



# **ACTUALIZACIÓN**

## **Lo último publicado en EPOC**

### **AVANCES EN COMORBILIDAD Y PREVENCIÓN**

**Maspalomas 23 de abril de 2010**



**Dr Jesús Recio Iglesias**



## Comorbilidades

Patología cardiovascular

Cáncer de pulmón

Osteoporosis

Depresión

## Prevención

Relevancia de la vacunación

Relación con el lugar de trabajo

Agenda de trabajo de la OMS

# Comorbilidad: ¿Repercusión en la EPOC?

Global Initiative for Chronic  
Obstructive  
Lung  
Disease



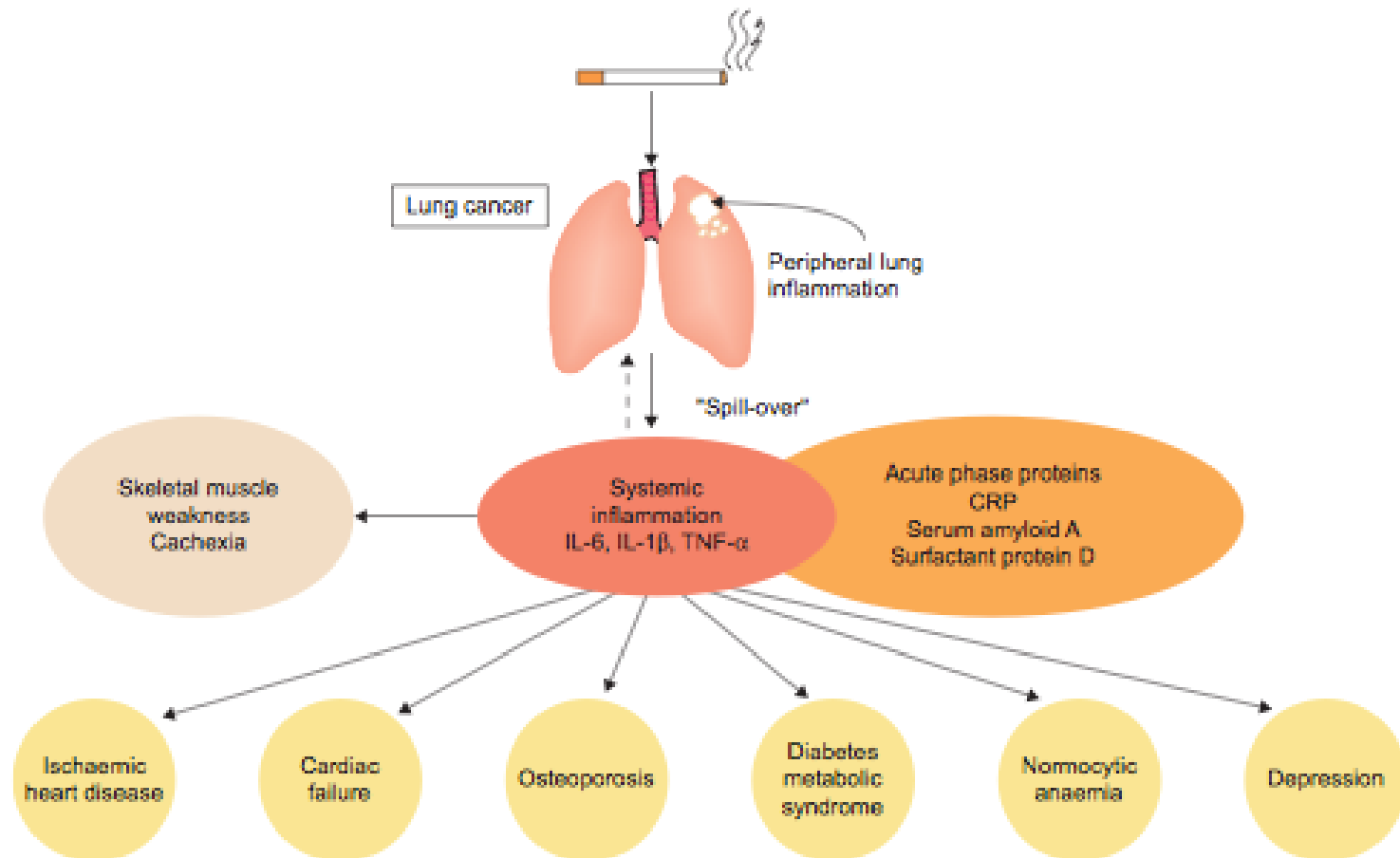
GLOBAL STRATEGY FOR THE DIAGNOSIS,  
MANAGEMENT, AND PREVENTION OF  
CHRONIC OBSTRUCTIVE PULMONARY DISEASE

- ✓ Influencia en tratamiento
- ✓ Importancia en exacerbaciones
- ✓ Influencia en los reingresos y en la duración de la estancia
- ✓ Influencia en la mortalidad



# Systemic manifestations and comorbidities of COPD

P.J. Barnes\* and B.R. Celli<sup>#</sup>





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# Revista Clínica Española

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## ORIGINAL

### Estudio de las comorbilidades en pacientes hospitalizados por descompensación de la enfermedad pulmonar obstructiva crónica atendidos en los servicios de Medicina Interna. Estudio ECCO

“confirma la **elevada** presencia de **comorbilidad** en los pacientes hospitalizados por descompensación de EPOC en nuestro país, con las implicaciones pronósticas y terapéuticas que comporta. La mayor parte de estos pacientes presenta además una **enfermedad pulmonar grave**, con limitación funcional por la disnea. Un adecuado diagnóstico y tratamiento de estas comorbilidades, junto al de la enfermedad pulmonar, es imprescindible para mejorar el tratamiento de estos pacientes, su calidad de vida y su supervivencia”

Tabla 3 Frecuencia de comorbilidades (n=398)

Comorbilidad	Total
<i>Incluidas en el índice Charlson</i>	
Enfermedad coronaria	68 (17%)
Insuficiencia cardíaca	107 (27%)
Enfermedad vascular periférica	50 (13%)
Enfermedad cerebrovascular	38 (10%)
Demencia	15 (4,4%)
Enfermedad del tejido conectivo	7 (2%)
Úlcus péptico	49 (12%)
Hepatopatía leve	29 (7,3%)
Diabetes sin complicaciones	103 (26%)
Diabetes con daño orgánico	14 (3,5%)
Hemiplejía	4 (1%)
Insuficiencia renal moderada	26 (6,5%)
Tumor sólido sin metástasis	26 (6,5%)
Leucemia	6 (1,5%)
Linfoma	2 (0,5%)
Enfermedad hepática moderada o severa	9 (2,3%)
Tumor sólido con metástasis	7 (1,8%)
Síndrome de inmunodeficiencia adquirida	1 (0,3%)
<i>Otras comorbilidades</i>	
Infarto de miocardio	34 (9%)
Hipertensión arterial	218 (55%)
Alcoholismo	56 (14%)
Enfermedad tromboembólica	13 (3%)
Arritmia	108 (27%)
Edemas	132 (33%)
Osteoporosis	37 (9,7%)
Anemia	265 (33%)

## Prevalence of Comorbidities in Patients with Chronic Obstructive Pulmonary Disease

Mario Cazzola<sup>a, b</sup>, Germano Bettoncelli<sup>c</sup>, Emiliano Sessa<sup>c</sup>, Claudio Cricelli<sup>c</sup>, Gianluca Biscione<sup>d</sup>

*Methods:* We conducted a population-based retrospective study

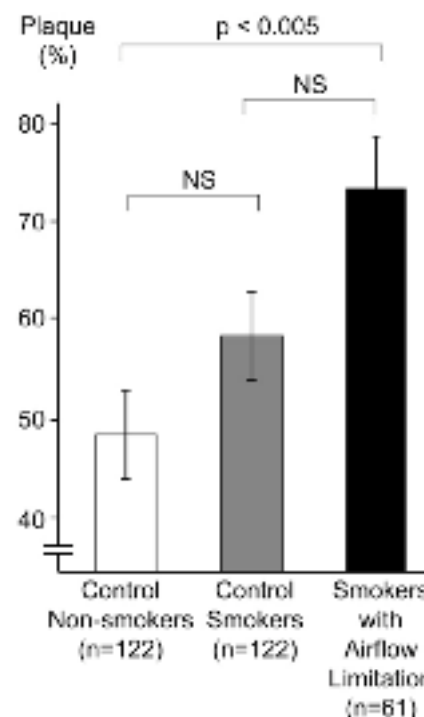
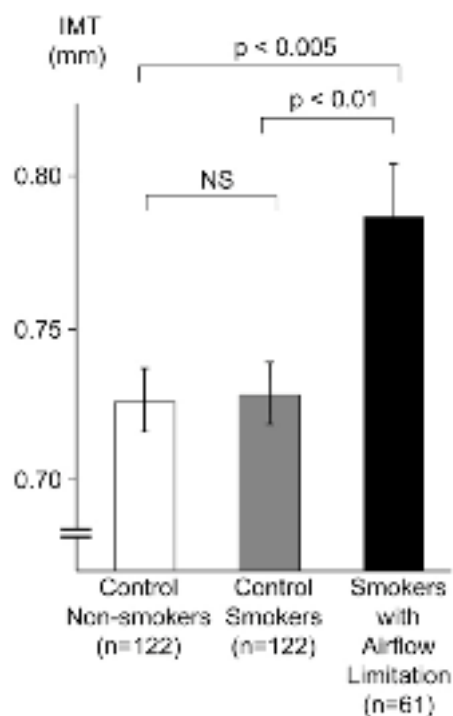
*Results:* Compared to the non-COPD people, COPD patients were at **increased risk for cardiovascular events** [ischemic heart disease (6.9% in the general population vs. 13.6% in COPD patients), **cardiac arrhythmia** (6.6% in the general population vs. 15.9% in COPD patients), **heart failure** (2.0% in the general population vs. 7.9% in COPD patients), and other forms of heart disease (10.7% in the general population vs. 23.1% in COPD patients); with a higher impact of COPD in the elderly]; non-psychotic mental disorders, including **depressive disorders** (29.1% in the general population vs. 41.6% in COPD patients; with a higher impact of COPD on women aged <75 years); **diabetes mellitus** (10.5% in the general population vs. 18.7% in COPD patients); **osteoporosis** (10.8% in the general population vs. 14.8% in COPD patients), with a higher impact of COPD on women aged <75 years, and **malignant pulmonary neoplasms** (0.4% in the general population vs. 1.9% in COPD patients). *Conclusions:* Our results indicate that COPD is a risk factor for these comorbid condition



# Airflow Limitation in Smokers Is Associated with Subclinical Atherosclerosis

Hiroshi Iwamoto<sup>1,2</sup>, Akihito Yokoyama<sup>2</sup>, Yoshihiro Kitahara<sup>1</sup>, Nobuhisa Ishikawa<sup>1</sup>, Yoshinori Haruta<sup>1</sup>, Kiminori Yamane<sup>1</sup>, Noboru Hattori<sup>1</sup>, Hitoshi Hara<sup>3</sup>, and Nobuoki Kohno<sup>3</sup>

“exaggerated subclinical atherosclerosis in smokers with airflow limitation, indicating that **atherosclerotic change occurs early** in the disease process of COPD. Systemic inflammation is predominantly associated with atheromatous plaque. **Reduced lung function is associated with thickened IMT**, but the underlying **mechanism** for this association is **unclear**”



## Increased risk of Myocardial Infarction and Stroke following Exacerbation of Chronic Obstructive Pulmonary Disease.

Gavin C. Donaldson, John R. Hurst, Christopher J. Smith, Richard B. Hubbard and Jadwiga A. Wedzicha

*Chest*; Prepublished online December 18, 2009;  
DOI 10.1378/chest.09-2029

**Objective:** The course of COPD is punctuated by exacerbations, which further increase systemic inflammation, but the **risk of vascular events in the post- exacerbation period** has never been defined.

**Design:** 25,857 COPD patients over a two year period. The risk of myocardial infarction (MI) and stroke in the post-exacerbation period ...

**Results:** There was a **2.27 fold (95% CI 1.1-4.7; P=0.03) increased risk of MI 1-5 days after exacerbation** (defined by prescription of both steroids and antibiotics). This relative risk diminished progressively over time and was not significantly different from the baseline MI risk at any other post-exacerbation time interval. One in 2,513 exacerbations was associated with MI within 1-5 days. There was a **1.26 fold (95% CI 1.0-1.6; P=0.05) increased risk of stroke 1-49 days after exacerbation.**

**Conclusion:** The results suggest that exacerbations of COPD increase the risk of myocardial infarction and stroke. This may have implications for therapy in both stable and exacerbated COPD.





## Original

## Enfermedad pulmonar obstructiva crónica en pacientes ingresados por insuficiencia cardiaca. Resultados del Grupo para el Estudio y Significado de la Anemia en la Insuficiencia Cardiaca (GESAIC)

	EPOC (n=98)	NO EPOC (n=293)	p
Varones / Mujeres	69/29	83/210	<0,05
Índice Charlson	3,7±1,9	2,7±1,9	0,04
Edad (años)	78,0±9,5	77,9±9,4	0,95
FEVI (%)	48,5±17,8	51,3±16,5	0,18
Hemoglobina (g/L)	12,3±1,9	11,9±2,1	0,12
Índice de masa corporal	27,3±5,2	28,8±6,1	0,028
NYHA	2,67±0,8	2,6±0,8	0,89
BB previo (%)	18 (23,2)	78 (6,9)	0,05
BB alta (%)	27 (27,5)	111 (37,88)	0,068

Antes del ingreso hospitalario tratamiento con BB en el 18,4 frente al 27,6% en el momento del alta ( $p<0,05$ ). Durante el ingreso se suspendió el tratamiento con BB en 31 de 111 pacientes (27,9%), sin observarse diferencia entre los grupos.

En el 29,6% de los pacientes con EPOC el BB se instauró durante el ingreso

Solo la FEVI ( $p<0,03$ ) y el tratamiento con BB previo ( $p<0,001$ ) se asociaron a una mayor prescripción de tratamiento BB al alta

- Estadio moderado o grave de EPOC en el 23,5%
- En dos tercios: diagnóstico sólo por criterios clínicos

### Conclusión

Aumento en el tratamiento con BB condicionado por el deterioro de la función del VI y que no se ve interferido por la presencia simultánea de EPOC.



# COPD prevalence is increased in lung cancer, independent of age, sex and smoking history

R.P. Young\*, R.J. Hopkins\*, T. Christmas<sup>#</sup>, P.N. Black<sup>†</sup>, P. Metcalf<sup>‡</sup> and G.D. Gamble\*

In the present study, the prevalence of COPD in patients diagnosed with lung cancer was 50% compared with 8% in a randomly recruited community control group, matched for age, sex and pack-yr smoking. After controlling for important variables, **the prevalence of COPD in newly diagnosed lung cancer cases was six-fold greater than in matched smokers**; this is much greater than previously reported. We conclude that COPD is both a common and important independent risk factor for lung cancer.

This strong association between COPD and lung cancer is the possibility that both diseases result from **shared pathogenic mechanisms**. It has been hypothesised that COPD is due to **an inherent susceptibility (exaggerated or maladaptive response) to chronic inflammation**

This association has clinical implications for the wider **use of spirometry** for the early identification of those at the greatest risk of lung cancer



### Prevalence and Progression of Osteoporosis in Patients With COPD

Results From the Towards a Revolution in COPD Health Study

#### Prevalence of Osteoporosis and Osteopenia

At baseline, the overall prevalence of osteoporosis and osteopenia was high (65%). More women (30%) than men (18%) had osteoporosis. In contrast, the prevalence of osteopenia was comparable between men (42%) and women (41%)

#### Incidence of Fractures

5.1% to 6.3%

There was no association between FEV1 impairment and BMD when adjusted by age and gender.

#### Conclusions

We observed a **high prevalence** of osteopenia and osteoporosis in men and women with COPD. It is important to remain aware of these potentially treatable conditions. Although safety concerns remain paramount in the care of patients with COPD, the results of the TORCH study are reassuring as we did **not detect** that either SFC or its individual components had a **significant effect on BMD** compared with placebo over 3 years.

# Pulmonary Perspective

## Vitamin D Beyond Bones in Chronic Obstructive Pulmonary Disease

### Time to Act

Wim Janssens<sup>1</sup>, An Lehouck<sup>1</sup>, Claudia Carremans<sup>1</sup>, Roger Bouillon<sup>2</sup>, Chantal Mathieu<sup>2</sup>, and Marc Decramer<sup>1</sup>

<sup>1</sup>Respiratory Division, University Hospital Gasthuisberg; and <sup>2</sup>Clinic and Laboratory of Experimental Medicine and Endocrinology, Katholieke Universiteit Leuven, Leuven, Belgium

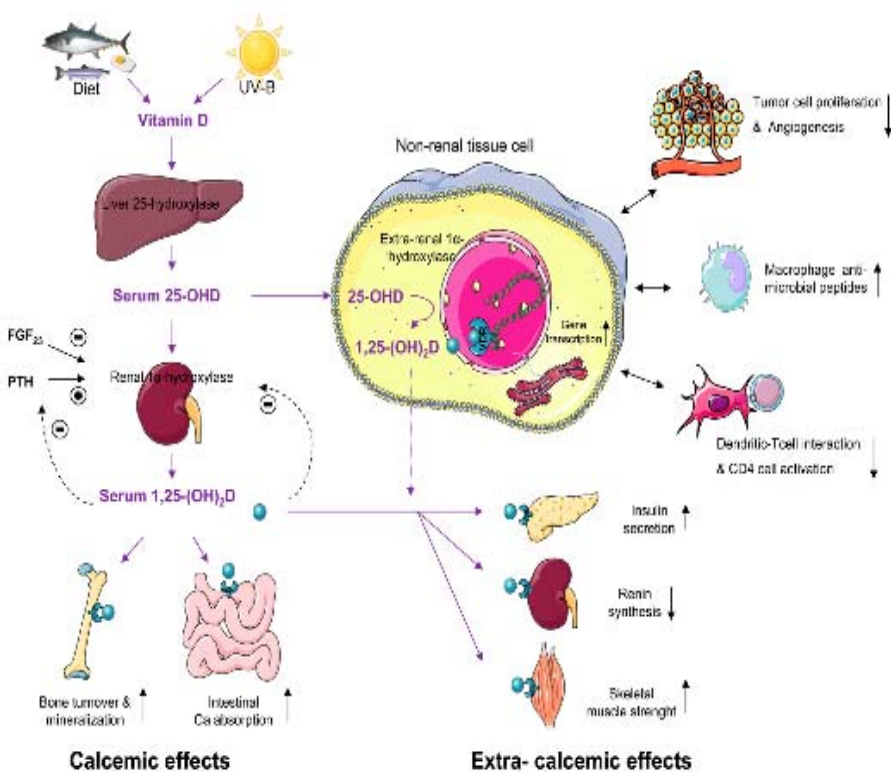


Figure 1. Schematic presentation of calcemic and extracalcemic effects of vitamin D that are potentially important in patients with COPD.

### CONCLUSIONS

Therapeutic benefits of vitamin D supplementation beyond bone and calcium homeostasis still **needs to be investigated**.

Given the increased risk for osteopenia and osteoporosis in COPD, vitamin D supplementation **should be considered for all patients with COPD**. Yet, a potential benefit of improved vitamin D status on noncalcemic endpoints in patients with severe COPD, in which deficiency or relative insufficiency of vitamin D is often present, has not been explored.

COPD is an optimal candidate .....the challenge in **such randomized controlled trials will be primarily to demonstrate efficacy and safety and secondarily to define optimal target serum levels for 25-OHD** in this disease as a proof of concept for other than calcemic endpoints.

## Depressive Symptoms as Predictors of Mortality in Patients With COPD\*

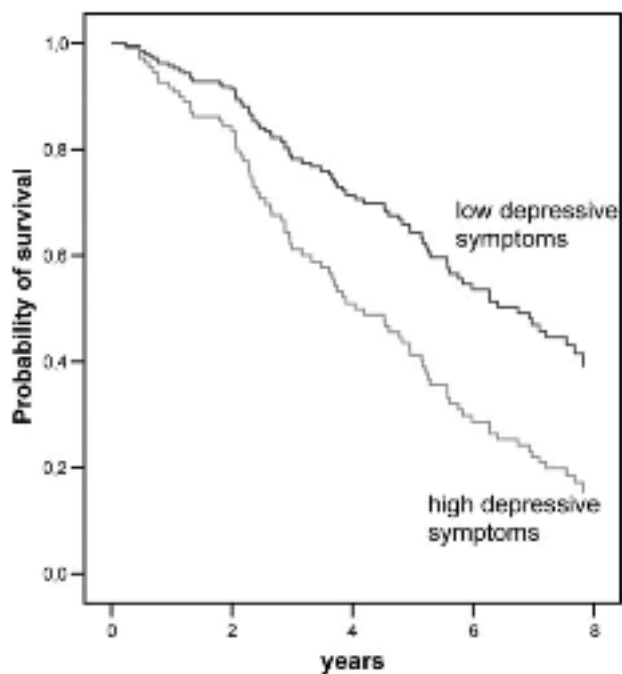


FIGURE 1. Kaplan-Meier curves for COPD patients with separate lines for high and low depressive symptoms (adjusted for the covariates sex, age, and Wpeak).

The baseline characteristics of 121 COPD patients (78 men and 43 women; mean  $\pm$ SD age,  $61.5 \pm 9.1$  years; and mean FEV<sub>1</sub>,  $36.9 \pm 15.5\%$  predicted). The vital status was ascertained using municipal registrations. In 8.5 years of follow-up, 76 deaths occurred (mortality rate, 63%). Survival time ranged from 88 days to 8.5 years (median survival time, 5.3 years). The Cox proportional hazard model was used to quantify the association of the baseline characteristics (ie, age, sex, marital status, smoking behavior, FEV<sub>1</sub>, BMI, Wpeak, and depressive symptoms) with mortality.

Conclusions: depressive symptoms assessed in stable patients with COPD are associated with their subsequent all-cause mortality.

Some possible explanations ... "first, depression can affect the **hypothalamic-pituitary-adrenal axis functioning**, which could make health status deteriorate. Second, depressive symptoms can **impair self-care**, as indicated by insufficient nutritional intake, continued smoking, lower activity levels, poor medication compliance, ....., which also could lead to an accelerated decline in health

## **Influenza but not pneumococcal vaccination protects against all-cause mortality in patients with COPD**

Influenza and pneumococcal vaccination are recommended in patients with chronic obstructive pulmonary disease (COPD).

### **Results**

177 120 patients with COPD (mean age 65 years) were identified, with a mean follow-up of 6.8 years between 1988 and 2006.

Vaccination rates against influenza rose from <30% before 1995 to >70% in 2005 in patients aged 60 years or more.

The cumulative vaccination rate against pneumonia rose from almost zero to 70% in patients aged 70 years or more over the same period.

For all-cause mortality the adjusted relative risks associated with influenza vaccination were 0.59 (95% CI 0.57 to 0.61) during the influenza season and 0.97 (95% CI 0.94 to 1.00) outside the season in patients not vaccinated against pneumonia, and 0.30 (95% CI 0.28 to 0.32) and 0.98 (95% CI 0.96 to 1.11), respectively, in patients vaccinated against pneumonia. The relative risk associated with pneumococcal vaccination was >1 at all times of the year

**Conclusions: Influenza but not pneumococcal vaccination was associated with a reduced risk of all-cause mortality in COPD.**



## **The effect of influenza vaccination on the incidence of chronic obstructive pulmonary disease (COPD) exacerbations in the immediate post-vaccination period**

**Background:** The administration of influenza vaccination is an important strategy in the prevention of exacerbations in patients with chronic obstructive pulmonary disease (COPD). Despite the proven benefits, there are patients who are reluctant to have this intervention for fear of triggering an exacerbation. There are very few studies looking at the effect of the vaccination on exacerbation rates of COPD in primary care.

**Methods:** “6 primary care practices in the Derbyshire area (UK) and obtained 293 pairs of patients. All patients had a diagnosis of COPD ..... The first group of patients received the influenza vaccination whilst the other group served as a control. (either never received the vaccination or received it at a later date). The incidence of COPD exacerbations of both groups were recorded.

**Results:** There were 21 exacerbations in the control group compared to 11 in the vaccinated group. In the 2 weeks after receiving the influenza vaccination, the risk of experiencing an exacerbation in this group of patients was 0.52 in the vaccinated group compared to the non vaccinated group (OR=0.52; CI 0.29-1.14)

**Conclusion:** Patients with COPD should be reassured that **the influenza vaccination is safe and does not cause an increase in exacerbations**. They should be encouraged to take up the vaccination annually before the onset of winter.



## Superior Immune Response to Protein-Conjugate versus Free Pneumococcal Polysaccharide Vaccine in Chronic Obstructive Pulmonary Disease

**Objectives:** serotype-specific IgG antibody concentration and functional antibody activity would be superior after PCV7 vaccination compared with PPSV23 in moderate to severe COPD. We also posited that older age and prior PPSV23 vaccination would be associated with reduced vaccine responsiveness.

**Methods:** One hundred twenty patients with COPD were randomized to PPSV23 (63 subjects) or PCV7 (57 subjects). IgG concentrations were determined by ELISAK at 1 month post

**Results:** Both vaccines were well tolerated. Adjusted for baseline levels, **postvaccination IgG was higher in the PCV7 group than the PPSV23 group for all seven serotypes**, reaching statistical significance for five ( $P < 0.05$ ). In multivariate analyses, younger age, vaccine naivety, and receipt of PCV7 were associated with increased OPK responses

**Conclusions:** PCV7 induces a superior immune response at 1 month post vaccination compared with PPSV23 in COPD. Older age and prior PPSV23 reduce vaccine responsiveness.

### Limitations

It cannot be inferred that **the more frequent achievement of serologic responses** after PCV7 would **definitively translate into improved clinical outcomes**

**PCV7 contain only about one-third** of pneumococcal isolates recovered from patients with COPD suffering an acute exacerbation



## Occupational exposures and the risk of COPD

**Background**—The contribution of occupational exposures to chronic obstructive pulmonary disease (COPD) and, in particular, their potential interaction with cigarette smoking remains underappreciated.

**Methods**—data from the FLOW study of 1,202 subjects with COPD and 302 referent subjects matched by age, sex, and race, recruited from a large managed care organization. Occupational exposures were assessed ....

Multivariate analysis was used to control for age, sex, race, and smoking history.

**Results**— exposure was associated with an increased risk of COPD (OR 2.11; 95% CI 1.59-2.82). Joint exposure to both smoking and occupational factors markedly increased the risk of COPD (OR 14.1; 95% CI 9.33-21.2).

**Conclusions**—Workplace exposures are strongly associated with an increased risk of COPD. On a population level, prevention of both smoking and occupational exposures, and especially both together, is needed to prevent the global burden of disease.



## Prioritized research agenda for prevention and control of chronic respiratory diseases

The **2008-13 WHO Action Plan** on noncommunicable diseases includes chronic respiratory diseases as one of the four priorities. Major chronic respiratory diseases (CRD) include chronic obstructive pulmonary disease (COPD),  
Effective intervention plans can prevent and control chronic respiratory diseases, thus reducing morbidity and mortality.

### Priorities in COPD from the public health perspective

#### Short term

To reach consensus on a universal definition of COPD, COPD exacerbations and risk factors.  
To estimate (and monitor yearly) the access to spirometry, essential medicines and adequate care.

#### Medium term

To assess the COPD prevalence, risk factors and co-morbidities (CVDs, cancer...) in population based studies



## En resumen.....

- La comorbilidad en la EPOC es frecuente y compleja.
- Por compartir factores de riesgo y sintomatología, la presencia simultánea de enfermedad cardiovascular y EPOC dificulta el diagnóstico.
- La comorbilidad puede interferir en el tratamiento y no siempre de manera justificada (BB en pacientes con EPOC e insuficiencia cardíaca)
- Un mejor diagnóstico representa un mejor tratamiento de la EPOC y de sus comorbilidades

*Todo ganado  
todo por ganar*

*El mejor logro es el  
queda por conquistar*

