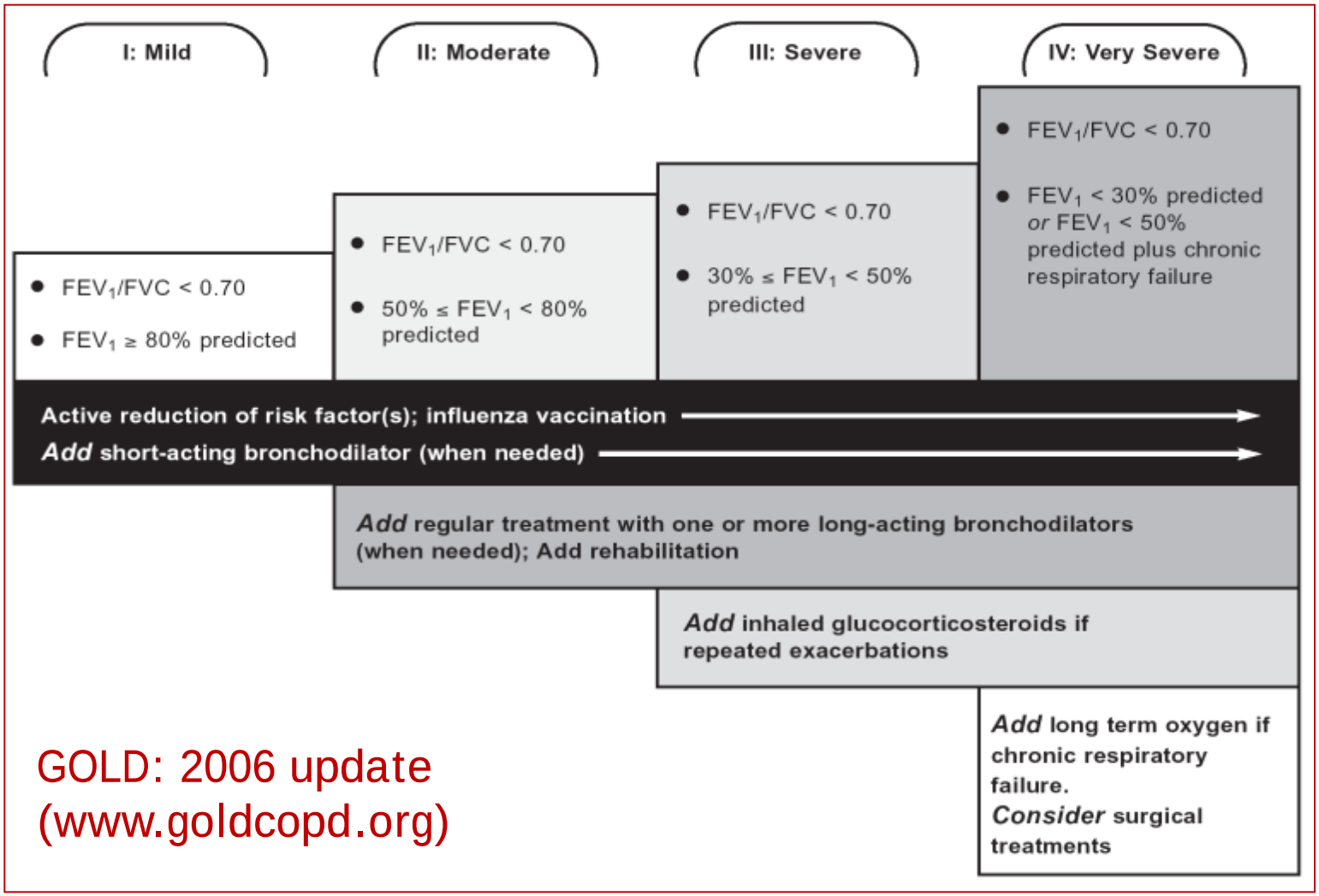
EPOC

Enfermedad Pulmonar Obstructiva Crónica

Treatment of COPD



GOLD: 2006 update
(www.goldcopd.org)

Fenotipos: Heterogeneidad genética de la EPOC

La EPOC es una enfermedad heterogénea que engloba múltiples subfenotipos.

Los diferentes fenotipos pueden tener distinta contribución genética por lo que los diferentes estudios deben considerar esta heterogeneidad.

Puede existir una variabilidad interindividual en respuesta al tratamiento con diferentes fármacos.

Hersh CP. Pharmacogenomics. 2010;11(2):237-47

Table 1. Genes associated with potential phenotypes for chronic obstructive pulmonary disease pharmacogenetics studies.

Phenotype	Genes with significant association
Lung function decline in chronic obstructive pulmonary disease	*SERPINA1** [37] *EPHX1* [37] *IL1B, IL1RN*‡ [91] *GSTP1, GSTT1, GSTM1*‡ [92] *MMP1* [93] *IL4RA* [94] *ADRB2* [68] *GC* [95] *HMOX1* [96] *IL6* [36] *CDC6* [97] *LEPR* [98]
Chronic obstructive pulmonary exacerbations	*SERPINA1** [56] *MBL2* [52] *CCL1* [53] *SFTPB* [54] *SOD3* [55]
Exercise capacity	*EPHX1* [58] *LTBP4* [58] *SFTPB* [58]
Symptoms (e.g., dyspnea)	*TGFB1* [58]
Emphysema on quantitative chest CT scan analysis	*GC* [95] *MMP9* [21] *EPHX1* [20] *GSTP1* [20] *ADRB2* [22] *TGFBR3* [99]

*Studies of α1-antitrypsin heterozygous carriers (PI MZ).
‡Combination of variants in multiple genes associated with lung function decline, but not each gene individually.

Cho et al. Respiratory Research 2010, 11:30
http://respiratory-research.com/content/11/1/30

RESPIRATORY

Arch Bronconeumol. 2009;45(3):129–138

RESEARCH

Cluster analysis in severe emp

ELSEVIER DOYMA

ARCHIVOS DE BRONCONEUMOLOGIA

www.archbronconeumol.org

Characteristics of COPD phenotypes classified according to the findings of HRCT☆

Yoshiaki Kitaguchi[a], Keisaku Fujimoto[a,*], Keishi Kubo[a], Takayuki Honda[b]

[a]Department of Internal Medicine, Shinshu University School of Medicine, Matsumoto 390-8621, Japan
[b]Department of Laboratory Medicine, Shinshu University School of Medicine, Matsumoto 390-8621, Japan

Belda[g], Eva Farrero[h], Antoni Ferrer[i],
z[f], Eduard Monsó[o], Josep Morera[p],
l Grupo de Trabajo sobre la
monary disease (PAC-COPD)

types

P M Shirtcliffe,[1]

CHEST Original Research
COPD

lys

The Role of CT Scanning in Multidimensional Phenotyping of COPD

Mona Bafadhel, M
Dhiraj D. Vara, B
Christopher E. Br

Respiratory Research

BioMed Central

Research

Open Access

COPD phenotype description using principal components analysis

Kay Roy*, Jacky Smith, Umme Kolsum, Zöe Borrill, Jørgen Vestbo and Dave Singh

Radiologic Phenotypes[1]

Fenotipos de la EPOC

“Aquellos atributos de la enfermedad que solos o combinados describen las diferencias entre individuos con EPOC en relación a parámetros que tienen significado clínico (síntomas, agudizaciones, respuesta al tratamiento, velocidad de progresión de la enfermedad, o muerte)”

Han et al. AJRCCM 2010; 182: 598-604

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Han et al. AJRCCM 2010; 182: 598-604

THE EMPHYSEMATOUS AND BRONCHIAL TYPES OF CHRONIC AIRWAYS OBSTRUCTION

A Clinicopathological Study of Patients in London and Chicago

B. BURROWS
M.D. Johns Hopkins
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SENIOR MEDICAL REGISTRAR

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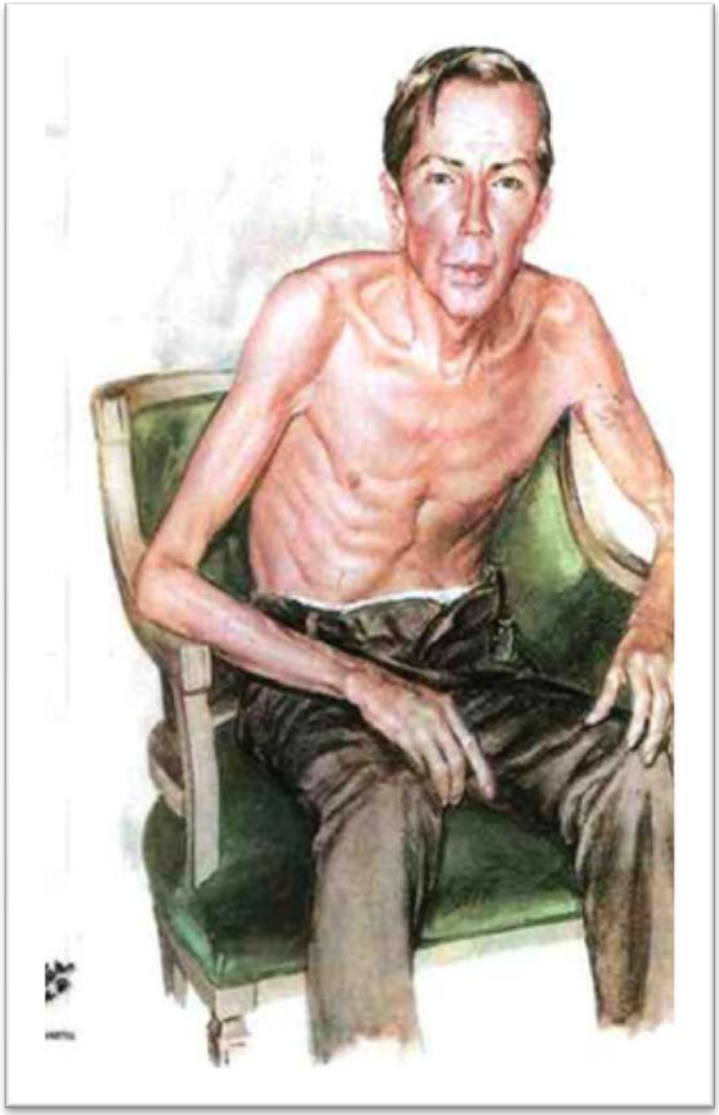
M.B. Manc., Dip.Path., D.C.P.
RESEARCH ASSISTANT IN PATHOLOGY

Lancet 1966 (April 16th)



¿Qué fenotipos son clínicamente relevantes?

Clinical Commentary

Chronic Obstructive Pulmonary Disease Phenotypes

The Future of COPD

MeiLan K. Han[1], Alvar Agusti[3], Peter M. Calverley[4], Bartolome R. Celli[5], Gerard Criner[6], Jeffrey L. Curtis[1,7], Leonardo M. Fabbri[8], Jonathan G. Goldin[9], Paul W. Jones[10], William MacNee[11], Barry J. Make[12], Klaus F. Rabe[13], Stephen I. Rennard[14], Frank C. Sciurba[15], Edwin K. Silverman[5,16], Jørgen Vestbo[17], George R. Washko[5], Emiel F. M. Wouters[18], and Fernando J. Martinez[2]

AJRCCM 2010; 182: 598-604

Bronquitis crónica

El % del área de la pared bronquial se asocia con:

IMC:

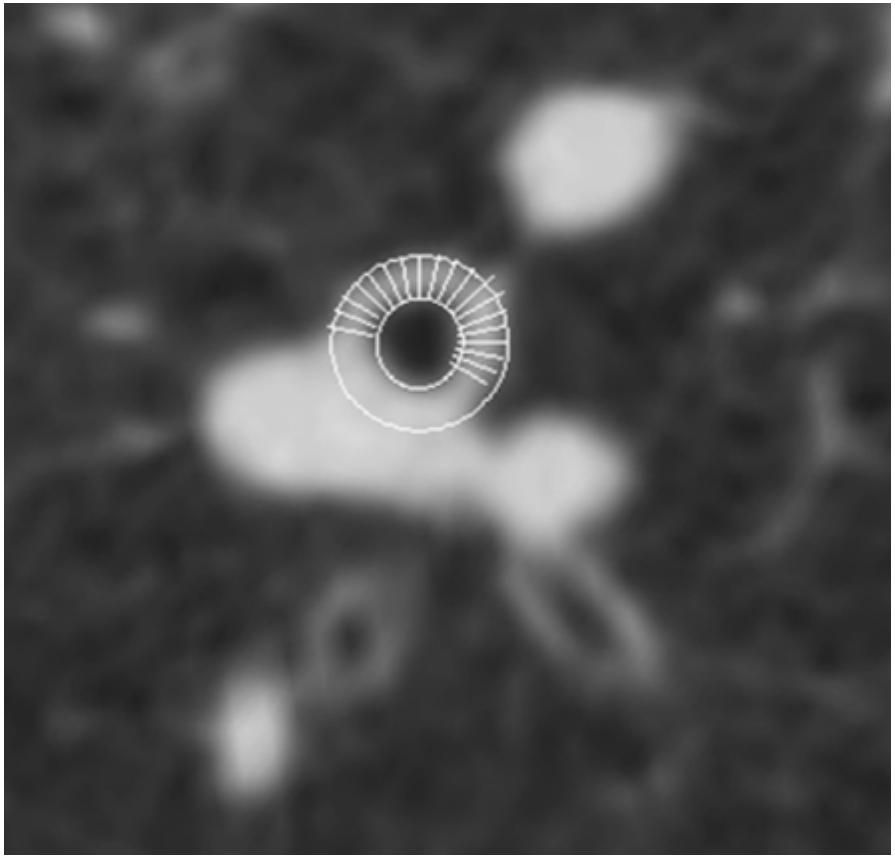
OR=0,25 (0,002-0,49; p=0,04)

Bronquitis crónica:

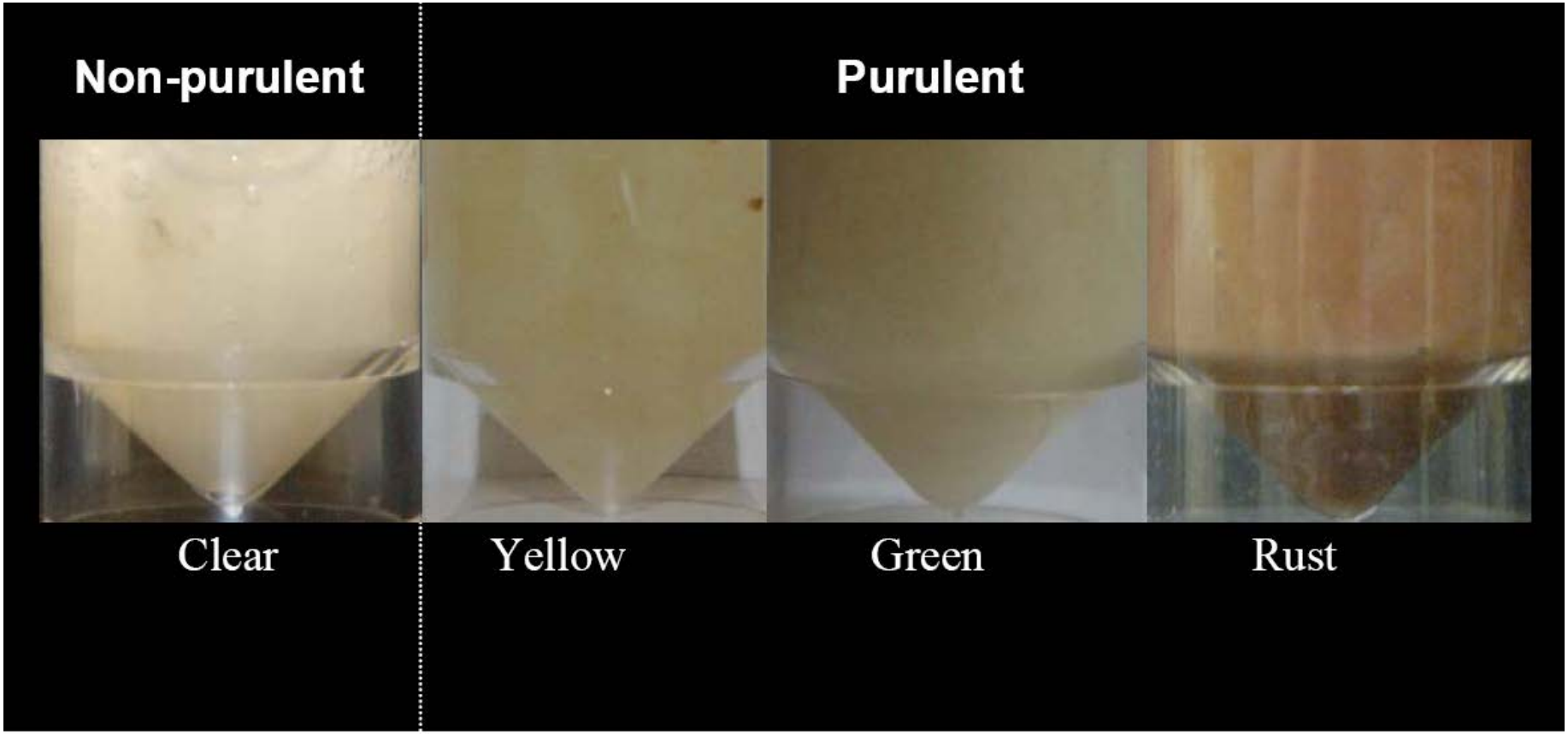
1,22 (1,07-1,39; p=0,003)

Agudizaciones frecuentes:

1,15 (1,03-1,29; p=0,017)



Mair et al. Respir Med 2010; 104: 1683-1690



Courtesy of R. Wilson. Host Defence Unit. Royal Brompton Hospital London, UK

Chronic Obstructive Pulmonary Disease Phenotypes

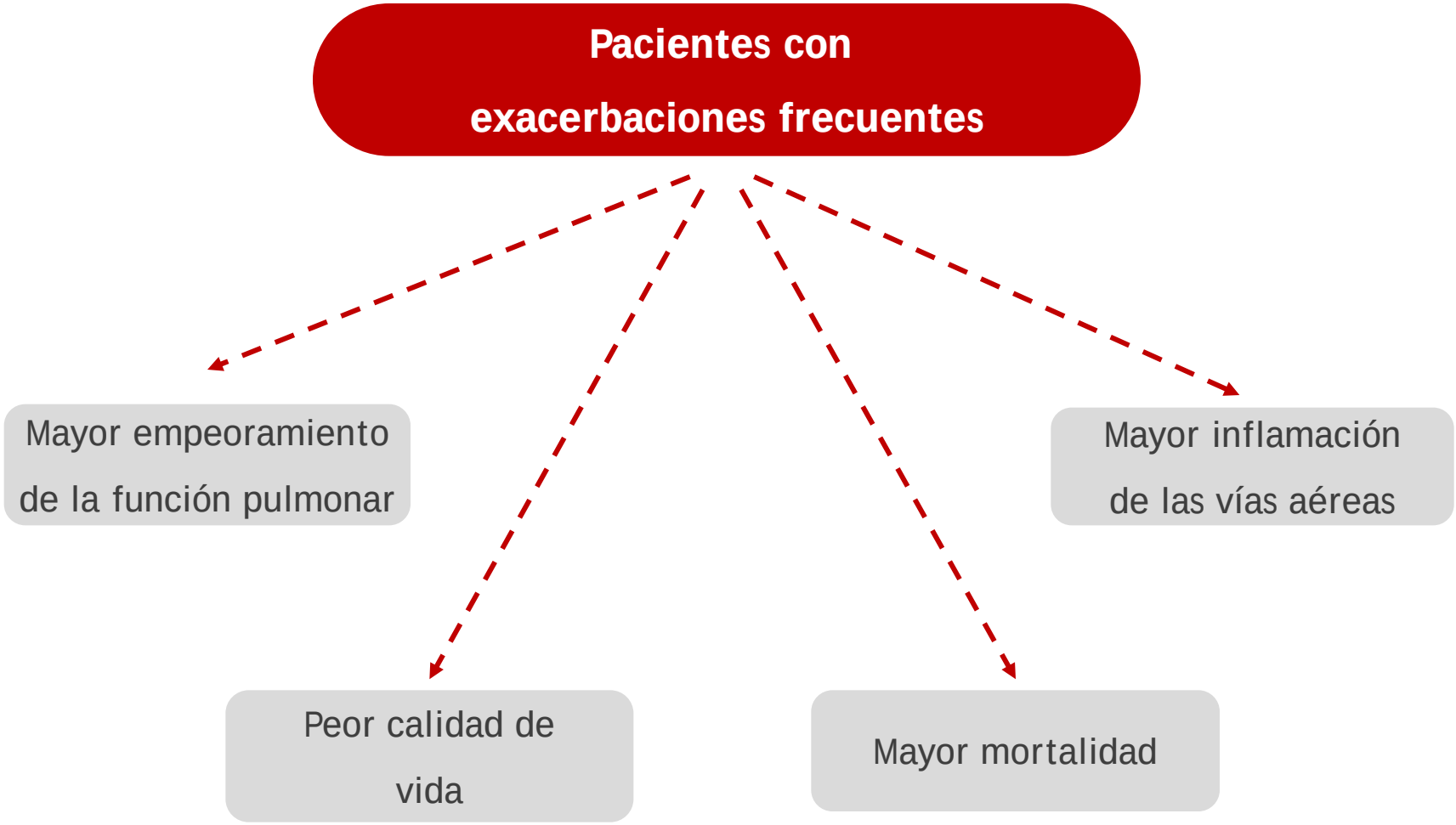
The Future of COPD

MeiLan K. Han[1], Alvar Agusti[3], Peter M. Calverley[4], Bartolome R. Celli[5], Gerard Criner[6], Jeffrey L. Curtis[1,7], Leonardo M. Fabbri[8], Jonathan G. Goldin[9], Paul W. Jones[10], William MacNee[11], Barry J. Make[12], Klaus F. Rabe[13], Stephen I. Rennard[14], Frank C. Sciurba[15], Edwin K. Silverman[5,16], Jørgen Vestbo[17], George R. Washko[5], Emiel F. M. Wouters[18], and Fernando J. Martinez[2]

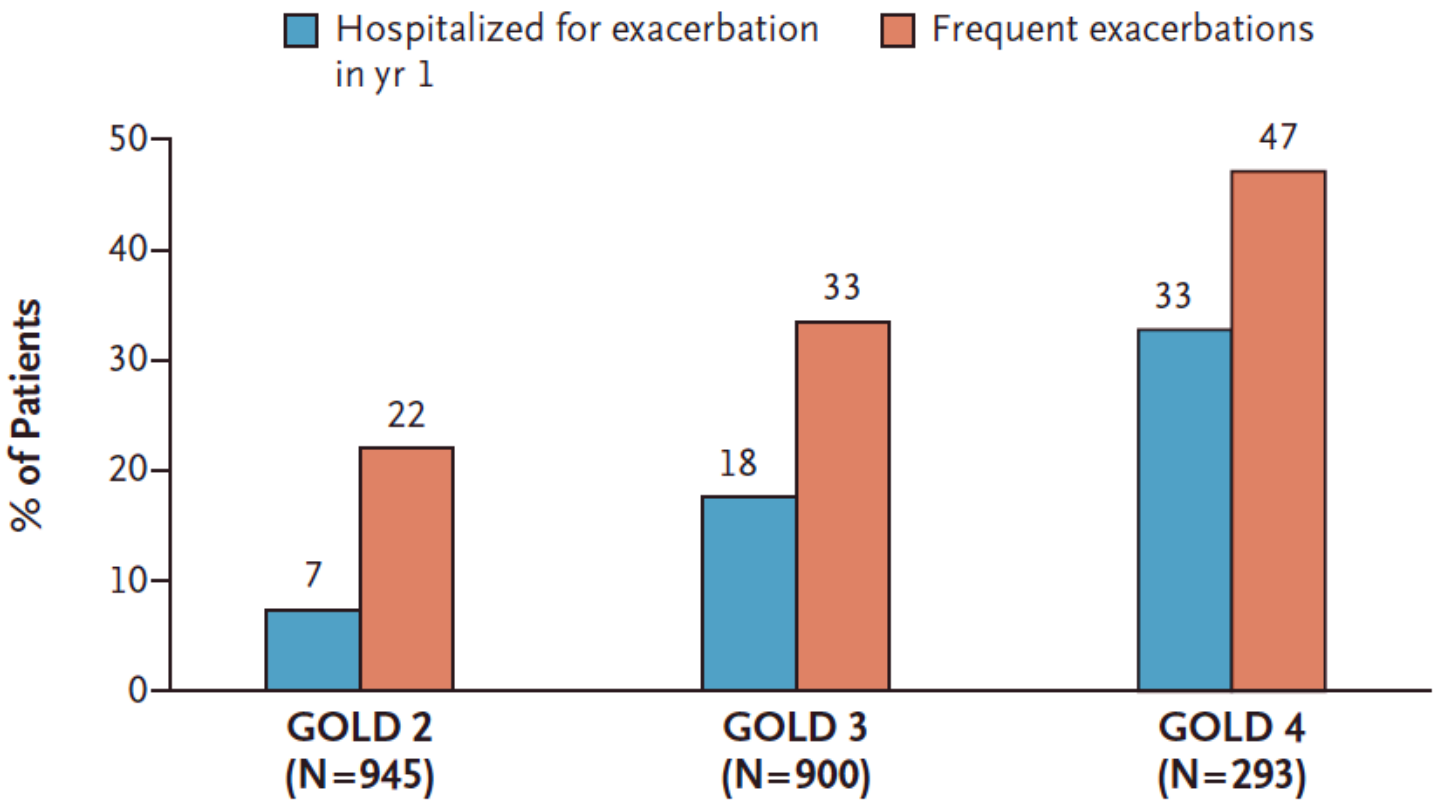
Significant heterogeneity of clinical presentation and disease progression exists within chronic obstructive pulmonary disease (COPD). Although FEV_1 inadequately describes this heterogeneity, a clear alternative has not emerged. The goal of phenotyping is to identify patient groups with unique prognostic or therapeutic characteristics, but significant variation and confusion surrounds use of the term "phenotype" in COPD. Phenotype classically refers to any observable characteristic of an organism, and up until now, multiple disease characteristics have been termed COPD phenotypes. We, however, propose the following variation on this definition: "a single or combination of disease attributes that describe differences between individuals with COPD as they relate to clinically meaningful outcomes (symptoms, exacerbations, response to therapy, rate of disease progression, or death)." This more focused definition allows for classification of patients into distinct prognostic and therapeutic subgroups for both clinical and research purposes.

Am J Respir Crit Care Med Vol 182. pp 598–604, 2010
Originally Published in Press as DOI: 10.1164/rccm.200912-1843CC on June 3, 2010
Internet address: www.atsjournals.org

Consecuencias clínicas



Fenotipo agudizador



Hurst et al. NEJM 2010; 363: 1128-38

Fenotipo agudizador

- ✓ Las agudizaciones son los eventos más importantes en la Hª natural de la EPOC.
- ✓ Diagnóstico fácil, rápido, barato y fiable.
- ✓ Impacto pronóstico.
- ✓ Tratamiento diferencial: antinflamatorios.
- ✓ Recordar la importancia de interrogar sobre las agudizaciones.

Hurst et al. NEJM 2010; 363: 1128-38

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Susceptibility to Exacerbation in Chronic Obstructive Pulmonary Disease

John R. Hurst, M.B., Ch.B., Ph.D., Jørgen Vestbo, M.D., Antonio Anzueto, M.D., Nicholas Locantore, Ph.D., Hana Müllerova, Ph.D., Ruth Tal-Singer, Ph.D., Bruce Miller, Ph.D., David A. Lomas, Ph.D., Alvar Agusti, M.D., Ph.D., William MacNee, M.B., Ch.B., M.D., Peter Calverley, M.D., Stephen Rennard, M.D., Emiel F.M. Wouters, M.D., Ph.D., and Jadwiga A. Wedzicha, M.D., for the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) Investigators*

EDITORIALS

Frequent Exacerbations of Chronic Obstructive Pulmonary Disease — A Distinct Phenotype?

Donald P. Tashkin, M.D.

Fenotipo mixto

Review

The overlap syndrome of asthma and COPD: what are its features and how important is it?

P G Gibson,[1,2] J L Simpson[1]

Thorax 2009; 64: 728-735

Research

Marc Miravitlles, Isabel Andreu, Yolanda Romero, Salvador Sitjar, Andreu Altés, and Esther Anton

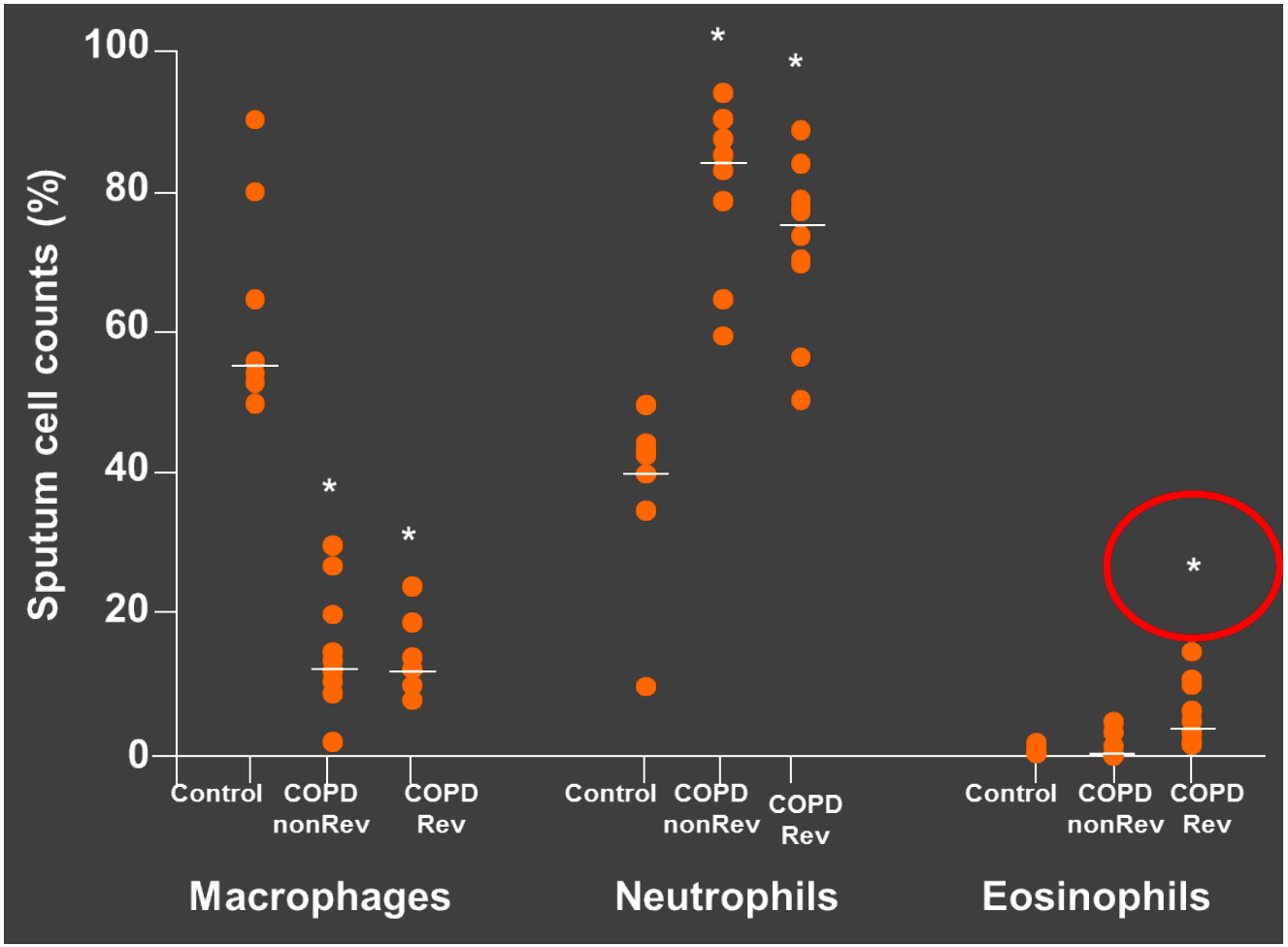
Difficulties in differential diagnosis of COPD and asthma in primary care

Table 2. Characteristics of eligible patients classified according to physican criteria

	All	COPD	Asthma	Indeterminate
	n = 324	*n* = 210	*n* = 50	*n* = 64
Mean age, years (SD)[a]	66.9 (11.2)	68.9 (9.7)	58.9 (13.1)	67.2 (11.2)
Sex, male, *n* (%)[a]	204 (63.8)	161 (77.4)	13 (26.0)	30 (48.4)
Mean BMI, kg/m^2(SD)	27.5 (4.8)	27.3 (4.1)	27.4 (6.1)	28.0 (5.8)

Br J Gen Pract 2012: DOI:10.3399

Fenotipos de la EPOC



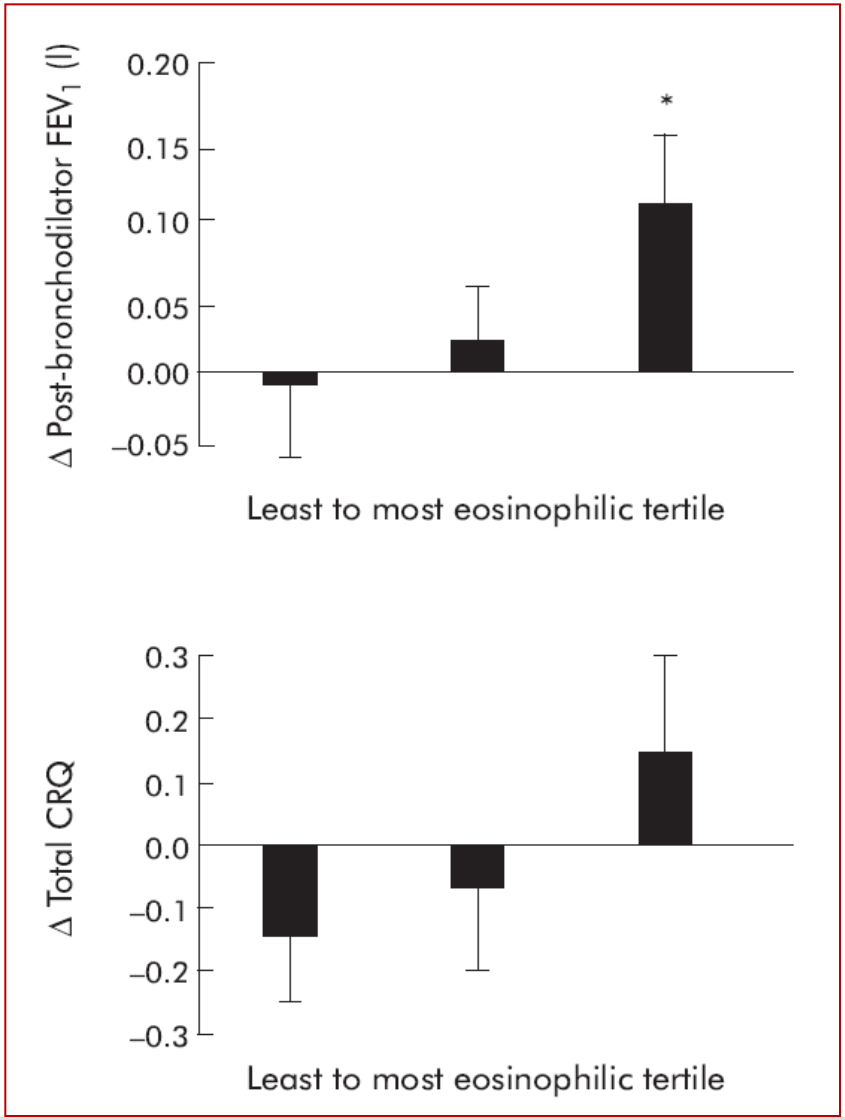
*p<0.01 vs control

Papi et al. AJRCCM 2000;162:1773-1777

Respuesta a CIs según eos en esputo

Respuesta al tratamiento con mometasona comparado con placebo para cada tercil de eosinofilia en esputo inducido

Brightling et al. Thorax 2005; 60: 193-198



Normativa Canadiense

- In patients in whom the asthma component is prominent, early introduction of ICS may be justified

- ICS should not be used as monotherapy in COPD and when used should be combined with a LABA

O'Donnell et al. Can Respir J 2007; 14 (Suppl B): 5-32

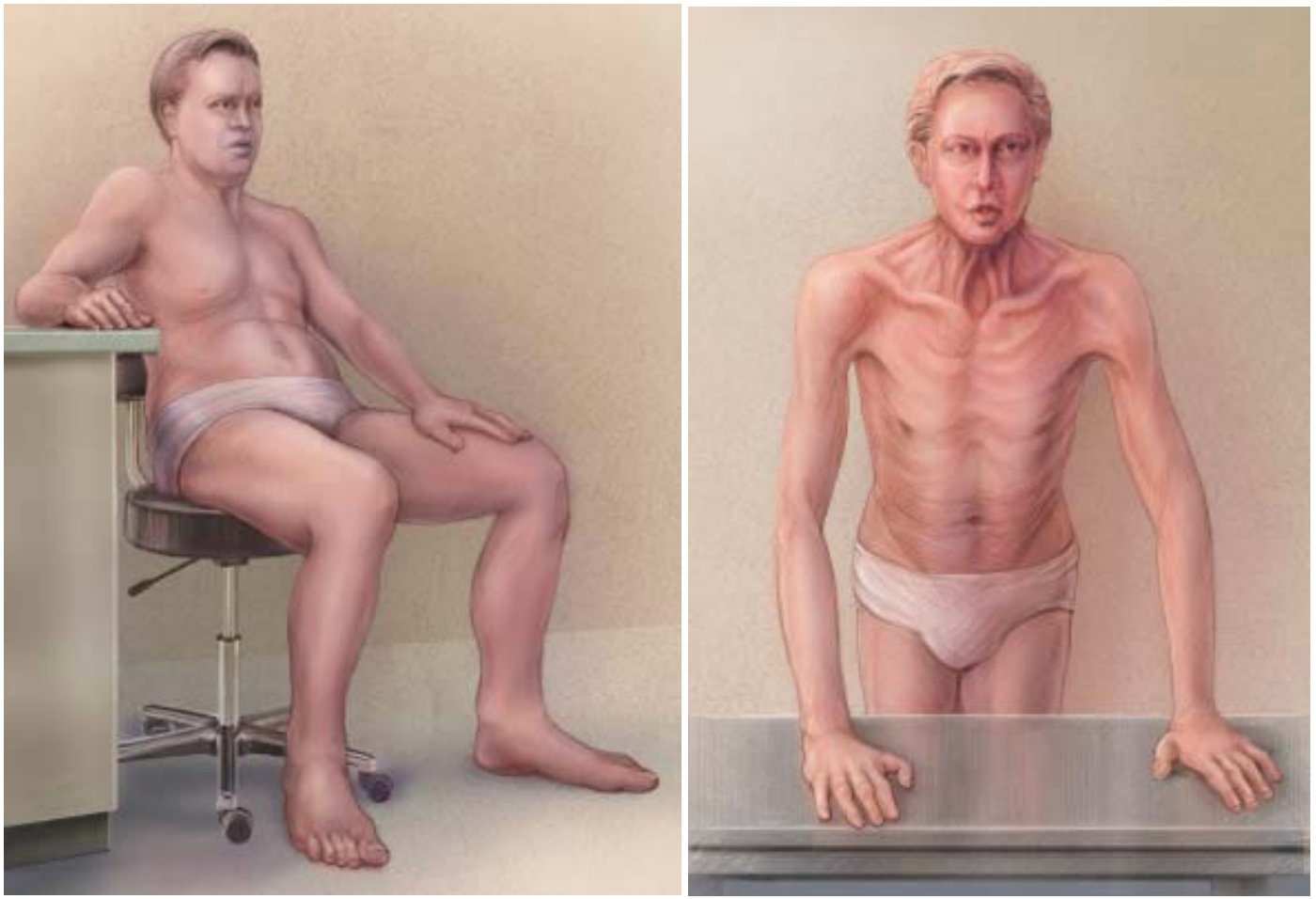
C-4. Treatment of COPD complicated by asthma

- Concurrent asthma is suspected in COPD patients with such symptoms as paroxysmal dyspnea, wheezing, and cough occurring predominantly during the night and in the early morning.
- Findings such as the presence of an atopic predisposition and increase eosinophil count in sputum and peripheral blood suggest complication by asthma.
- Corticoid inhalation therapy should be used in cases of COPD complicated by asthma, regardless of the severity of the COPD.
- Either an anticholinergic agent or β_2-agonist can be used as a long-acting bronchodilator in combination with an inhaled corticosteroid. Both of an anticholinergic agent and a β_2-agonist should be used concomitantly when combination treatment with a single bronchodilator is ineffective.
- Combined use of a leukotriene receptor antagonist is also effective.

Diagnostic indices for concurrent asthma

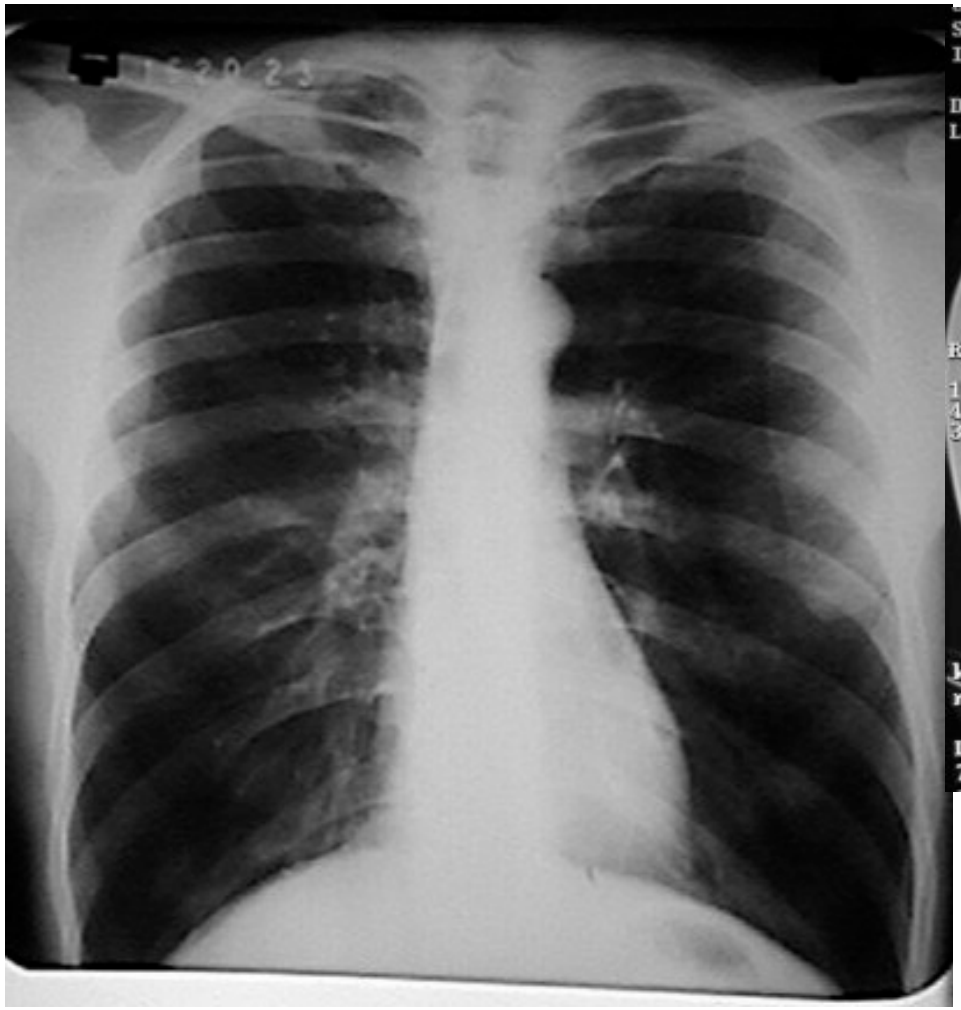
1. Paroxysmal dyspnea
2. Wheezing and cough, especially when they occur during the night and in the early morning
3. Presence of atopic predisposition (IgE antibodies to environmental allergens)
4. Increased eosinophil count in sputum and peripheral blood

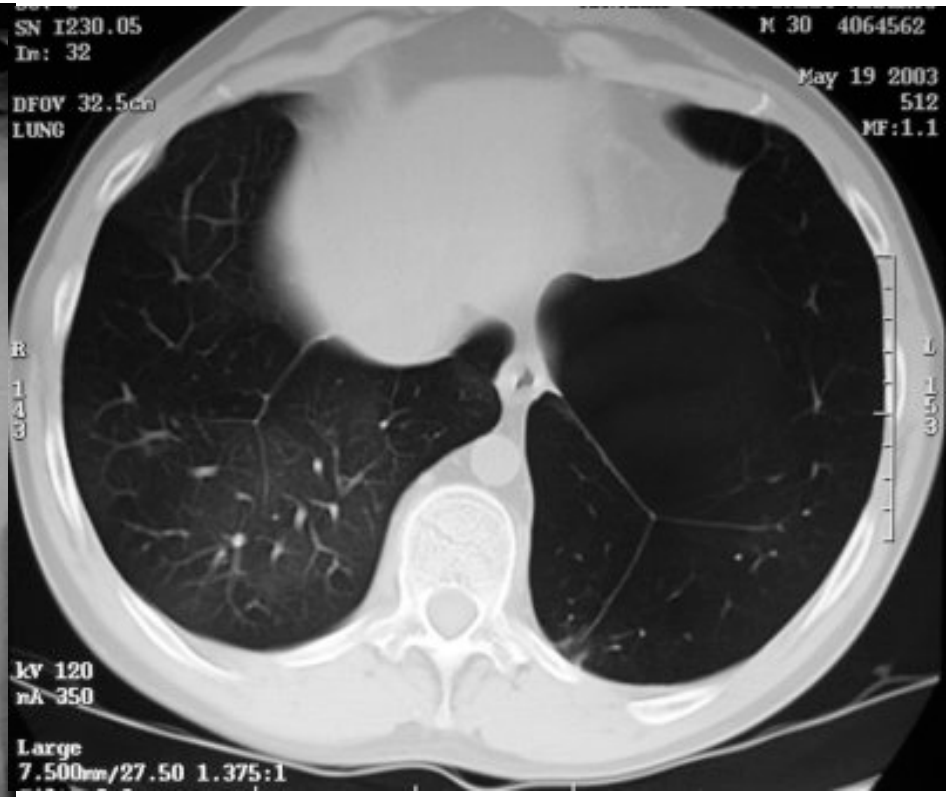
Looking at the patient



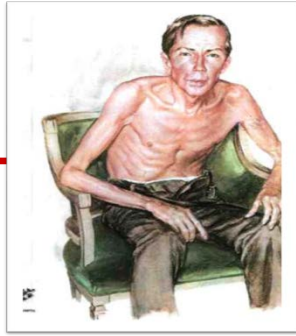
Rennard. NEJM 2004; 350: 965-966

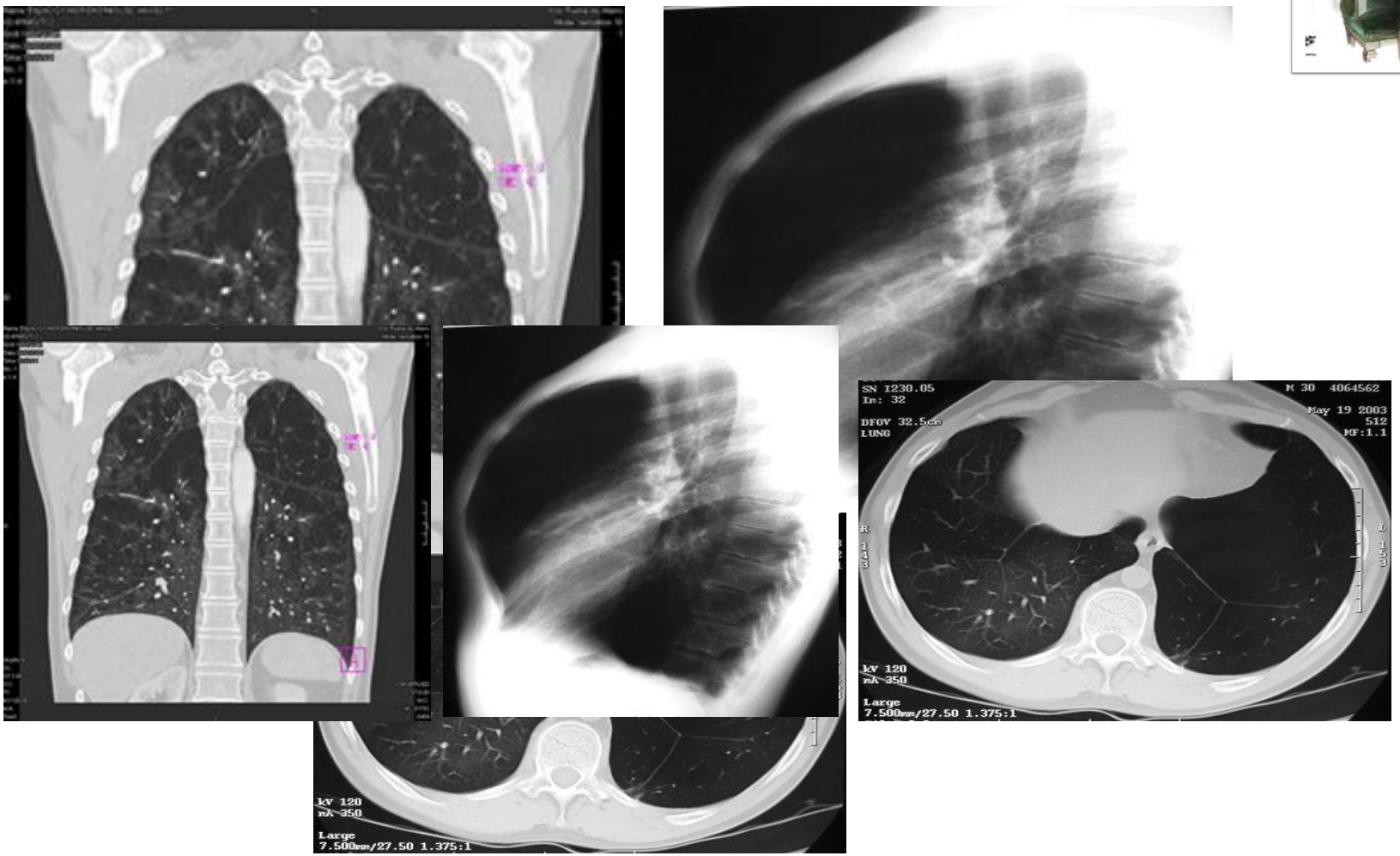
Fenotipo enfisema





Consecuencias clínicas

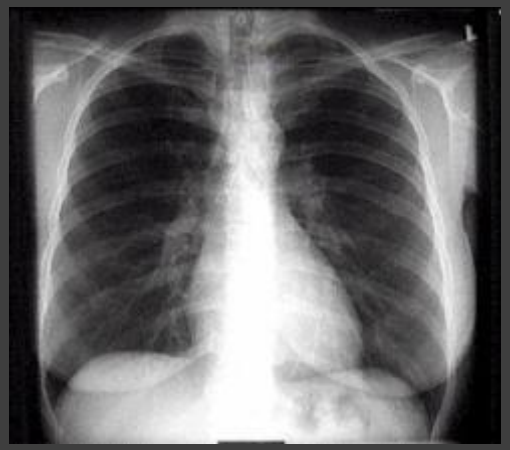


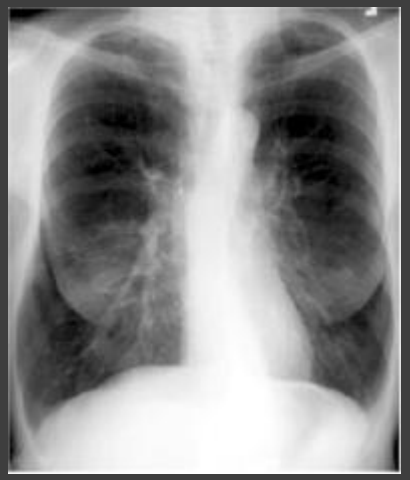


Atrapamiento aéreo

- Lo presentan las personas que sufren EPOC.
- Provoca un mayor trabajo respiratorio.
- Sitúa a los músculos respiratorios en desventaja mecánica.
- Contribuye a la sensación de falta de aire (disnea).

Normal

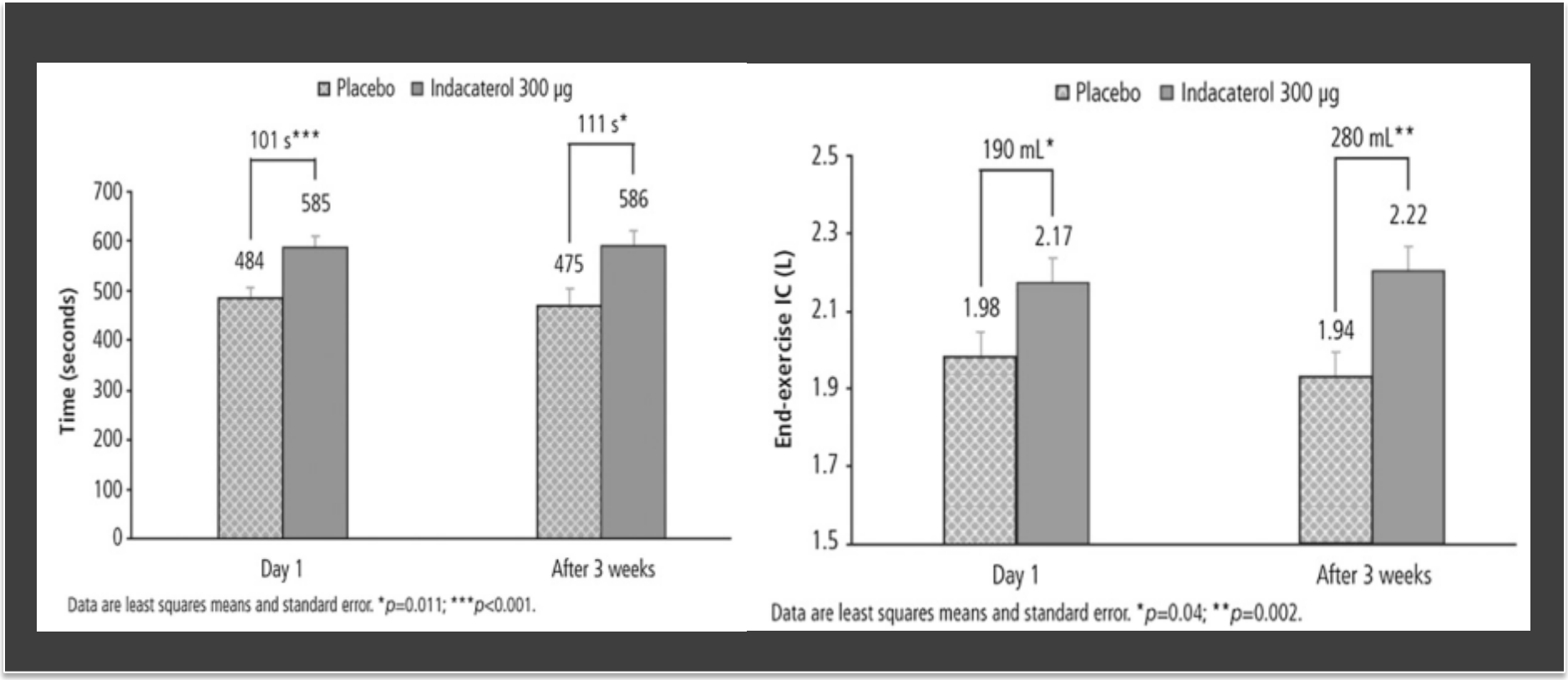




Hiperinsuflación

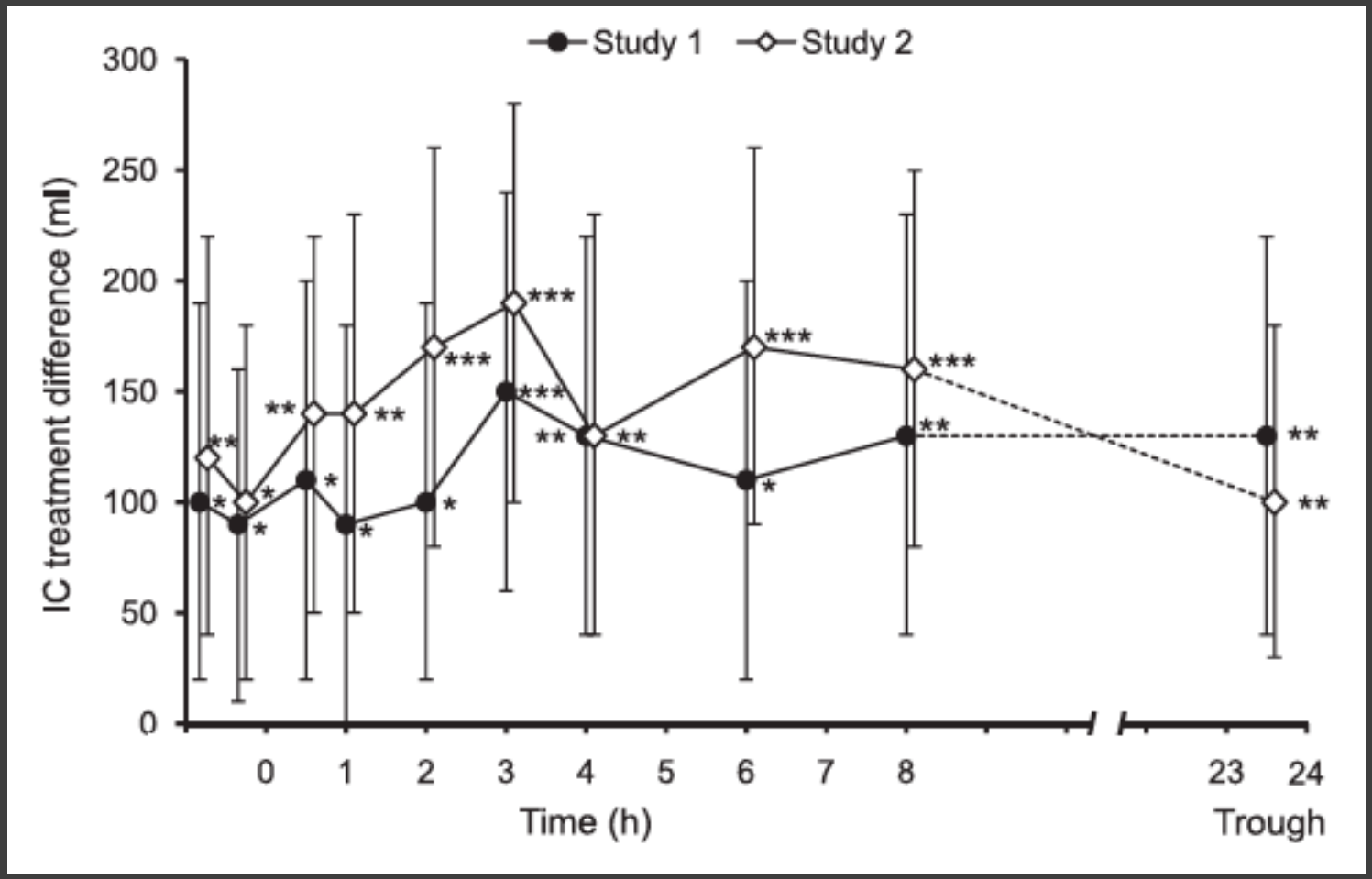
Imágenes cortesía de Denis O'Donnell, Queen's University, Kingston (Canadá

Indacaterol and exercise endurance



O'Donnell et al. Respir Med 2011; 105: 1030-1036

Indacaterol + Tiotropium



Mahler et al. Thorax 2012; 67: 781-788

EPOC: TRATAMIENTO SEGUN GesEPOC 2012

Fenotipo	I (Leve)	II (Moderada)	III (Grave)	IV (Muy grave)
A Fenotipo no agudizador, con enfisema o bronquitis crónica	LAMA o LABA SABA o SAMA*	LABA o LAMA LABA+ LAMA	LABA + LAMA	LABA + LAMA+Teofilinas
B Fenotipo mixto EPOC-Asma (± agudizac.)	LABA + CI	LABA + CI	LABA + LAMA + CI	LABA + LAMA+ CI Valorar añadir teofilina o IPE4 si hay expectoración
C Fenotipo agudizador con enfisema	LAMA o LABA	(LABA o LAMA) + CI LABA + LAMA LABA o LAMA	LABA + LAMA + CI	LABA + LAMA+Ci Valorar añadir teofilina
D Fenotipo agudizador con bronquitis crónica	LAMA o LABA	(LABA o LAMA) + (CI o IFDE4) LABA + LAMA LABA o LAMA	LABA+LAMA + (CI o IPE4) (LABA o LAMA) + CI + IPE4 Valorar añadir carbocisteína	LABA + LAMA + CI + IPE4 LABA+LAMA + CI o IPE4 Valorar añadir carboscisteína Valorar añadir teofilinas Valorar añadir antibióticos

Grupo de Trabajo de GesEPOC, Arch Bronconeumol. 2012

Moltes gràcies a tots!

Amb el patrocini de Novartis