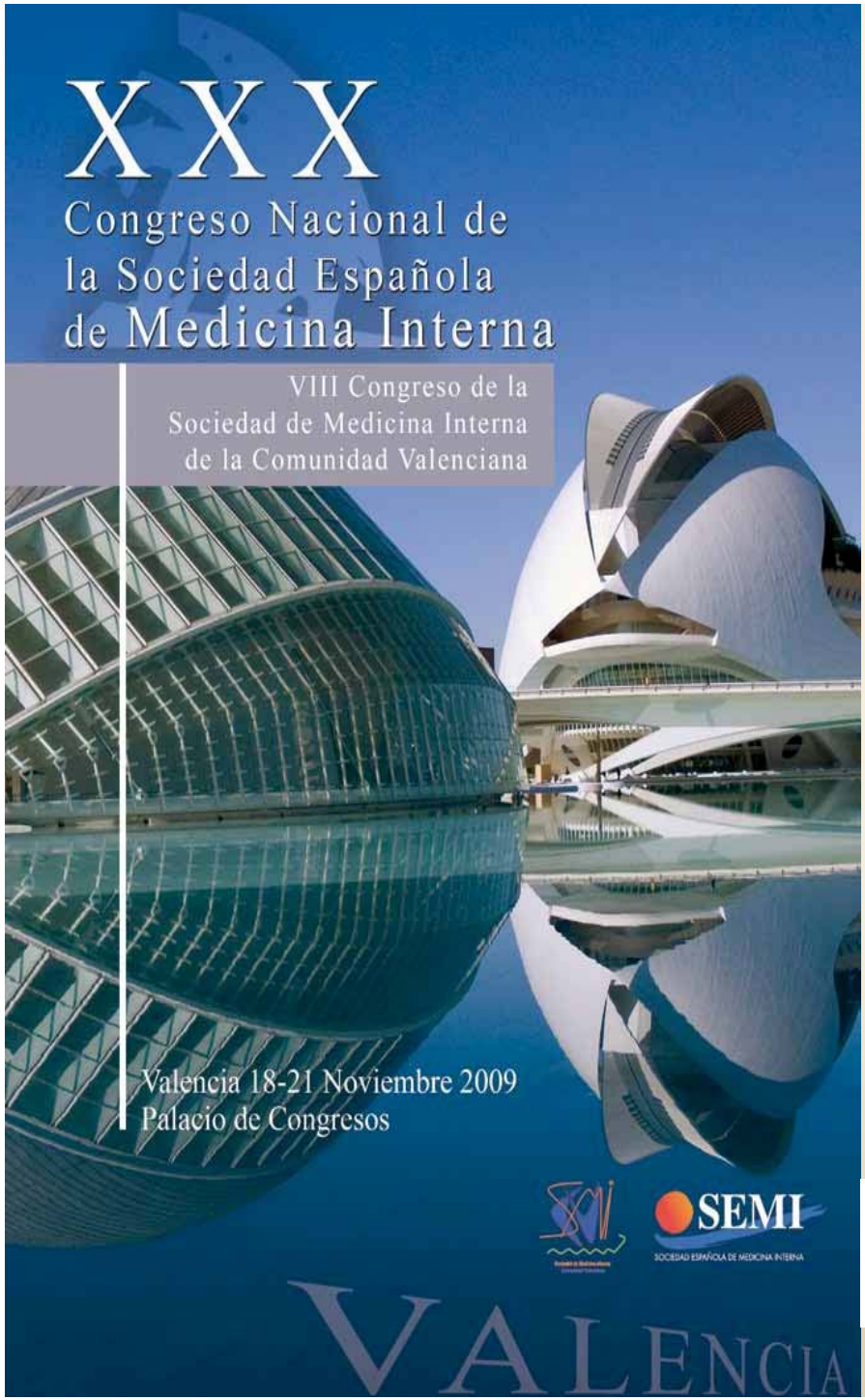


FÁRMACOS MODIFICADORES DEL PRONÓSTICO EN LA EPOC

ALMAGRO P

VALENCIA 18.11.2009

Hospital Universitari MútuaTerrassa

UNIVERSITAT DE BARCELONA

Medications to Modify Lung Function Decline in Chronic Obstructive Pulmonary Disease

Some Hopeful Signs

SAMY SUISSA, PH.D.

AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 178 2008

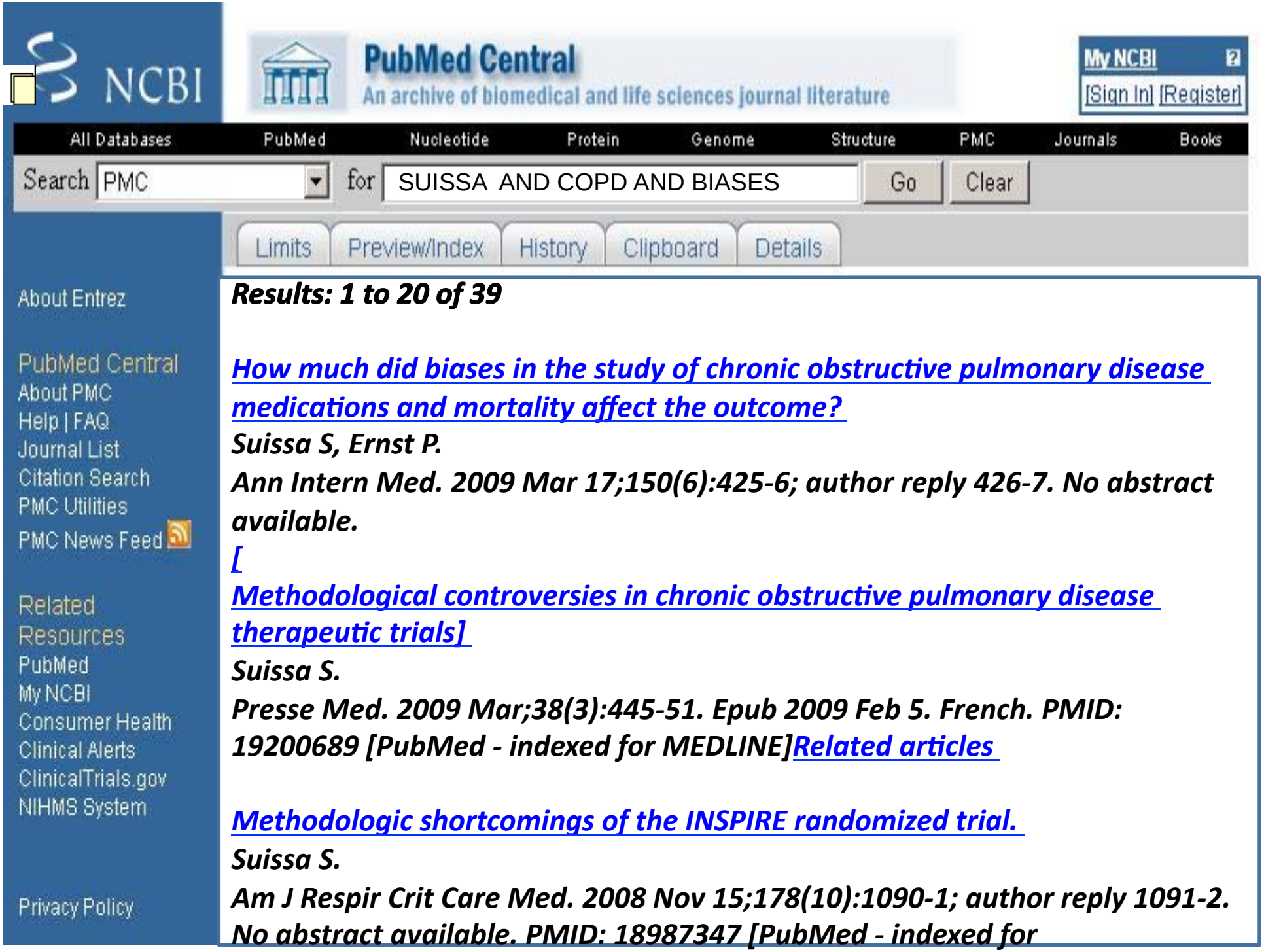
Chronic Obstructive Pulmonary Disease

From Unjustified Nihilism to Evidence-based Optimism

Bartolome R. Celli

Department of Medicine, Tufts University; and Pulmonary and Critical Care Division, St. Elizabeth's Medical Center, Boston, Massachusetts

Proc Am Thorac Soc Vol 3. pp 58–65, 2006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Journal List
Citation Search
PMC Utilities
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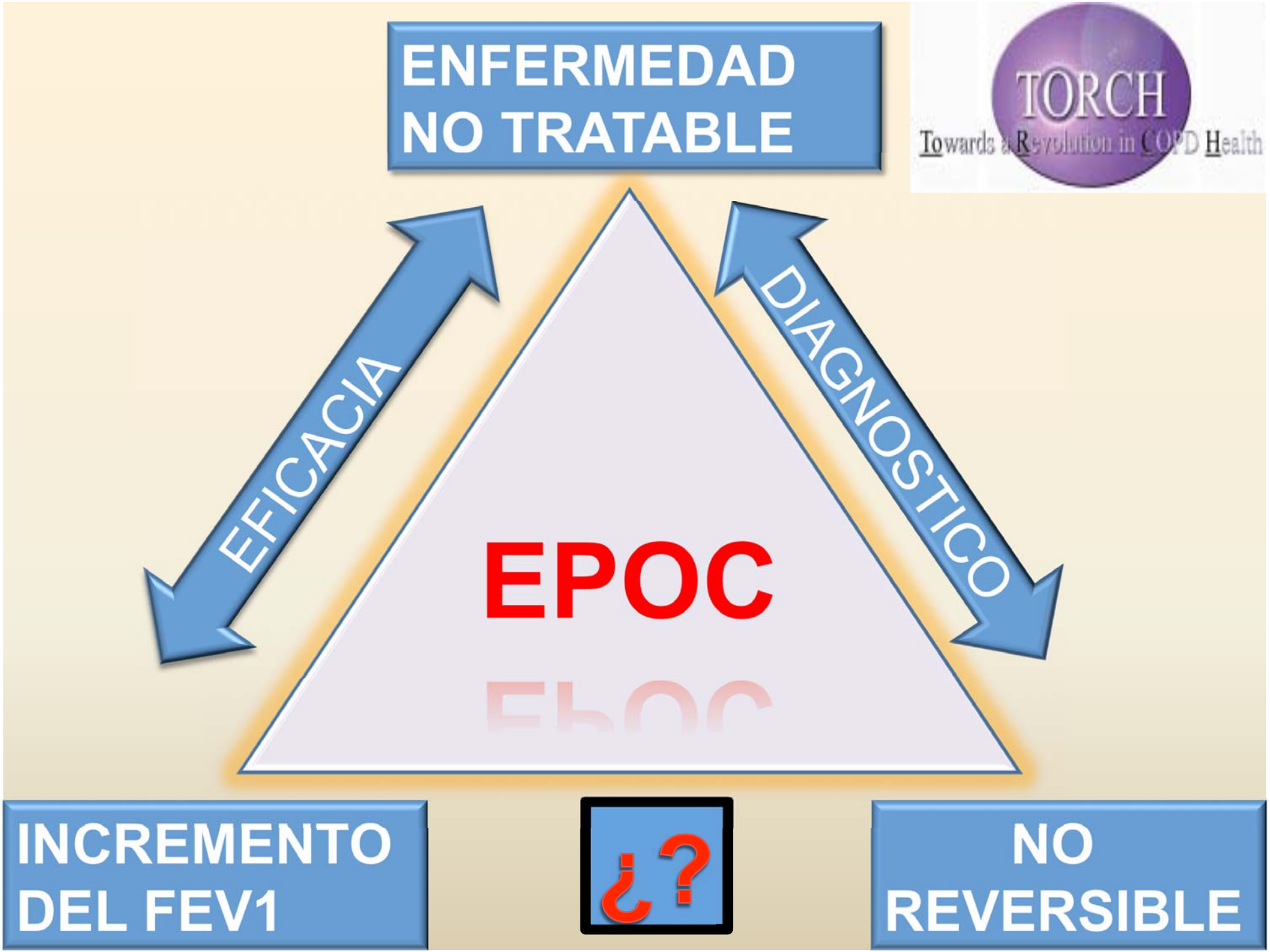
Related Resources
PubMed
My NCBI
Consumer Health
Clinical Alerts
ClinicalTrials.gov
NIHMS System
Privacy Policy
Results: 1 to 20 of 39
How much did biases in the study of chronic obstructive pulmonary disease medications and mortality affect the outcome?
Suissa S, Ernst P.
Ann Intern Med. 2009 Mar 17;150(6):425-6; author reply 426-7. No abstract available.
[
Methodological controversies in chronic obstructive pulmonary disease therapeutic trials]
Suissa S.
Presse Med. 2009 Mar;38(3):445-51. Epub 2009 Feb 5. French. PMID: 19200689 [PubMed - indexed for MEDLINE]Related articles
Methodologic shortcomings of the INSPIRE randomized trial.
Suissa S.
Am J Respir Crit Care Med. 2008 Nov 15;178(10):1090-1; author reply 1091-2. No abstract available. PMID: 18987347 [PubMed - indexed for


ENFERMEDAD NO TRATABLE
TORCH
Towards a Revolution in COPD Health
EFICACIA
DIAGNOSTICO
EPOC
INCREMENTO DEL FEV1
¿?
NO REVERSIBLE

AUMENTO SUPERVIVENCIA

FUNCION RESPIRATORIA

EXACERBACIONES

CALIDAD DE VIDA

ESTUDIOS POBLACIONALES

Survival in COPD patients after regular use of fluticasone propionate and salmeterol in general practice

Eur Respir J 2002; 20: 819–825

J.B. Soriano*,+, J. Vestbo§, N.B. Pride^{f}, V. Kiri#, C. Maden¶, W.C. Maier*

Inhaled Corticosteroids and the Risk of Mortality and Readmission In Elderly Patients with Chronic Obstructive Pulmonary Disease

DON D. SIN and JACK V. TU

Am J Respir Crit Care Med Vol 164. pp 580–584, 2001

Effectiveness of Inhaled Corticosteroids in Chronic Obstructive Pulmonary Disease

Immortal Time Bias in Observational Studies

Samy Suissa

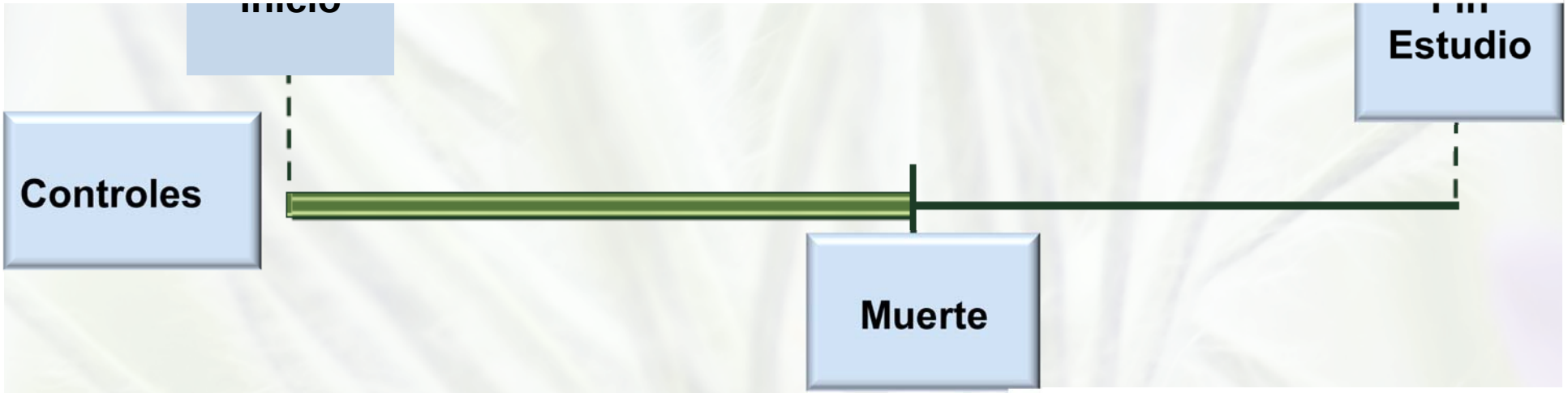
Immortal time bias must be considered in observational studies

Sesgo de inmortalidad

Inhaled Corticosteroids in Chronic Obstructive Pulmonary Disease

Results from Two Observational Designs Free of Immortal Time Bias

Victor A. Kiri, Neil B. Pride, Joan B. Soriano, and Jørgen Vestbo

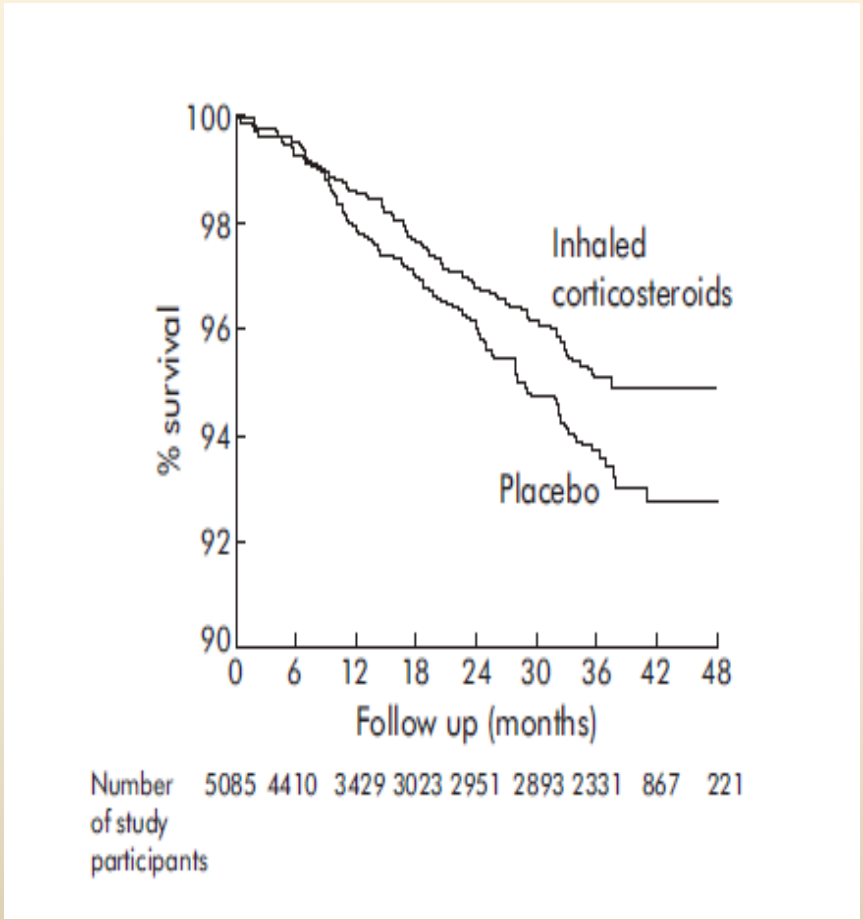


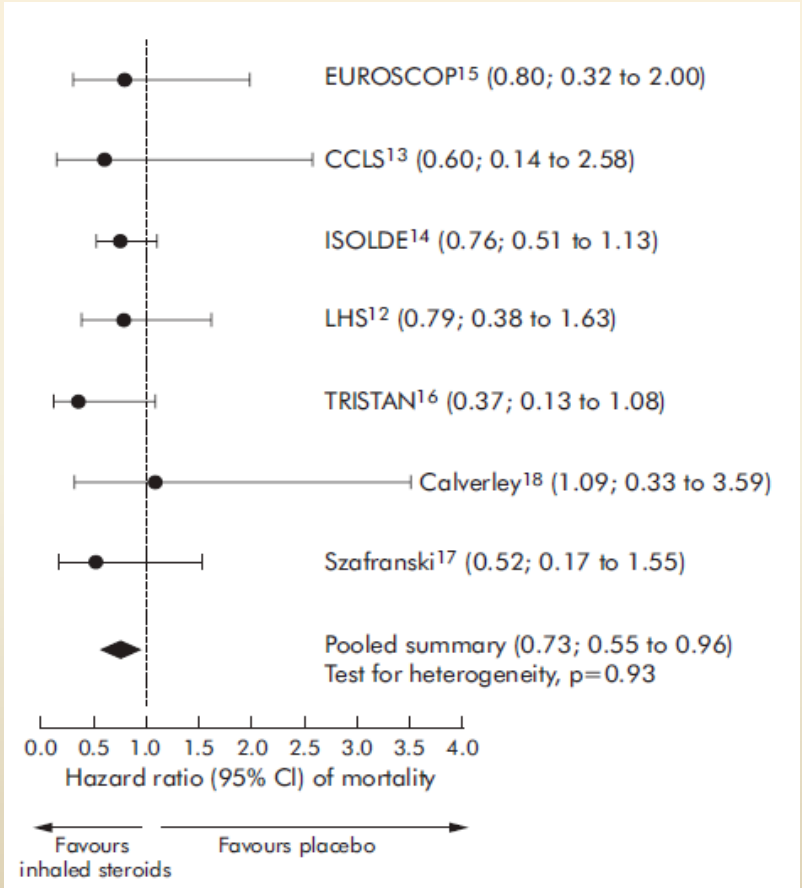
Am J Respir Crit Care Med Vol 172. pp 460–464, 2005

Inhaled corticosteroids and mortality in chronic obstructive pulmonary disease

D D Sin, L Wu, J A Anderson, N R Anthonisen, A S Buist, P S Burge, P M Calverley, J E Connett, B Lindmark, R A Pauwels†, D S Postma, J B Soriano, W Szafranski, J Vestbo

Thorax 2005;**60**:992–997. doi: 10.1136/thx.2005.045385





The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 22, 2007 VOL. 356 NO. 8

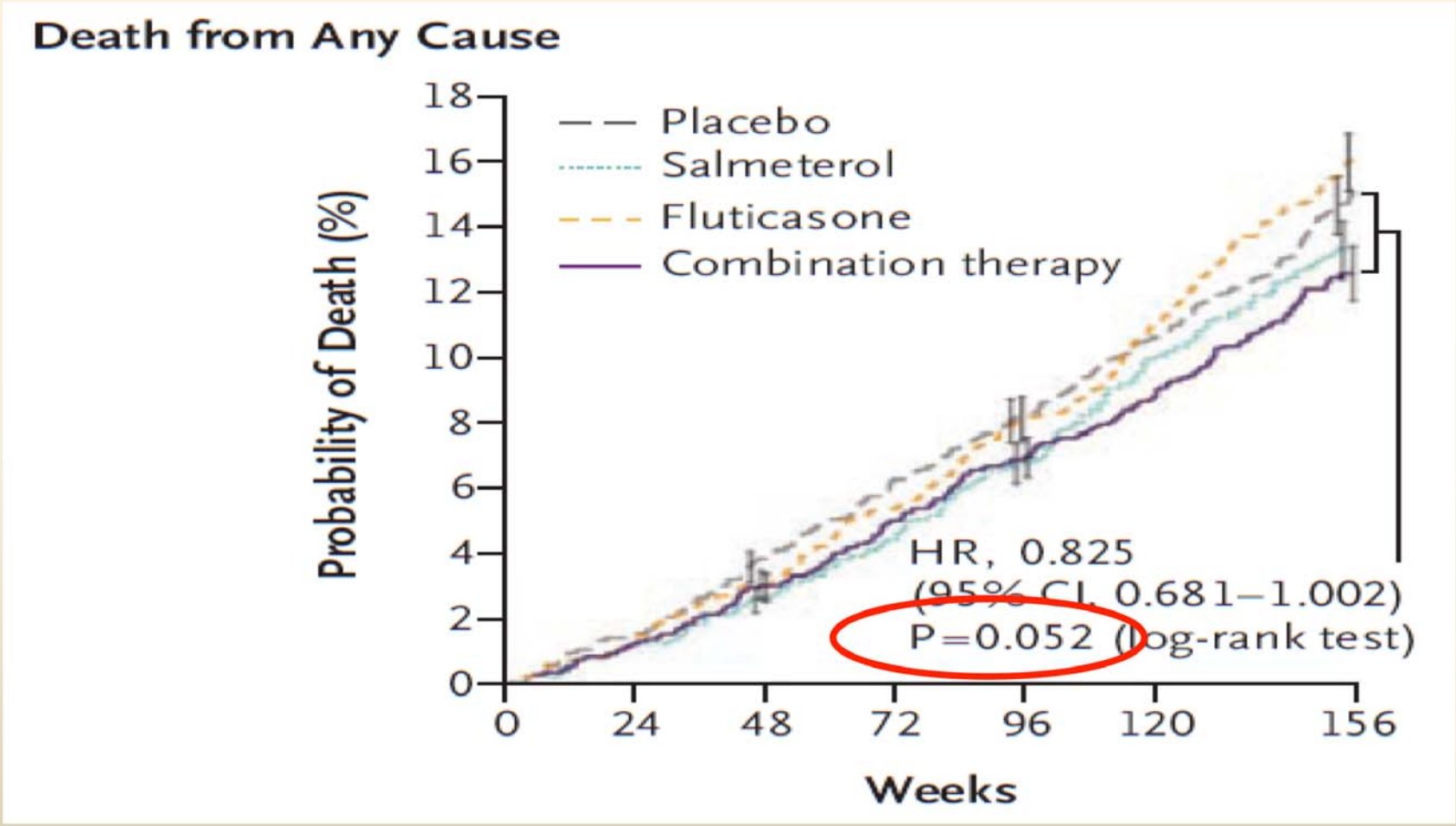
Salmeterol and Fluticasone Propionate and Survival in Chronic Obstructive Pulmonary Disease

- ***6184 PACIENTES***
- ***OBJETIVO PRINCIPAL, DISMINUCIÓN DE LA MORTALIDAD***
- ***3 AÑOS DE SEGUIMIENTO***
- ***EPOC POCO REVERSIBLE (PBD <10%)***
- ***4 RAMAS (PB)-(SML)-(FTC)-(SML+FTC)***
- ***PLACEBO "PURO"***

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



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

CALCULO DEL TAMAÑO MUESTRAL

MORTALIDAD PREVISTA 17% → OBSERVADA 14%

PLACEBO "PURO"

¿A quién incluyo?

PRUEBA BRONCODILATADORA <10%

Selecciona pacientes con peor respuesta

Eur Respir J 2008; 31: 742–750
DOI: 10.1183/09031936.00129607

Bronchodilator responsiveness in patients with COPD

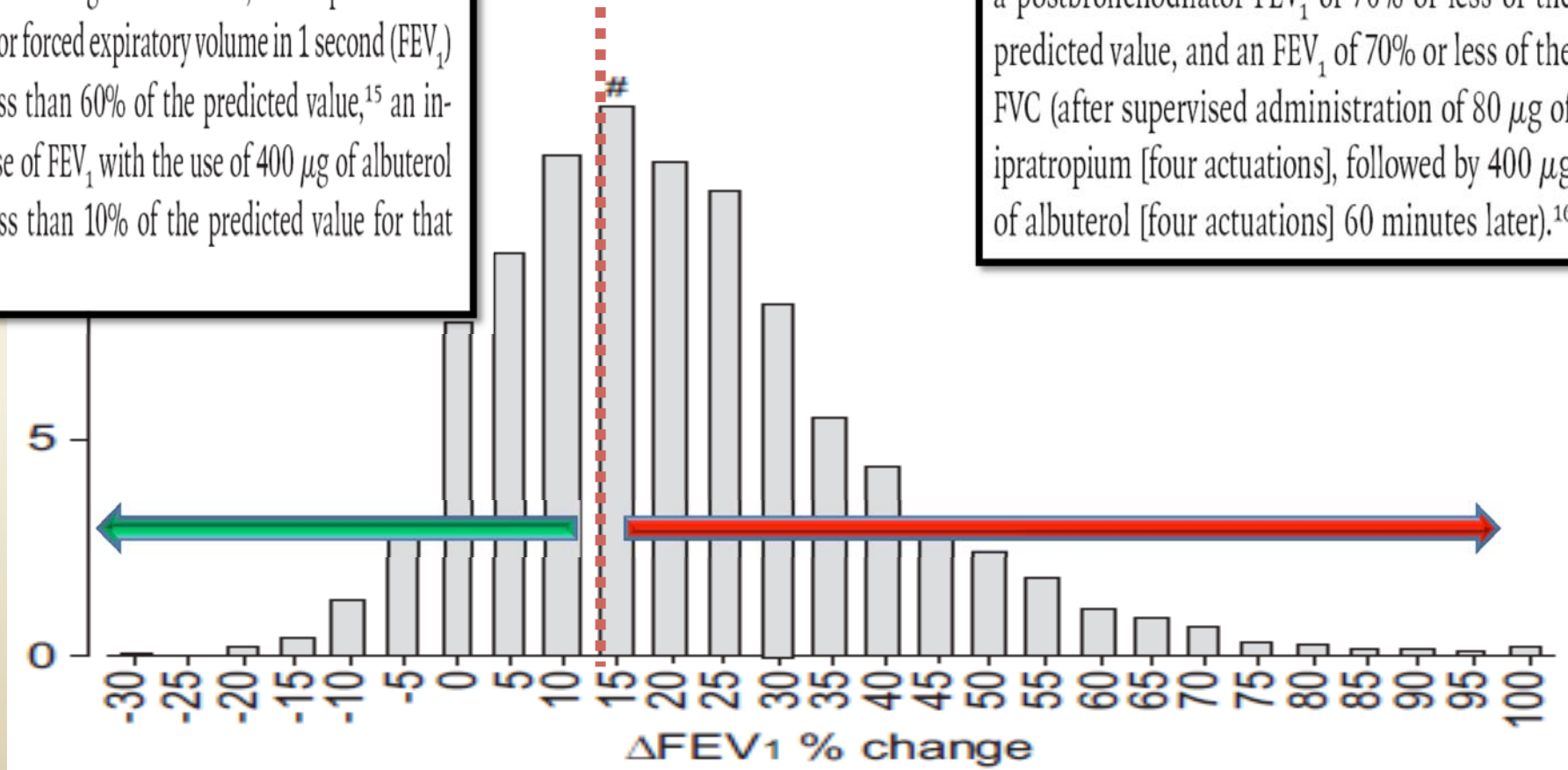
D.P. Tashkin*, B. Celli#, M. Decramer¶, D. Liu+, D. Burkhart+, C. Cassino+ and S. Kesten§

TORCH

received a diagnosis of COPD, with a prebronchodilator forced expiratory volume in 1 second (FEV_1) of less than 60% of the predicted value,[15] an increase of FEV_1 with the use of 400 μg of albuterol of less than 10% of the predicted value for that

UPLIFT

a postbronchodilator FEV_1 of 70% or less of the predicted value, and an FEV_1 of 70% or less of the FVC (after supervised administration of 80 μg of ipratropium [four actuations], followed by 400 μg of albuterol [four actuations] 60 minutes later).[16]



ANALISIS POR INTENCION DE TRATAR

PLACEBO

Eur Respir J 2009; 34: 1018–1023
DOI: 10.1183/09031936.00122608

PERSPECTIVE

Methods for therapeutic trials in COPD: lessons from the TORCH trial

O.N. Keene*, J. Vestbo[#,¶], J.A. Anderson*, P.M.A. Calverley[+], B. Celli[§], G.T. Ferguson[ƒ], C. Jenkins** and P.W. Jones[##]

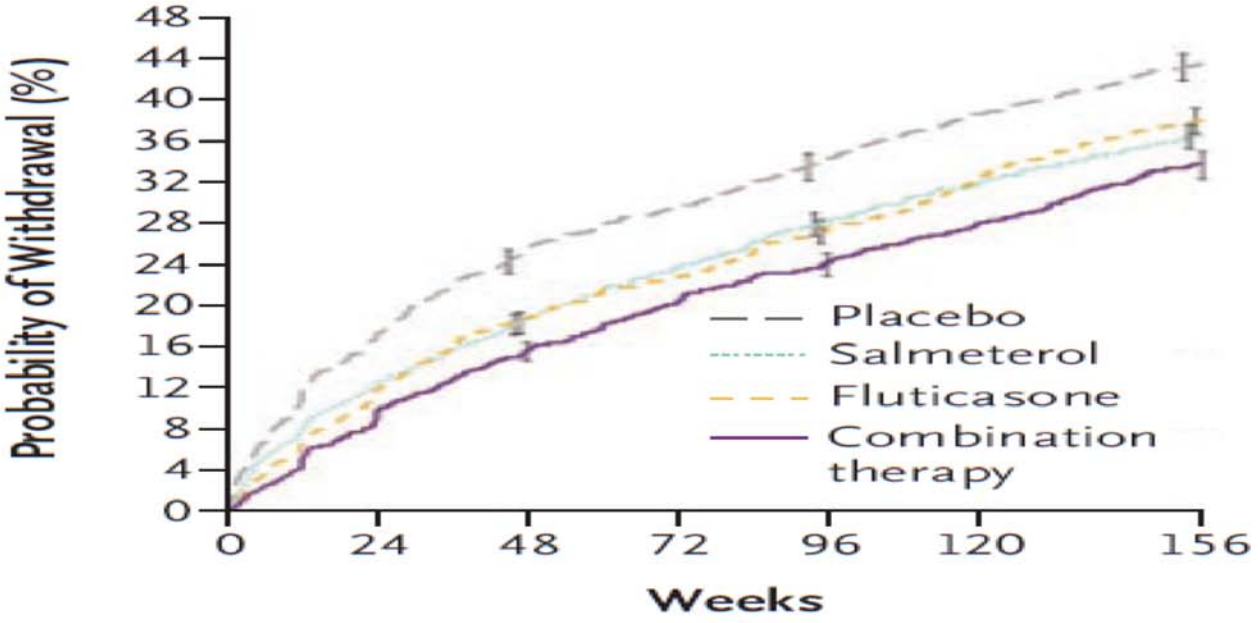
LABA | LABA+CI | ANTCLN

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

A Discontinuation of Study Drug



No. of Patients							
Placebo	1524	1264	1141	1074	1005	937	640
Salmeterol	1521	1336	1240	1160	1093	1036	717
Fluticasone	1534	1361	1247	1184	1112	1039	681
Combination therapy	1533	1397	1296	1224	1164	1104	758

Respiratory Research

BioMed Central

Research

Open Access

Efficacy of salmeterol/fluticasone propionate by GOLD stage of chronic obstructive pulmonary disease: analysis from the randomised, placebo-controlled TORCH study

Published: 30 June 2009

Christine R Jenkins*†1, Paul W Jones†2, Peter MA Calverley†3, Bartolome Celli†4, Julie A Anderson†5, Gary T Ferguson†6, Julie C Yates†7, Lisa R Willits†5 and Jörgen Vestbo†8,9

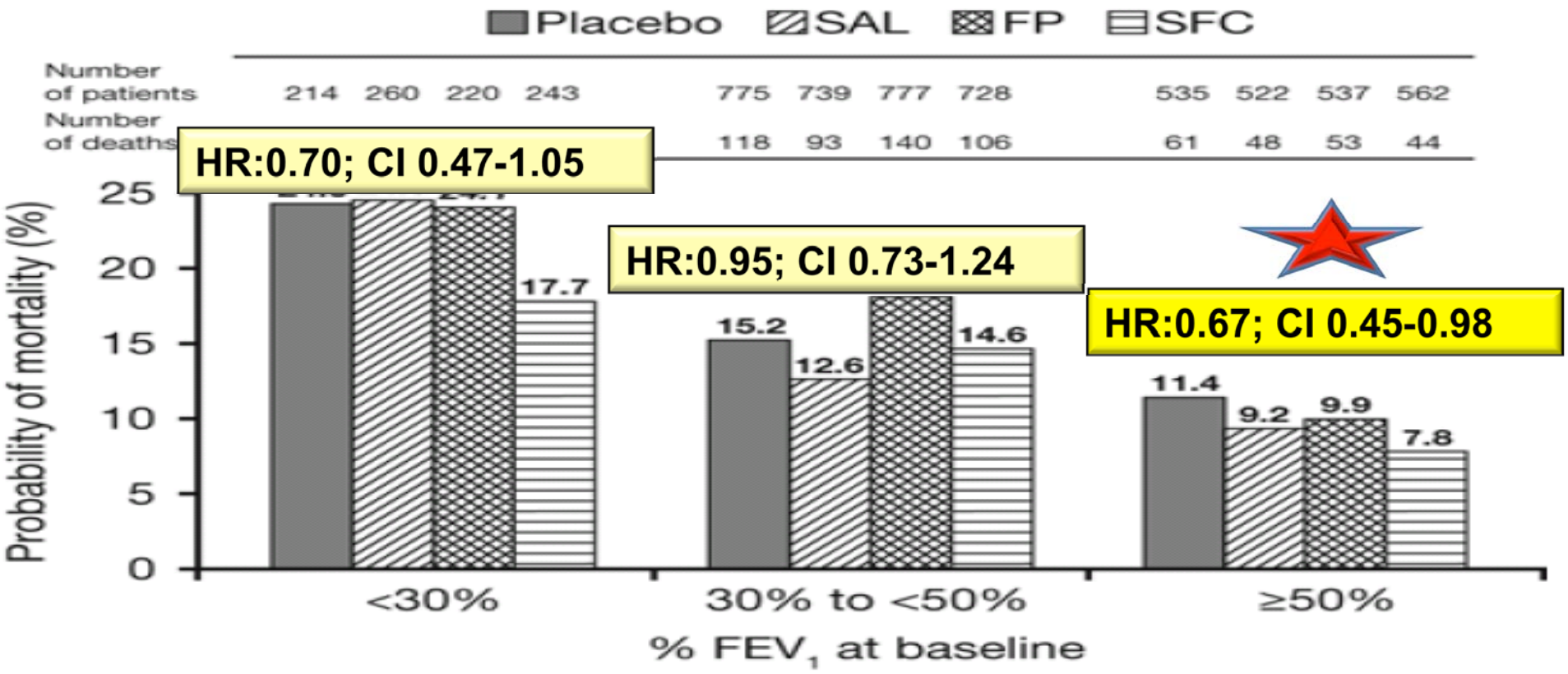


Figure 2
All-cause mortality by baseline post-bronchodilator FEV_1 % predicted.

THORAX

Adherence to inhaled therapy, mortality, and hospital admission in COPD

Jørgen Vestbo, Julie A Anderson, Peter Calverley, Bartolome Celli, Gary T Ferguson, Christine Jenkins, Katharine Knobil, Lisa R Willits, Julie C Yates and Paul Jones

Thorax published online 23 Aug 2009;

P=0.023

	Pb	SMT	FC	SMT/FC
Cumplidores	12%	10.7%	12.9%	9.5%
No cumplidores	26.7%	25.2%	28.7%	24.9%

Intención de tratar	HR 0.4; C.I. 0.35-0.46; p<0.001
Tratamiento	HR 0.25; CI 0.20-0.30

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 9, 2008 VOL. 359 NO. 15

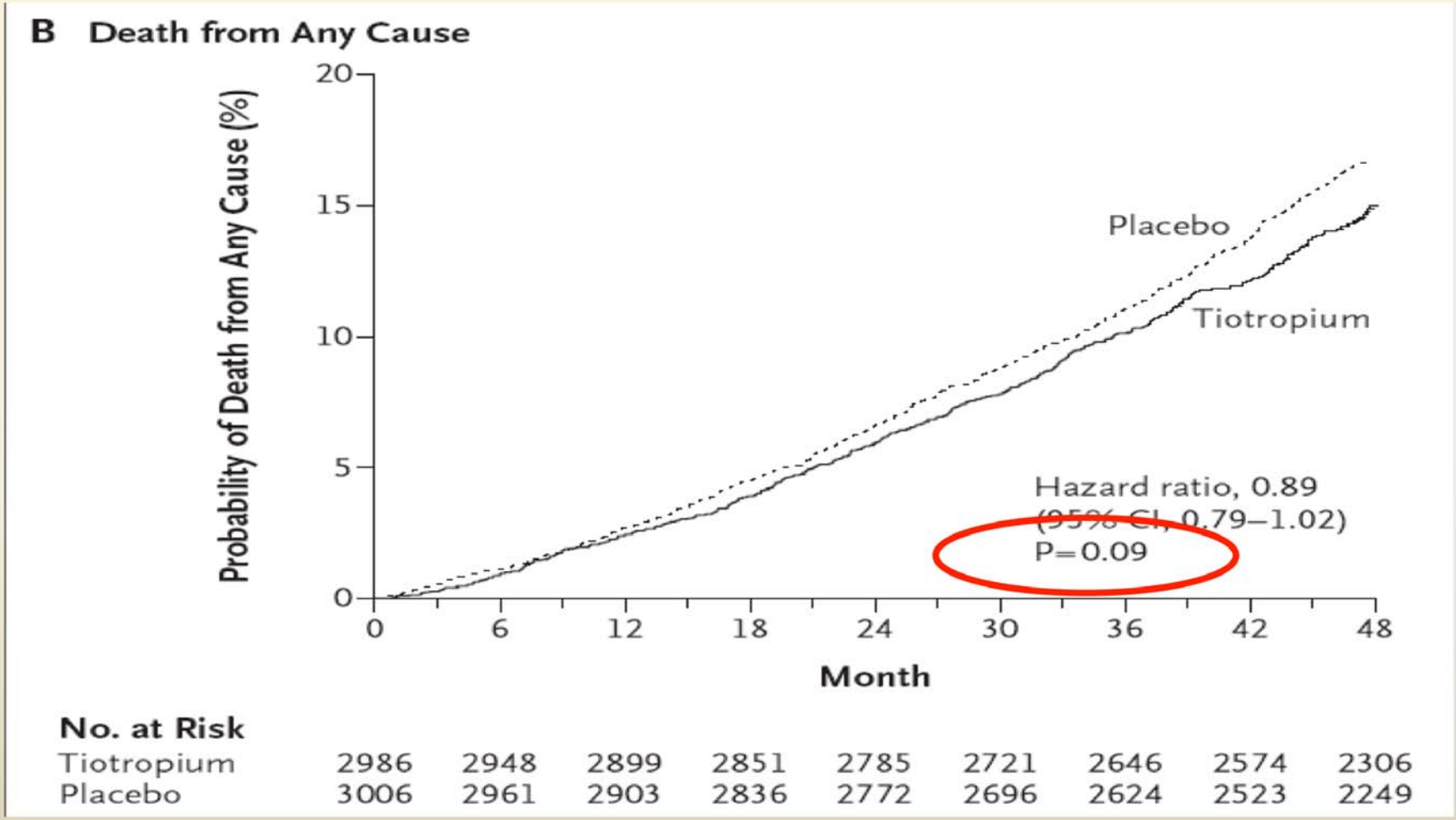
A 4-Year Trial of Tiotropium in Chronic Obstructive Pulmonary Disease

- ***5993 PACIENTES***
- ***OBJETIVO PRINCIPAL, DISMINUCIÓN DE LA CAIDA DEL FEV1***
- ***4 AÑOS DE SEGUIMIENTO***
- ***FEV1 <70% TRAS PBD***
- ***RAMAS ("PLACEBO"-TIOTROPIO)***
- ***Un 68% de los pacientes llevaba tratamiento con Betamiméticos (60% de larga duración).***
- ***Un 61% recibía tratamiento con C. I.***

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



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

Mortalidad a 4 años

14.4% en Tiotropium vs 16.3% en placebo

H.R. 0.87, 95% C.I. , 0.76-0.99

Porcentaje de pérdidas 5%

Mortalidad a 4 años + 30 días

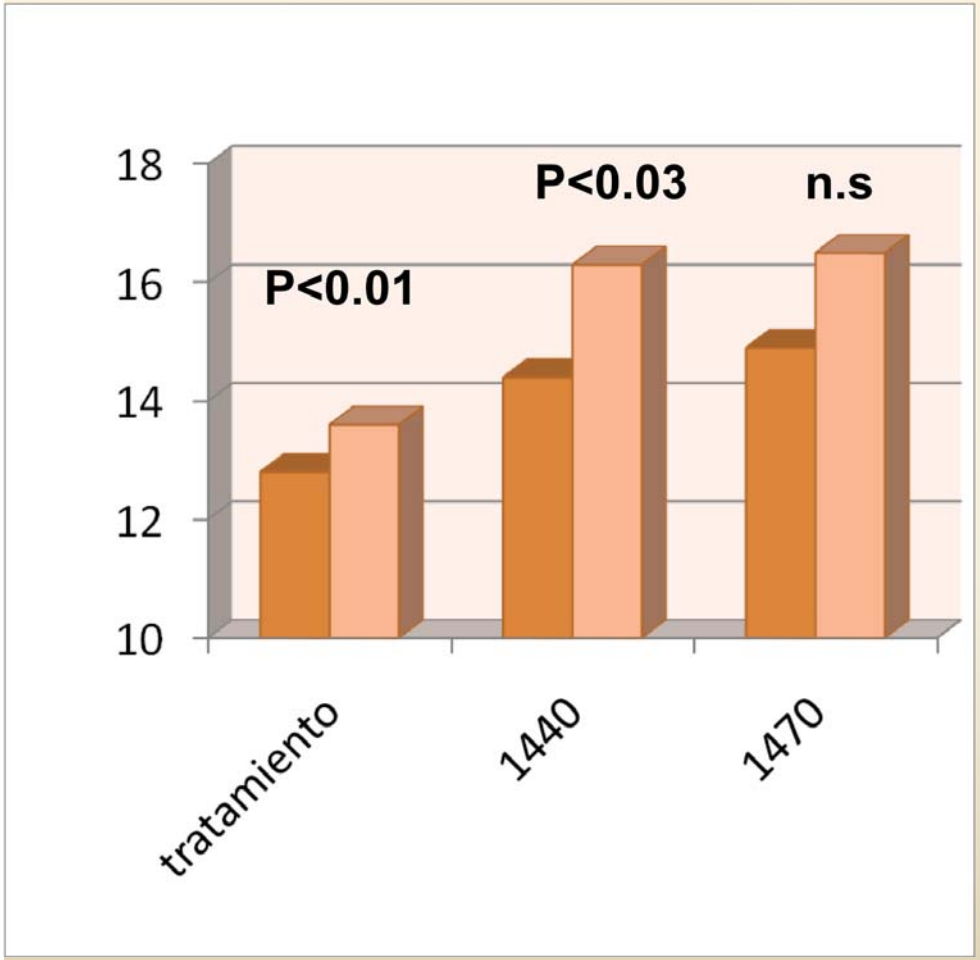
14.9% en Tiotropium vs 16.5% en placebo

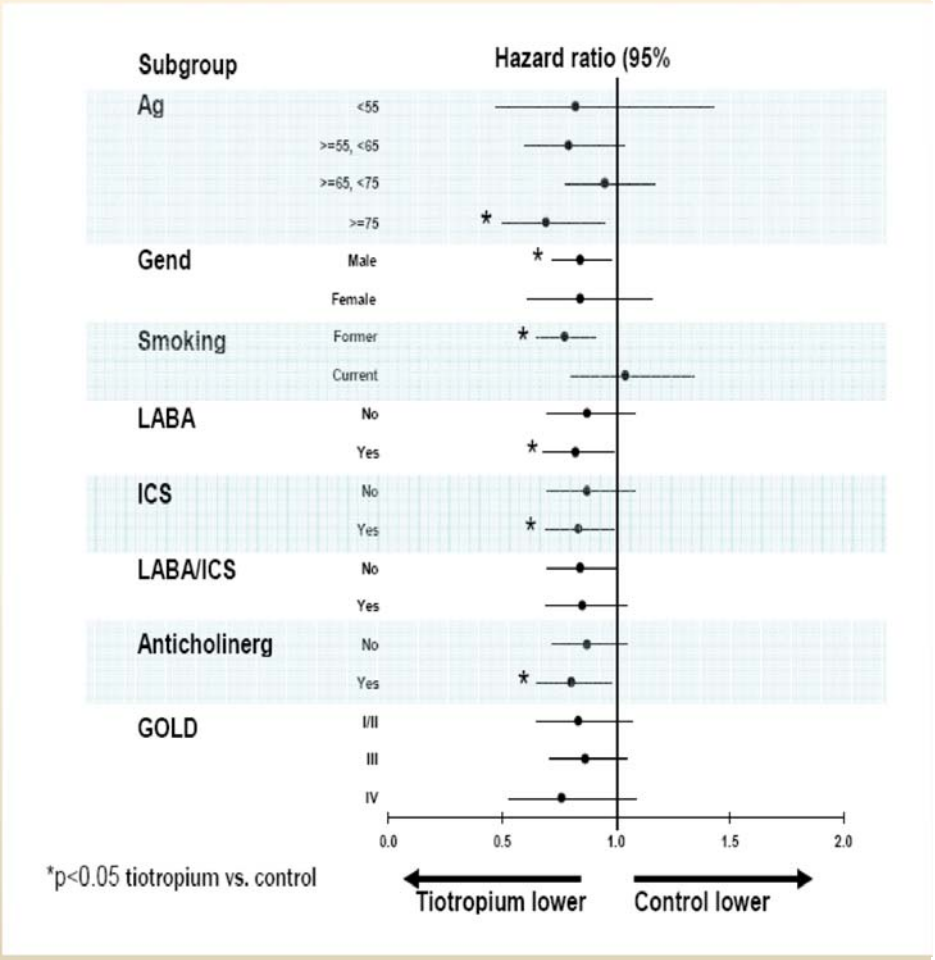
Porcentaje de pérdidas 25%

Mortality in the 4-Year Trial of Tiotropium (UPLIFT) in Patients with Chronic Obstructive Pulmonary Disease

Bartolome Celli[1], Marc Decramer[2], Steven Kesten[3], Dacheng Liu[3], Sunil Mehra[4], and Donald P. Tashkin[5], on behalf of the UPLIFT Study Investigators*

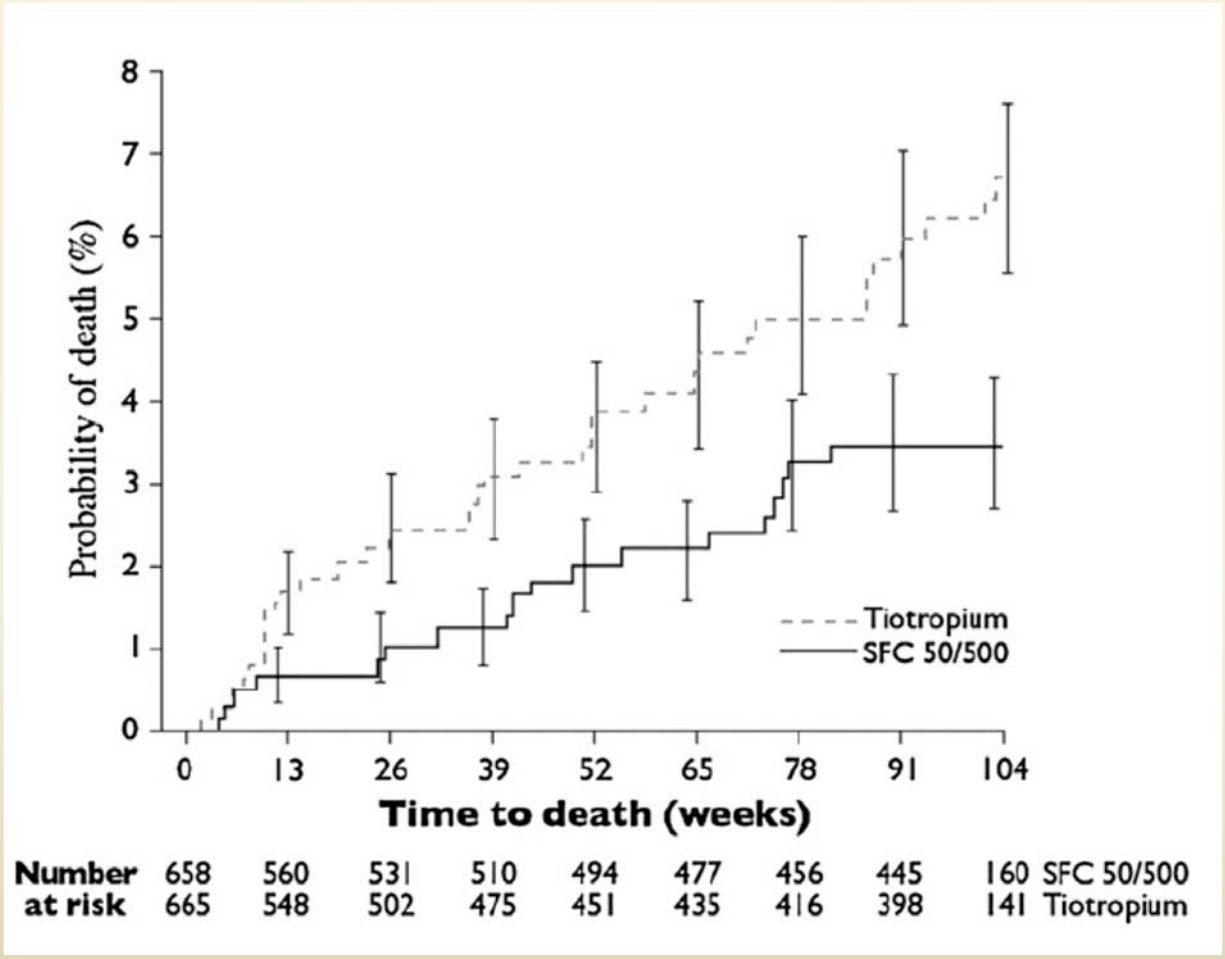
Am J Respir Crit Care Med Vol 180. pp 948–955, 2009





The Prevention of Chronic Obstructive Pulmonary Disease Exacerbations by Salmeterol/Fluticasone Propionate or Tiotropium Bromide

Am J Respir Crit Care Med Vol 177. pp 19–26, 2008



Respiratory Research

BioMed Central

Research

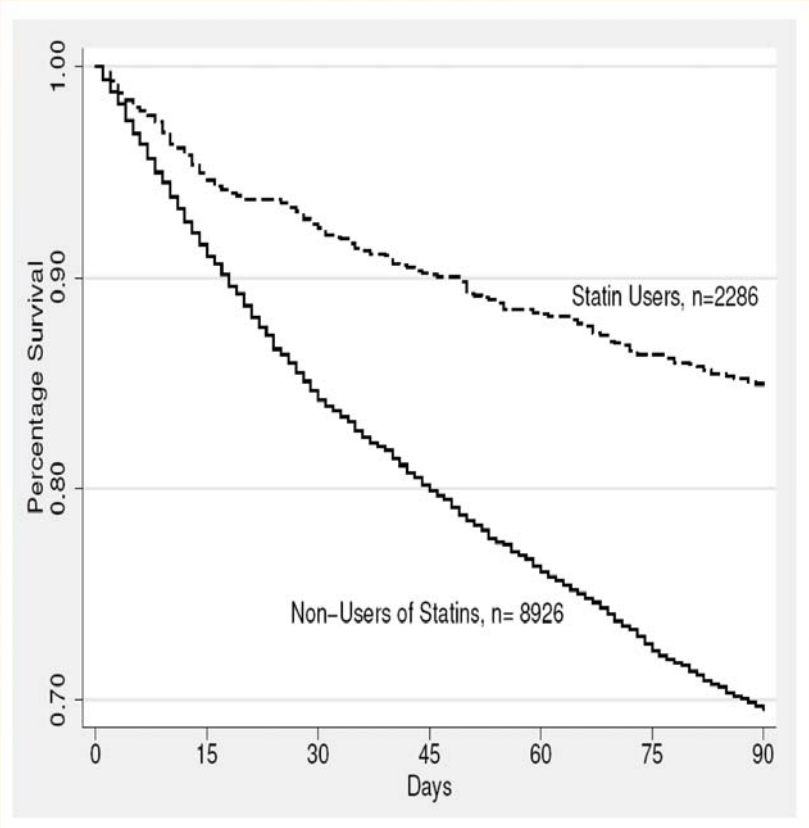
Open Access

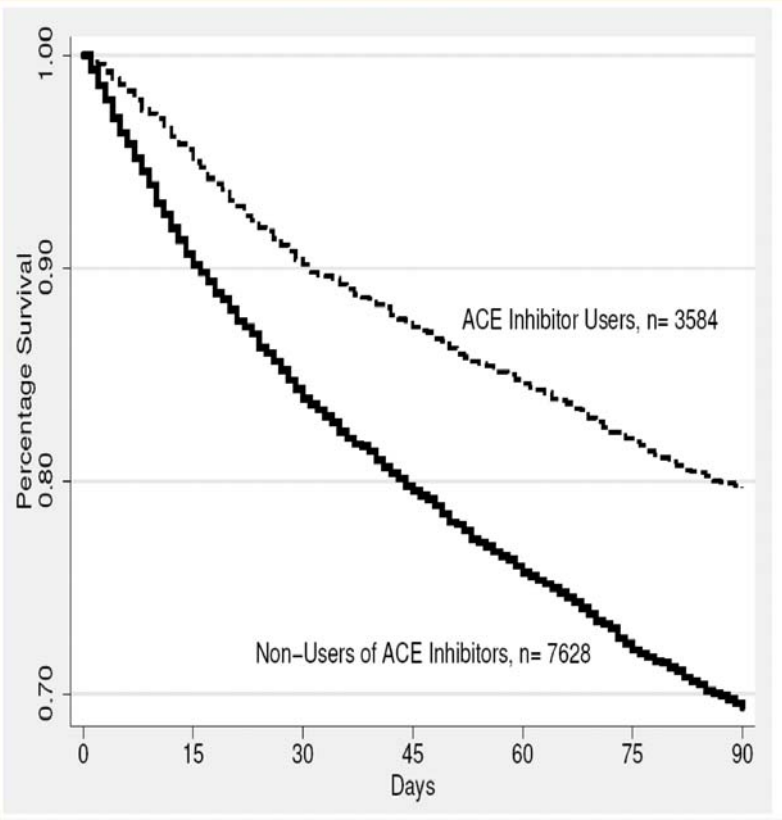
Impact of statins and ACE inhibitors on mortality after COPD exacerbations

Eric M Mortensen*[1,2], Laurel A Copeland[1,3], Mary Jo V Pugh[1,4], Marcos I Restrepo[1,5], Rosa Malo de Molina[1,5], Brandy Nakashima[1] and Antonio Anzueto[1,5]

Respiratory Research 2009, **10**:45

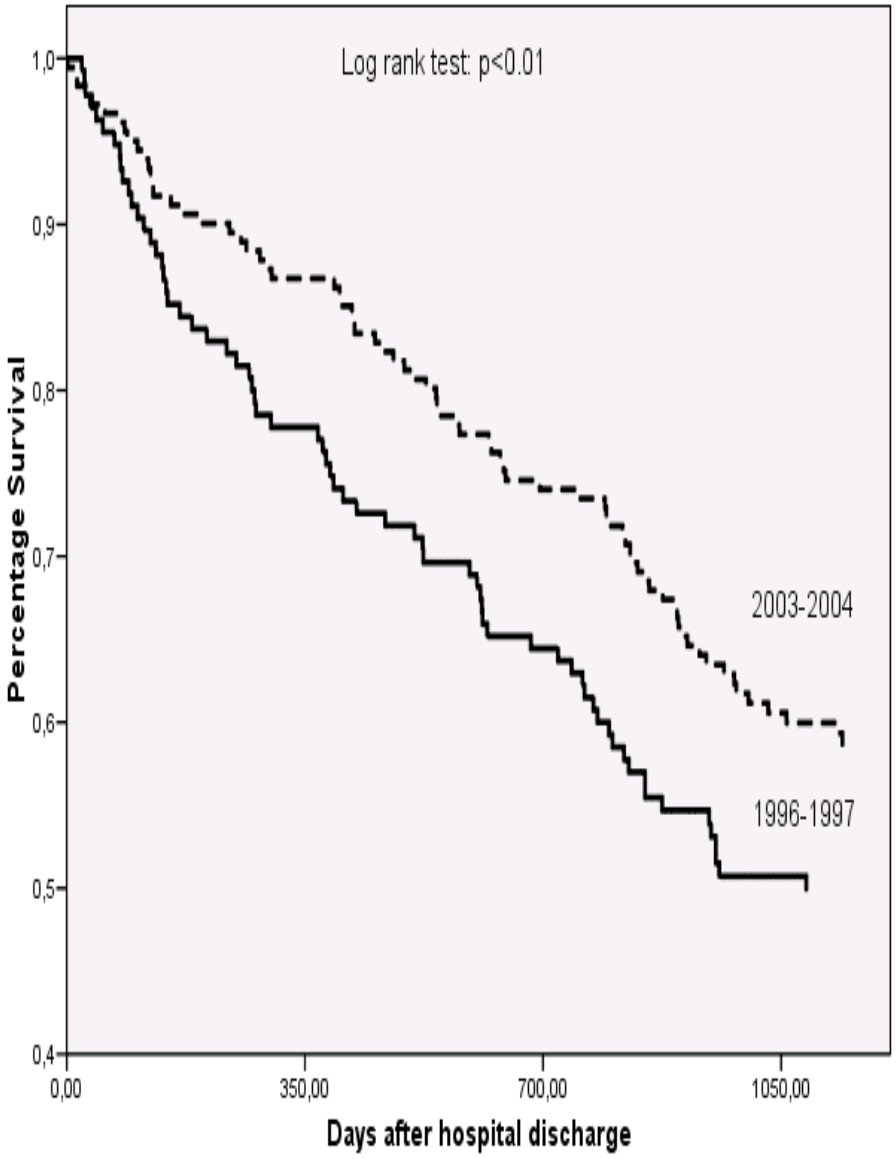
- ***Estudio observacional de 11.212 pacientes (98%H), hospitalizados por EPOC***
- ***Tratamiento con estatinas (20%)***
- ***Tratamiento con IECA-ARAII (30%)***
- ***Mortalidad a los 90 días del alta (12.4%)***
- ***Análisis multivariante ajustado por edad, comorbilidad, variables sociodemográficas…..***





	O.R.	95 % C.I.
IECA /ARAII	0.62	0.53-0.73
ESTATINAS	0.49	0.39-0.61
AMBOS	0.40	0.32-0.52

Recent improvement in long-term survival after a COPD hospitalization *(Almagro P.Thorax 2009)*



	p	H.R.	C.I.95 %
Cohort	.038	.661	0.447-0.977
Age*	.000	1.050	1.025-1.075
Gender	.498	1.261	0.645-2.463
BMI*	.052	.962	0.924-1.000
Comorbidity	.000	1.346	1.179-1.536
FEV_1 %*	.036	.984	0.969-0.999
mMMRC*	.046	1.186	1.003-1.403

TABLE 4. Treatment at discharge, by cohort

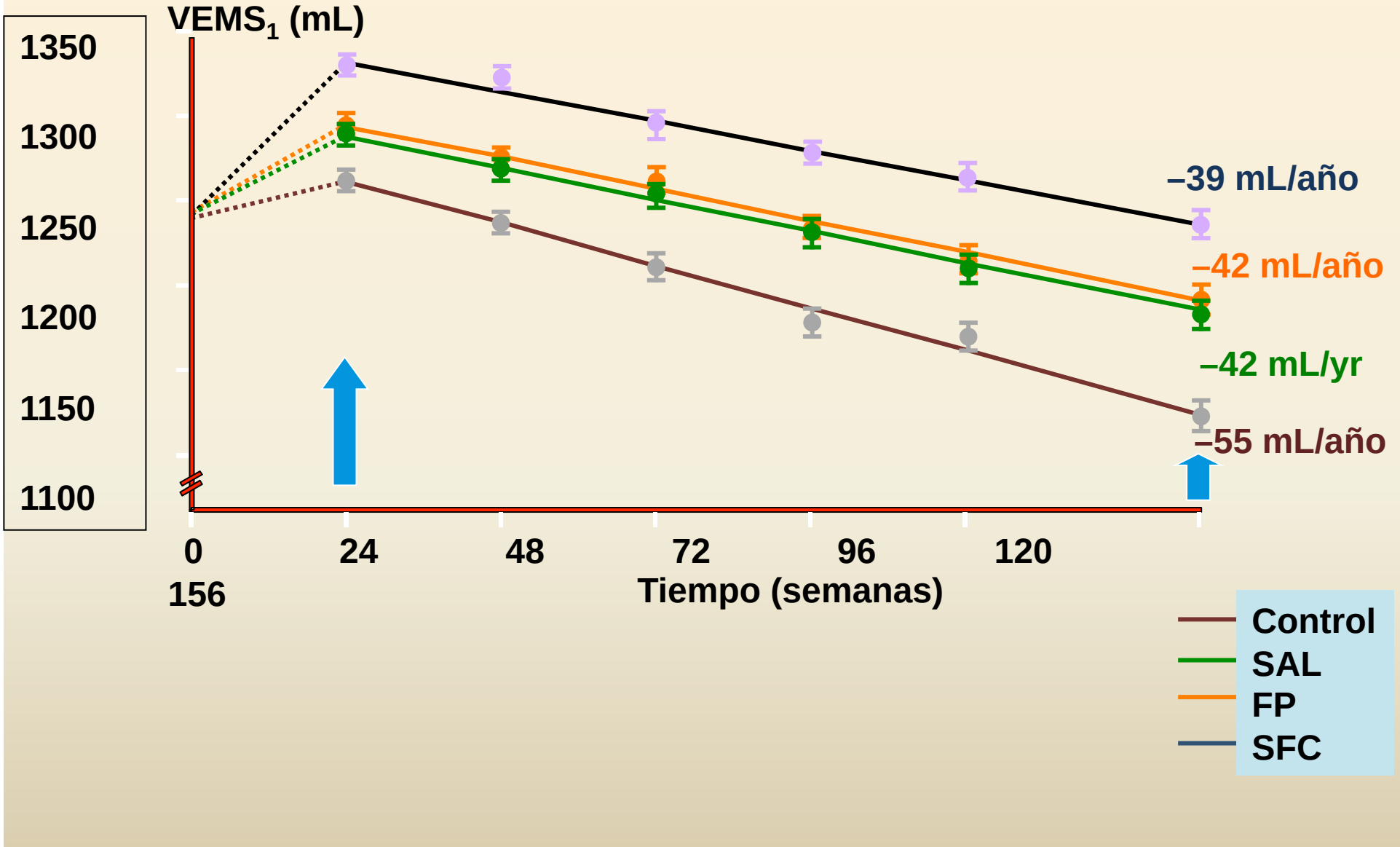
	1996-1997	2003-2004	p
	%	%	
Short-acting B_2 agonists	97.6	78.5	0.0001
Long-acting B_2 agonists	1.2	77.9	0.0001
Ipratropium bromide	89	58.1	0.0001
Tiotropium	0	33.1	0.0001
Inhaled corticosteroids	87.4	84.9	0.3
Chronic systemic corticosteroids	2.4	2.3	0.6
Statins	1.6	16.9	0.001
ACE inhibitors	27.6	27.3	0.5
Angiotensin II receptor antagonist	0	7.6	0.001
B-blockers	1.6	5.8	0.057
Antiplatelet drugs	16.5	30.2	0.004

¿PODEMOS DISMINUIR LA MORTALIDAD EN LOS PACIENTES CON EPOC?

Effect of Pharmacotherapy on Rate of Decline of Lung Function in Chronic Obstructive Pulmonary Disease

Results from the TORCH Study

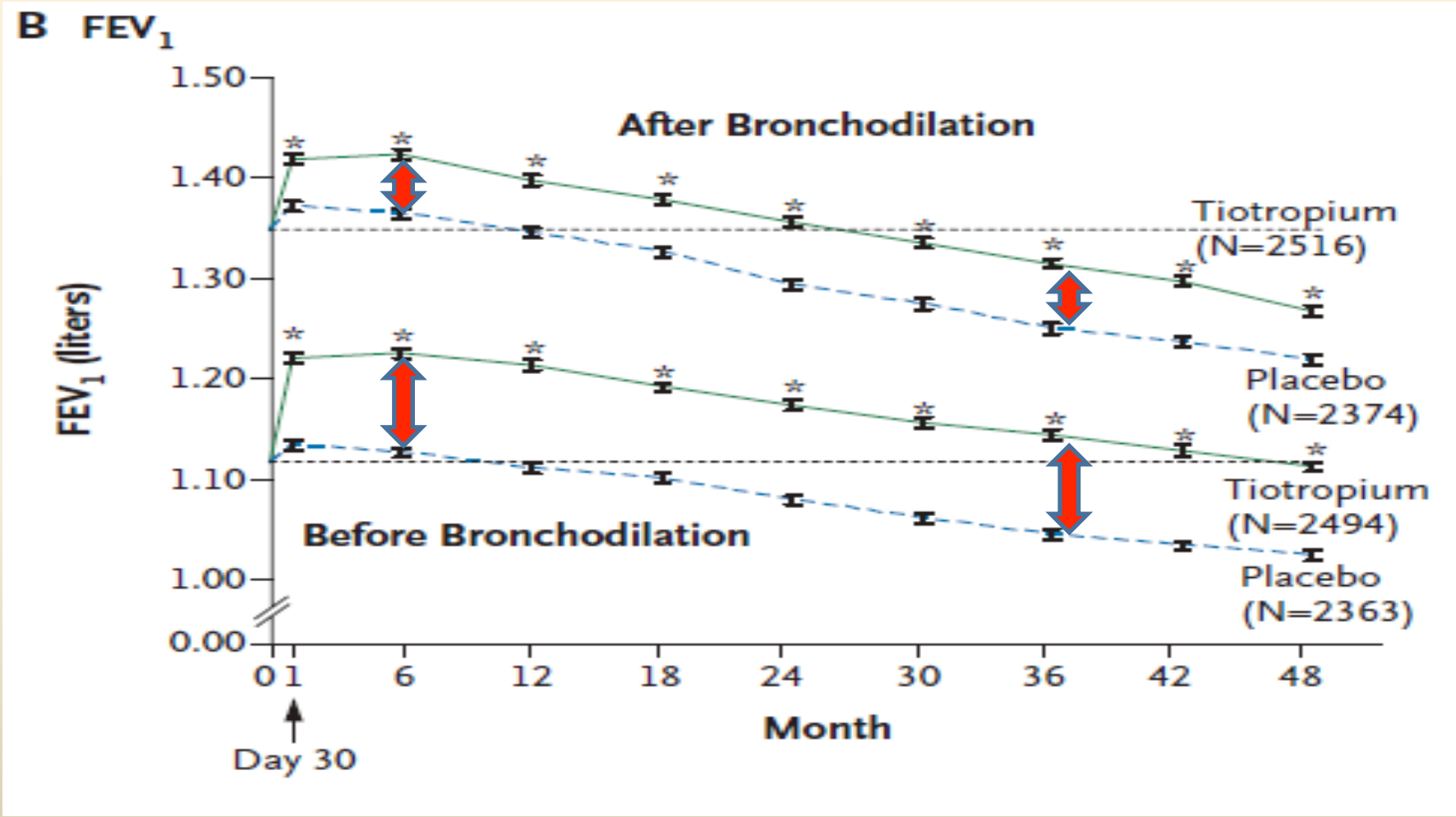
Am J Respir Crit Care Med Vol 178. pp 332–338, 2008



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



Effect of tiotropium on outcomes in patients with moderate chronic obstructive pulmonary disease (UPLIFT): a prespecified subgroup analysis of a randomised controlled trial

Published Online
August 28, 2009

*Marc Decramer, Bartolome Celli, Steven Kesten, Theodore Lystig, Sunil Mehra, Donald P Tashkin, for the UPLIFT investigators**

	Tiotropium		Control		Difference between tiotropium and control (mL per year [95% CI])	p value
	n	Mean decline (mL per year [SE]])	n	Mean decline (mL per year [SE])		
Primary analysis*						
FEV_1						
Prebronchodilator	1221	35 (2)	1158	37 (2)	2 (−3 to 7)	0·38
Postbronchodilator	1218	43 (2)	1157	49 (2)	6 (1 to 11)	0·024

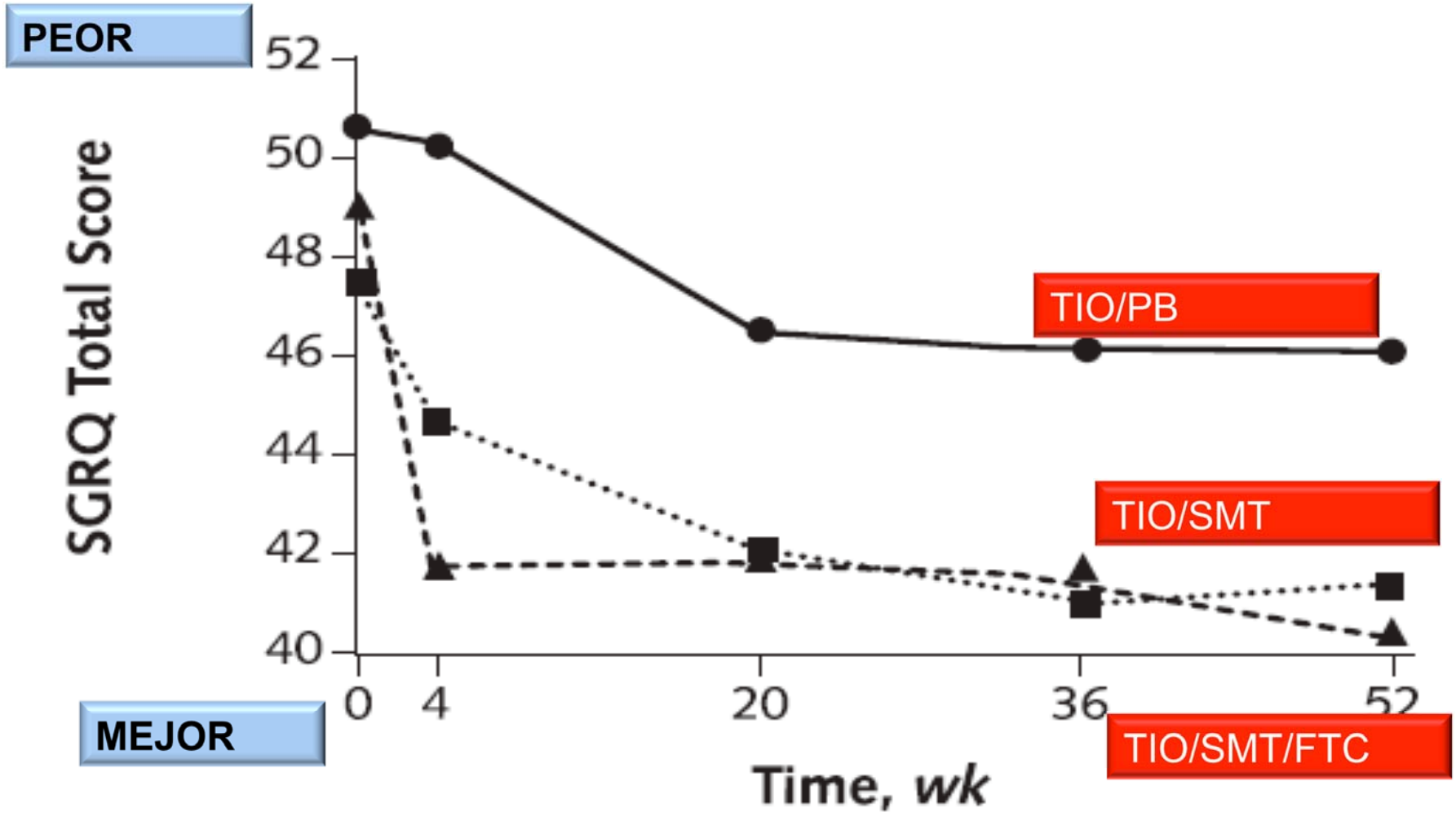
	Baseline		During study	
	Tiotropium (n=1384)	Control (n=1355)	Tiotropium (n=1384)	Control (n=1355)
Longacting β agonists*	771 (56%)	751 (55%)	955 (69%)	962 (71%)
Inhaled corticosteroids*	810 (59%)	772 (57%)	996 (72%)	989 (73%)
Combination longacting β agonist and inhaled corticosteroids	627 (45%)	598 (44%)	841 (61%)	827 (61%)

OPTIMAL Study: Hospitalizations for AECOPD

	Tio + Placebo	Tio + Salmeterol	Tio + Flut./Salm.
Hospitalizations for AECOPD	49	38	26
Rate ratio vs placebo		0.83 (0.54-1.27)	0.53 (0.33-0.86)
p value		0.38	0.01

Aaron S, et al. AIM 2007; 146:545-555.

Tiotropium in Combination with Placebo, Salmeterol, or Fluticasone–Salmeterol for Treatment of Chronic Obstructive Pulmonary Disease



Inhaled Corticosteroids in Chronic Obstructive Pulmonary Disease

Samy Suissa[1], Ryan McGhan[2], Dennis Niewoehner[3], and Barry Make[4]

Proc Am Thorac Soc Vol 4. pp 535–542, 2007

TABLE 1. PROJECTED POTENTIAL EFFECTS OF COMBINATION INHALED CORTICOSTEROID/LONG-ACTING β-AGONIST THERAPY IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE BY DISEASE SEVERITY BASED ON BODE QUARTILE

BODE Quartile	Expected Mortality at 36 mo* (%)	Calculated Absolute Risk Reduction with ICS/LABA† (%)	Calculated Number of Patients Needed to Treat with ICS/LABA for 3 yr to Save One Life‡
I	10	1.8	56
II	15	2.6	39
III	25	4.4	23
IV	45	7.9	13

Medications to Modify Lung Function Decline in Chronic Obstructive Pulmonary Disease

Some Hopeful Signs

" A pesar de sus limitaciones metodológicas, este estudio demuestra que el no tratamiento (placebo) no es una opción para pacientes con EPOC moderada- severa y que cualquiera de los 3 tratamientos (SM, FC o SM-FC) disminuye la pérdida acelerada de función pulmonar en los pacientes con EPOC".

Suissa S. AJRCCM 2008

Medications to Modify Lung Function Decline in Chronic Obstructive Pulmonary Disease

Some Hopeful Signs

component (6, 8). Moreover, inhaled corticosteroids alone or in combination have been associated with increased risks of glaucoma and possibly osteoporotic fractures (9–11), and have been shown to increase the risk of cataract and pneumonia, particularly with the high doses currently in use (12–16).

On the whole, this study offers two major advances that benefit the patient with COPD. It provides the first possible evidence that lung function decline can be slowed with medications. It also provides further evidence that the use of inhaled corticosteroids, alone or in combination, in COPD is unnecessary and thus inappropriate.

9. Garbe E, LeLorier J, Boivin JF, Suissa S. Risk of ocular hypertension or open-angle glaucoma in elderly patients on oral glucocorticoids. *Lancet* 1997;350:979–982.

Inhaled and Nasal Corticosteroid Use and the Risk of Fracture

Am J Respir Crit Care Med Vol 169. pp 83–88, 2004

The implications of our results for the treatment of respiratory disease are important. The fact that long-term use of inhaled

Samy Suissa, Marc Baltzan, Richard Kremer, and Pierre Ernst

high doses, suggests that the doses corresponding to the current treatment guidelines are safe.

EN RESUMEN.....

- ***B2 de larga y CI mejoran la supervivencia, en análisis poblacionales y metaanálisis.***

- ***B2 de larga y CI mejoran la supervivencia a tres años, aunque la diferencia no llega a alcanzar significación estadística.***

- ***Tiotropio añadido a la medicación habitual del paciente aumenta la supervivencia a 4 años.***

EN RESUMEN.....

- ***Estatinas e IECAS mejoran la supervivencia en estudios observacionales y caso-control.***

- ***Tanto la combinación de B2 de larga con CI, como el Tiotropio sólo o en combinación, mejoran la función pulmonar, disminuyen las exacerbaciones y aumentan la calidad de vida.***

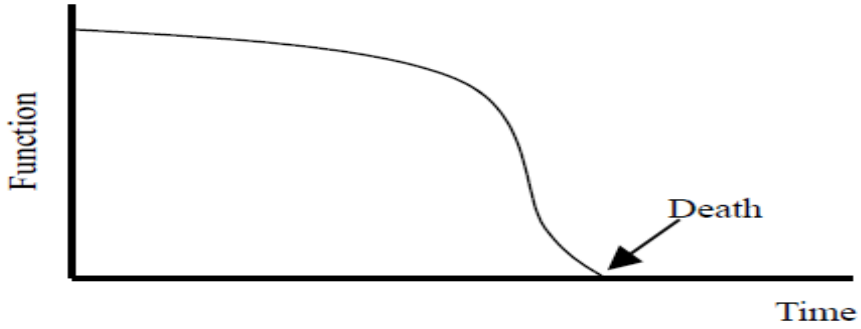

Pep CT 2007
GRACIAS

Illness trajectories and palliative care

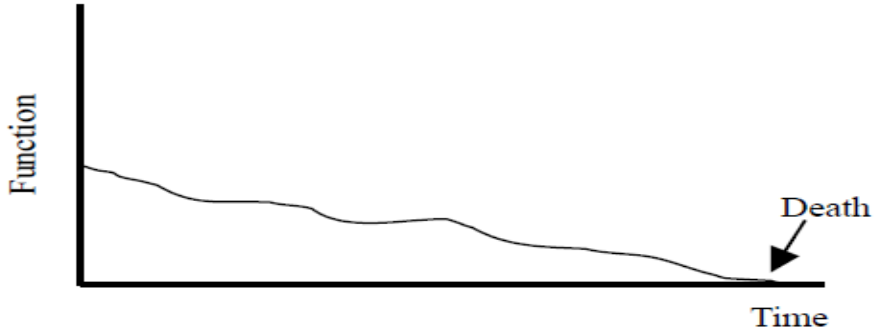
Scott A Murray, Marilyn Kendall, Kirsty Boyd, Aziz Sheikh

BMJ 2005;330:1007–11

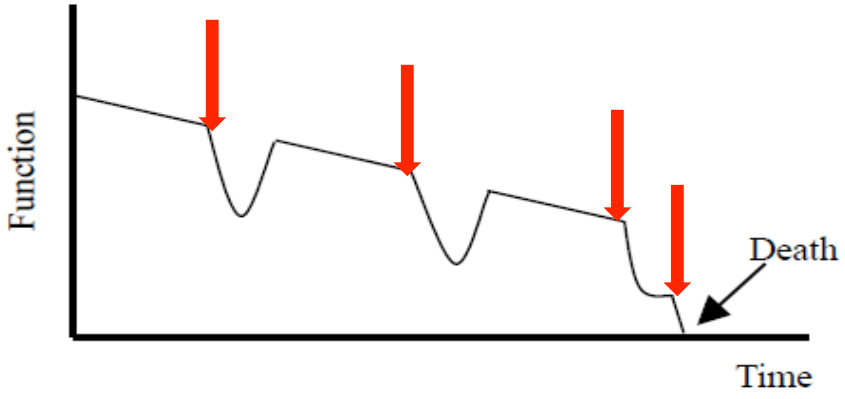
NEOPLASIAS



DEMENCIAS



E. CRÓNICAS



¿PODEMOS DISMINUIR LA MORTALIDAD EN LOS PACIENTES CON EPOC?

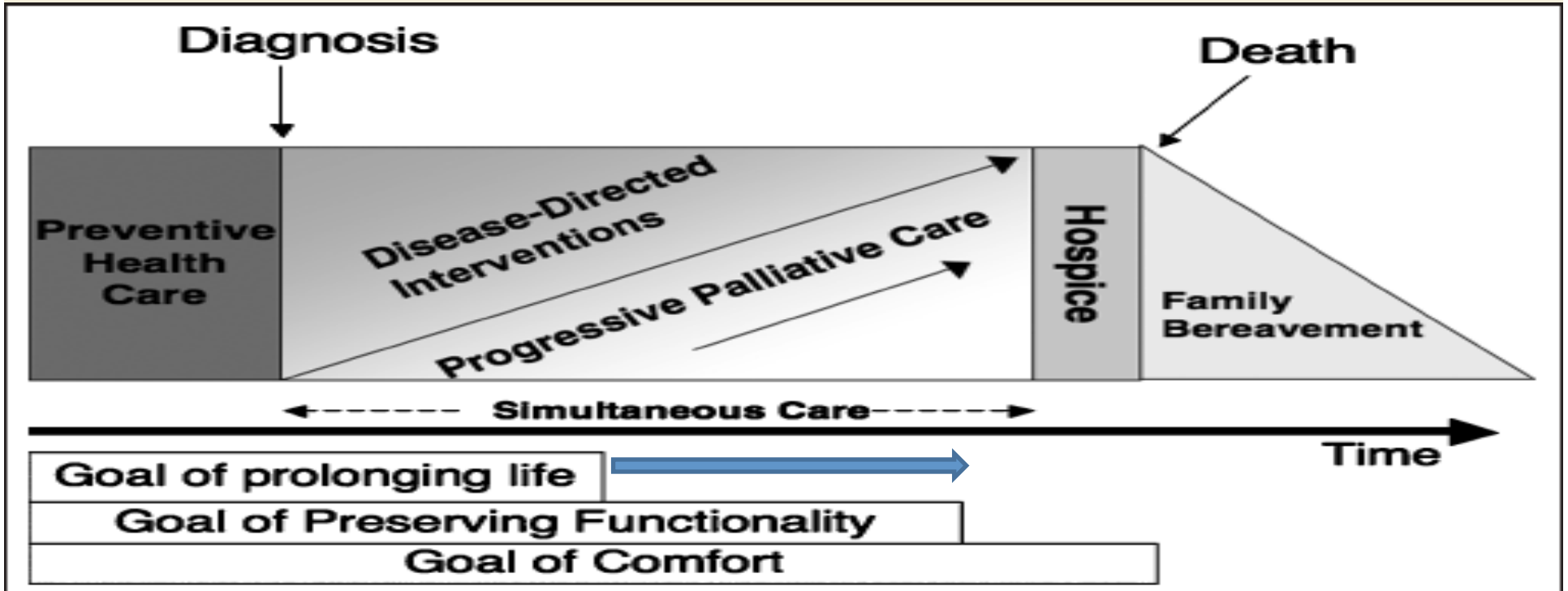


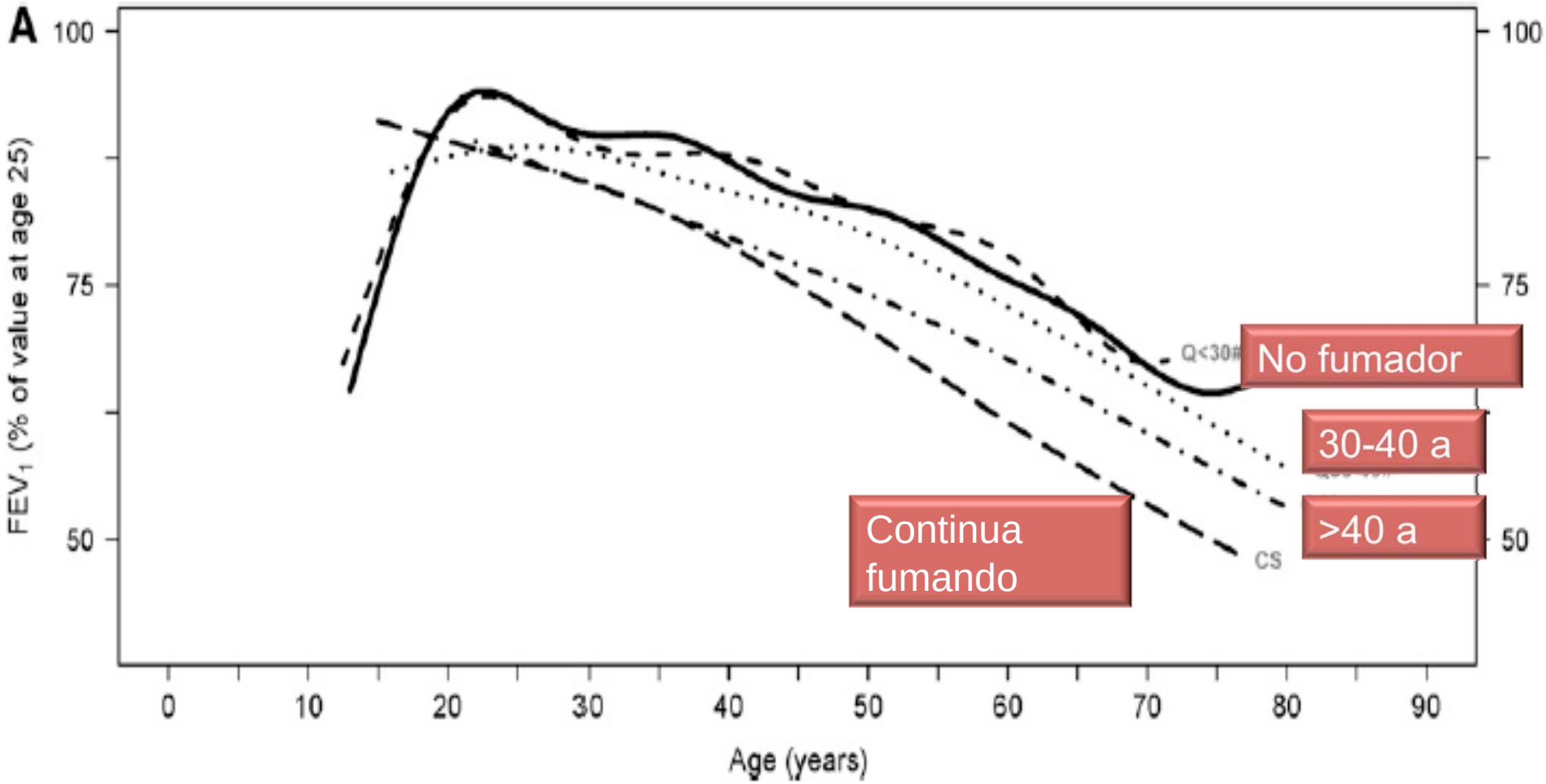
Figure 1. Integrated palliative care for COPD patients and families.

The Natural History of Chronic Airflow Obstruction Revisited

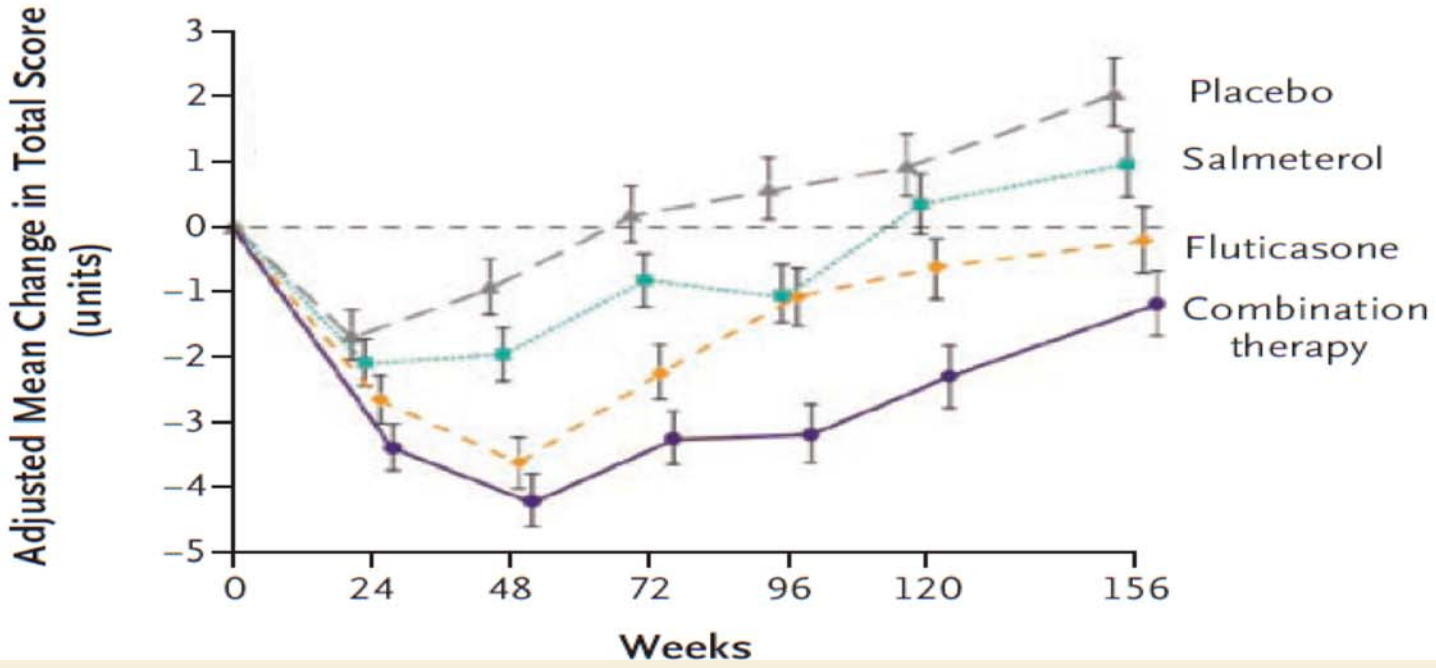
An Analysis of the Framingham Offspring Cohort

Robab Kohansal[1,2], Pablo Martinez-Camblor[1,3], Alvar Agustí[1,4,5], A. Sonia Buist[6], David M. Mannino[7], and Joan B. Soriano[1,4]

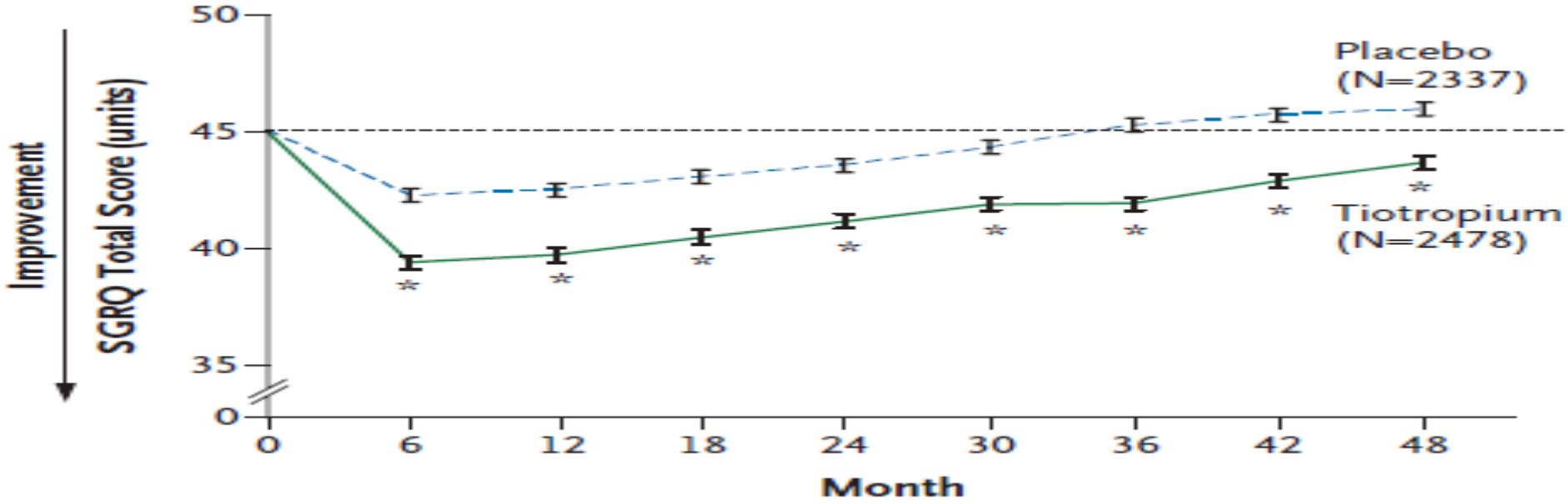
Am J Respir Crit Care Med Vol 180. pp 3–10, 2009



Health Status



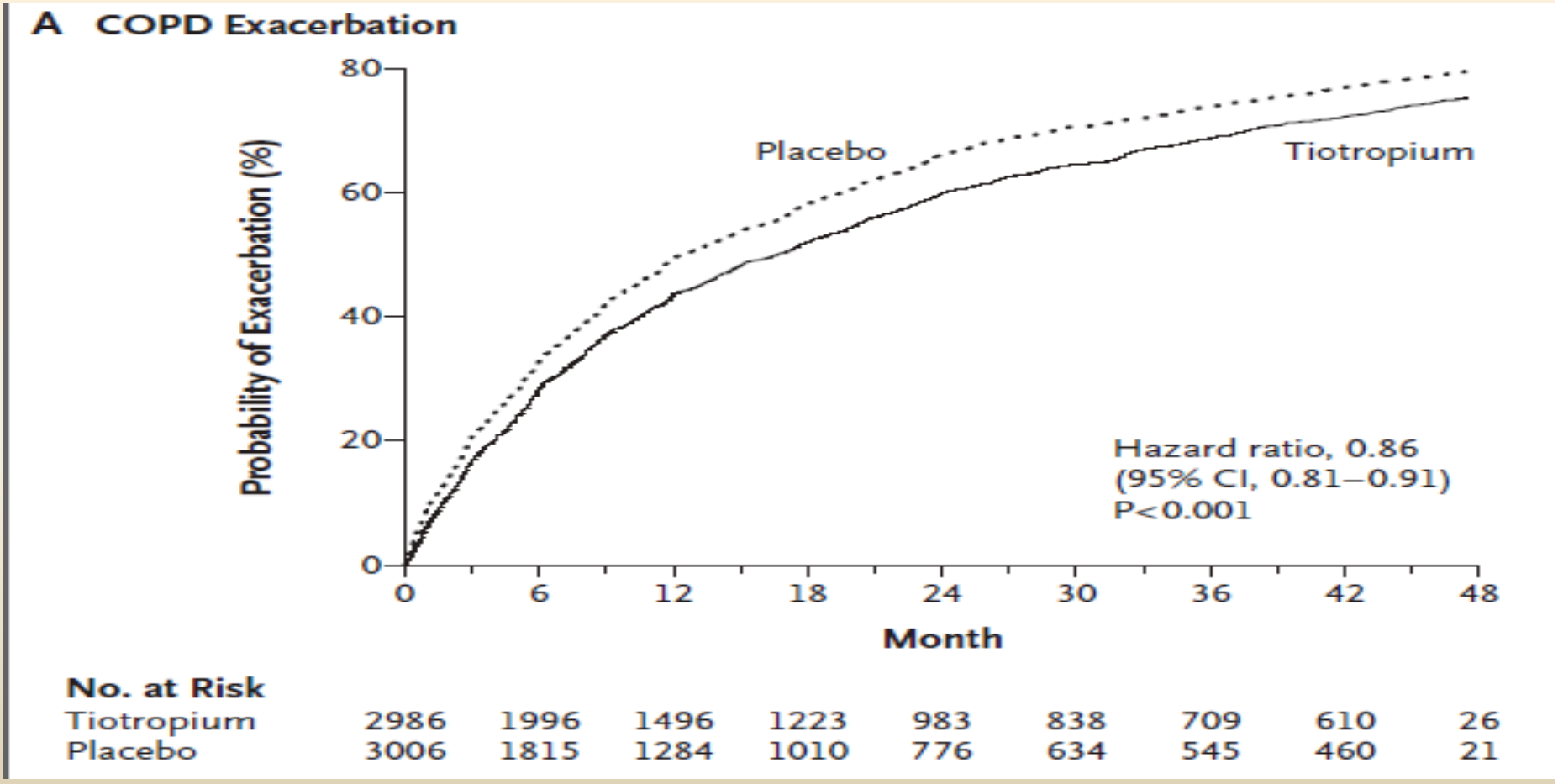
D SGRQ Total Score

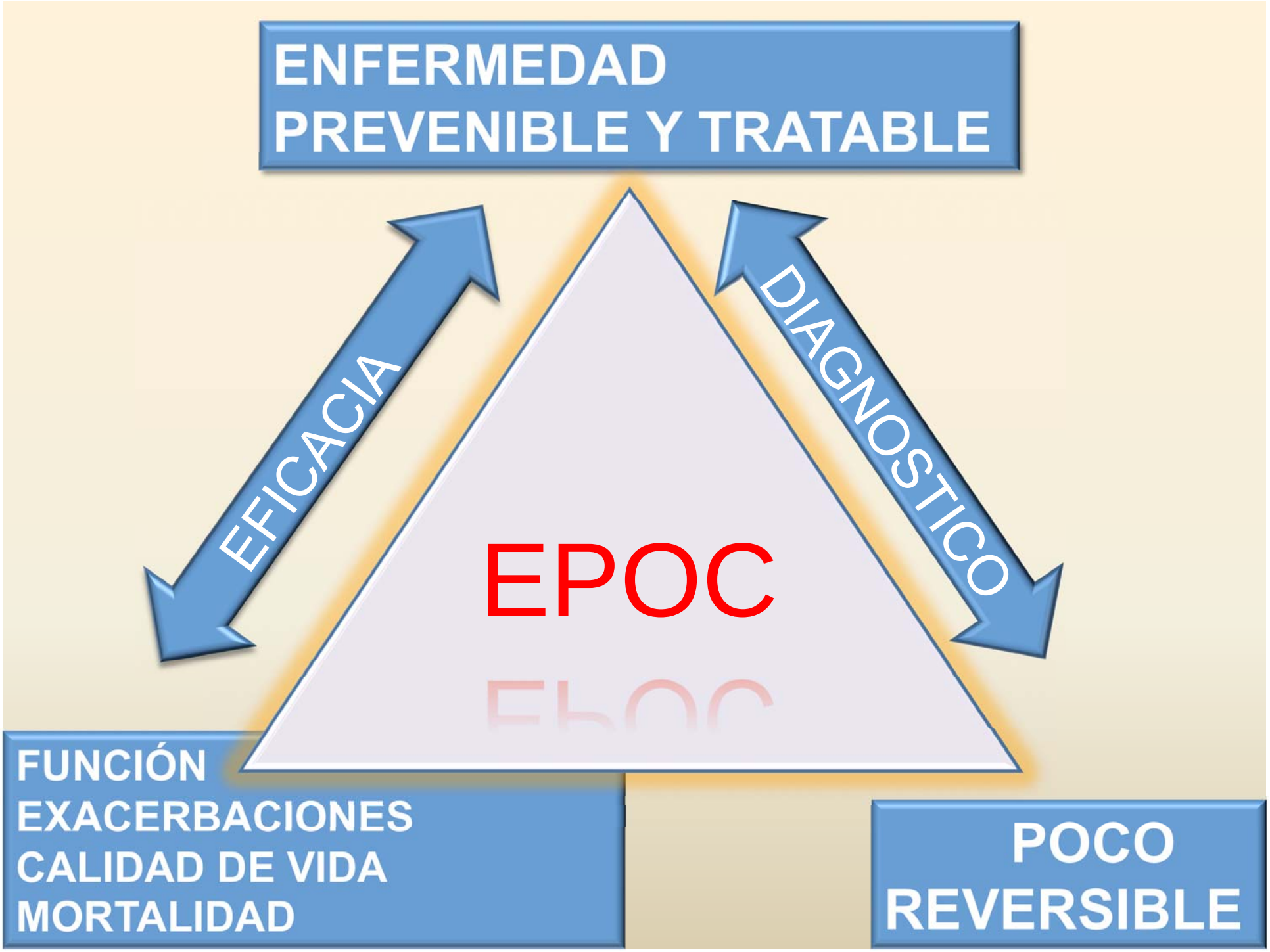


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 9, 2008 VOL. 359 NO. 15

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




ENFERMEDAD
PREVENIBLE Y TRATABLE
EFICACIA
DIAGNOSTICO
EPOC
FUNCIÓN
EXACERBACIONES
CALIDAD DE VIDA
MORTALIDAD
POCO
REVERSIBLE

Eur Respir J 2008; 31: 927–933
DOI: 10.1183/09031936.00098307

PERSPECTIVE

Methodological issues in therapeutic trials of COPD

S. Suissa*,#, P. Ernst*,#, K.L. Vandemheen¶ and S.D. Aaron¶

TABLE 4 Factorial analysis of Towards a Revolution in COPD Health (TORCH) data of the independent effects of fluticasone and salmeterol on the 3-yr incidence of all-cause mortality

	Medication allocated		Crude RR	Adjusted RR (95% CI)
	Yes deaths/total n	No deaths/total n		
Medication				
Fluticasone	439/3067	436/3045	1.00	1.00 (0.89–1.13)
Salmeterol	398/3054	477/3058	0.83	0.83 (0.74–0.95)

RR: relative rate ratio; CI: confidence interval.