ASMA GRAVE (DE DIFICIL CONTROL)

La opción de la fisiopatología

L. Prieto

Asociación Valenciana de Investigaciones Clínicas

Valencia

ASMA DE DIFICIL CONTROL
PROBABLES ESCENARIOS

ASMA DE DIFICIL CONTROL

(precisa tratamiento de alta intensidad)

Buen control solo con tratamiento de alta intensidad

Mal control a pesar de tratamiento de alta intensidad

Taylor DR, et al. Eur Respir J. 32: 545. 2008

ASMA DE DIFICIL CONTROL

PROBABLES FACTORES CAUSALES

Factores no identificados
- Alergenos no identificados
- Exposición ocupacional
- Afectación vía aérea superior
  - Rinitis
  - Sinusitis
  - Apnea de sueño obstruciva
- Reflujo gastro-esofágico
- Enfermedades sistémicas
  - Hipertiroidismo
  - S carcinoide
  - Churg-Strauss
- Fármacos
  - β-bloqueantes, AINES, inh ACE
- Infecciones crónicas
  - Clamidofilia y micoplasma

Incorrecto diagnóstico
- COPD
- Insuficiencia cardiaca izquierda
- Obstrucción localizada
- Fibrosis quística
- Disfunción c vocales

Mal cumplimiento terapéutico

Factores psicológicos

Asma inestable
- Nocturna
- Premenstrual
- Labil

Asma cortico-resistente

Asma cortico-dependiente

Barnes PJ, et al. ERJ. 12: 1209. 1998; ten Brinke et al. ERJ. 26: 812. 2005

Strek ME. Proc Am Thorac Soc. 3: 116. 2006

ASMA DE DIFICIL CONTROL

COMORBILIDADES

Que factores condicionan la dificultad para el control del asma?

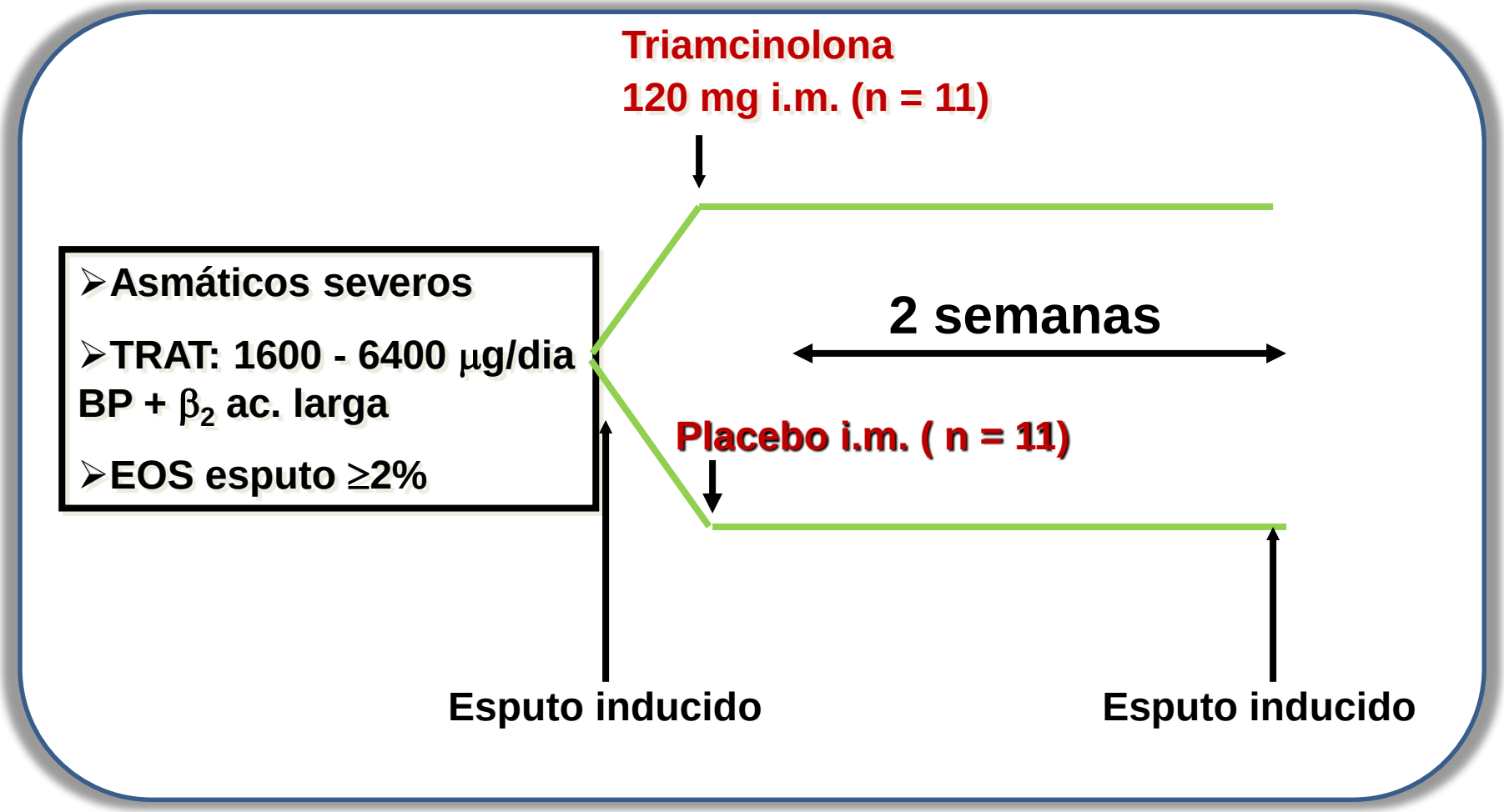
1. Diferentes fenotipos inflamatorios?

2. Diferentes fenotipos funcionales?

Boulet LP. Eur Respir J. 33: 897. 2009

INFLAMACION EOSINOFILICA

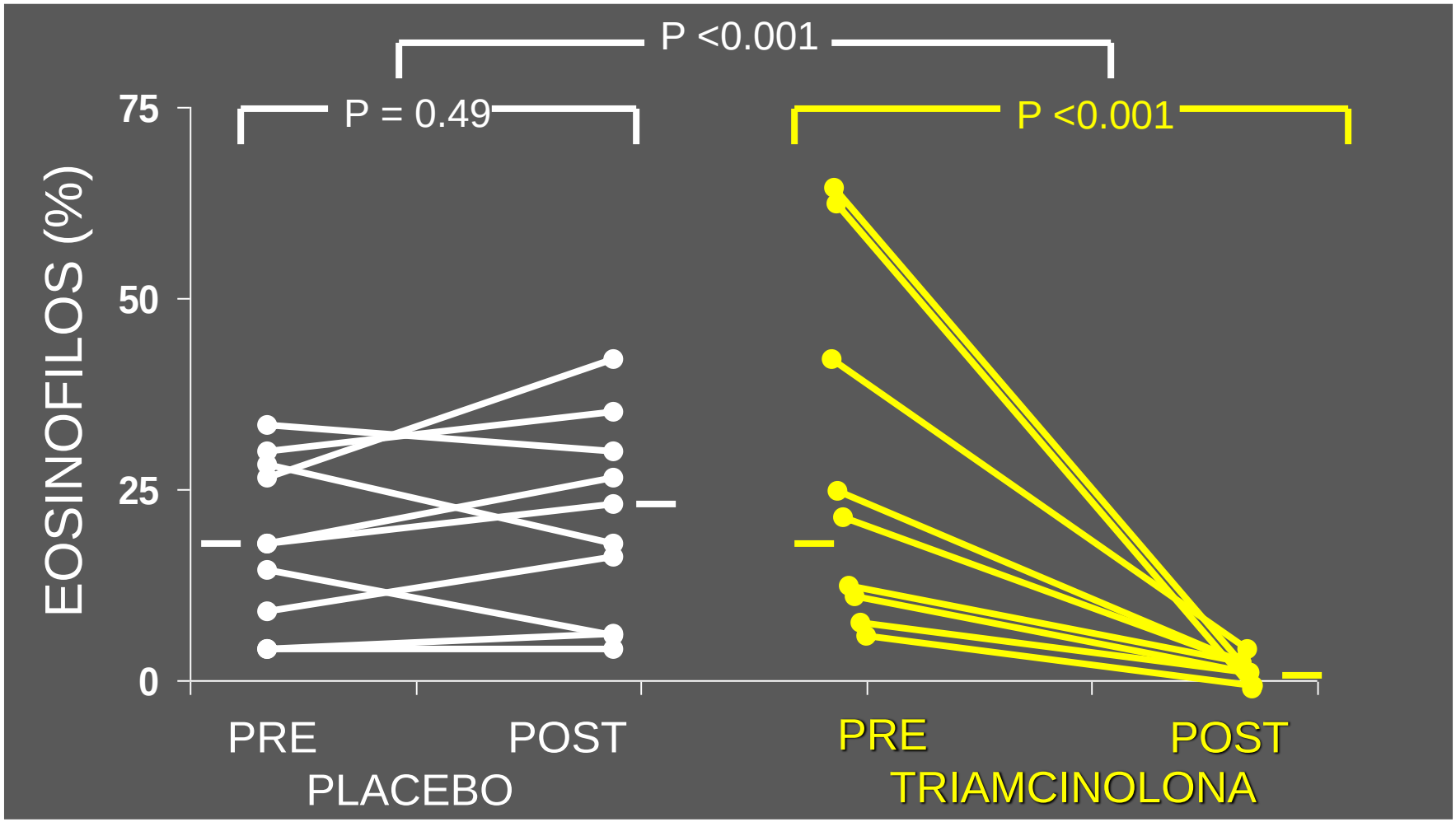
PERSISTENCIA A PESAR DE EST. INHALADOS



Ten Brinke A, et al Am J Respir Crit Care Med. 170: 601. 2004

INFLAMACION EOSINOFILICA

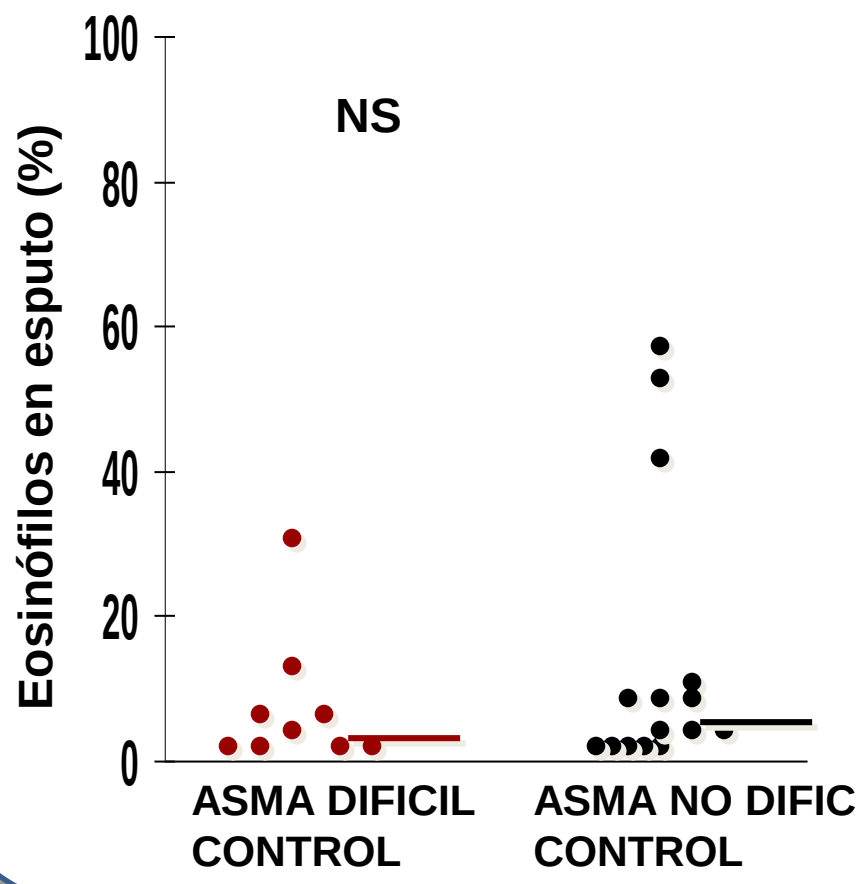
PERSISTENCIA A PESAR DE EST. INHALADOS

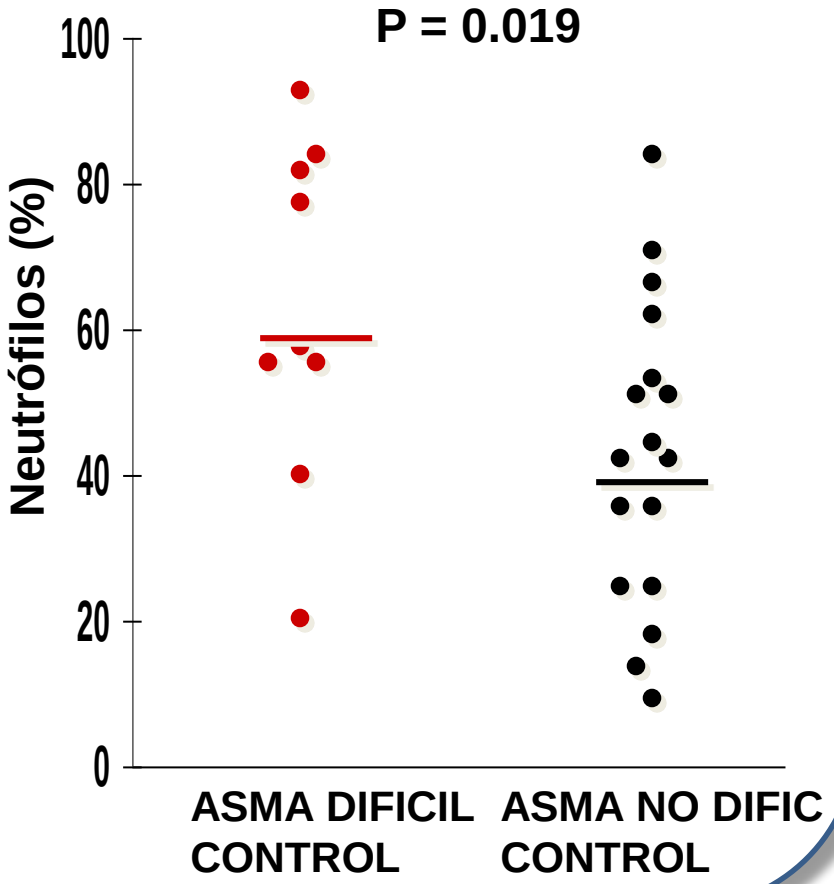


Ten Brinke A, et al Am J Respir Crit Care Med. 170: 601. 2004

ASMA DE DIFICIL CONTROL

IMPORTANCIA DE INFLAMACION NEUTROFILICA

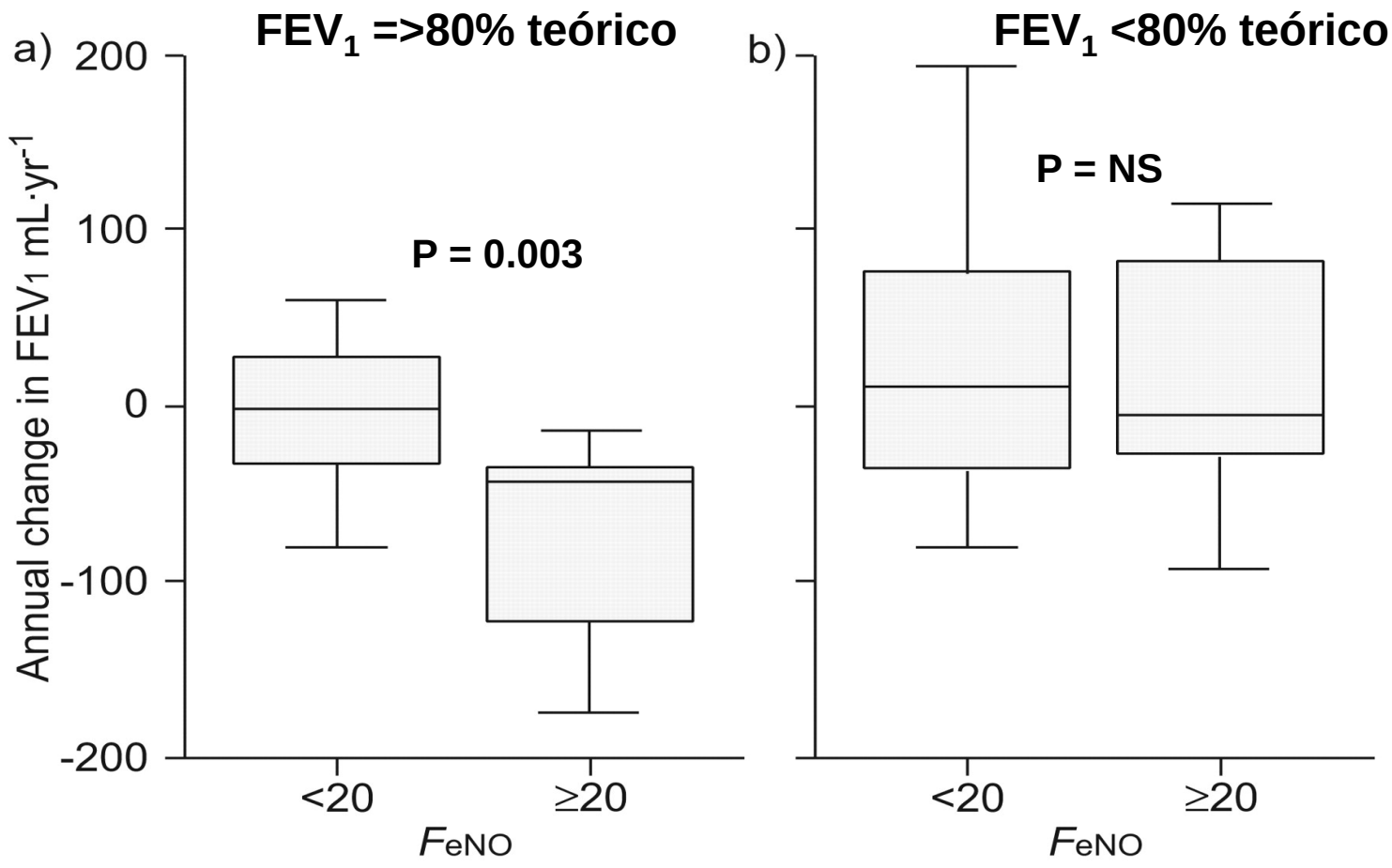




Boulet LP, et al. Respir Med. 97: 739. 2003

DETERIORO FUNCIONAL EN ASMA

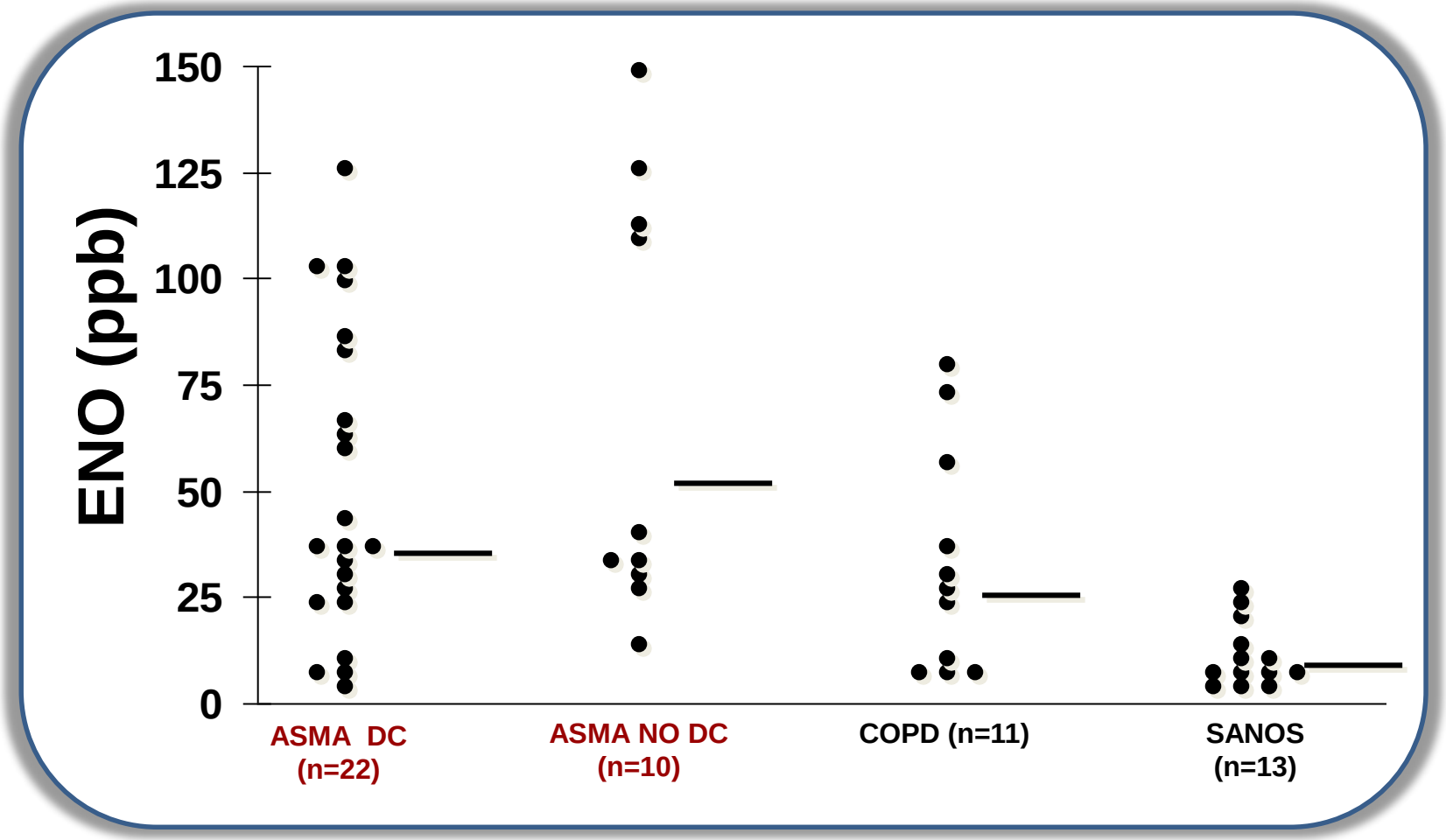
RELACION CON ENO BASAL



Van Veen IH, et al. Eur Respir J. 32: 344. 2008

OXIDO NITRICO EXHALADO

ASMA DC vs ASMA NO DC

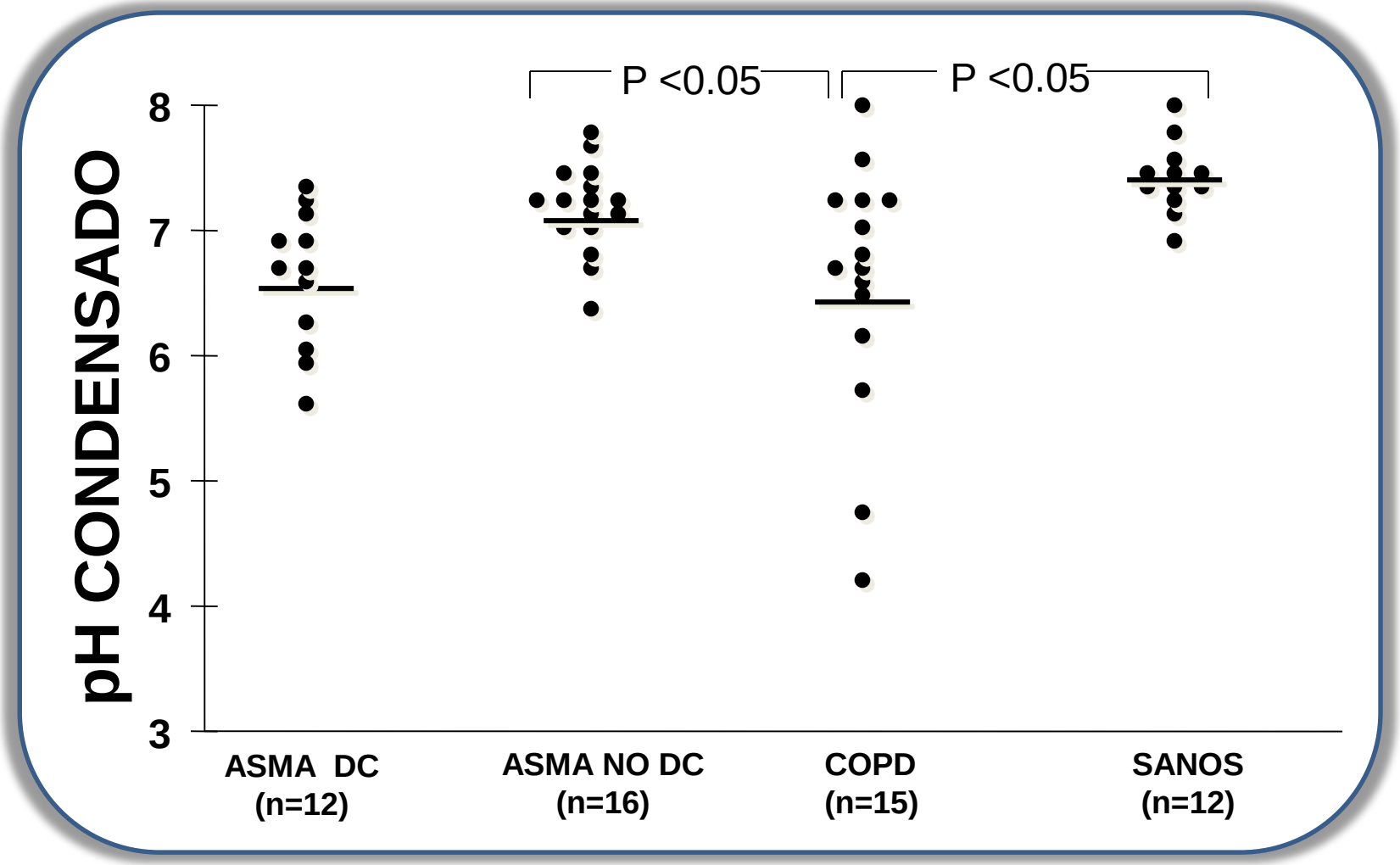


Asma DC, no DC y COPD vs sanos, P <0.05

Asma DC vs no DC vs COPD, P = NS

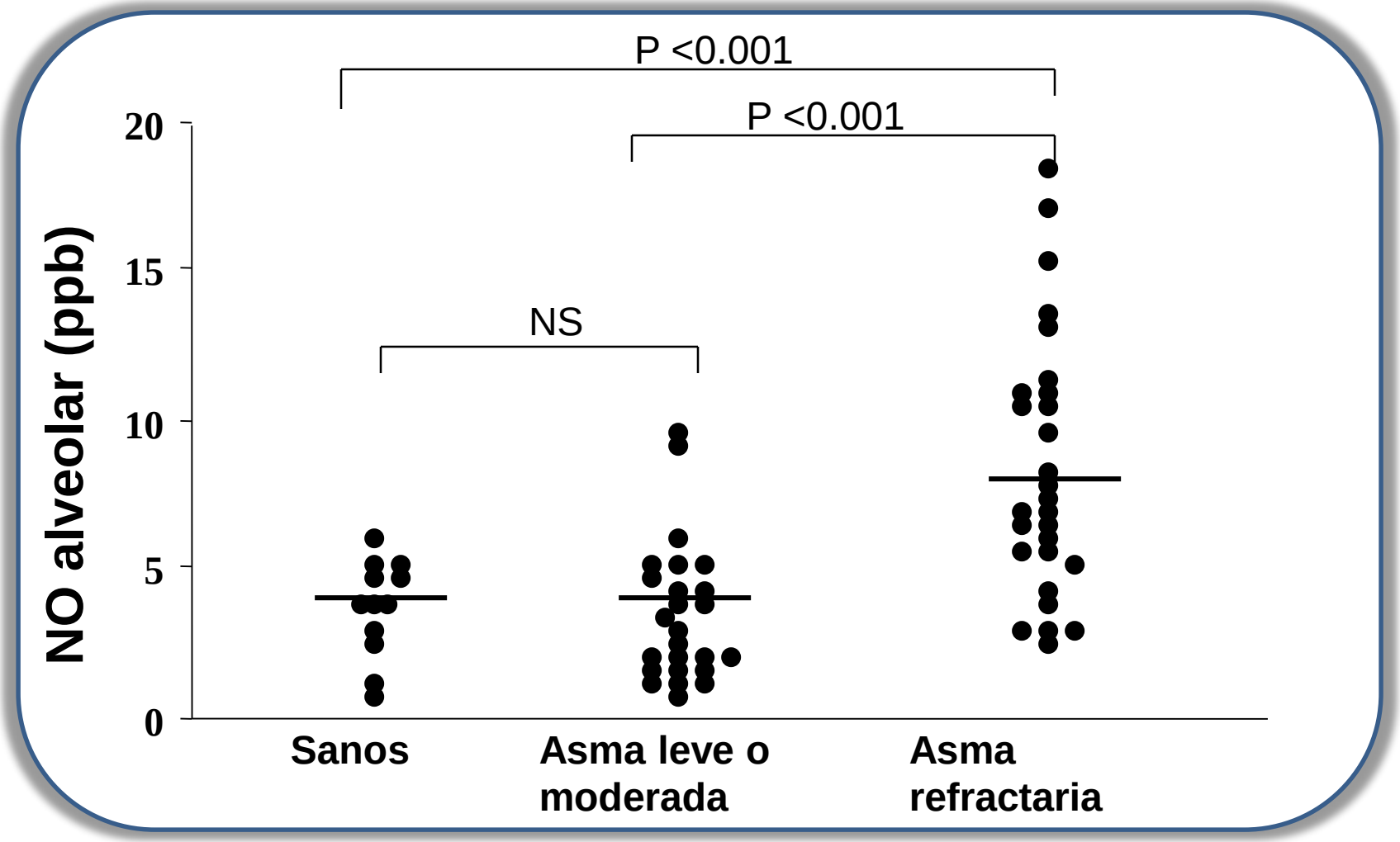
pH del EBC

ASMA DC vs ASMA NO DC



PERSISTENCIA DE INFLAMACION

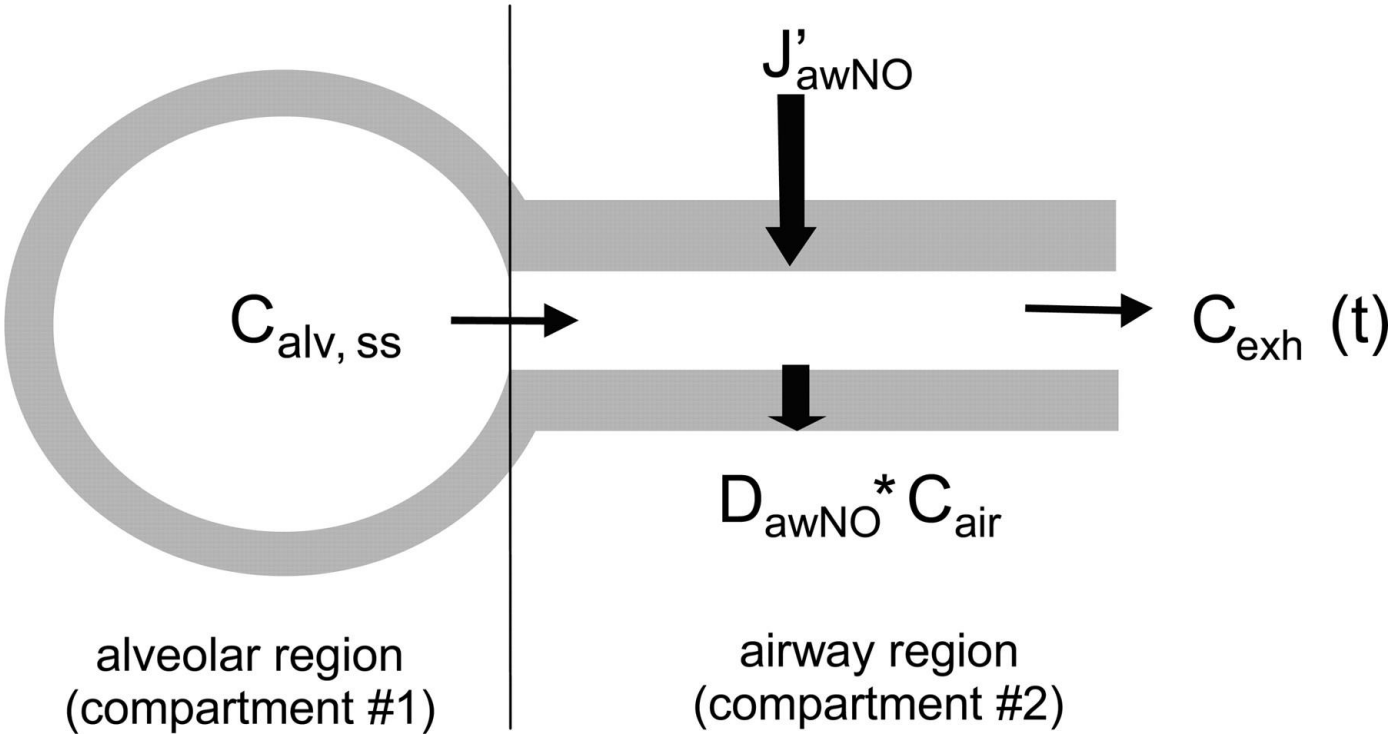
ASMA REFRACTARIA



Berry M, et al. Eur Respir J. 25: 986. 2005

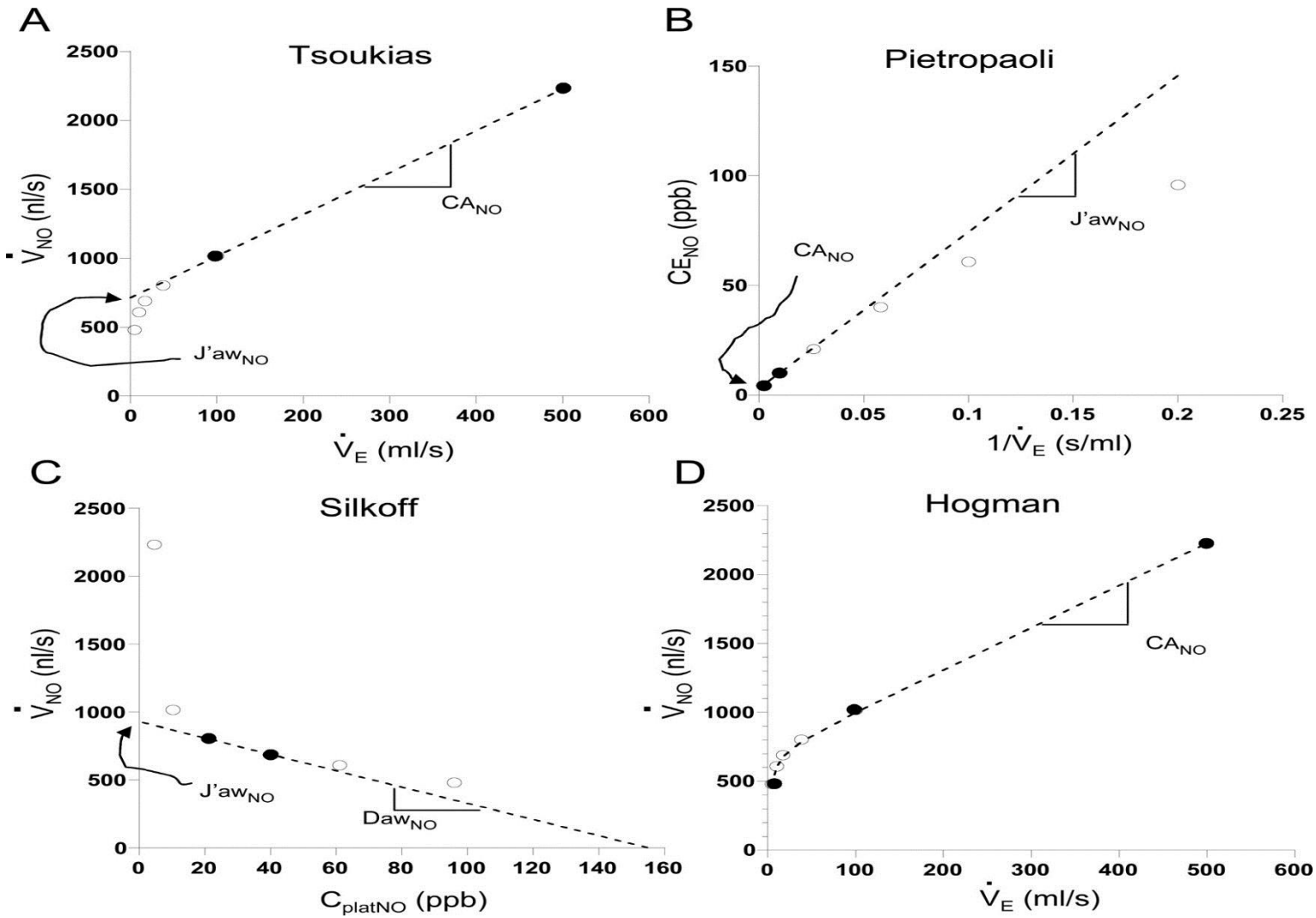
Schematic of 2-compartment model used to describe NO exchange dynamics

$$J_{awNO} = J'_{awNO} - D_{awNO} C_{air}$$



Shin, H.-W. et al. J Appl Physiol 96: 65-75 2004

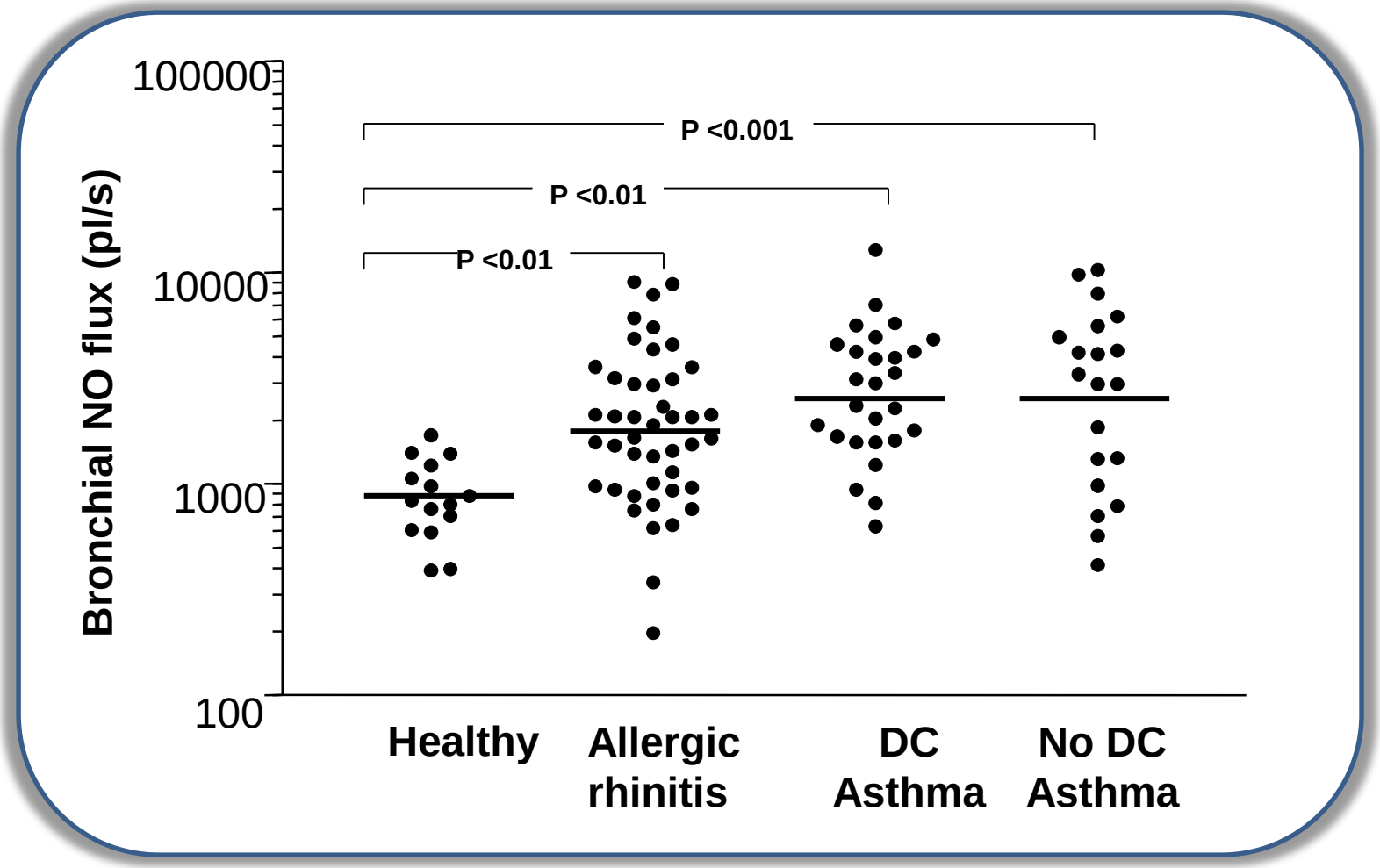
Determination of NO_A by using 2 or 3 exhalation flow rates



George, S. C. et al. J Appl Physiol 96: 831-839 2004

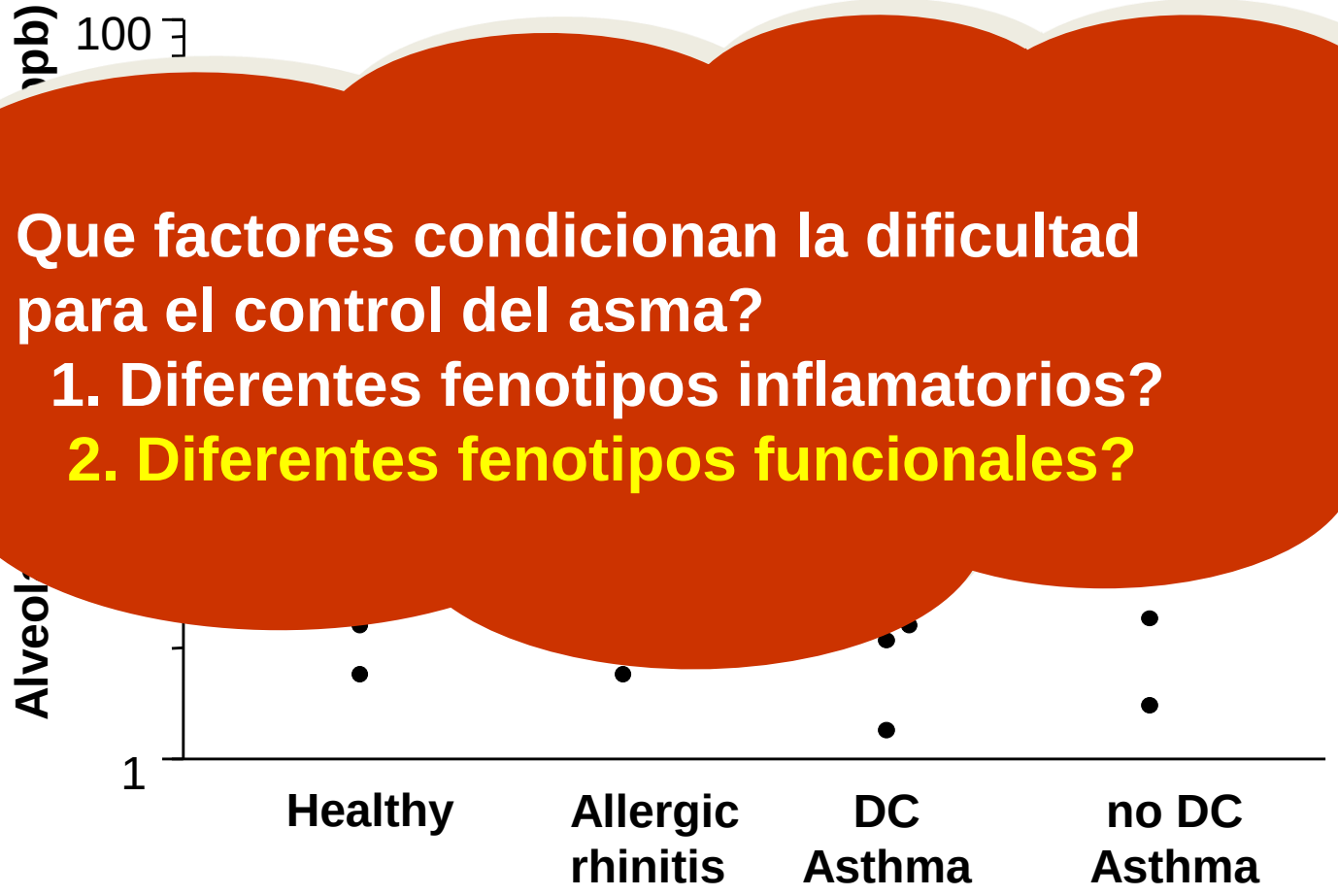
ASMA DC vs ASMA NO DC

OXIDO NITRICO BRONQUIAL



ASMA DC vs ASMA NO DC

OXIDO NITRICO ALVEOLAR

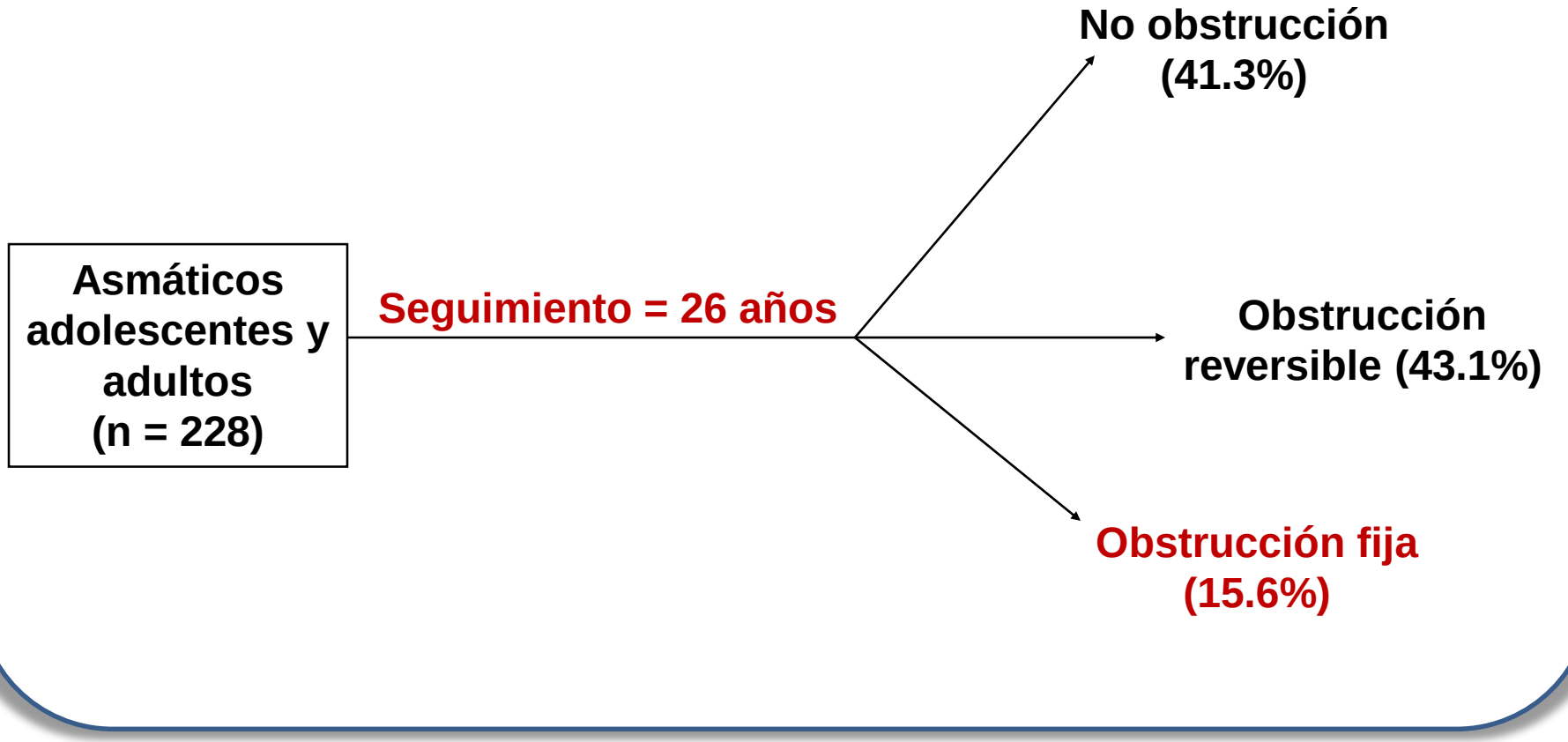


Que factores condicionan la dificultad para el control del asma?

1. **Diferentes fenotipos inflamatorios?**
2. **Diferentes fenotipos funcionales?**

OBSTRUCCION FIJA EN ASMA

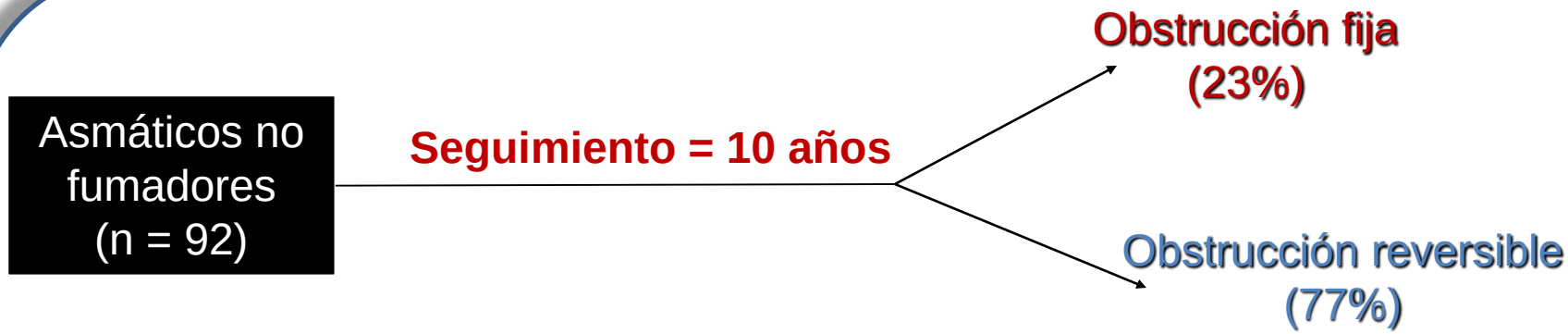
PREVALENCIA



Vonk JM, et al. Thorax. 58: 322. 2003.

OBSTRUCCION FIJA EN ASMA

PREVALENCIA Y FACTORES DE RIESGO



CARACTERISTICAS BASALES

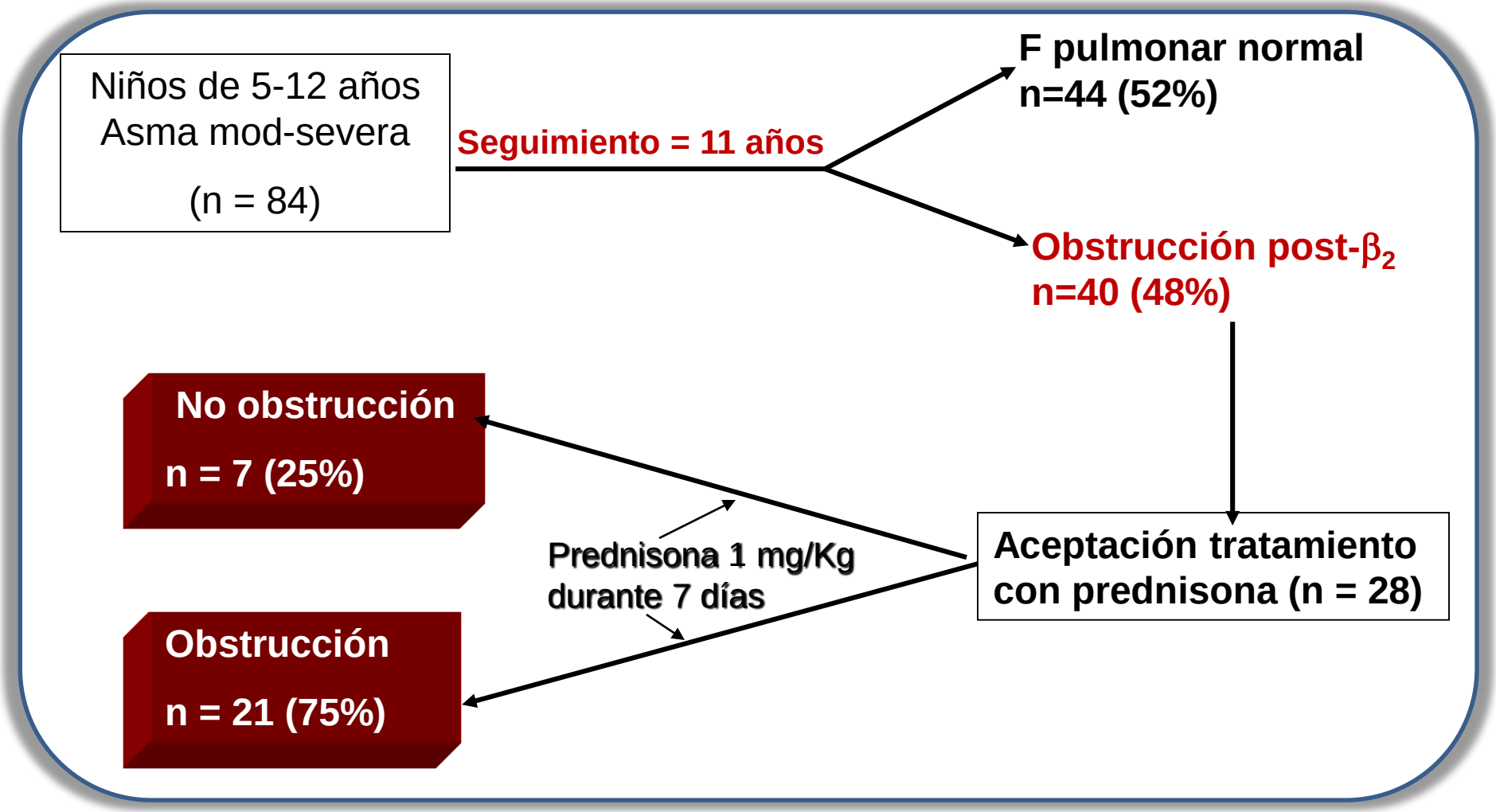
	Obstr. Fija	Obstr. Reversible
Edad (años)	32±12	38±12
ΔFEV_1 con β_2 (%)	17.2±3.1	12.8±3.8*
FEV_1 basal (% teórico)	77.6±19.7	89.1±18.0

* = P < 0.003

Ulrik and Backer. Eur Respir J. 14: 892. 1999.

OBSTRUCCION FIJA EN ASMA

PREVALENCIA



Limb SL, et al. J Allergy Clin Immunol. 116: 1213. 2005

Asthma and lower airway disease

Body mass index, weight gain, and other determinants of lung function decline in adult asthma

Alessandro Marcon, MSc,[a] Angelo Corsico, MD, PhD,[b] Lucia Cazzoletti, MSc,[a] Massimiliano Bugiani, MD,[c] Simone Accordini, MSc,[a] Enrique Almar, MD,[d] Isa Cerveri, MD,[b] David Gislason, MD,[e] Amund Gulsvik, MD, PhD,[f] Christer Janson, MD,[g] Deborah Jarvis, MD,[h] Jesús Martínez-Moratalla, MD,[i] Isabelle Pin, MD,[j] Roberto de Marco, PhD,[a] and the Therapy and Health Economics Group of the European Community Respiratory Health Survey Verona, Pavia, and Turin, Italy, Albacete, Spain, Reykjavik, Iceland, Bergen, Norway, Uppsala, Sweden, London, United Kingdom, and Grenoble, France

Background: Little is known about factors associated with lung function decline in asthma.

Objective: To identify the determinants of FEV_1 decline in adults with asthma with and without airflow obstruction at baseline.

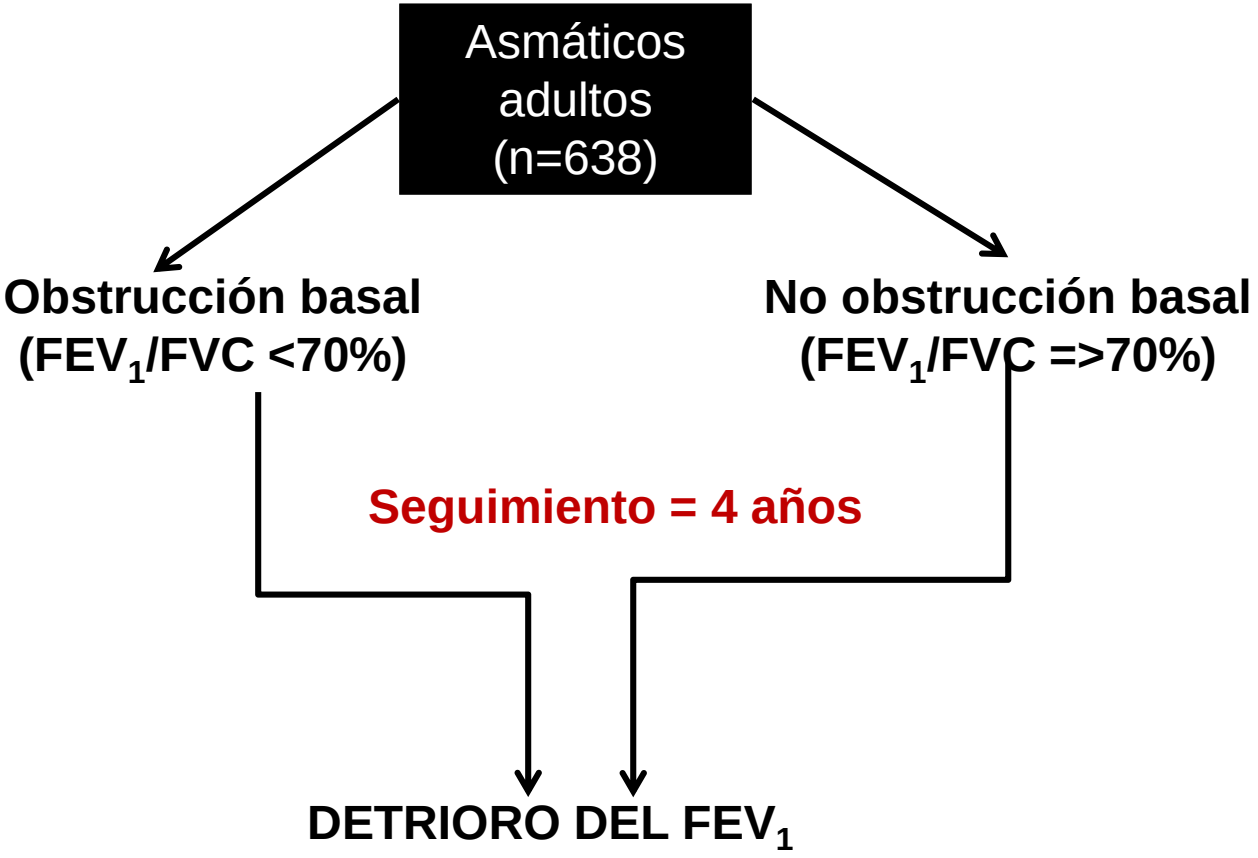
Methods: An international cohort of 638 subjects with asthma (20-44 years old) was identified in the European Community Respiratory Health Survey (1991-1993) and followed up from 1998 to 2002. Spirometry was performed on both occasions. FEV_1 decline was related to potential determinants evaluated at

airflow obstruction (n = 94), the absence of allergen sensitization and a low BMI at baseline were associated with a faster FEV_1 decline, whereas weight gain was not associated with decline.

Conclusions: The detrimental effect of weight gain on FEV_1 decline is particularly relevant in subjects with asthma who still do not have an established airflow obstruction. Our findings support the importance of weight management in asthma and recommend weight loss in overweight or obese individuals with asthma. (J Allergy Clin Immunol 2009;123:1069-74.)

DETERIORO FUNCIONAL EN ASMA

OBESIDAD COMO FACTOR DE RIESGO



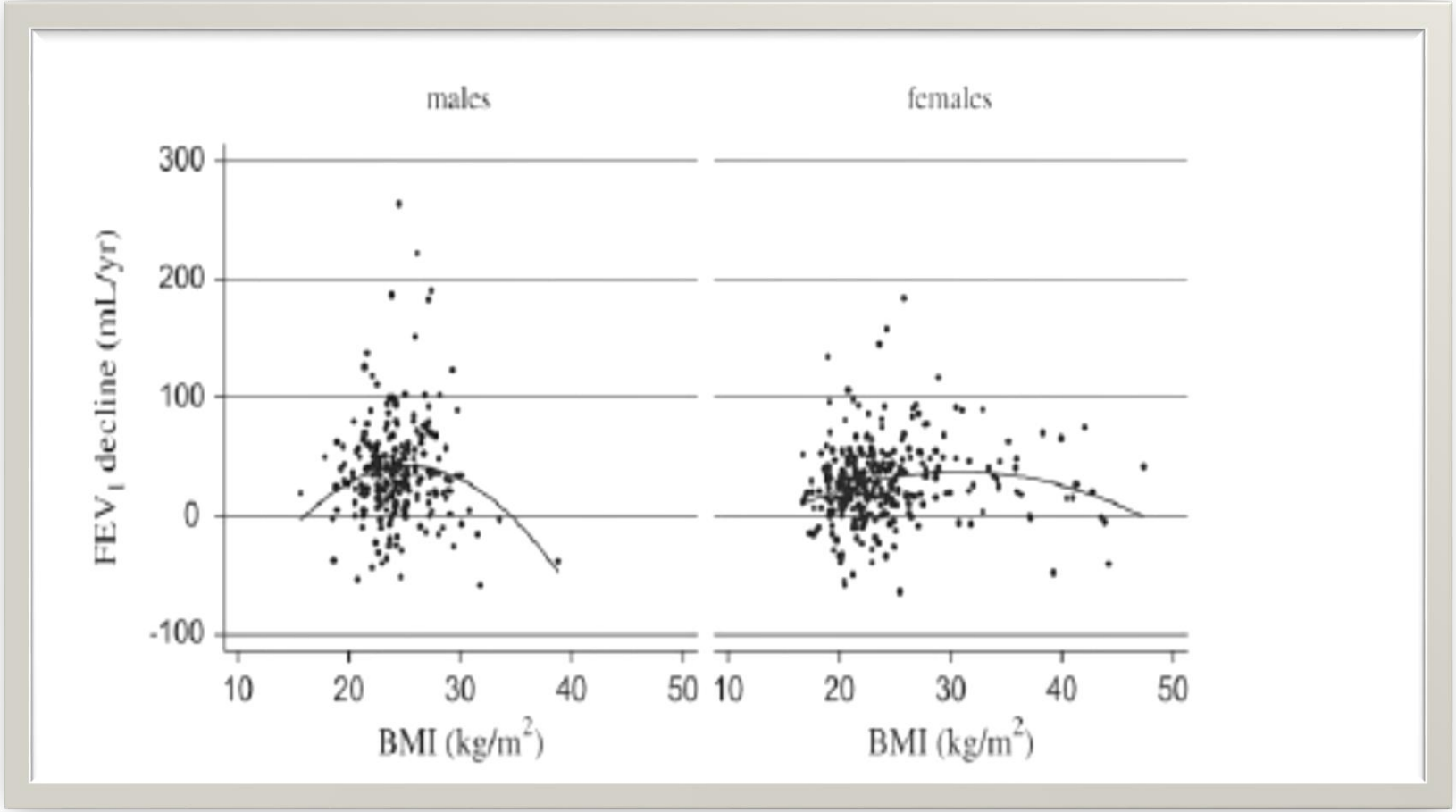
Marcon A, et al. J Allergy Clin Immunol. 123: 1069. 2009

DETERIORO FUNCIONAL EN ASMA

OBESIDAD COMO FACTOR DE RIESGO

No obstruction at baseline

BMI at baseline



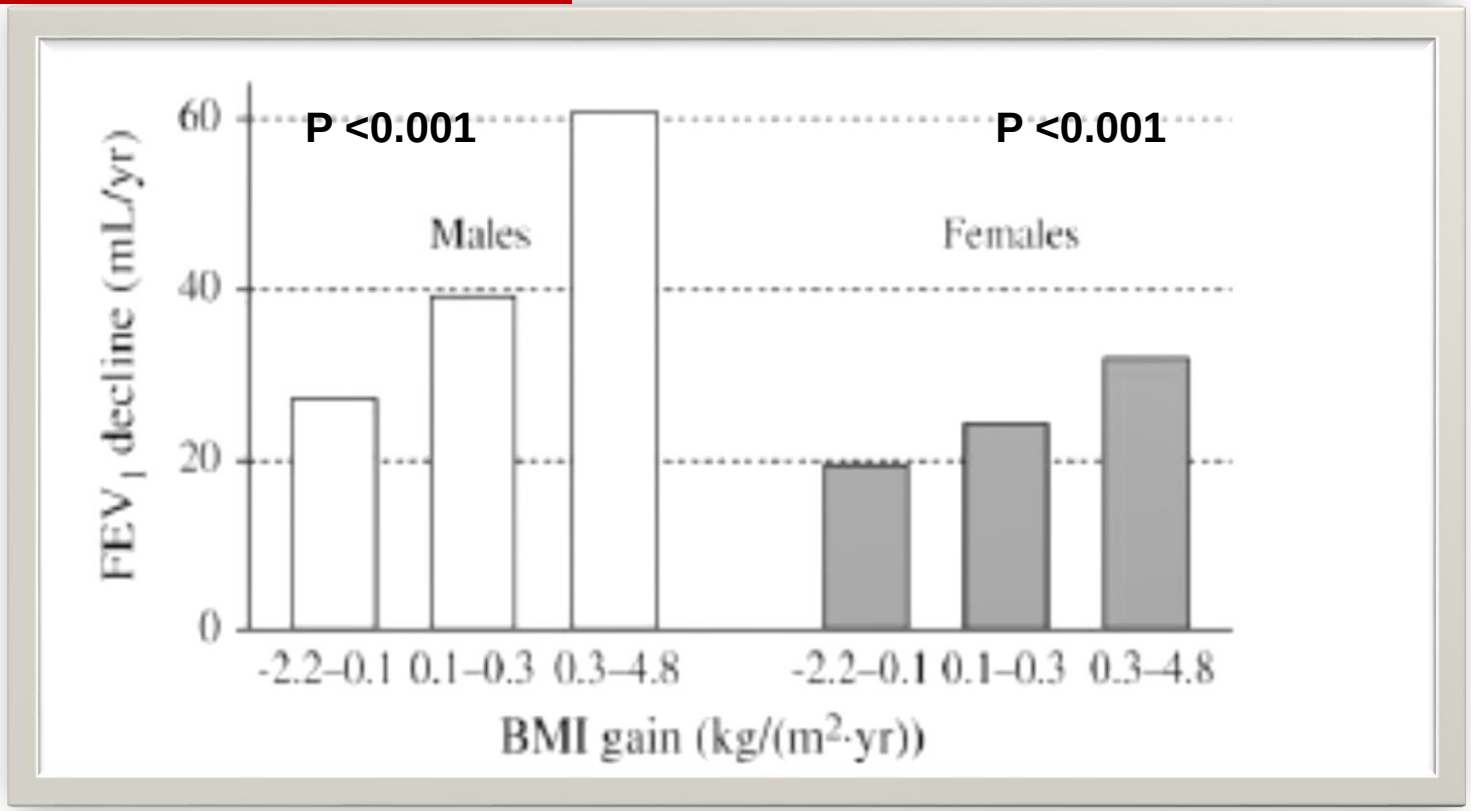
Men and women with an intermediate BMI had the greatest FEV_1 decline

Marcon A, et al. J Allergy Clin Immunol. 123: 1069. 2009

DETERIORO FUNCIONAL EN ASMA

OBESIDAD COMO FACTOR DE RIESGO

No obstruction at baseline



FEV_1 decline in men: 61.8 ml/y greater for every BMI unit (1 Kg/m^2) gained
FEV_1 decline in women: 20.2 “ “ “ “ “ “

Marcon A, et al. J Allergy Clin Immunol. 123: 1069. 2009

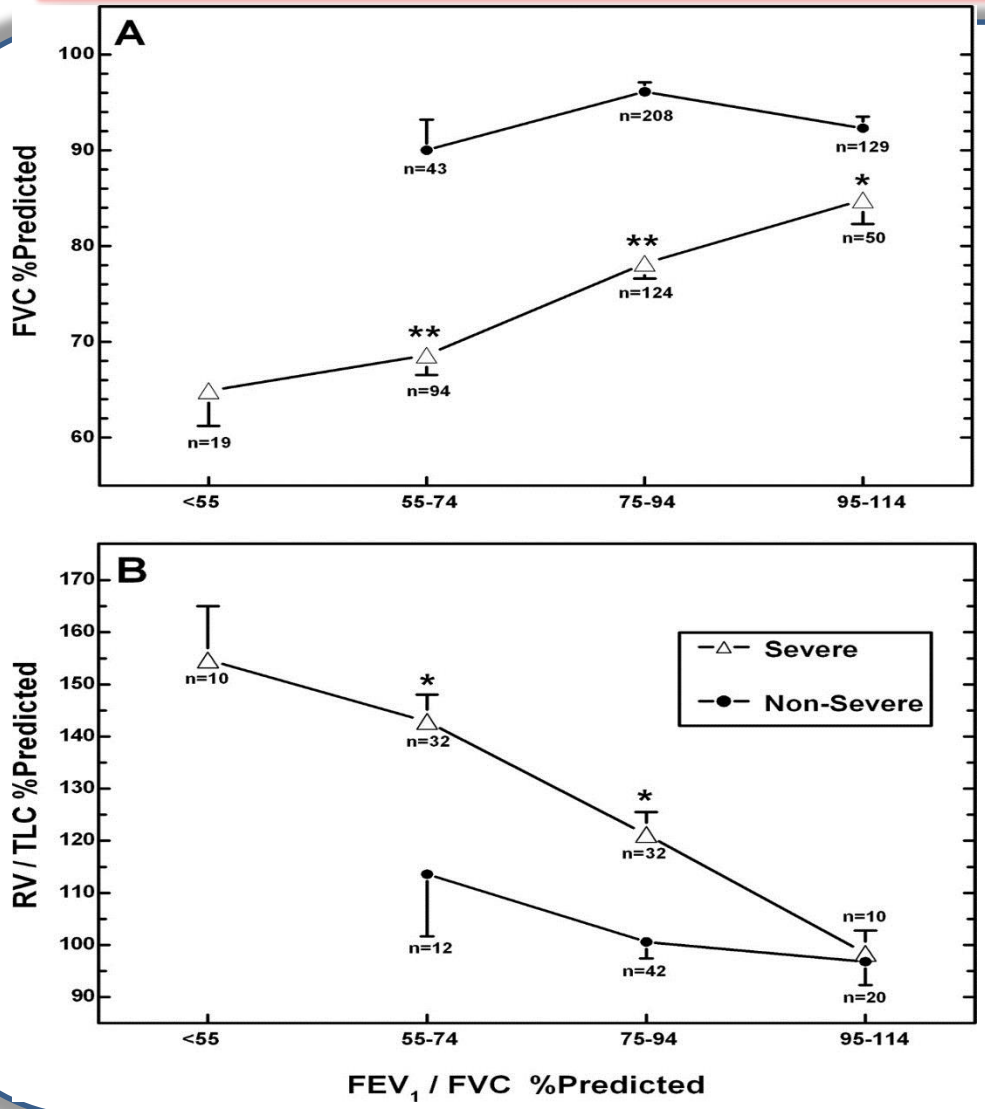
J Appl Physiol 104: 394–403, 2008.
First published November 8, 2007; doi:10.1152/japplphysiol.00329.2007.

Lung function in adults with stable but severe asthma: air trapping and incomplete reversal of obstruction with bronchodilation

Ronald L. Sorkness,[1] Eugene R. Bleecker,[2] William W. Busse,[1] William J. Calhoun,[3,4] Mario Castro,[5] Kian Fan Chung,[6] Douglas Curran-Everett,[7] Serpil C. Erzurum,[8] Benjamin M. Gaston,[9] Elliot Israel,[10] Nizar N. Jarjour,[1] Wendy C. Moore,[2] Stephen P. Peters,[2] W. Gerald Teague,[11] and Sally E. Wenzel,[7] for the National Heart, Lung, and Blood Institute Severe Asthma Research Program

[1]University of Wisconsin, Madison, Wisconsin; [2]Wake Forest University, Winston-Salem, North Carolina; [3]University of Pittsburgh, Pittsburgh, Pennsylvania; [4]University of Texas Medical Branch, Galveston, Texas; [5]Washington University, St. Louis, Missouri; [6]Imperial College, London, United Kingdom; [7]National Jewish Medical and Research Center, Denver, Colorado; [8]Cleveland Clinic, Cleveland, Ohio; [9]University of Virginia, Charlottesville, Virginia; [10]Brigham & Women's Hospital, Boston, Massachusetts; and [11]Emory University, Atlanta, Georgia

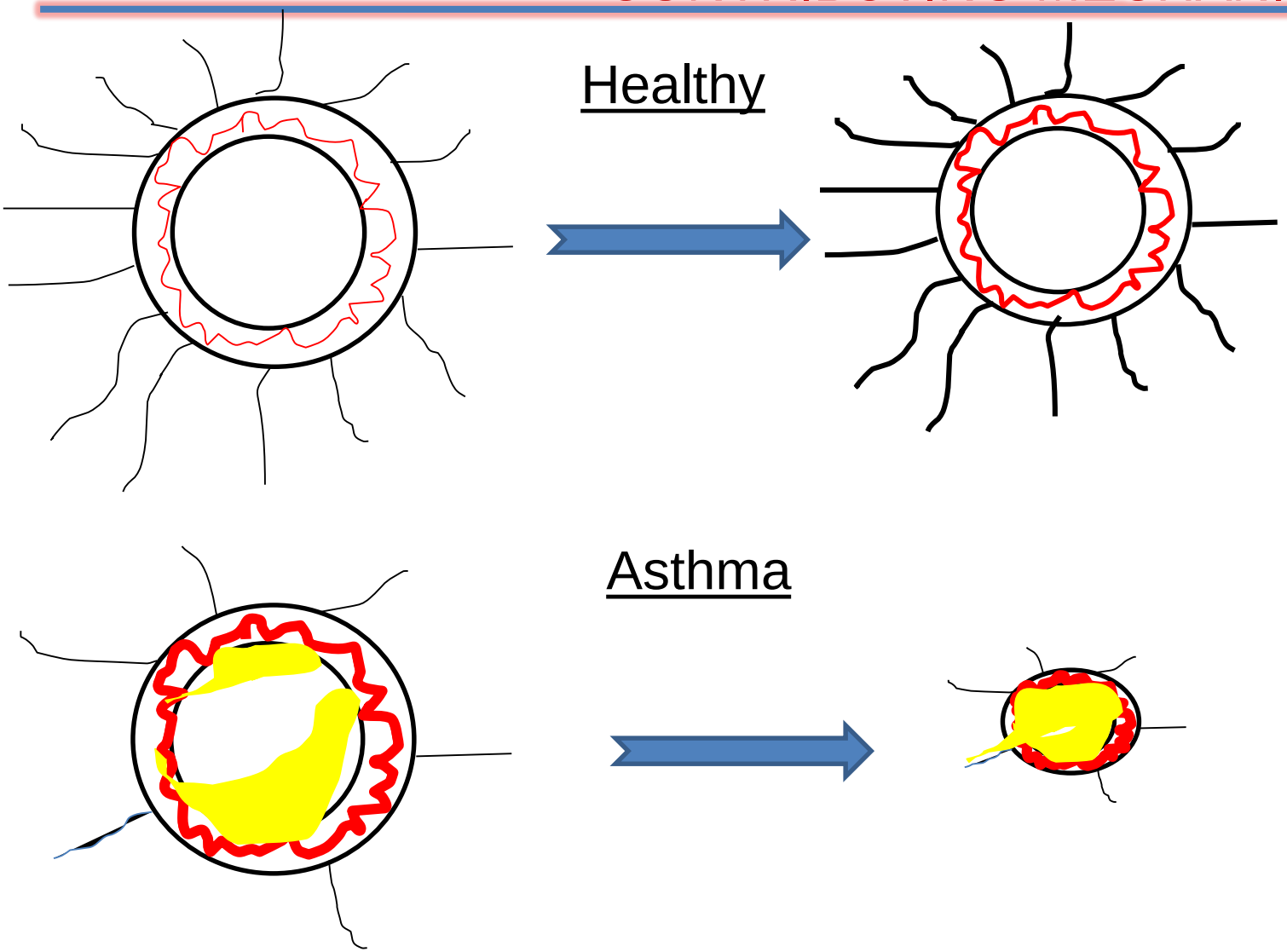
PAPEL DEL ATRAPAMIENTO EN DETERIORO DEL FEV_1



En los pacientes con asma grave, las reducciones del FEV_1 son achacables a atrapamiento aéreo en una medida significativamente mayor que en los asmáticos no graves.

Sorkness, R. L. et al. J Appl Physiol 104: 394-403 2008;

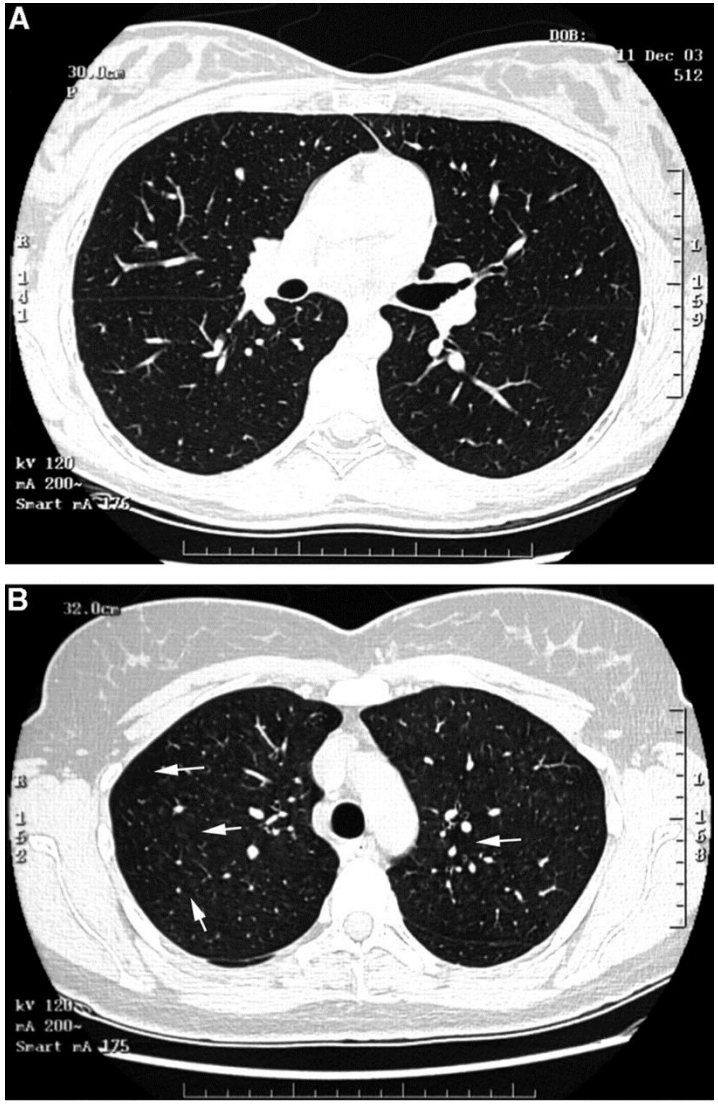
AIRWAY CLOSURE
CONTRIBUTING MECHANISMS



ASTHMATIC SUBJECTS
ATENUATION AREAS

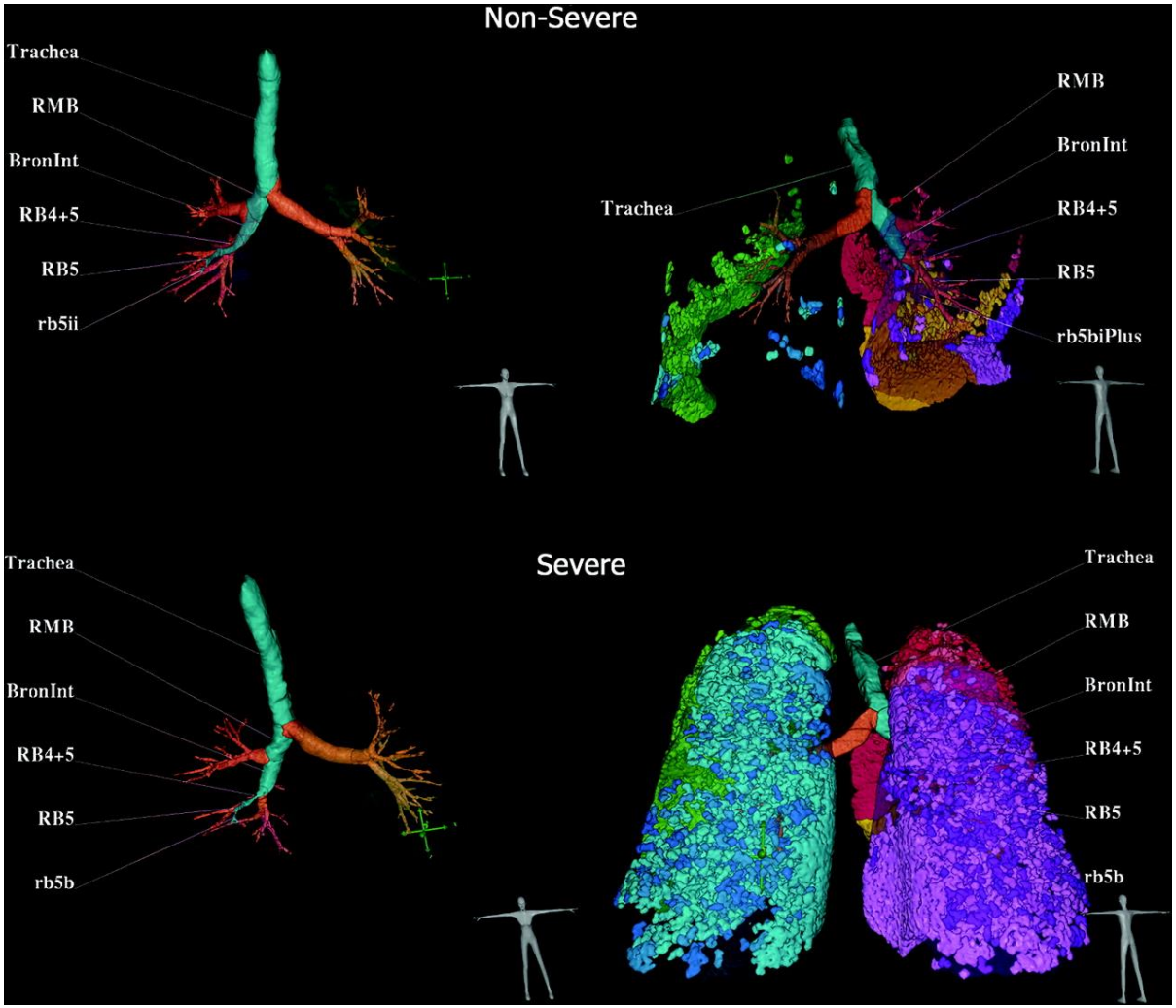
Healthy nonsmoker

Asthmatic nonsmoker



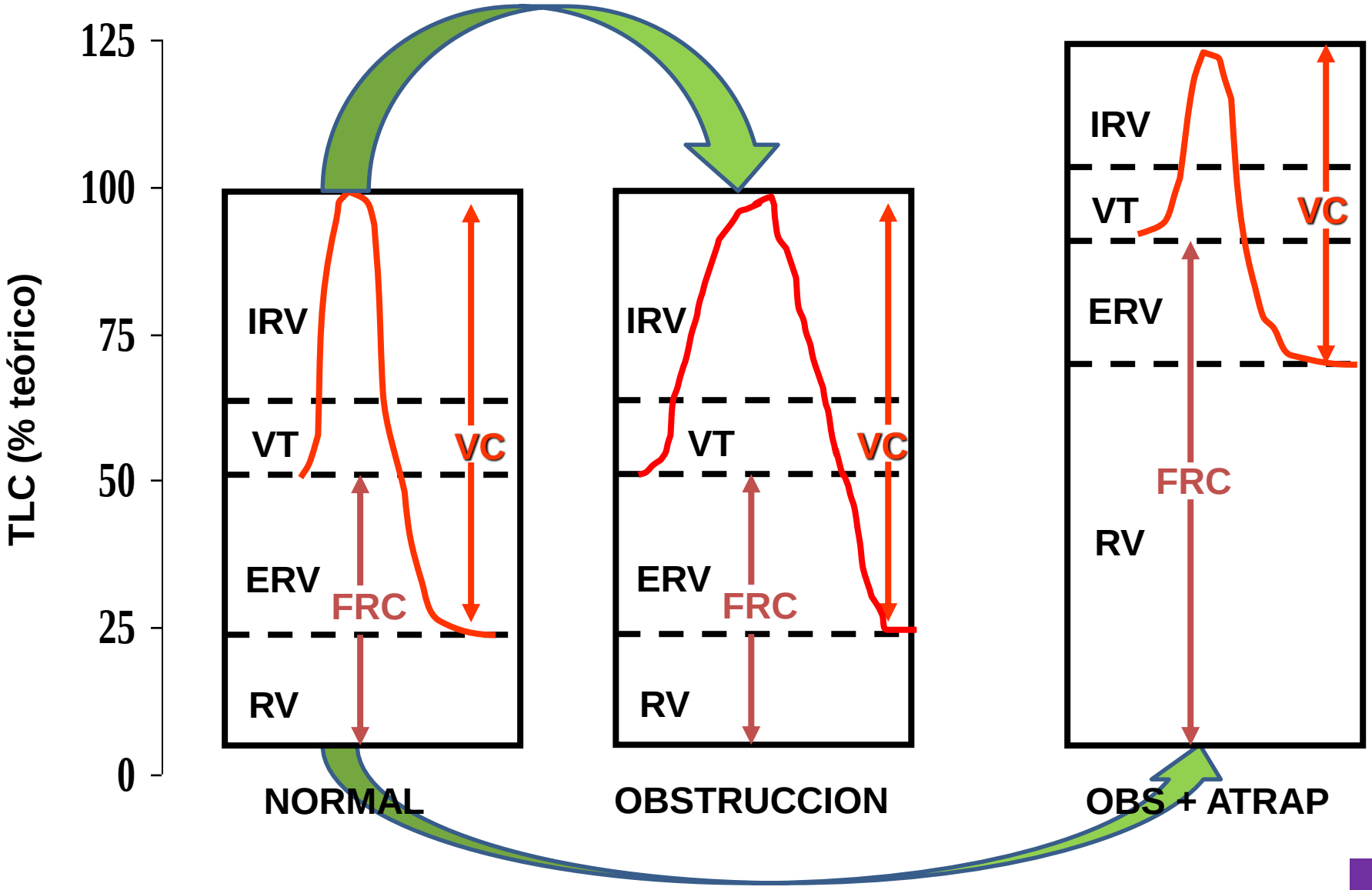
Boulet, L.-P. et al. Chest 2006;129:661-668

CT-derived three-dimension display of the lungs, airways, and regions of air trapping

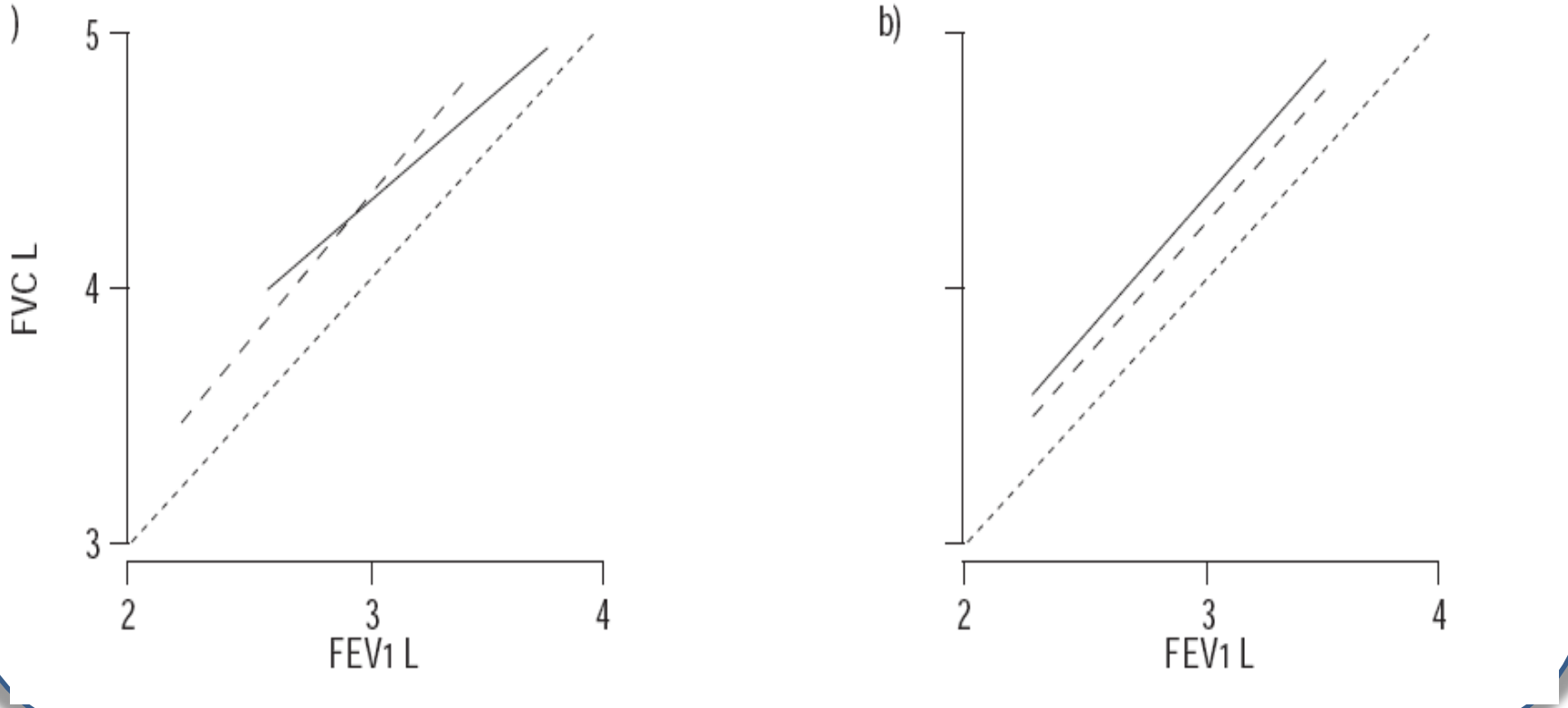


Busacker A. et.al. Chest 2009;135:48-56

FENOTIPOS DE RESPUESTA OBSTRUCTIVA



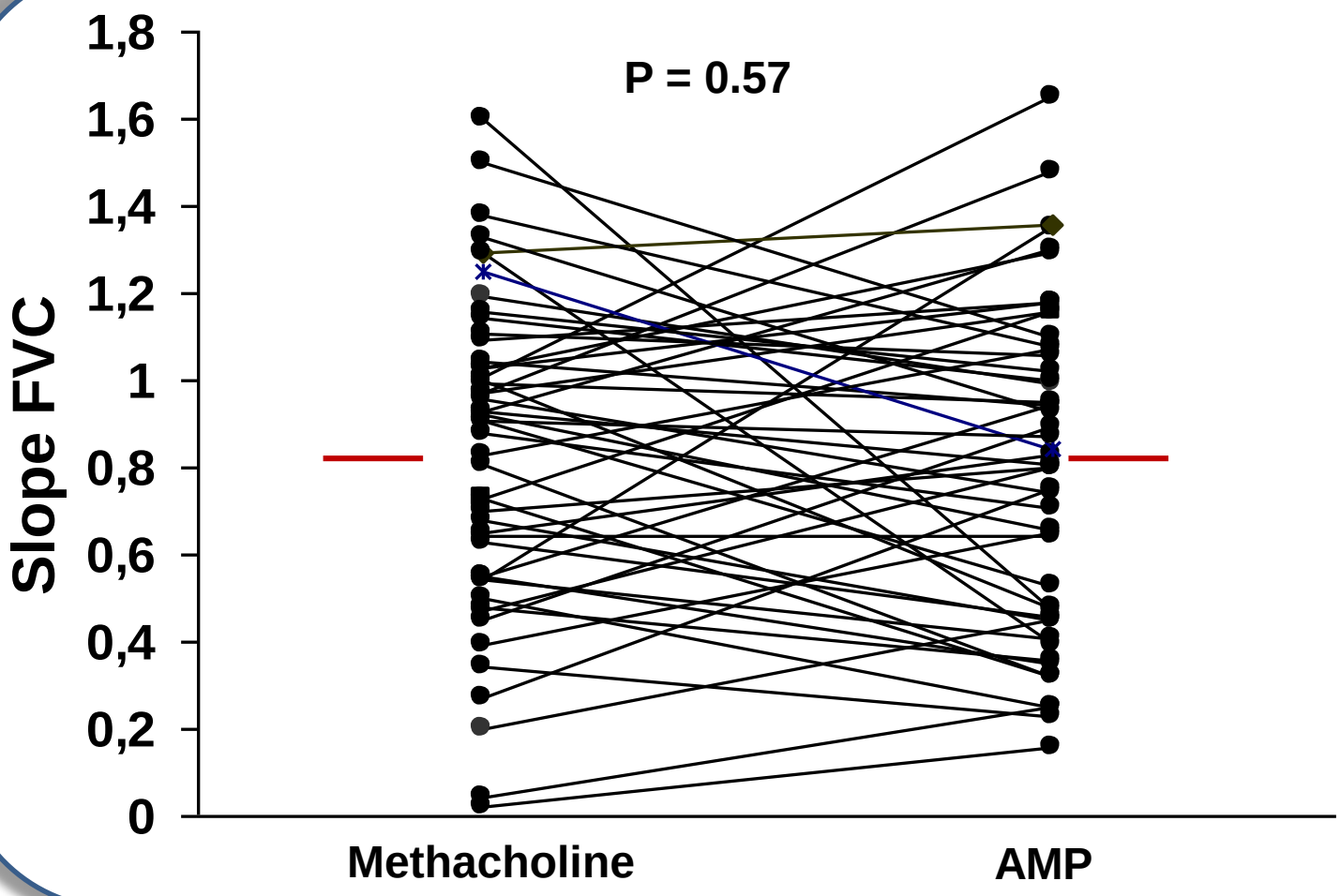
IDENTIFICACION DE ATRAPAMIENTO
PENDIENTE E INTERCEPCION



Corsico A, et al. Eur Respir J. 2000; 15: 687.

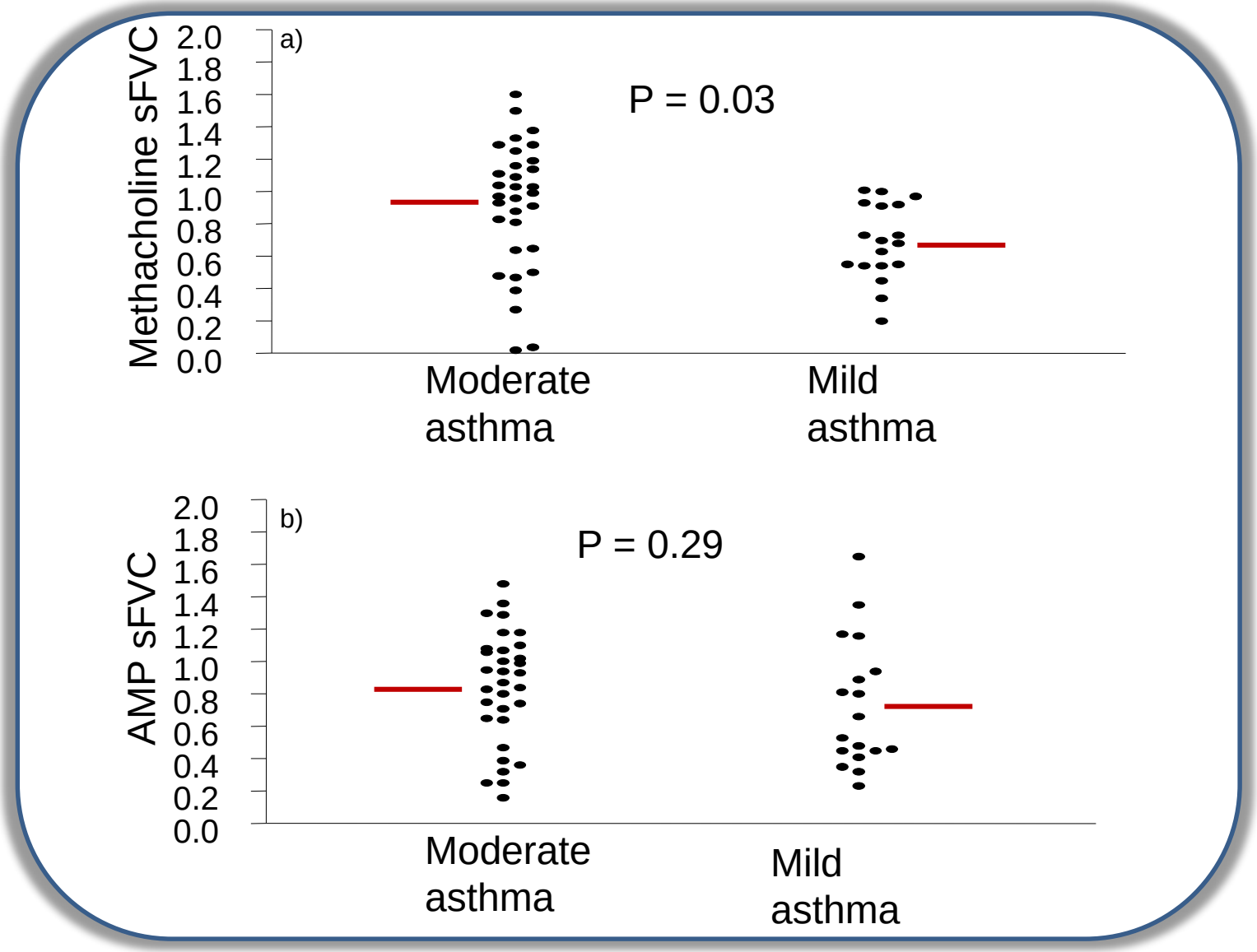
ATRAPAMIENTO AEREO

METACOLINA vs AMP



Prieto L, et al. Ann Allergy Asthma Immunol. 102: 239. 2009.

ATRAPAMIENTO AEREO: METACOLINA vs AMP



Prieto L, et al. Ann Allergy Asthma Immunol. 102: 239. 2009.