

LA VALUTAZIONE DEL PAZIENTE NON CONTROLLATO E POSSIBILITA' TERAPEUTICHE

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XXX CONGRESSO NAZIONALE

SIAAIC

Società Italiana di Allergologia,
Asma ed Immunologia Clinica



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Italian Society for Allergy, Asthma & Clinical Immunology



Controllo dell'asma

Studi a confronto

	Quota controllati	Metodo raccolta dati	Numerosità campione (Italia)	Provenienza del campione	Valutaz. controllo	Valutazione parametri spirometrici
AIRE Study ERJ 2000	5,3%	Questionario telefonico	400 asmatici	Francia, Germania Italia, Olanda, Spagna, Svezia, Regno Unito.	GINA 1995	NO
ISAYA Study Allergy 2003	10%	Questionario postale + intervista telefonica	649 asmatici 9 centri pneum.	Italia	questionario	NO
Cazzoletti Study J All Clin Immun 2007	32%	Questionari postali + visita pneumologica	4002 asmatici 3 centri pneum.	Italia, Svizzera, Regno Unito, Svezia, Spagna, Belgio, Germania, Francia, Norvegia, Islanda	GINA 2006	SI
PRISMA Study Resp Med 2012	64,3%	Pazienti del centro pneumologico	2.853 asmatici 56 centri pneum.	Italia	ACT	NO

Il costo dell'asma aumenta nell'asma non controllato

	REC (95%CI)	p-value
Uncontrolled vs controlled/partly controlled asthma	3.02 (2.06-4.44)	<0.001
Female	1.37 (0.97-1.94)	0.07
Age (years), 5-year increase	1.05 (0.91-1.21)	0.51
BMI (Kg/m ²), 1-unit increase	1.03 (1.00-1.05)	0.03
Low socio-economic class	0.81 (0.53-1.24)	0.34
Smoking habits, vs non smoker		
• past smoker	1.02 (0.67-1.56)	0.93
• current smoker	0.74 (0.46-1.19)	0.22
Age at onset (years), vs [0-10)		
• [10-20)	0.88 (0.66-1.18)	0.40
• ≥20	0.90 (0.59-1.36)	0.61
Chronic cough or phlegm	2.22 (1.52-3.25)	<0.001
Allergic rhinitis	0.89 (0.54-1.46)	0.65
IgE sensitization	0.63 (0.39-1.00)	0.051

BMI: body mass index; IgE: Immunoglobulin E
REC: Mutually adjusted ratios of expected individual total costs (REC) obtained by using a negative binomial regression model with adjusted standard errors for intra-centre correlation

Evoluzione della definizione di asma

1962

***Malattia episodica
caratterizzata da:***

- **Ostruzione reversibile**
- **Iperreattività bronchiale**

American Thoracic Society

1997

***Malattia cronica
caratterizzata da:***

- **Infiammazione cronica
delle vie aeree**
- **Ostruzione con quota
di non reversibilità**
- **Iperreattività bronchiale**

NHLBI Expert Panel Report



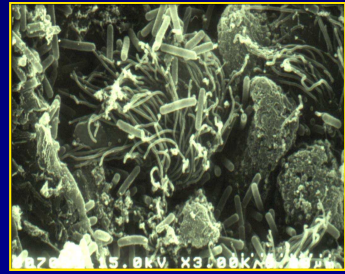
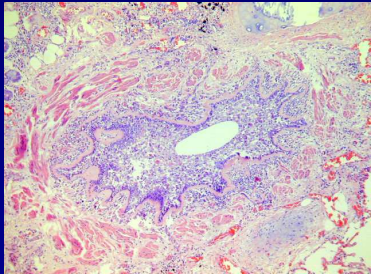
ASSESSMENT OF ASTHMA – KEY POINTS

- Assess asthma control in terms of its two domains: symptom control (previously called 'current clinical control') and future risk of adverse outcomes.
- Assess symptom control from the frequency of daytime and night-time asthma symptoms and reliever use, and from activity limitation. Poor symptom control is burdensome to patients and is a risk factor for future exacerbations.
- Lung function is most useful as part of an assessment of the future risk of adverse outcomes. It should be recorded at diagnosis, 3–6 months after starting treatment, and periodically thereafter. Discordance between symptoms and lung function should prompt further investigation.
- Assess each patient's future risk for exacerbations, fixed airflow limitation and medication side-effects, even when symptom control is good. Identified risk factors for exacerbations that are independent of symptom control include a history of one or more exacerbations in the previous year, poor adherence, incorrect inhaler technique, low lung function, smoking, and blood eosinophilia.
- Poor control of symptoms and poor control of exacerbations may have different contributory factors and may need different treatment approaches.
- Asthma severity is assessed from the level of treatment required to control symptoms and exacerbations. It is important to distinguish between severe asthma and asthma that is uncontrolled due to common problems, such as incorrect inhaler technique or poor adherence.

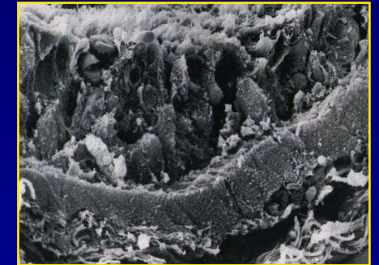
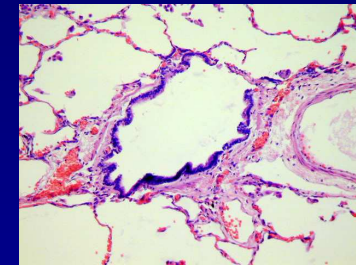
Asma: dalla fisiopatologia alla clinica

Grandi e piccole vie aeree

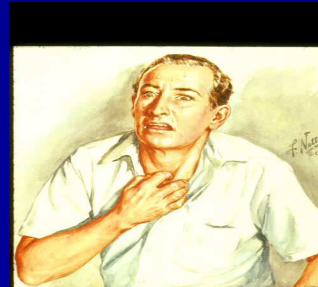
infiammazione



rimodellamento



sintomi

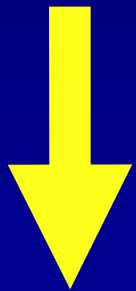


Controllo dell'asma

Tre domini

Sintomi

*(diurni e notturni,
limitazione delle
attività, necessità di
farmaco al bisogno)*



1. Valutare il quadro clinico

Funzione respiratoria

(PEF or FEV1)



2. Eseguire la spirometria

Riacutizzazioni

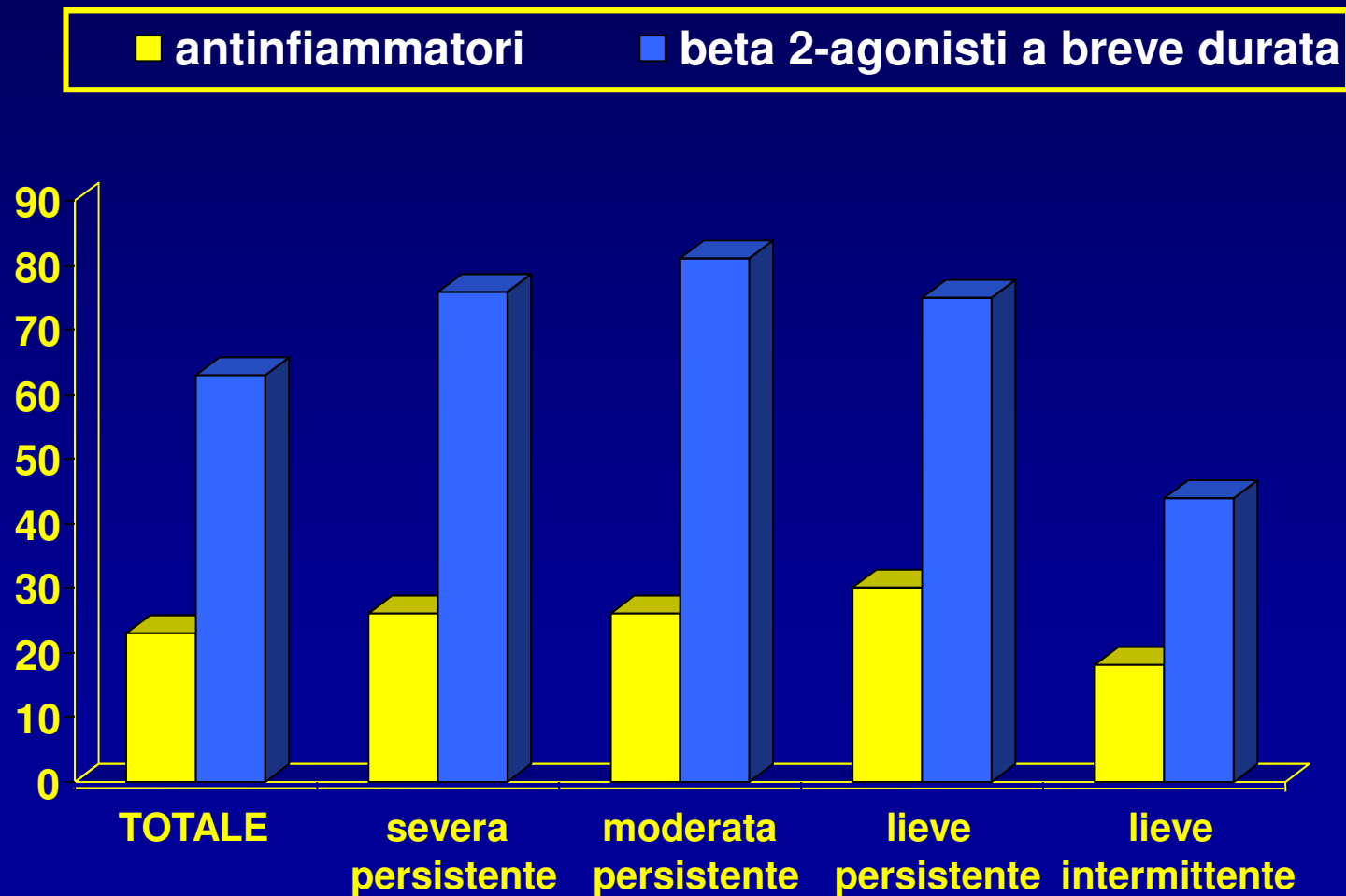
(frequenza e gravità)



3. Rivedere la storia clinica

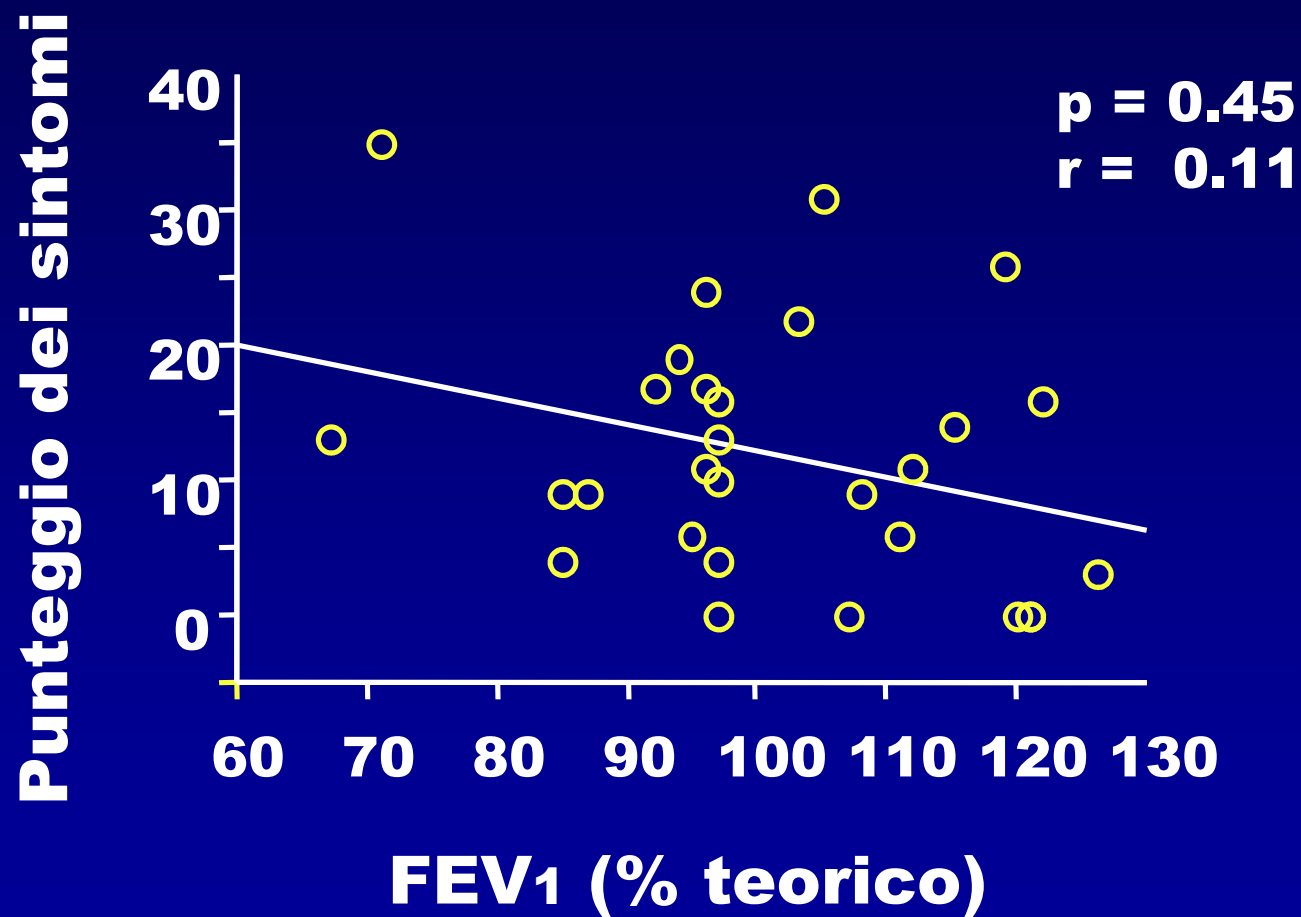
I fatti:

Terapia rivolta a risolvere gli episodi acuti piuttosto che a prevenirne l'insorgenza



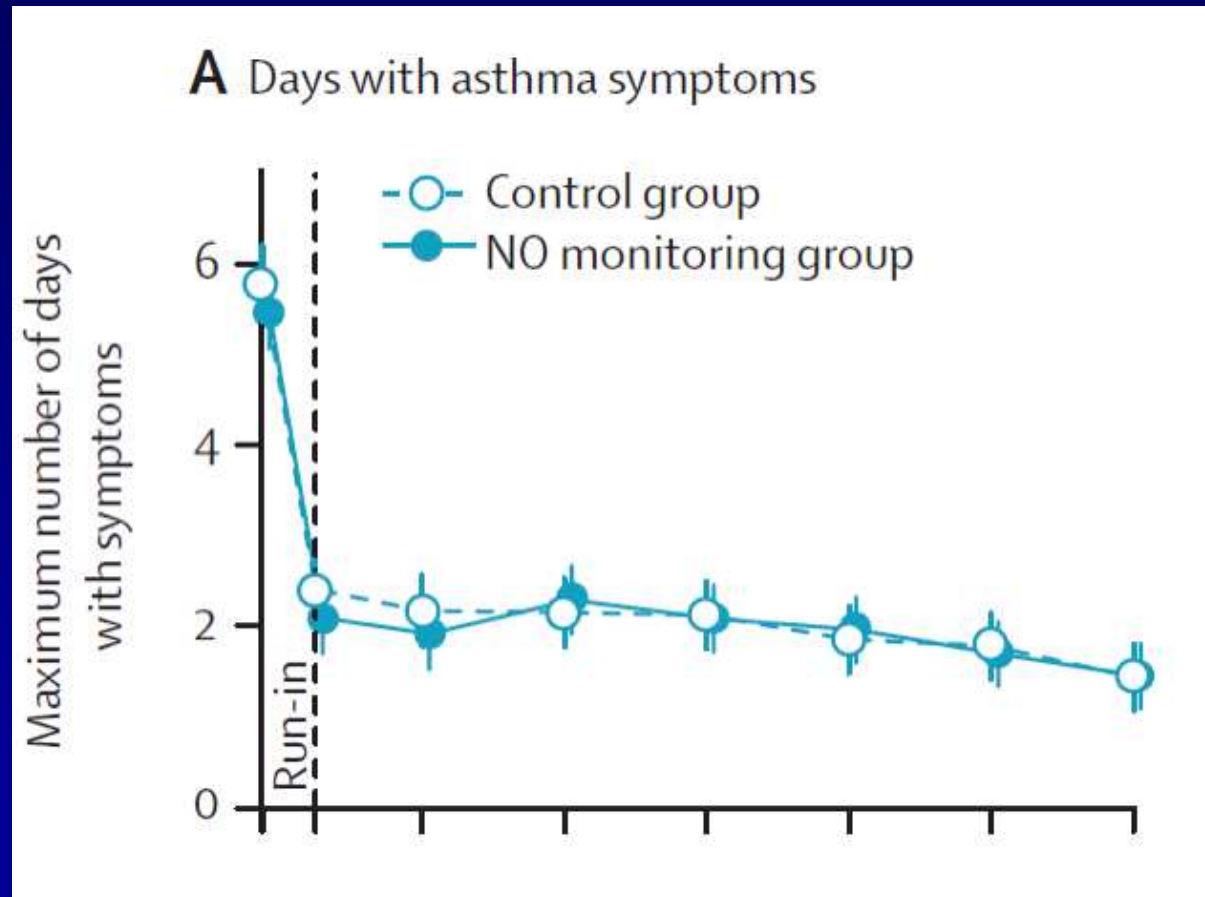
I fatti:

La funzione respiratoria non si associa alla gravità dell'asma



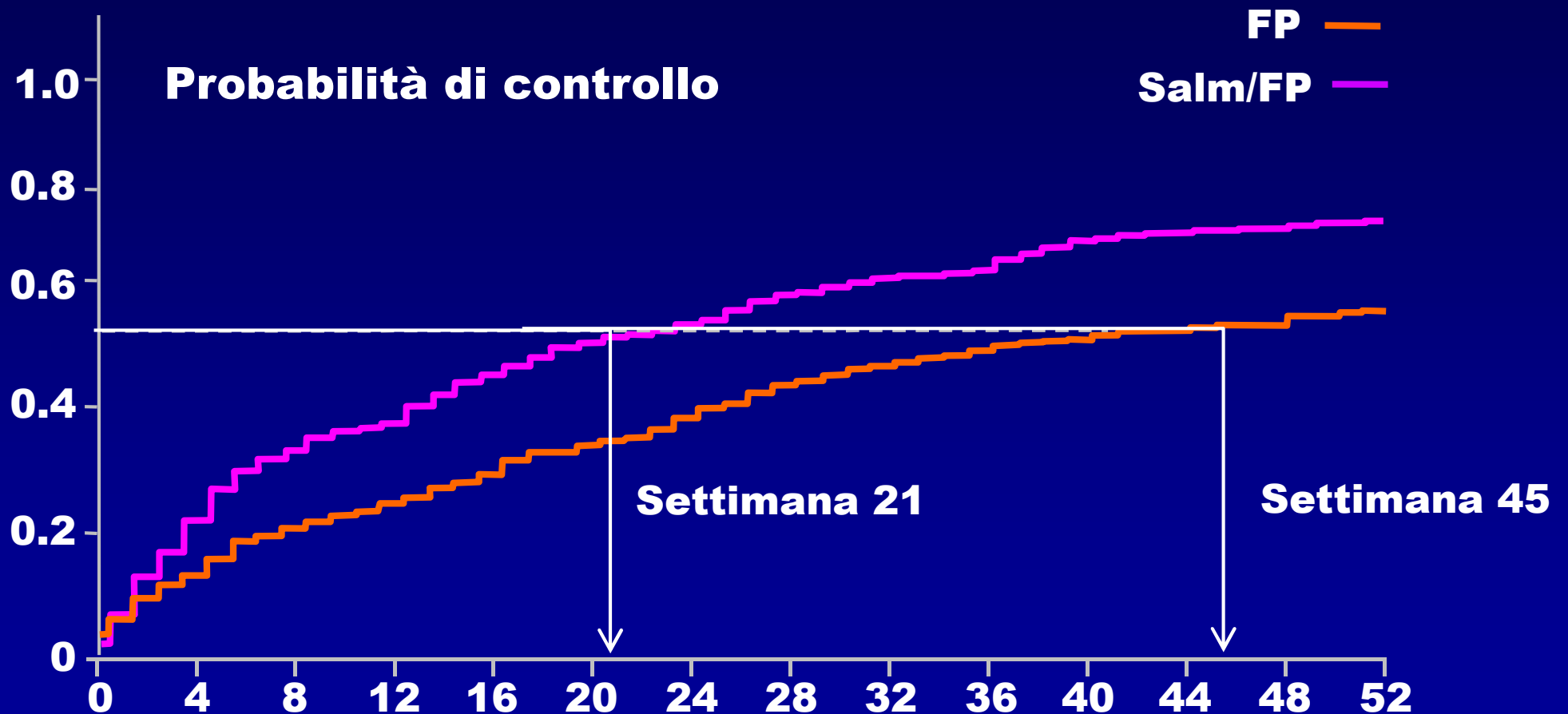
I fatti:

Gestione dell'asma basata sulle misurazioni di ossido nitrico non migliora il controllo



Szeffler et al. Lancet 2008

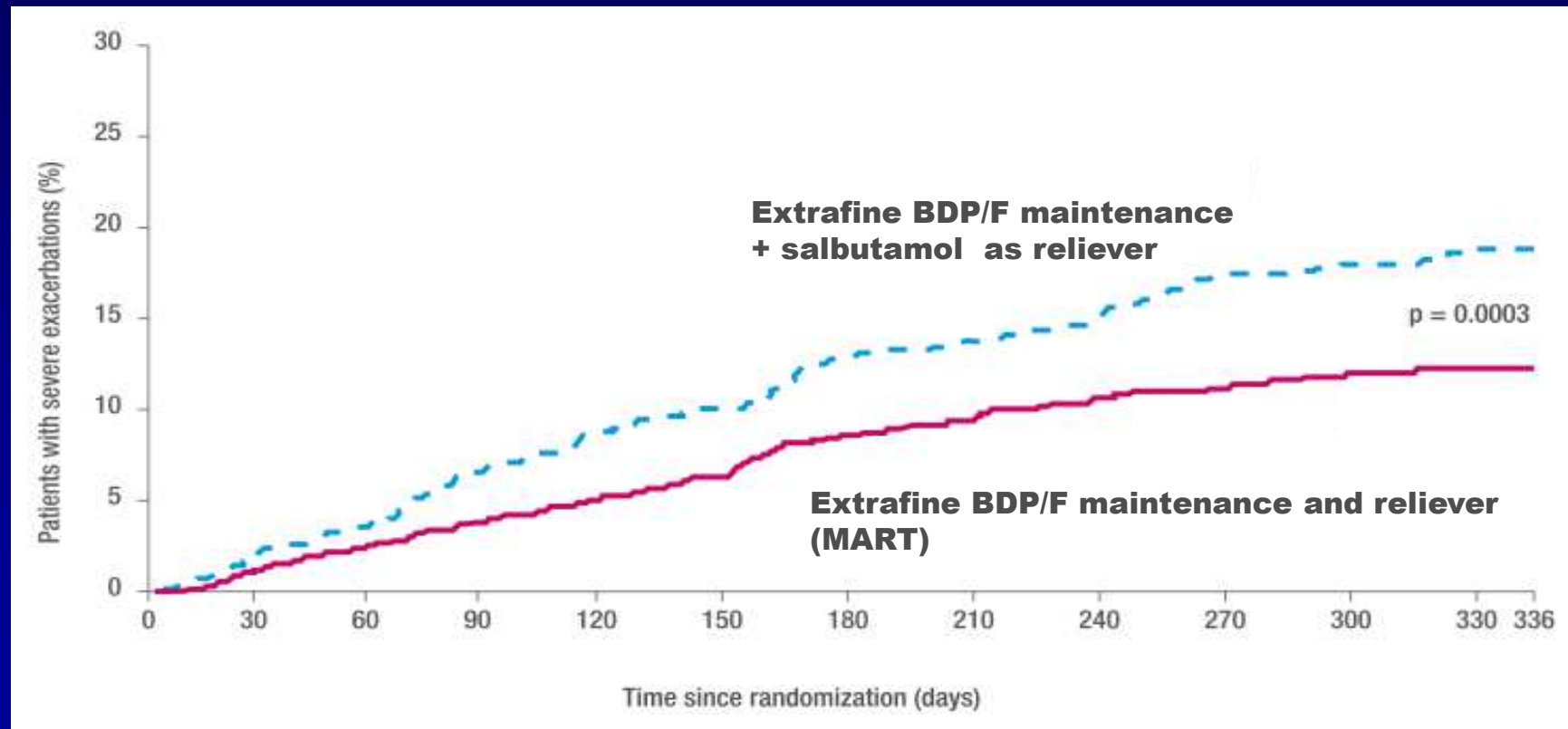
Aumento progressivo della percentuale di pazienti controllati nel tempo



Tempo per il raggiungimento della prima settimana di Controllo Totale
Pazienti precedentemente in trattamento con basse dosi di ICS (Strato 2)

La strategia MART (BDP/Form extra-fine mantenimento e bisogno)

1714 patients with asthma and history of exacerbation



Papi et al, The Lancet Respir Med 2013

Le piccole vie aeree hanno un ruolo nel controllo dell'asma?

Vi è evidenza di infiammazione nelle piccole vie aeree?

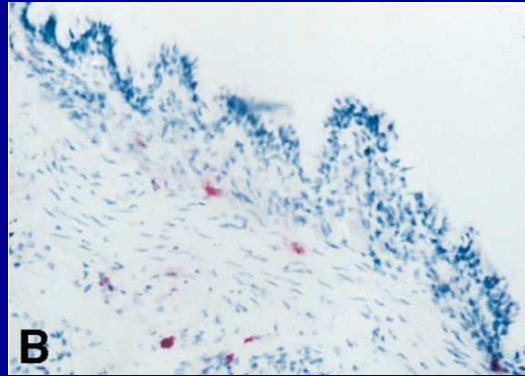
Vi è evidenza di rimodellamento nelle piccole vie aeree?

L'infiammazione e il rimodellamento delle piccole vie aeree si traducono in alterazioni funzionali?

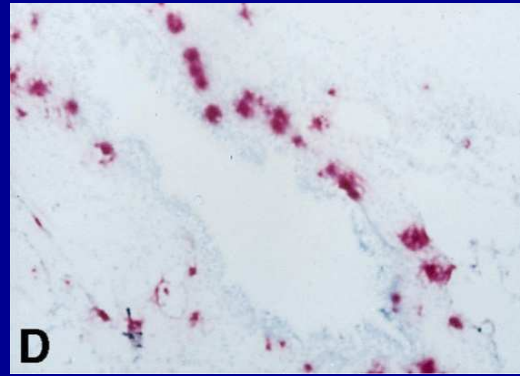
Le alterazioni funzionali delle piccole vie aeree si traducono nella comparsa di sintomi respiratori?

Infiammazione allergica e piccole vie aeree nell'asma

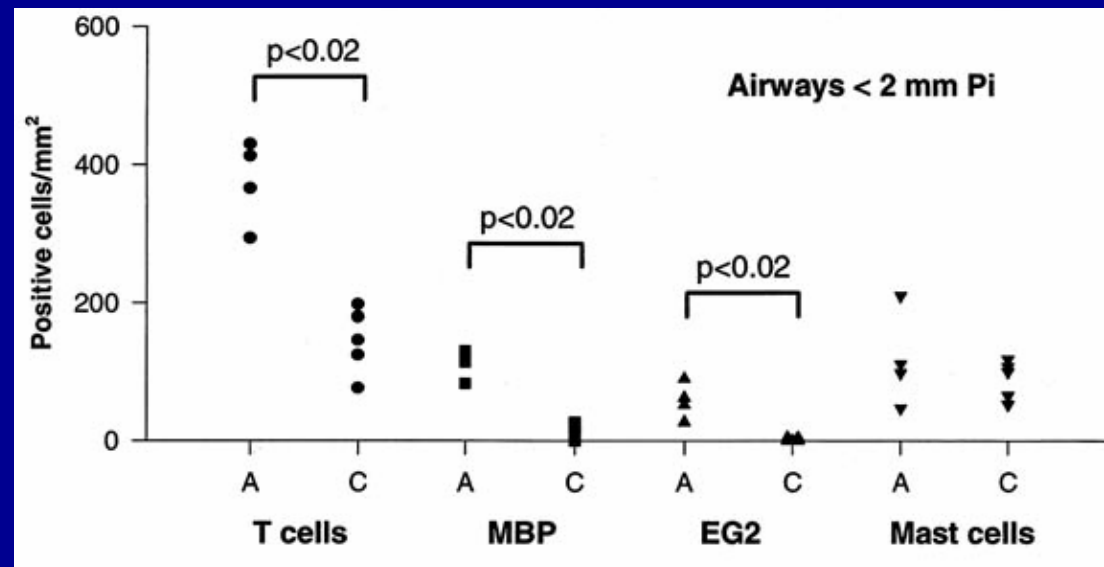
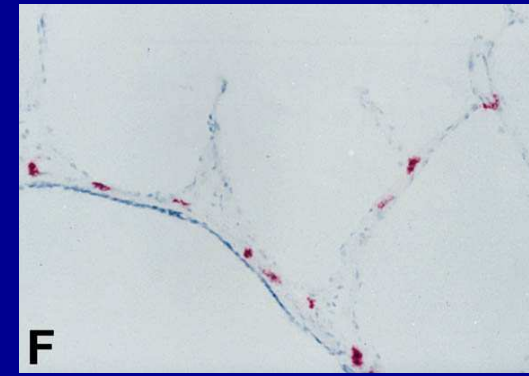
Large airways



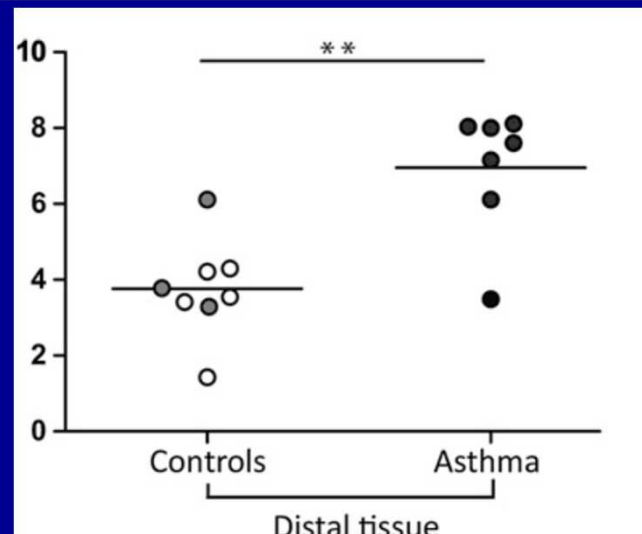
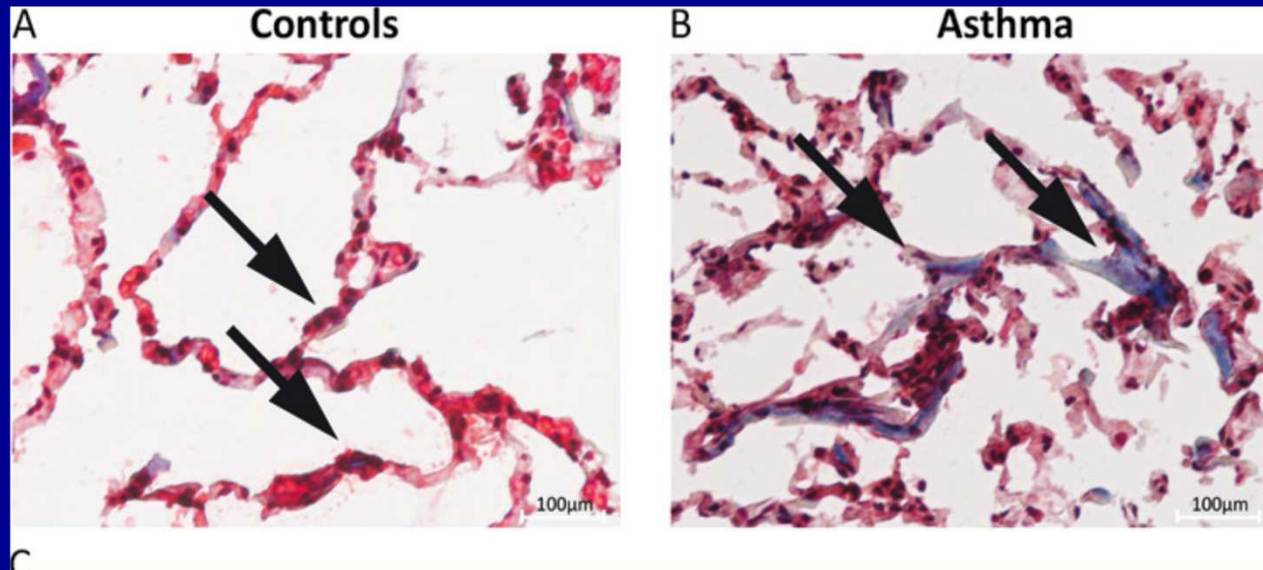
Small airways



Parenchyma



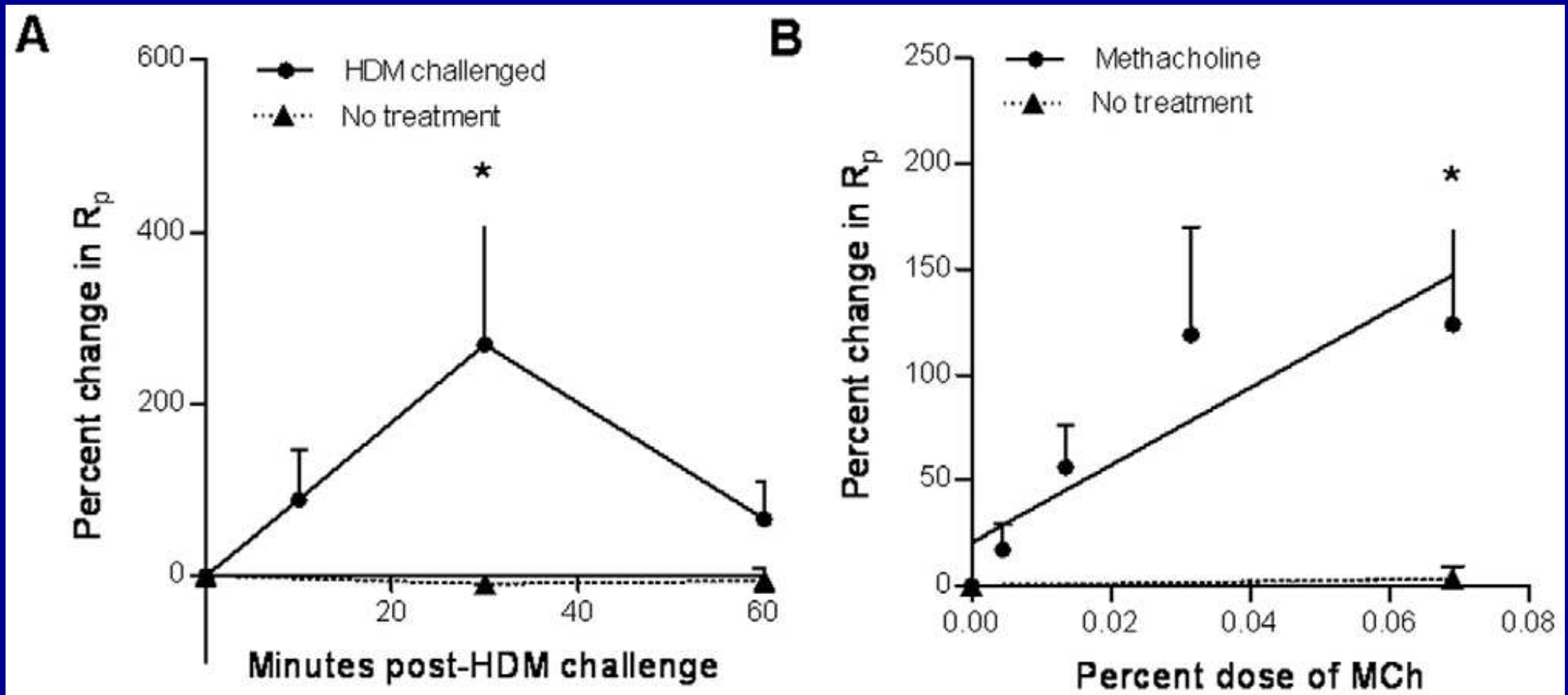
Altered matrix production in the distal airways of mild asthmatics



L'inflammatione e il rimodellamento delle piccole vie aeree si traducono in alterazioni funzionali?

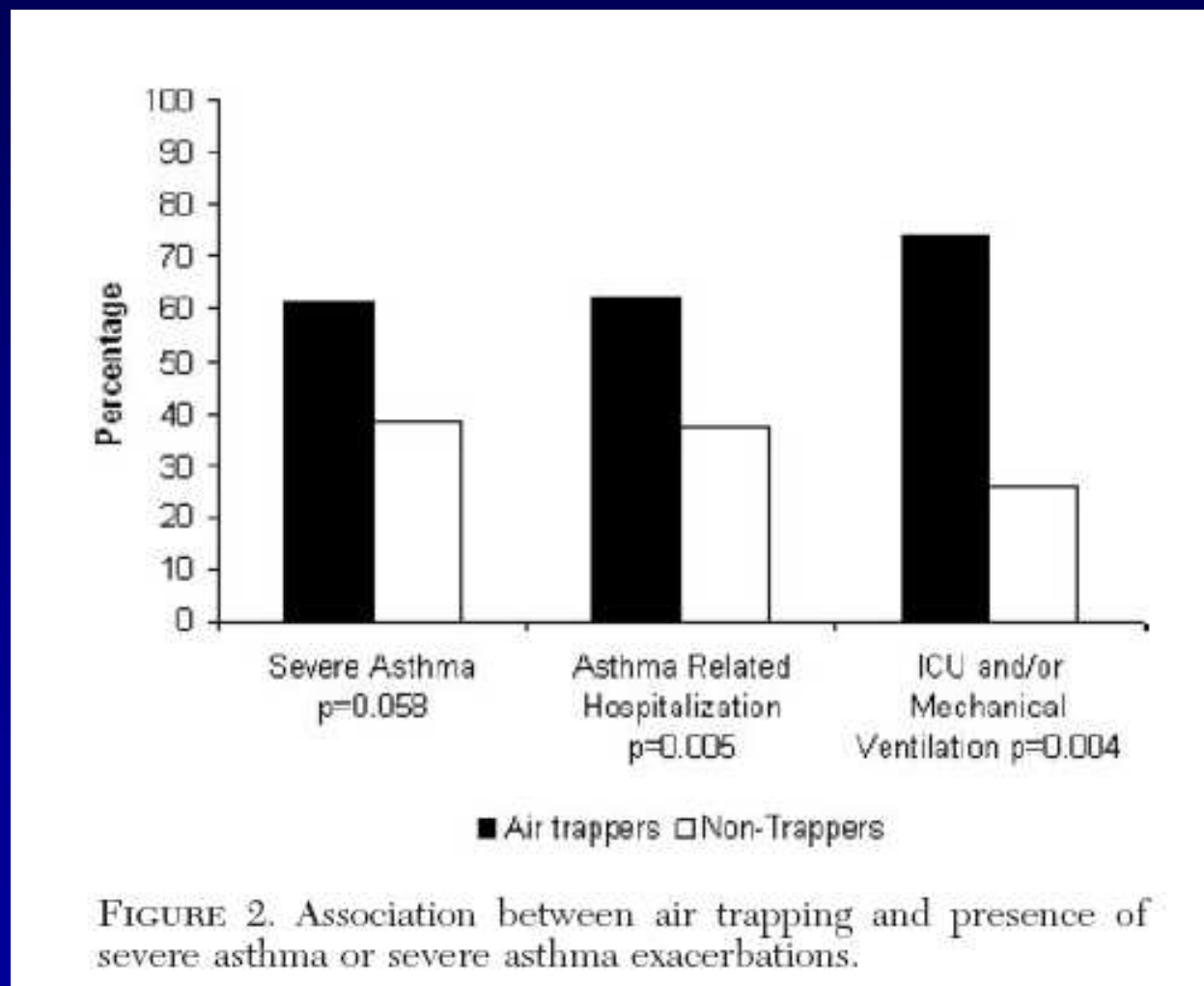
House dust mite challenge

Methacholine challenge

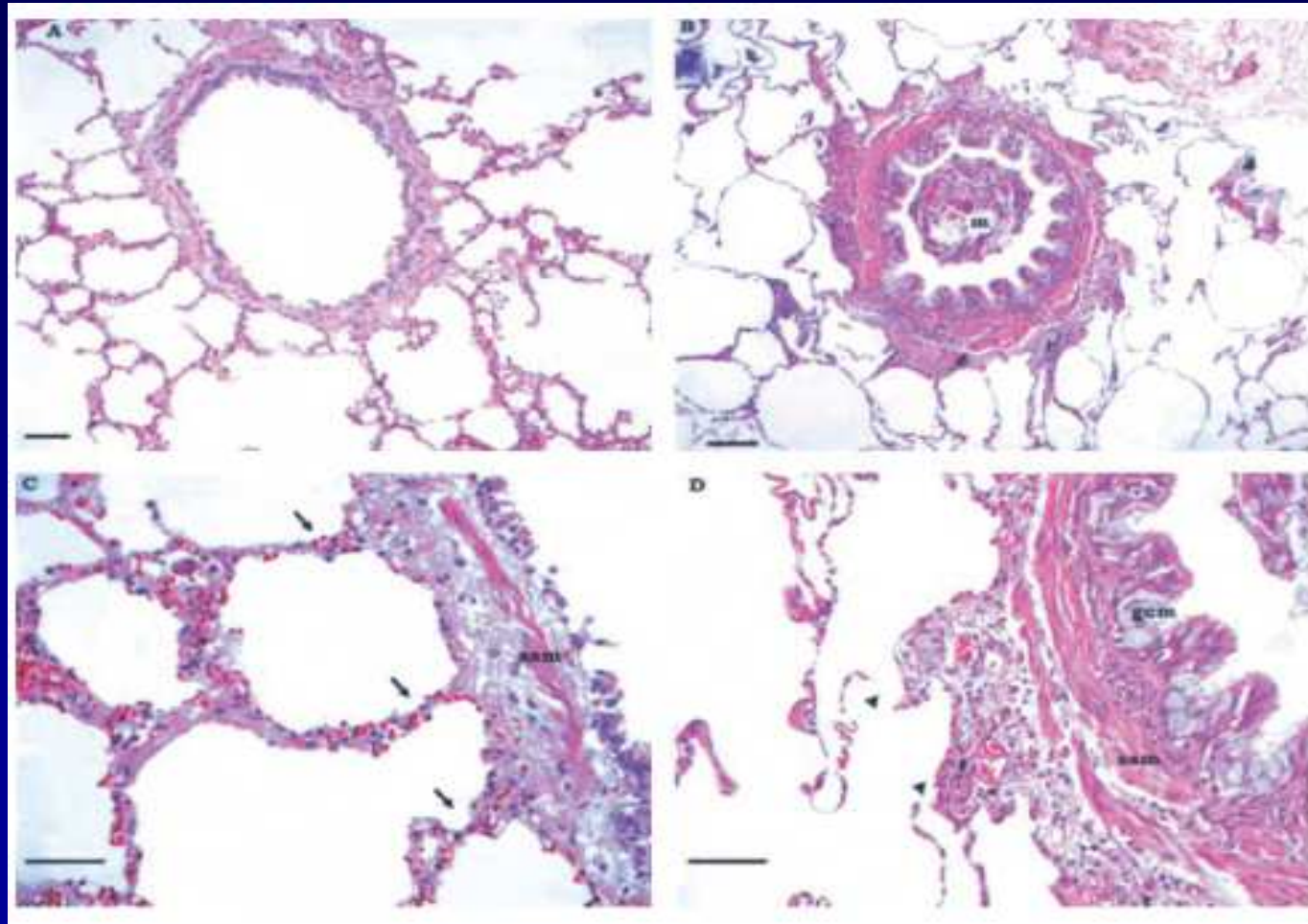


Functional changes of small airways and severity of asthma

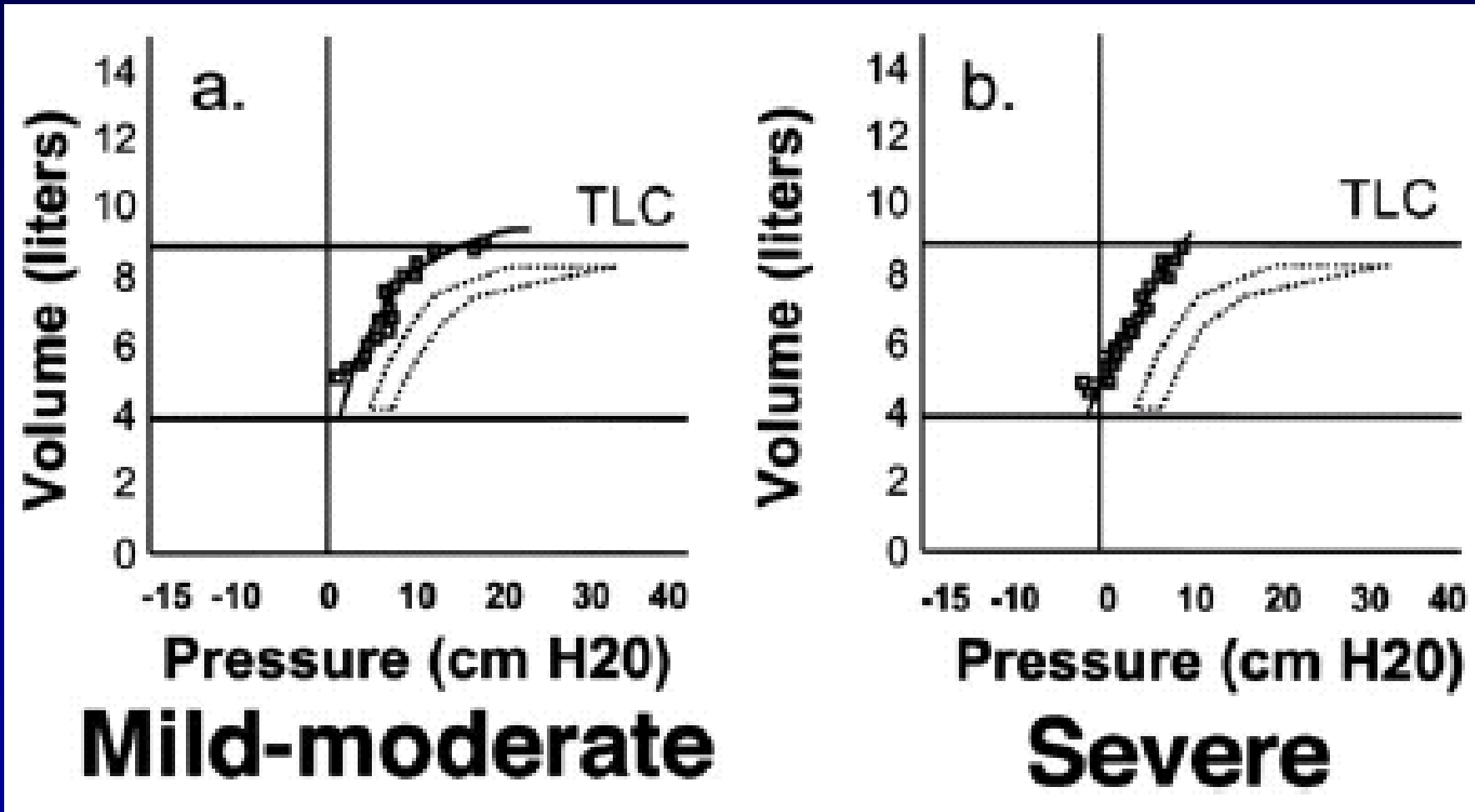
Air trapping



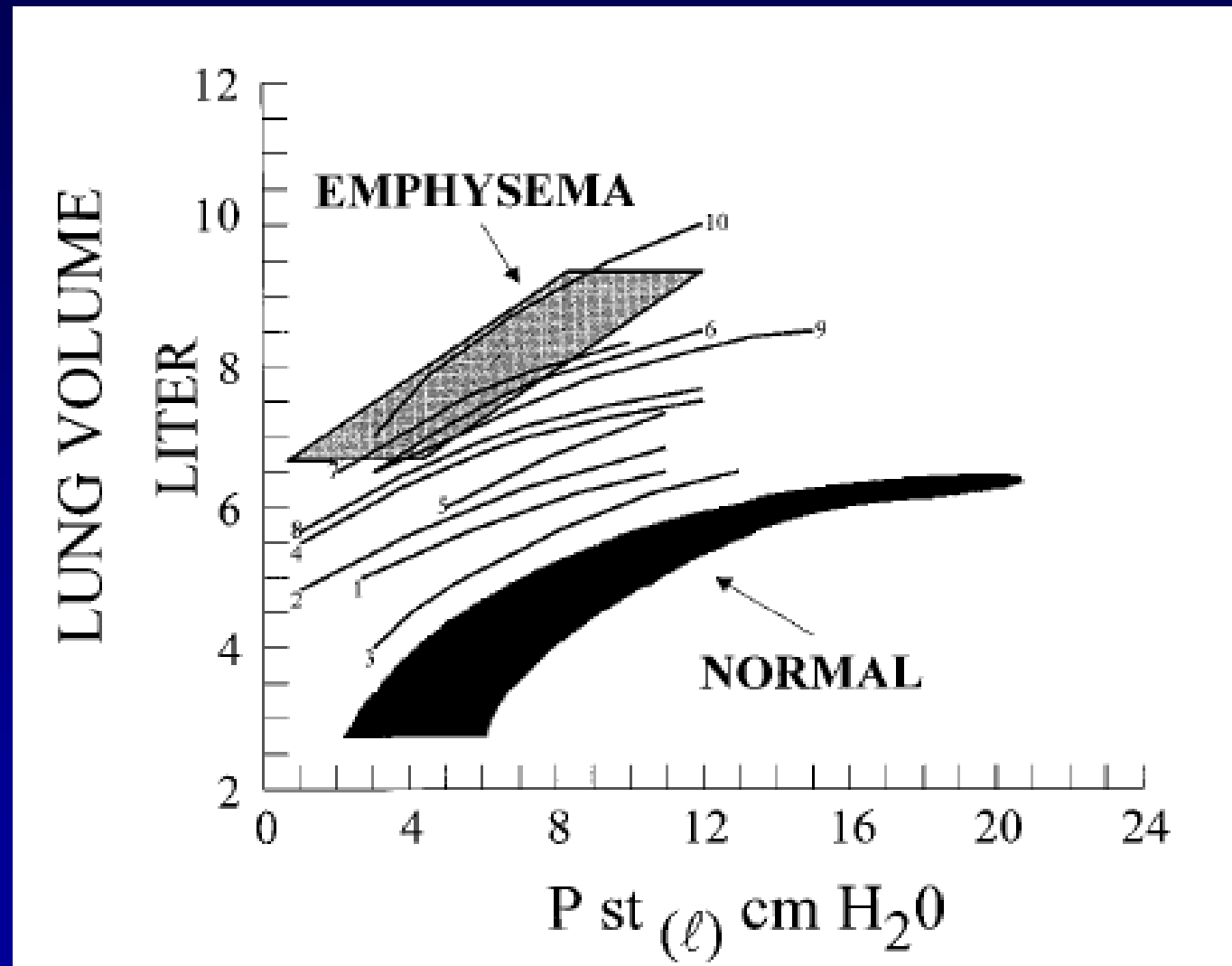
Riduzione delle fibre elastiche del polmone distale nell' asma grave



PRESSURE-VOLUME CURVES IN ASTHMA



Enfisema pseudofisiologico nel coinvolgimento severo delle piccole vie aeree

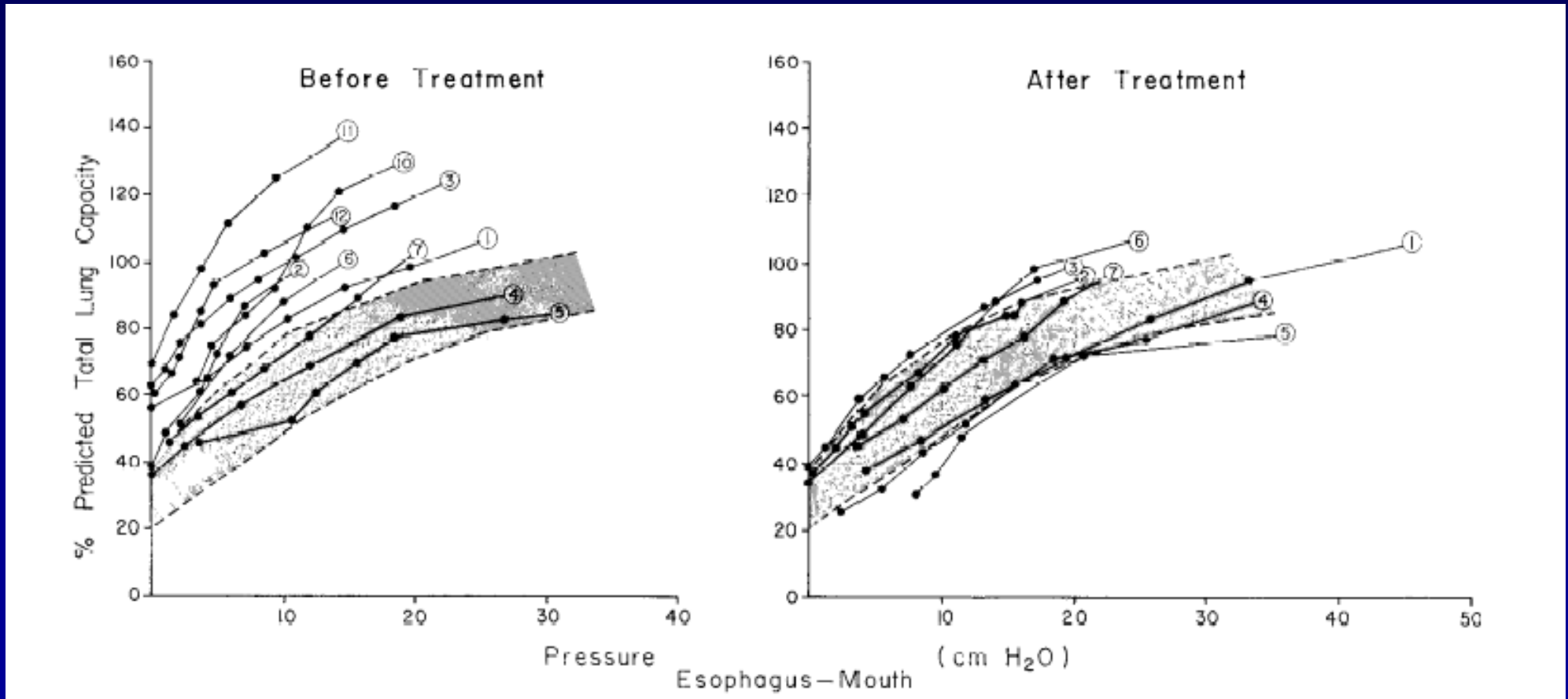


Unsuspected loss of lung elastic recoil in chronic persistent asthma

***Conclusion:* Patients with chronic moderate and severe persistent asthma, despite optimal therapy, have reduced maximum expiratory airflow limitation for many years in part due to (early?) loss of lung elastic recoil from unknown mechanism(s).**

This challenges current concept of airway remodeling.

Pressione di ritorno elastico nell'asmatico prima e dopo terapia con steroide sistemico



Overall Asthma Control

achieving

Current Control

defined by

Symptoms

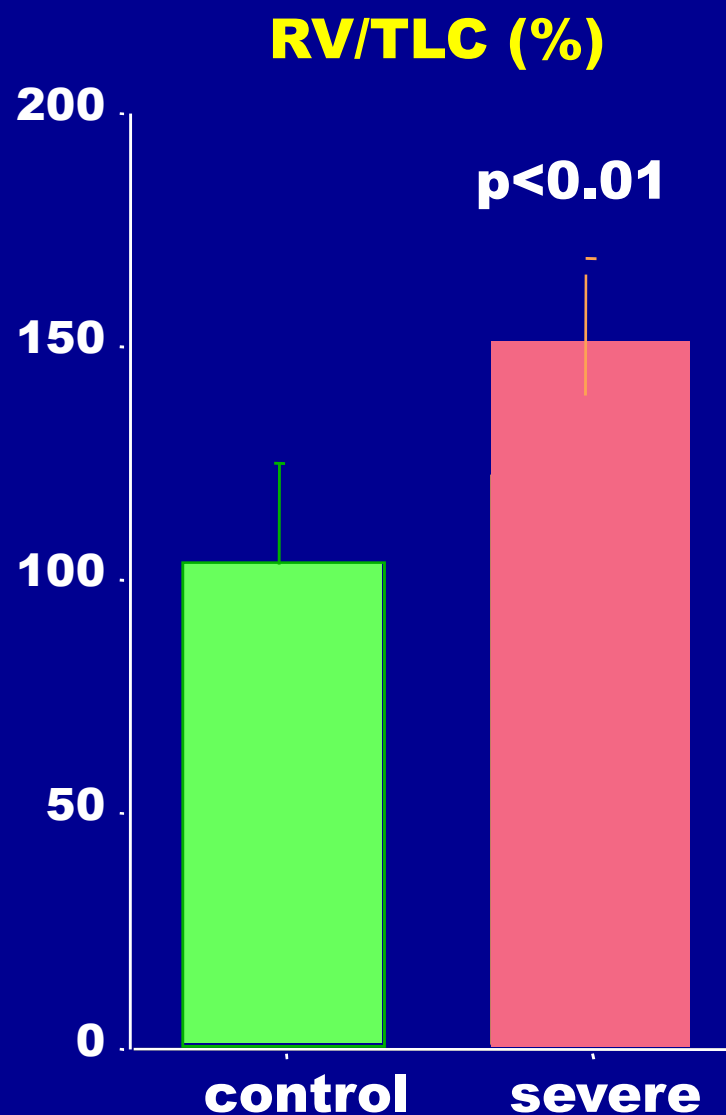
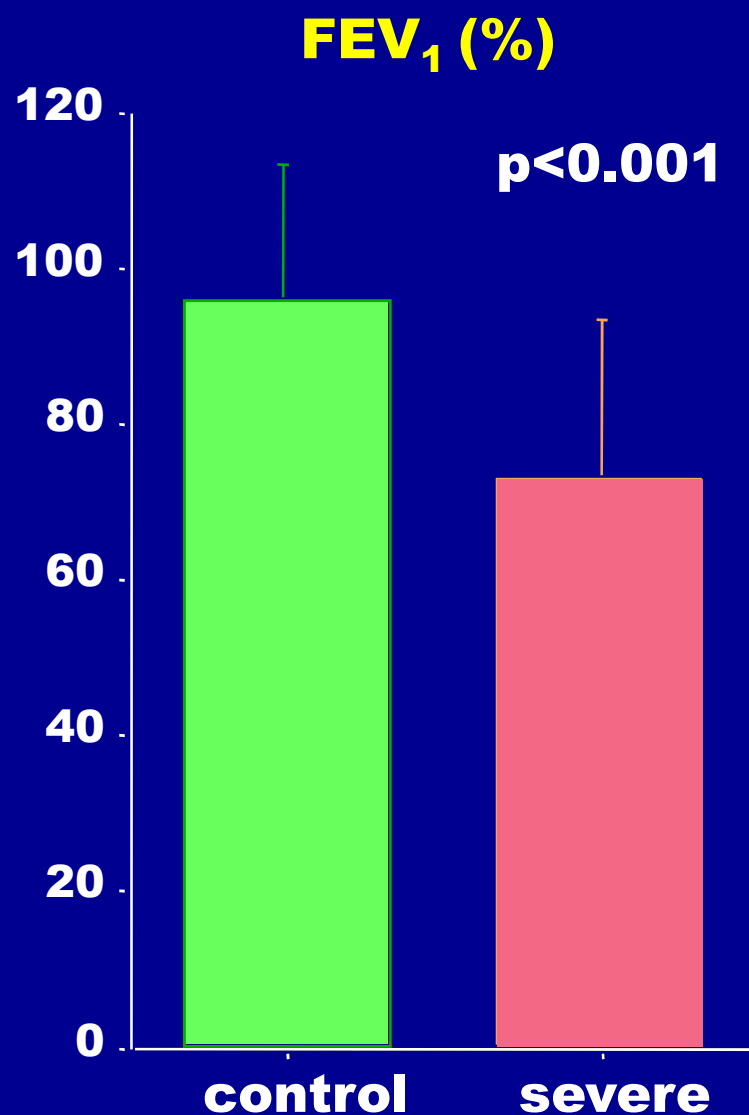
Reliever use

Activity

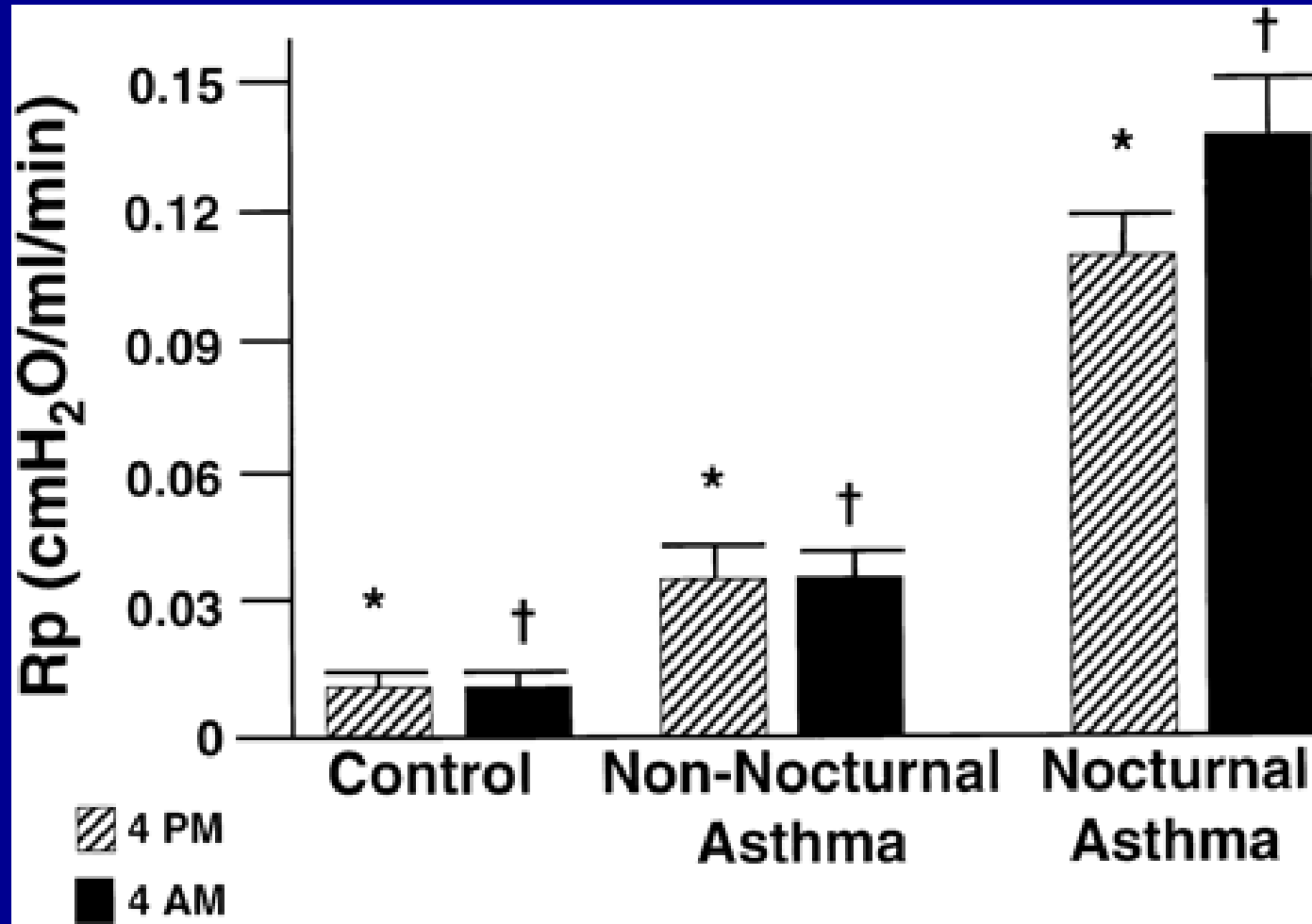
Lung function

Asthma not responsive to treatment
Nocturnal asthma
Recurrent exacerbations

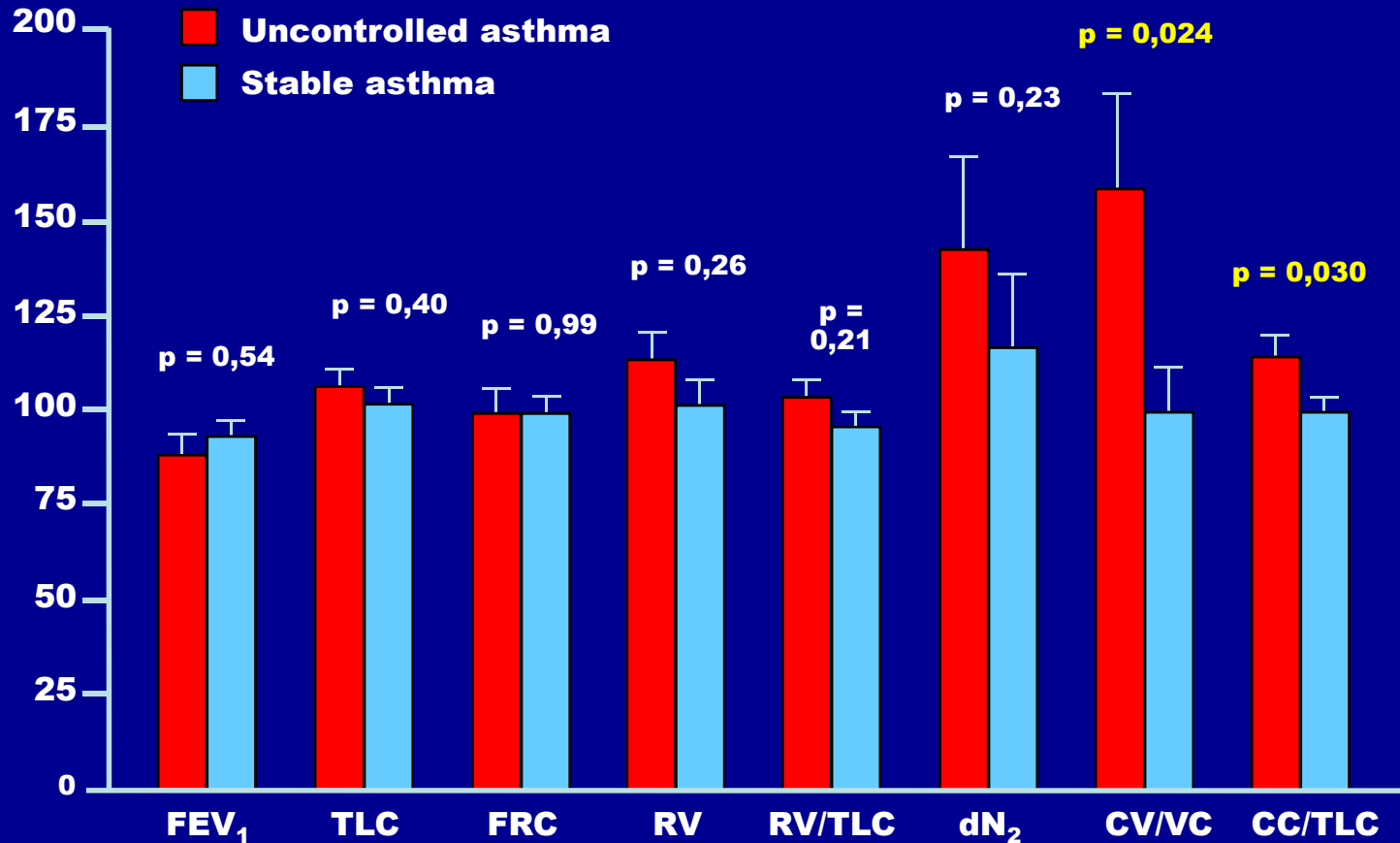
Functional parameters in severe asthma



Peripheral resistance is increased in nocturnal asthma



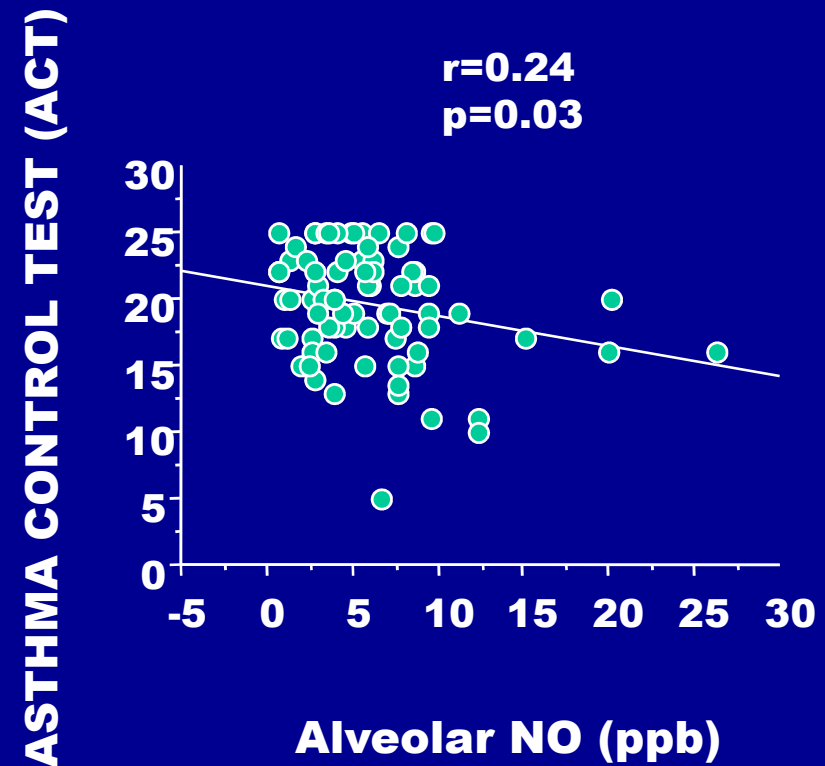
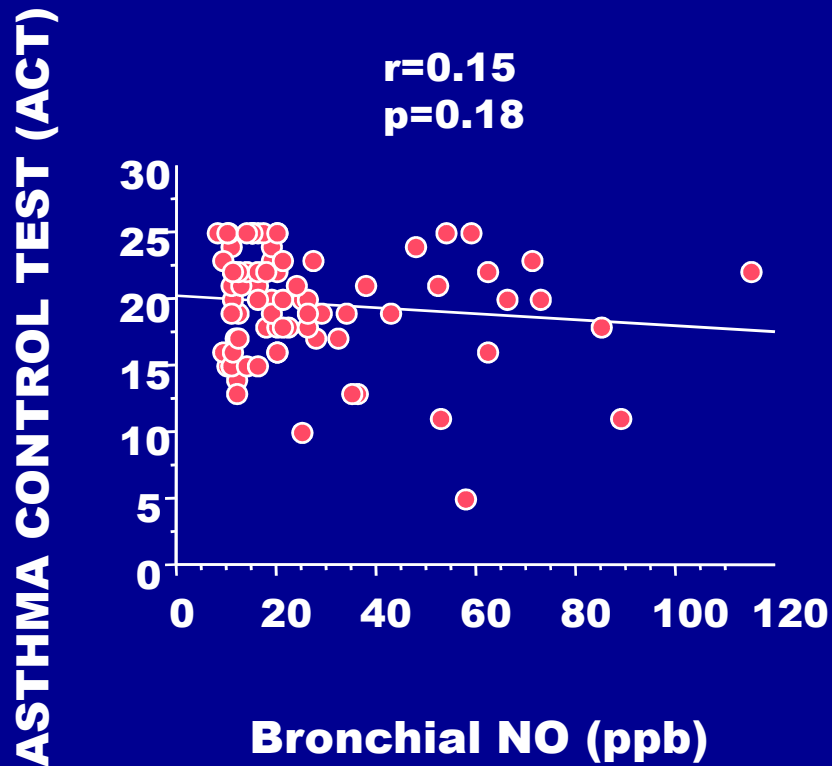
Uncontrolled asthma is associated with enhanced small airway closure



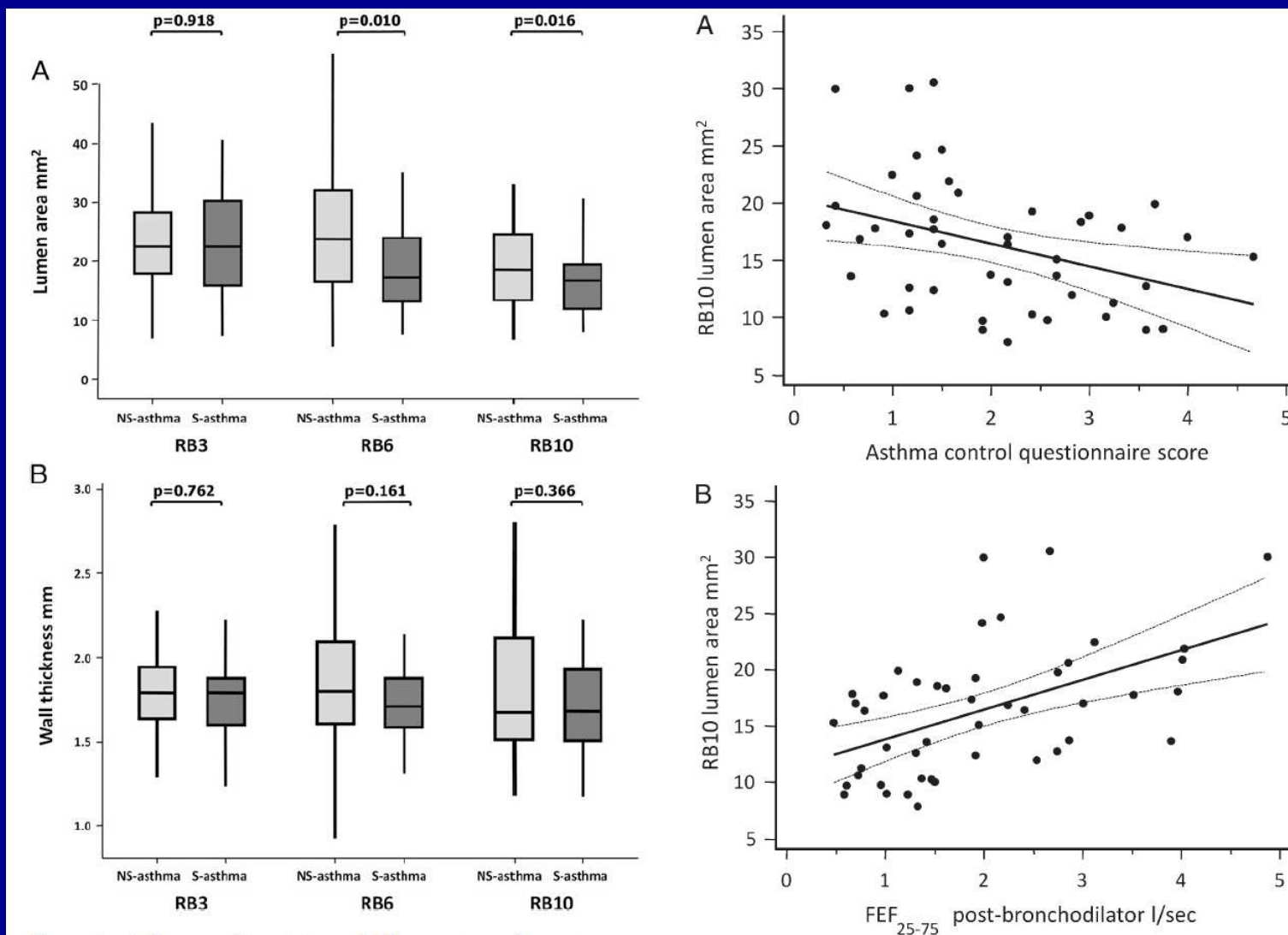
in 't Veen et al. Am J Respir Crit Care Med 2000

L'asma non controllato si associa ad alterazioni infiammatorie delle piccole vie aeree

Alveolar NO



La riduzione del lume delle piccole vie aeree all'imaging correla con lo scarso controllo di asma



La disfunzione delle piccole vie aeree si associa allo scarso controllo dell'asma

	Adjusted	
	OR (95% CI)	p-value
FEF_{25-75%} <70% (n=157) versus FEF_{25-75%} >70% (n=145)		
Oral steroid use	1.50 (0.91–2.48)	0.11
SABA use	1.91 (1.19–3.07)	0.007
FEV₁/FVC <0.80 (n=167) versus FEV₁/FVC >0.80 (n=135)		
Oral steroid use	1.85 (1.10–3.12)	0.02
SABA use	1.54 (0.95–2.51)	0.08
R_{5-R20} >0.07 kPa·L⁻¹·s (n=135) versus R_{5-R20} <0.07 kPa·L⁻¹·s (n=167)		
Oral steroid use	1.80 (1.09–2.98)	0.02
SABA use	1.87 (1.15–3.01)	0.01
FEF_{25-75%} <70% and R_{5-R20} >0.07 kPa·L⁻¹·s (n=83) versus FEF_{25-75%} >70% and R_{5-R20} <0.07 kPa·L⁻¹·s (n=93)		
Oral steroid use	2.34 (1.20–4.58)	0.01
SABA use	3.16 (1.64–6.07)	0.001
FEF_{25-75%} <70%, R_{5-R20} >0.07 kPa·L⁻¹·s and FEV₁/FVC <0.80 (n=72) versus FEF_{25-75%} >70%, R_{5-R20} <0.07 kPa·L⁻¹·s and FEV₁/FVC >0.80 (n=75)		
Oral steroid use	2.78 (1.28–6.04)	0.01
SABA use	2.96 (1.44–6.12)	0.003

DEFINIZIONE: 2006

Other clinical signs are only likely to be present if patients are examined during symptomatic periods. Features of hyperinflation result from patients breathing at a higher lung volume in order to increase outward retraction of the airways and maintain the patency of smaller airways (which are narrowed by a combination of airway smooth muscle contraction, edema, and mucus hypersecretion). The combination of hyperinflation and airflow limitation in an asthma exacerbation markedly increases the work of breathing.



GLOBAL STRATEGY FOR
ASTHMA MANAGEMENT AND PREVENTION

REVISED 2006

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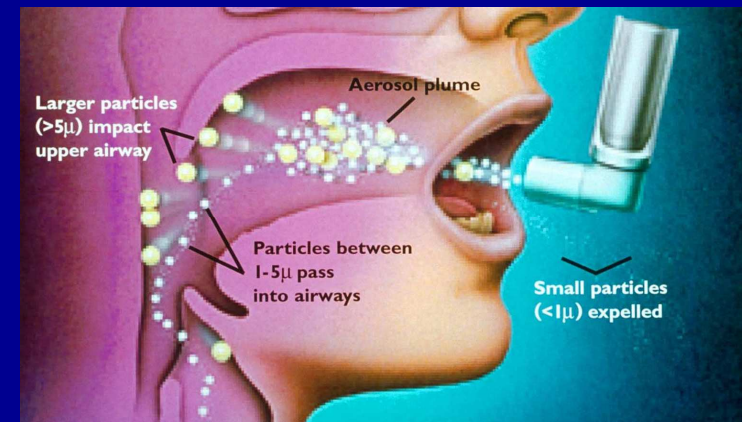
Assessing and accessing the small airways; implications for asthma management

Nicola Scichilone^{a,*}, Marco Contoli^b, Davide Paleari^c, Pietro Pirina^d, Andrea Rossi^e,
Claudio Maria Sanguinetti^f, Pierachille Santus^g, Matteo Sofia^h, Nicola Sverzellatiⁱ

Inhaler device

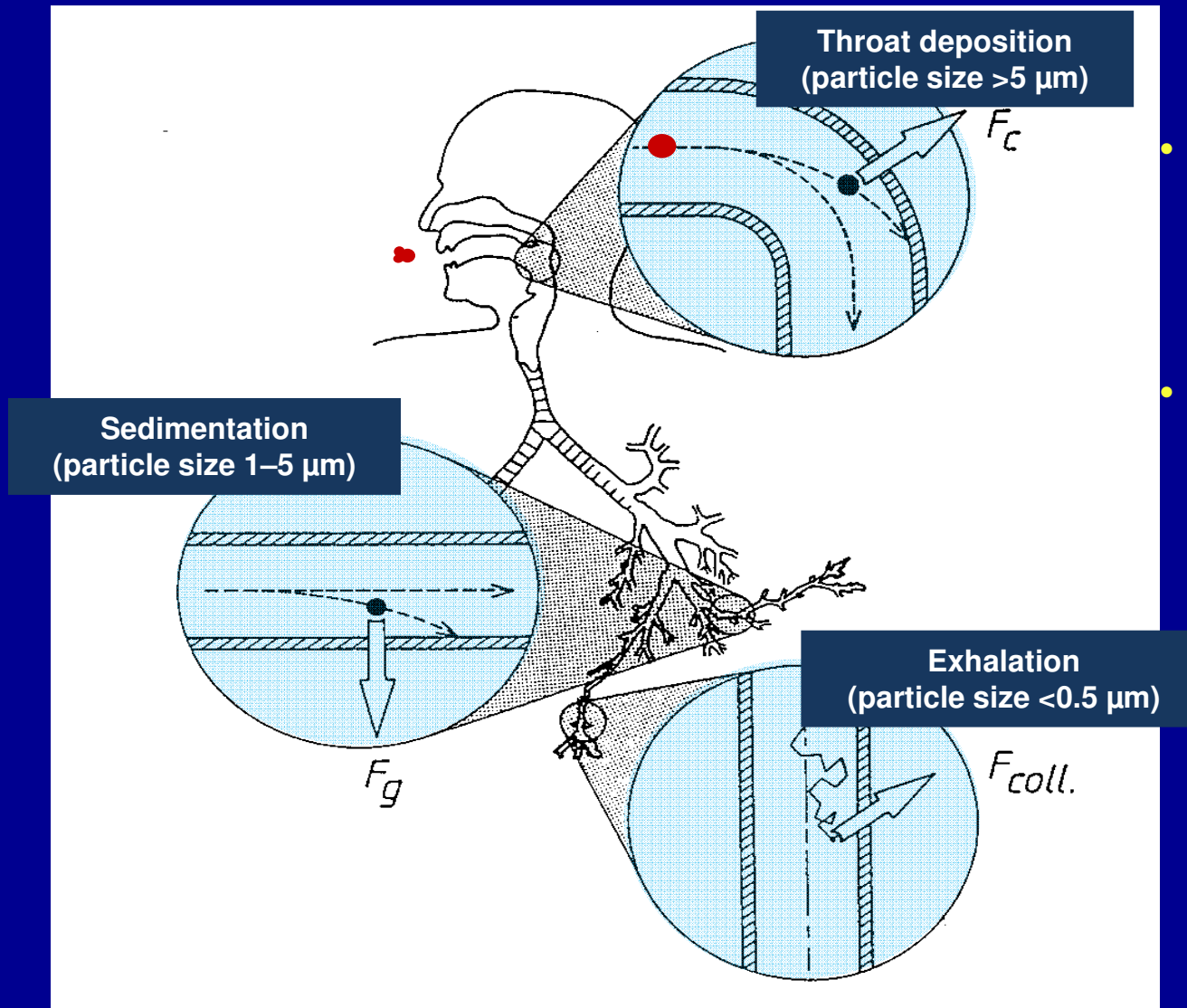


Particle size



How particle size affects penetration and deposition

- The efficacy with which inhaled drug particles reach the target site in the lung is determined by:

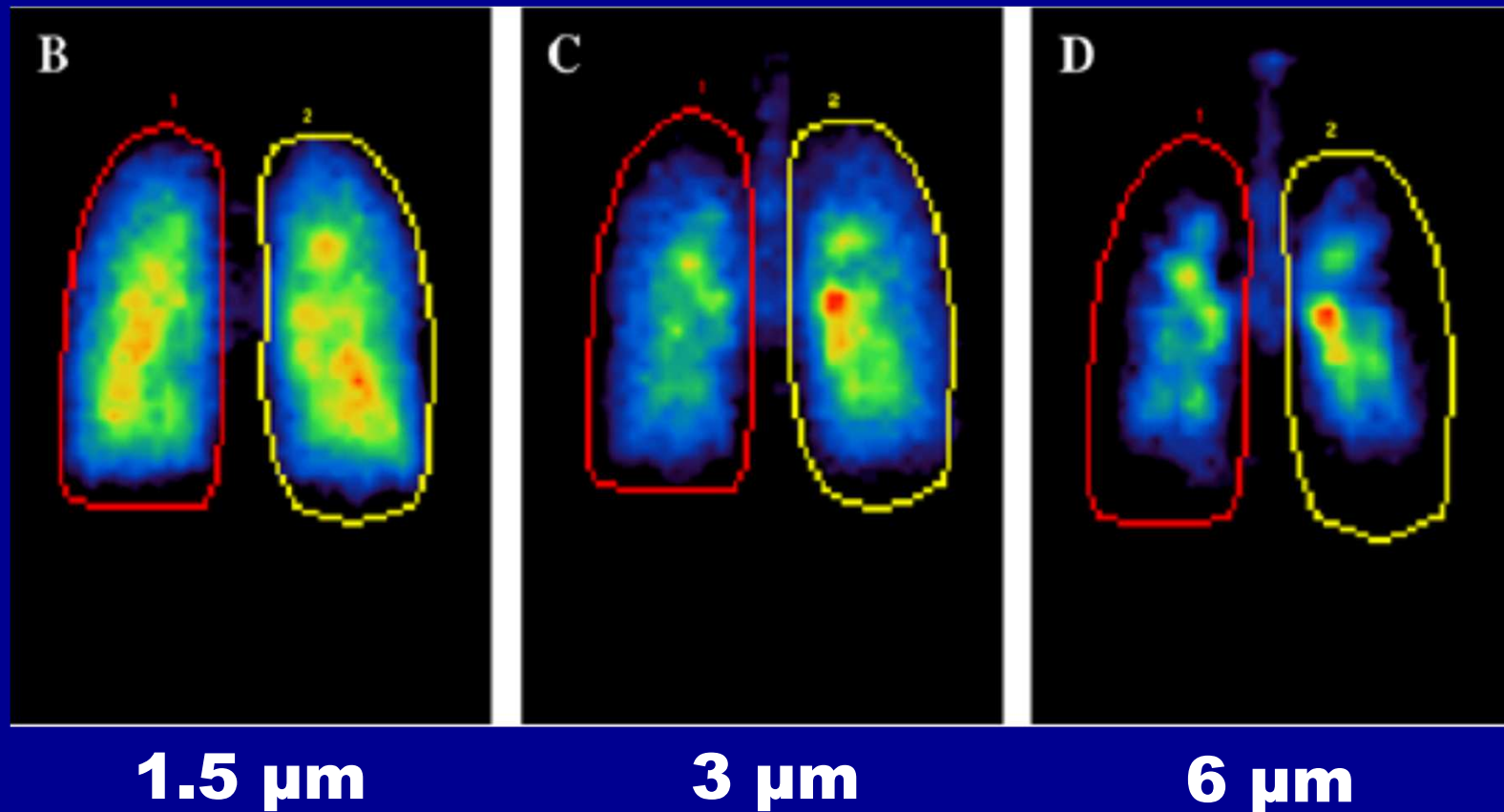


- Penetration of the particles into the airways
- Deposition of the particles on the wall of the airways

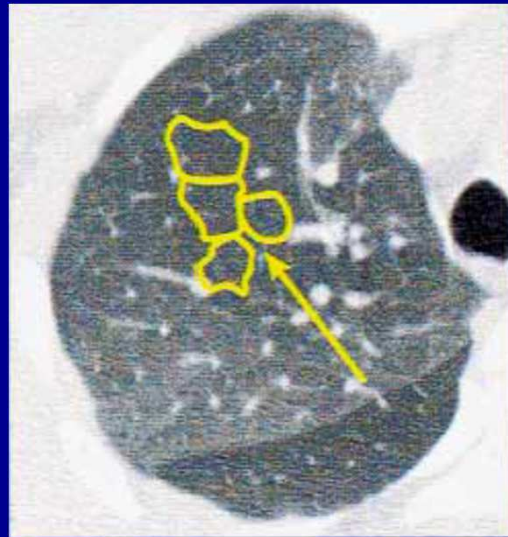
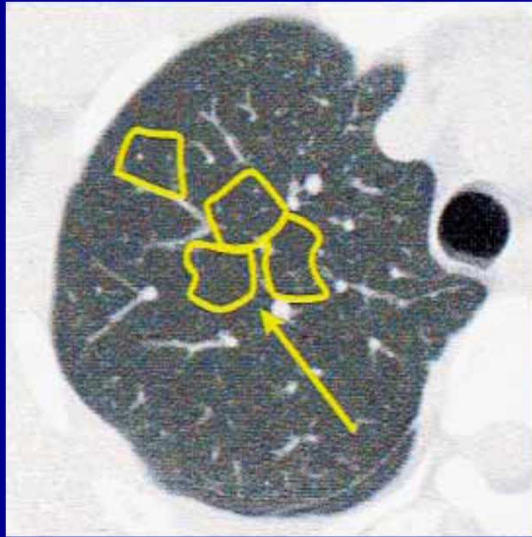
Regional Lung Deposition and Bronchodilator Response as a Function of β_2 -Agonist Particle Size

Omar S. Usmani, Martyn F. Biddiscombe, and Peter J. Barnes

National Heart and Lung Institute, Imperial College London; Royal Brompton Hospital, London, United Kingdom



Reduction in air trapping measured through HRCT in asthmatics treated with extrafine BDP compared with non extrafine BDP



Non extrafine BDP



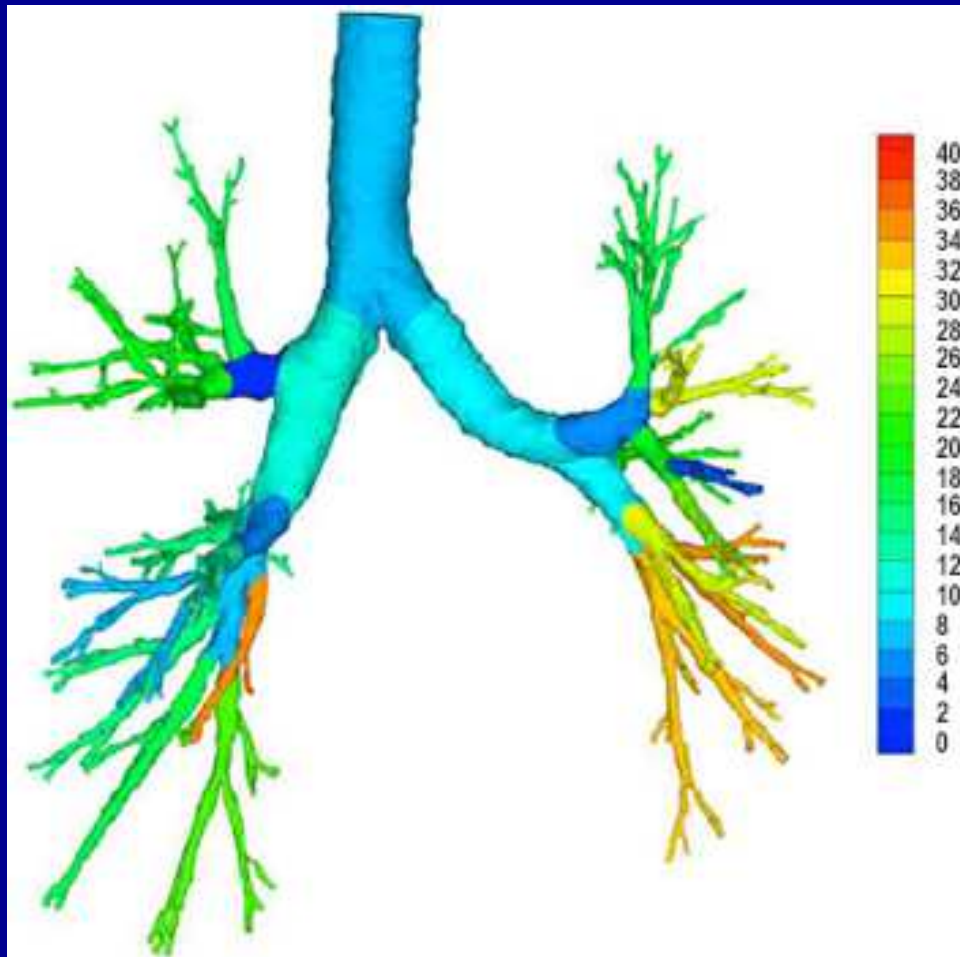
Extrafine BDP

baseline

4 weeks

*Goldin. JACI 1999;104:S258-
Vanden Burgt. JACI 2000;106:1209-*

Extrafine BDP/F guarantees uniform treatment of inflammation and bronchoconstriction both in large and small airways

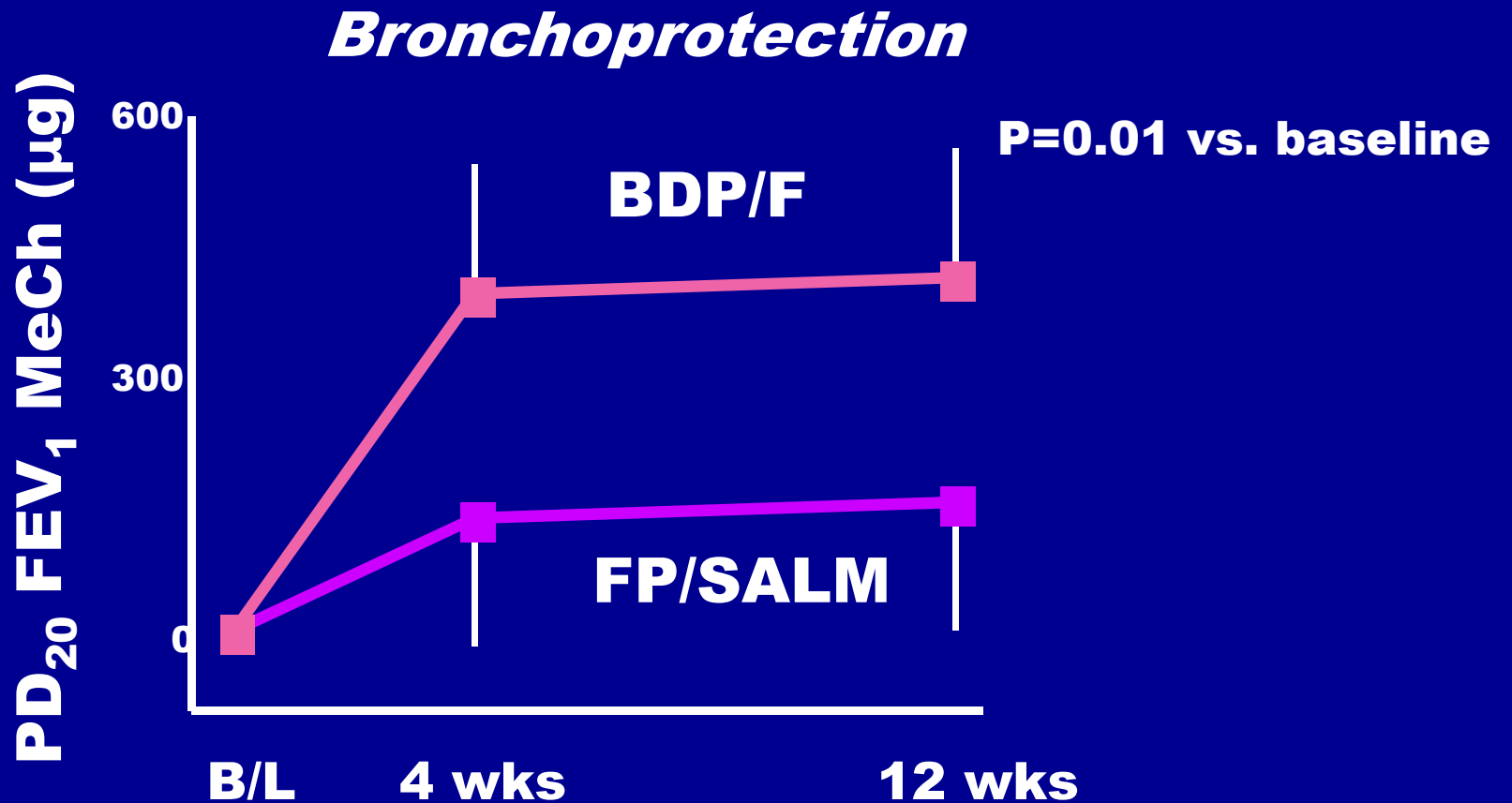


Airway volume changes from baseline (%) after 6 months of treatment and appropriate wash-out period for SABA.

Open-label clinical trial, 24 stable asthma patients, extrafine BDP/F fixed-dose combination vs baseline

Additional effects of extra-fine BDP/F on small and large airways

30 moderate-to-severe asthmatic patients



Controllo dell'Asma

- **L'obiettivo principale del trattamento è ottenere il “buon controllo” dell'asma**
- **Tale indice composito include tutte le principali misure cliniche e funzionali, ed è realisticamente raggiungibile in una alta percentuale di pazienti**
- **Il solo controllo delle riacutizzazioni, senza tener conto dei sintomi quotidiani e del livello di funzione polmonare, non è sufficiente**

REVIEW ARTICLE

DRUG THERAPY

Asthma

Christopher H. Fanta, M.D.

Controllo = prevenzione delle manifestazioni cliniche mediante soppressione dell'infiammazione bronchiale

“When asthma symptoms are infrequent, shortlived, and mild, occasional administration of a quick-acting bronchodilator to reverse smoothmuscle constriction in the airways is an acceptable approach. However, as symptoms become more frequent or more severe, the emphasis changes to prevention of symptoms (and of asthmatic attacks)... by suppressing airway inflammation”

Miglioramento della morbilità e mortalità per asma negli ultimi anni, grazie ad un maggiore uso preventivo della terapia di fondo

Despite the persistently high prevalence of disease, the most recently available data indicate improved outcomes, with fewer annual hospitalizations for asthmatic attacks and fewer asthma-related deaths. Among the possible explanations for these favorable trends are the more widespread preventive use of inhaled corticosteroids

Fanta CH, New Engl J Med 2009

Asthma Management Failure: A Flaw in Physicians' Behavior or in Patients' Knowledge?

FULVIO BRAIDO,^{1,*} ILARIA BAIARDINI,¹ STEFANIA MENONI,² VITO BRUSASCO,³ STEFANO CENTANNI,⁴
GIUSEPPE GIRBINO,⁵ ROBERTO DAL NEGRO,⁶ AND GIORGIO WALTER CANONICA¹

Why do doctors and patients not follow guidelines? Iliaria Baiardini, Fulvio Braido, Matteo Bonini, Enrico Compalati and Giorgio Walter Canonica

Allergy and Respiratory Diseases, Department of Internal Medicine (DIMI), University of Genoa, Genoa, Italy

Correspondence to Giorgio Walter Canonica, Allergy and Respiratory Diseases, Department of Internal Medicine (DIMI), 10 Pad Maragliano, Largo Rosanna Benzi, 16132 Genoa, Italy
Tel: +39 01 03538933; fax: +39 01 03538904;
e-mail: canonica@unige.it

Purpose of review

The aim of this review is to evaluate the factors related to the doctor and the patient that could make following the guidelines difficult. It also underlines the importance of the adherence to guidelines themselves in order to ameliorate both the control of healthcare and the patients' quality of life.

Recent findings

Following guidelines not only depend on factors related to guidelines themselves,