Exercise and Asthma: What patients and doctors can do to improve outcomes

Timothy Craig, DO
Professor of Medicine and Pediatrics
Distinguished Educator
Program Director
Penn State University
Hershey, PA, USA

Conflicts of Interest

Research

- Novartis
- GSK
- Forest
- Genentech
- Merck

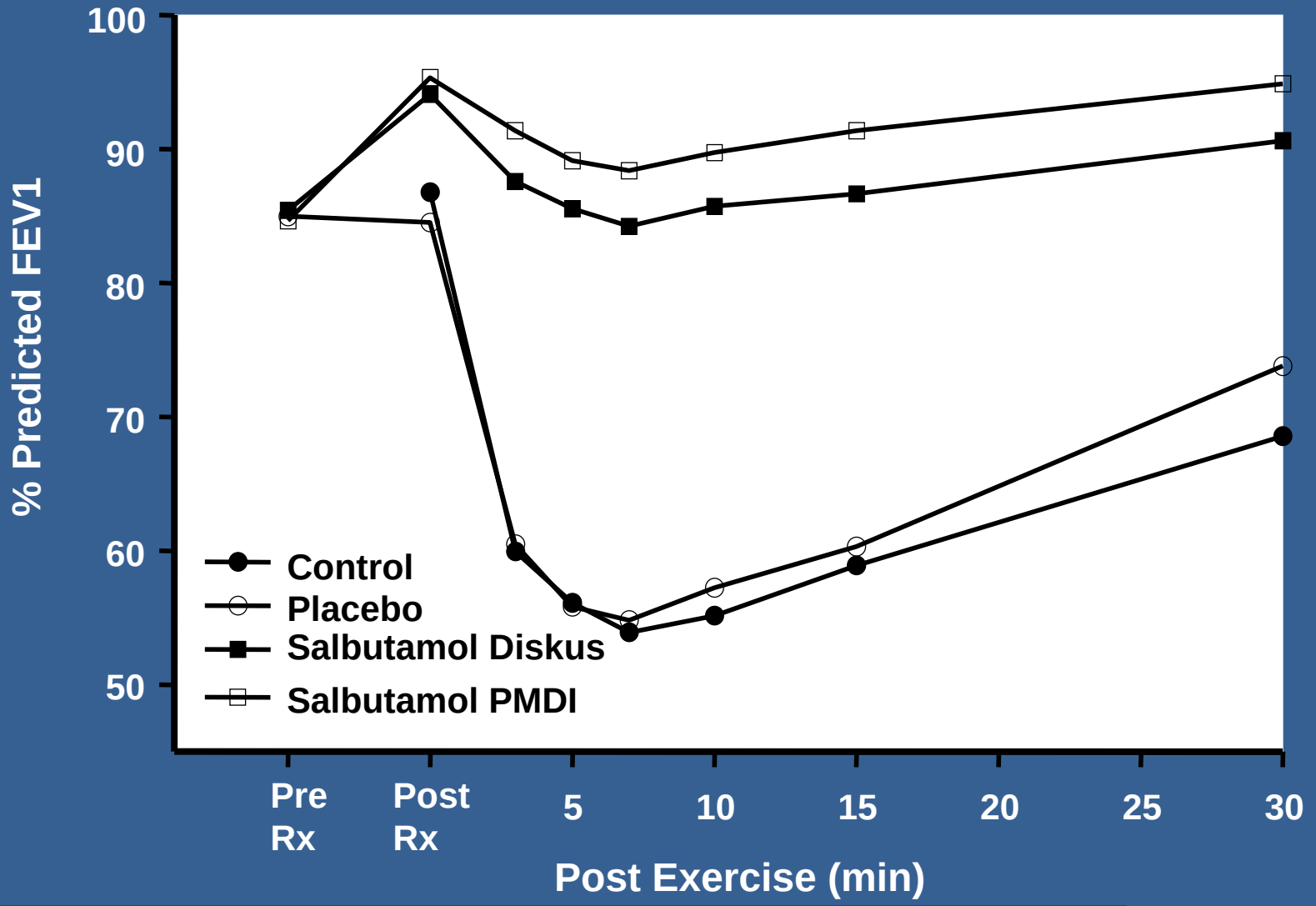
Speaker

- Teva
- Merck

Objectives

- ***1. To understand the physiology of EIB***
- ***2. To be able to diagnose EIB***
- ***3. To successfully treat EIB***
- ***4. To understand that patients with asthma avoid exercise***
- ***5. Demonstrate the importance of exercise in mice and humans with asthma***

Changes in FEV1 Before & After 8 minutes Cycling Exercise in 27 adult asthmatics



Anderson SD et al Med Sci Sports Exerc 2001; 33:893-900.

What causes EIB?

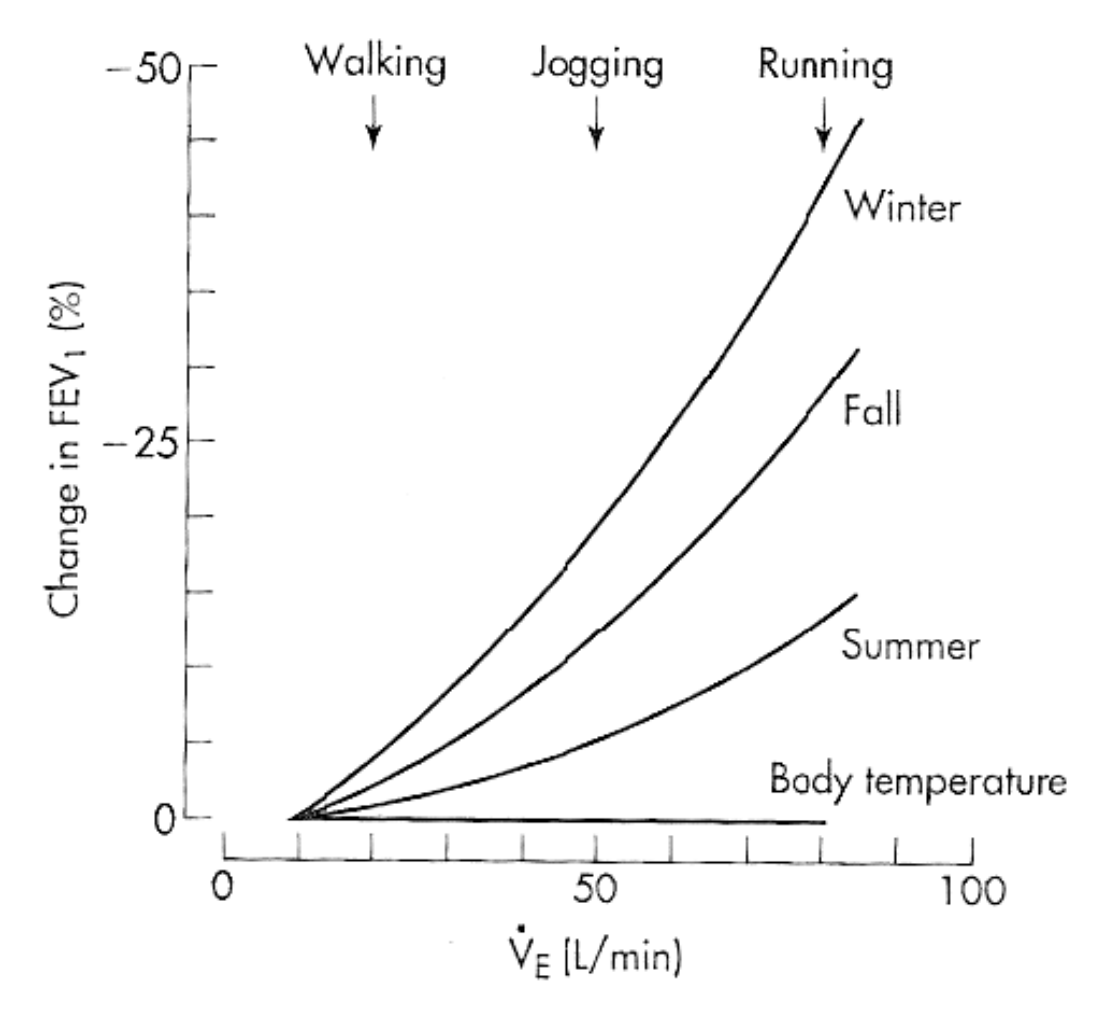
- A. Hot humid air
- B. Cold air
- C. Dry air
- D. Ozone
- E. Both cold and dry air

- Ans:

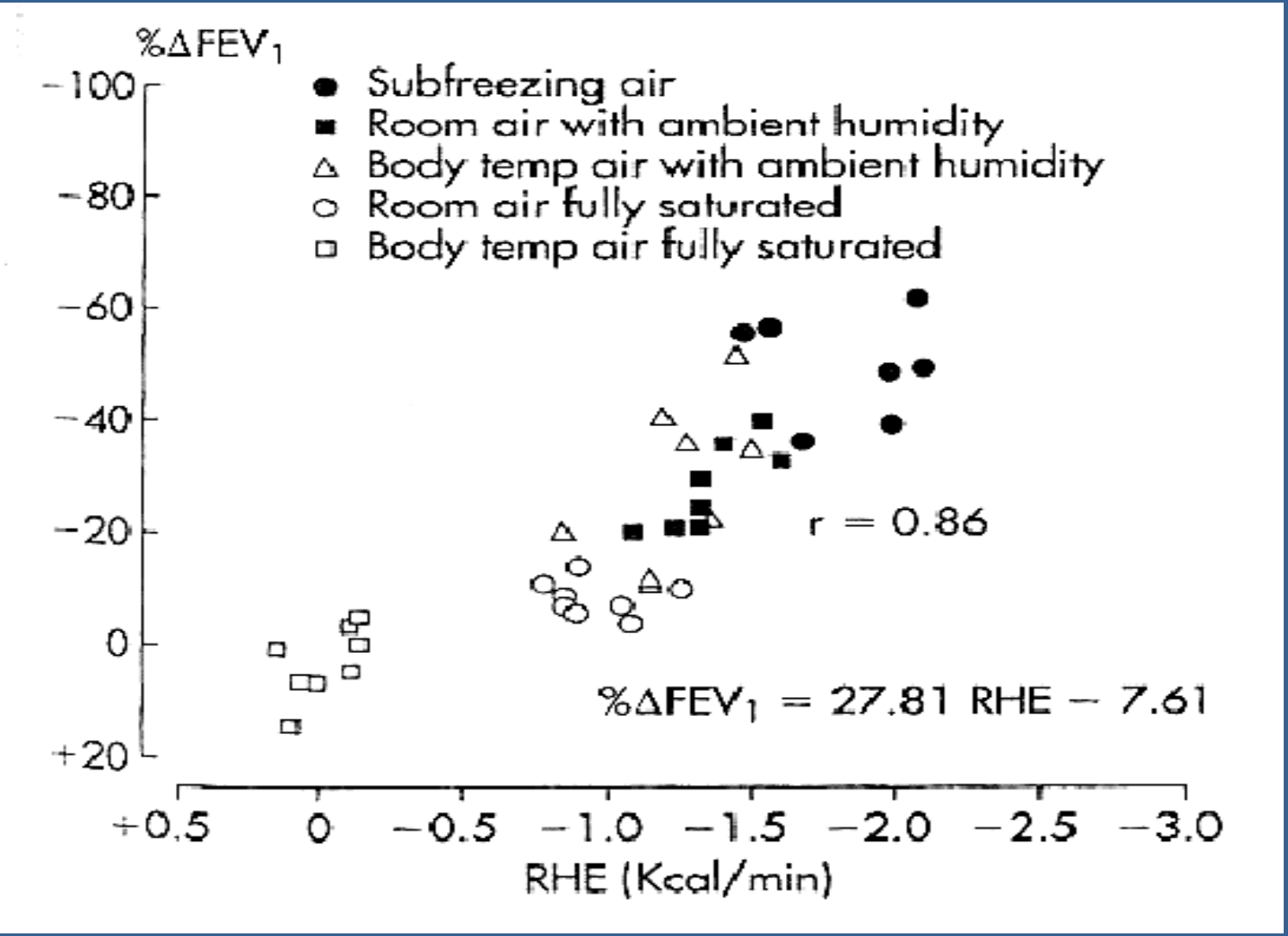
What causes EIB:

- A. Hot humid air
- B. Cold air
- C. Dry air
- D. Ozone
- E. Both cold and dry air

- Ans: C

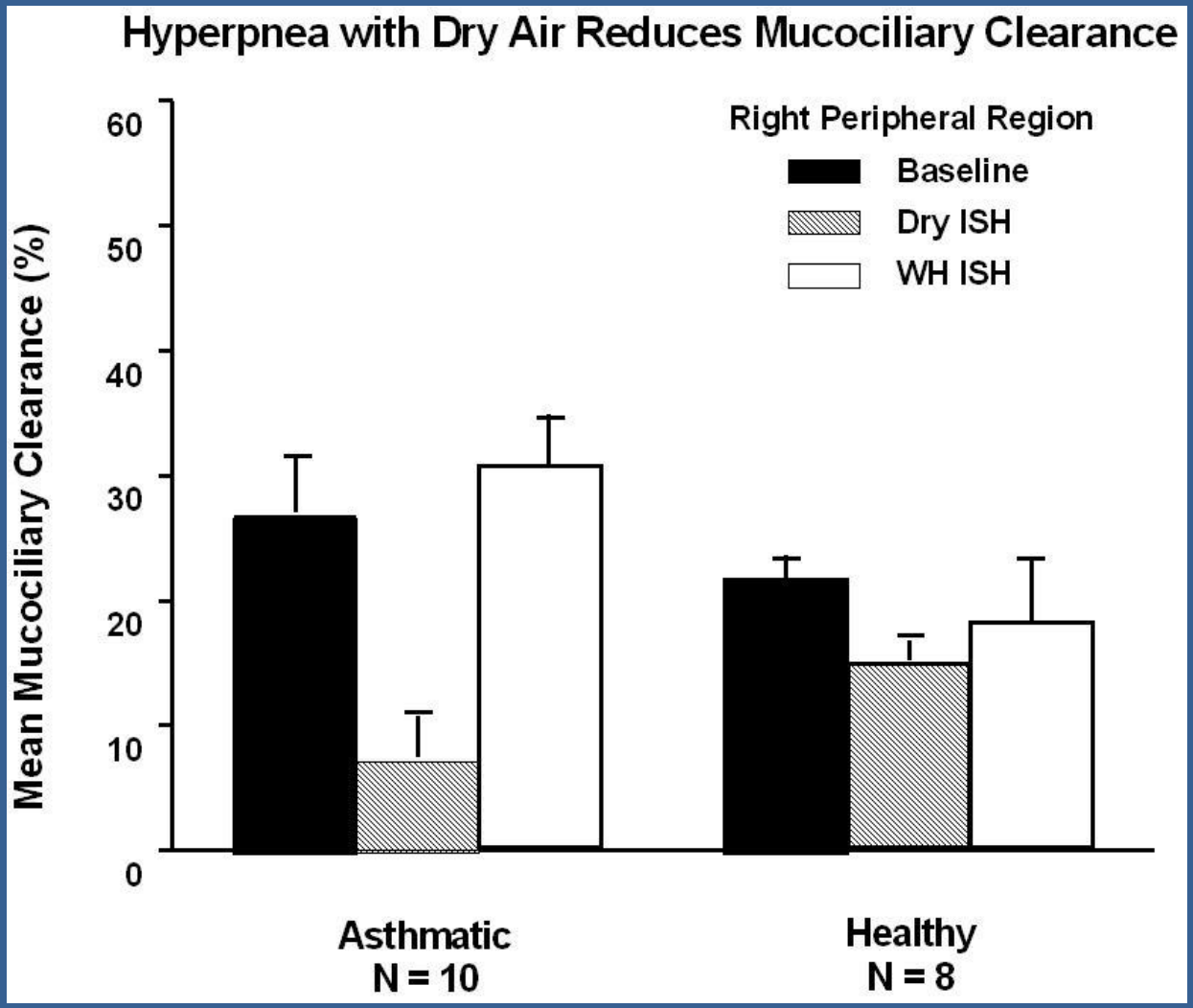


- McFadden ER, Gilbert IA. Exercise-induced asthma, NEJM 1994;330 (19):1362-7.



RHE= Respiratory Heat Exchange

- From Deal ECJr,McFaddenERJr,Ingram RH Jr,et al:J Appl Physiol 57:608-609,1984



Reproduced from Daviskas E, Anderson SD, Gonda I, Chan HK, Cook P, Fulton R. Changes in mucociliary clearance during and after isocapnic hyperventilation in asthmatic and healthy subjects. Eur Respir J 1995;8:742-751.

Inflammatory Cells in sputum with EIB

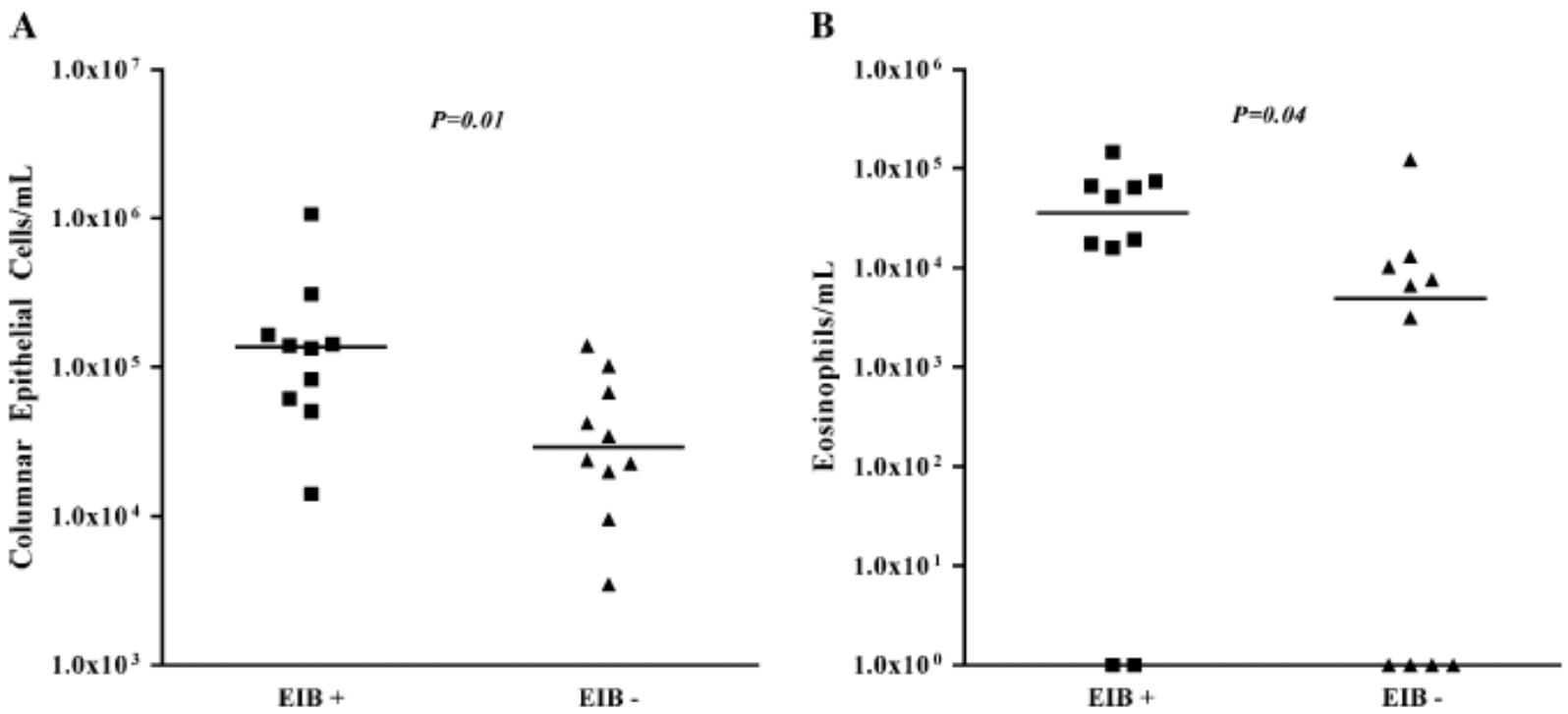
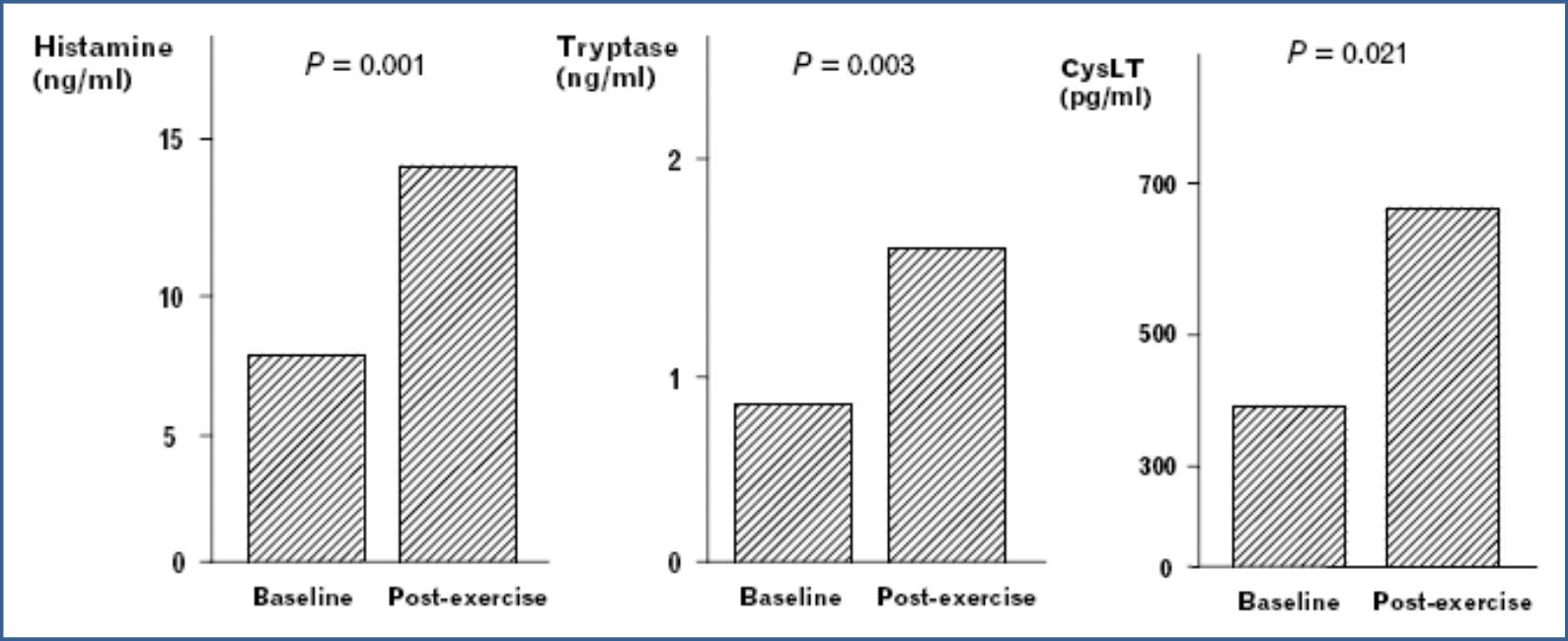


FIG 3. Comparison of the concentration of columnar epithelial cells (A) and the concentration of eosinophils (B) in induced sputum between asthmatic subjects with EIB and asthmatic control subjects without EIB. The median concentration of columnar epithelial cells and eosinophils was higher in the group with EIB.

Hallstrand et al, JACI 2005;116:586-593

Inflammatory mediators in EIB



Curr Opin Allergy Clin Immunol 2006,6:37-42

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DIFFERENTIAL DIAGNOSIS FOR EIB

- Asthma
- Pulmonary diseases other than asthma: bronchitis, pneumonia, emphysema, pulmonary embolism, CF, croup, bronchiolitis
- GE reflux
- Anaphylaxis
- Severe nasal congestion
- Laryngeal dysfunction, VCD
- Carcinoid tumor
- Cardiac
- Poor conditioning

Storms, WW. *Medical Science and Sports Exercise* (1 Suppl):S33-8.1999

What percent of children with dyspnea will have EIB on exercise challenge test?

- A. 1
- B. 11
- C. 55
- D. 85
- E. 95

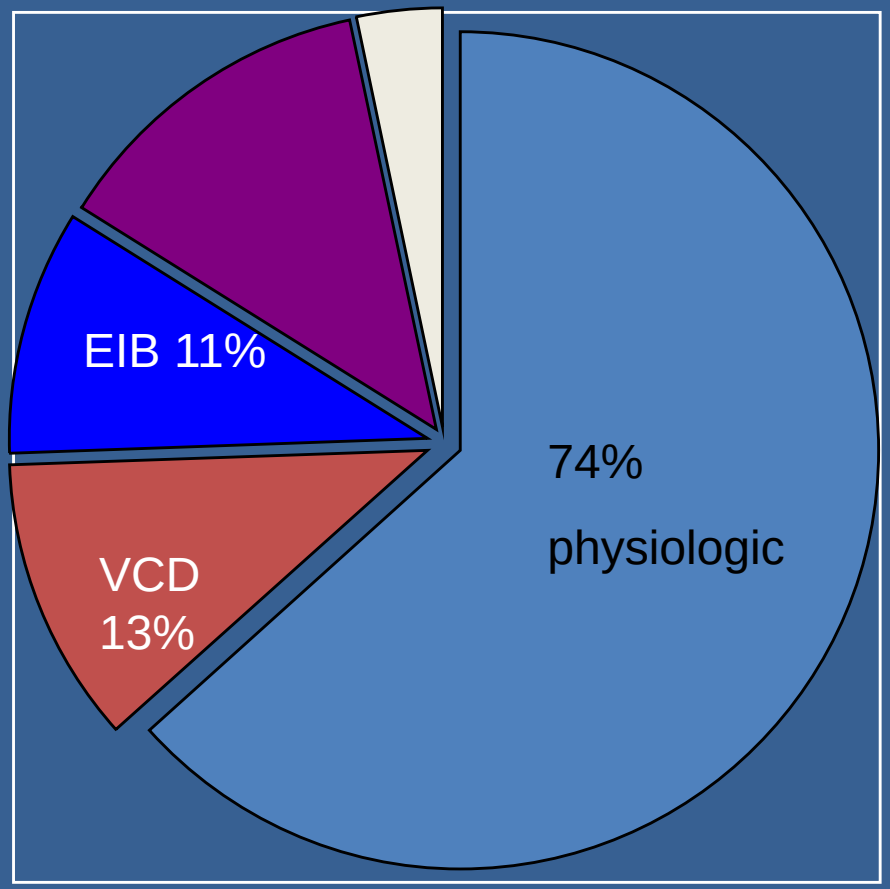
- Ans:

What percent of children with dyspnea will have EIB on exercise challenge test?

- A. 1
- B. 11
- C. 55
- D. 85
- E. 95

- Ans: B

Percent diagnosis of 117 children with exercised induced dyspnea diagnosed by treadmill



Weinberger et al 2008

Is the history of EIB reliable in athletes?

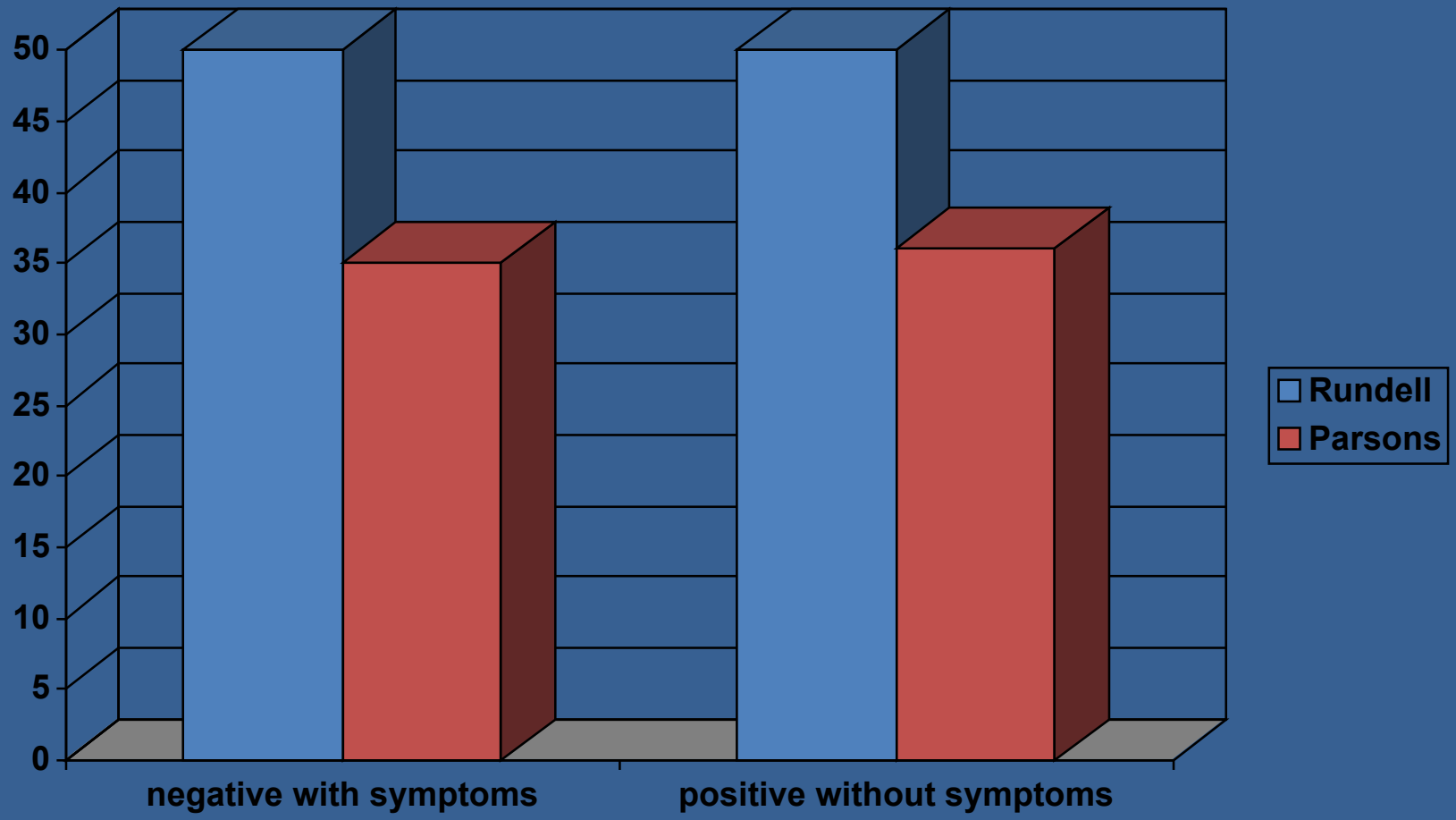
- A. No
- B. Yes

Is the history of EIB reliable in athletes?

- A. No
- B. Yes

- Answer: no

Exercise challenge Results in Athletes with Symptoms of EIB



Evaluation:

- Detailed history and exam
- Prevented by albuterol before exercise.
- PFT pre and post beta-agonists
- Challenge test, but what type?
  - free run
  - controlled exercise challenge
  - surrogate challenge

Exercise Challenge: external source dry air

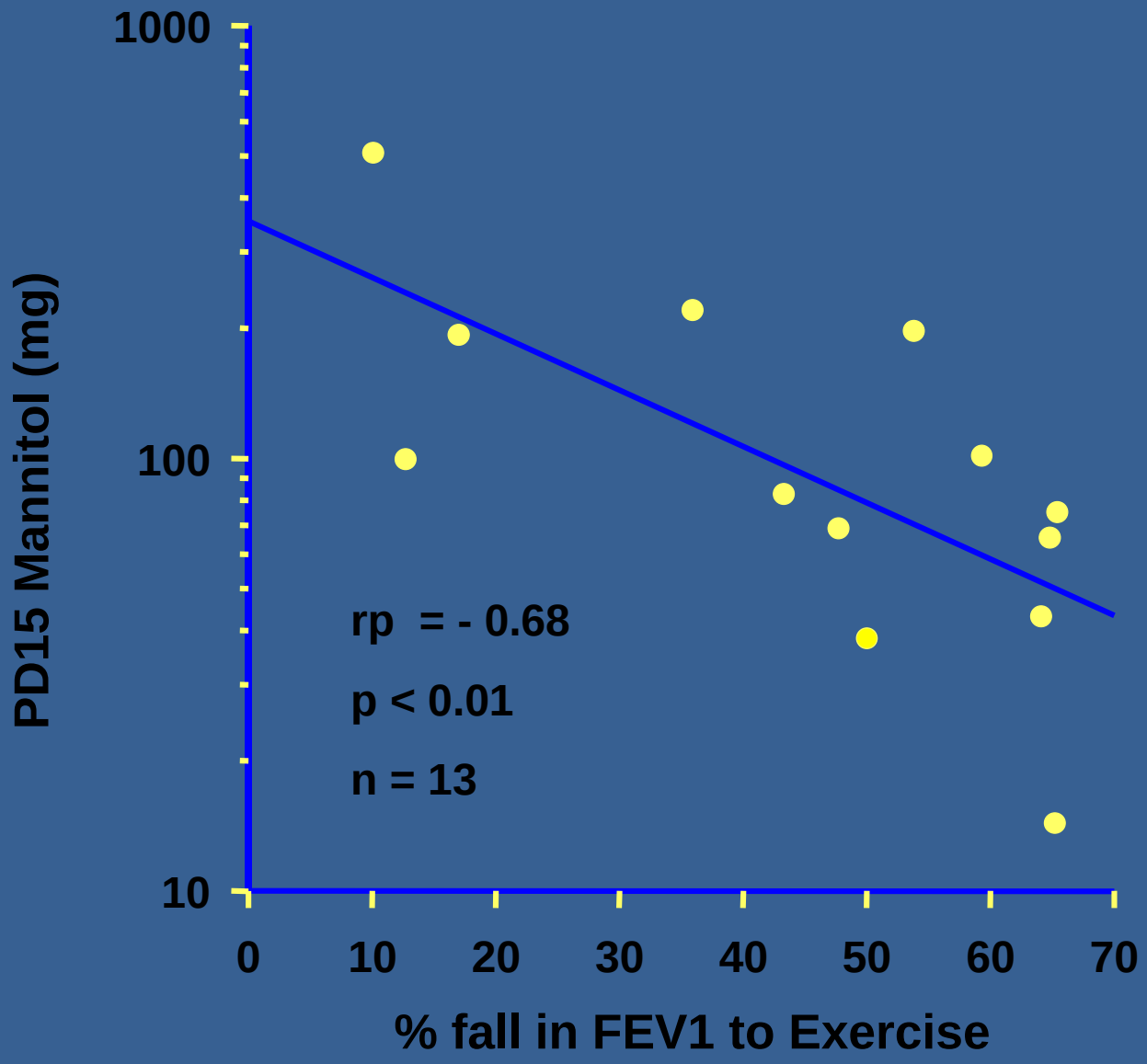
Step	Duration	Target HR	Treadmill Rate	Treadmill Incline
1	2 minutes	50% MHR	2.5 mph	0%
2	2 minutes	70% MHR	increase	increase
3	6 minutes	>80% MHR	increase	increase

ACRN Manual of Operations

Positive test

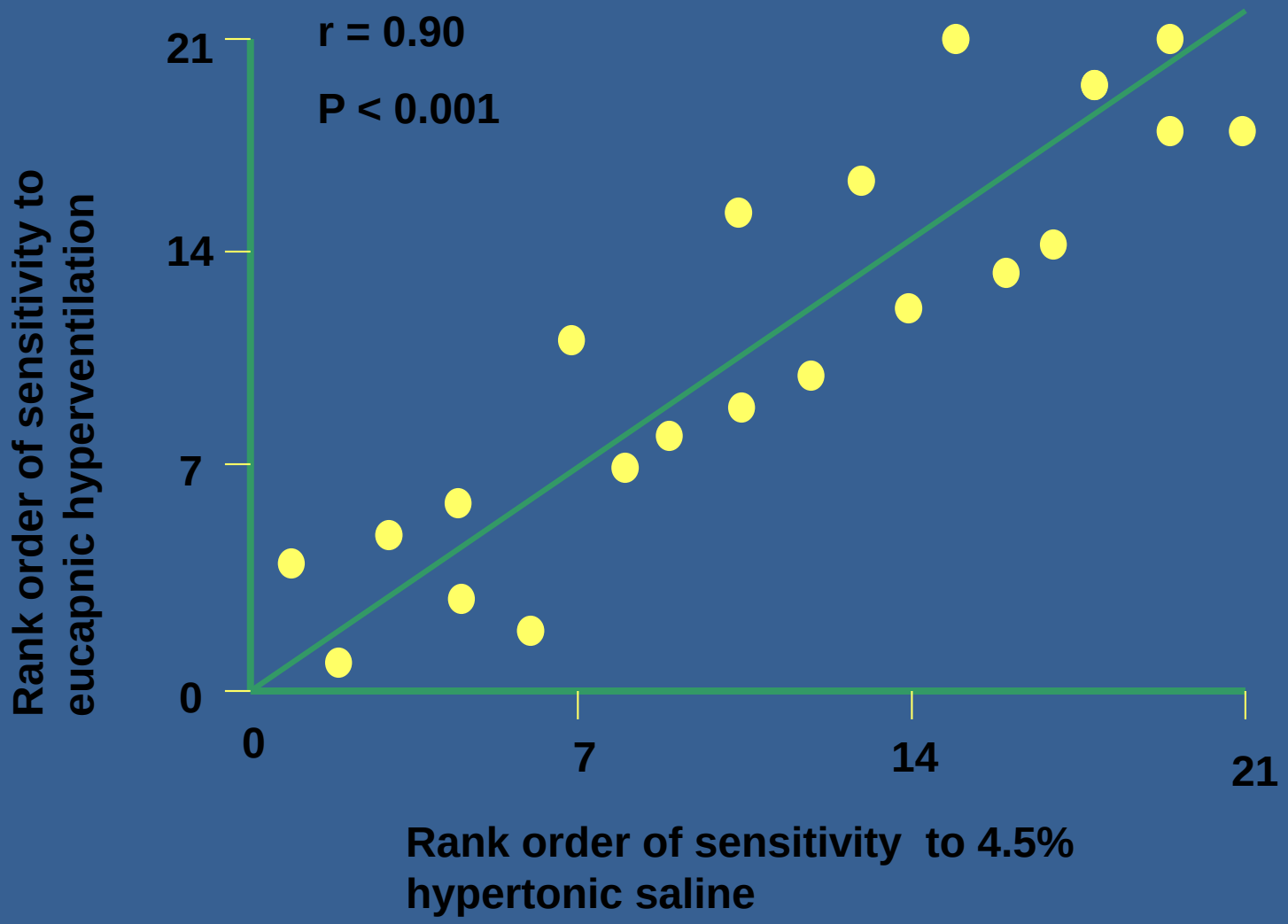
- Adequate test is 8 minutes with >80% MHR achieved in 2 minutes, with 6 minutes at MHR
- Ventilation should be 40-60% MVV
- Positive EST: symptoms with 10% or more drop in FEV-1
- If negative on treadmill do a “in venue challenge” in children or surrogate test for adults

% fall in FEV1 after exercise in relation to PD15 to mannitol



Brannan et al, AJRCCM 1998; 158:1120-6

Relationship of sensitivity to EVH & sensitivity to 4.5% saline



Smith CM & Anderson SD Eur Respir J 1989; 2: 36-43

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The effect of inhaled corticosteroids on EIB is?

- 1. not effective to eliminate EIB
- 2. reduces EIB by 10%
- 3. reduces EIB by 25%
- 4. reduces EIB by 50%
- 5. reduces EIB by greater than 75%

- Ans:

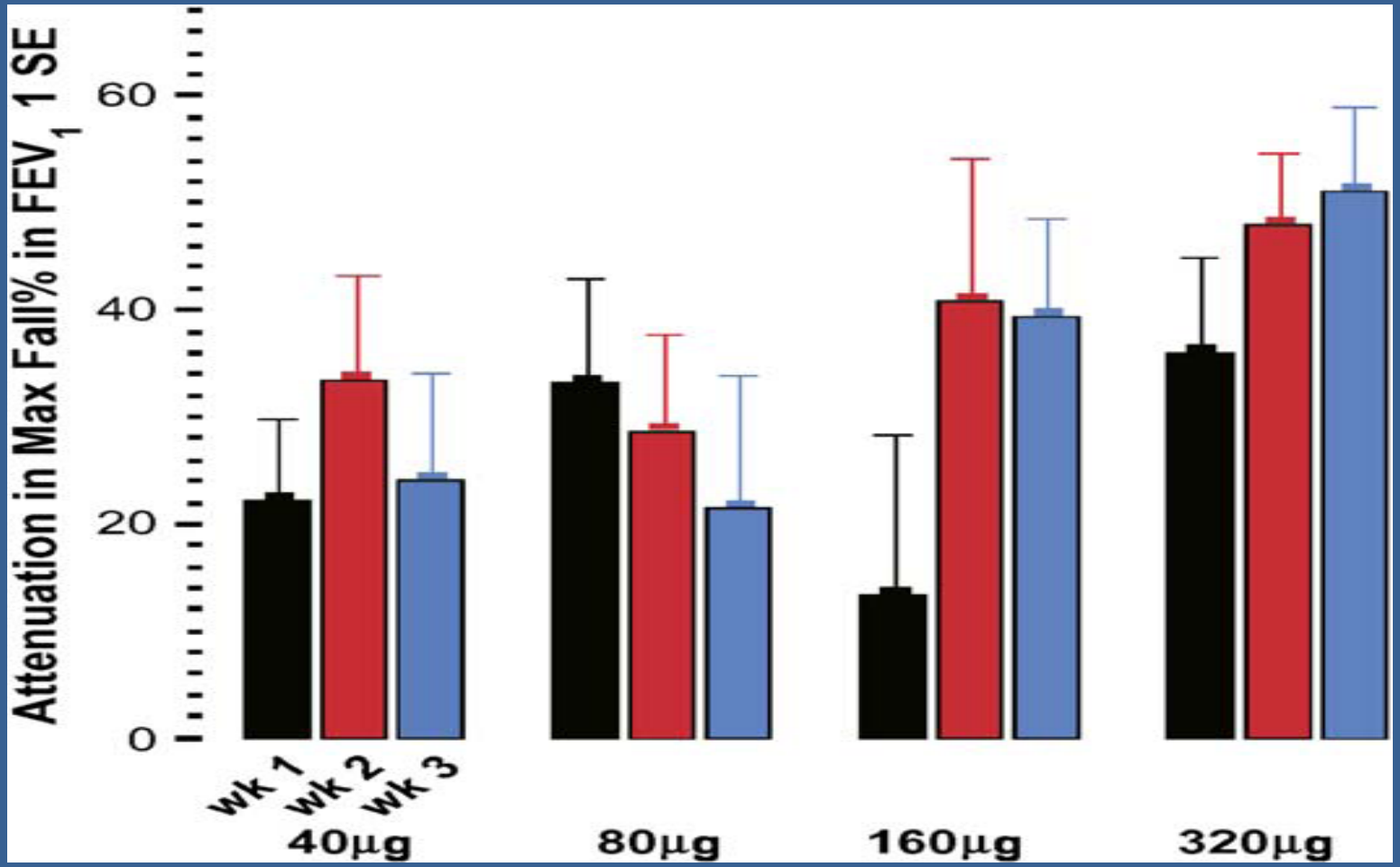
The effect of inhaled corticosteroids on EIB is?

- 1. not effective to eliminate EIB
- 2. reduces EIB by 10%
- 3. reduces EIB by 25%
- 4. reduces EIB by 50%
- 5. reduces EIB by greater than 75%

- Ans: 5

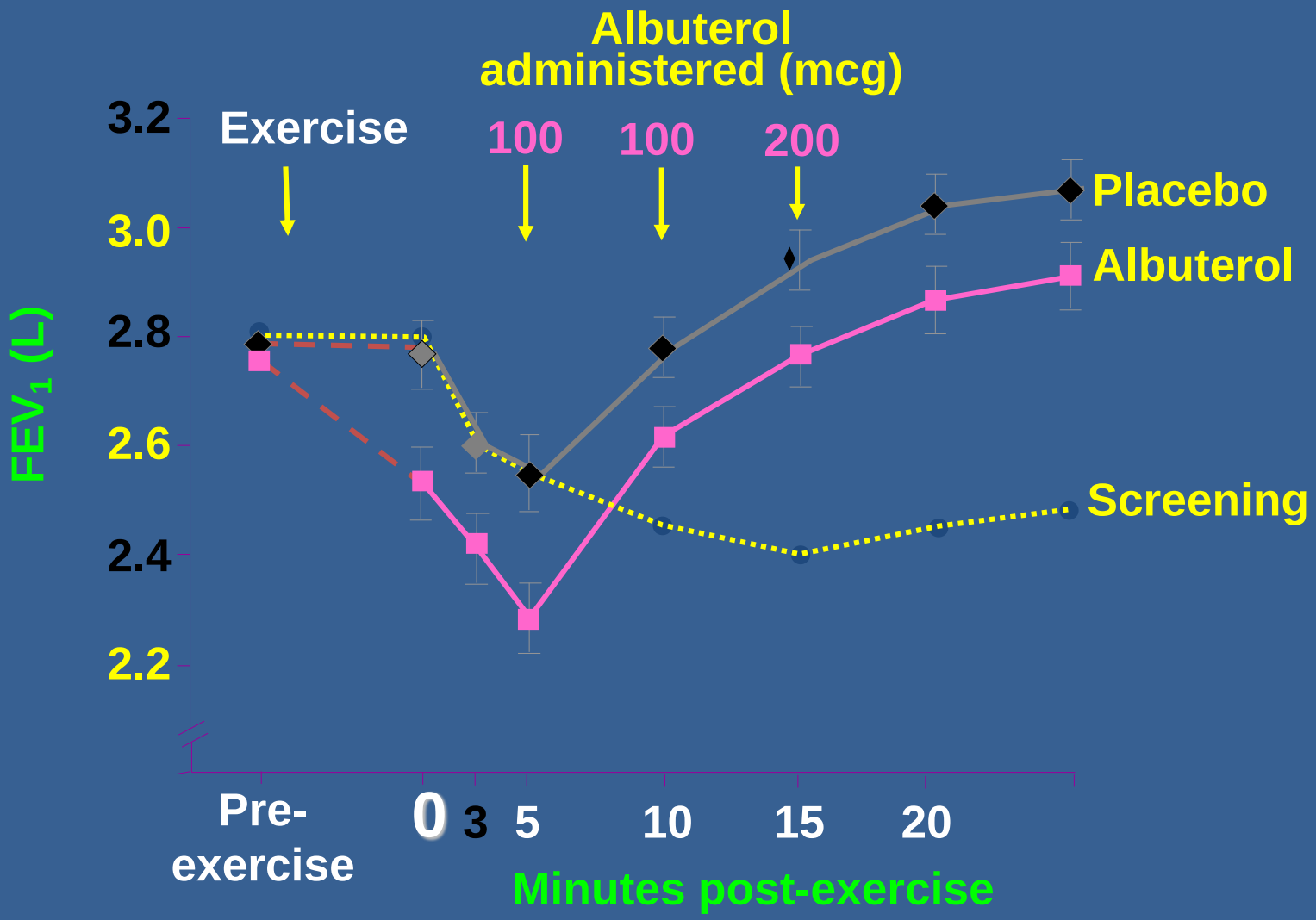
Effect of progressive doses of ICS on EIA

Average attenuation of EIA was 30% for all doses, but with 25% in low doses and 50% in higher doses of qd ciclesonide, compared to up to 65 to 80% in other bid studies



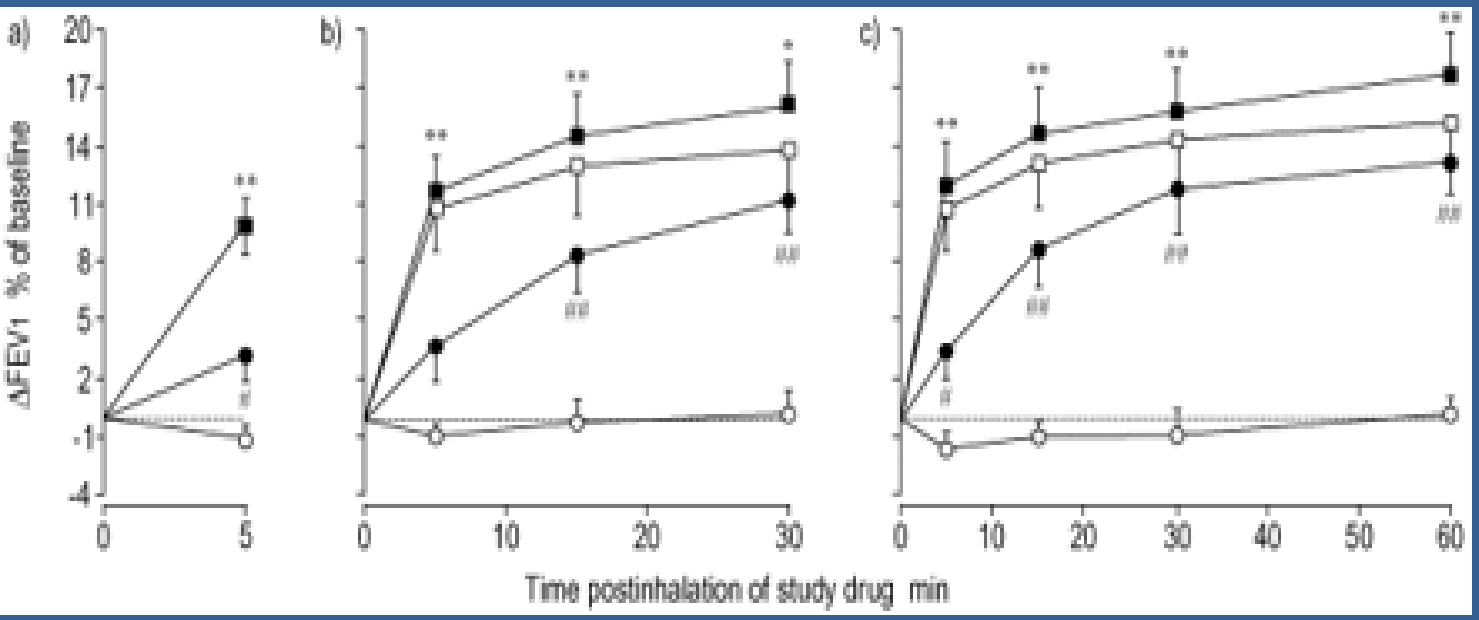
Subbarao. JACI 2006; 117: 1008

Regular Use of Beta-agonists May Lead to Increased EIB



Hancox RJ, et al. *Am J Respir Crit Care Med*. 2002; 65(8):1068–1070.

Comparing salmeterol, formoterol and terbutaline for EIA by change in % FEV-1 over time

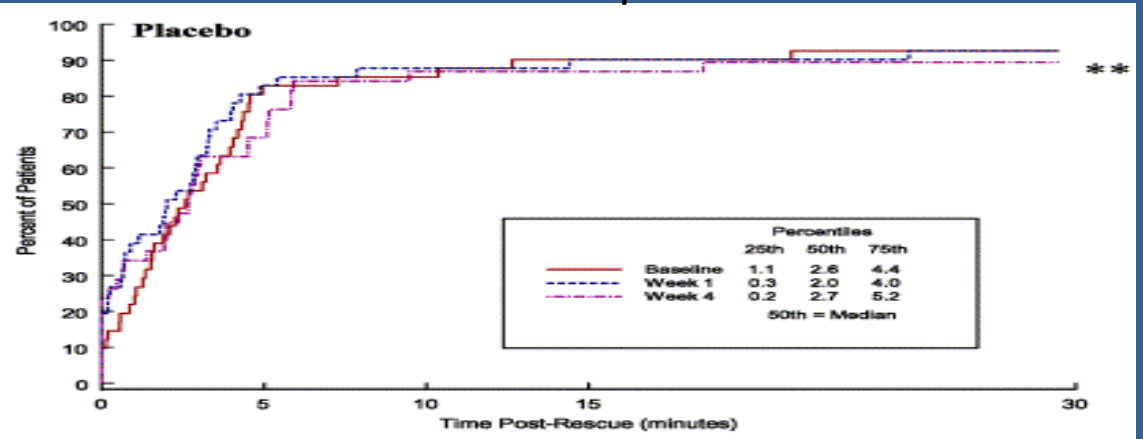


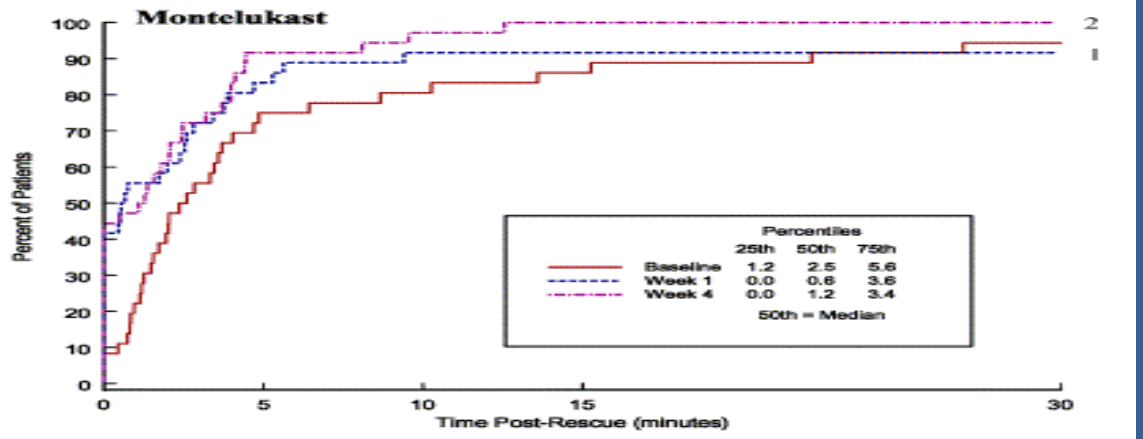
formoterol
terbutaline
salmeterol

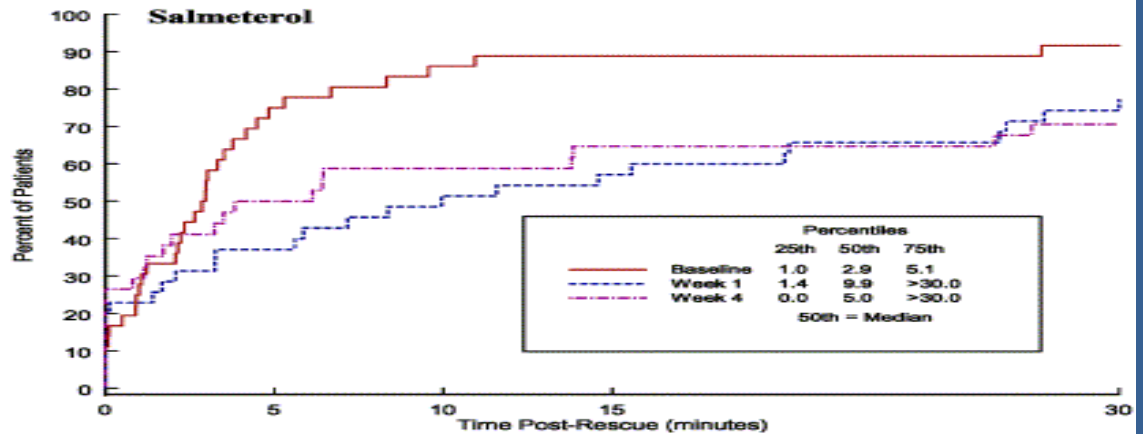
placebo

Richter. Eur Resp J. 2002; 19; 865

Storms. Resp Med 2004





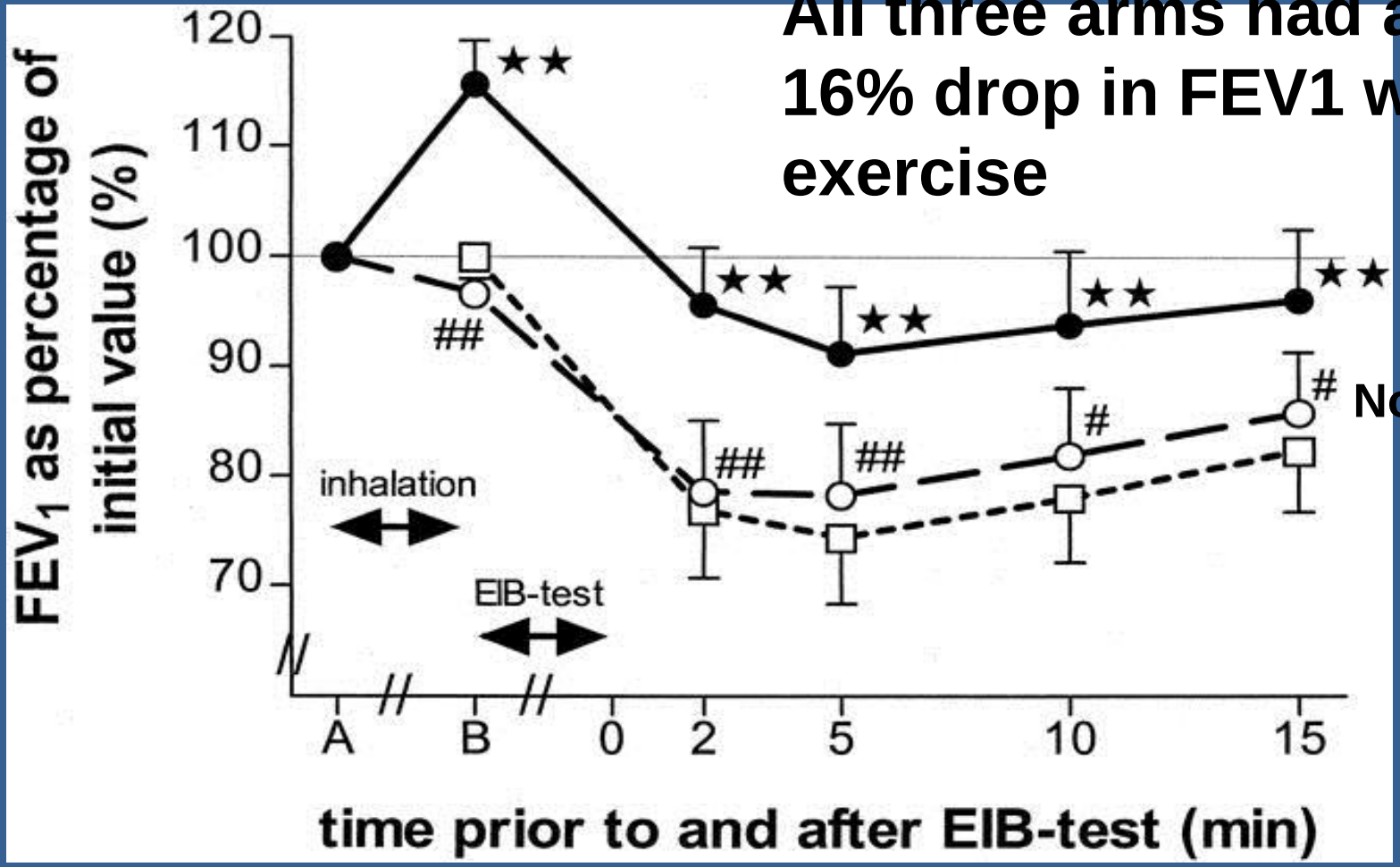


Placebo's effect on % of patients responding post albuterol in minutes at week 0, 1 and week 4

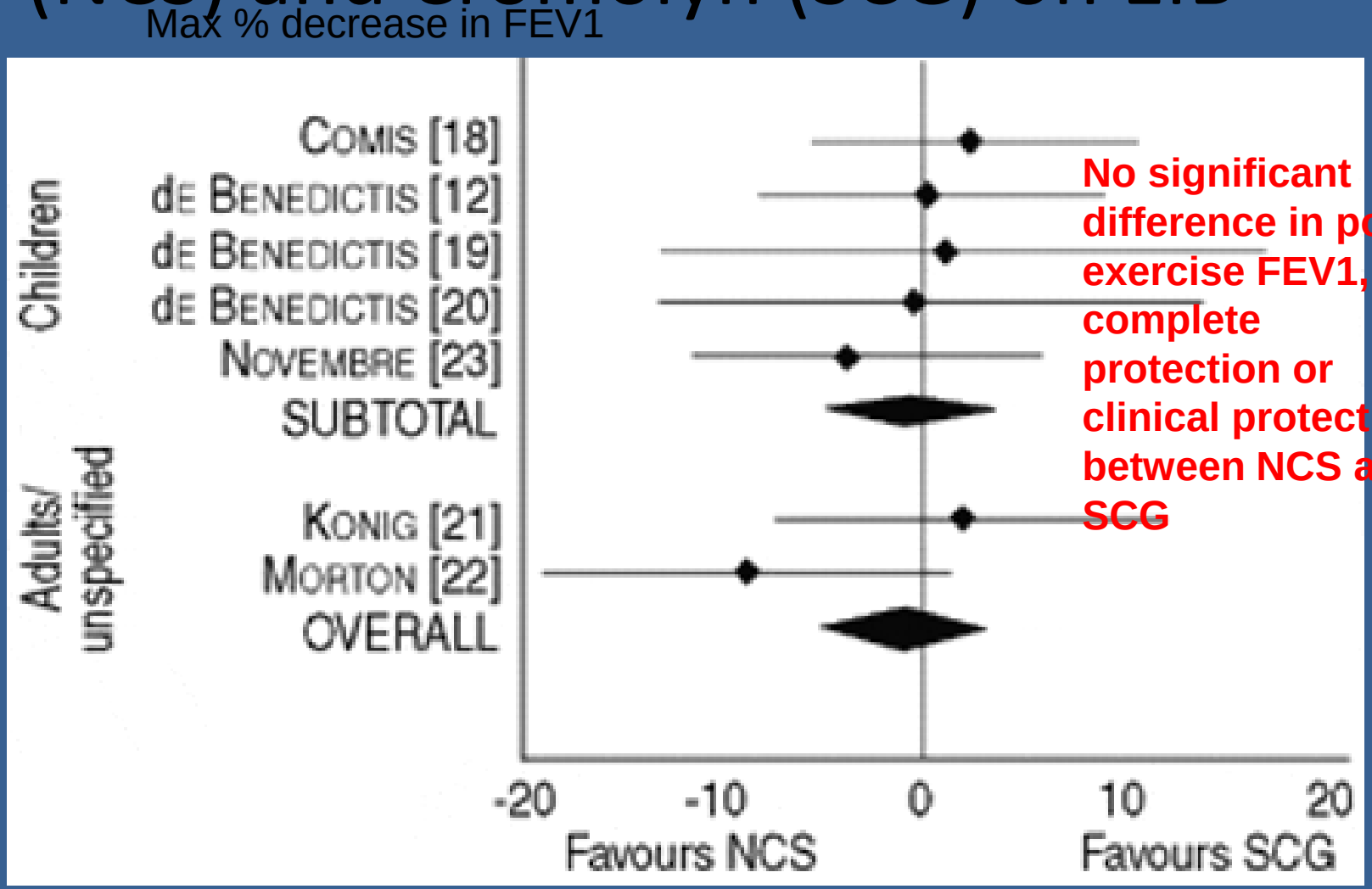
Montelukast's effect on % of patients responding post albuterol in minutes at week 0, 1 and week 4

Salmeterol's effect on % of patients responding post albuterol in minutes at week 0, 1 and week 4

Effect of ipratropium bromide on EIA

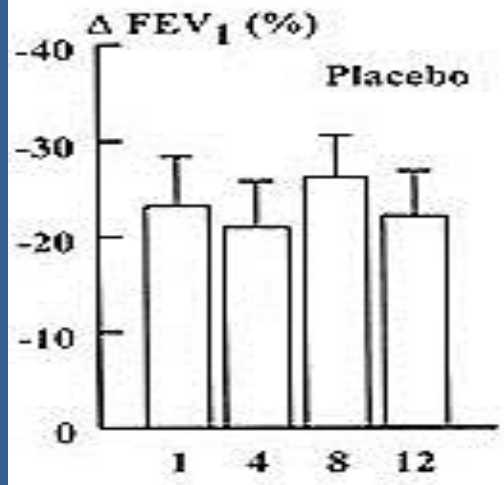


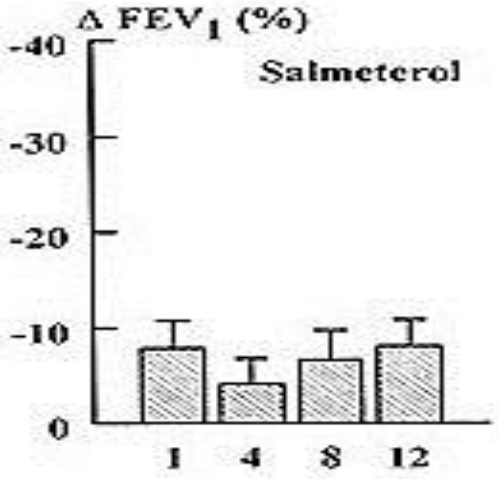
Assessing effect of Nedocromil (NCS) and Cromolyn (SCG) on EIB

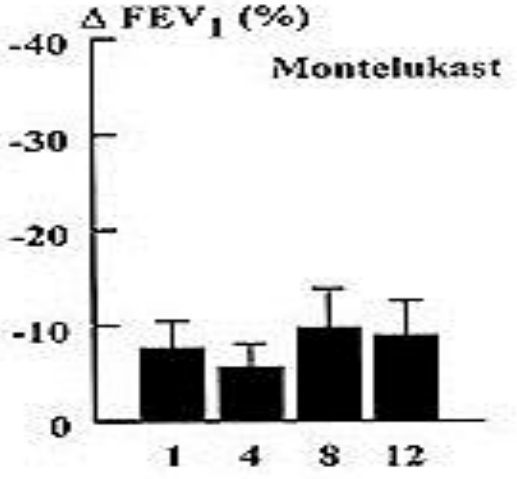


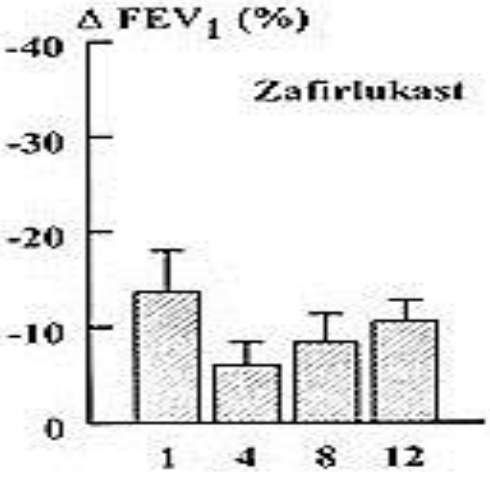
Kelly. Eur Resp J 2001; 17: 39

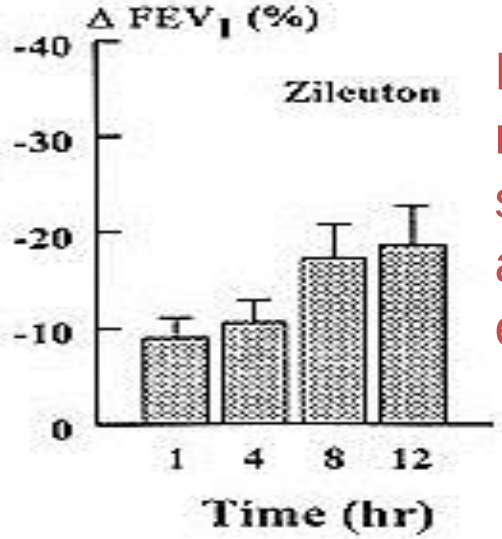
Comparing salmeterol, montelukast, zileutin and placebo in change of FEV1 over hours after exercise











No difference between montelukast, zafirlukast or salmeterol, but zileutin at 8 and 12 hours was less effective

Coreno et al. JACI. 2000: 106; 500-6

Other Therapies

- Warming up
- Salt restriction
- Hydration
- Fish oil
- Magnesium
- Anti-oxidants vitamins

- Alternative therapies should not replace traditional therapies since data supporting their use are limited.

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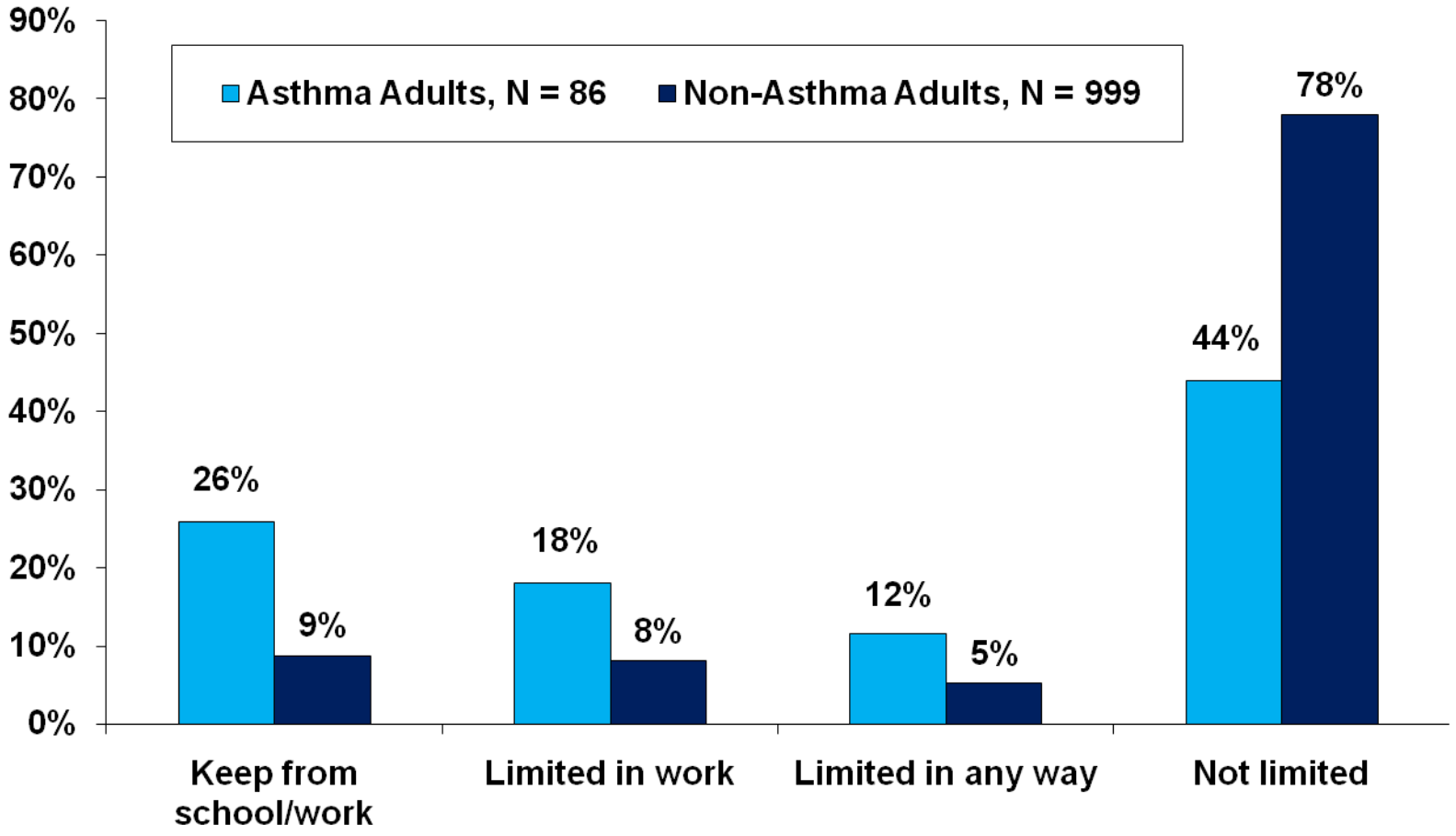
Impact of Health on Activities



Q2a. Does your health keep you from going to school or working?

Q2b. Are you limited in the kind or amount of work you can do because of your health?

Q2c. Are your activities limited in any way by your health?

Base: Adult cross-section

What % of Children with asthma admitted that asthma interfered with participation in school sports?

- A. 10
- B. 26
- C. 50
- D. 76
- E. 90

- Answer:

What % of Children with asthma admitted that asthma interfered with participation in sports?

- A. 10
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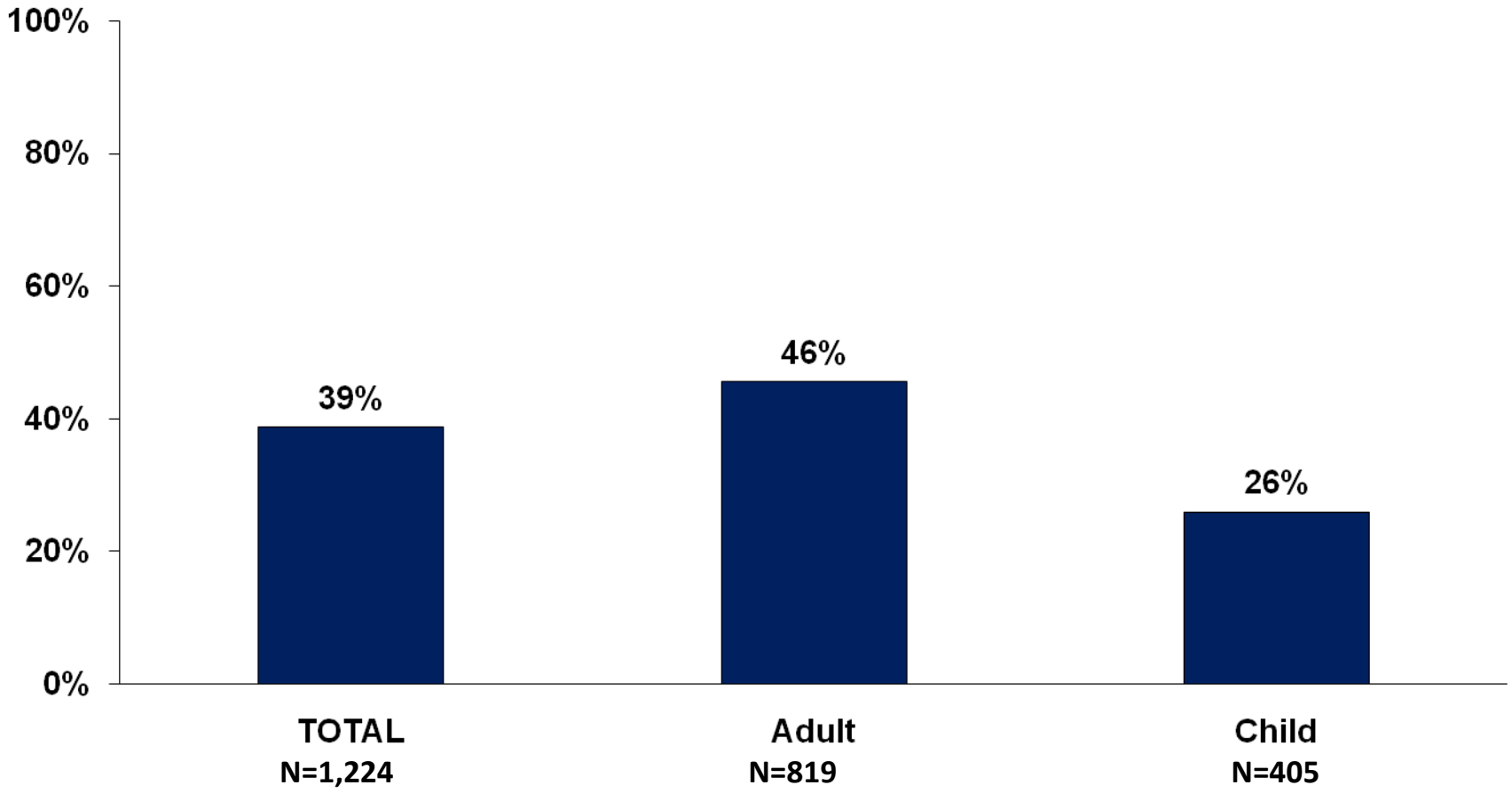
- D. 76
- E. 90

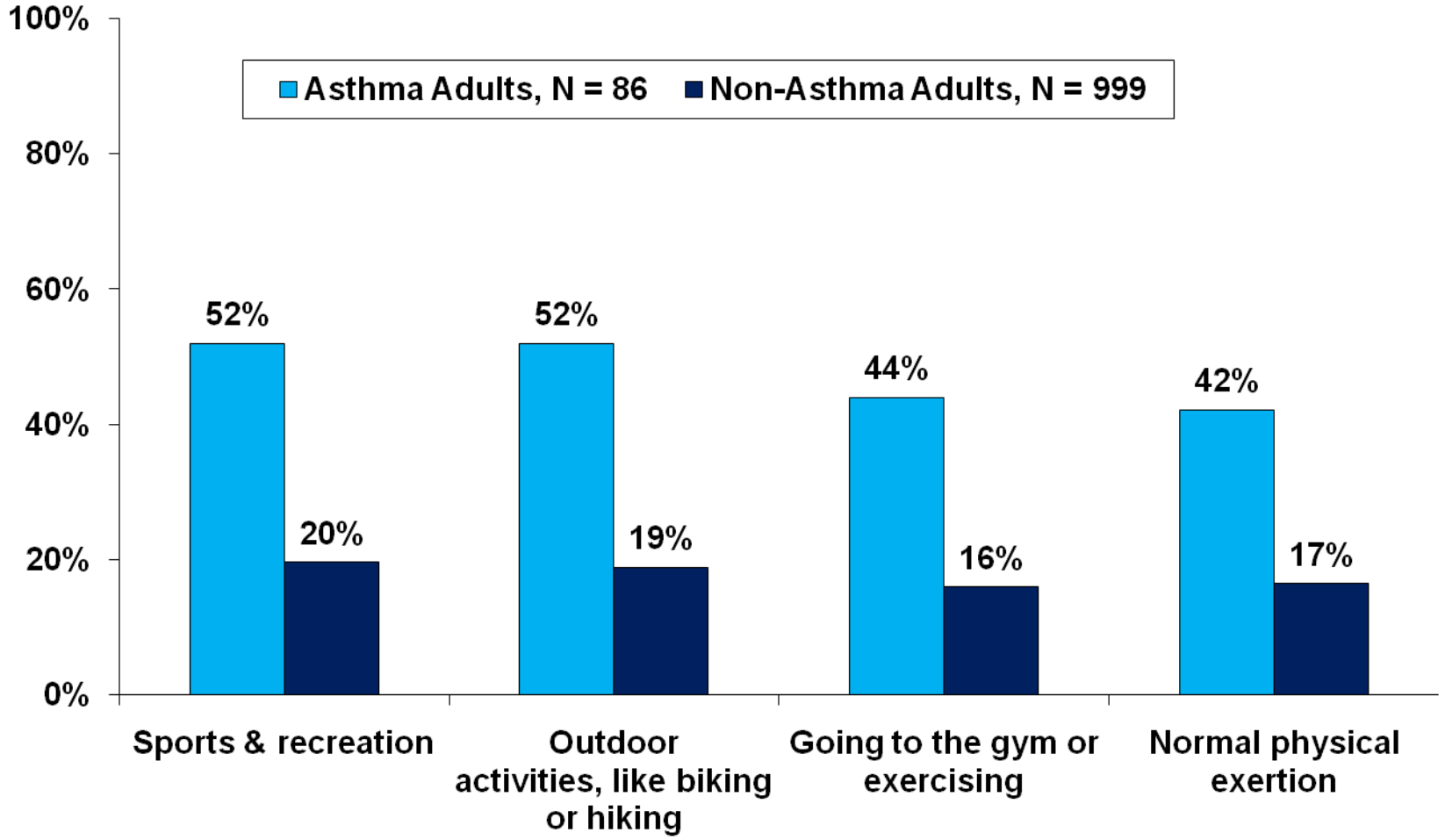
- Answer: B

Avoid Activities Because of Symptoms



Q22a. Are there any activities that you would like to do, but avoid doing because of coughing, wheezing, shortness of breath after exercise, play or exertion?
Base: Asthma patients that experience symptoms DURING OR SHORTLY AFTER exercise

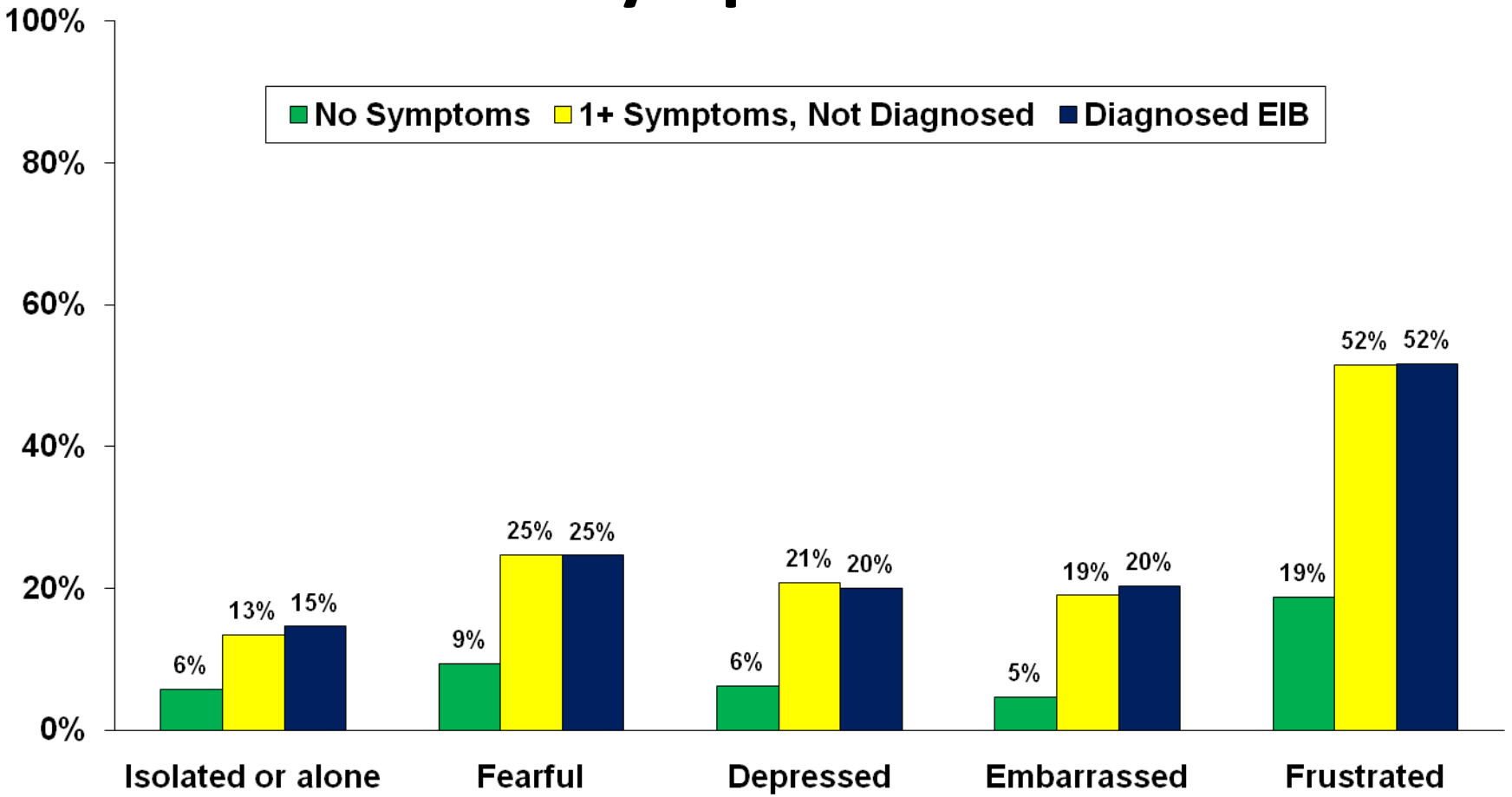
Health Limits Activities: A Lot or Some



Q49. How much do you feel that your health limits what you can do in each of the following areas. Do you feel your health restricts you – a lot, some, only a little or not at all in….

Base: Adult cross-section

Emotional Burden of Asthma by Symptoms



Q55. As a result of your asthma, how often do you feel . . . ? Often, sometimes, rarely, or never?

Base: All Asthma Patients, Unweighted N=1,517

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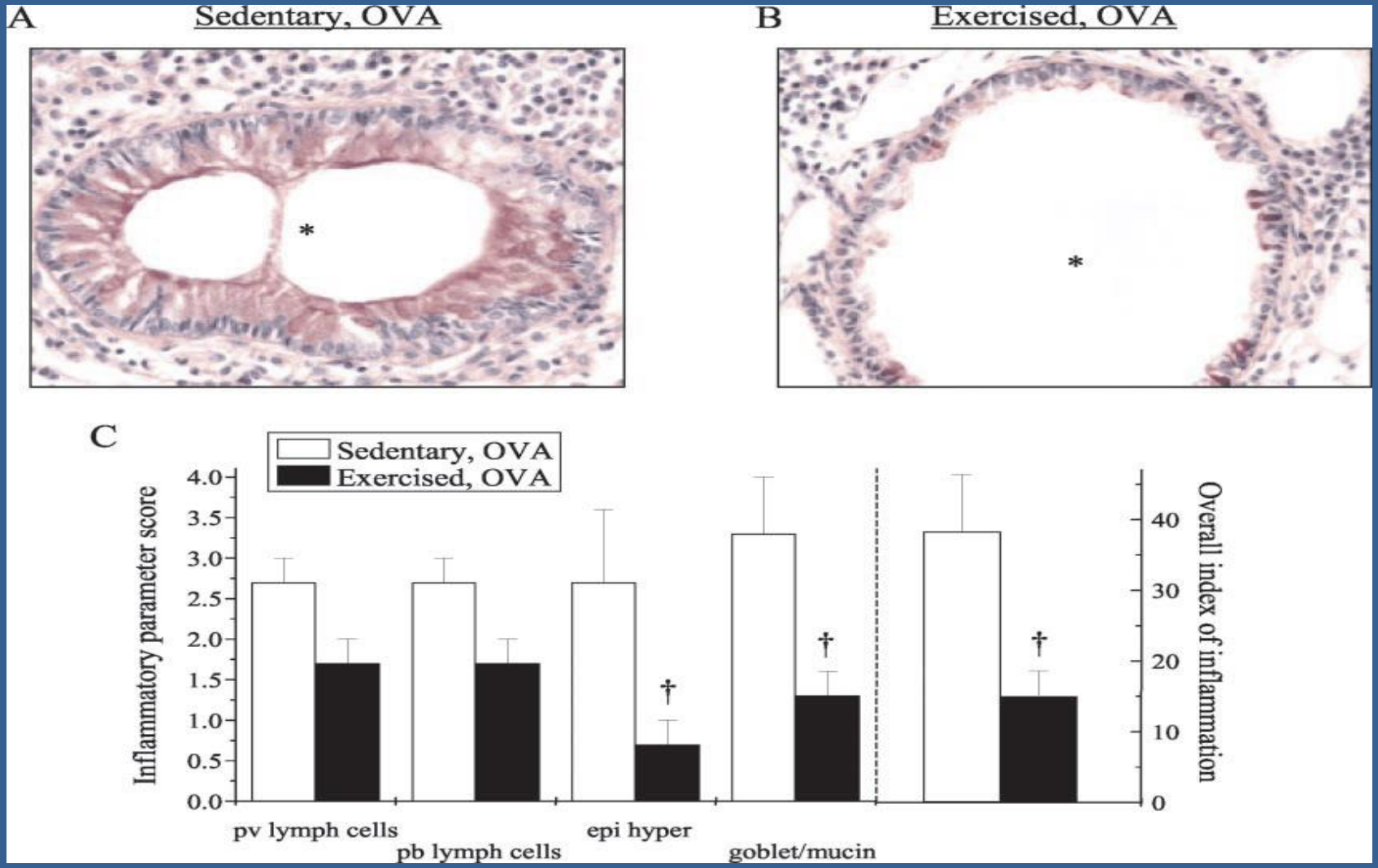
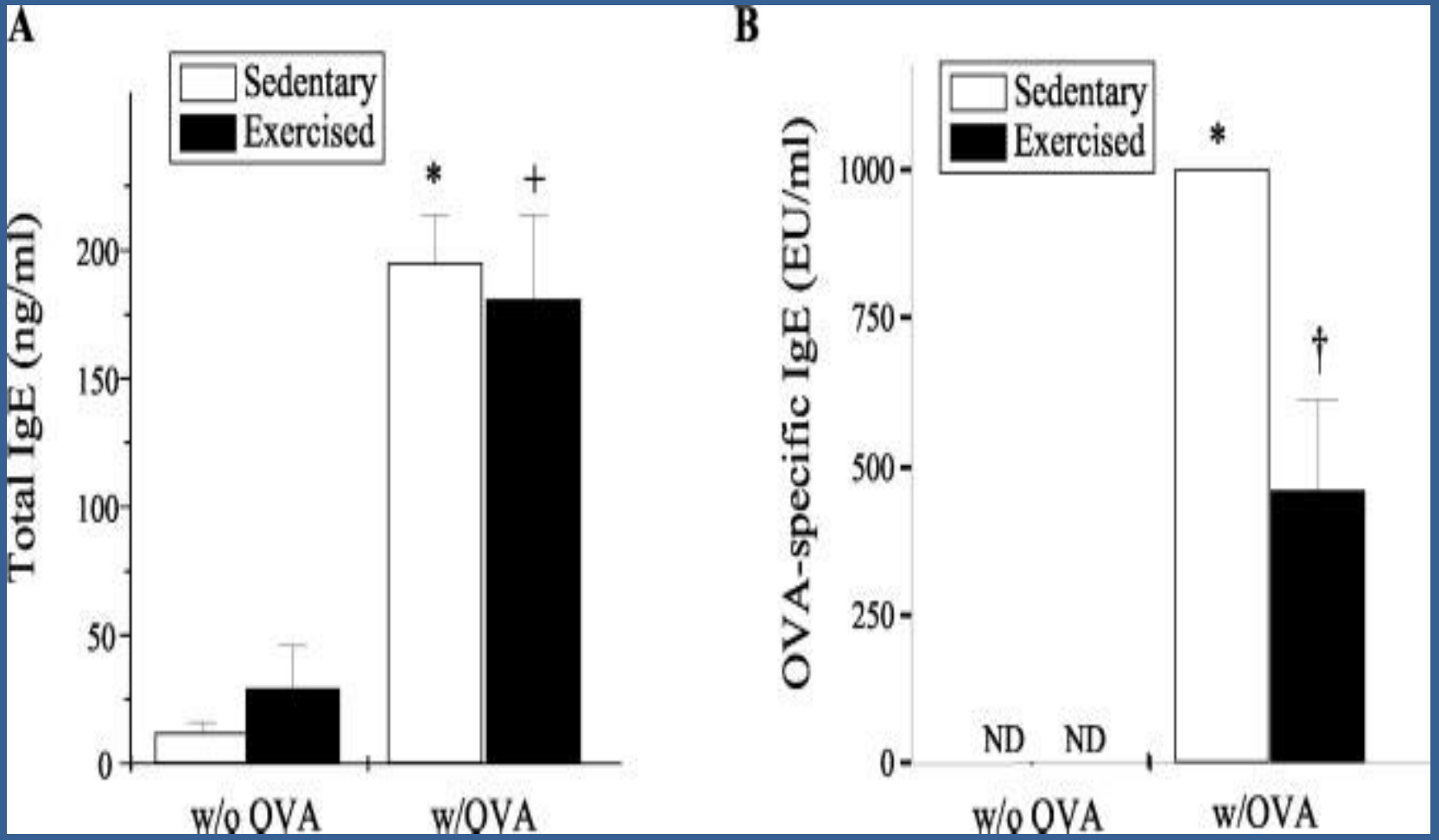
What is the importance of exercise in the mouse model with asthma

Effect of exercise on inflammatory mediators of asthma



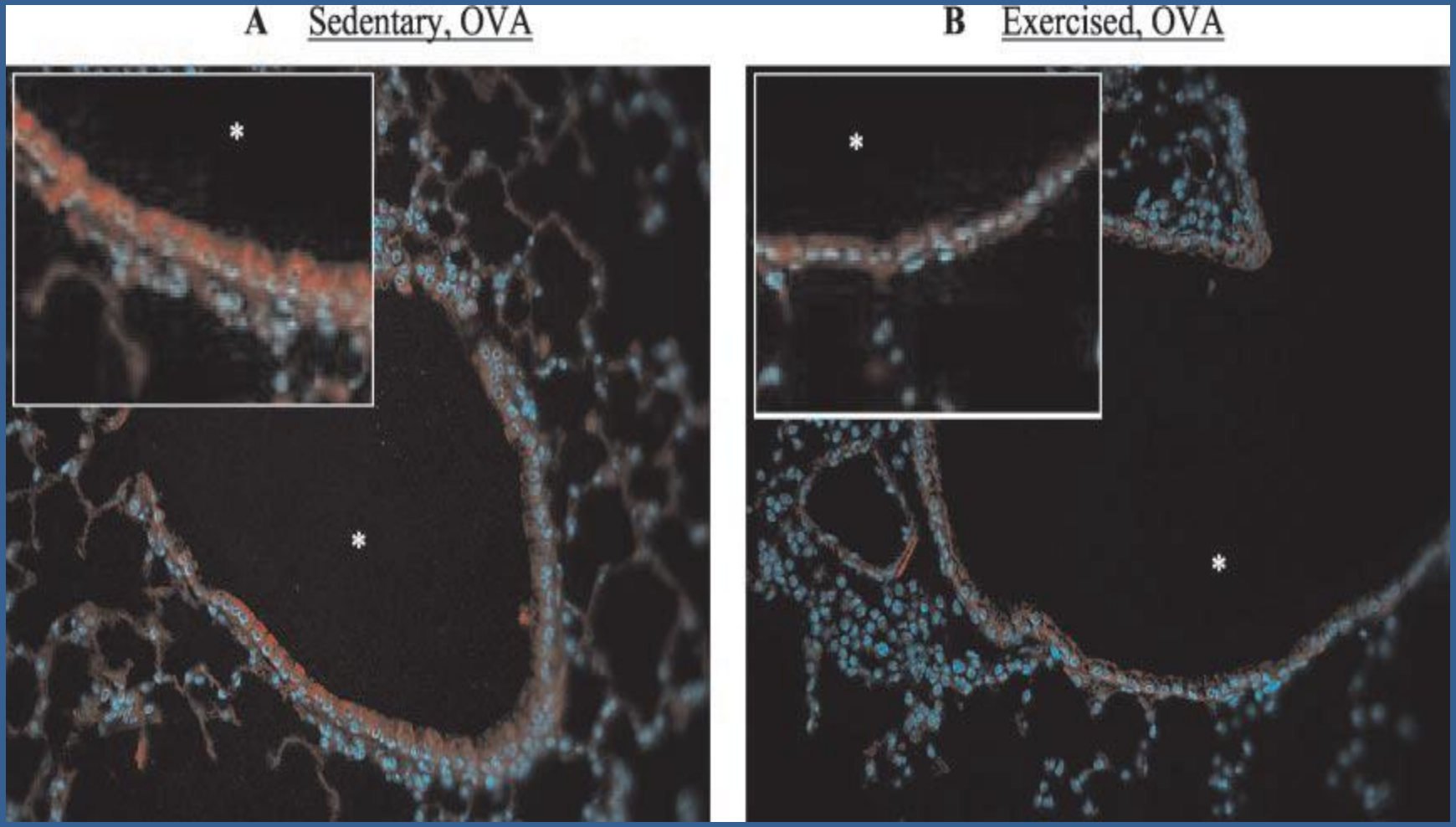
Pastva. J Immunol 2004;172;4520-4526

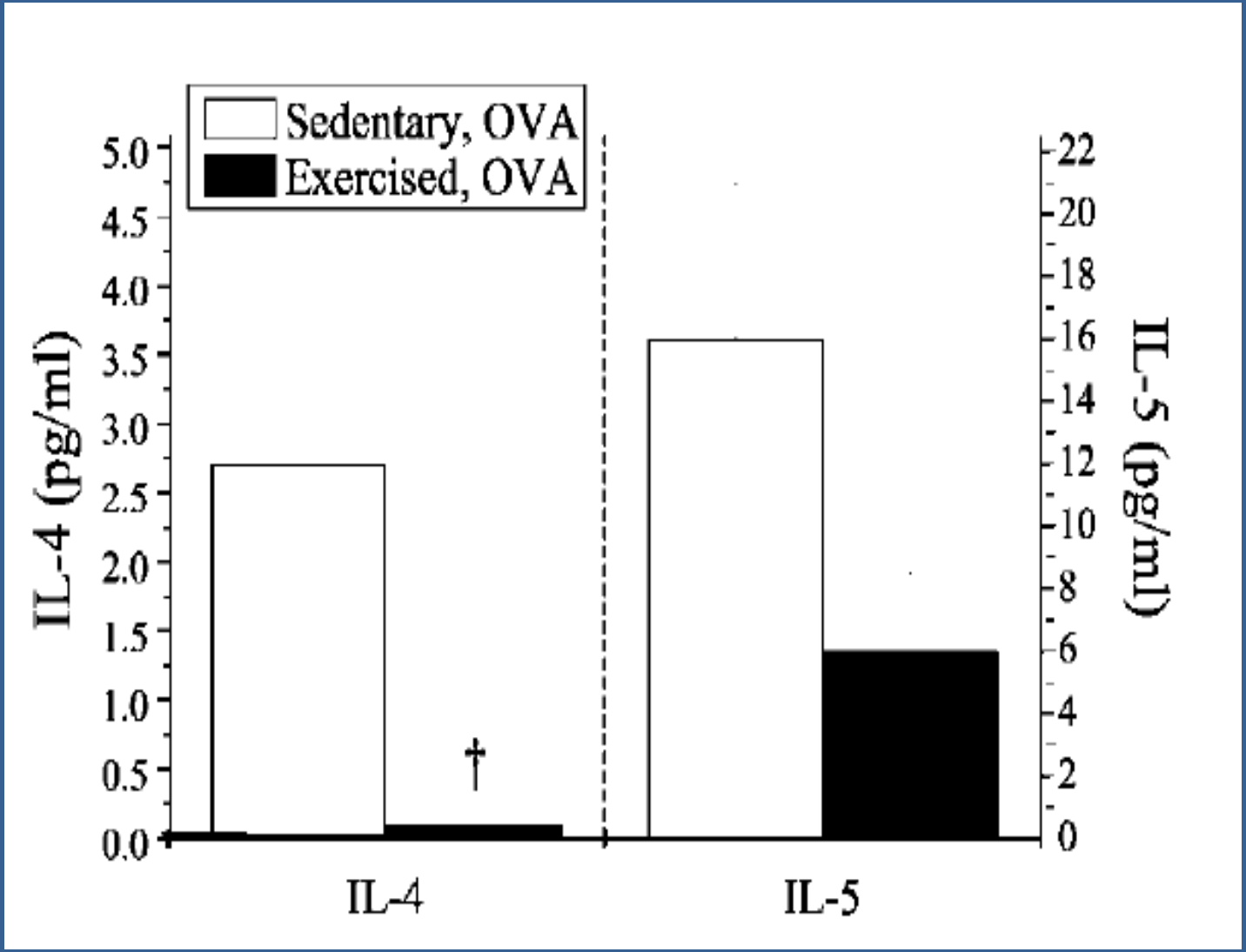
IgE production in sedentary and exercising mice



Pastva. J Immunol 2004;172;4520-4526

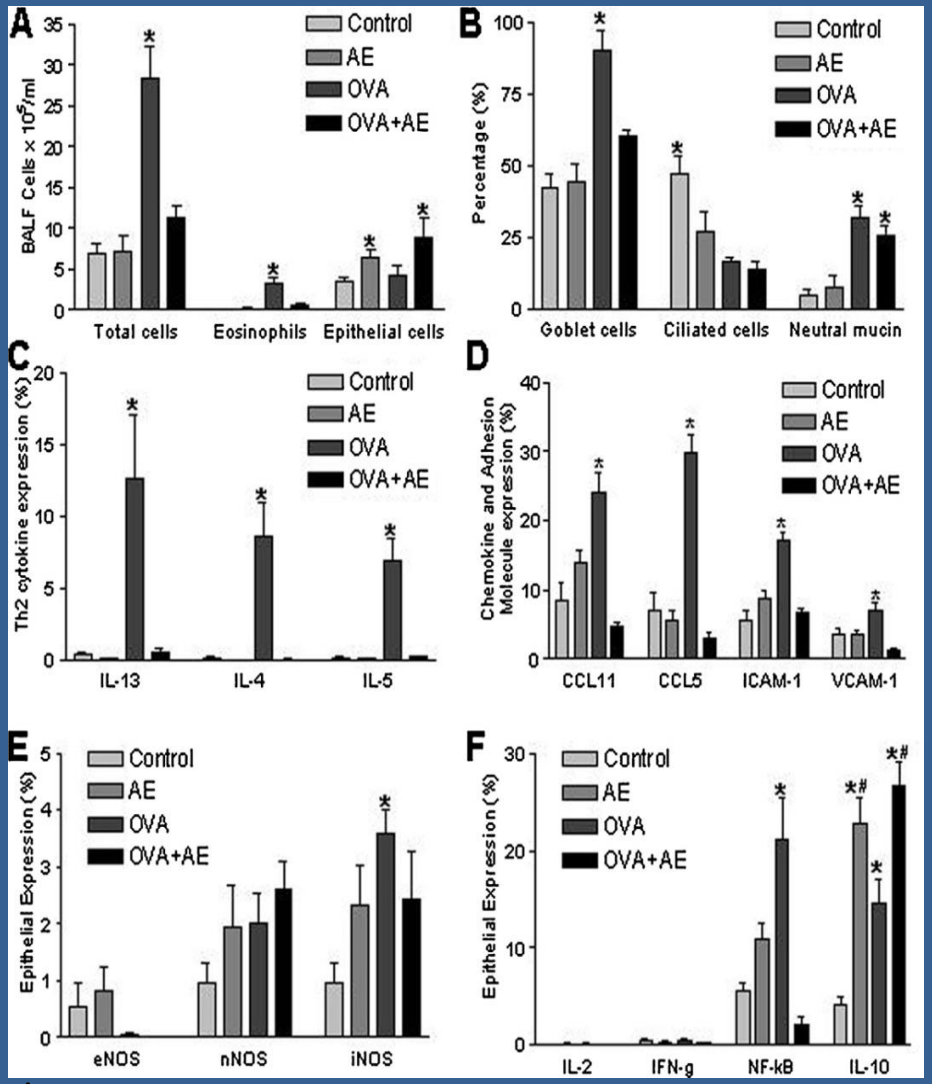
Exercise decreased VCAM-1 surface expression in the lungs of OVA-sensitized mice





Pastva. J Immunol 2004;172;4520-4526

The number of total cells, eosinophils and epithelial cells in the bronchoalveolar lavage



R.P. Vieira et al. / Respiratory Physiology & Neurobiology *175 (2011) 383–389*

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Exercise Improves Asthma Outcomes "Quality of Life"

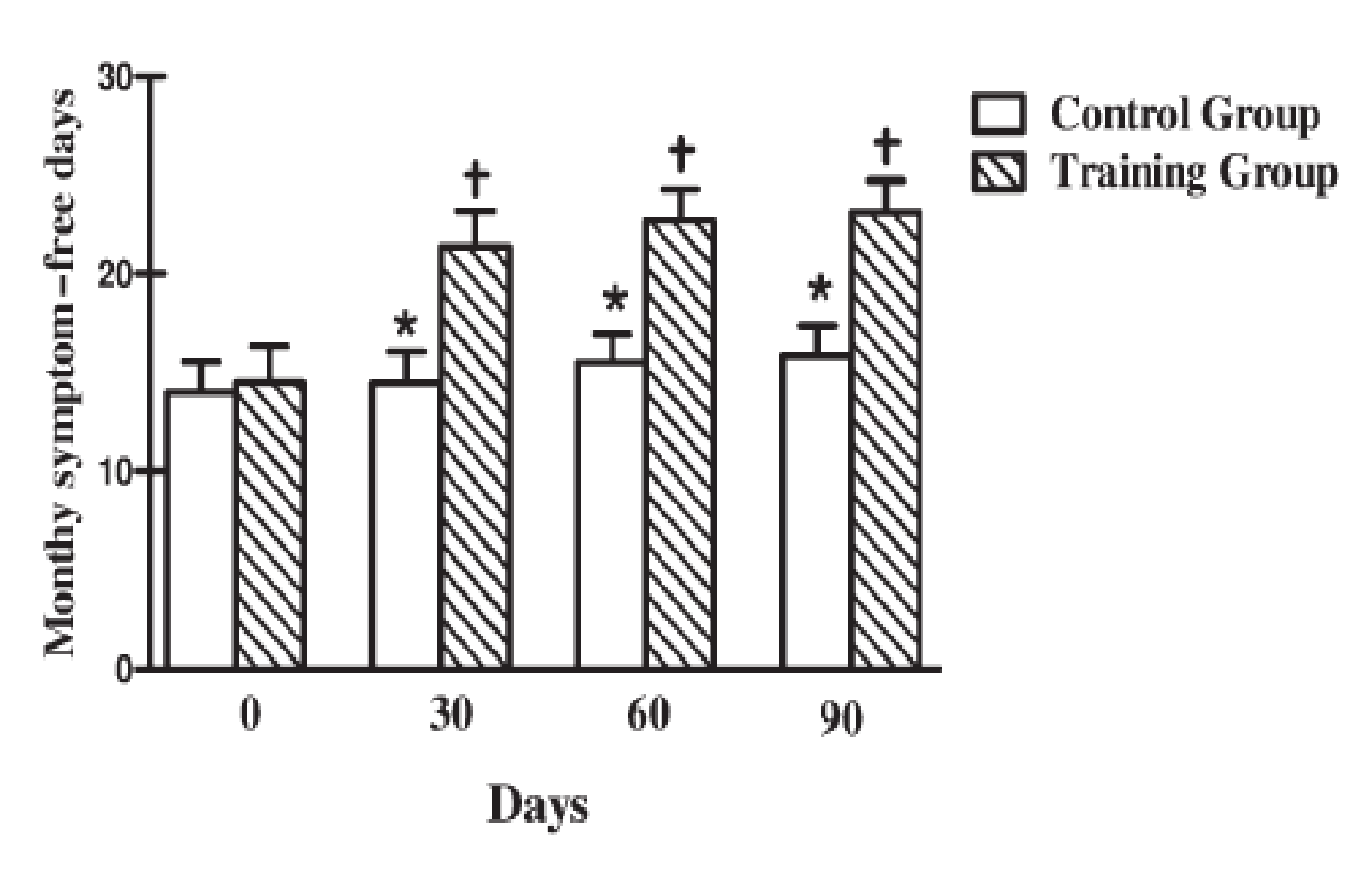
	Control Group		Exercise Group		
	Baseline (n=12)	Week 12 (n=11†)	Baseline (n=18)	Week 12 (n=18)	Week 24 (n=15‡)
ACQ Questionnaire	0.90±0.15	0.99±0.16†	1.30±0.19	0.72±0.10*	0.72±0.17‡***
ACQ with Spirometry	1.06±0.10#	0.80±0.14	1.37±0.21	0.95±0.11	1.02±0.18
Perceived Asthma Control	2.33±0.19	2.25±0.18†	2.56±0.15	1.94±0.10^	2.00±0.13‡***
Mini-AQLQ	5.79±0.15	5.90±0.17†	5.01±0.21	5.84±0.17	6.11±0.21‡**,***
Maximal VO_2	2.66±0.27	2.77±0.29	2.63±0.20	2.88±0.21	3.00±0.27***
Submaximal V_E/VO_2	23.21±0.73	23.64±0.80	24.89±1.08	23.78±0.74^	24.35±0.90
Maximal V_E/VO_2	28.46±0.88	28.65±1.39	28.84±1.02	27.44±0.78	28.48±1.17
Submaximal DI	0.42±0.03	0.42±0.02	0.45±0.02	0.48±0.03^	0.54±0.03***
Maximal DI	0.68±0.04	0.69±0.04	0.73±0.04	0.77±0.04	0.84±0.04

ACQ: Asthma Control Questionnaire; AQLQ: Asthma Quality of Life Questionnaire; VO_2: Oxygen uptake; V_E: Ventilation; DI: Dyspnea Index

†n=12 for paper measurements only; ‡n=17 for paper measurements only; # significant differences at baseline between control and exercise group; *p<0.05 between groups from T1 to T2; ** p< 0.05 within exercise group from T2 to T3; ***p<0.05 within exercise group from T1 to T3; ^ statistical trend from T1 to T2; p<0.10.

Dogra. ERJ June 7, 2010

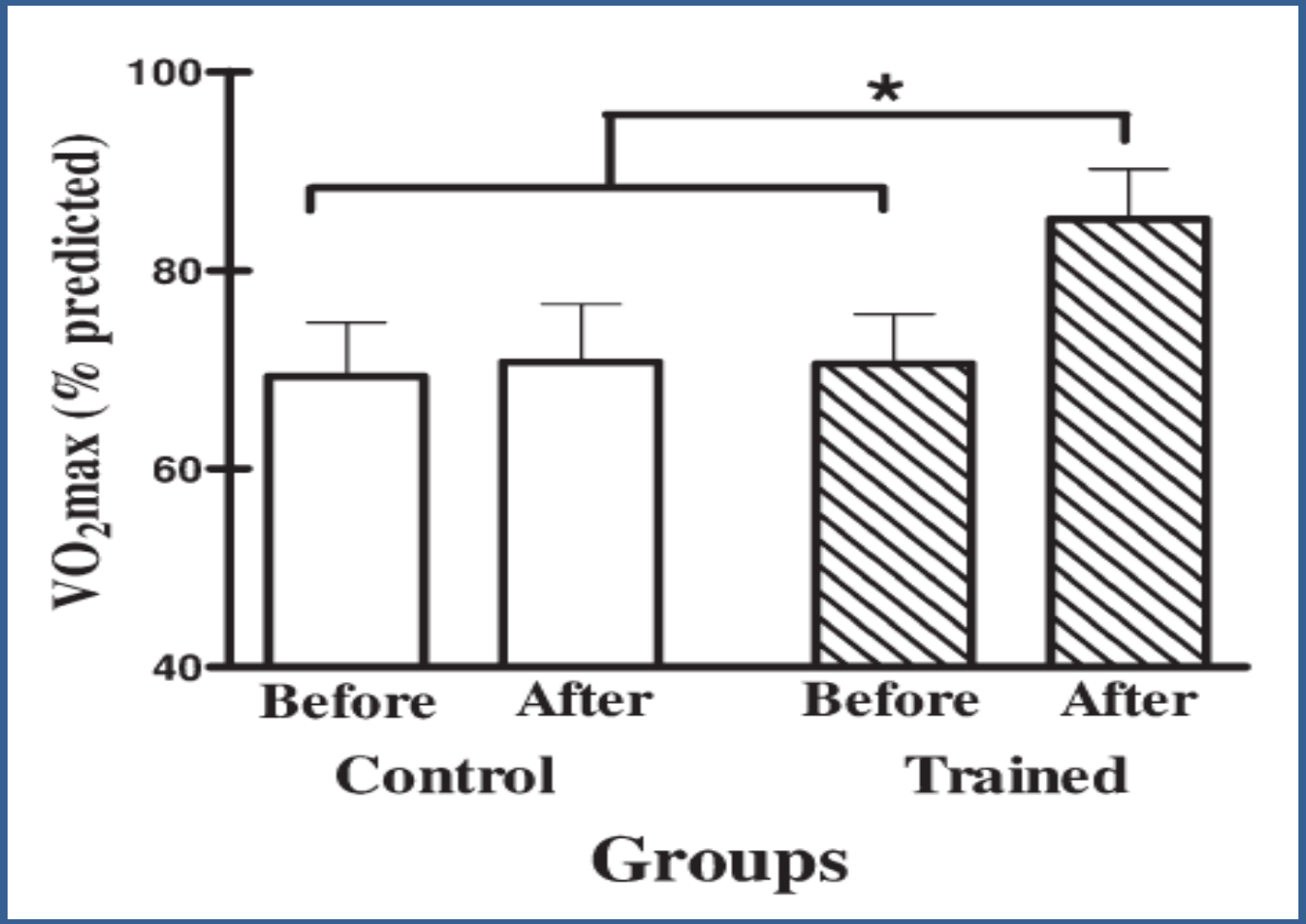
Exercise Improves Asthma Outcomes
"Symptom Free Days"



Mendes. CHEST / 138 / 2 / AUGUST, 2010

Exercise Improves Asthma Outcomes

" Oxygen consumption"



Mendes. CHEST / 138 / 2 / AUGUST, 2010

Exercise in children: all compared to open label conventional treated group

author	duration	frequency	type	P value Subject #
Basaran 2006	2 months	1 hour, 3X a week	Aerobic, moderate	0.001 62
Fanelli 2007	4 months	1.5 hours, 2X a week	Aerobic to 70%	0.03 38
Flapper 2008	3 months	2.5 hours, 1 time a week	Aerobic	0.02 36
Moreira 2008	3 months	50 minutes, 2X weekly	Aerobic	0.004 34

D. Pacheco, J of Asthma, 2012

Exercise in adults: all compared to open label conventional treated group

author	duration	frequency	type	P value Subject #
Turner 2010	6 weeks	1.5 hour, 3X a week	Aerobic, moderate	0.04 34
Goncalves 2008	3 months	0.5 hours, 2X a week	Aerobic to 70%	0.001 20
Mendes 2010	3 months	0.5 hours, 2X a week	Aerobic to 70%	0.001 101

D. Pacheco, J of Asthma, 2012

Exercise in Adults, non aerobic: all compared to open label conventional treated group

author	duration	frequency	type	P value Subject #
Sabina 2005	1 month	1.5 hour, 2X a week	Yoga	NS 62
Thomas 2009	1 and 6 months	3 sessions	Breathing exercises	NS 183
Vempati 2009	2 months	1.5 hours, daily	Yoga	0.013 57

D. Pacheco, J of Asthma, 2012

Summary:

Patients can improve their asthma by:

- 1. Using maintenance medications regularly can decrease EIB
- 2. Pre-medicating before exercise with albuterol can eliminate EIB in some
- 3. Warming up, hydrating and cooling down is important to decrease EIB
- 4. Exercising regularly can improve quality of life, improve asthma control and reduce T-helper cell induced inflammation

Please contact me at

tcraig@psu.edu

Have a great day