

Severe asthma
Definition, epidemiology and
risk factors

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Difficult asthma

Defined as

- "asthma, poorly controlled in terms of chronic symptoms, with episodic exacerbations, persistent and variable airway obstruction and continued requirement for short-acting beta-2-agonists and a reasonable dose of inhaled corticosteroids"

ERS definition-Eur Respir J 1999; 13:1198-208



Refractory asthma

Major criteria

- Treatment with oral corticosteroids > 50% of the time
- High doses inhaled corticosteroids (>1200 μg beclomethasone equivalent)

Minor criteria

- requirement for daily treatment with long-acting beta-agonists, theophylline or leukotriene antagonists
- daily asthma symptoms requiring rescue medication
- persistent airway obstruction ($\text{FEV}_1 < 80\%$ predicted); diurnal PEF variability > 20%
- 1 or more urgent care visits for asthma per year
- 3 or more oral steroid bursts per year
- prompt deterioration with < 25% reduction in oral or inhaled corticosteroid dose
- near fatal asthma event in the past

ATS Definition- Am J Respir Crit Care Med 2000; 162:2341-51.

Severe asthma

The term, "severe asthma" applies to patients who have refractory asthma who remain difficult to control despite an extensive re-evaluation of diagnosis, management, and following an observational period of at least 6 months by an asthma specialist.

Chanez et al, JACI 2007

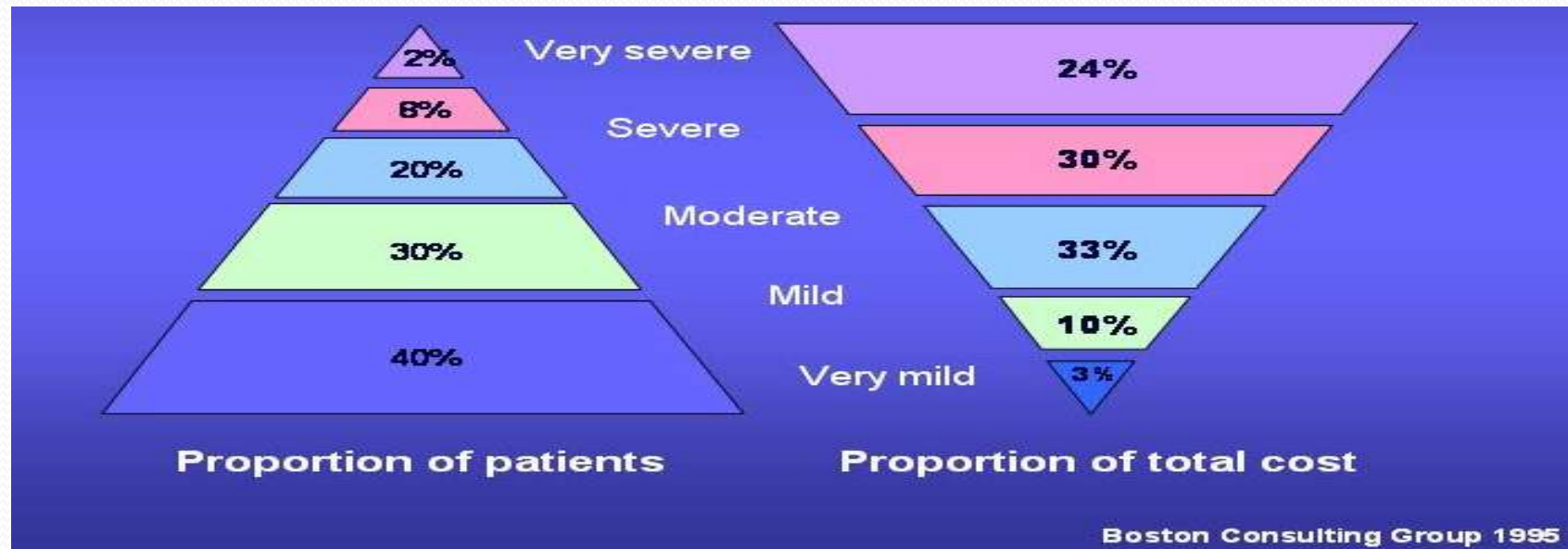
Severe asthma

The term, “severe refractory asthma” should apply to patients who remain difficult to control despite an extensive re-evaluation of diagnosis, avoidance or treatment of exacerbating factors and following a period of at least 6 months of close follow up and tailored and rigorous management by an asthma specialist.

Gaga et al, Eur Respir Rev in press

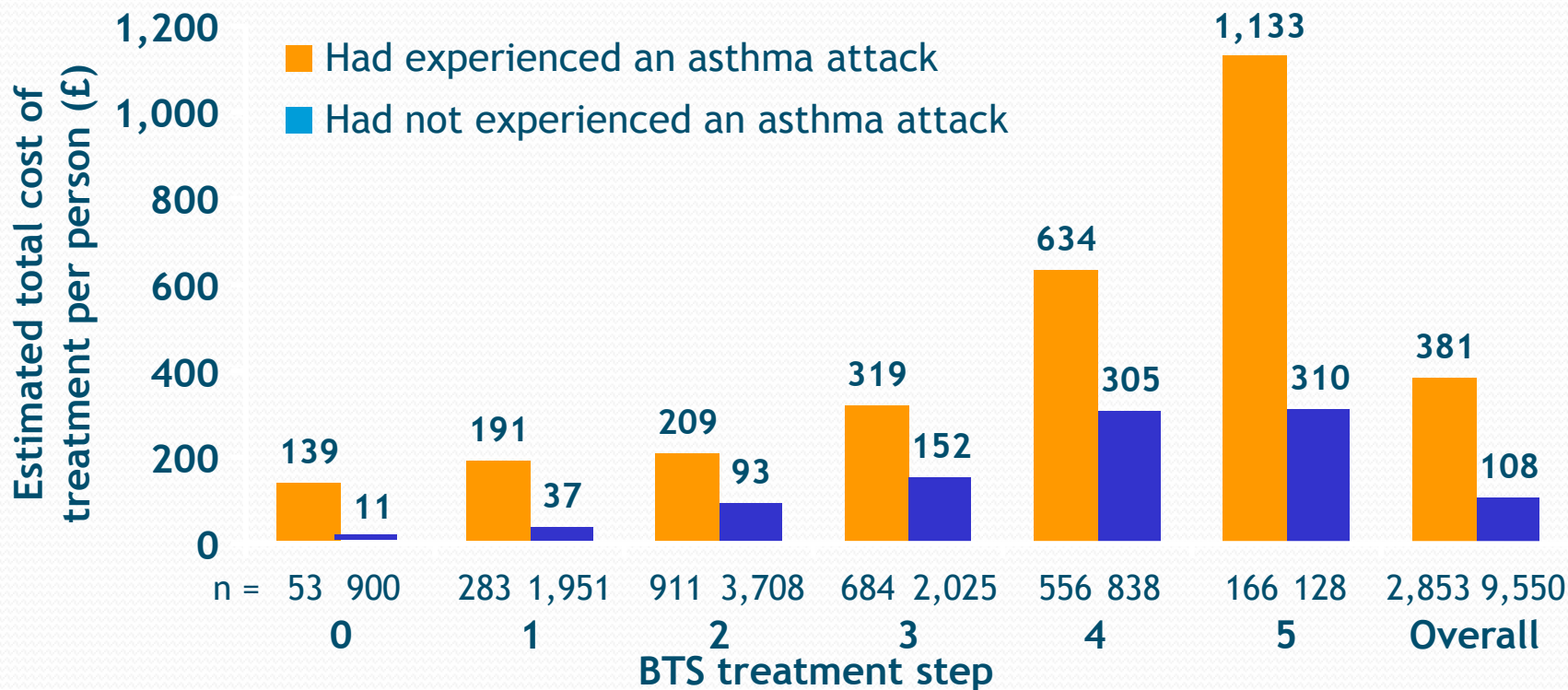
Severe and difficult to treat asthma

- 2-12% of asthmatic patients
- 50% of asthma costs
- Severe impact on health and QoL



Poor asthma control contributes to substantial healthcare and societal costs

Average total cost of treatment by BTS treatment step and occurrence of asthma attack in the previous 12 months



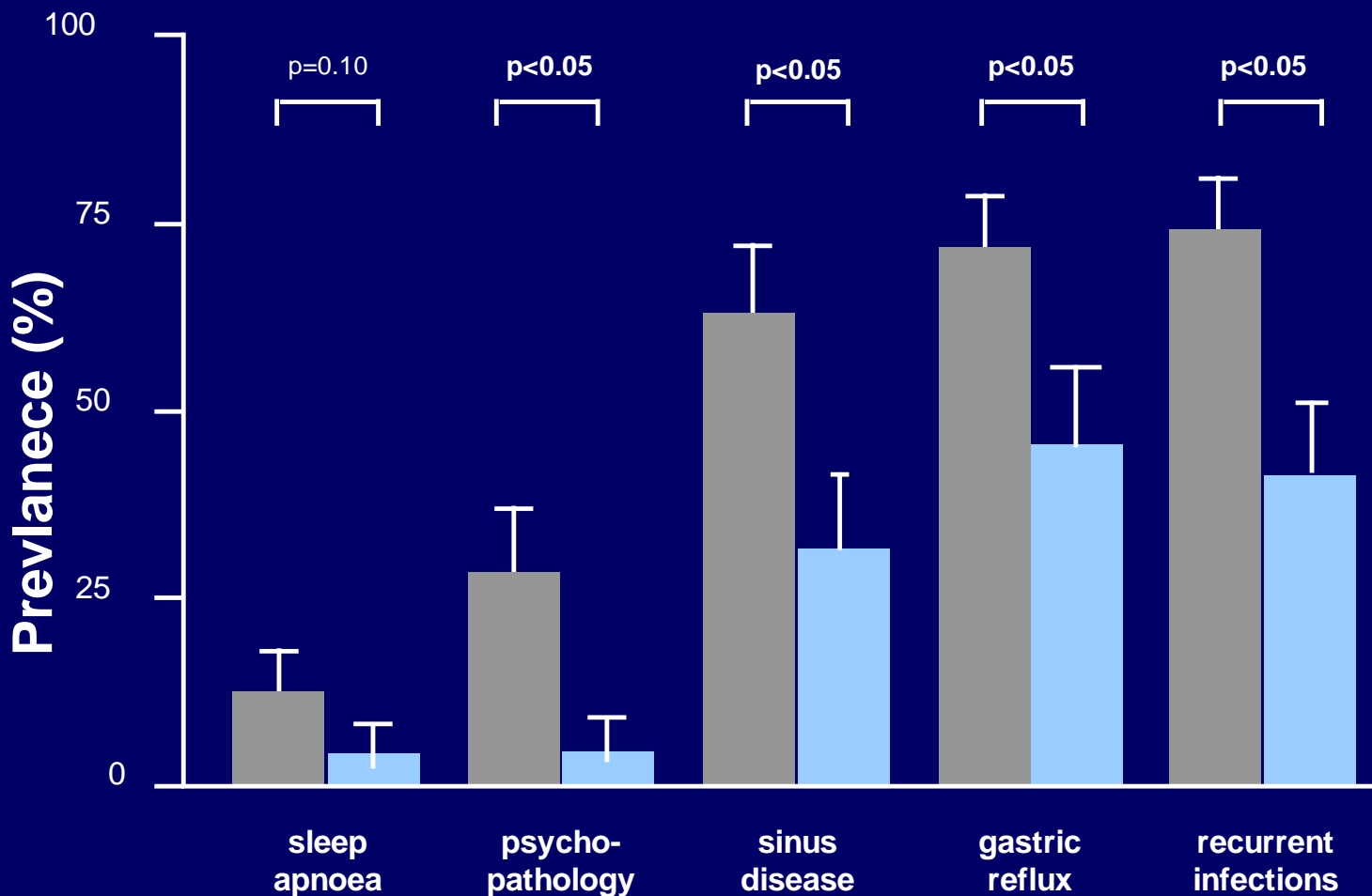
75% of asthma costs relate to poor asthma control²

BTS = British Thoracic Society

1. Asthma UK Asthma Audit, 1999; 2. Barnes PJ, et al. Eur Respir J 1996;9:636-42.

- Costs for uncontrolled patients were more than double those of controlled patients
- 14,212 vs 6,452 US Dollars; $P < 0.0001$
- Few severe or difficult-to-treat asthma patients achieved control over a 2-year period and the economic consequence of uncontrolled disease is substantial.

Risk Profile of Patients with Frequent Asthma Exacerbations



ten Brinke et al, ERJ 2005

Epidemiology-Genetics

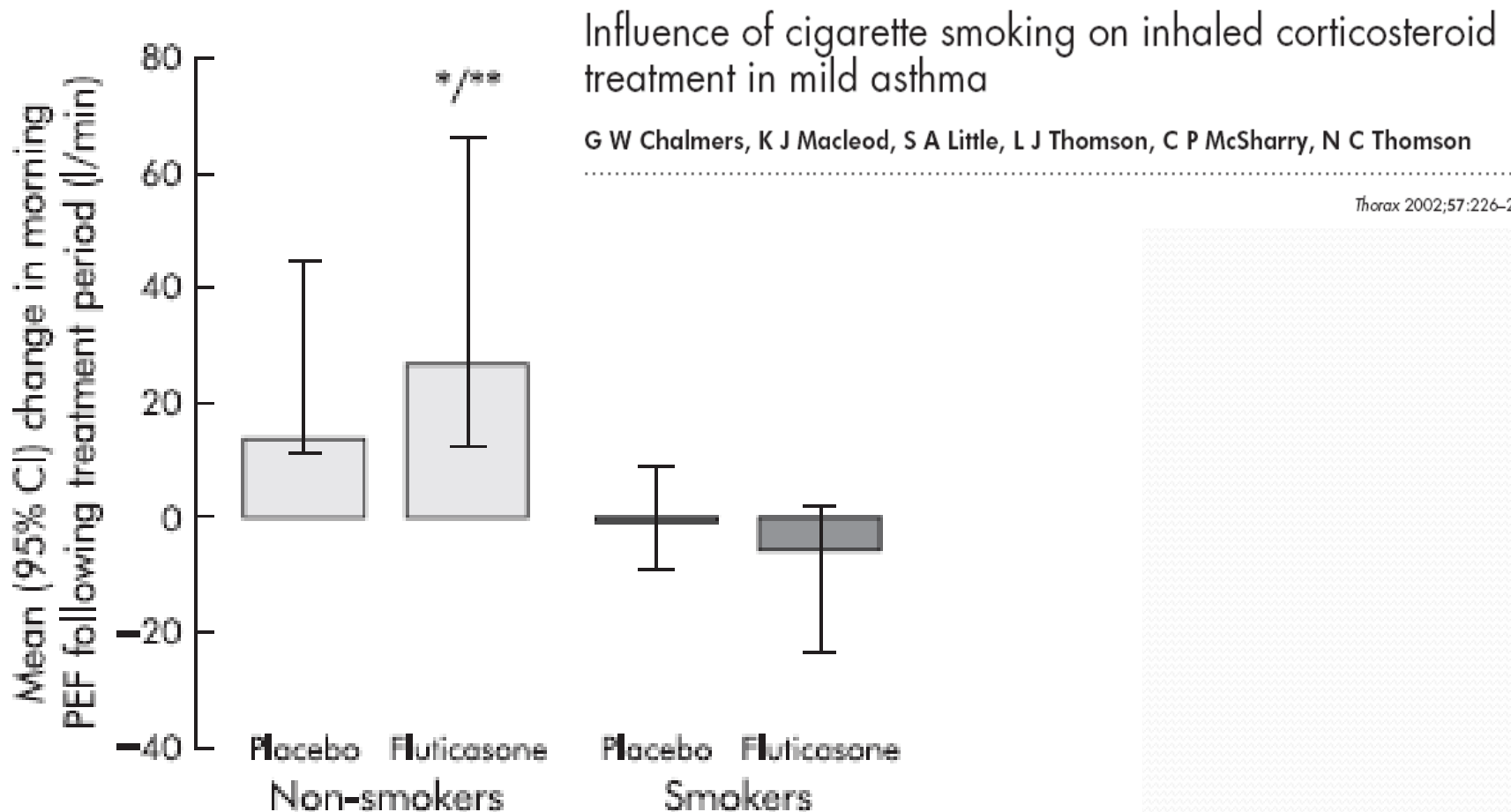
Genes and genetic-environmental interactions are associated with severity

- ADAM₃₃ BHR, decline in lung function
- TGF- β ₁ lower FEV₁
- IL-4 lower FEV₁, severe exacerbations
- IL-4R α lower FEV₁, severe exacerbations

Jongepier et al, Clin Exp Allergy 2004
Pulleyn et al, Hum Genet 2001
Sandford et al, JACI 2000
Lee et al Am J Respir Crit Care Med 2006

Genes and genetic-environmental interactions are associated with disease severity and poor response to treatment

Studies focusing on severe asthma are needed



Epidemiology- Infections

- *Respiratory viruses (and some bacteria) contribute to severe exacerbations of asthma*
- *Viruses can persist in the airways for long periods after the exacerbation*
- *their role in the development of severe persistent asthma remains poorly understood.*

Everard, Curr Opin Allergy Clin Immunol 2006

Epidemiology

- Severe asthma is associated with an increased risk of hospitalization and death.
- Severe asthma in children, but not adults, is associated with elevated IgE (Europe vs USA).
- Female gender, obesity and smoking are associated with more severe asthma and a poor response to therapy.

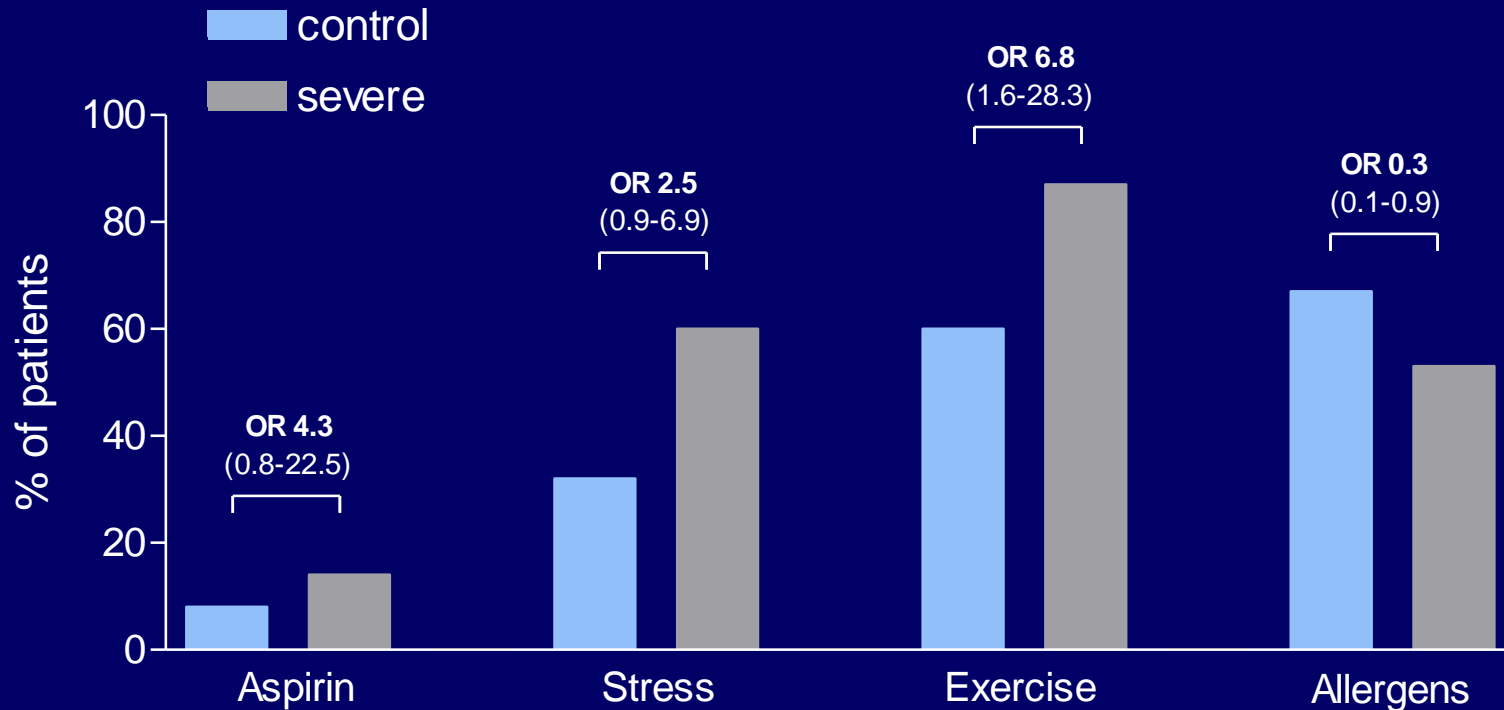
Prediction

TENOR study, risk score

- Age 3
- Gender 1
- Race 2
- BMI 1
- Lung Function 2
- Previous history of pneumonia 1
- Diabetes 1
- Cataracts 1
- Previous intubation 1
- Steroid bursts 3
- Nebuliser ipratropium bromide 1
- Systemic corticosteroids 1

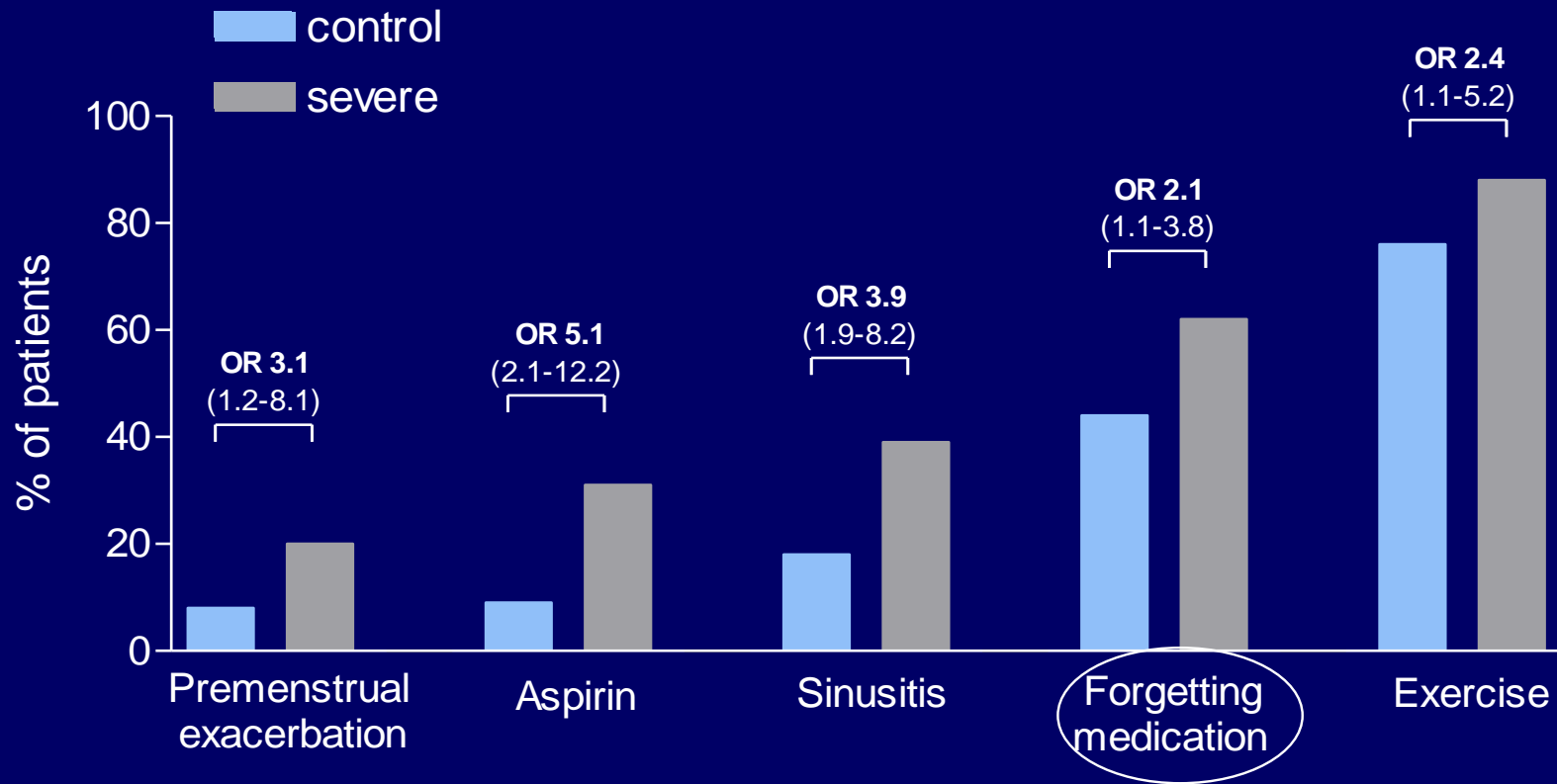
Total score 0-18
High risk score >8

Trigger factors for asthma attacks Men



OR=Odds ratios for severe asthma
Each OR is adjusted by all the other trigger factors and age

Trigger factors for asthma attacks Women



OR=Odds ratios for severe asthma
Each OR is adjusted by all the other trigger factors and age


Risk factors

- In children and adolescents, increased body weight was found to be associated with asthma severity in girls

Sullivan et al, Allergy 2007

- ATAQ
- a validated questionnaire may help clinicians identify patients requiring intervention to prevent future severe asthma-related events

Chipps et al, JACI, 2007

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- Studies focused in severe asthma are urgently needed
 - Καλό τριημέρο!