

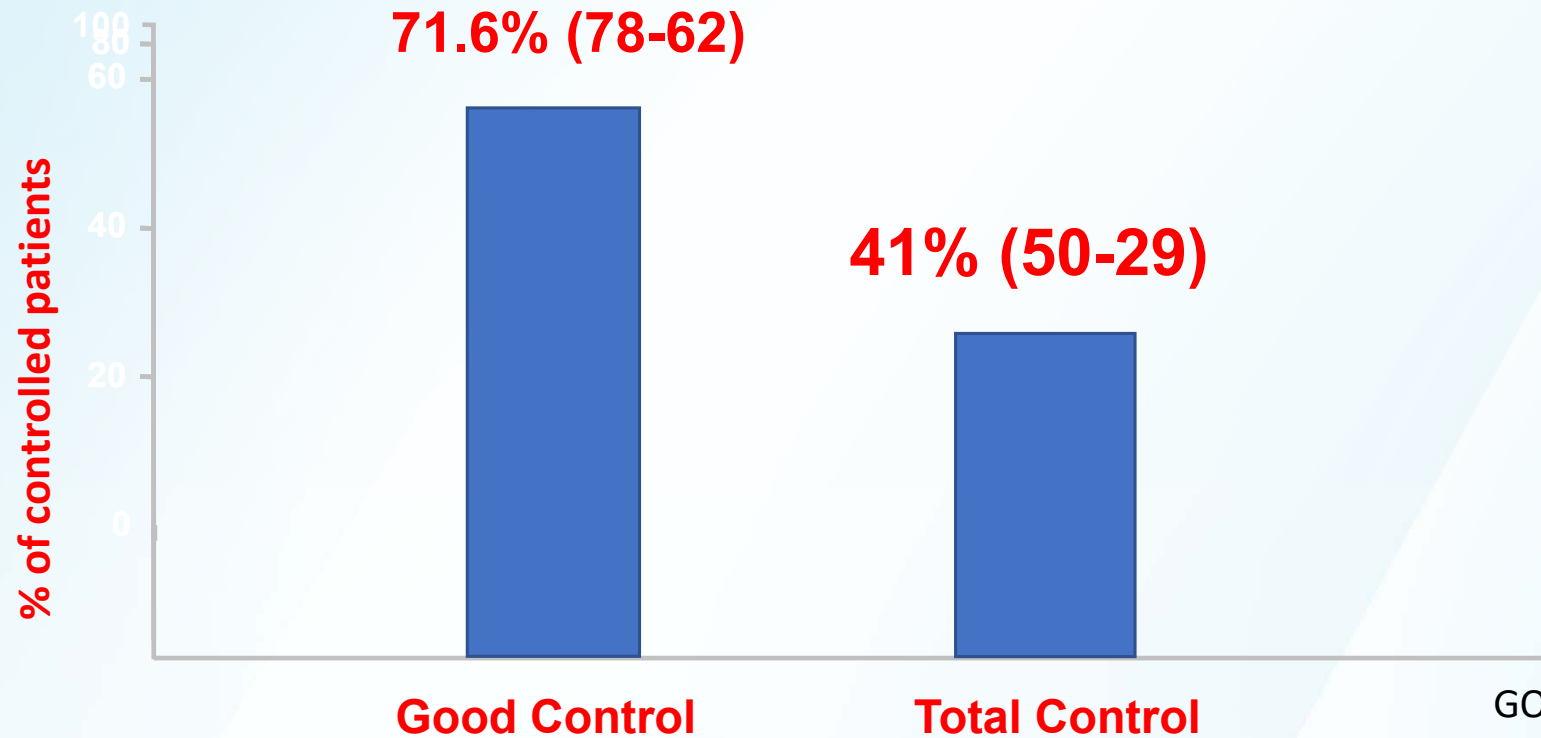
Asma grave: definizione, burden e costi sociali

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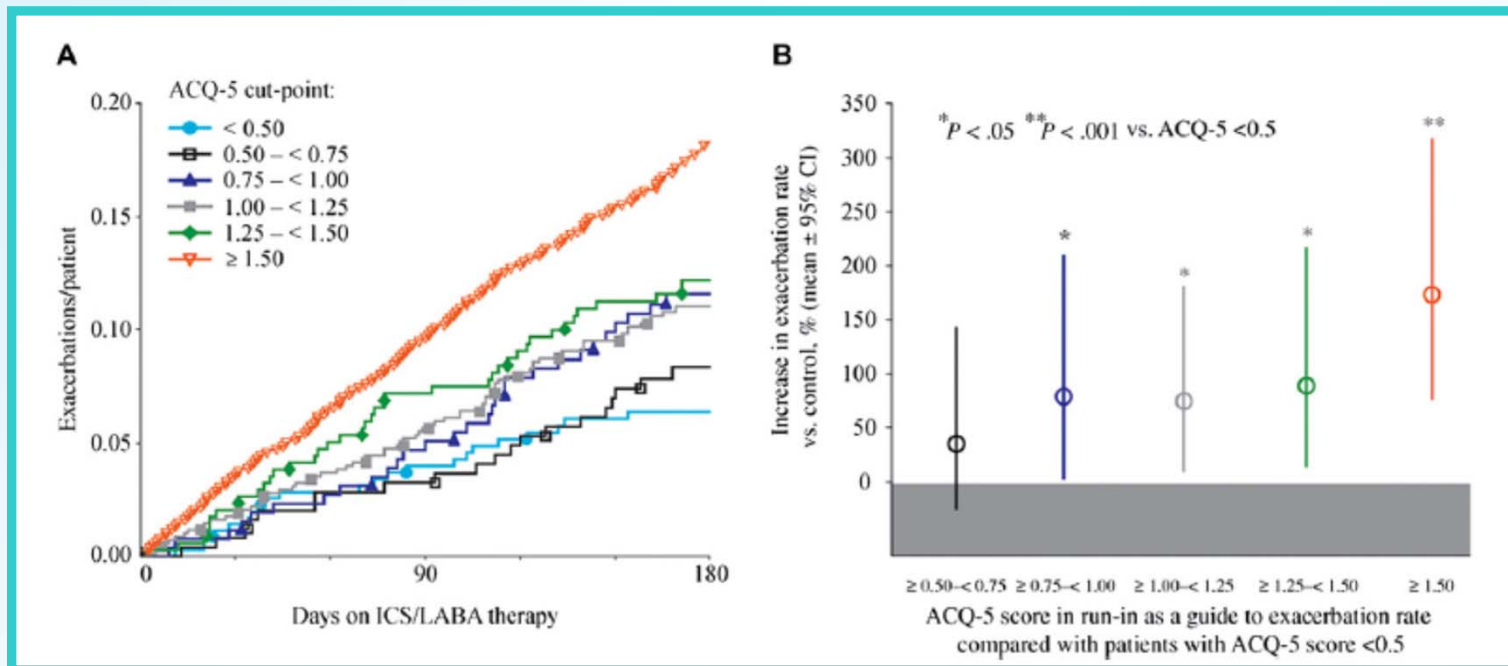
Mean Percentage of “Controlled” patients

Modified by Bateman et al, ARJCCM 2004



GOAL Study 2004

The current level of control can predict the risk of future exacerbations

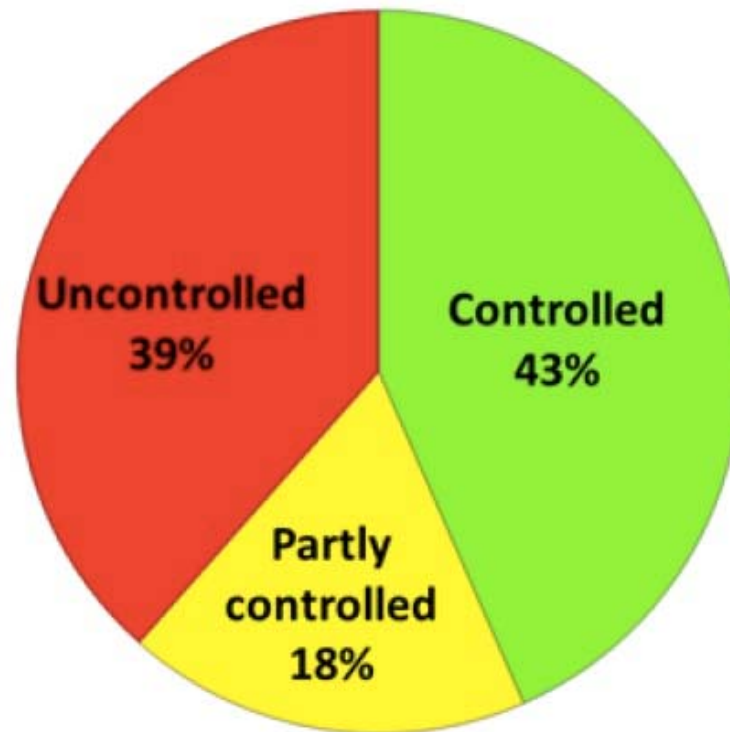


Bateman et al, JACI 2010

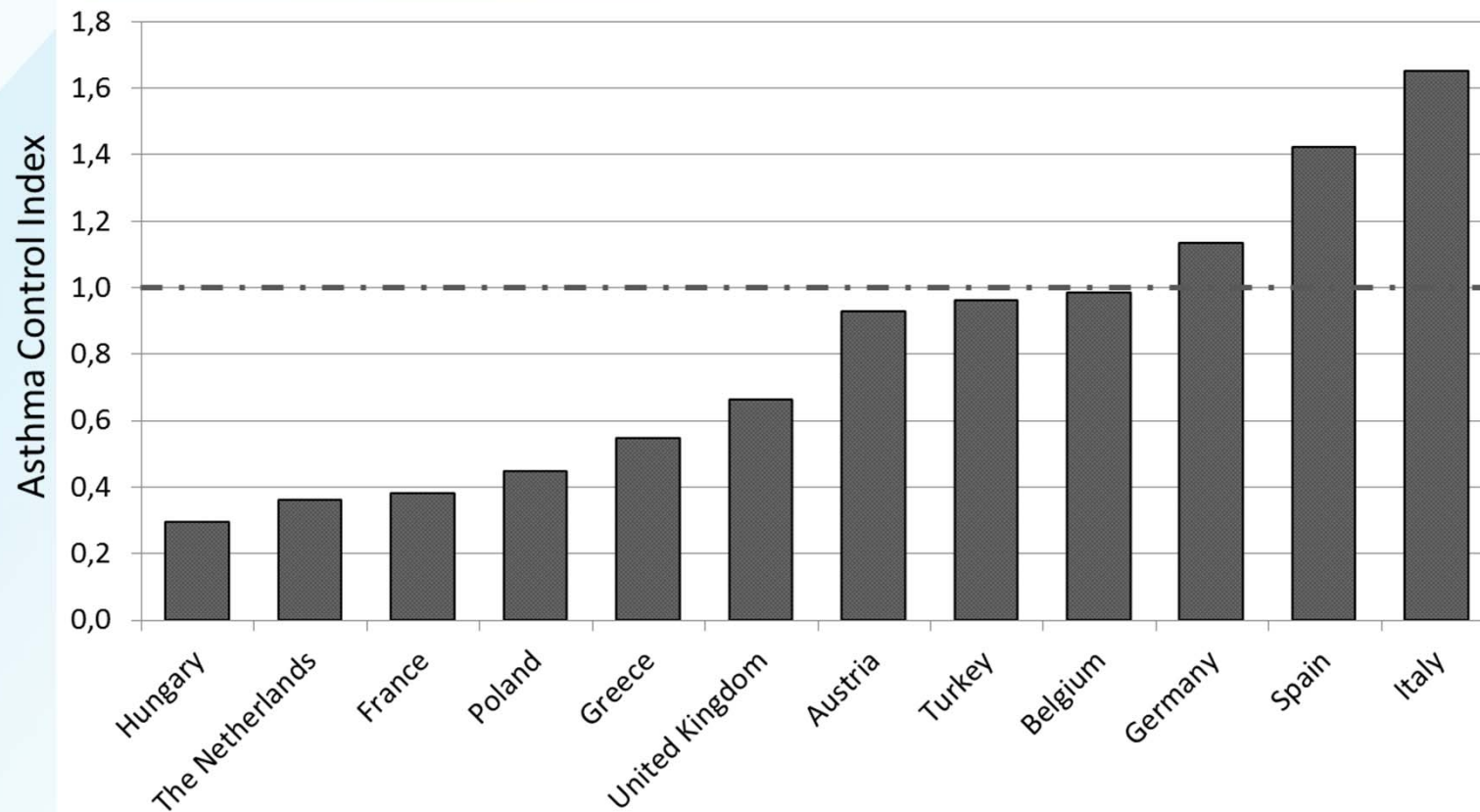
Asthma Control Index in European countries: the LIAISON (International cross-sectional and longitudinal assessment on asthma control) study cross-sectional results

Braido F, Brusselle 2, Guastalla D, Ingrassia E, Nicolini G, Price D, Roche N, Soriano J B and Worth H on behalf of the LIAISON study group

Prevalence of asthma control in Europe



Asthma Control Index



Asthma Control Index >1: greater proportion of patients with controlled asthma ($ACQ \leq 0.75$)

Asthma Control Index <1: greater proportion of patients with not well-controlled asthma ($ACQ > 0.75$)



TASK FORCE REPORT
ERS/ATS GUIDELINES ON SEVERE ASTHMA

International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma

Kian Fan Chung^{1,2,21}, Sally E. Wenzel^{3,21}, Jan L. Brozek⁴, Andrew Bush^{1,2}, Mario Castro⁵, Peter J. Sterk⁶, Ian M. Adcock¹, Eric D. Bateman⁷, Elisabeth H. Bel⁶, Eugene R. Bleecker⁸, Louis-Philippe Boulet⁹, Christopher Brightling¹⁰, Pascal Chanez¹¹, Sven-Erik Dahlen¹², Ratko Djukanovic¹³, Urs Frey¹⁴, Mina Gaga¹⁵, Peter Gibson¹⁶, Qutayba Hamid¹⁷, Nizar N. Jajour¹⁸, Thais Mauad¹⁹, Ronald L. Sorkness¹⁸ and W. Gerald Teague²⁰

Expert Panel → State of the art on Severe Asthma

Grade System → Specific Topics Recommendation

ERS taskforce (1999) definition of
“**Difficult Asthma**”



Eur Respir J. 1999;13:1198-6

ATS workshop (2000) definition of
“**Refractory Asthma**”



AJRCCM 2000; 162:2341-51

WHO definition of severe asthma
2009-2010





Definition of severe asthma for patients aged ≥ 6 years

Asthma which requires treatment with guidelines suggested medications for GINA steps 4–5 asthma (high dose ICS[#] and LABA or leukotriene modifier/theophylline) for the previous year or systemic CS for $\geq 50\%$ of the previous year to prevent it from becoming “uncontrolled” or which remains “uncontrolled” despite this therapy

Uncontrolled asthma defined as at least one of the following:

- 1) Poor symptom control: ACQ consistently >1.5 , ACT <20 (or “not well controlled” by NAEPP/GINA guidelines)
- 2) Frequent severe exacerbations: two or more bursts of systemic CS (>3 days each) in the previous year
- 3) Serious exacerbations: at least one hospitalisation, ICU stay or mechanical ventilation in the previous year
- 4) Airflow limitation: after appropriate bronchodilator withhold $FEV_1 < 80\%$ predicted (in the face of reduced FEV_1/FVC defined as less than the lower limit of normal)

Controlled asthma that worsens on tapering of these high doses of ICS or systemic CS (or additional biologics)

Inhaled corticosteroid	Threshold daily dose in μg considered as high	
	Age 6–12 years	Age >12 years
Beclomethasone dipropionate	≥ 800 (DPI or CFC MDI) ≥ 320 (HFA MDI)	≥ 2000 (DPI or CFC MDI) ≥ 1000 (HFA MDI)
Budesonide	≥ 800 (MDI or DPI)	≥ 1600 (MDI or DPI)
Ciclesonide	≥ 160 (HFA MDI)	≥ 320 (HFA MDI)
Fluticasone propionate	≥ 500 (HFA MDI or DPI)	≥ 1000 (HFA MDI or DPI)
Mometasone furoate	≥ 500 (DPI)	≥ 800 (DPI)
Triamcinolone acetonide	≥ 1200	≥ 2000

When the asthma diagnosis is confirmed and comorbidities addressed

Diseases which can masquerade as severe asthma

Children

- Dysfunctional breathing/vocal cord dysfunction
- Bronchiolitis
- Recurrent (micro)aspiration, reflux, swallowing dysfunction
- Prematurity and related lung disease
- Cystic fibrosis
- Congenital or acquired immune deficiency
- Primary ciliary dyskinesia
- Central airways obstruction/compression
- Foreign body
- Congenital malformations including vascular ring
- Tracheobronchomalacia
- Carcinoid or other tumour
- Mediastinal mass/enlarged lymph node
- Congenital heart disease
- Interstitial lung disease
- Connective tissue disease

Adults

- Dysfunctional breathlessness/vocal cord dysfunction
- Chronic obstructive pulmonary disease
- Hyperventilation with panic attacks
- Bronchiolitis obliterans
- Congestive heart failure
- Adverse drug reaction (e.g. angiotensin-converting enzyme inhibitors)
- Bronchiectasis/cystic fibrosis
- Hypersensitivity pneumonitis
- Hypereosinophilic syndromes
- Pulmonary embolus
- Herpetic tracheobronchitis
- Endobronchial lesion/foreign body (e.g. amyloid, carcinoid, tracheal stricture)
- Allergic bronchopulmonary aspergillosis
- Acquired tracheobronchomalacia
- Churg–Strauss syndrome



Comorbidities and contributory factors

- 1) Rhinosinusitis/(adults) nasal polyps
 - 2) Psychological factors: personality trait, symptom perception, anxiety, depression
 - 3) Vocal cord dysfunction
 - 4) Obesity
 - 5) Smoking/smoking related disease
 - 6) Obstructive sleep apnoea
 - 7) Hyperventilation syndrome
 - 8) Hormonal influences: premenstrual, menarche, menopause, thyroid disorders
 - 9) Gastro-oesophageal reflux disease (symptomatic)
 - 10) Drugs: aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), β -adrenergic blockers, angiotensin-converting enzyme inhibitors
-

Tabella 1. Fattori che influenzano il controllo dell'asma

Fattori correlati alla malattia	Comorbidità	Rinite, rinosinusite, poliposi nasale, reflusso gastro-esofageo, OSAS, obesità
	Fattori esacerbanti	Esposizione ad allergeni ambientali e occupazionali
Fattori relativi al paziente	Fattori socio-demografici	Sesso femminile, basso livello culturale, età avanzata
	Aderenza	Modifiche del regime terapeutico, irregolarità nelle visite di follow-up, inadeguato monitoraggio dei sintomi, mancate modificazioni dello stile di vita (fumo, obesità, scarsa attività fisica)
	Comorbidità psichiatrica	Ansia, disturbi depressivi
	Caratteristiche psicologiche	Alessitimia (tratto di personalità caratterizzato dalla difficoltà a identificare ed esprimere le emozioni)
	Percezioni e adattamento	Tendenza a tollerare i sintomi e ad adattarsi ai limiti imposti dalla malattia
	Aspettative	Basse aspettative personali rispetto alla possibilità di raggiungere il controllo
	Comportamenti	Fumo Tecnica inalatoria inadeguata
	Conoscenze	Informazioni inadeguate su malattia e trattamento
Fattori assistenziali	Mancata diagnosi di asma	Inadeguata consapevolezza della prevalenza di asma – relazione medico/paziente
	Conoscenza delle linee guida	Scarsa familiarità con le linee guida
	Atteggiamento rispetto alle linee guida	Difficoltà ad accettare un particolare documento, o il concetto stesso di linee guida Scarsa fiducia nelle proprie possibilità di applicare le linee guida alla pratica clinica Aspettative di difficoltà e fallimento nel seguire le linee guida
	Implementazione delle linee guida	Difficoltà a modificare procedure e routine ormai consolidate
Fattori legati al rapporto medico-paziente	Comunicazione medico-paziente	Comunicazione inefficace Cattiva intesa Inadeguatezza nel comportamento o nell'atteggiamento da parte del medico e/o del paziente Incapacità del medico a cogliere il punto di vista del paziente rispetto alla malattia e al trattamento Insoddisfazione da parte del medico e del paziente

OSAS: sindrome delle apnee ostruttive nel sonno

Why are we interested in severe asthma?

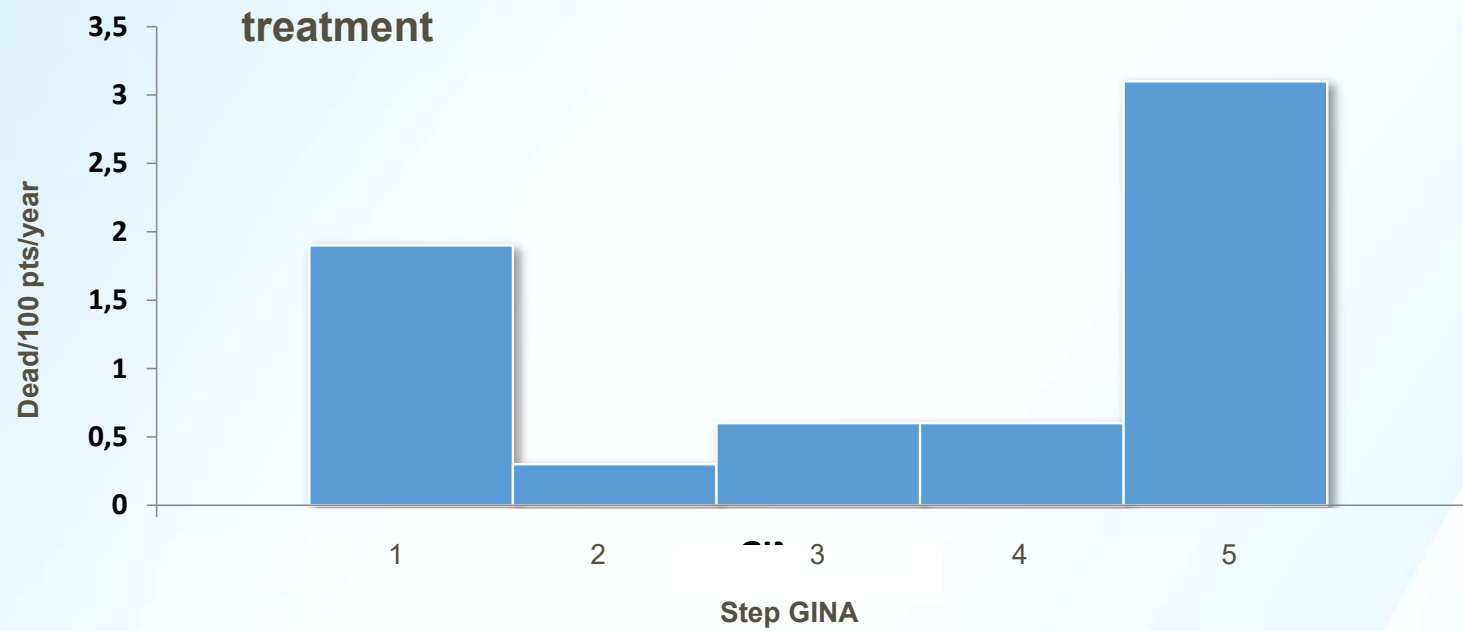
- Although affecting 10-15% of all asthma, this is likely an underestimate
- This phenotype has the greatest disease burden from asthma
 - Highest costs
 - Most compromised to quality of life
 - Greatest frequency of treatment side-effects, particularly systemic corticosteroids
- Treatments, until now, have not been highly effective in severe asthma

Asma grave refrattario

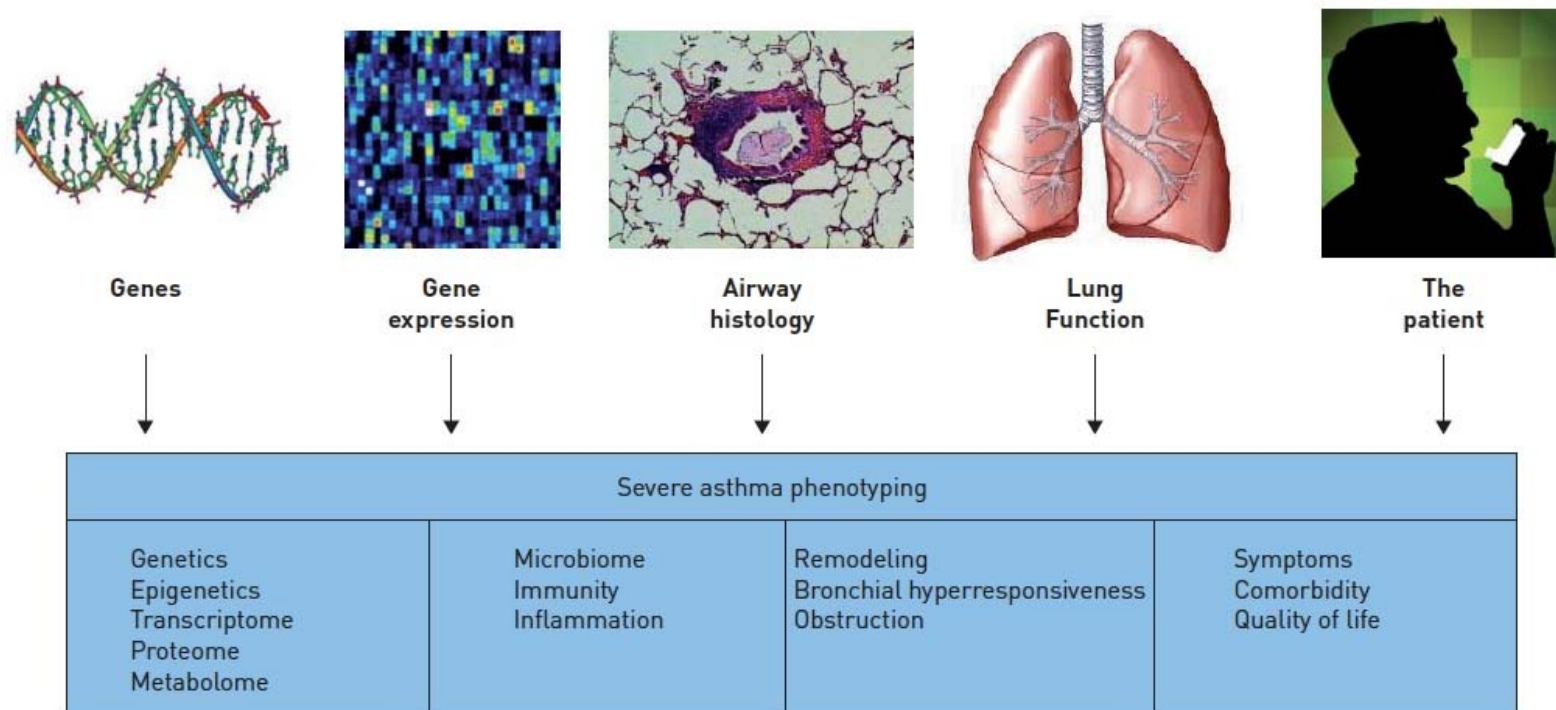


Uno studio di coorte su 1006 asmatici ha evidenziato che le tre definizioni non sono del tutto sovrapponibili; in questa popolazione, infatti, la prevalenza di asma grave era del 3.6% usando la definizione SARP, del 4.8% secondo ERS/ATS e del 6.1% secondo GINA.⁴

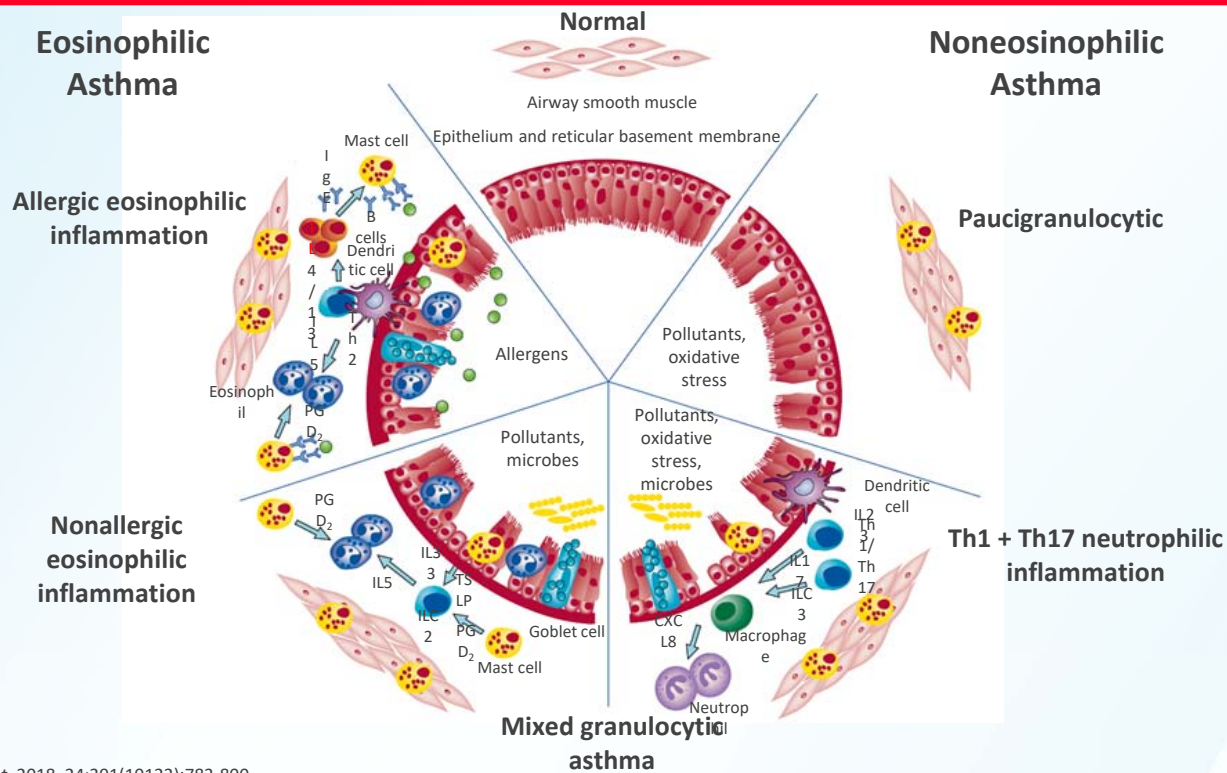
Mortality rate according with GINA steps of treatment



Integration of factors, beginning with genetics, which may contribute to the ultimate phenotype of the severe asthma patient



What are the patterns of inflammation in the pathophysiology of severe asthma?



Papi A, et al. *Lancet*. 2018. 24;391(10122):783-800.

Control

Severity