

# UCDAVIS

**PULMONARY, CRITICAL CARE  
AND SLEEP MEDICINE**

## Providers' Best Practices Update: Asthma and COPD

Indian Health Service Conference  
Sacramento, CA  
May 4<sup>th</sup>, 2015

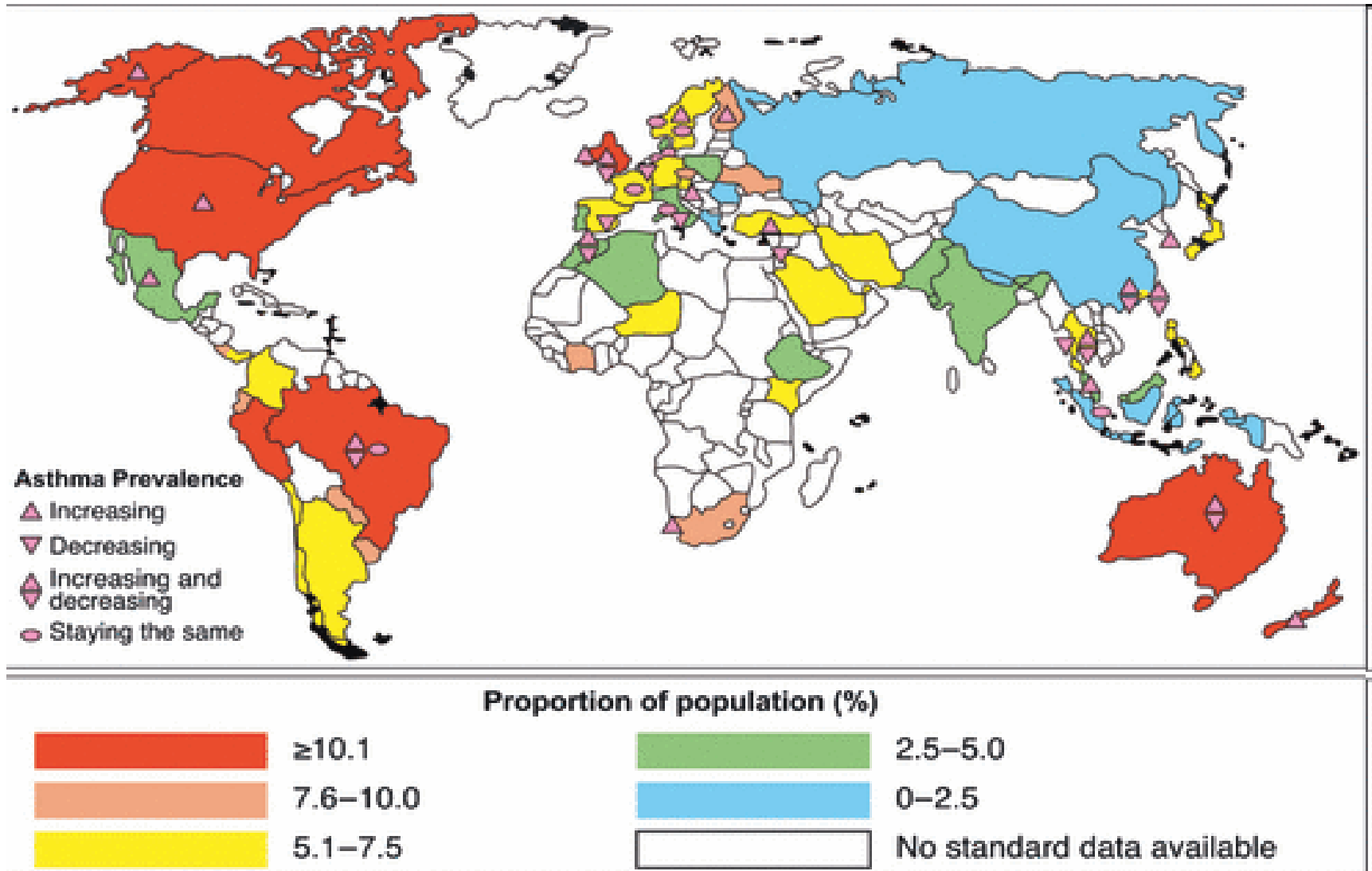
Nicholas Kenyon, MD

Professor and Chief  
Division of Pulmonary, Critical Care, Sleep Medicine  
Co-Director, UC Davis Asthma Network  
University of California, Davis

## Summary: Management of COPD & Asthma

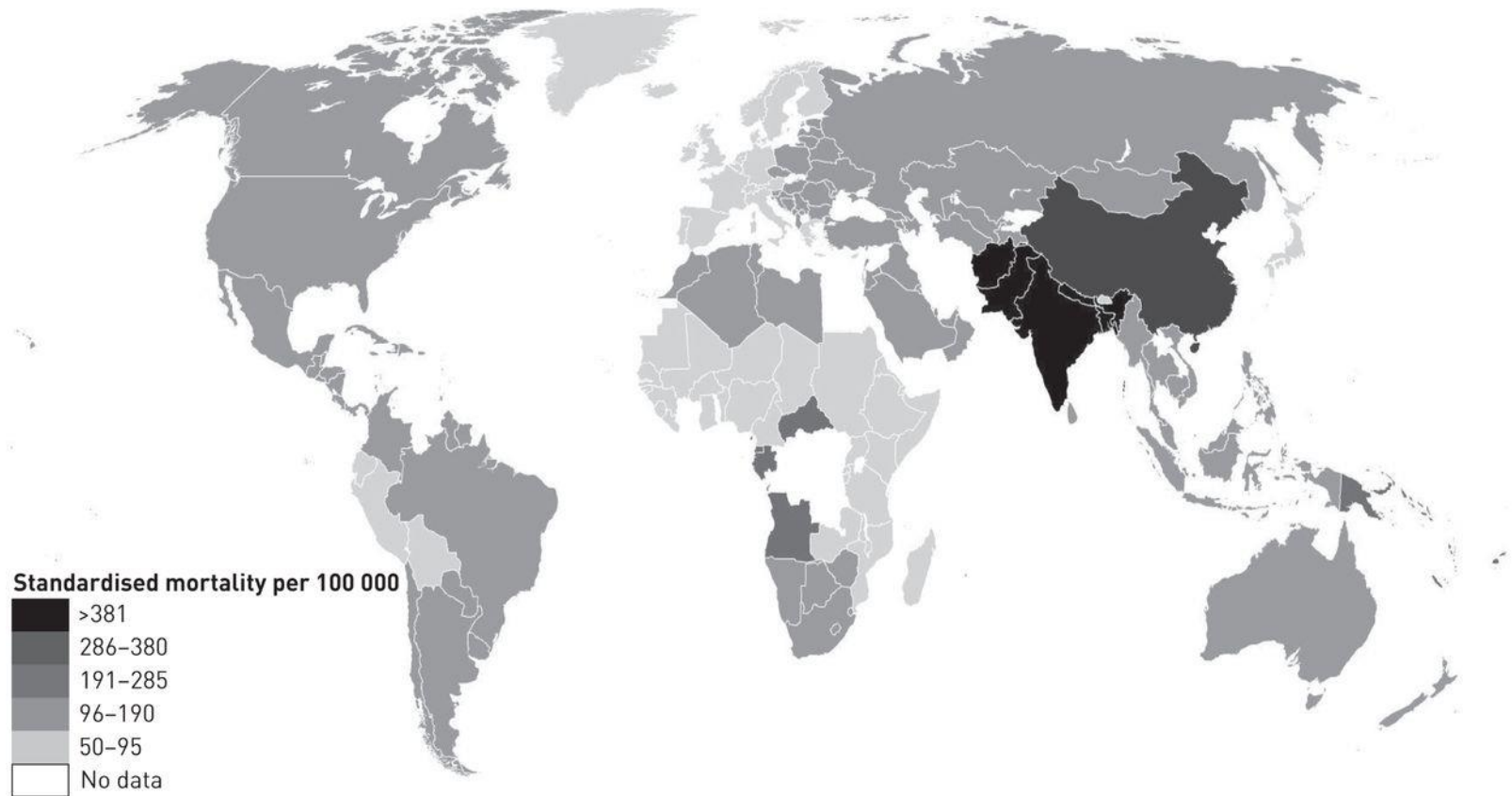
- Epidemiology Trends for Asthma and COPD
- Definitions and Diagnostic Concerns
- Updates with the Management Guidelines
  - Similarities and Differences
- Treating Exacerbations of Asthma and COPD
- Novel Therapies for Asthma
- UC Davis Asthma and COPD Management Programs

# Asthma in the Developed World, 1990-2008



# Global and regional trends in COPD mortality, 1990–2010

Burney et al. ERJ 2015



# The Soaring Cost of a Simple Breath, NY Times

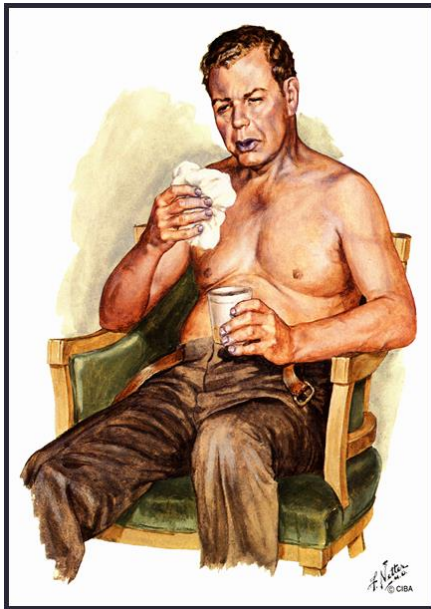
October 12<sup>th</sup>, 2013

40 million asthmatics in US; Asthma Costs are \$56 billion/yr

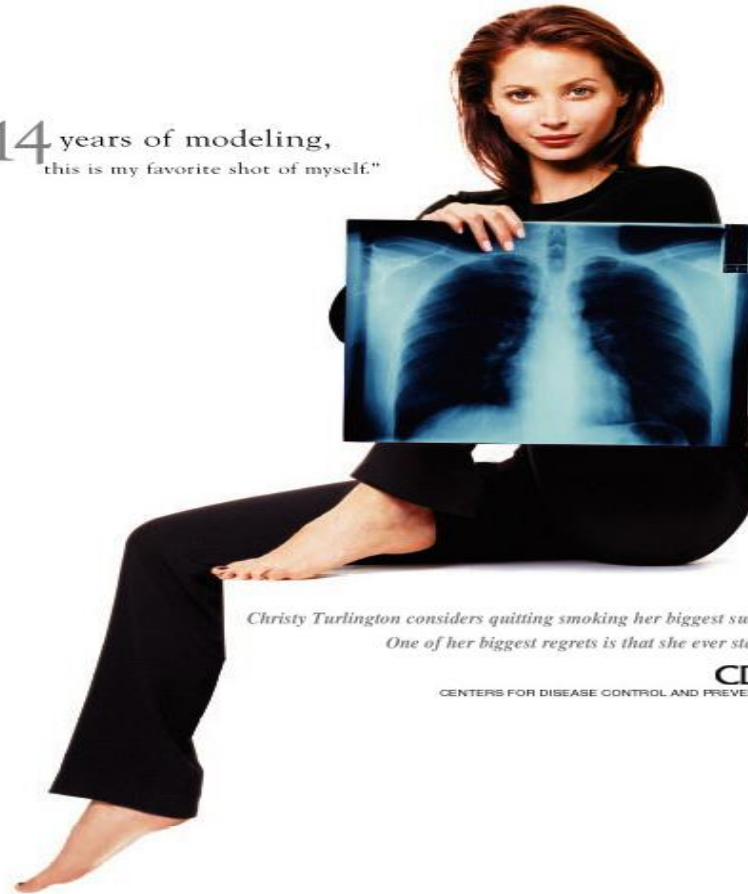


# The New Face of COPD

30 million COPD patients in US; COPD costs are \$49 billion/yr



"In 14 years of modeling,  
this is my favorite shot of myself."



*Christy Turlington considers quitting smoking her biggest success.  
One of her biggest regrets is that she ever started.*

**CDC**  
CENTERS FOR DISEASE CONTROL AND PREVENTION



# COPD is much larger burden in hospital

- 1.5 million Emergency Department (ED) visits for severe COPD exacerbations in United States
  - 726, 000 hospitalizations annually (48%)
  - 270,000 require mechanical ventilation
  - 120,000 deaths annually      CDC, 2000
- 2 million Emergency Department (ED) visits attributed to acute asthma exacerbations annually in United States
  - 500,000 hospitalizations annually (25% of visits)
  - 25,000 intubations annually (5% of hospitalizations)
  - 5,000 deaths annually, majority occur outside hospital

# California Department of Public Health, 2010

## Summary of Asthma Measures by Race/Ethnicity

Measures (All Ages Unless Otherwise Specified)	Black	AI/AN	White	Hispanic	A/PI
Lifetime Asthma Prevalence (p. 31)	20.8%	21.2%	14.9%	10.0%	12.1%*
Current Asthma Prevalence (p. 31)	13.0%	15.6%	9.0%	5.9%	6.5%*
Percent with Well-Controlled Asthma (adults with current asthma, p. 52)	45.8%	52.0%†	54.7%	48.5%	58.1%*†
Asthma ED Visit Rate (per 10,000, p. 114)	157.5	26.9	38.6	43.2	17.9
Medi-Cal Asthma ED Visit Rate (per 10,000, p. 147)	317.0	227.7	164.9	115.1	60.8
Asthma Hospitalization Rate (per 10,000, p. 128)	29.0	4.7	7.6	8.7	6.1
Percent with Repeat Asthma Hospitalizations (p. 140)	18.8%	4.3%	11.3%	8.9%	10.5%
Medi-Cal Asthma Hospitalization Rate (per 10,000, p. 151)	63.0	31.1	25.3	19.5	17.4
Asthma Death Rate (per million, p. 161)	32.7	6.8	11.5	9.0	15.2*

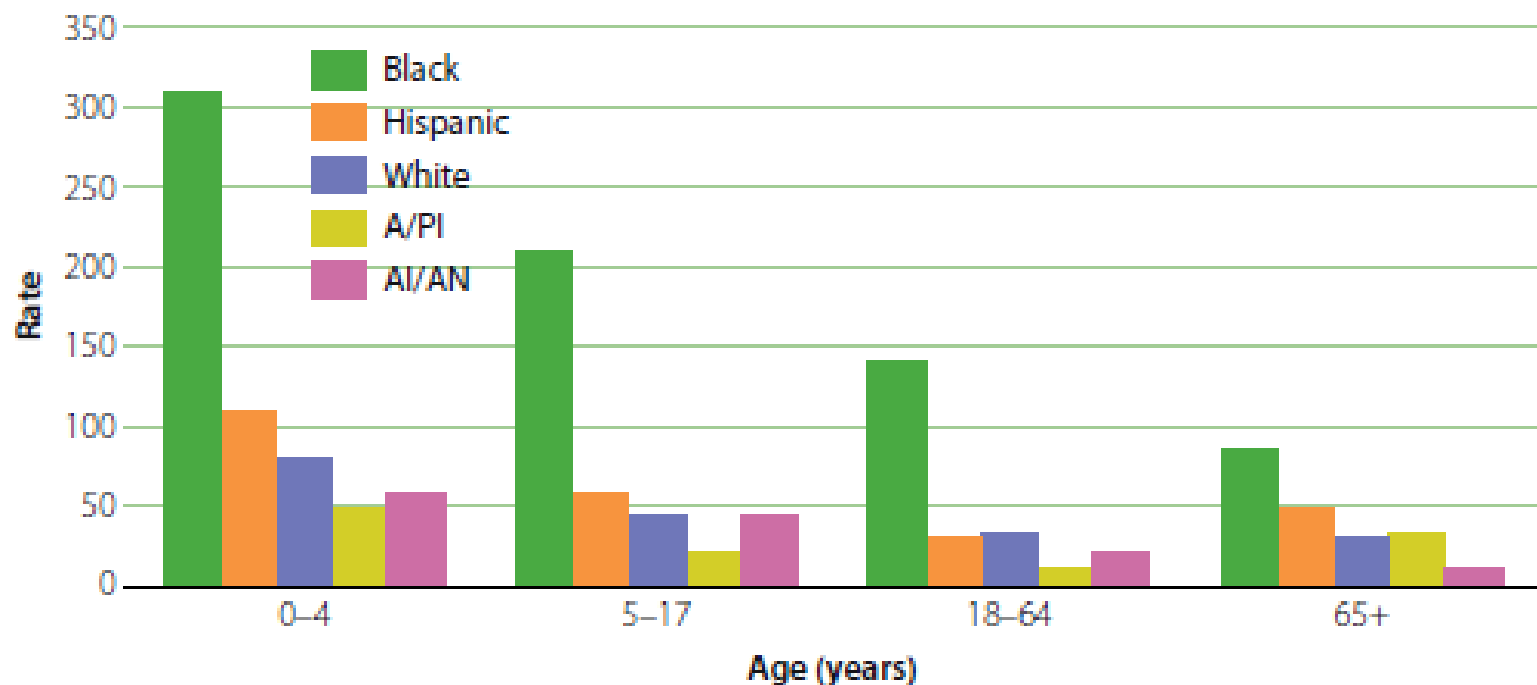
\* Asian only (does not include Pacific Islanders)

† Unstable estimate – please note the wide confidence interval (see Technical Notes for details).

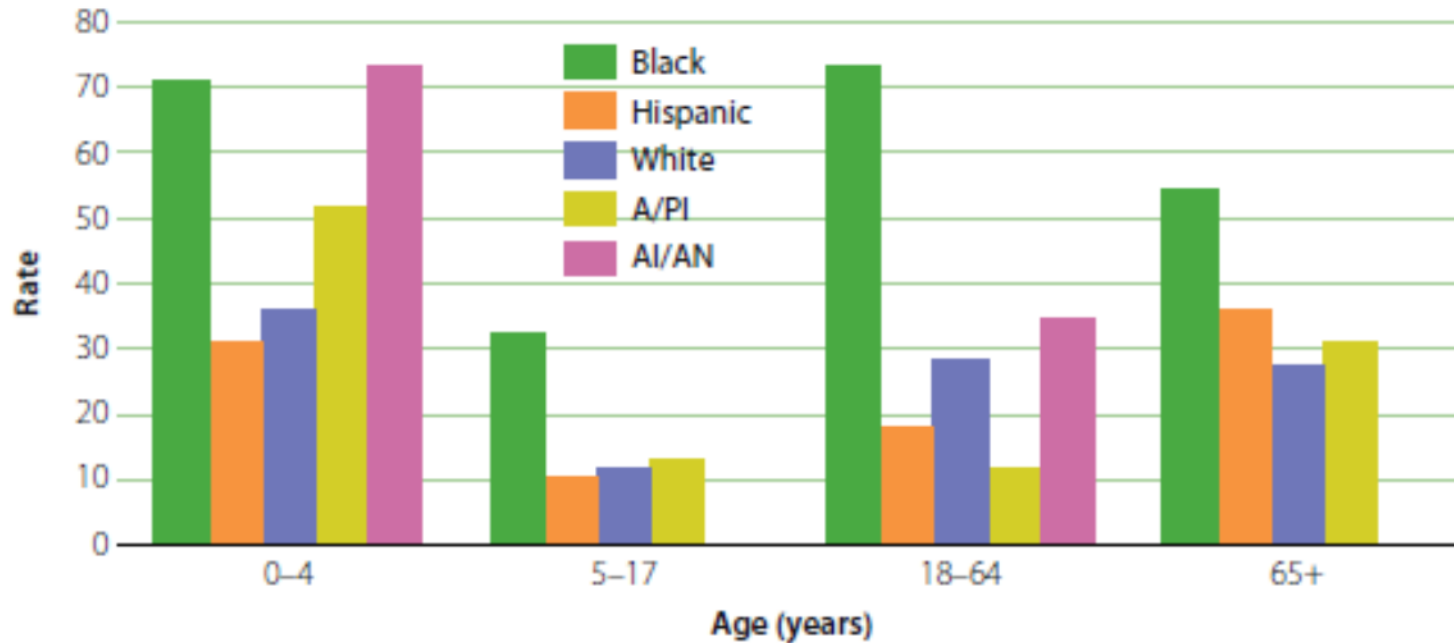


## Age-Adjusted Asthma ED Visits per 10,000 California Residents by Race/Ethnicity and Age, 2010

Racial disparities persist across all ages, with Blacks having asthma ED visit rates that are 3–5 times higher than Whites. In the 65+ age group, the A/PI rate is slightly higher than among Whites, whereas their rate is much lower than Whites in all of the younger age groups.



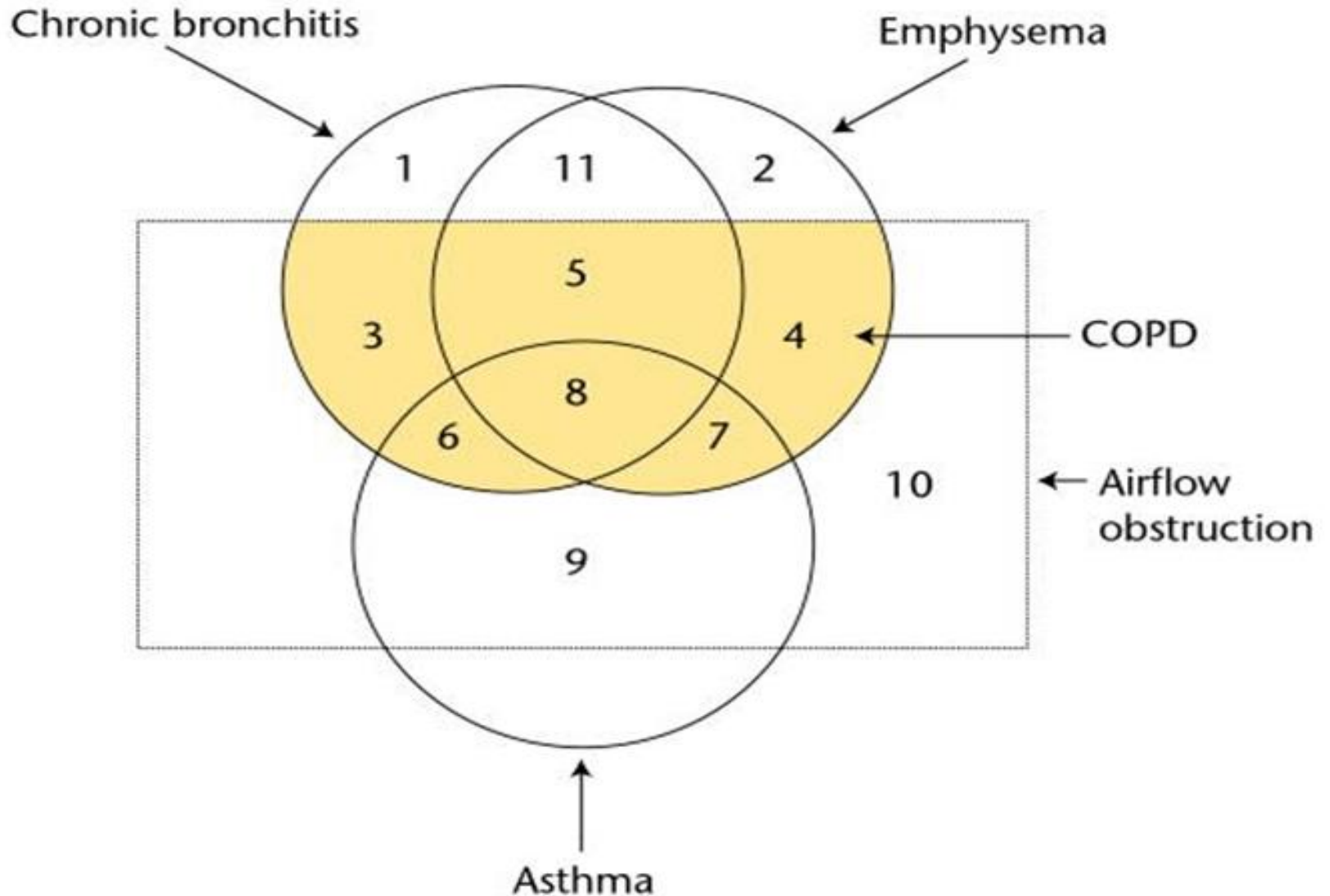
# California Department of Public Health, 2010



**Medi-Cal Asthma Hospitalizations per 10,000 Continuously Enrolled Beneficiaries by Age and Race/Ethnicity, 2010**

# ACOS: Asthma COPD Overlap Syndrome

Zeki et al. J Asthma 2011; Louie et al. 2013





## Definition of Asthma

A chronic inflammatory disorder of the airways in which many cells and elements play a role

Chronic inflammation leads to an increase in airway hyper-responsiveness with recurrent episodes of wheezing, coughing, and shortness of breath

Widespread, variable, and often reversible airflow limitation

## Definition of COPD



### SYMPTOMS

cough  
sputum  
dyspnea

### EXPOSURE TO RISK FACTORS

tobacco  
occupation  
indoor/outdoor  
pollution



**SPIROMETRY**

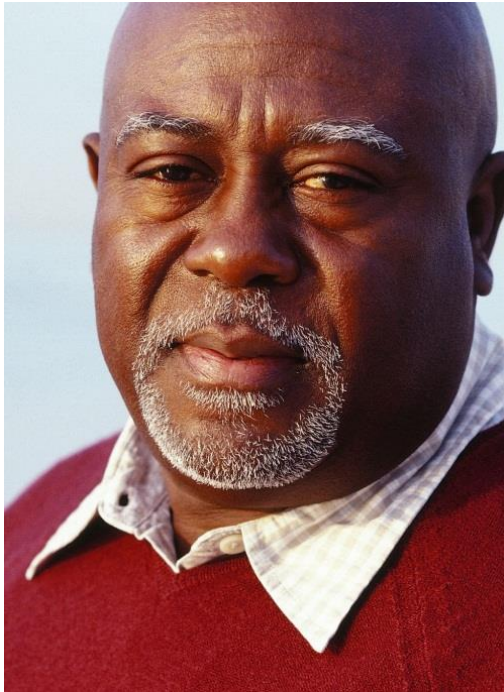
# COPD : ATS/ERS Definition

- “COPD is a *preventable and treatable* disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal *inflammatory response* of the lungs to noxious particles or gases, primarily caused by cigarette smoking. Although COPD affects the lungs, it also produces *systemic consequences*.”
- Progressive disorder even when contributing factors are eliminated and aggressive therapy is instituted

American Thoracic Society 2004

[www.thoracic.org/sections/copd/resources/copddoc.pdf](http://www.thoracic.org/sections/copd/resources/copddoc.pdf)

# Asthma, or COPD or ACOS



## 59-year-old man

- FEV<sub>1</sub> 69% predicted
- Current smoker
- Productive cough in the morning
- No longer can walk up stairs
- ? Osteoporosis, coronary artery disease



## 42-year-old woman

- FEV<sub>1</sub> 66% predicted
- 10 pack-year history of smoking
- Increased shortness of breath when gardening
- ? Osteoporosis, coronary artery disease

# ACOS: Asthma COPD Overlap Syndrome

Zeki et al. J Asthma 2011; Louie et al 2013

Louie et al.

Major criteria:

1. Physician diagnosis of asthma and COPD in the same patient
2. History or evidence of atopy—such as hay fever and elevated total IgE
3. >40 years old
4. Smoking >10 pack years
5. Post-Bronchodilator FEV1 < 80 % predicted and COPD per GOLD definition.

Minor criteria:

1.  $\geq 15$  % increase in post-bronchodilator FEV1 or
2.  $\geq 12$  % and  $\geq 200$  ml in post-bronchodilator FEV1

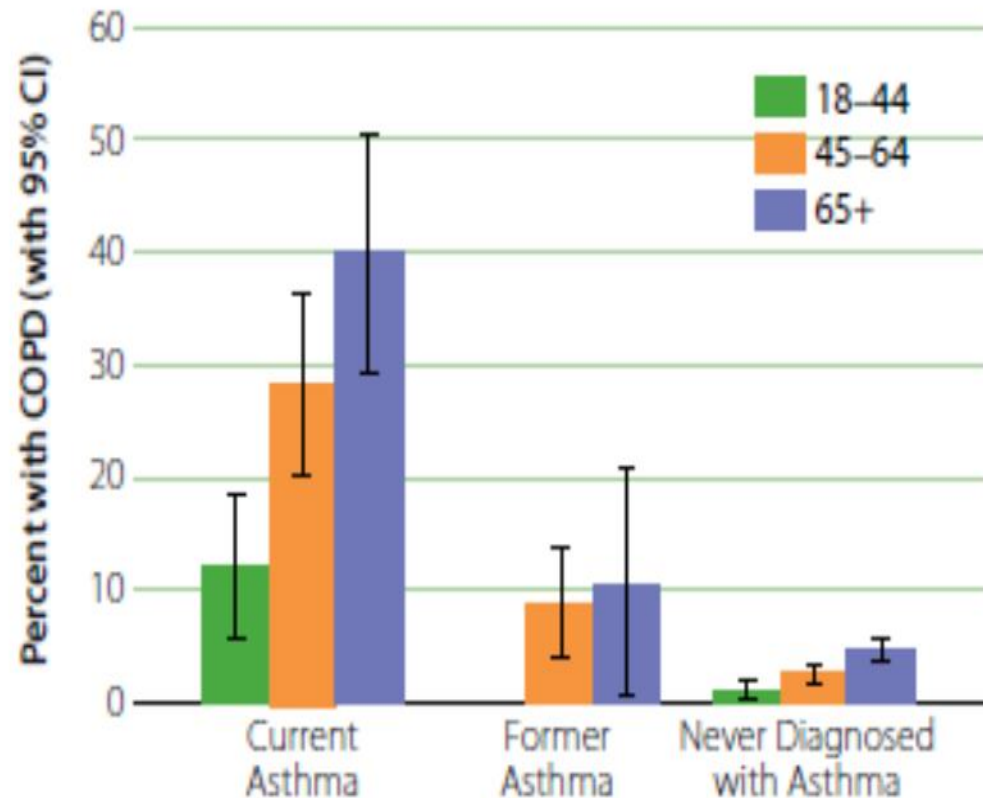


# California Department of Public Health, 2010

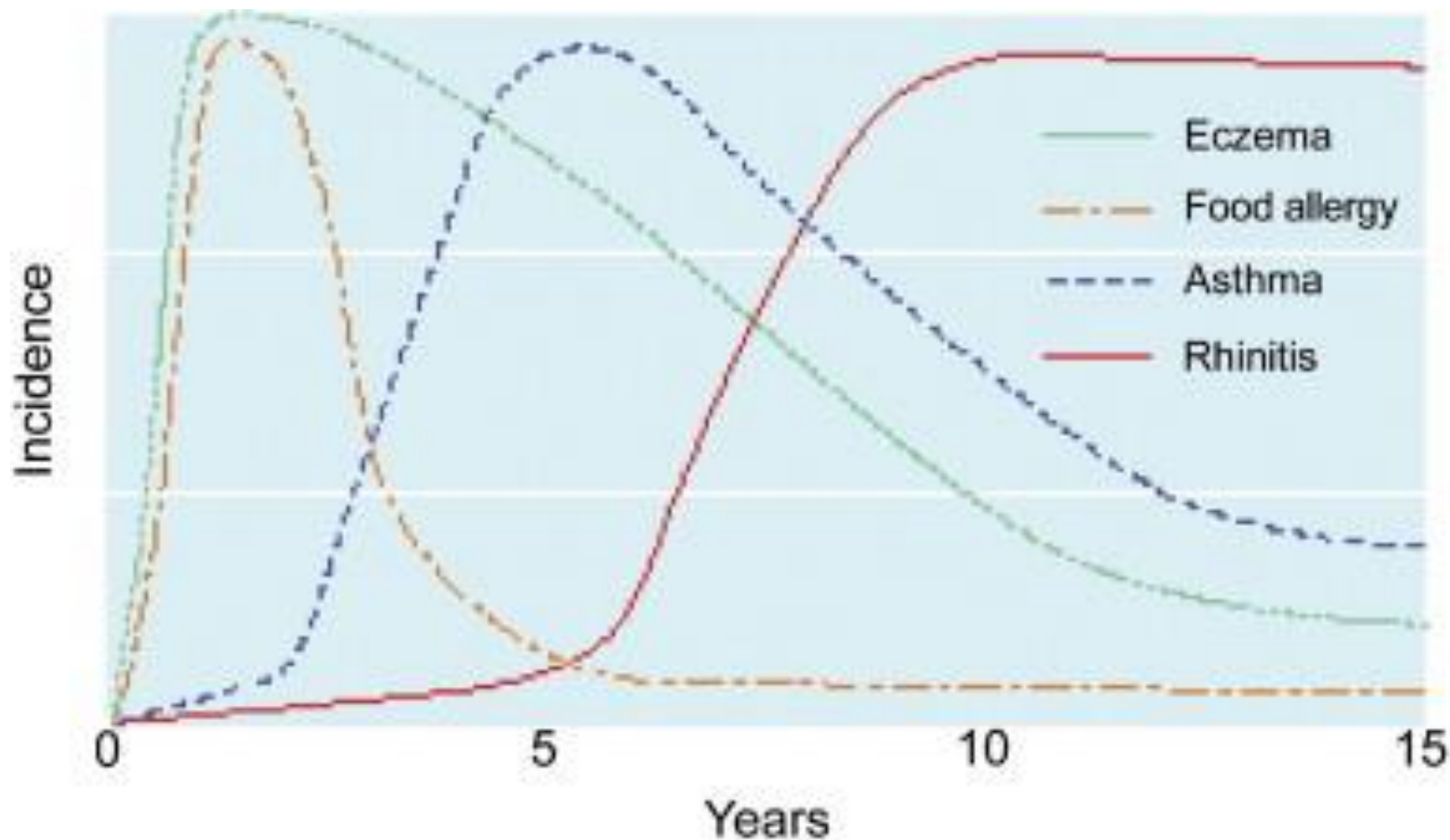
## Percent of Adults Ever Diagnosed with COPD, by Asthma Status and Age, California 2009

Adults with current asthma are almost 8-10 more likely to have COPD than adults who have never had asthma.\*

\*Chi-square  $p < 0.01$  for all age groups

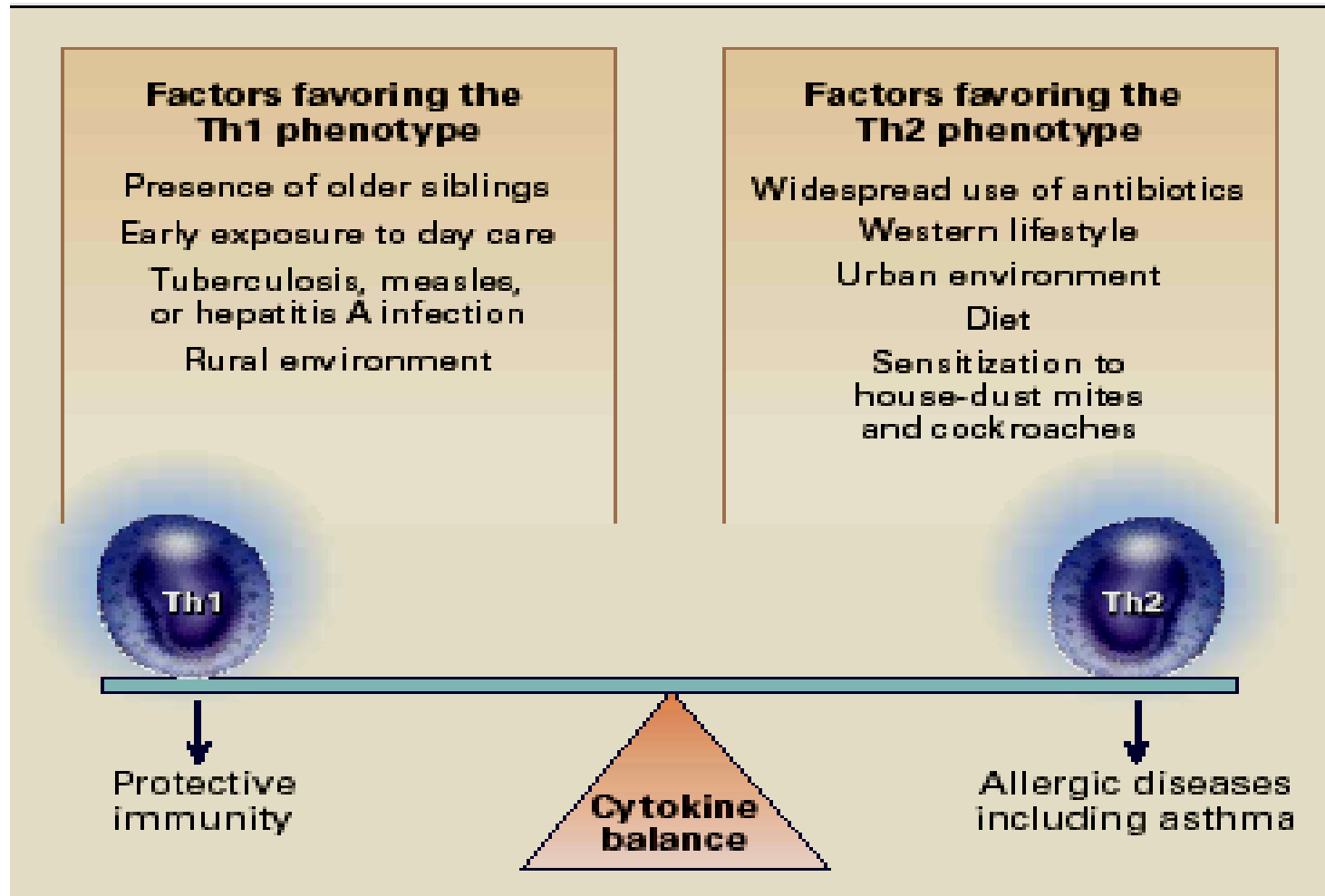


Atopic March—Allergic airway inflammation may begin in the skin and intestine.

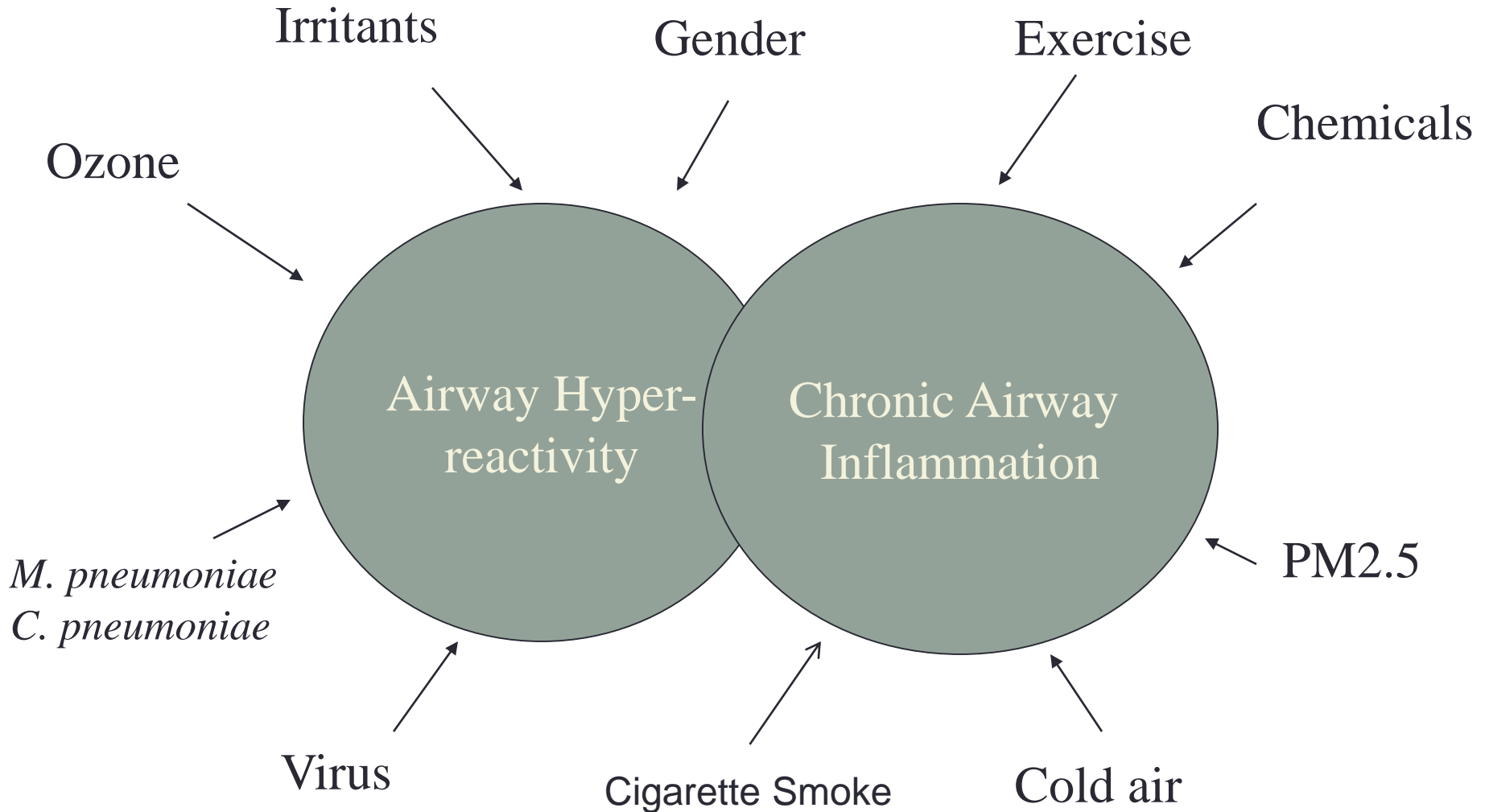


# The Hygiene Hypothesis

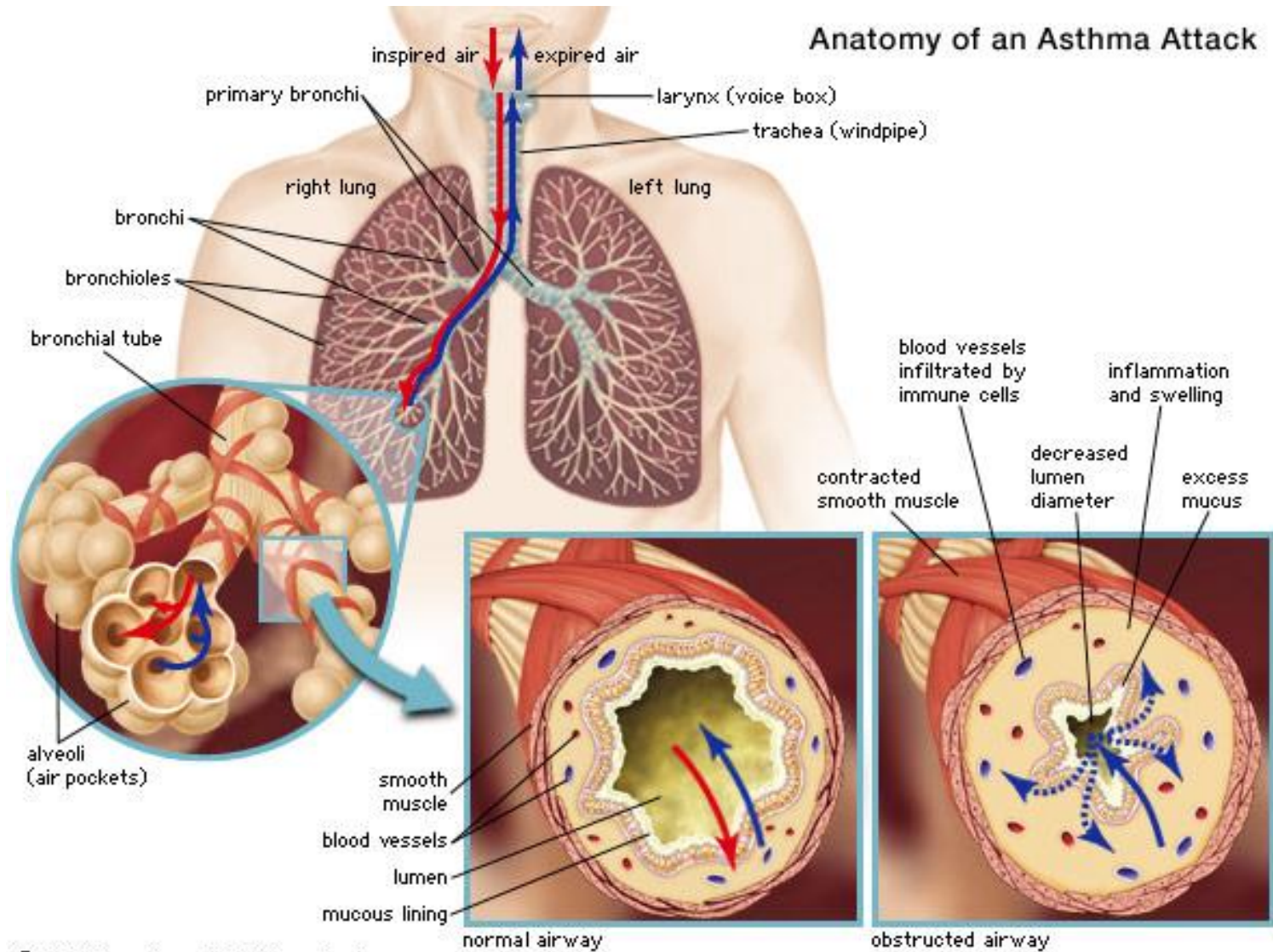
Busse et al. NEJM 2000



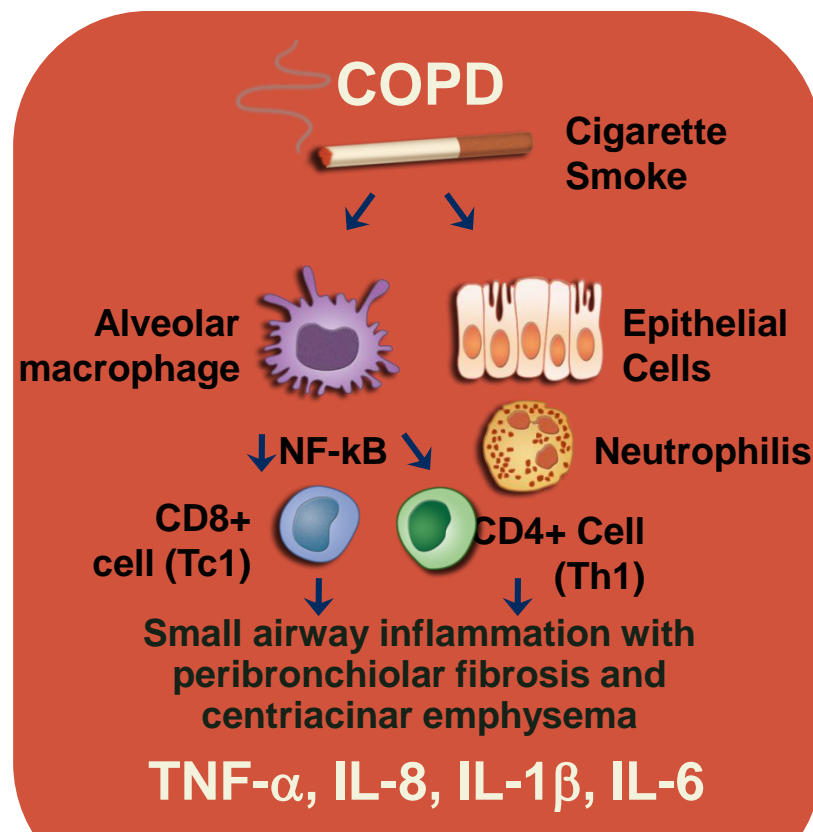
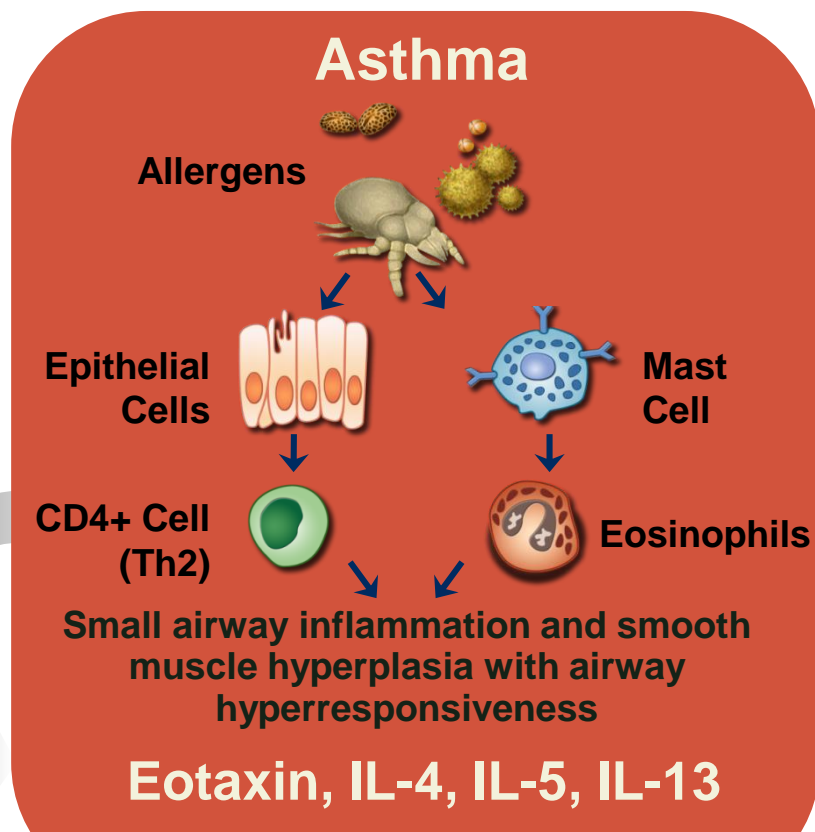
Neither asthma nor chronic bronchitis is a single disease. It is a spectrum of airway disorders with common features.



# What happens to the airway over a lifetime?



# Asthma versus COPD: Pathobiology



NOT FULLY  
REVERSIBLE

**Airflow Limitation**

NOT FULLY  
REVERSIBLE

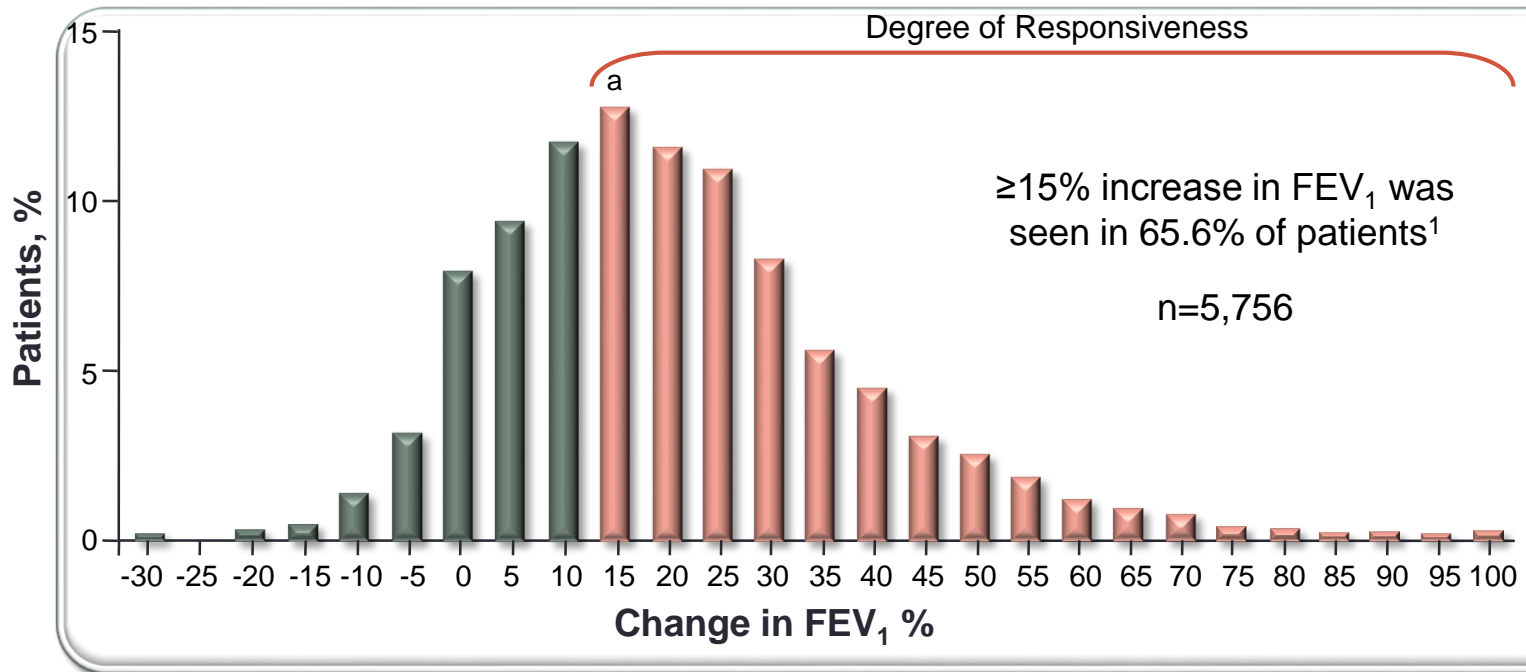
IL = interleukin; TNF = tumor necrosis factor.

Adapted from Global Initiative for Chronic Obstructive Lung Disease. <http://www.goldcopd.org/Guidelineitem.asp?l1=2&l2=1&intlId=989>. Accessed November 21, 2008.

# COPD: Yes, there is bronchodilator reversibility.

## Short- and long-acting bronchodilators

- May improve airflow obstruction and lung volumes<sup>2</sup>
- Play a central role in the treatment of COPD<sup>2</sup>



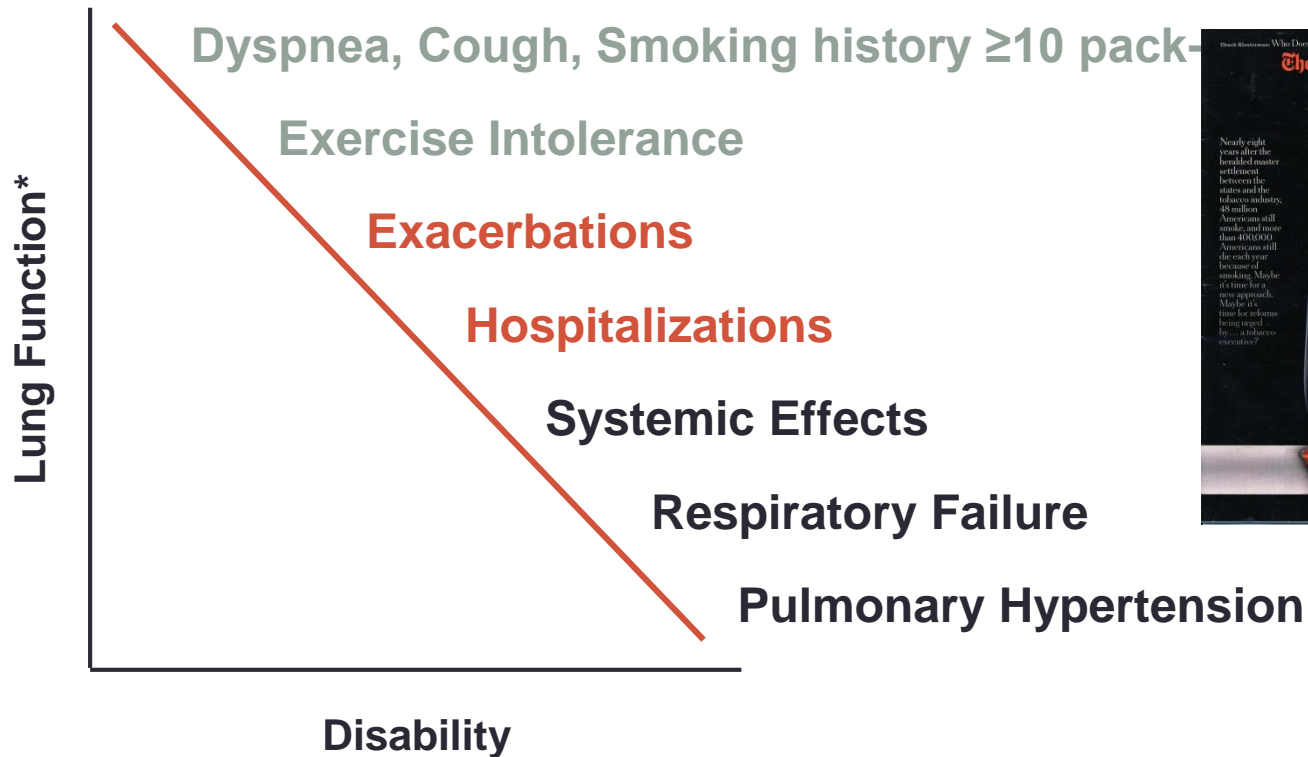
**~54% of patients met ATS responsiveness criteria (≥12% + ≥200 mL)<sup>2</sup>**

1. Tashkin DP, et al. *Eur Respir J*. 2008;31(4):742-750. 2. Global Initiative for Chronic Obstructive Lung Disease. [http://www.goldcopd.org/uploads/users/files/GOLD\\_Report\\_2013\\_Feb20.pdf](http://www.goldcopd.org/uploads/users/files/GOLD_Report_2013_Feb20.pdf). Accessed August 6, 2013.



# COPD : Early Diagnosis Difficult

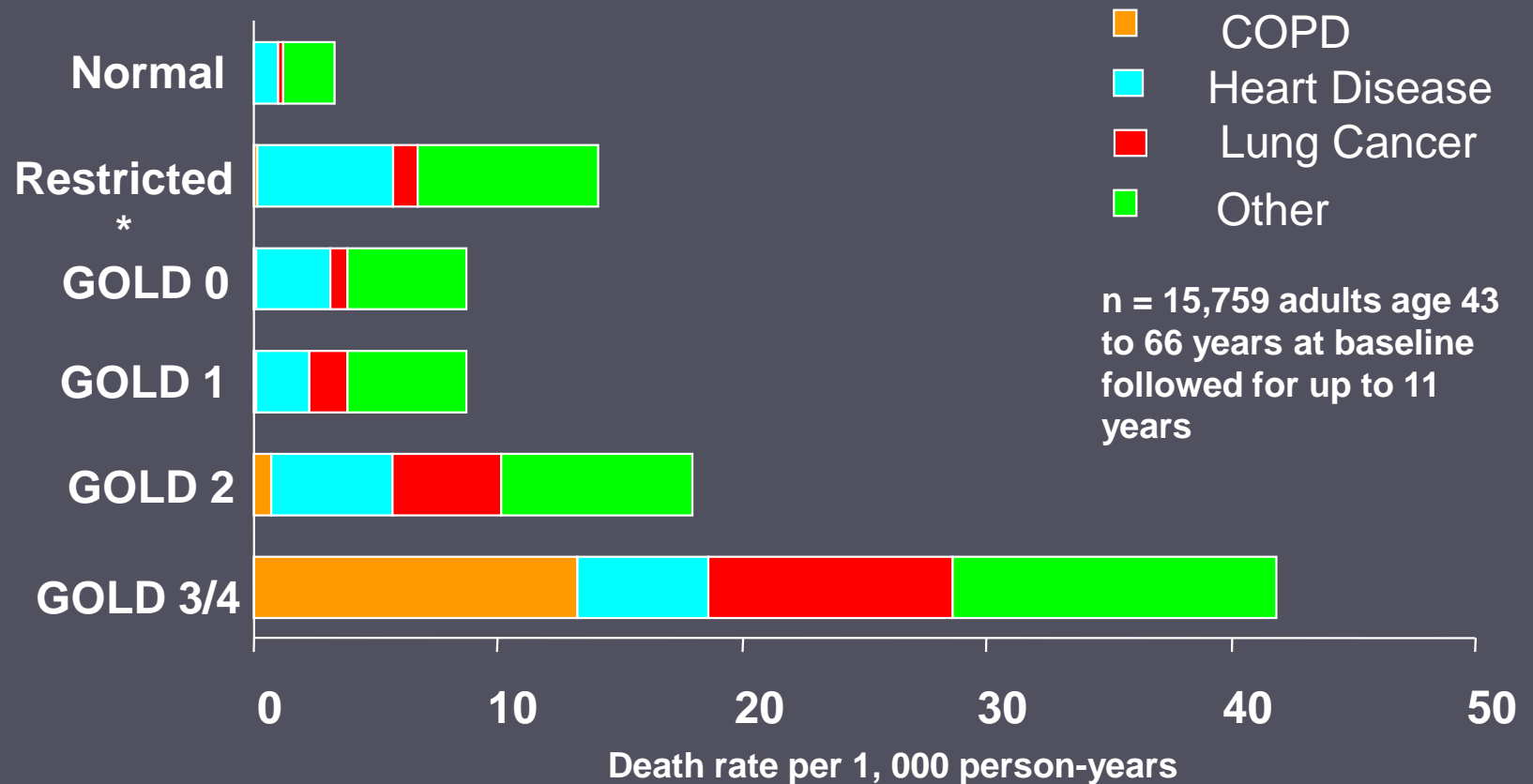
Significant Drops (50%) in Lung Function Are Often Required for Patients to Become Severely Symptomatic



\*FEV<sub>1</sub> % predicted

Adapted from Fletcher C and Peto R. *Br Med J* 1977; 1: 1645-1648.

# COPD : What do patients die from?



\* Restricted category defined by FEV1/FVC > 0.70 and FVC < 80% predicted

Mannino DM et al. *Respir Med.* 2006;100(1):115-122. Global Initiative for Chronic Obstructive Lung Disease (GOLD) Executive Summary. Updated 2009. <http://www.goldcopd.com>.

# COPD : Spirometry = Severity

**Post-bronchodilator FEV<sub>1</sub>/FVC < 0.70 supports a COPD diagnosis**  
**Post-bronchodilator FEV<sub>1</sub> % predicted determines severity:**

GOLD 1: Mild

FEV<sub>1</sub> ≥ 80% predicted

GOLD 2: Moderate

50% ≤ FEV<sub>1</sub> < 80% predicted

GOLD 3: Severe

30% ≤ FEV<sub>1</sub> < 50% predicted

GOLD 4: Very Severe

FEV<sub>1</sub> < 30% predicted

Table adapted from the Global Strategy for Diagnosis, Management and Prevention of COPD 2013, © Global Initiative for Chronic Obstructive Lung Disease (GOLD), all rights reserved. Available from <http://www.goldcopd.org>.

# COPD : WHO/NIH GOLD Guidelines

Figure 5-3-8. Therapy at Each Stage of COPD					
Old	0: At Risk	I: Mild	II: Moderate IIA IIB		III: Severe
New	0: At Risk	I: Mild	II: Moderate	III: Severe	IV: Very Severe
Characteristics	<ul style="list-style-type: none"> <li>Chronic symptoms</li> <li>Exposure to risk factors</li> <li>Normal spirometry</li> </ul>	<ul style="list-style-type: none"> <li>FEV<sub>1</sub>/FVC &lt; 70%</li> <li>FEV<sub>1</sub> ≥ 80%</li> <li>With or without symptoms</li> </ul>	<ul style="list-style-type: none"> <li>FEV<sub>1</sub>/FVC &lt; 70%</li> <li>50% ≤ FEV<sub>1</sub> &lt; 80%</li> <li>With or without symptoms</li> </ul>	<ul style="list-style-type: none"> <li>FEV<sub>1</sub>/FVC &lt; 70%</li> <li>30% ≤ FEV<sub>1</sub> &lt; 50%</li> <li>With or without symptoms</li> </ul>	<ul style="list-style-type: none"> <li>FEV<sub>1</sub>/FVC &lt; 70%</li> <li>FEV<sub>1</sub> &lt; 30% or FEV<sub>1</sub> &lt; 50% predicted plus chronic respiratory failure</li> </ul>
	Avoidance of risk factor(s); influenza vaccination				
		Add short-acting bronchodilator when needed			
			Add regular treatment with one or more long-acting bronchodilators Add rehabilitation		
				Add inhaled glucocorticosteroids if repeated exacerbations	
					Add long-term oxygen if chronic respiratory failure Consider surgical treatments

# COPD Assessment Scores

## mMRC Dyspnea Score

- Grade 0: SOB w/ strenuous exercise
- Grade 1: SOB w/ hurrying on level ground or slight hill
- Grade 2: SOB w/ normal walking >100 meters; slower than others my age
- Grade 3: SOB after 100 meters
- Grade 4: SOB w/ ADLs or leaving the house

## How is your COPD? Take the COPD Assessment Test (CAT)

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

If you wish to complete the questionnaire by hand on paper, [please click here](#) and then print the questionnaire.

If you complete the questionnaire on-line, for each question below, click your mouse to place a mark (X) in the box that best describes you currently.

Example: I am very happy (0)  (1) (2) (3) (4) (5) I am sad

Question	Score
I never cough (0) (1) (2) (3) <input checked="" type="radio"/> (5) I cough all the time	4
I have no phlegm (mucus) in my chest at all (0) (1) (2) (3) <input checked="" type="radio"/> (5) My chest is full of phlegm (mucus)	4
My chest does not feel tight at all (0) (1) (2) (3) <input checked="" type="radio"/> (5) My chest feels very tight	4
When I walk up a hill or one flight of stairs I am not breathless (0) (1) (2) (3) (4) <input checked="" type="radio"/> (5) When I walk up a hill or one flight of stairs I am very breathless	5
I am not limited doing any activities at home (0) (1) (2) (3) (4) <input checked="" type="radio"/> (5) I am very limited doing activities at home	5
I am confident leaving my home despite my lung condition (0) (1) (2) (3) (4) <input checked="" type="radio"/> (5) I am not at all confident leaving my home because of my lung condition	5
I sleep soundly (0) (1) (2) (3) (4) <input checked="" type="radio"/> (5) I don't sleep soundly because of my lung condition	5
I have lots of energy (0) (1) (2) (3) (4) <input checked="" type="radio"/> (5) I have no energy at all	5
<b>CLICK TO GET YOUR TOTAL SCORE!</b>	
<b>37</b>	

# Management of COPD: WHO/NIH GOLD Guidelines

**Symptoms:** Based on mMRC or CAT scores

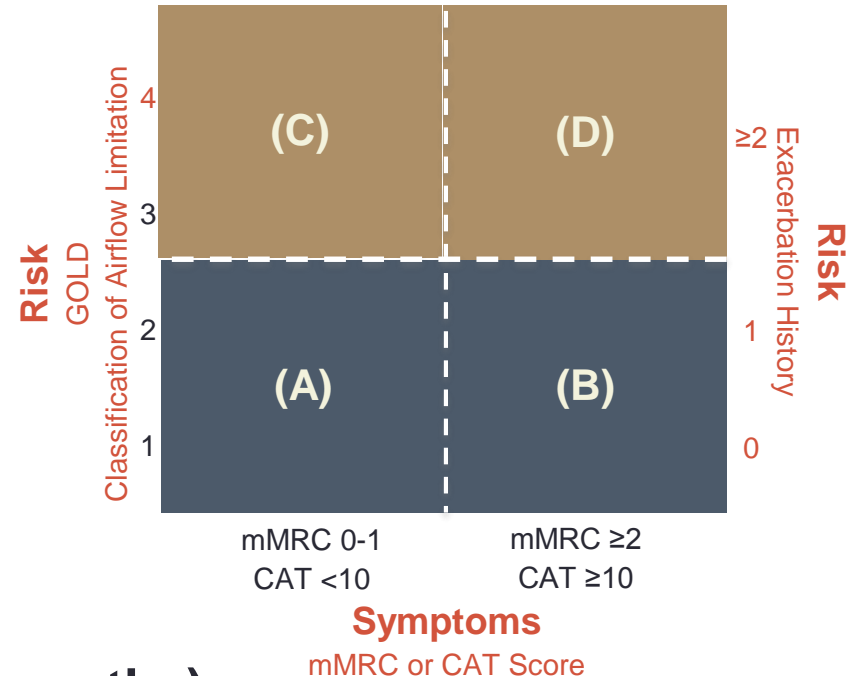
**Risk:** Based on GOLD grades and/or exacerbation history

## Spirometric Classification

- Low risk: GOLD grades 1 and 2
- High risk : GOLD grades 3 and 4

## Exacerbation history (previous 12 months)

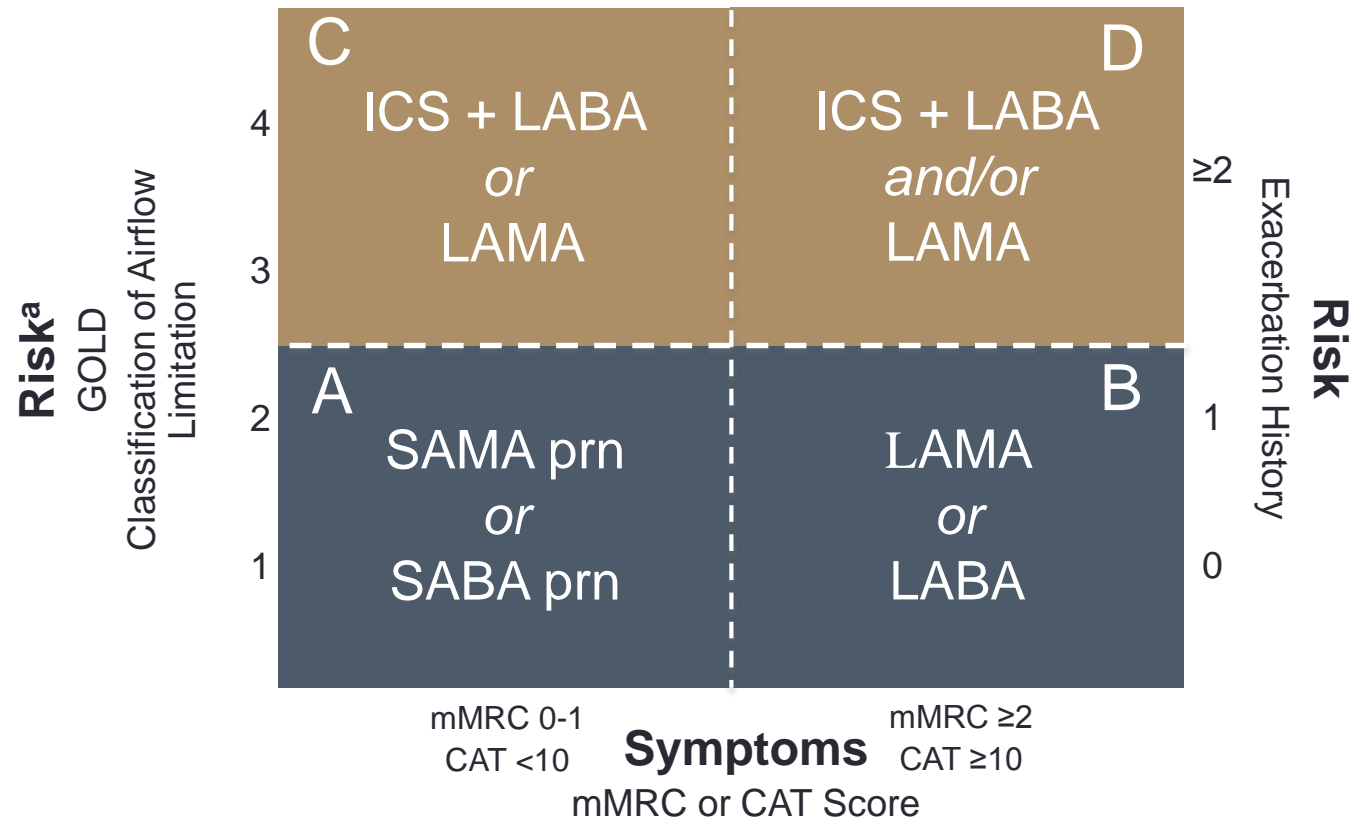
- Low risk: 0 or 1
- High risk: >2 (or any hospitalization due to COPD)



When assessing risk, choose the highest risk according to GOLD grade or exacerbation history. (One or more hospitalizations for COPD exacerbations should be considered high risk.)

Figure adapted from the Global Strategy for Diagnosis, Management and Prevention of COPD 2013, © Global Initiative for Chronic Obstructive Lung Disease (GOLD), all rights reserved. Available from <http://www.goldcopd.org>.

# Management of COPD : WHO/NIH GOLD Guidelines



<sup>a</sup>When assessing risk, choose the highest risk according to GOLD grade or exacerbation history. (One or more hospitalizations for COPD exacerbations should be considered high risk.)

Medications listed within each of the quadrants above are not necessarily in order of preference.

CAT=COPD assessment test; ICS=inhaled corticosteroid; LABA=long-acting beta agonist; LAMA=long-acting muscarinic antagonist; mMRC=modified British medical research council; SABA=short-acting beta agonist; SAMA=short-acting muscarinic antagonist

Figure adapted from the Global Strategy for Diagnosis, Management and Prevention of COPD 2013, © Global Initiative for Chronic Obstructive Lung Disease (GOLD), all rights reserved. Available from <http://www.goldcopd.org>.



# COPD: The Goals of Care

## Reduce Symptoms

- Relieve symptoms
- Improve exercise tolerance
- Improve health status

**AND**

## Reduce Risk

- Prevent disease progression
- Prevent and treat exacerbations
- Reduce mortality

COPD management includes both pharmacologic and non-pharmacologic measures

# COPD : Key Activities

Early and correct diagnosis, i. e. FEV1 % < 70%

Staging disease severity, e. g. FEV1 % predicted

Phenotyping disease heterogeneity

Tobacco smoking cessation

Regular exercise and individualized pharmacotherapy

Palliative care with COPD action plan

Influenza vaccinations annually

Preventing acute COPD exacerbations

Consultation with pulmonologist in difficult cases

Providing education on patient self-management

Adapted after Center for Disease Control & Prevention

*MMWR* 2003; 52 (No. RR-6 ):1-8

# Asthma: The Goals of Care

## Reduce Symptoms

- Relieve symptoms
- Improve exercise tolerance
- Improve health status

+

## Reduce Risk

- Prevent disease progression
- Prevent and treat exacerbations
- Reduce mortality

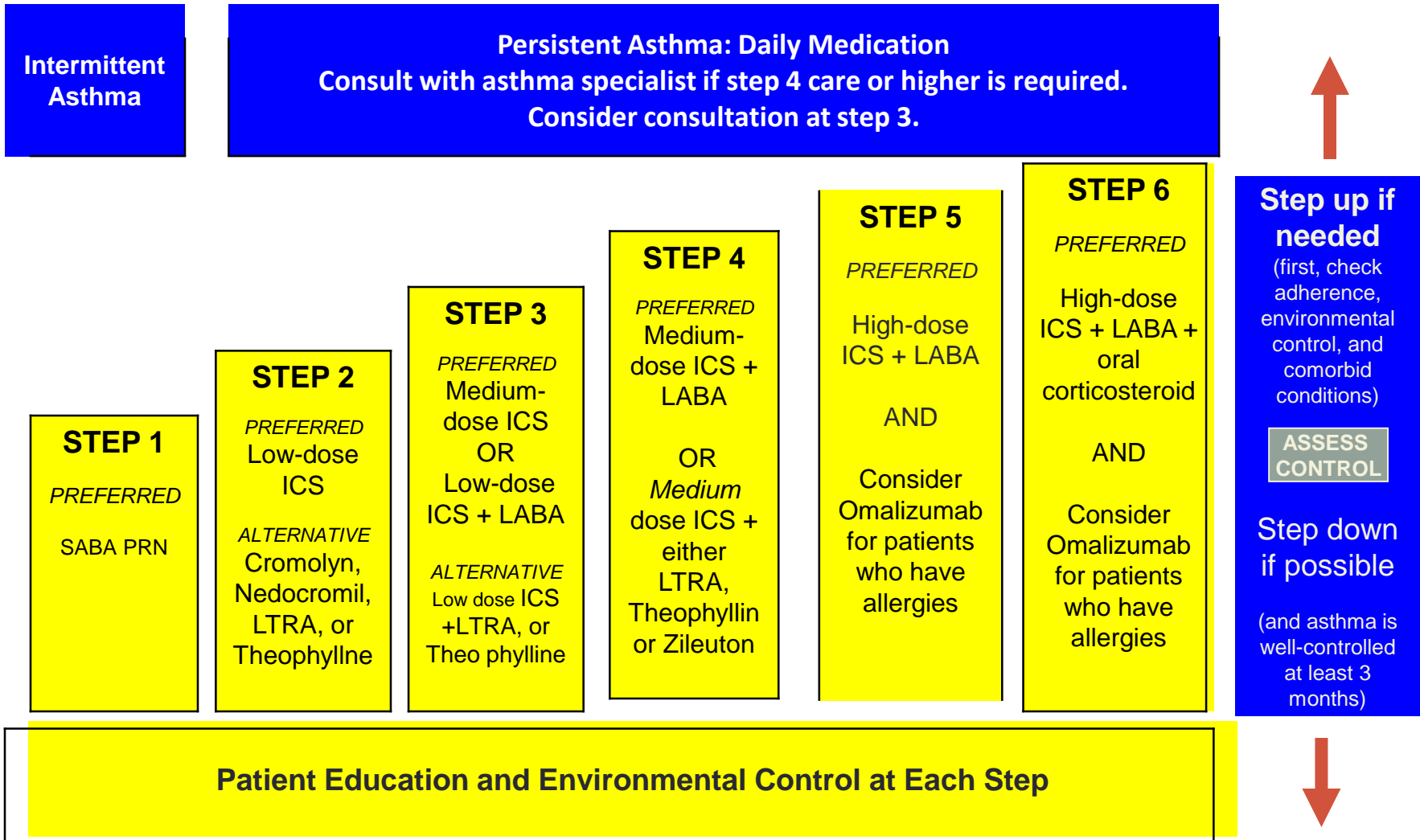
**Asthma management includes both pharmacologic and non-pharmacologic measures**

Figure adapted from NHLBI. National Asthma Education and Prevention Program. Full report of the Expert Panel: guidelines for the diagnosis and management of asthma (EPR-3), <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm>

# Approach to Asthma: Classifying Control in Patients $\geq 12$ Years

Components of Control		Classification of Asthma Control (Youths $\geq 12$ years of age and adults)		
		Well-Controlled	Not Well-Controlled	Very Poorly Controlled
Impairment	Symptoms	$\leq 2$ days/week	$> 2$ days/week	Throughout the day
	Nighttime awakenings	$\leq 2$ x/month	1-3x/month	$\geq 4$ x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short-acting beta <sub>2</sub> -agonist use for symptom control	$\leq 2$ days/week	$> 2$ days/week	Several times per day
	FEV <sub>1</sub> or peak flow	$> 80\%$ predicted/ personal best	60-80% predicted/ personal best	$< 60\%$ predicted/ personal best
	Validated questionnaires ATAQ ACQ ACT	0 $\leq 0.75$ $\geq 20$	1-2 $\geq 1.5$ 16-19	3-4 N/A $\leq 15$
Risk	Exacerbations	0-1 per year	2-3 per year	$> 3$ per year
	Reduction in lung growth	Evaluation requires long-term follow-up care.		
	Treatment-related adverse effects	Medication side effects vary in intensity. Level of intensity does not correlate to specific levels of control but should be considered in overall assessment of risk.		

# Approach for Managing Asthmatics ≥ 12 Years of Age

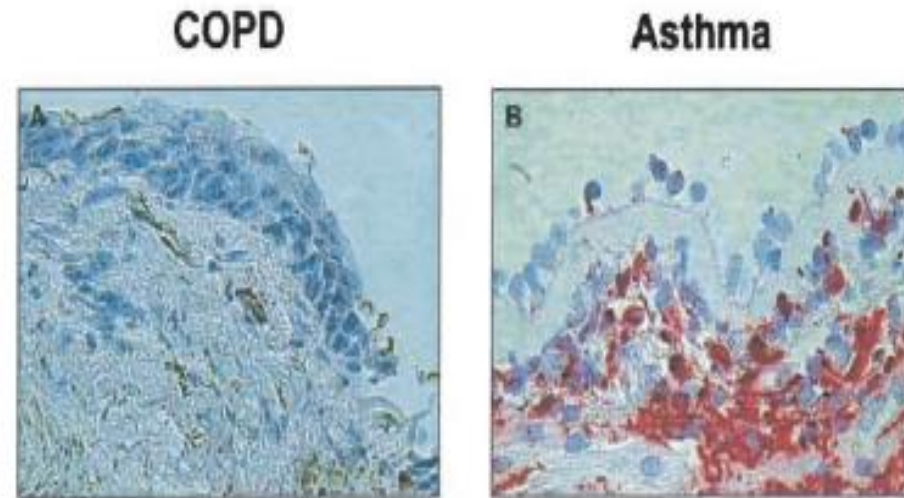
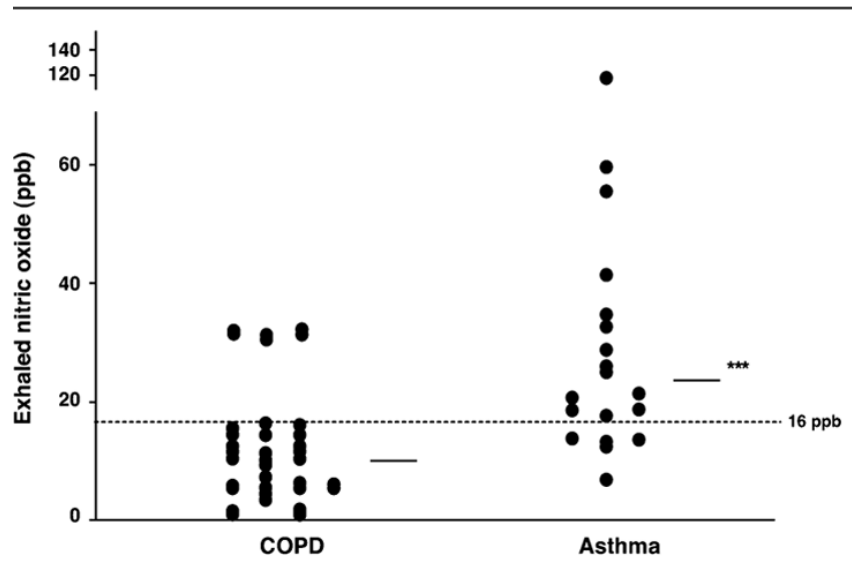


## How might you differentiate Asthma from COPD?

- Childhood history of asthma
- Family history of asthma
- Atopy: RAST panel and total serum IgE
- Pulmonary Function Test: DLCO
- 6 min walk test: Oxygen saturation
- Methacholine challenge testing
- CXR/ Chest CT scan
- Exhaled Nitric Oxide FeNO

# Exhaled breath nitric oxide predicts response to steroids in elderly patients with fixed airflow obstruction

46 patients, >50 yrs of age referred with fixed airflow obstruction. Subjects had bronchoscopic biopsy and HRCT + PFTs.



Stain with anti- EG2 for eosinophil cationic protein

# American Thoracic Society Documents

## **An Official ATS Clinical Practice Guideline: Interpretation of Exhaled Nitric Oxide Levels (FeNO) for Clinical Applications**

Raed A. Dweik, Peter B. Boggs, Serpil C. Erzurum, Charles G. Irvin, Margaret W. Leigh, Jon O. Lundberg, Anna-Carin Olin, Alan L. Plummer, D. Robin Taylor, on behalf of the American Thoracic Society Committee on Interpretation of Exhaled Nitric Oxide Levels (FeNO) for Clinical Applications

THIS OFFICIAL CLINICAL PRACTICE GUIDELINE OF THE AMERICAN THORACIC SOCIETY (ATS) WAS APPROVED BY THE ATS BOARD OF DIRECTORS, MAY 2011

- ATS recommends using FeNO in:
  - diagnosing of eosinophilic airway inflammation
  - determining likelihood of steroid responsiveness
  - supporting the diagnosis of asthma
  - monitoring airway inflammation



AJRCCM Sept 2011



# Common Initial Management

- **Anti-Inflammatory drugs**

- ED: IV corticosteroids within 1 hour *Cochrane Review 2002; (4): AB002178*
  - 120 – 500 mg/d methylprednisolone
- Inhaled corticosteroids
- Oral prednisone for exacerbation

- **Bronchodilator drugs**

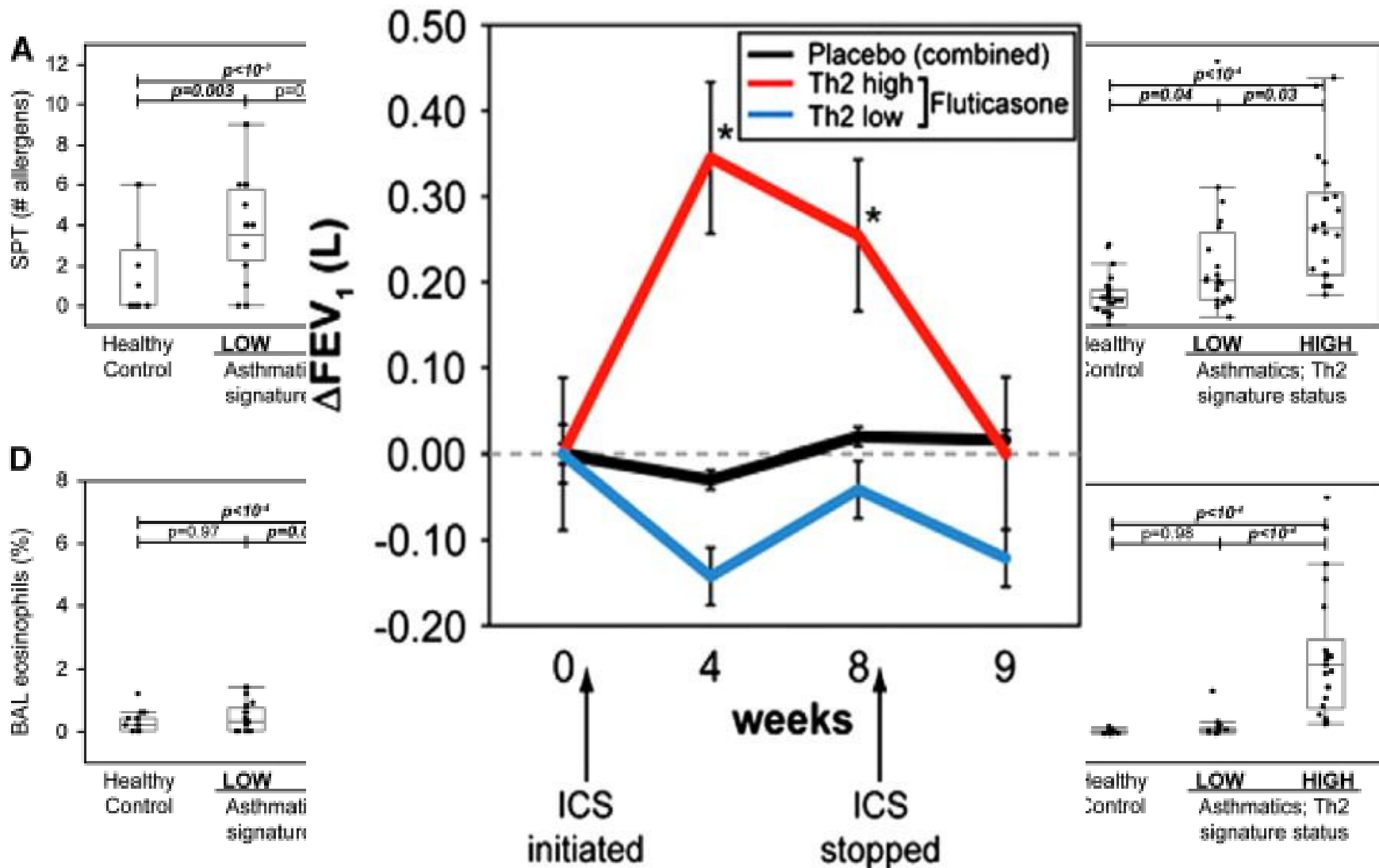
- Short-acting  $\beta_2$  agonists + ipratropium *Chest 1998; 114: 365 • Am J Med 1999; 107: 363 • Am J Respir Crit Care Med 2000; 161: 1862*
- Long acting  $\beta_2$  agonists + tiotropium

-

# Not all asthmatics respond the same to steroids.

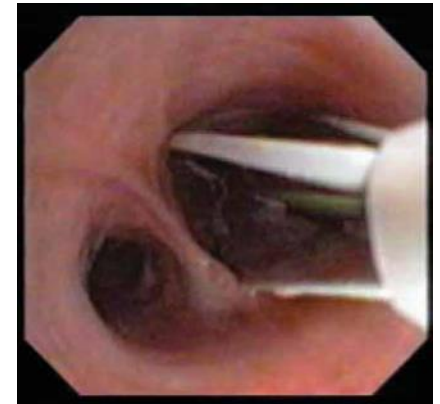
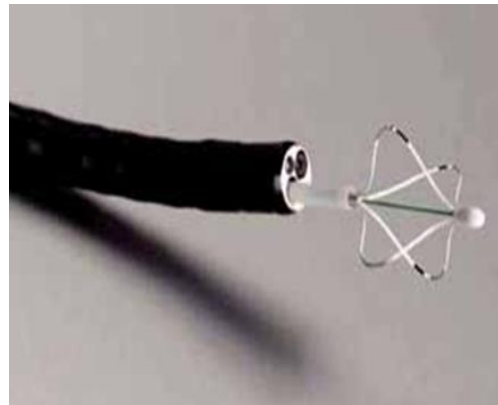
## Th2 High vs. Low Phenotype

Woodruff et al. AJRCCM 2009



# More 'targeted' treatments : Asthma vs. COPD

- Leukotriene antagonists
  - Lipoxygenase inhibitor
  - LT receptor antagonist
- Magnesium
- Omalizumab (anti-IgE)
- Bronchial Thermoplasty
  - Roflumilast
  - Azithromycin
- Anti-IL5
  - Mepolizumab
- Anti-IL13
  - Lebrikizumab
- Anti-IL4/Anti-IL13
  - Dupilumab



# Effectiveness of magnesium sulfate as initial treatment of acute severe asthma in children: a randomized, controlled trial

Torres et al Arch Pediatr 2012

SBT salbutamol  
MPD methylprednisolone  
CRIA respiratory failure

TABLE 2A. Treatment group

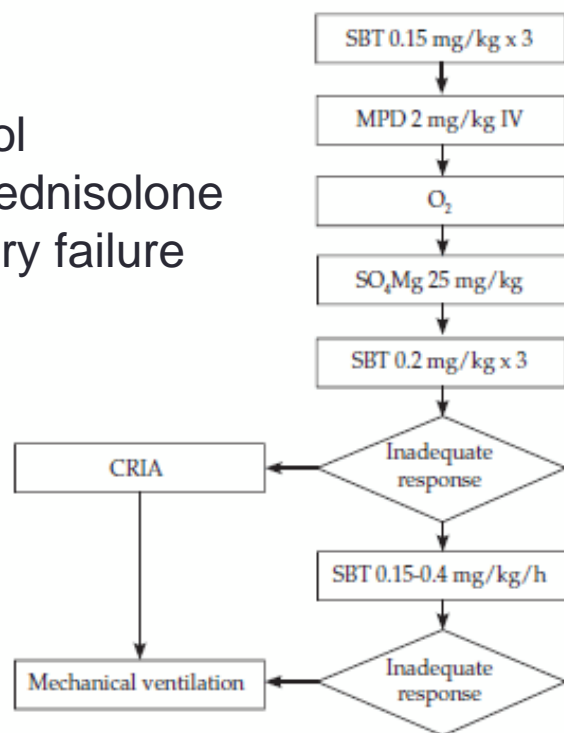
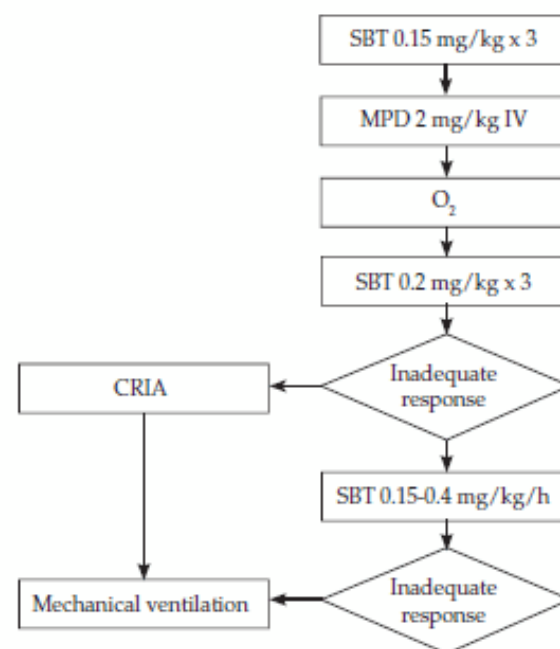


TABLE 2B. Control group



	Treatment group n= 76	Control group n= 67	p-value
Need of MV	5% (n= 4)	33% (n= 22)	0.001
Length-of-stay in MV (days) α	3 (1-6)	5 (2-12)	0.087
Total hospital length-of-stay α	7 (3-12)	19 (14-29)	0.046
Length-of-stay in PICU (days) α	2 (1-4)	10 (6-18)	0.0376

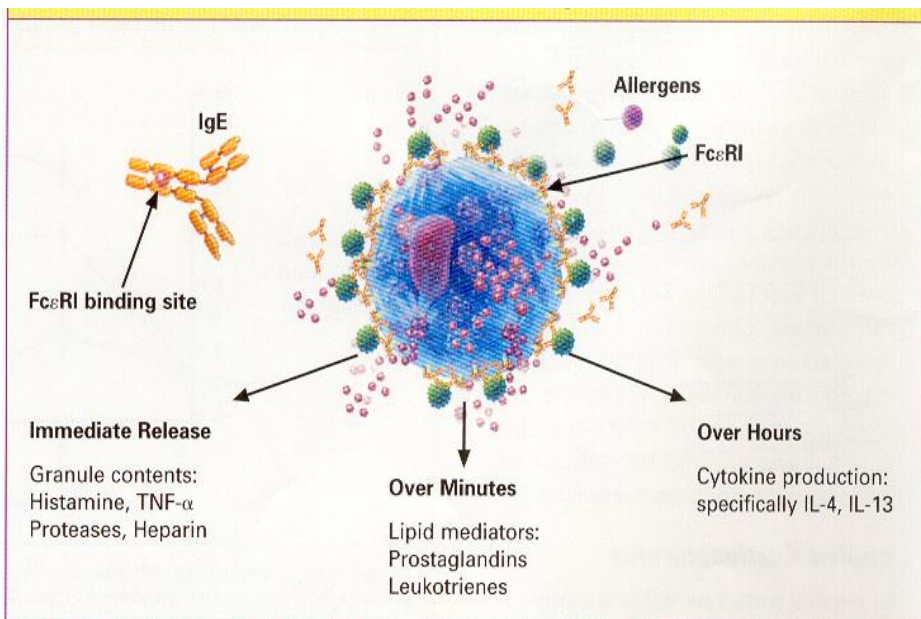
## Effect of oral magnesium supplementation on measures of airway resistance and subjective assessment of asthma control and quality of life in men and women with mild to moderate asthma: a randomized placebo controlled trial.

Kazaks et al. J Asthma 2010

- **OBJECTIVE:** To determine if long term(6.5 month) treatment with oral Mg would improve asthma control and increase serum measures of Mg status in men and women with mild-to-moderate asthma.
- **SUBJECTS:** 55 males and females aged 21 to 55 years with mild to moderate asthma according to the 2002 National Heart, Lung, and Blood Institute(NHLBI) who used only beta-agonists or inhaled corticosteroids(ICS) as asthma medications were enrolled.
- **DESIGN:** Subjects were randomly assigned to consume 340 mg(170 mg twice a day) of Mg or a placebo for 6.5 months.
- **CONCLUSION:** Adults who received oral Mg supplements showed improvement in objective measures of bronchial reactivity to methacholine and PEFr and in subjective measures of asthma control and quality of life.

## Anti-IgE (Omalizumab)

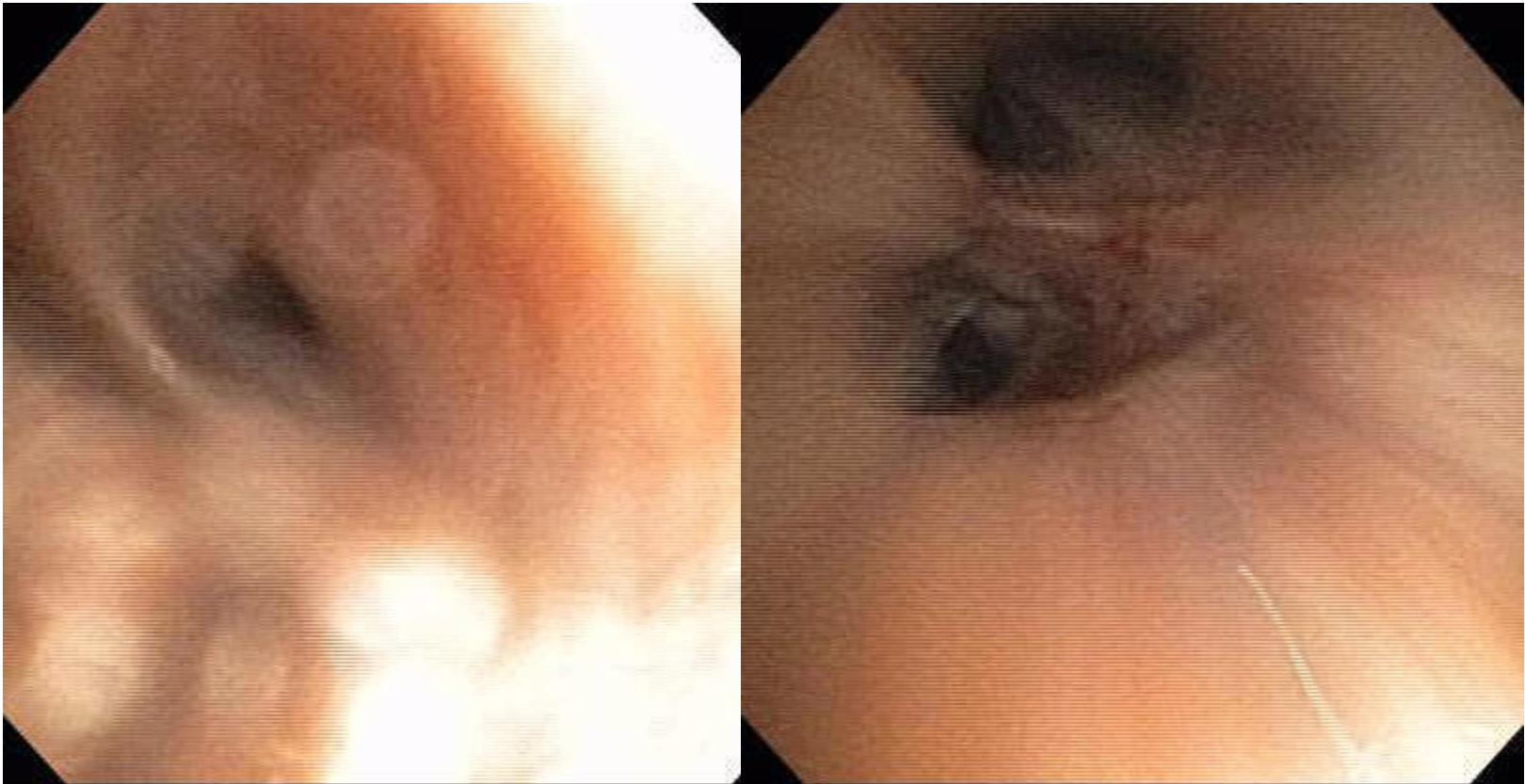
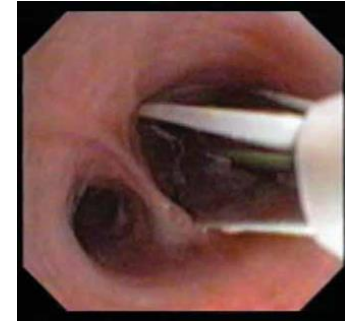
2003 FDA Approval ; JACI 2007 Joint Task Force Report on omalizumab-associated anaphylaxis.



**TABLE II.** Summary of timing of Xolair (omalizumab) adverse reactions

Timing of the reaction	First-third Xolair (omalizumab) dose (no. of events)	Fourth or later Xolair (omalizumab) dose (no. of events)	Total
<30 min	11	5	16
30-60 min	6	1	7
1-2 h	5	0	5
2-12 h	4	1	5
>12 h	3	0	3
Unknown	3	2	5
<b>Total</b>	<b>32</b>	<b>9</b>	<b>41</b>

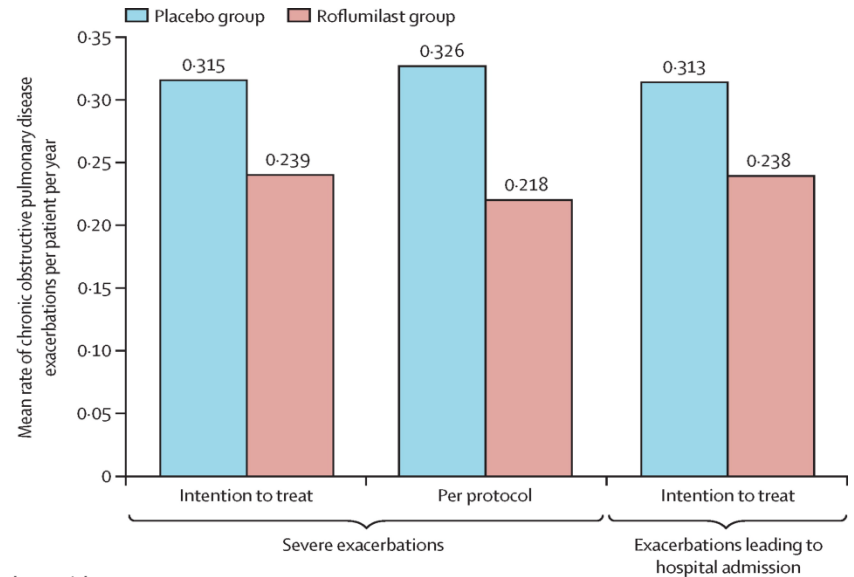
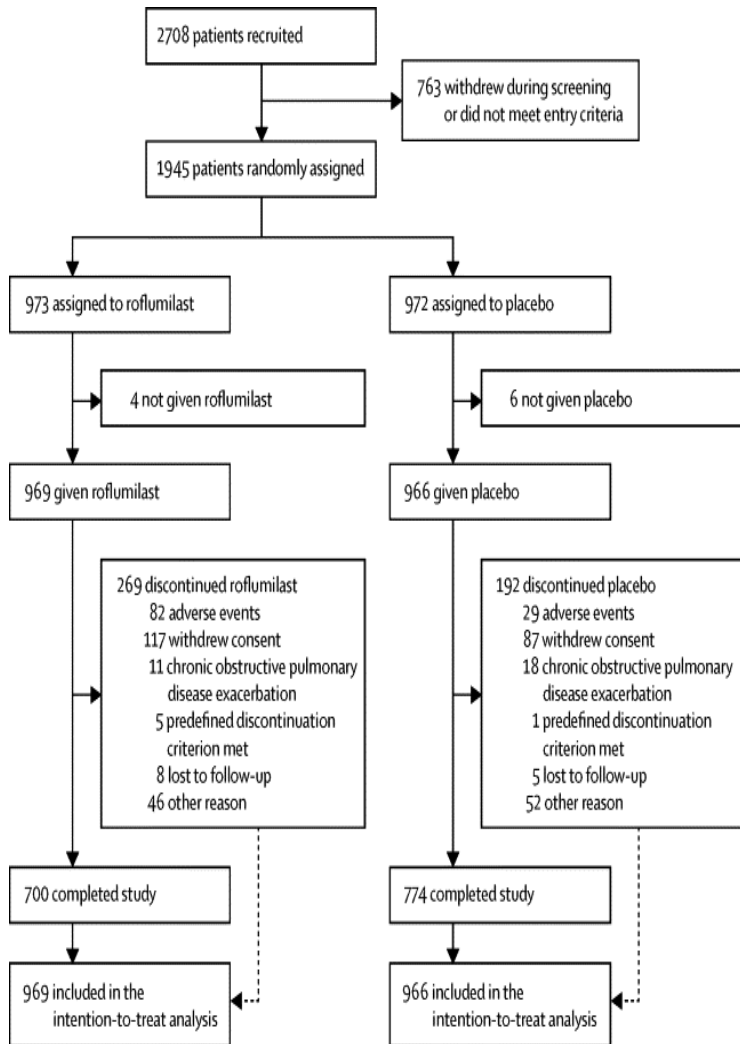
Bronchial Thermoplasty #2:  
Left: LLL Untreated, Right: RLL Treated





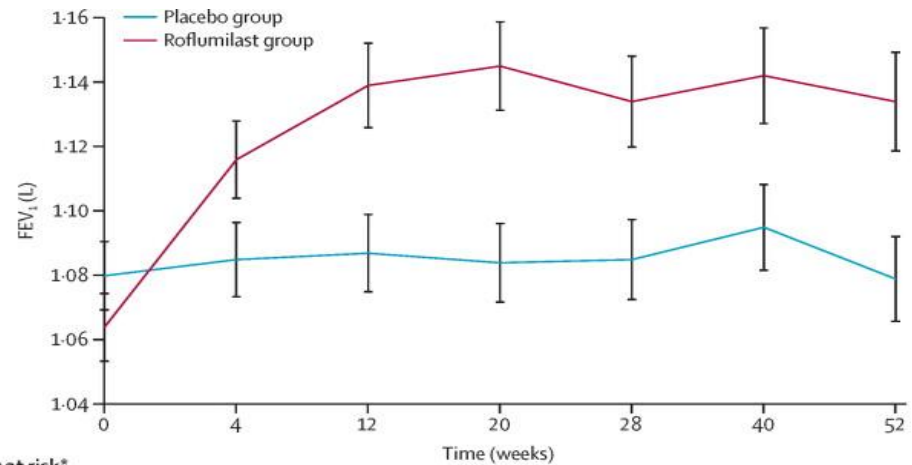
# Effect of roflumilast on exacerbations in patients with severe chronic obstructive pulmonary disease uncontrolled by combination therapy (REACT): a randomised controlled trial.

Martinez et al Lancet 2015



**Number at risk**  
Patients with at least one exacerbation (n)  
Rate ratio (95% CI)  
Two-sided p value

Exacerbation Type	Placebo (n)	Roflumilast (n)	Rate ratio (95% CI)	Two-sided p value
Severe exacerbations	192	151	0.757 (0.601-0.952)	0.0175
Exacerbations leading to hospital admission	167	120	0.668 (0.518-0.861)	0.0018
Intention to treat	190	150	0.761 (0.604-0.960)	0.0209



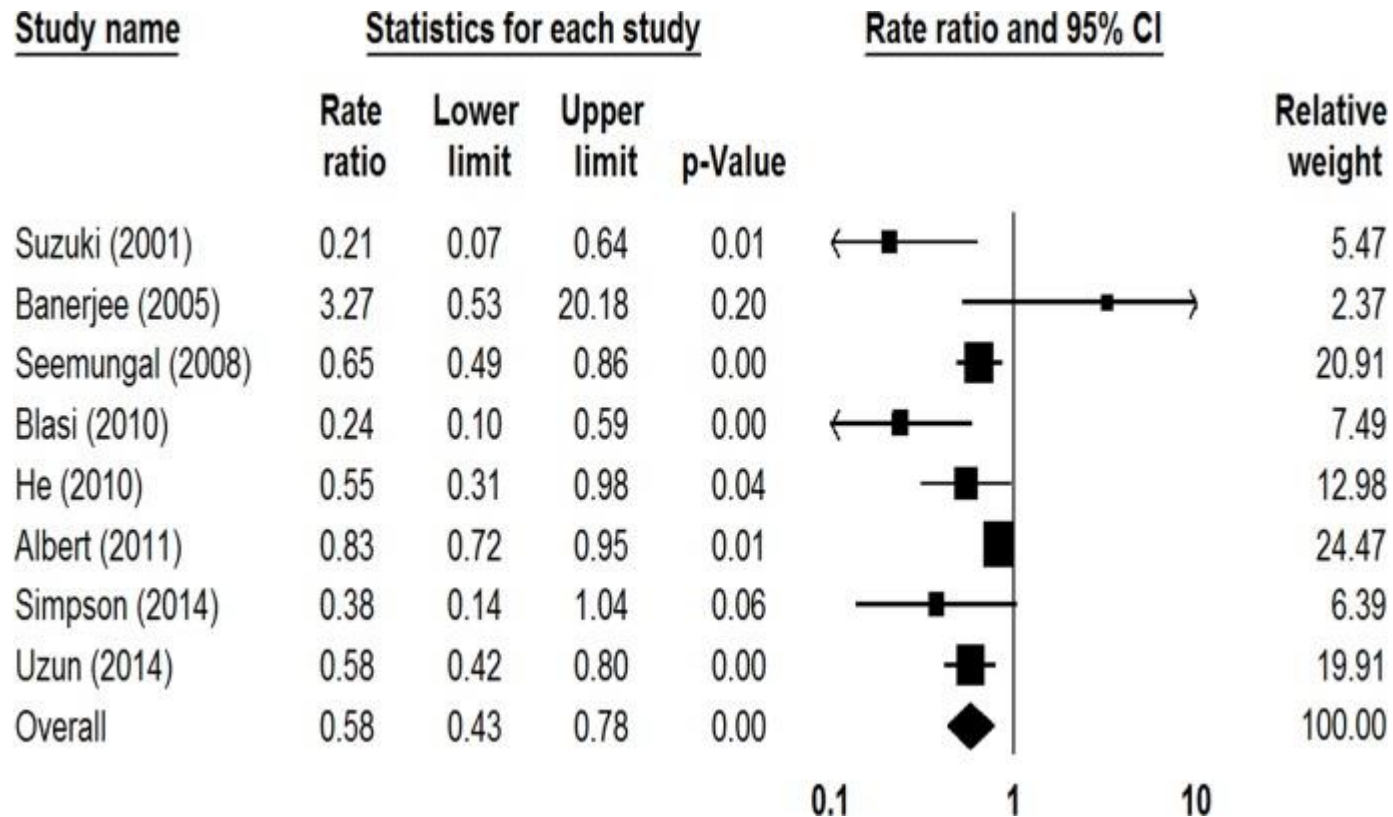
Number at risk\*



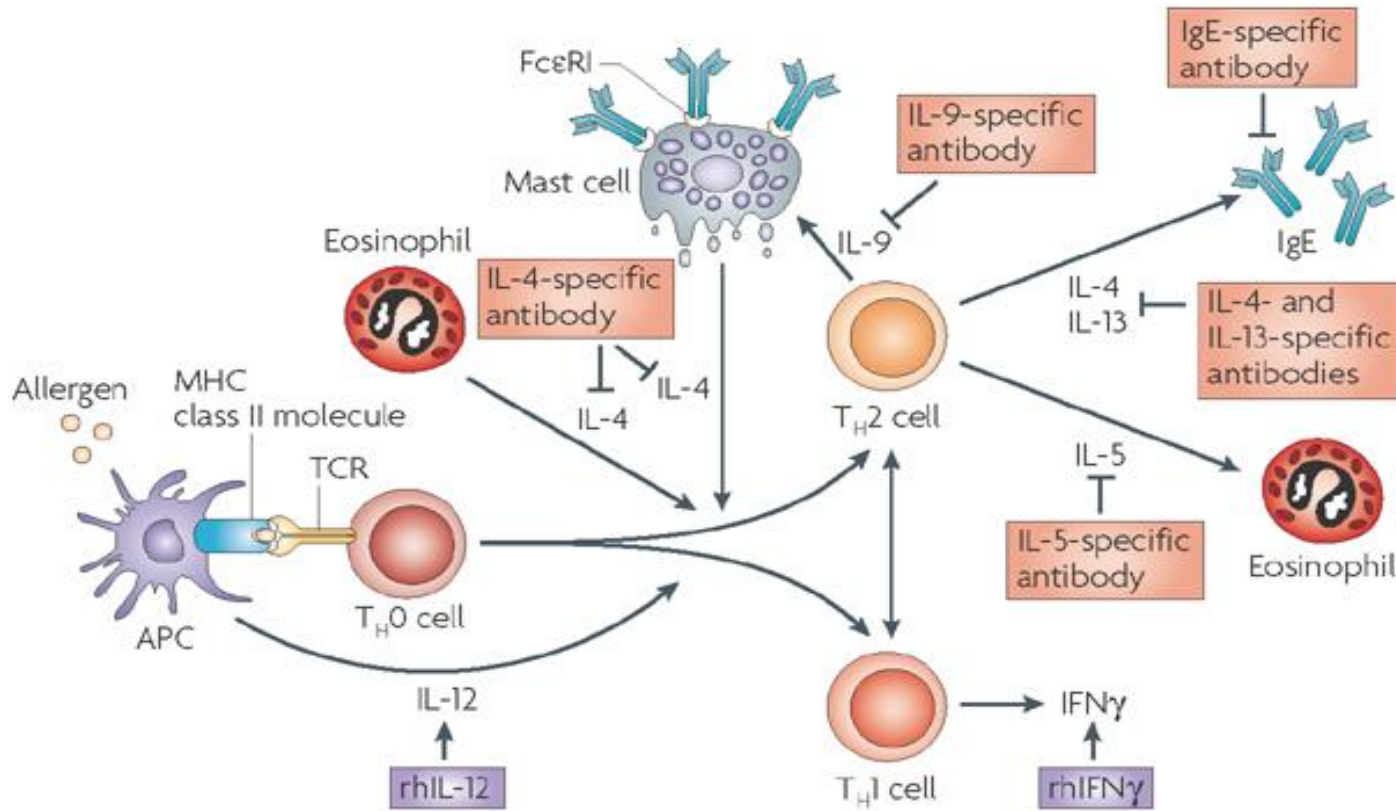
# Prophylactic use of macrolide antibiotics for the prevention of chronic obstructive pulmonary disease exacerbation: a meta-analysis.

Ni et al. PLOS One 2015

**Forest plot of risk ratios for exacerbations per patient per year treated with macrolides compared with the control.**



# Cytokines and Effector Cells of Interest in Asthma



## Key Cells

Eosinophil

Mast cell

Th2 lymphocyte

Dendritic cell

## Key Cytokines

IL-4

IL-5

IL-13

IL-17

Nature Reviews | Immunology

# Asthma: Genotyping studies have led to new research avenues, but little change in therapeutics, in asthma.

CHIA (0)	COX2 (1)	KCNS33	NAT2	GSTM1	IL4
VCAM1 (0)	AGT (1)	ACP1	DEFB1	IL10	IL13
CLCA1 (0)	HMNT (3)	IL1RN	TLR4	CTLA4	CD14
DAP3 (0)	STAT4 (1)	IL1A	C5	SPINK5	ADRB2
SELP (0)	CCR3 (2)	IL1B	GATA3	LTC4S	HLA-DRB1
CHRM3 (0)	TLR9 (3)	<u>DPP10</u>	ALOX5	LTA	HLA-DQB1
ST2 (0)	IL8 (1)	CCR5	CRTH2	<u>GRPA</u>	TNF
ICOS (0)	EDNRA (1)	IL5RA	IL18	NOD1	FCER1B
IL8RA (0)	UGRP1 (3)	TLR6	AICDA	CC16	IL4RA
MUC7 (0)	EDN1 (1)	TLR10	VDR	GSTP1	<u>ADAM33</u>
PGDS (0)	IKAP (2)	TLR2	IFNG	STAT6	
IL15 (0)	FLAP (2)	CSF2	<u>PHF11</u>	NOS1	
IRF2 (0)	MCP1 (3)	IL5	CYSLTR2	CCL5	
IRF1 (0)	IFNGR2 (1)	IL12B	TCRA/D	TBXA2R	
IL3 (0)	IL13RA1 (1)	TIM1	CMA1	TGFB1	
<u>CYFIP2</u> (0)		TM3	PTGDR		
SDF1 (0)		<u>HLA-G</u>	CARD15		
C3AR1 (0)		HLA-DQA1	NOS2A		
PTGER2 (0)		HLA-DPB1	CRHR1		
AACT (0)		TAP1	CCL11		
IL12RB1 (0)		PAFAH	TBX21		
SSCE (0)		EDN1	STAT3		
TIMP1 (0)		IFNGR1	ITGB3		
CXCR3 (0)		CCL24	ACE		
		CCL26	C3		
		CFTR	GSTT1		
		NOS3	MIF		

- >100 genes associated with either asthma or atopy
- Most genes are related to either Th2 lymphocyte mediated inflammation or smooth muscle reactivity



IL4
IL13
CD14
ADRB2
HLA-DRB1
HLA-DQB1
TNF
FCER1B
IL4RA
<u>ADAM33</u>

# The Black Box Warning on $\beta$ -agonists



“We’ve got case reports of people dying, clutching their Serevent inhaler. But Serevent is still on the market.”

Dr. David Graham, October 2004

# Salmeterol Multi-center Asthma Research Trial (SMART)

Hypothesis: Long-acting  $\beta$ -agonists would decrease near-fatal and fatal respiratory-related events

Goal: Enroll 60,000 patients

Design: RCT, 28 wk intervention of placebo vs. salmeterol

## Interim analysis (25,858 patients)

- v Non-significant increase in severe respiratory related events (<1% of subjects) in salmeterol group
- v African Americans (17% of those enrolled) there was a significant increase in events (19 vs. 4; RR=4.6)
- v 62% of African Americans were not on inhaled steroids

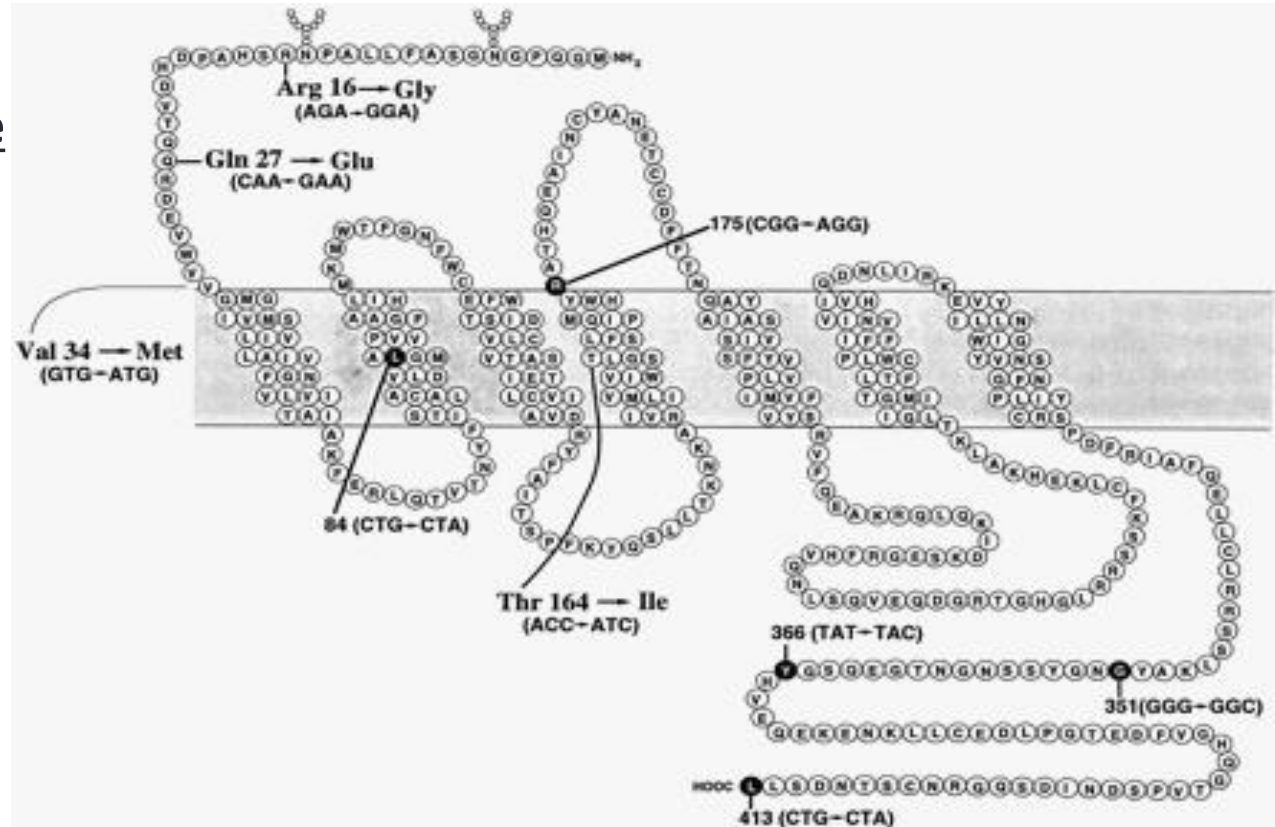
# Polymorphisms of the $\beta_2$ -adrenergic receptor

## Population Genotype Prevalence

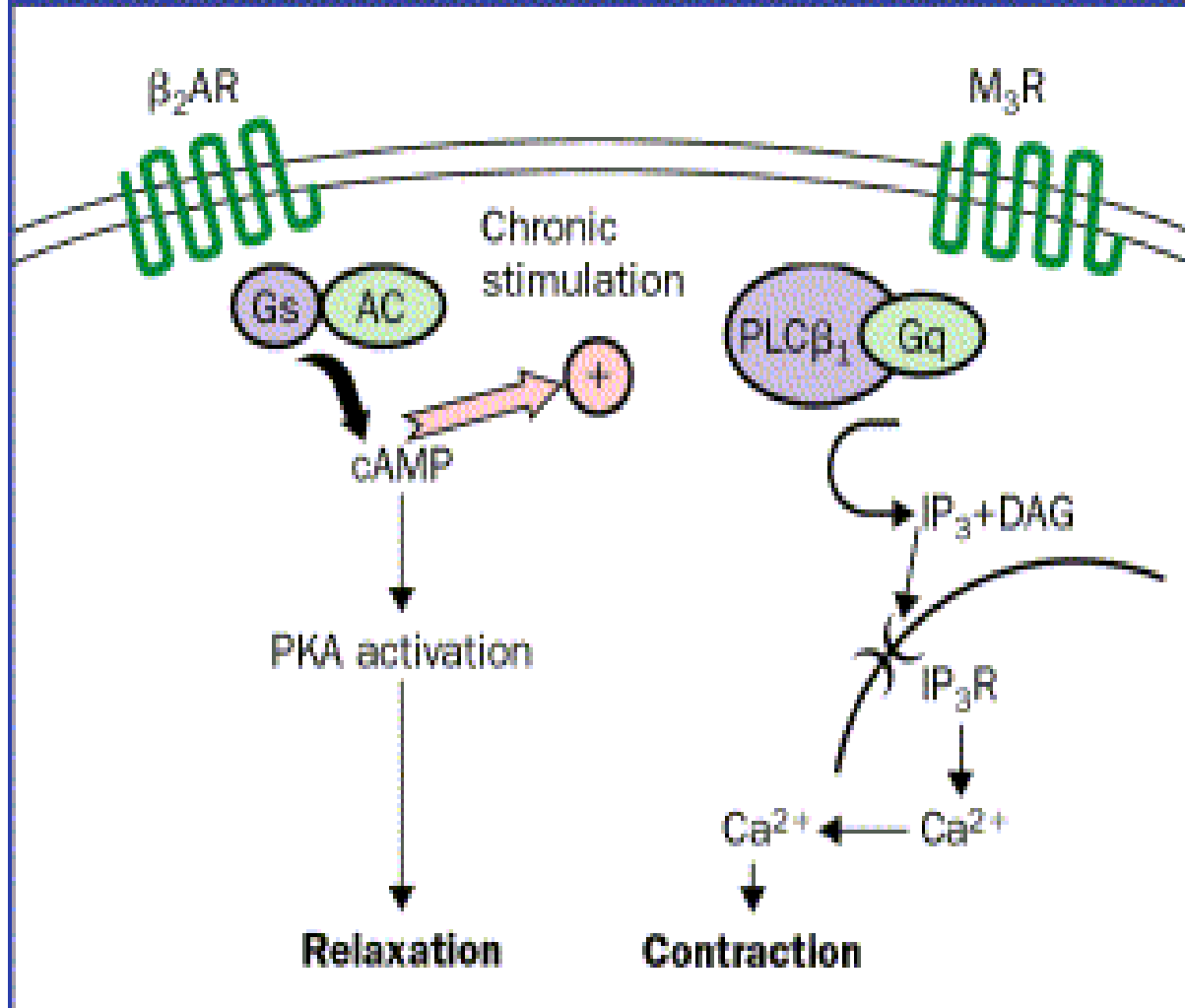
16% Arg/Arg

37% Arg/Gly

47% Gly/Gly



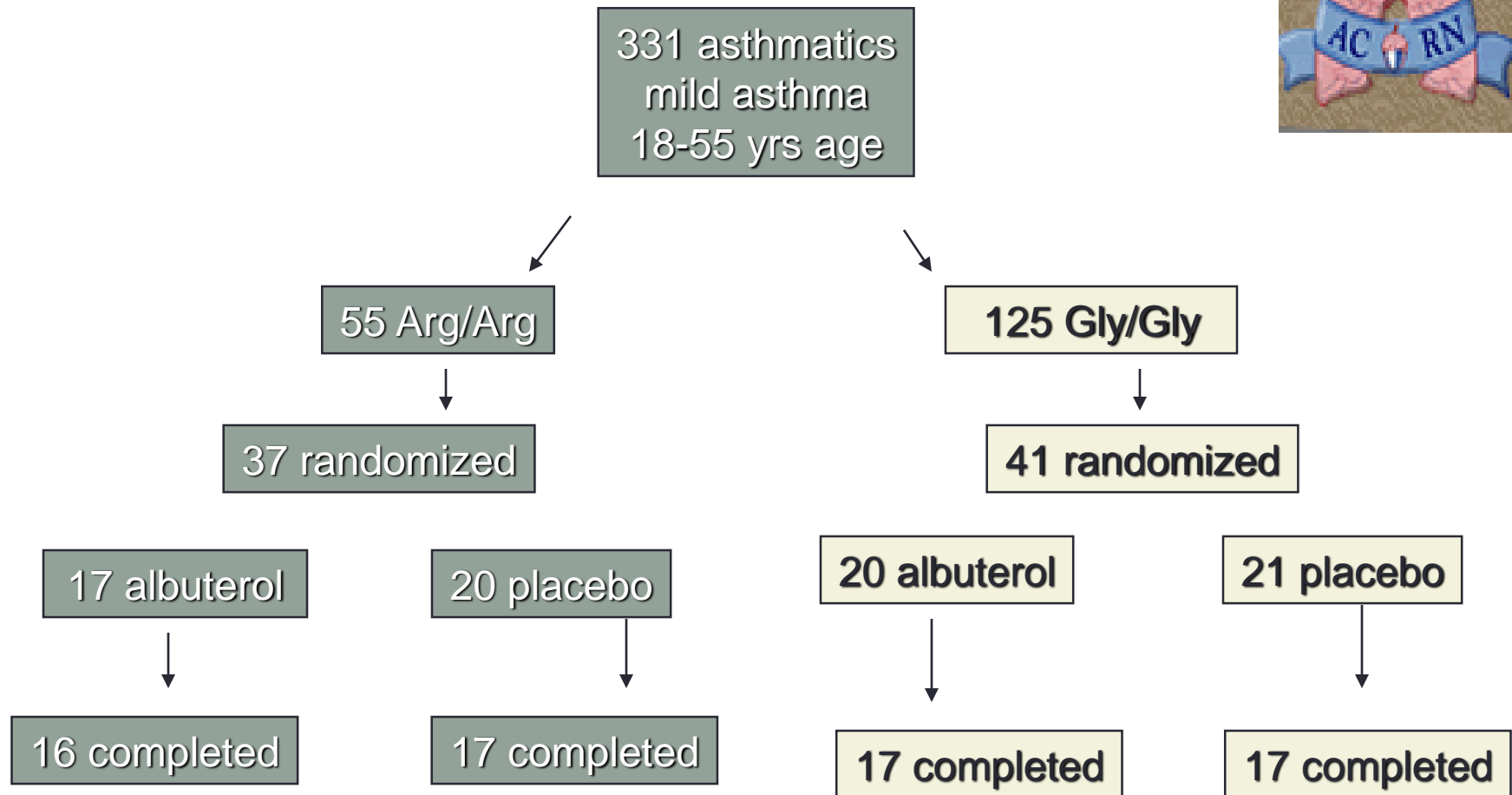
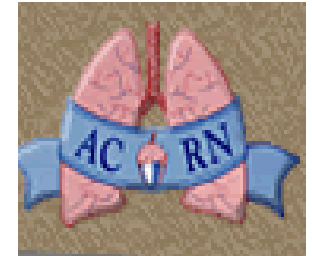
## Relaxant and contractile pathways in airway smooth-muscle



Hall Lancet 2004; 363:183-4.

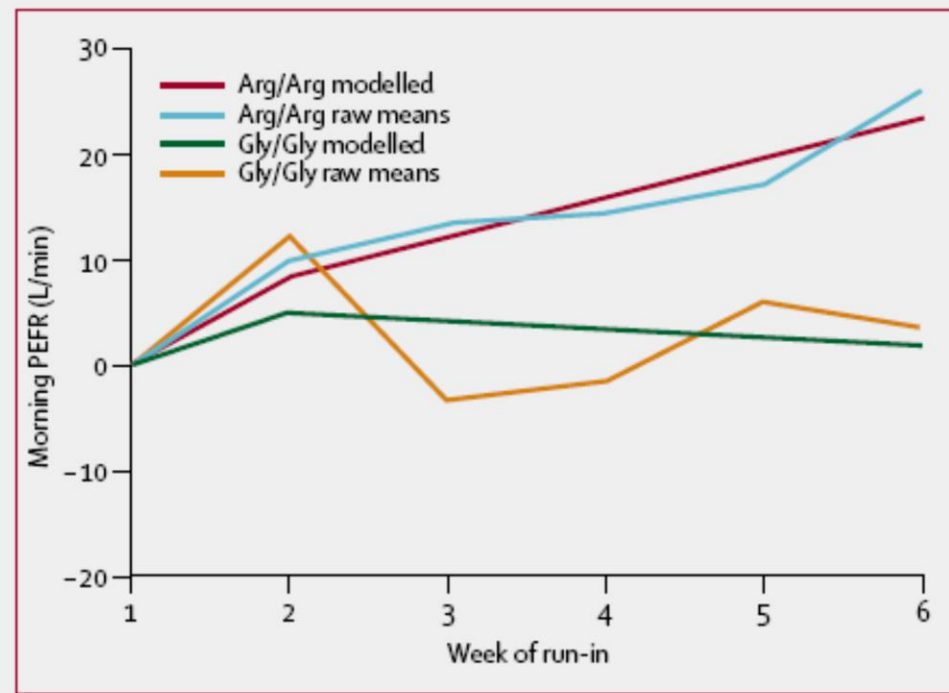
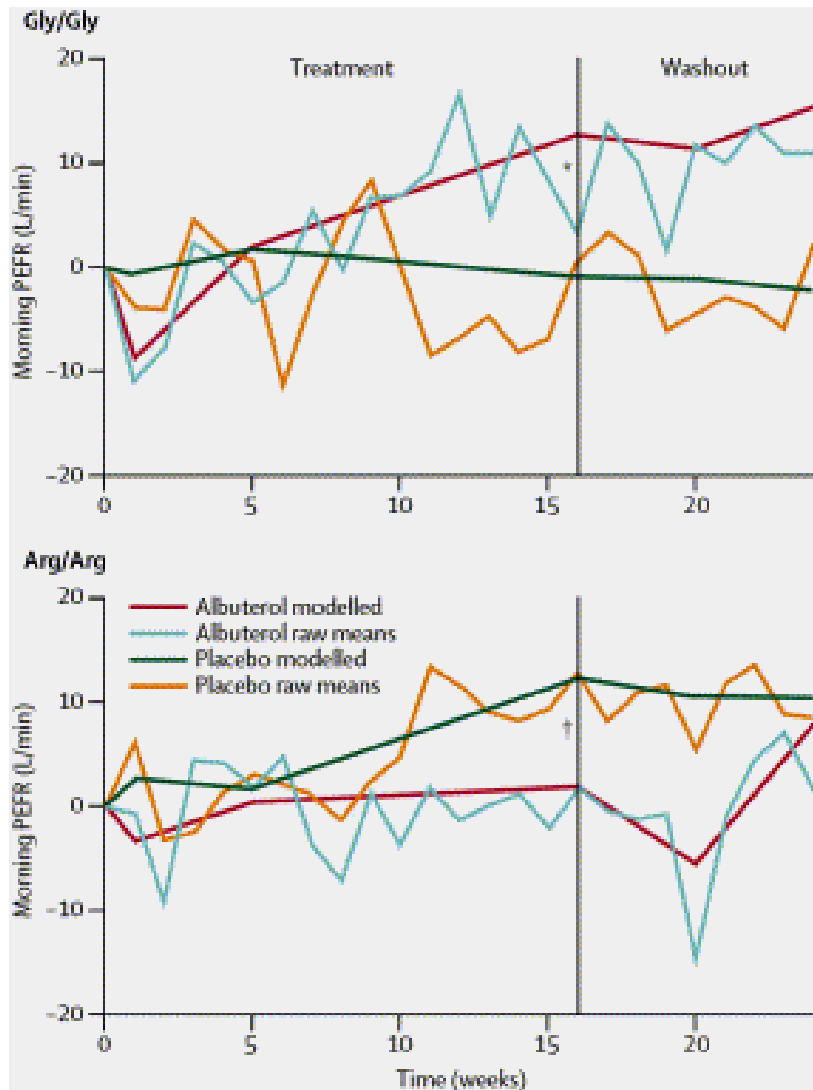
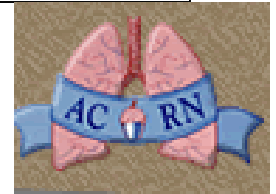


# Prospective trial of scheduled albuterol use by genotype (BARGE)





# Response to bronchodilators by genotype



Response to anti-cholinergic

# UCAN Asthma Team (1998-2015)

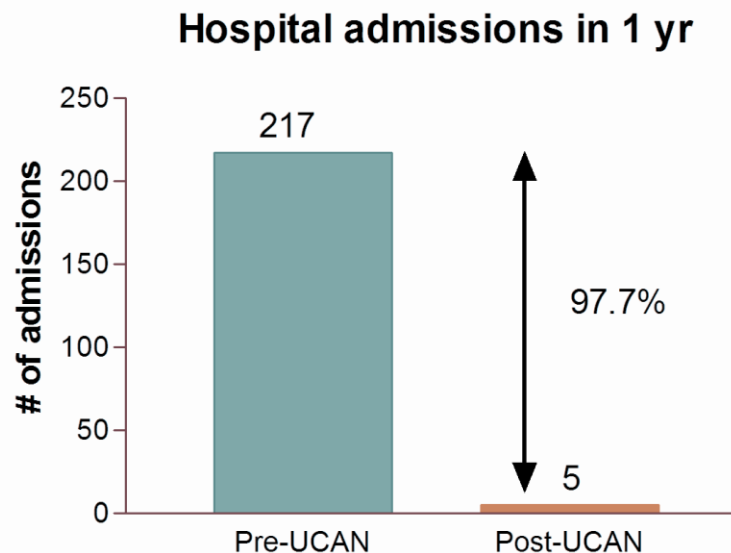
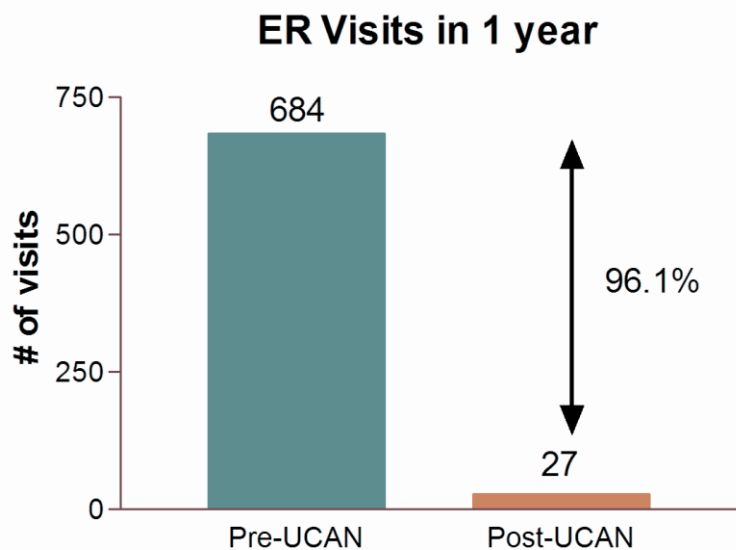
- UCAN Clinic
  - Two pulmonary asthma specialists
  - Two full time respiratory therapists
  - “UCAN Quit” smoking cessation clinic,
  - Omalizumab clinic
  - Videolaryngoscopy clinic
  - Bronchial thermoplasty program
- Three additional bronchoscopists integrated into the UCAN team specifically to perform BT
- Authorization coordinator
- Bronchoscopy suite: Interventional pulmonary laboratory nurses and respiratory therapists specifically trained in BT

## UC Davis Asthma Network (UCAN) clinics (1999-2008)

850 patients--74% Female, mean age  $46.3 \pm 15.3$

58.6% Severe persistent, 33.9% Moderate persistent

ER visits and admissions in the year before and after clinic enrollment



## 2012 UC Davis ROAD: Inpatient COPD program

COPD hospitalizations increased from 459 in 2009 to 587 in 2011

Average cost per case increased nearly 2-fold from \$14,259 to \$26,355

Average LOS increased from 6.27 to 7.57 days in FY 2011

Total direct cost in FY 2011 for inpatient COPD care was 587 patients = \$15,470,385

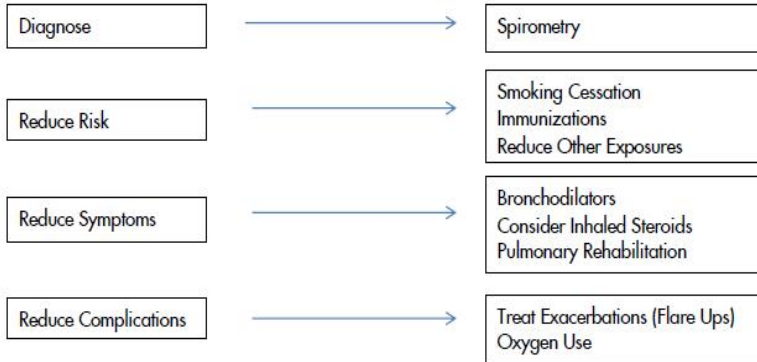


# COPD Case Management Program

- Registered Respiratory Therapist COPD Case Manager Program at UCDCMC (916)762-COPD from 7am-7pm
  - 130 Patients Hospitalized for AECOPD seen by CMs
    - Mean Age: **69 years** (range 46-88)
    - Men: **47%**
    - Women: **53%**
    - Patients with Prior COPD Education: **5%**
  - Referral Source
    - Referred by MD: **21%**
    - Referred by RT: **15%**
    - Referred by EMR Screening Tool: **12%**
      - Use of this tool after development began 6/30/2012
    - Identified by Case Managers by Dx Code in EMR: **52%**

# UC DAVIS HEALTH SYSTEM

## COPD is Treatable



We know there is no cure for COPD as of yet, but COPD is treatable. By taking your medications as prescribed to help slow the progression of this disease, you can reduce complications, such as an exacerbation. Slowing the progression of COPD can be done by:

**Quitting smoking** - You can add years on to your life and breathe better during those years if you quit smoking. Continuing to smoke reduces your lung function and can cause bad breathing days or flare ups.

**Immunizations** - Getting your flu shot and pneumonia vaccine when they are due can prevent respiratory illnesses that can lead to a COPD exacerbation.

**Washing your hands** - This is another way to help avoid infection. Approximately 60% of COPD exacerbations are caused by some sort of infection. We can reduce our risk by washing our hands as well as not touching our hands to our face. Waterless soap, wet wipes, and hand sanitizer can be kept handy.

**Avoiding others who are sick** - Staying away from friends and family who have a "cold" will prevent you from possibly contracting whatever bug they may have. When you have COPD, your "cold" can turn into an exacerbation. One week away from family and friends may save you a hospital visit!



# UC DAVIS HEALTH SYSTEM

## Traveling with Oxygen

It is ok to travel with oxygen. It just requires some planning. It's a good idea to call your healthcare provider before making travel arrangements and obtaining a copy of your oxygen prescription and any other paperwork you may need. Allow for plenty of time to have oxygen delivered, depending on where you are going, and how you plan to travel. Your healthcare provider or medical equipment company will help you with this. Before booking your trip, call the carrier or travel agent to find out the requirements for traveling with oxygen.

### By Car

When traveling by car you will want to keep windows cracked for good air circulation. If you are using liquid oxygen, be sure to store the unit upright and secure it with a seatbelt if possible. **DO NOT STORE OXYGEN IN THE TRUNK.** It is too hot! **DO NOT SMOKE** or let anyone else smoke in the car.

### By Bus or Train

You will likely be able to take your own oxygen delivery system on board, but you will need to call in advance to tell them you are traveling with oxygen. They may need to see a copy of your prescription prior to travel.

### By Plane

Oxygen tanks are not allowed on airplanes. Many airlines supply oxygen for a fee. Call the airline well in advance to make arrangements. Keep in mind that airlines may supply oxygen on the plane, but not in the airport. You will need to arrange to have oxygen delivered to your destination, or on hand during a layover. If you are using oxygen at rest, you will need it on your flight. Discuss these travel plans with your doctor and discuss your oxygen use. Different airlines have different requirements, so check with your airline in advance to facilitate your travel.

### By Ship

You can likely bring your own oxygen on board the cruise ship, but they may need a letter from your doctor along with a brief medical history and copy of your oxygen prescription. You must arrange for oxygen to be delivered to the cruise ship.



# COPD Case Management Program

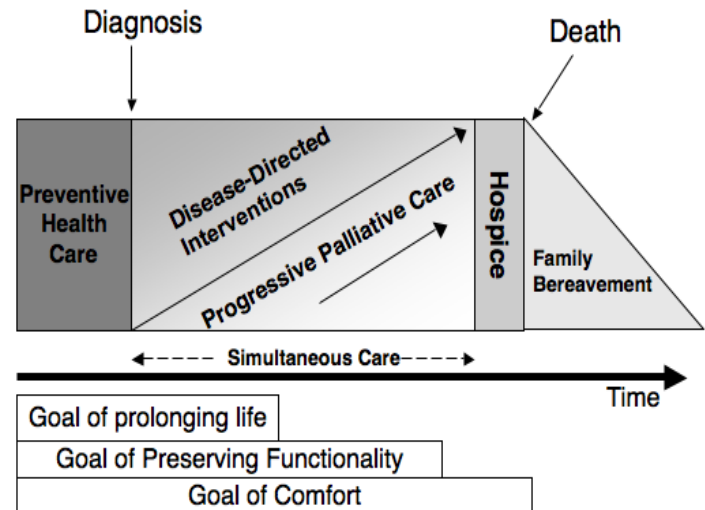
- COPD Care Coordination and Self Management proves to reduce Healthcare Resource Utilizations and Improve Patient Outcomes
  - Average LOS: **5.4 days**
    - **Decreased from 7.57 days for FY 2011**
    - **Projected cost savings of ~ \$7,555 per admission**
  - Average Hospitalizations in Past Year: **2.13**
  - Bounce Back Rate to Date(<30 days after D/C): **6%**
    - **Decreased from 16% for FY 2011**
    - **Projected cost savings of ~ \$1,300,000**
  - Readmission Rate (>30 days after D/C): **23%** (14 pts total)
  - Deaths After Enrolled In Program: **5**
  - Patients Followed by PCP: **85%**
    - UC Davis Patients: **60%**
  - Patients with Follow Up Visit to PCP after D/C: **77%**



# COPD : Rehabilitation and Integrated Palliative Care

## Who should we refer?

- COPD GOLD Stages II through IV
- Difficult-to-control after rehabilitation
- Oxygen requirement
- $\geq 2$  hospitalization for COPD per yr
- BMI < 21 kg/m<sup>2</sup>
- ICU admission for COPD
- Concomitant CHF
- Presence of anxiety or depression
- Patients unable to meet their ADLs





# Clinical Pearls

1. There will be fewer asthmatics and more COPD patients requiring hospitalization in the future.
2. ACOS will continue to be a diagnostic conundrum.
3. Therapeutic considerations:
  - Consider magnesium
  - Roflumilast or azithromycin for COPD patients with frequent exacerbations
  - New small molecule therapies being developed for severe asthma
4. We must develop hospital programs to better manage the discharged COPD and COPD patient.
5. Fight the indifference of managing COPD.