



Asthma and COPD: 2011

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Trends of Asthma Morbidity/ Mortality

Asthma by the Numbers

25 million Americans have asthma
up from 20 million in 2001
(Population of Australia: 22 million)

3,447 asthma deaths per year
9 deaths per day

Emergency visits for asthma:

1.6 million a year

456,000 admitted to hospital in 2007
Average length of stay: 3.4 days

8.2% of adults have asthma

9.6% of children or 7.1 million kids

50% increase in asthma among black kids (2001-2009)

1 in 6 African-American children lives with asthma

57% of kids with asthma had an attack in 2008

GRASP OF CONTROL

Under **50%** learned about avoiding triggers

Under **50%** of those who were taught it currently practise avoidance

ECONOMIC BURDEN

Costs of Asthma:

\$56 billion

in 2007. Up 6% from 2002

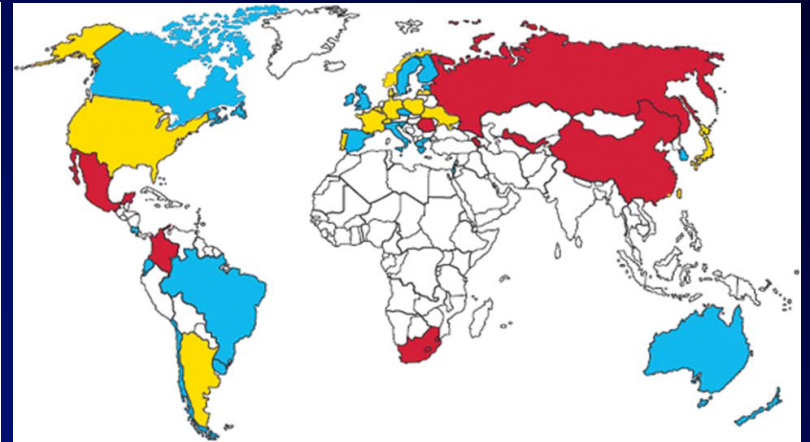
Medical expense portion:

\$50.1 billion

\$3,300 per asthmatic: Average annual asthma medical costs

1 in 9 insured can't afford prescription meds

Sources: Centers for Disease Control and Prevention, May 2011 Vital Signs report and CDC 2007 asthma data; 2008 Asthma Gap II survey from the Asthma and Allergy Foundation of America.



- Asthma deaths per 100,000 population age 5-34
- Red > 10
- Yellow 5-10
- Blue < 5

Papirus, Drugs 2009; 69 (17):2366-87

Asthma 2010-2011: Epidemic rise in America

Why Are We Here?

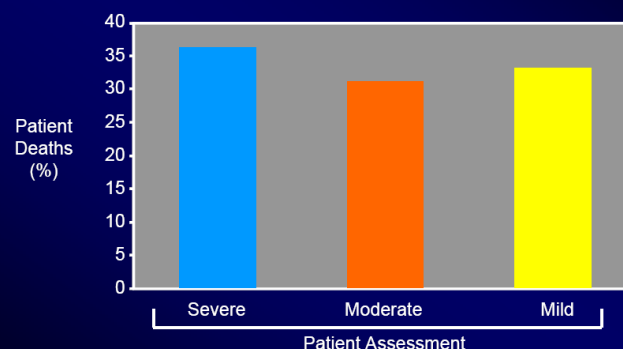
- 22 yo student in Northern Iowa
- Senior year: special Ed teacher
- “Mild Asthma” per MD
- Phoned her mother each day:
 - Roommates opening apartment windows at night
 - Erin using MDI 3-5 x/night
 - Went out dancing with friends
- Erin’s mother called by police and told to get to hospital as soon as possible!



Why did this 22 year old girl die?

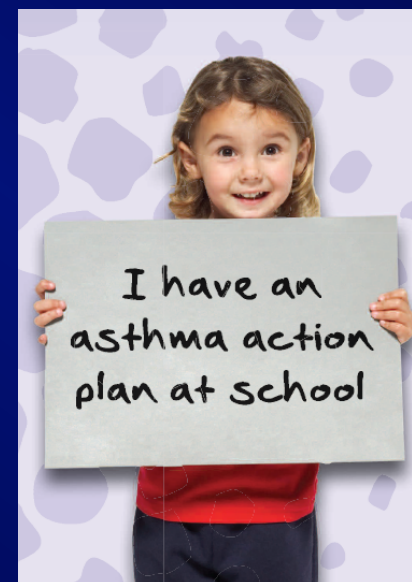
- Neither she nor her mother knew her asthma was “out of control”
- They were on the “wrong side of the information gap: just like 7/10 asthmatics
- Erin’s mother went on to become an Asthma Educator

Pediatric Asthma Deaths:
Mild Patients Are Also at Risk



Findings from a cohort study reviewing all pediatric asthma-related deaths (n=51) in the Australian state of Victoria from 1986 to 1989.

Robertson et al. *Pediatr Pulmonol.* 1992;13:95-100.



Risk Factors for Severe Asthma Exacerbation

- Equal among mild, moderate, and severe asthma*
- Key risk factors:
 - Ever been intubated or in ICU for asthma
 - Hospitalized in last year
 - Deficiency in self-management skills
- Predictors of health care utilization:
 - Score of < 20 on Asthma Control Test (ACT)
 - Poor perception of dyspnea

*Clin & Exper Allergy 2007; 37:552-557

Asthma Control Test™ (ACT)

1. In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school, or at home?

Score

All of the time

1

Most of the time

2

Some of the time

3

A little of the time

4

None of the time

5

2. During the past 4 weeks, how often have you had shortness of breath?

More than once a day

1

Once a day

2

3 to 6 times a week

3

Once or twice a week

4

Not at all

5

3. During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness, or pain) wake you up at night, or earlier than usual in the morning?

4 or more nights a week

1

2 or 3 nights a week

2

Once a week

3

Once or twice

4

Not at all

5

4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?

3 or more times per day

1

1 or 2 times per day

2

2 or 3 times per week

3

Once a week or less

4

Not at all

5

5. How would you rate your asthma control during the past 4 weeks?

Not controlled at all

1

Poorly controlled

2

Somewhat controlled

3

Well controlled

4

Completely controlled

5

Well controlled ≥ 20 ; 16-19 not well controlled, ≤ 15 very poorly controlled
Available at: <http://www.asthmacontrol.com>.

Patient Total Score

- ACT < 20 best predictor of asthma control

Factors Influencing the Heterogeneity of Asthma Control: Poor Perception of Dyspnea (POD)

113 Asthmatics Evaluated

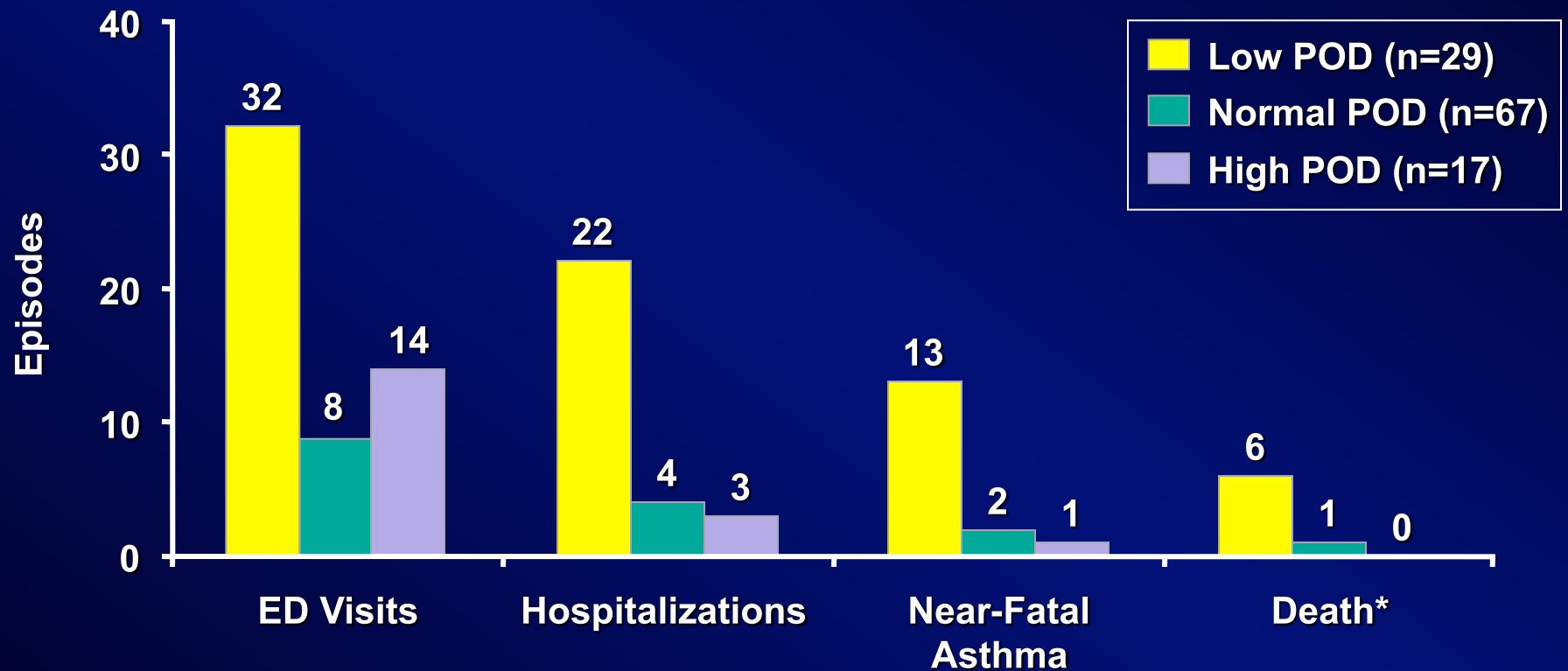
- Breathe against 2-way valve load of 0-, 5-, 10-, 20-, and 30-cm H₂O for 1 minute
- Dyspnea defined as modified Borg scale
- POD
 - Low 29 (26%)
 - Normal 67 (59%)
 - High 17 (15%)

- β_2 -Agonist use in 4 weeks*
 - Low 1.7/day
 - Normal 2.4/day
 - High 4.1/day
- Patients with asthma and a low POD had tendency toward
 - Older age
 - More females
 - Longer duration
 - More severe
- Documented events over 2 years

*Puffs/day.

Magadle R et al. *Chest*. 2002;121:329-333.

Poor Perception of Dyspnea (POD)



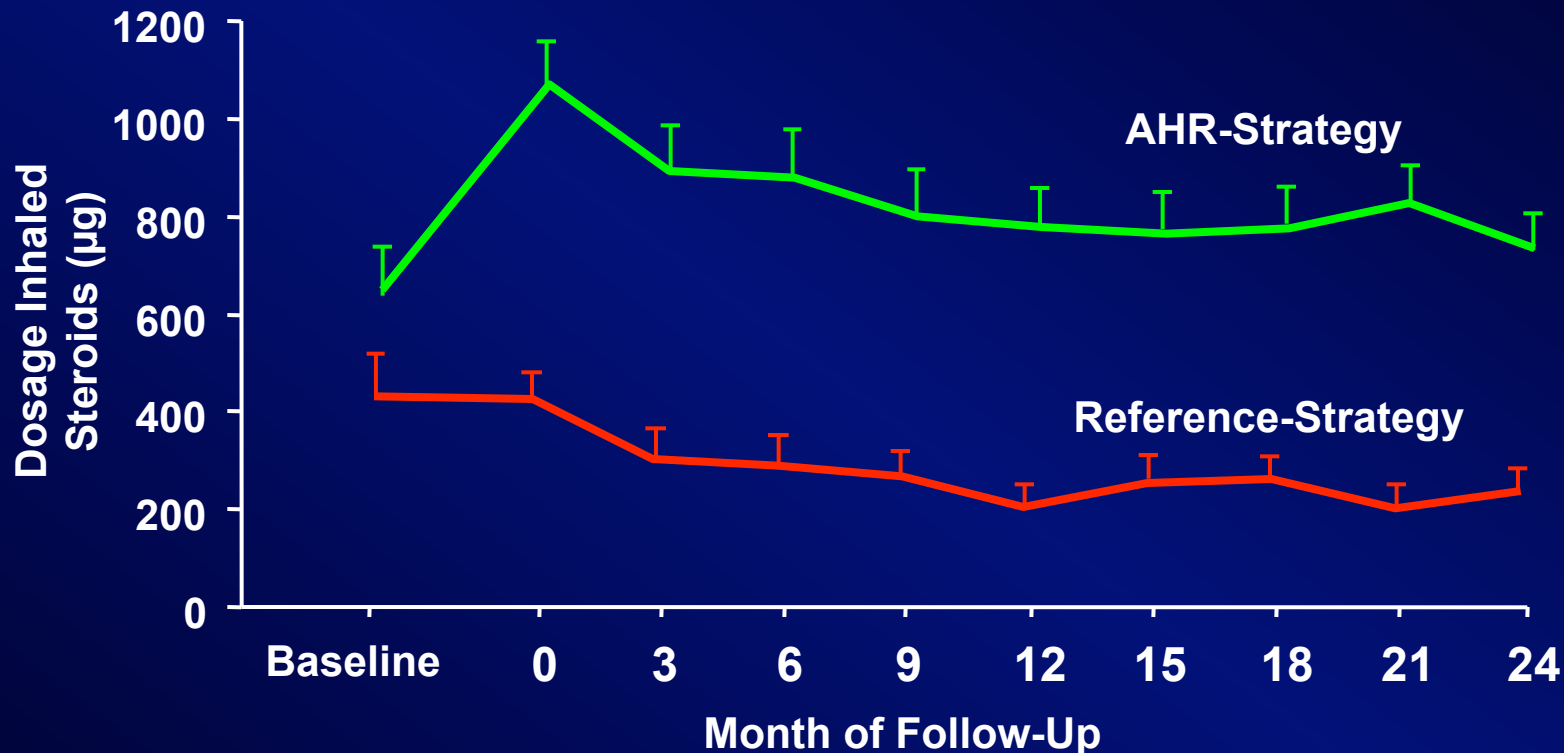
*Of deaths in the low POD group, 4 were asthma related, 2 were unknown.

Multiple studies now that show underperceivers and life-threatening asthma may have a 20% mortality from asthma

ASTHMA 2011

- **Maximizing therapy**

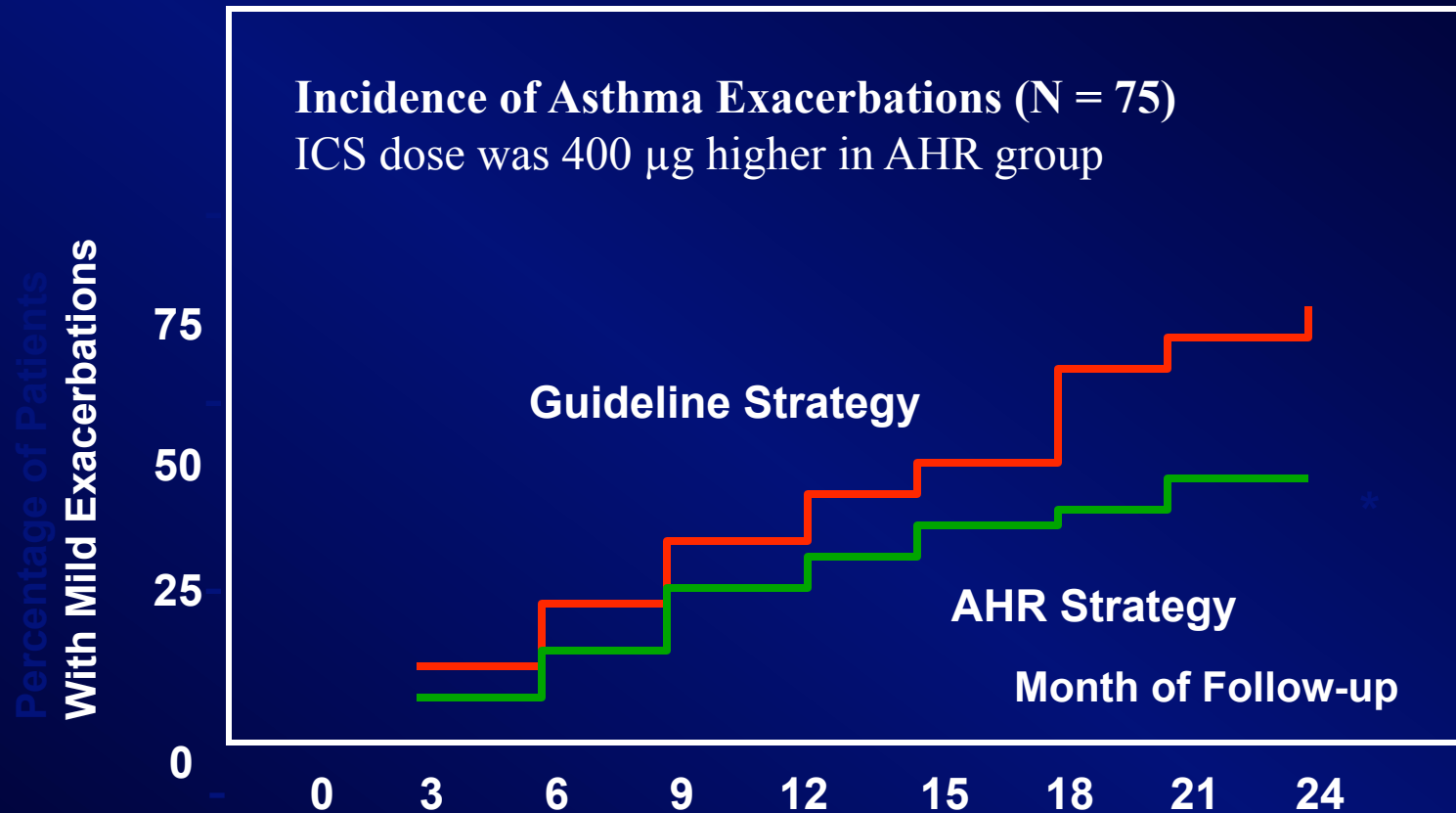
Utility of AHR in Asthma



- Asthma severity is related to the severity of AHR
- AHR is diagnostic tool for asthma

Sont JK, et al. *Am J Respir Crit Care Med*. 1999;159:1043-1051

Control of AHR: Mild Exacerbations



* 1.8-fold decrease in exacerbation rate vs guideline strategy ($P=0.03$).

Mild exacerbations = increase of ≥ 3 points in total asthma score.

Sont JK, et al. *Am J Respir Crit Care Med*. 1999;159:1043-1051.

2010: Studies on inhaled mannitol to assess AHR

Reasons to Measure Nitric Oxide

- **Identify the eosinophilic asthma phenotype**
- **Assess potential response or failure to ICS**
- **Establish a baseline**
- **Guide changes in doses of anti-inflammatory medications**
- **Assist in the evaluation of adherence to anti-inflammatory medications**
- **Assess whether airway inflammation is multifactorial**

Measurement ATS Guidelines: 2011

- **< 25 ppb (20 ppb in children) - eosinophilic inflammation and responsiveness to corticosteroids are less likely**
- **>50 ppb (> 35 ppb in children) eosinophilic inflammation and responsiveness to corticosteroids in sx patients is more likely**
- **25-50 ppb (20–35 ppb in children) depends on the clinical context**

Causes of High FENO

In a symptomatic patient (chronic cough and/or wheeze and/or shortness of breath during past > 6 wks) presenting for the first time, possible etiologies:

- **Atopic asthma**
- **Eosinophilic bronchitis**
- **COPD with mixed inflammatory phenotype**
- **That the patient is likely to benefit from a trial of inhaled corticosteroid treatment**

ASTHMA 2011

- What have we learned ?

On line February 2010

Long-acting Beta-Agonists with and without Inhaled Corticosteroids and Catastrophic Asthma Events

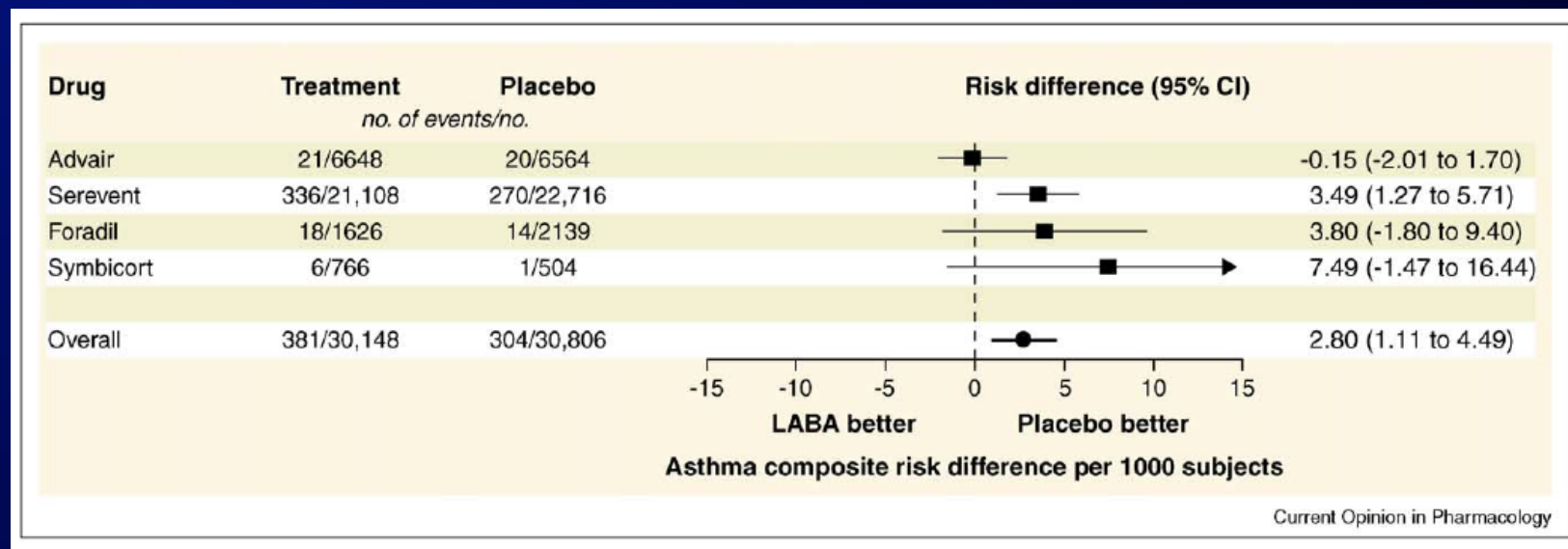
Shelley R. Salpeter, MD, FACP,^{a,b} Andrew J. Wall, MD,^{a,b} Nicholas S. Buckley^c

^aStanford University School of Medicine, Stanford, Calif; ^bSanta Clara Valley Medical Center, San Jose, Calif; ^cCalifornia Institute for Technology, Pasadena.

“There is a 3-fold increase in asthma-related intubations and deaths in those taking long-acting β -agonists with concomitant corticosteroids compared with corticosteroids alone”

The LABA controversy continues.....

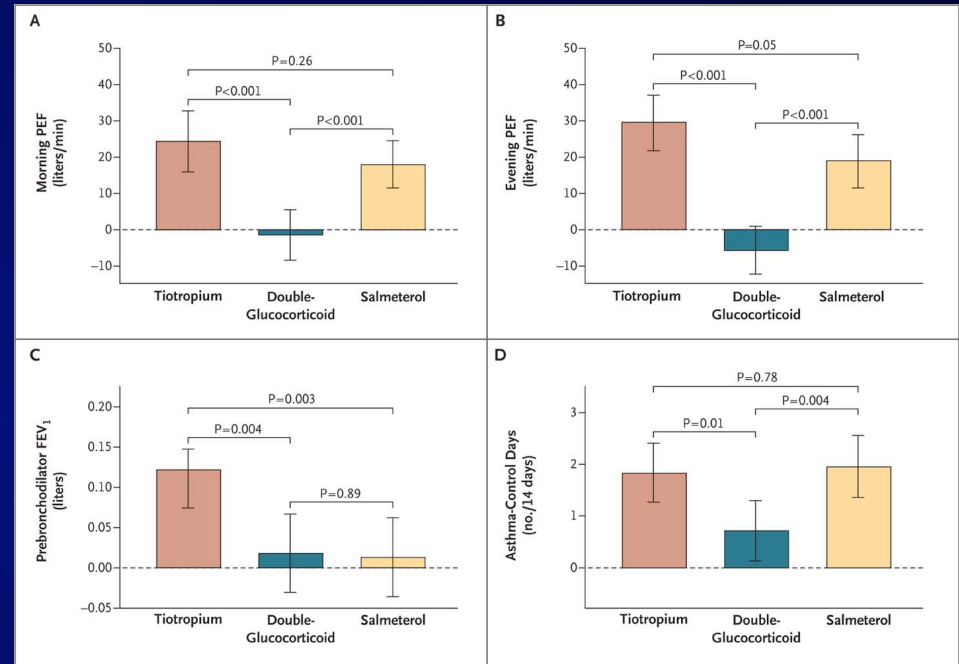
Safety of LABAs: Views from the FDA



- LABA alone without ICS dangerous
 - Yet 7-11% PCPs use LABA alone for asthma
- Use of ICS with LABA reduces but may not completely eliminate possible risk
- 4 adult/1 pedi study mandated: completion 2016

Tiotropium Bromide Step-Up Therapy for Adults with Uncontrolled Asthma

- TALC study
 - Poorly controlled on ICS
 - Double ICS
 - LABA (salmeterol)
 - LAMA (Tio)
- Primary endpoints
 - PEFR
 - FEV₁
 - Asthma control days
- LAMA = LABA > ↑ ICS
- No long term data; select subset of subjects



N Engl J Med 2010;363:1715-26
October 28, 2010

Update in Asthma 2010

- Epigenetic: environment changes functioning of genes
 - Smoke, hydrocarbons, diesel exhaust, or allergens
 - Converts naive T cells to TH-2 (allergic) T cells
- Prenatal exposure to tylenol increases risk of asthma
- Vitamin D deficiency ($< 2\text{ng/ml}$)
 - Increases risk and severity of asthma
 - Associated with poor response to ICS
- **Drug therapy** (in addition to ICS)
 - Macrolide Rx x16 weeks reduced airway hyperreactivity
 - Statins: reduced inflammation & improved spirometry in COPD but showed less effect in asthma

Update in Asthma 2010

- **What reduces exacerbations of asthma**
- Environmental tobacco smoke (ETS) = strongest predictor of respiratory illness in children
 - **Ban on ETS** in Scotland decreased asthma hospitalization by 18.2%
- Exercise can induce bronchospasm
 - 3 months of **aerobic exercise training** significantly improved asthma QOL and asthma free days ($p=0.001$)
- **Medication compliance**
 - Indacaterol – once a day LABA
 - Ciclesonide – once a day high potency ICS
- **MOST IMPORTANT**

Environment

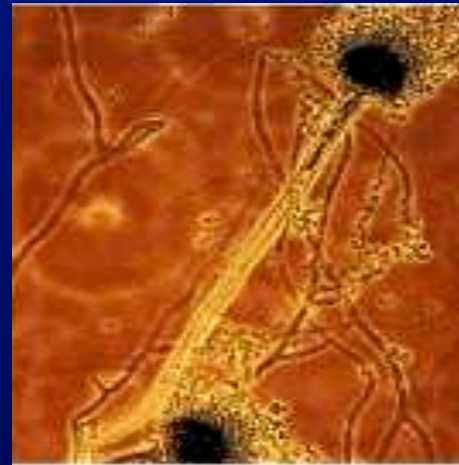
- Allergens avoidance in asthma:
 - House dust mite
 - Cat dander
 - Cockroach antigen
 - Alternaria/fungi
- **Most forgotten component in asthma education**



Mites



Cockroach



Fungi



Cat

COPD 2011

- What have we learned about COPD?

Three Things You Should Know about COPD

- 1- This a treatable and reversible disease.**
- 2- Management of COPD should include: encouragement of exercise; tobacco cessation, and pharmacotherapy.**
- 3- Inhaled long acting bronchodilators alone or combined with ICS are the appropriate therapy for the management of stable COPD patients.**

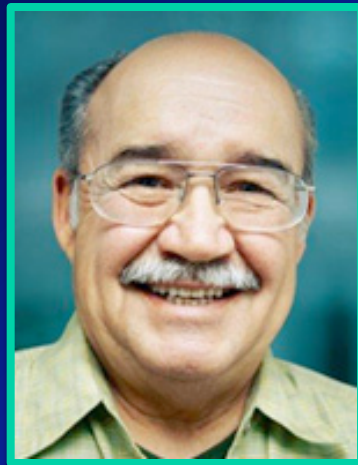
What do we mean by “Disease Modification” ?



Myth:
COPD is a disease of old
man

The Changing Face of COPD

Younger



- ~70% of patients with COPD are <65 years old,¹ accounting for: 67% of COPD office visits
— 43% of hospitalizations²

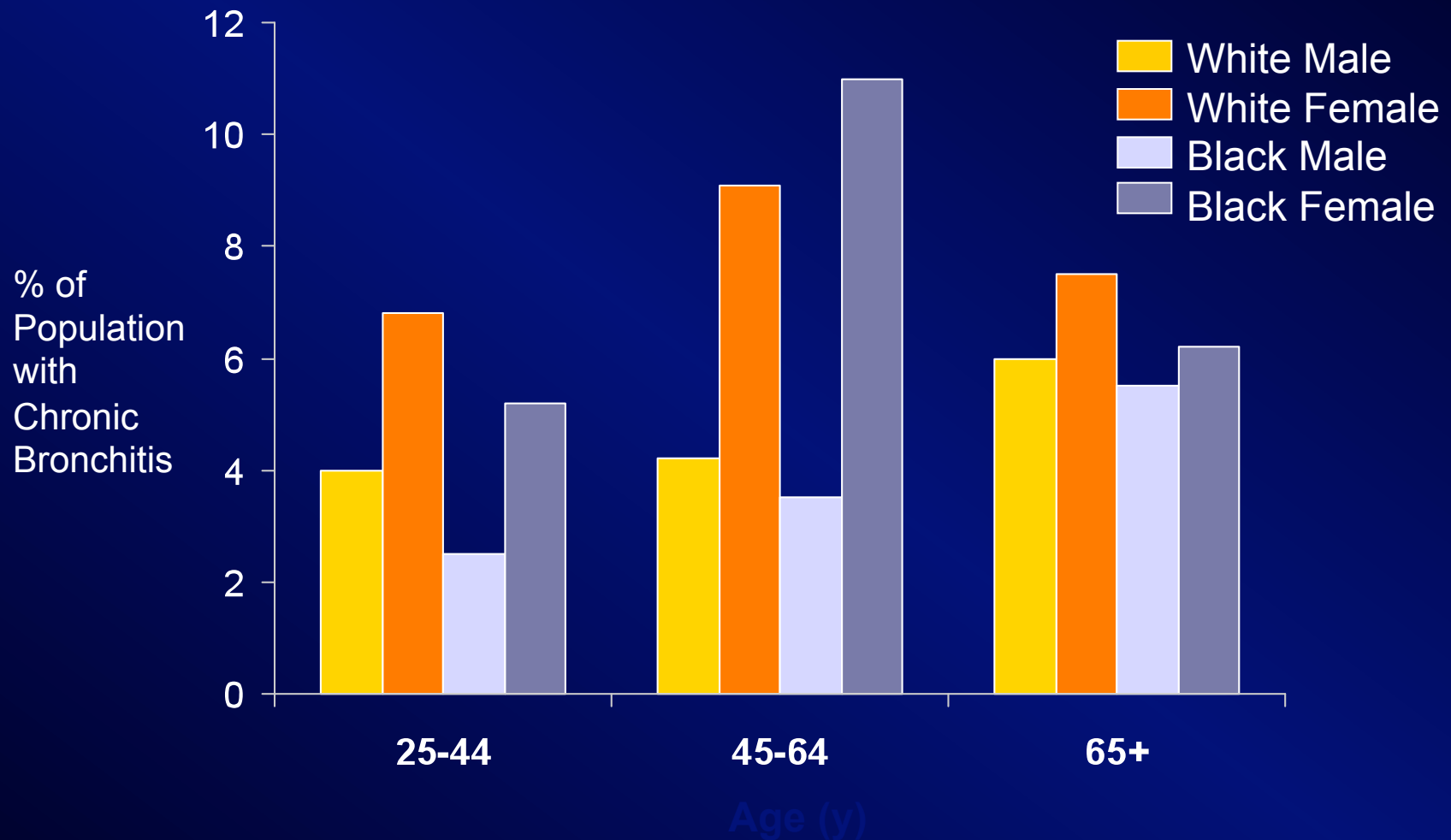
More Women



- ◆ In 2004, women accounted for ~63% of all self-reported COPD cases¹
- ◆ 1980–2009: COPD mortality rates for women nearly tripled³

1. Lethbridge-Çejku M et al. NHIS 2004. *Vital Health Stat.* 10(228). 2006; 2. Sin DD, et al. *Am J Respir Crit Care Med.* 2002;165:704-707; 3. CDC. Facts About Chronic Obstructive Pulmonary Disease. August 2003. Available at: <http://www.cdc.gov>.

Shifting Patient Profile in COPD: 2010



NHLBI. *COPD Data Fact Sheet*. Available at: www.nhlbi.nih.gov/health/public/lung/other/copd_fact.pdf.

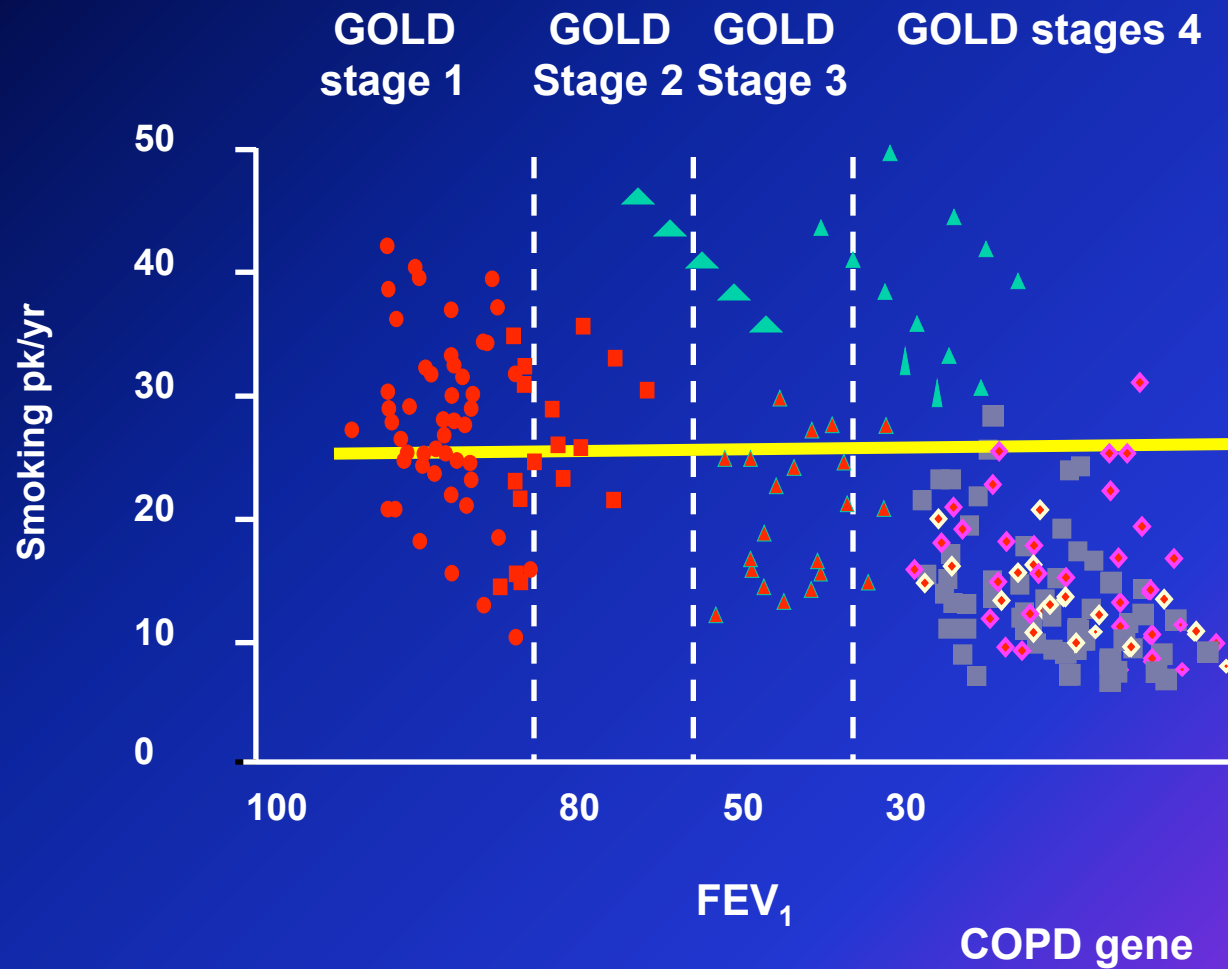
Myth:

The more you smoke the worse your disease gets....

Fact:

**There is no correlation between
pack years and disease
severity**

Smoking and disease severity



COPD: Disease Progression



age 40-50

50-55

55-60

60-70

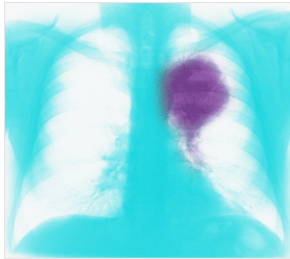


COPD

Lung cancer



Chest x-ray showing a primary lung cancer



Cachexia vs myopathy

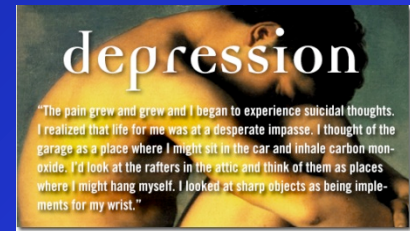


9 - 20%

20-60%

Anxiety and

depression



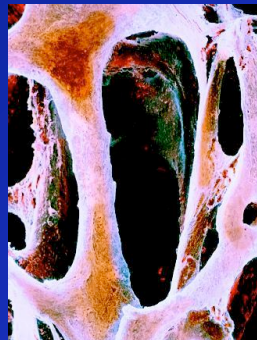
30%

30-50%

17%

30-50%

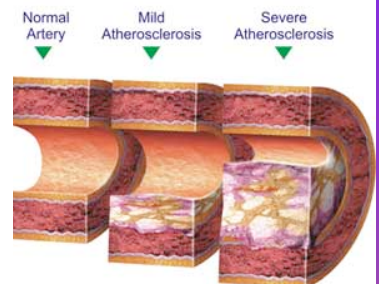
Osteoporosis



Anemia

CAD/CHF

ATHEROSCLEROSIS



Barnes et al GOLD 2009

Myth:

**Exacerbations are not
that bad.....**

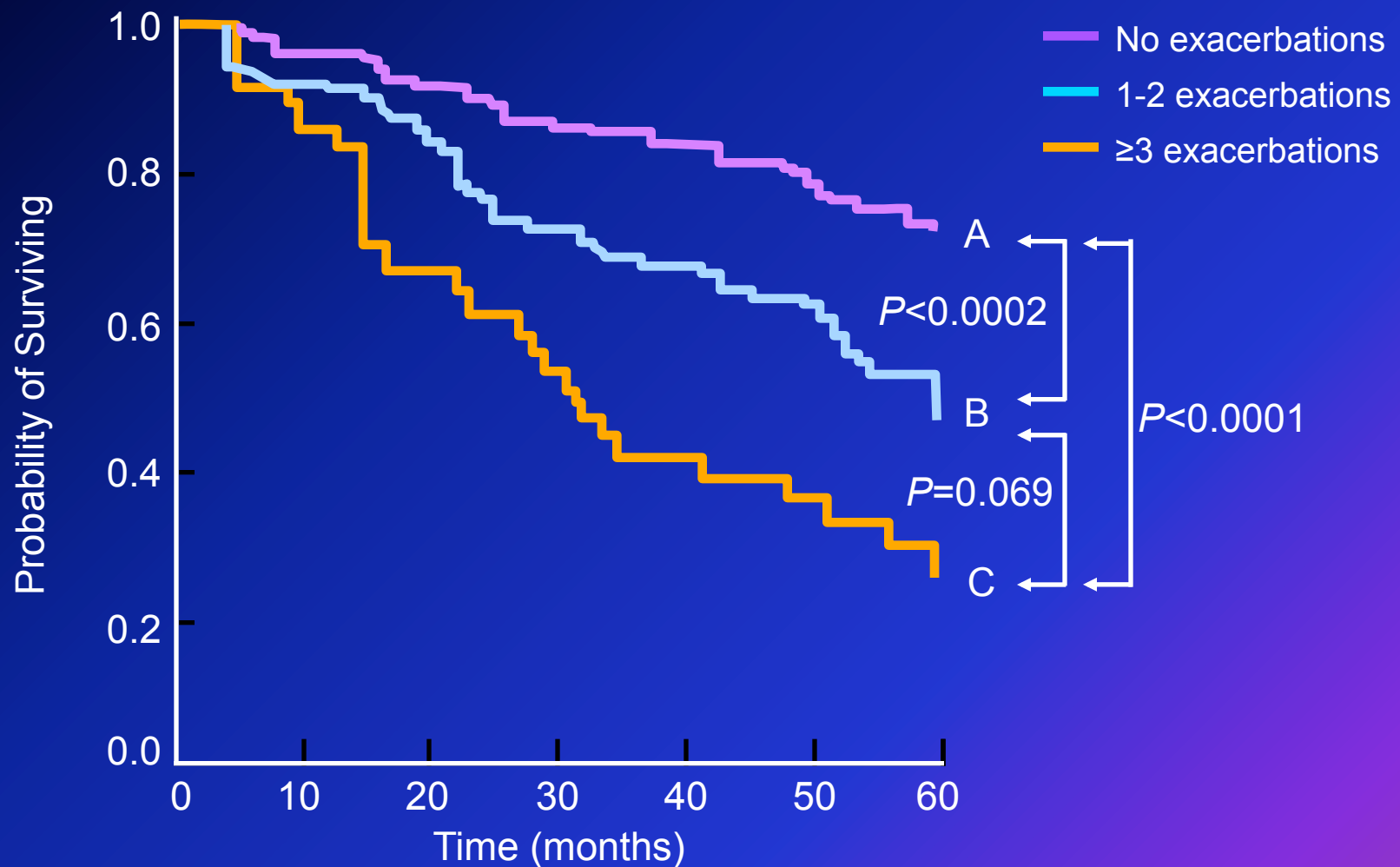
Recovery of Lung Function and Symptoms Following an Exacerbation Is Often Prolonged and Sometimes Incomplete

	PEF	Symptoms
Time to recovery,* median days (IQR)	6 (1-14)	7 (4-14)
Exacerbations recovering within 35 days	75.2%	86.1%
Exacerbations recovering within 91 days	80.2%	90.9%
Exacerbations that did not recover within 91 days	7.1%	4.6%

IQR=interquartile range.

Seemungal T, et al. *Am J Respir Crit Care Med*. 2000;161:1608-1613.

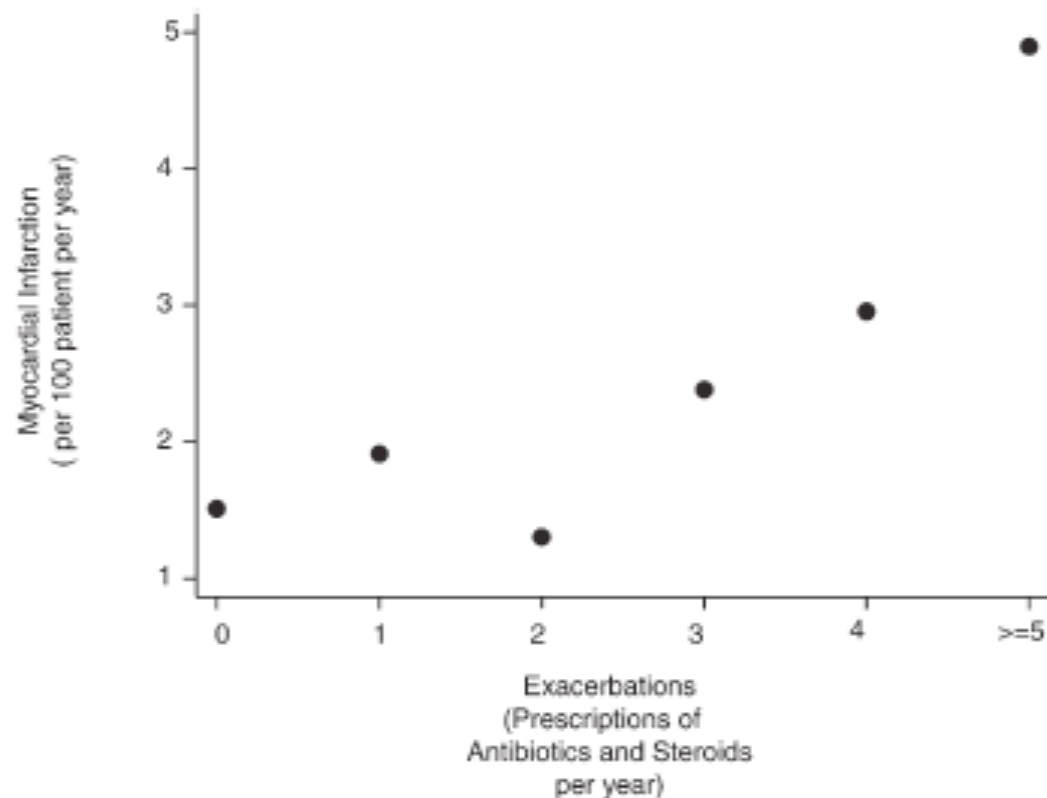
COPD Patients With a Greater Frequency of Severe Exacerbations* Per Year Have a Higher Risk of All-Cause Mortality



*Severe exacerbations = exacerbation required emergency visits or hospital admissions.

Soler-Cataluna JJ, et al. *Thorax*. 2005;60:925-931.

Increased Risk for MI and Stroke Following COPD Exacerbations

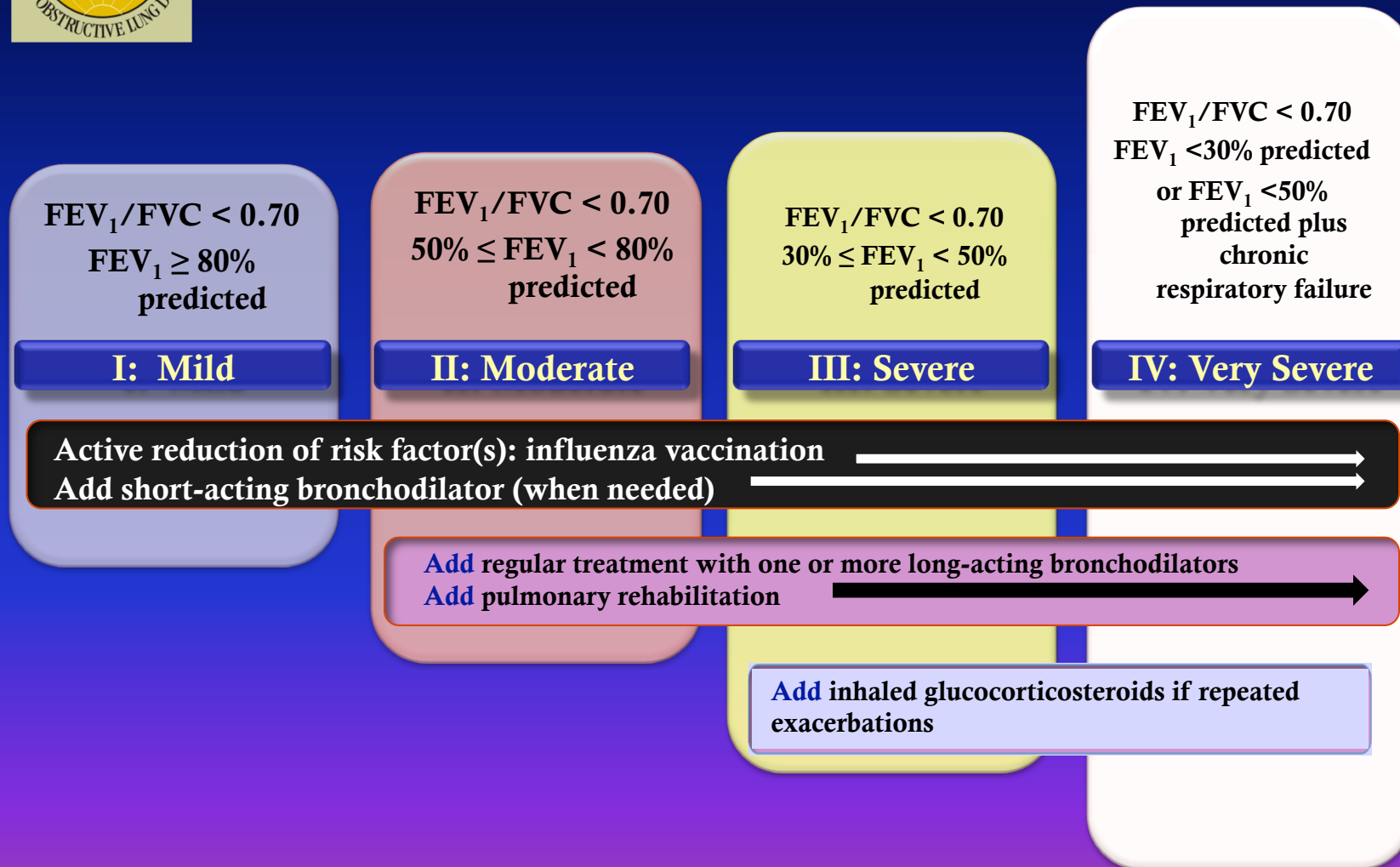


Increased risk 1-49
(2.27 [1.1-4.7]; $P=.03$)

Donaldson CG et al. *Chest*. 2010;137:1091-1097.



GOLD Therapy at Each Stage of COPD



Basics of Treating COPD: 2011

- **Initiation of long-acting bronchodilator**
 - Canadian guidelines suggest cost-effective to start with a LABA (salmeterol/formoterol) or LAMA (tiotropium)
 - Less exacerbations & better quality of life
 - Much better compliance
- **Inhaled Corticosteroids: Risk vs. Benefit**
 - Risk: Increase risk of pneumonia with RR= 1.6
 - Benefit: $FEV_1 < 50\%$ or "asthma/atopic" features with eosinophils, frequent exacerbations, or positive BD test
- **Home oxygen**
 - Saturation $\leq 88\%$ (or $\leq 89\%$ with Cor Pulmonale)
 - Must wear oxygen 15 hours/day for survival benefit

GOLD Pharmacologic Treatment Options

Bronchodilators

Short-acting

β-agonists
Albuterol
Levalbuterol
Pirbuterol
Anticholinergic
Ipratropium
Combination
Combivent

Long-acting

β-agonists
Salmeterol
Formoterol
Arformoterol
Indacaterol
Anticholinergic
Tiotropium
Theophylline

Anti-inflammatory

Corticosteroids

Combination
Salmeterol + Fluticasone
Formoterol + Budesonide

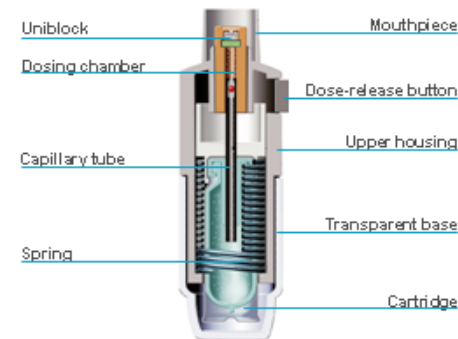
Phosphodiesterase inhibitor

PDE-4 Inhibitor
Roflumilast

Respimat: soft mist inhaler

- Spring powered inhaler
- No preservative; better delivery
- Approved 2011 for Combivent
- How to use:
 - ✓ Load cartridge into device
 - ✓ Rotate counter clockwise
 - ✓ Insert mouthpiece
 - ✓ Push dosing button during inspiration (1 actuation QID)

Schematic diagram of Respimat® SMI



How to use Respimat® SMI



1. Insert the Respimat® SMI cartridge into the inhaler. Push the cartridge into the inhaler until it is fully seated. The inhaler will make a clicking sound when the cartridge is fully seated.



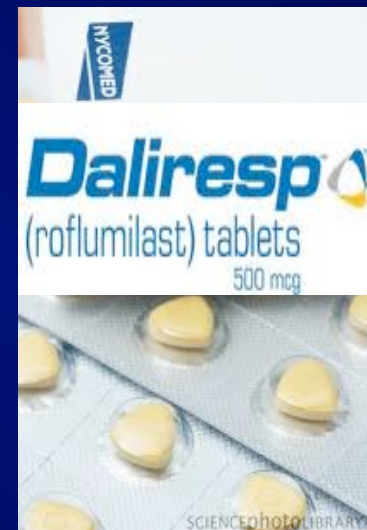
2. Rotate the inhaler counter-clockwise. The inhaler will make a clicking sound when it is fully rotated. The inhaler will now be ready for use.



3. Breathe your breath out for 10 seconds before you breathe in. Breathe in slowly and deeply. The inhaler will make a clicking sound when you breathe in. Breathe out for 10 seconds before you breathe in again.

Roflumilast: PDE4- inhibitor

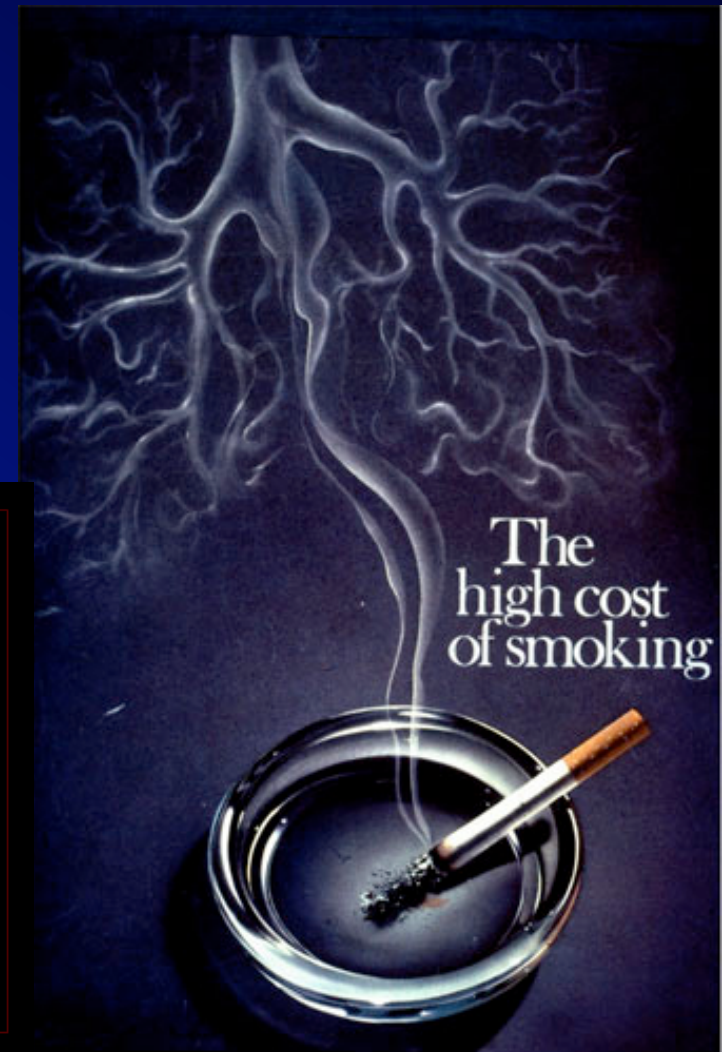
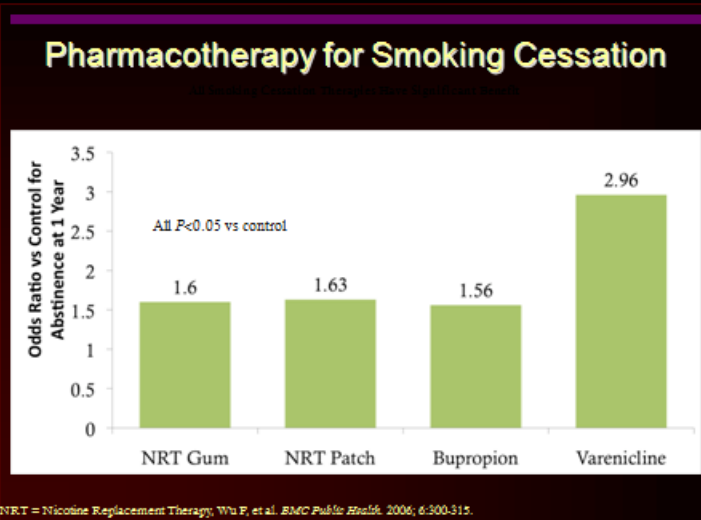
- Selection of patients who will benefit:
 - Severe COPD with chronic bronchitis
 - On LABA/ICS and LAMA (tiotropium)
 - Exacerbation requiring steroids/hospitalization
- Mechanism of action: anti-inflammatory medication
- Benefits: reduced exacerbations
- Side effects:
 - Nausea/diarrhea (10 – 20%)
 - Weight loss (7.5%)
 - Anxiety/depression (6%)



500 mg 1x/day

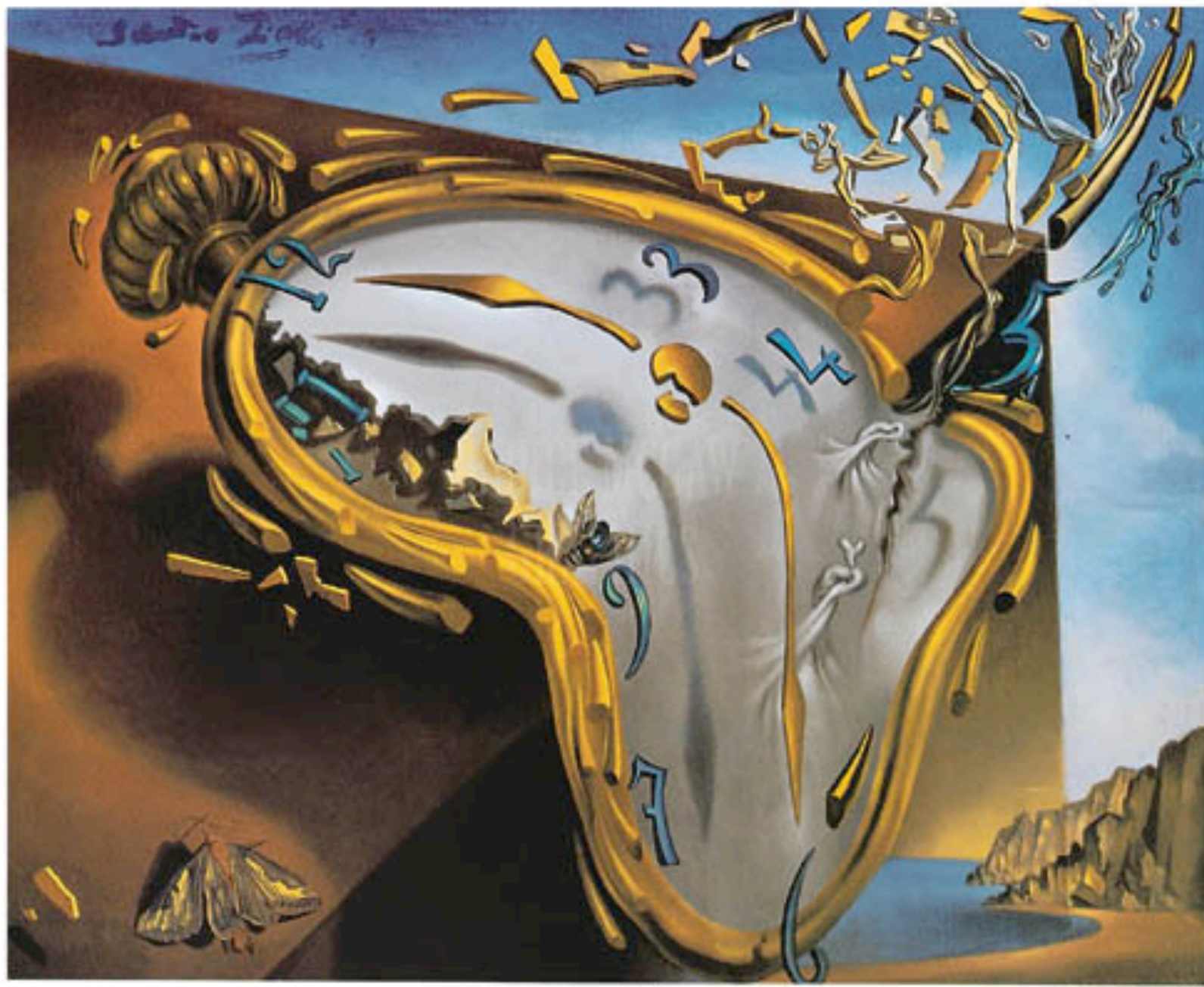
The Key to Treating COPD: Smoking Cessation

- **Smoking cessation (Lung Health Study)**
 - Reduced all cause mortality (MI/ Cancer)
 - Only therapy proven to prevent ↓ FEV₁
 - Average smoker quits 5 times prior to success





Questions?



Salvador Dalí