Managing the Risk of COPD Exacerbations: The GOLD Recommendations

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Disclaimer

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Index Case

MR MS – presented to IALCH in April 2012

- Chronic productive cough – daily for 12 years
- Dyspnoea on minimal exertion (mMRC 3)
- Progressive worsening of effort tolerance
- Occasional tight chest and wheezing – worse at night
- 6 hospital admissions in the prior 6 months for chest infections and worsening symptoms

Index Case

Background:

- Smoking Hx: **20 cigarettes/day for 30 years**
- → was still smoking on presentation

- Smoked cannabis and mandrax for > 15 years

- **Diabetes and Hypertension**
- No Hx of IHD
- No previous Dx of asthma/family hx/known allergies
- No previous TB
- Employment: upholstery factory

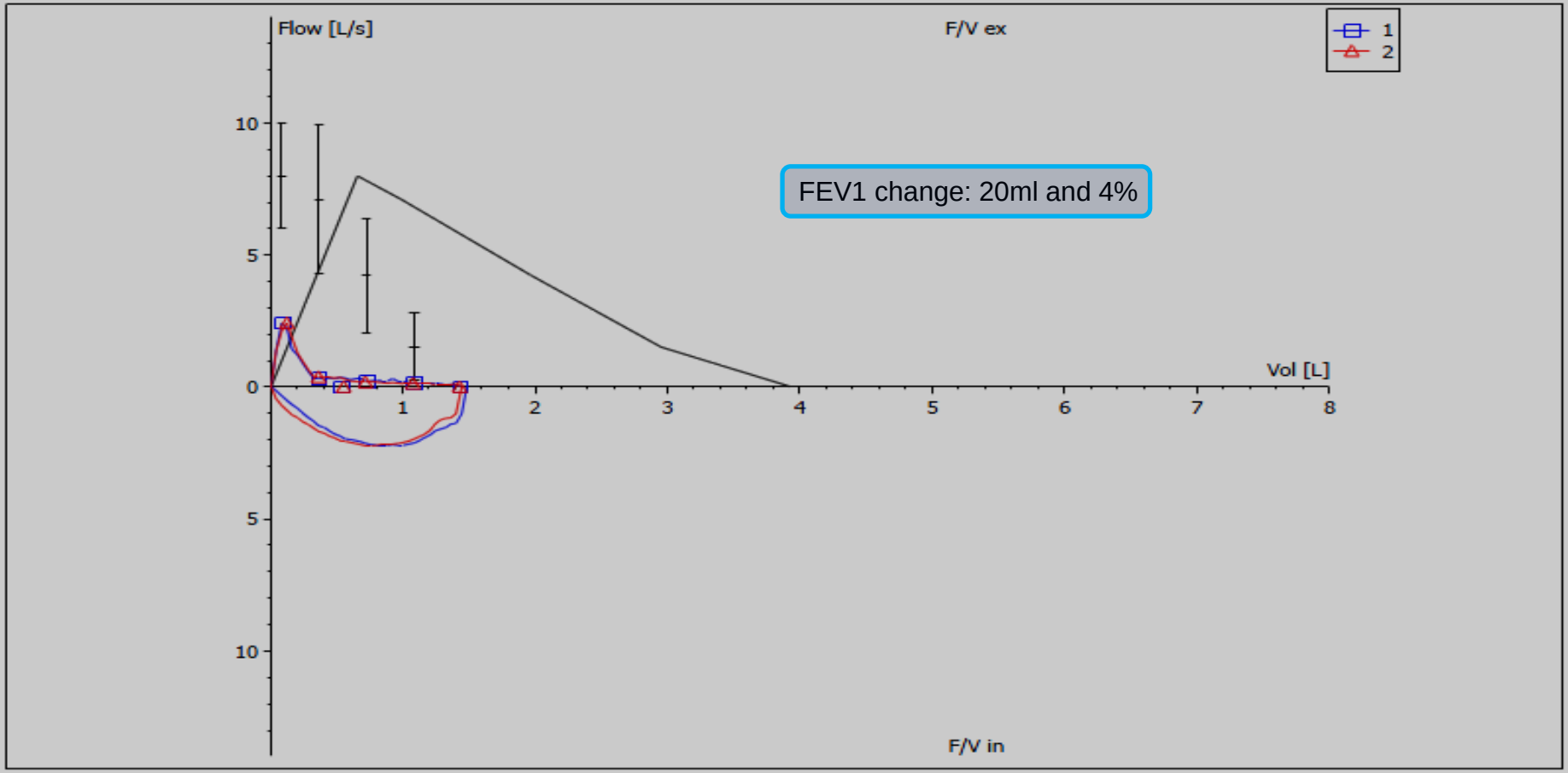
Medication:

- Started on **SABA** (Salbutamol) and **ICS** (budesonide) – **minimal improvement** in symptoms (3 years of treatment)
- **High dose oral steroids** (prednisone) with acute exacerbations
- Oral anti-**diabetic** medication and anti-**hypertensives**

Examination:

- Emaciated
- RR 24 **Resting SaO2: 90%**
- Early digital clubbing no palpable LN's
- No clinical features of respiratory failure
- Clinical features of **chest hyperinflation with wheezing**
- No cor pulmonale

	Pred	Pre	%Pred	Post	%Pred	%Diff
VC MAX	4.08	1.44	35.4	1.43	35.1	-0.9
IC	2.99					
ERV	1.09					
FVC	3.93	1.43	36.4	1.43	36.3	-0.3
FEV 1	3.08	0.53	17.2	0.55	17.9	4.0
FEV1%F		36.94		38.56		4.4
PEF	8.00	2.43	30.3	2.41	30.1	-0.7
MEF 75	7.09	0.31	4.4	0.36	5.1	16.1
MEF 50	4.22	0.22	5.2	0.18	4.3	-18.2
MEF 25	1.51	0.14	9.3	0.13	8.6	-7.1
PIF		2.23		2.25		0.9
Date		17/04/12		17/04/12		
Time		08:15:14		08:29:29		



FEV1 change: 20ml and 4%

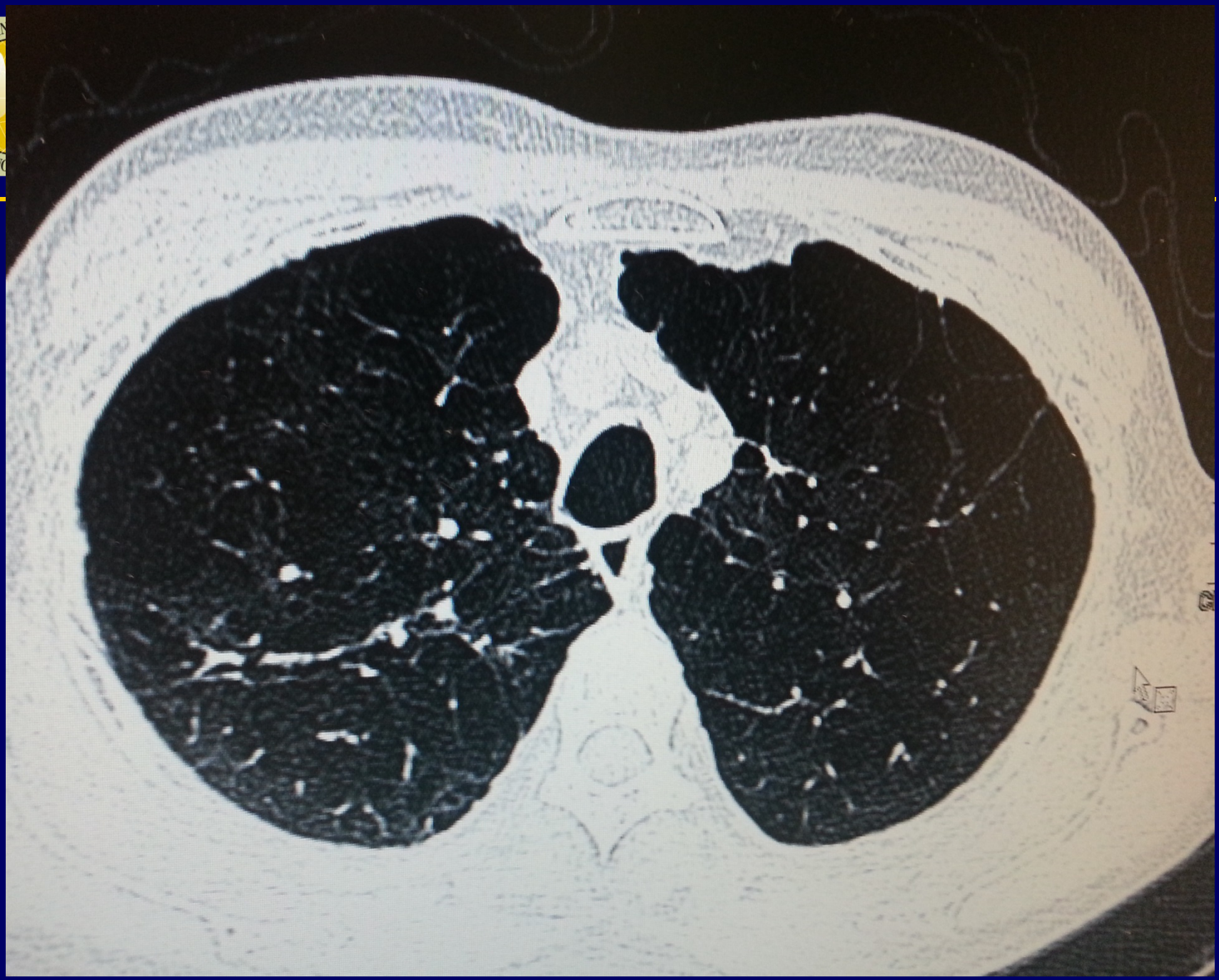
- 6MWT:

170m in 3 min

- BORG 2/4

BORG

Borg Rating Perceived Exertion Scale	
0	Nothing at all
0.5	Very, very weak (just noticeable)
1	Very weak
2	Weak (light)
3	Moderate
4	Somewhat strong
5	Strong (heavy)
6	
7	Very Strong
8	
9	
10	Maximal



Assessment:

- COPD **GOLD stage 4** – related to cigarette smoking. Other risk factors: Cannabis
- Comorbidities: Hypertension and Diabetes mellitus

Treatment:

- **Budesonide/Formoterol** DPI (Symbicord®)
- **Tiotropium** (Spiriva®)
- **Smoking cessation emphasised**

Assessment of COPD

- Assess symptoms
- Assess degree of airflow limitation

Use spirometry for grading severity according to spirometry, using four grades split at **80%, 50% and 30%** of predicted value

Classification of Severity of Airflow Limitation in COPD*

In patients with $FEV_1/FVC < 0.70$:

GOLD 1: Mild	**$FEV_1 \geq 80\%$ predicted**
GOLD 2: Moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3: Severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4: Very Severe	$FEV_1 < 30\%$ predicted

**Based on Post-Bronchodilator FEV_1*

Objectives

1. *Definition and Overview*
2. Pathogenesis and Risk Factors
3. Pathophysiology and Assessment
4. Therapeutic options
5. Management of stable COPD
6. Management of Exacerbations

Definition

*COPD, a **common preventable** and **treatable** disease*

- *Is characterised by persistent airflow limitation that is **usually progressive** and associated with an enhanced **chronic inflammatory** response in the airways and the lung to noxious particles or gases.*

- ***Exacerbations** and **comorbidities** contribute to overall severity in individual patients.*

Not only a progressive disease … *but the*

airflow limitation is not fully reversible

C.O.P.D

COPD has long been regarded as an ***incurable condition*** for which there is very little therapy available.

- It has also been **confused with asthma**.
- Apathy towards COPD treatment may be attributed to an **overemphasis on FEV1** as a marker of treatment success or failure.
- While it is true that **little can done to restore destroyed lung tissue** and disordered pulmonary physiology,
- **much can be done to improve quality of life**, increase exercise capacity and
- **reduce morbidity and mortality.**

Aim

- Outline the latest international COPD guidelines
- Discuss implications of guidelines for clinical practice

Definition of COPD

- Common
- Preventable
- Treatable disease
- Persistent airflow limitation
  - noxious particles or gases→ progressive + enhanced chronic inflammatory response in the airways and the lung
- Exacerbations + comorbidities

Mechanisms Underlying Airflow Limitation in COPD

Small Airways Disease

- Airway inflammation
- **Airway fibrosis**, luminal plugs
- Increased airway resistance

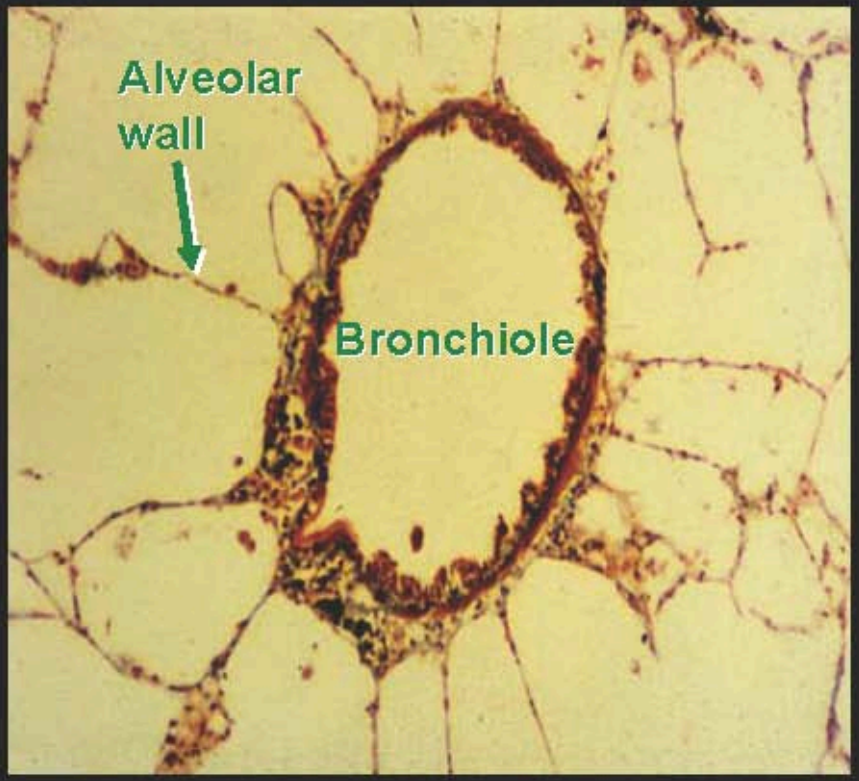
Parenchymal Destruction

- **Loss of alveolar attachments**
- Decrease of elastic recoil

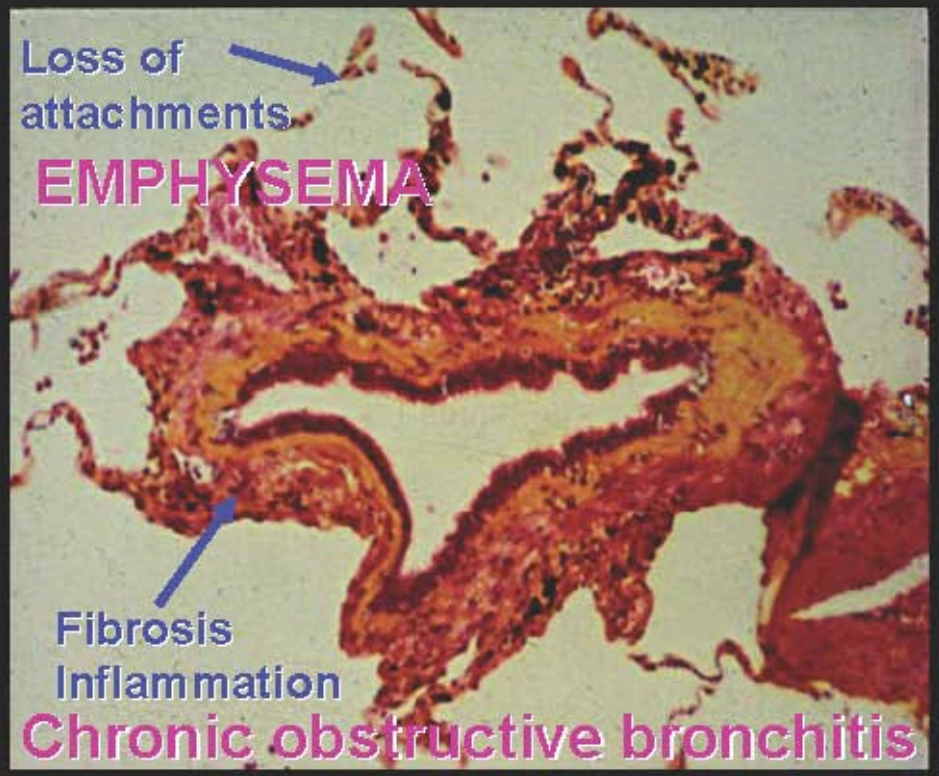
AIRFLOW LIMITATION

PATHOLOGY OF COPD

Peripheral lung



Normal



COPD

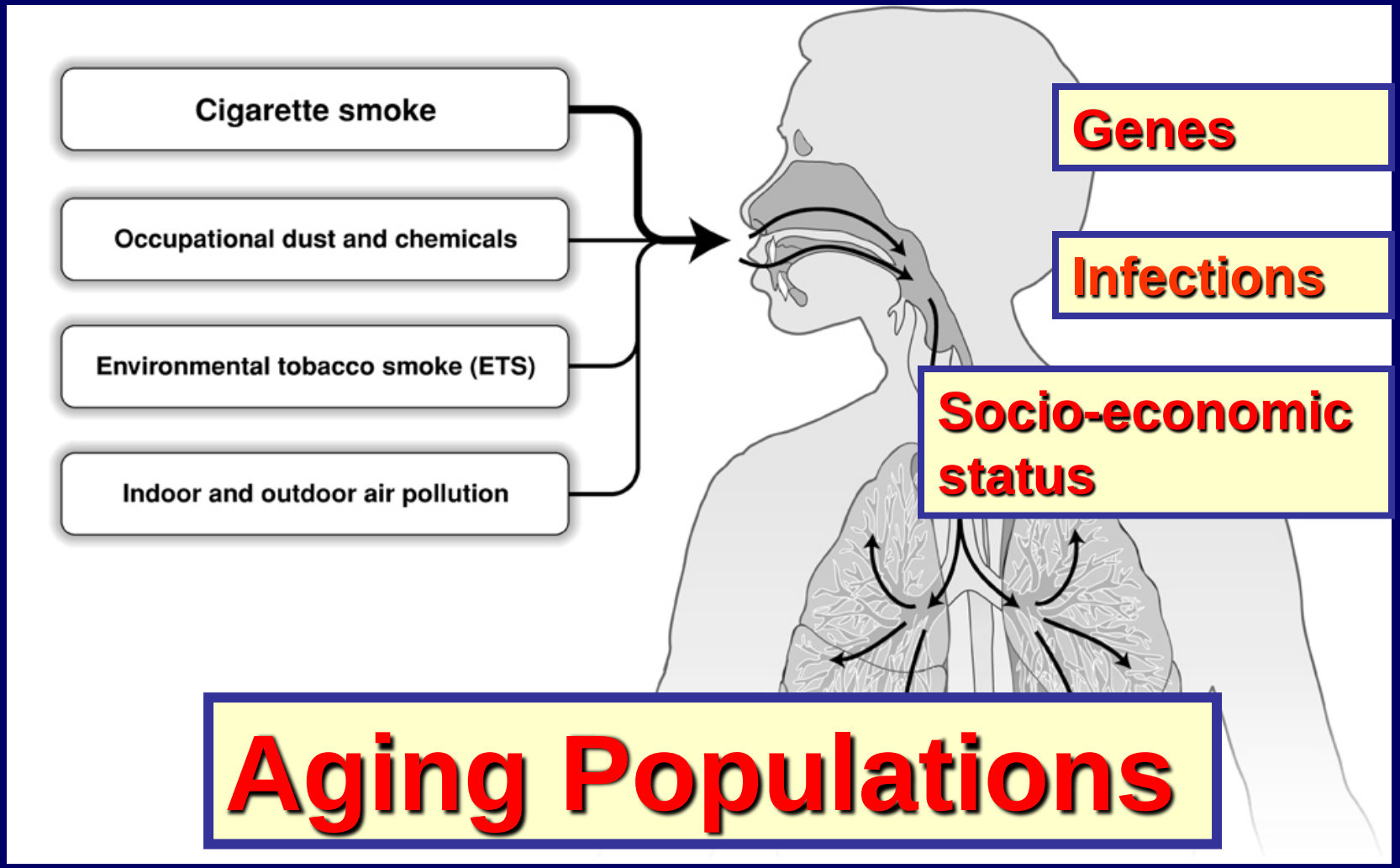
Dr Manuel Cosio

Burden of COPD

- A leading cause of morbidity and mortality worldwide.
- **Burden of COPD projected to increase in coming decades:**
  - continued exposure to COPD risk factors and
  - aging of the world's population.

Global Strategy for Diagnosis, Management and Prevention of COPD

Risk Factors for COPD



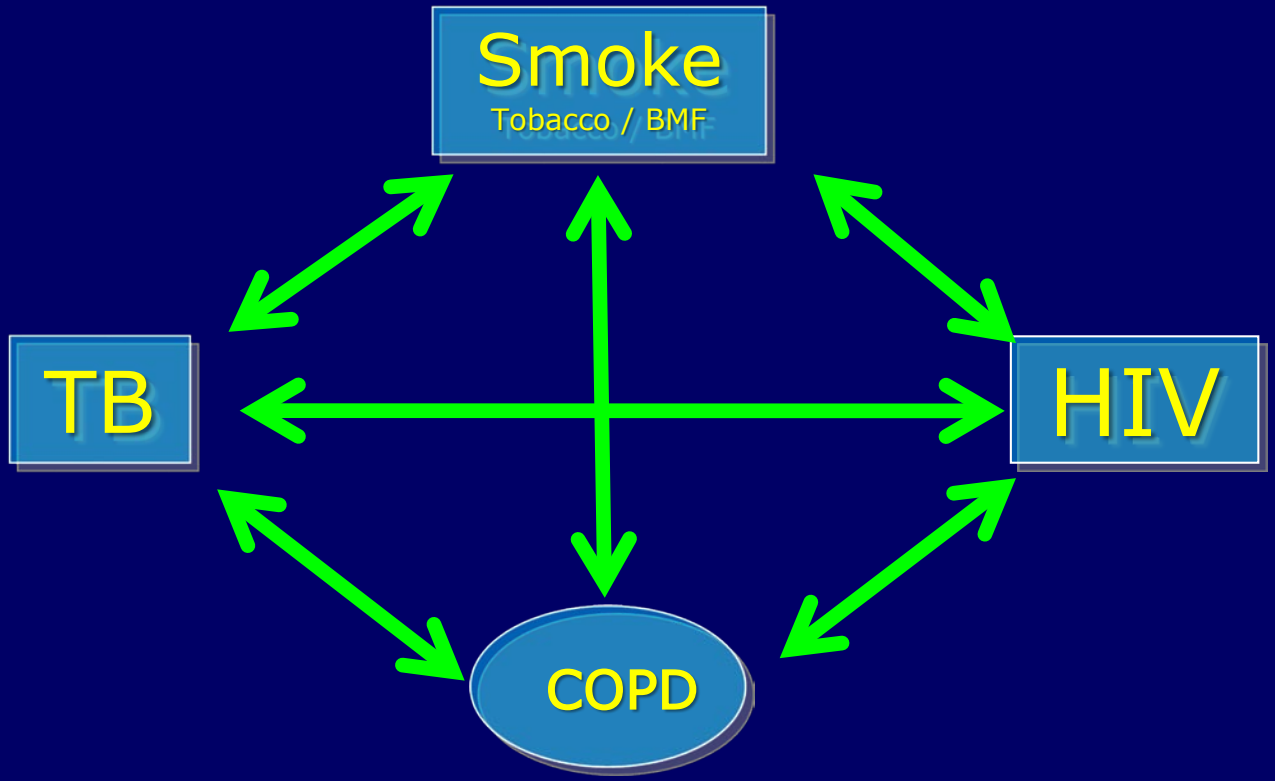
C.O.P.D

- **Cigarette smoking** is the **most important** aetiological factor in the development of COPD

- It is estimated that in **Western societies** cigarette smoking accounts for about **85% of the risk of developing COPD**

- There is a **close relationship between the amount of tobacco smoked** and the rate of **decline in FEV 1**

Colliding Epidemics….



HIV and COPD

- Increased risk of emphysema
  (114 HIV+ve pts **15% had radiographic emphysema** vs **2%** of 44 HIV –ve pts)

  Diaz et al Ann Intern Med 2000; 132:369–372

- Increased airway hyper-responsiveness
  (**30% HIV** +ve vs 13% HIV –ve)

  Poirier et al AJRCCM2001; 164:542–545

- HIV may accelerate smoker's COPD
- HIV pts who smoke have double the risk of TB

  Miguez-Burbano MJ,Addict Biol 2003;8:39-43

- **HIV pts 50-60% more likely to have COPD** vs HIV –ve pts (after correction)

  Crothers K et al *CHEST 2006; 130:1326 –1333*

Post TB COPD

- Incidence rates ranging from **27% to 50.8 %**
- Prior TB is still not recognized as a risk factor for COPD in most countries

Rabe KF Am J Respir Crit Care Med. 2007 ; 176 (6): 532 - 555

- TB COPD (vs. smokers' COPD) :
- **lower FEV1 values**
- lower degrees of reversibility
- no differences in the frequencies of dyspnoea, cough and exacerbations
- higher risk of ventilatory failure
- **higher risk of mortality**

Park JH . Int J Tuberc Lung Disease 5 : 963-7

Diagnosis of COPD

SYMPTOMS

shortness of breath

chronic cough

sputum

EXPOSURE TO RISK FACTORS

tobacco

occupation

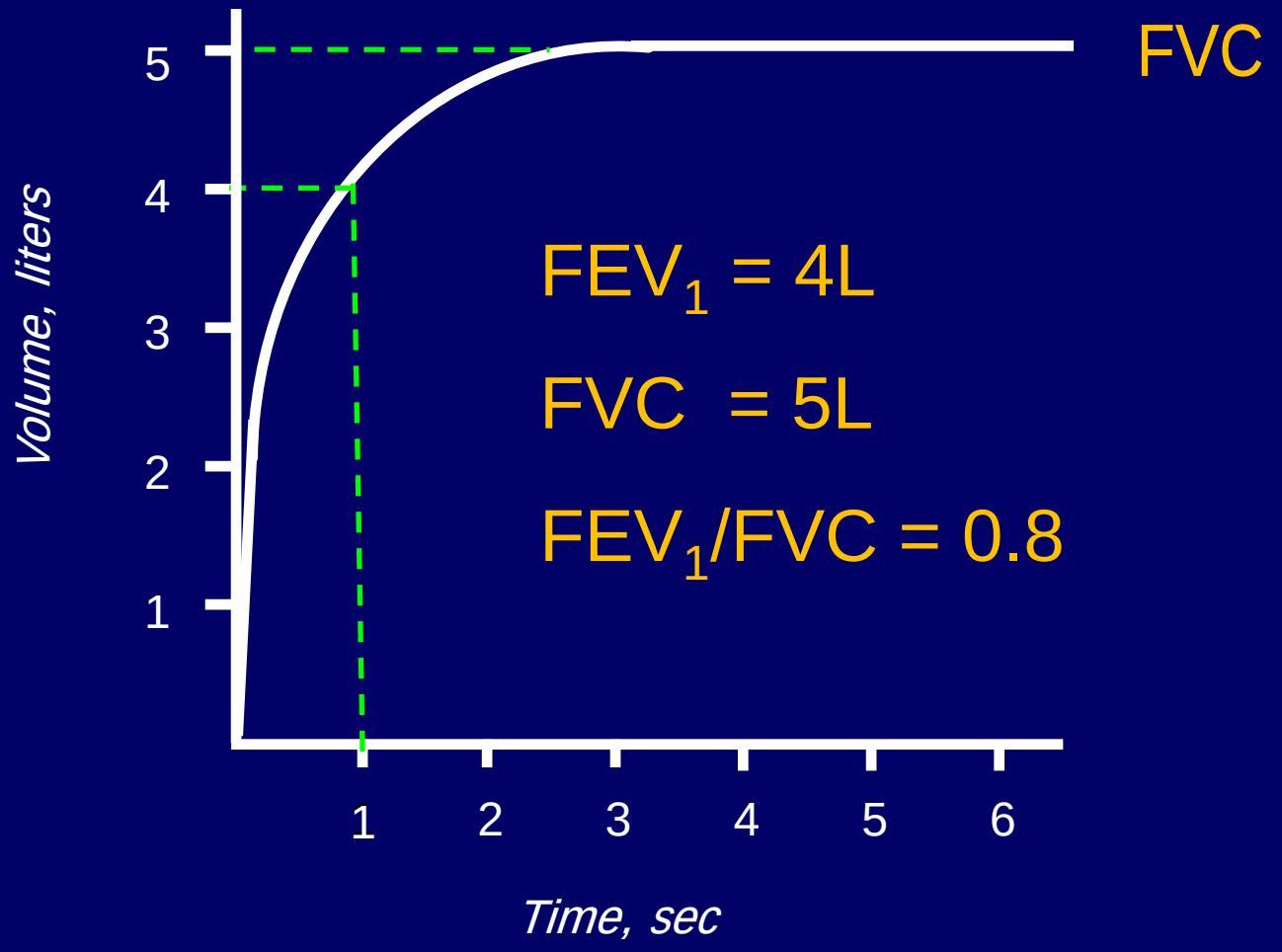
indoor/outdoor pollution

SPIROMETRY: Required to establish diagnosis

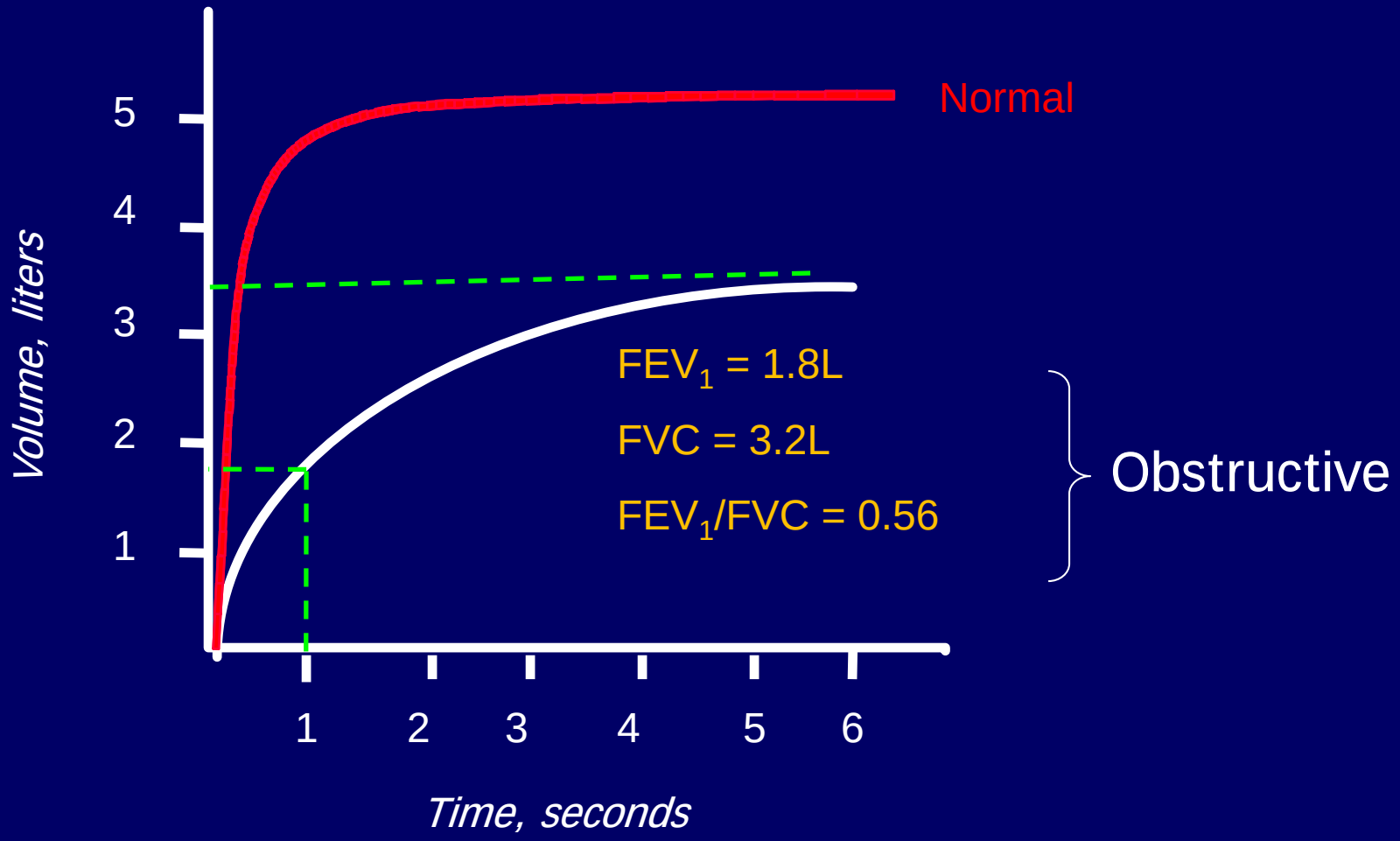
Assessment of Airflow Limitation: Spirometry

- A post-bronchodilator **$FEV_1/FVC < 0.70$** confirms the presence of airflow limitation.
- Where possible, values should be compared to age-related normal values

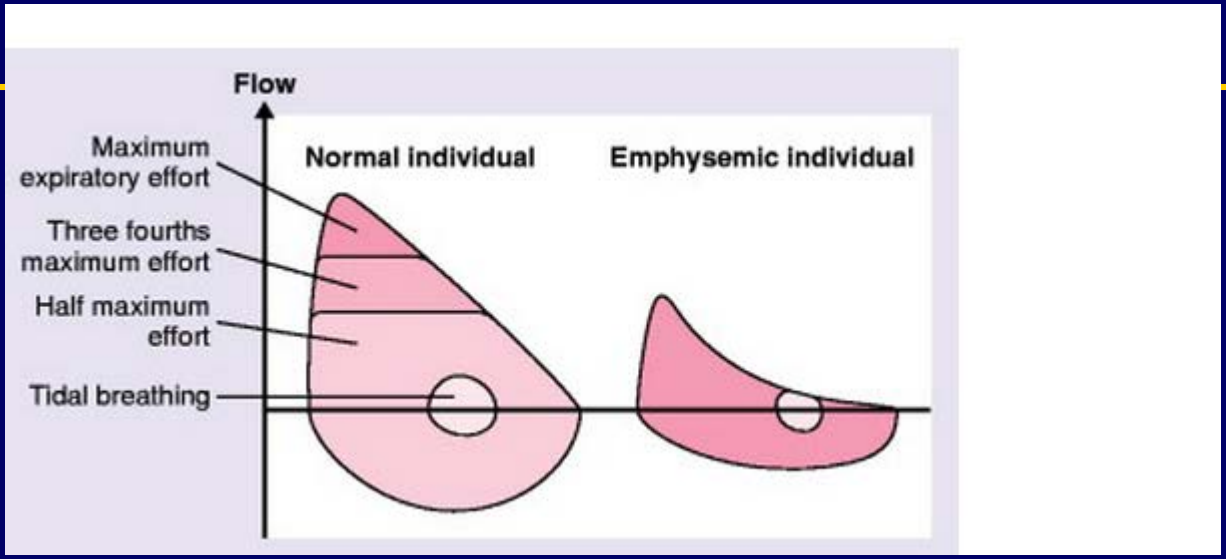
Spirometry: Normal Trace Showing FEV_1 and FVC

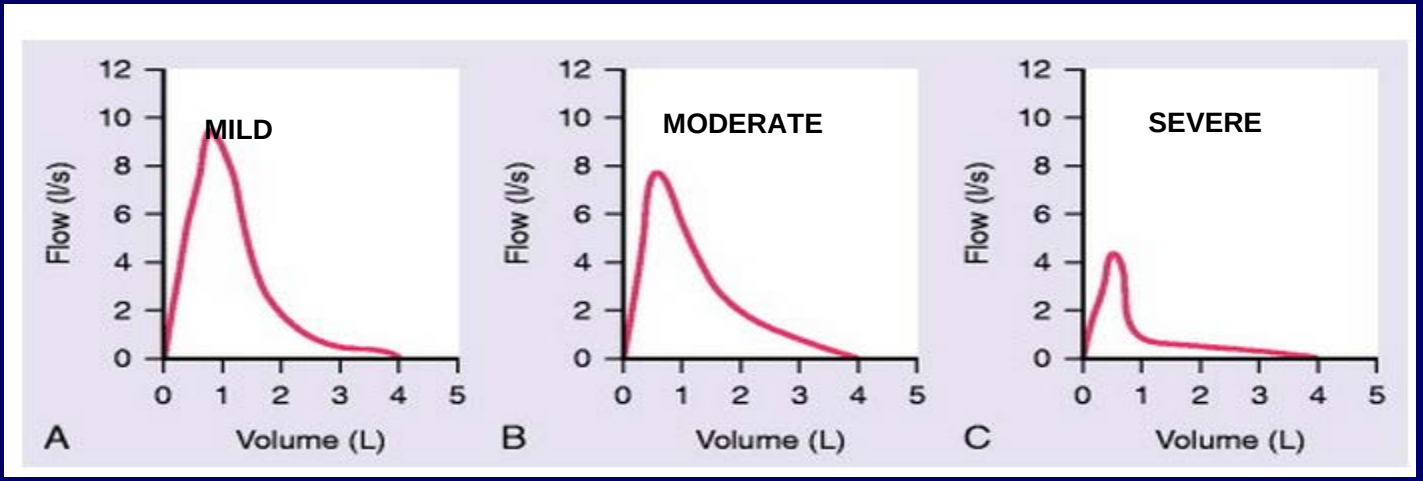


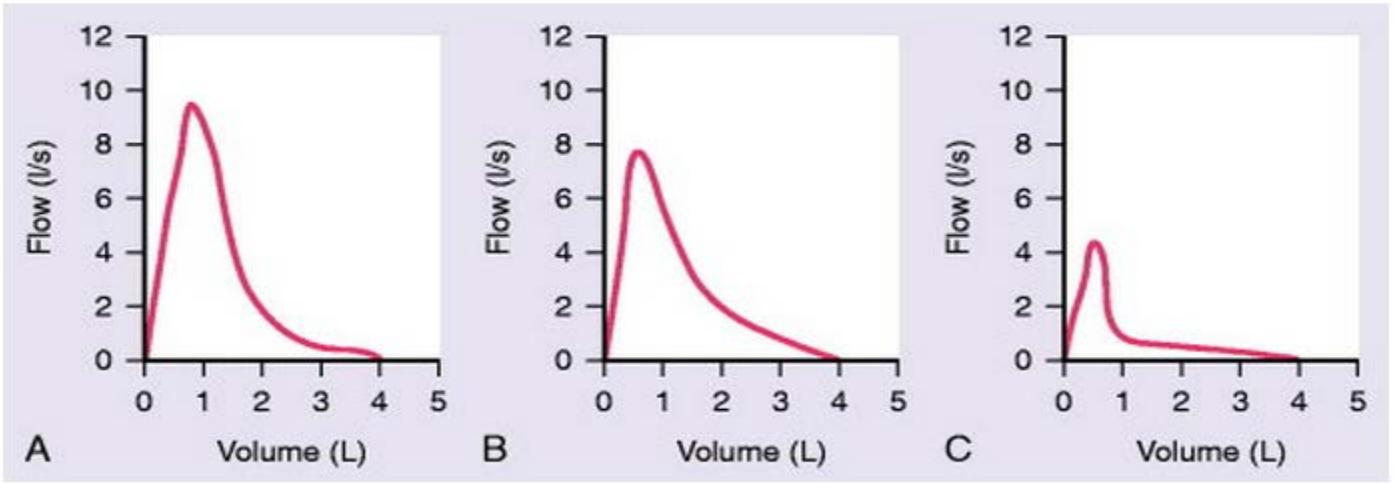
Spirometry: Obstructive Disease

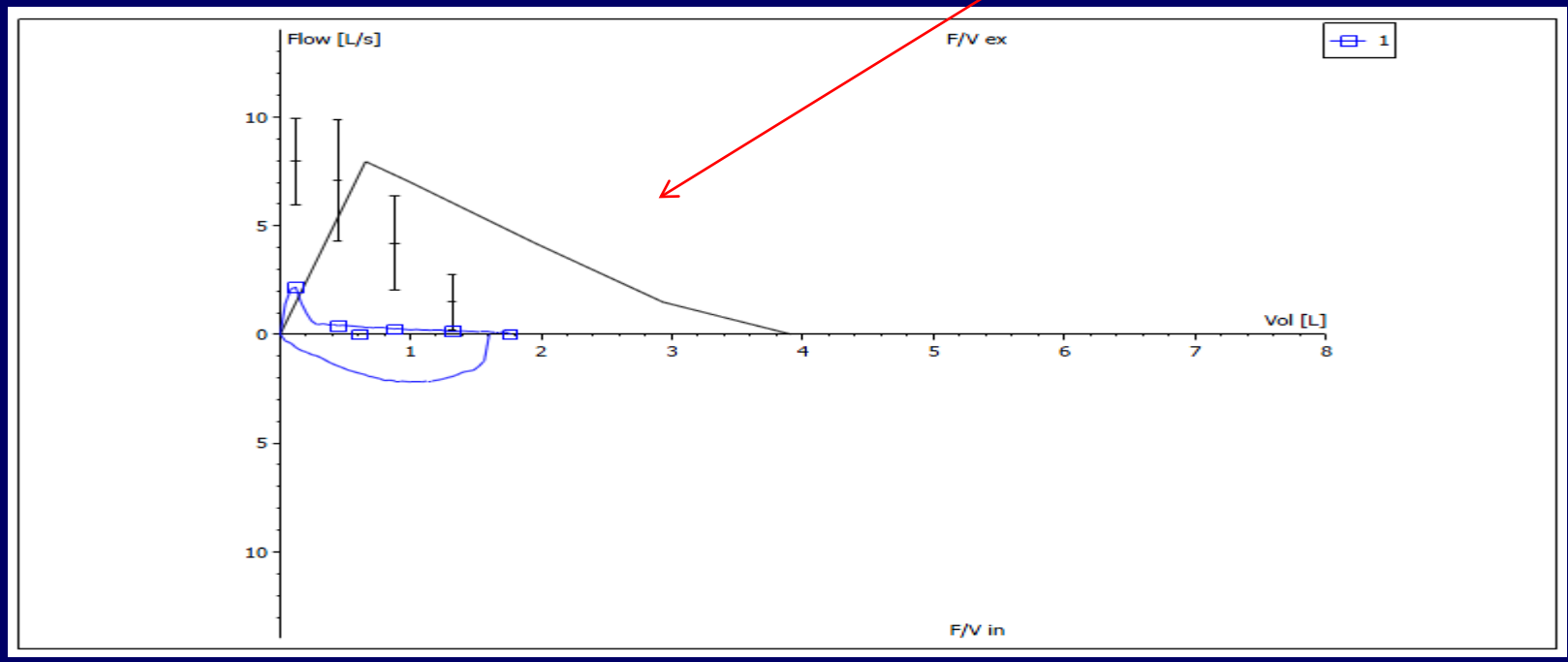


Flow-Volume loops






Flow (l/s)
Volume (L)
A
B
C

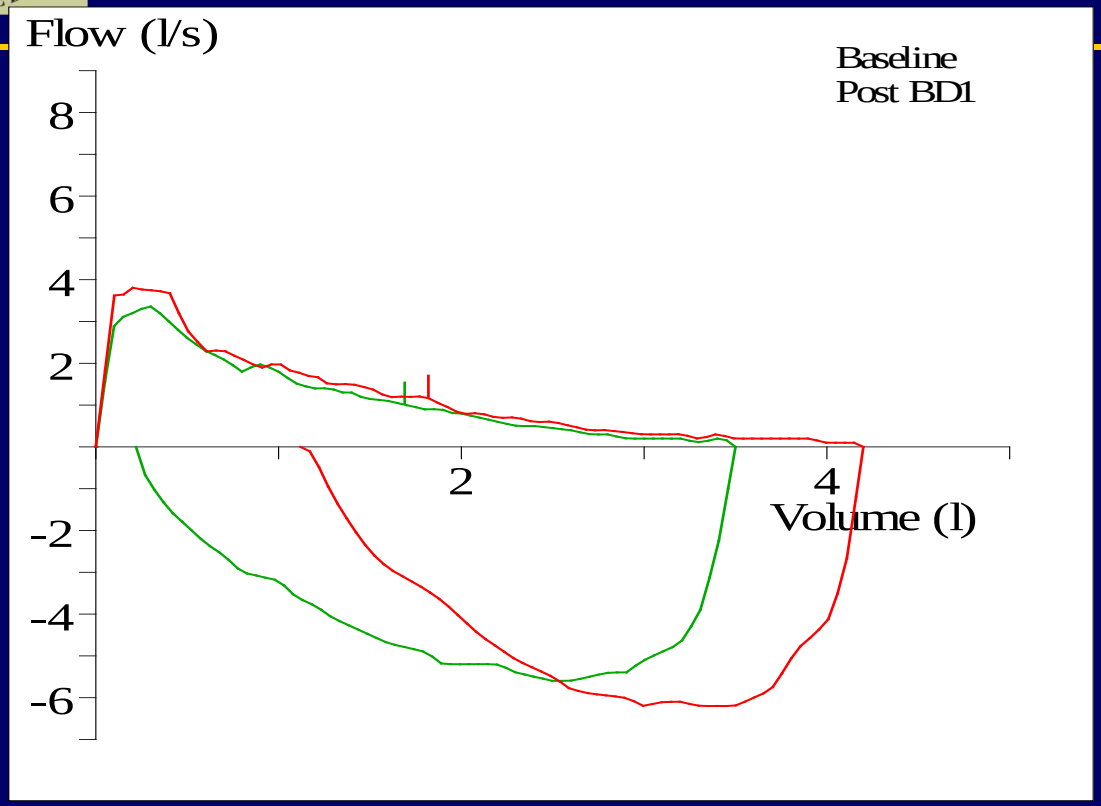

Flow [L/s]
F/V ex
1
Vol [L]
F/V in

P.3 A.T

- Re: A.T
- D.O.B. **1928**
- **Presenting Symptoms:**
- Cough
- Wheeze
- **Shortness of breath**
- Chest tightness
- **Marked sputum production**
- Periodic rhinorrhea
- Nasal congestion
- Periodic heart burn.

NAIROBI CHEST CLINIC

P.3 A.T



NAIROBI CHEST CLINIC

Reversibility testing

- Should be done to distinguish COPD vs. Asthma

- Significant reversibility: ***increase in FEV1 of 200ml AND 12%***

(Post BD FEV1 10mins after 400mcg salbutamol inhaled)

Differential Diagnosis: COPD and Asthma

COPD

- Onset in mid-life
- **Symptoms slowly progressive**
- Long smoking history

ASTHMA

- Onset early in life (often childhood)
- **Symptoms vary from day to day**
- Symptoms worse at night/early morning
- **Allergy**, rhinitis, and/or eczema also present
- **Family history of asthma**

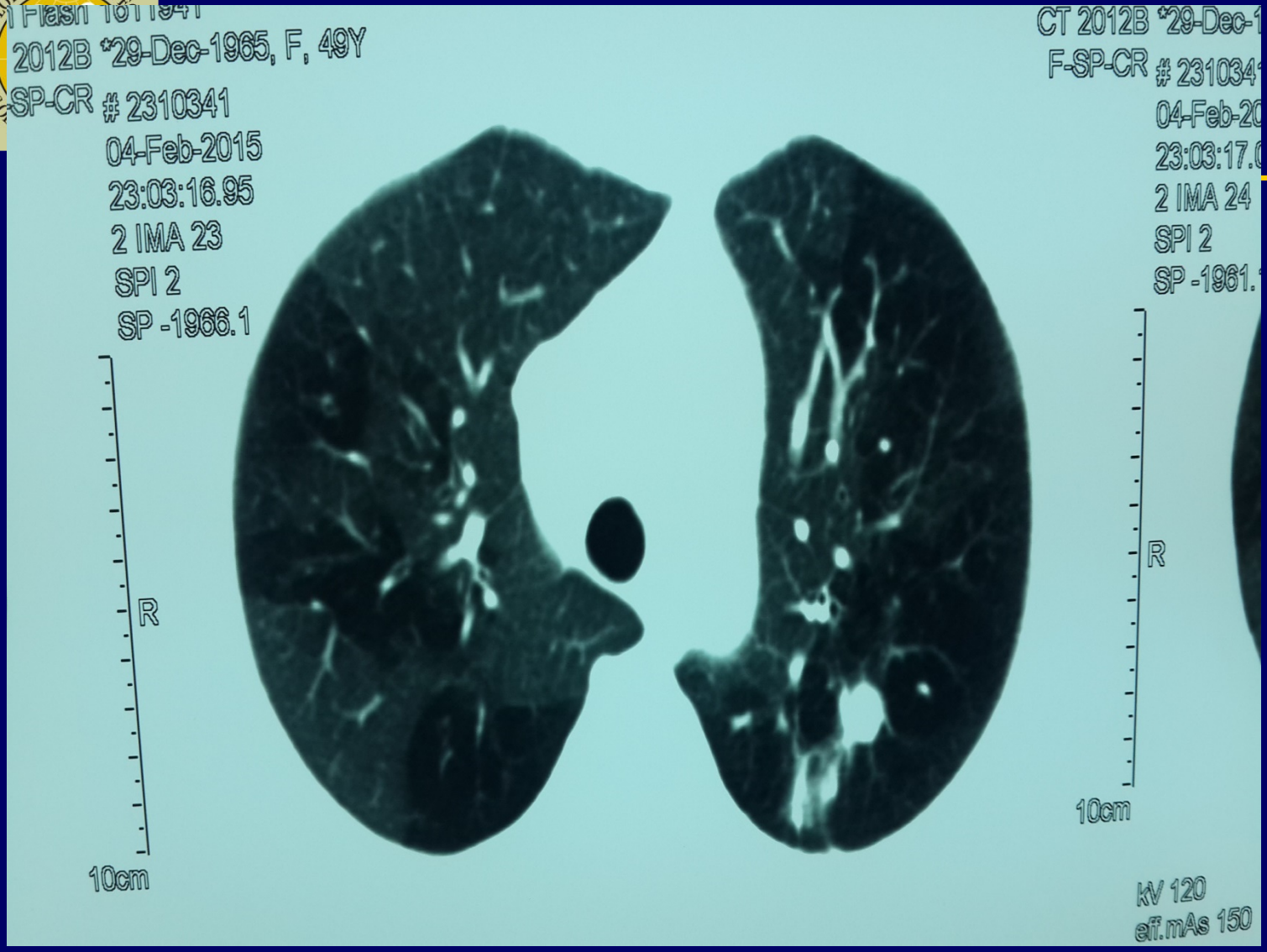
Additional Investigations

Chest X-ray

Lung Volumes and Diffusing Capacity

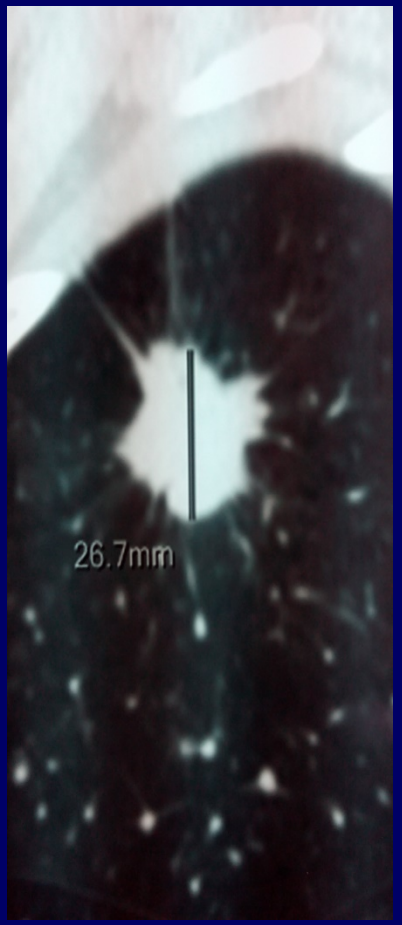
Oximetry and Arterial Blood Gases

Alpha-1 Antitrypsin Deficiency Screening



NAIROBI CHEST CLINIC

NAIROBI CHEST CLINIC


26.7mm

Additional Investigations

Exercise Testing:

- powerful indicator of health status impairment
- predictor of prognosis

C.O.P.D

A simple plan for patient care– the COPD-X Plan

- C Confirm diagnosis & assess severity
- O Optimise function
- P Prevent deterioration
- D Develop support network and self-management plan
- X eXacerbations – manage appropriately

Therapeutic Options: Key Points

- Smoking cessation
- **Pharmacotherapy**
- Lung Rehabilitation
- **Regular physical activity**

Therapeutic Options: Key Points

- Appropriate pharmacologic therapy:
  - can reduce COPD symptoms
  - reduce the frequency and severity of exacerbations
  - improve health status and exercise tolerance.
- None of the existing medications for COPD has been shown conclusively to modify the long-term decline in lung function
- Vaccination

Global Strategy for Diagnosis, Management and Prevention of COPD

Therapeutic Options: COPD Medications

Beta$_2$-agonists
Short-acting beta$_2$-agonists
Long-acting beta$_2$-agonists
Anticholinergics
Short-acting anticholinergics
Long-acting anticholinergics
Combination short-acting beta$_2$-agonists + anticholinergic in one inhaler
Combination long-acting beta$_2$-agonists + anticholinergic in one inhaler
Methylxanthines
Inhaled corticosteroids
Combination long-acting beta$_2$-agonists + corticosteroids in one inhaler
Systemic corticosteroids
Phosphodiesterase-4 inhibitors

Global Strategy for Diagnosis, Management and Prevention of COPD

Therapeutic Options: Bronchodilators

- **Bronchodilator** medications central to the symptomatic management of COPD.
- Bronchodilators are prescribed on an as-needed or on a regular basis to prevent or reduce symptoms.
- The principal bronchodilator treatments are **beta$_2$-agonists, anti-cholinergics, theophylline** or **combination** therapy.

Therapeutic Options: Bronchodilators

- Long acting bronchodilators more convenient and more effective for symptom relief than SABAs.

- LABAs reduce exacerbations and related hospitalizations and improve symptoms and health status.

Therapeutic Options: Inhaled Corticosteroids

- Regular treatment with **inhaled corticosteroids** improves symptoms, lung function and quality of life and reduces **frequency of exacerbations** for COPD patients with an **FEV_1 < 60% predicted**.
- Inhaled corticosteroid therapy is associated with an increased **risk of pneumonia**.
- Withdrawal from treatment with inhaled corticosteroids may lead to exacerbations in some patients.

Therapeutic Options: Combination Therapy

- ICS+LABA > individual components in improving lung function and health status and reducing exacerbations in moderate to very severe COPD.
- **ICS+LABA → increased risk of pneumonia.**
- **ICS+LABA+LAMA** appears to provide additional benefits.

Therapeutic Options: Systemic Corticosteroids

- Chronic treatment with systemic corticosteroids should be avoided

Therapeutic Options: Phosphodiesterase-4 Inhibitors

- In patients with severe and very severe COPD (GOLD 3 and 4) and a history of **exacerbations** and **chronic bronchitis**, the **phospodiesterase-4 inhibitor, roflumilast**, reduces exacerbations treated with oral glucocorticosteroids.

Therapeutic Options: Theophylline

- Theophylline
  - **less effective** and **less well tolerated** than inhaled long-acting bronchodilators
  - Not recommended if those drugs are available and affordable.

Therapeutic Options: Other Pharmacologic Treatments

Influenza vaccines

Antibiotics ?

Therapeutic Options: Other Pharmacologic Treatments

Alpha-1 antitrypsin augmentation therapy*:*

Mucolytics: Patients with viscous sputum may benefit from **mucolytics**; overall benefits are very small.

Antitussives: Not recommended.

Therapeutic Options: Rehabilitation

- All COPD patients benefit from *exercise training programs* with improvements in exercise tolerance and symptoms of dyspnea and fatigue.
- **Effective pulmonary rehabilitation program is 6 weeks**, the longer the program continues, the more effective the results.
- If **exercise training is maintained at home**, the patient's health status remains above pre-rehabilitation levels.

Therapeutic Options: Other Treatments

Oxygen Therapy:

Long-term administration of oxygen (> 15 hours per day) to patients with chronic respiratory failure has been shown to increase survival in patients with severe, resting hypoxemia

- *PaO2 at or below 7.3 kPa (**55mmHg**) or SaO2 at or below **88%,** with or without hypercapnia confirmed twice over three week period*

- ***PaO2 between 7.3 and 8 kPa (55-60mmHg), or SaO2 of 88%, if there is evidence of PHT, peripheral oedema suggesting CCF, or Polycythemia (HCT > 55%)***

C.O.P.D

- he development of **hypoxaemic respiratory failure** is an independent predictor of mortality with a **three year survival of about 40%**

- Survival is increased by long-term administration of oxygen to about **50% with nocturnal oxygen**

- About **60% with administration for greater than 15 hours per day**

Therapeutic Options: Surgical Treatments

Lung Volume Reduction Surgery (LVRS)

Bronchoscopic Lung Volume Reduction (BLVR)

Lung Transplantation

Therapeutic Options: Other Treatments

Palliative Care, End-of-life Care, Hospice Care

Manage Stable COPD: Key Points

- Identification and reduction of exposure to risk factors
- Individualized assessment of symptoms, airflow limitation, and future risk of exacerbations should be incorporated into the management strategy.
- All COPD patients benefit from rehabilitation and maintenance of physical activity.
- Pharmacologic therapy is used to
  - reduce symptoms
  - reduce frequency and severity of exacerbations
  - and improve health status and exercise tolerance.

Manage Stable COPD: Key Points

- Long-acting formulations of beta$_2$-agonists and anti-cholinergics are preferred over short-acting formulations.
- Long-term treatment with **inhaled corticosteroids** added to long-acting bronchodilators is recommended for patients with **high risk of exacerbations**.

Manage Stable COPD: Key Points

- Long-term monotherapy with oral or inhaled corticosteroids is not recommended in COPD.
- The phospodiesterase-4 inhibitor roflumilast may be useful to reduce exacerbations for patients with **FEV_1 < 50% of predicted, chronic bronchitis, and frequent exacerbations.**

Manage Stable COPD: Goals of Therapy

- Relieve symptoms
- Improve exercise tolerance
- Improve health status

Reduce symptoms

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

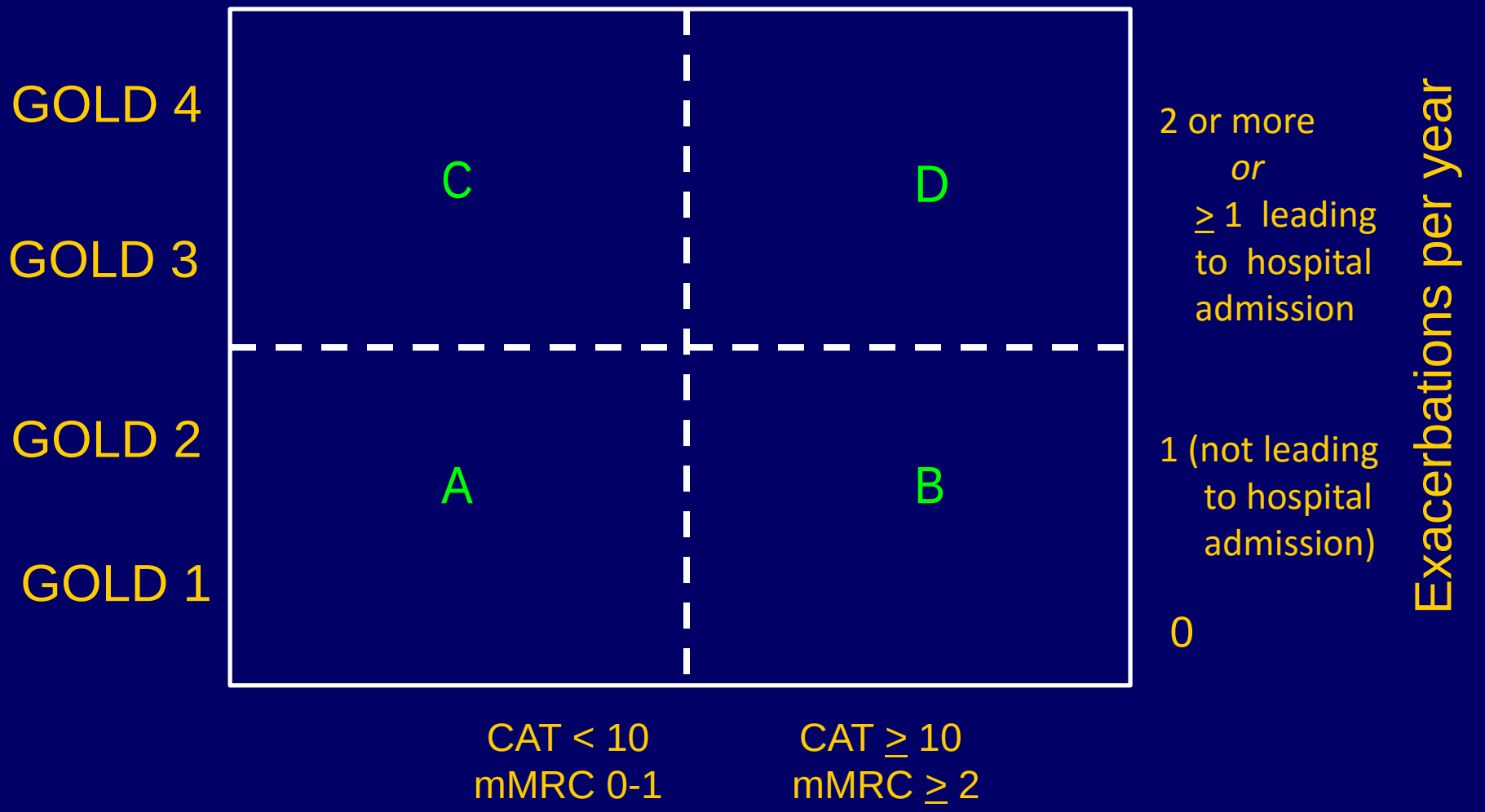
Reduce risk

Manage Stable COPD: All COPD Patients

- Avoidance of risk factors
  - smoking cessation
  - reduction of indoor pollution
  - reduction of occupational exposure
- Influenza vaccination

Manage Stable COPD: Pharmacologic Therapy

RECOMMENDED FIRST CHOICE



MRC Dyspnoea Scale

Grade 1 **"I only get breathless with strenuous exercise"**

Grade 2 "I get short of breath when hurrying on the level or walking up a slight hill"

Grade 3 "I walk slower than most people of the same age on the level because of breathlessness or have to stop for breath when walking at my own pace on the level"

Grade 4 "I stop for breath after walking about 100 yards or after a few minutes on the level"

Grade 5 **"I am too breathless to leave the house" or " I am breathless when dressing"**

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Manage Stable COPD: Non-pharmacologic

Patient Group	Essential	Recommended	Depending on local guidelines
A	Smoking cessation (can include pharmacologic treatment)	Physical activity	Flu vaccination Pneumococcal vaccination
B, C, D	Smoking cessation (can include pharmacologic treatment) Pulmonary rehabilitation	Physical activity	Flu vaccination Pneumococcal vaccination

Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Stable COPD: Pharmacologic Therapy

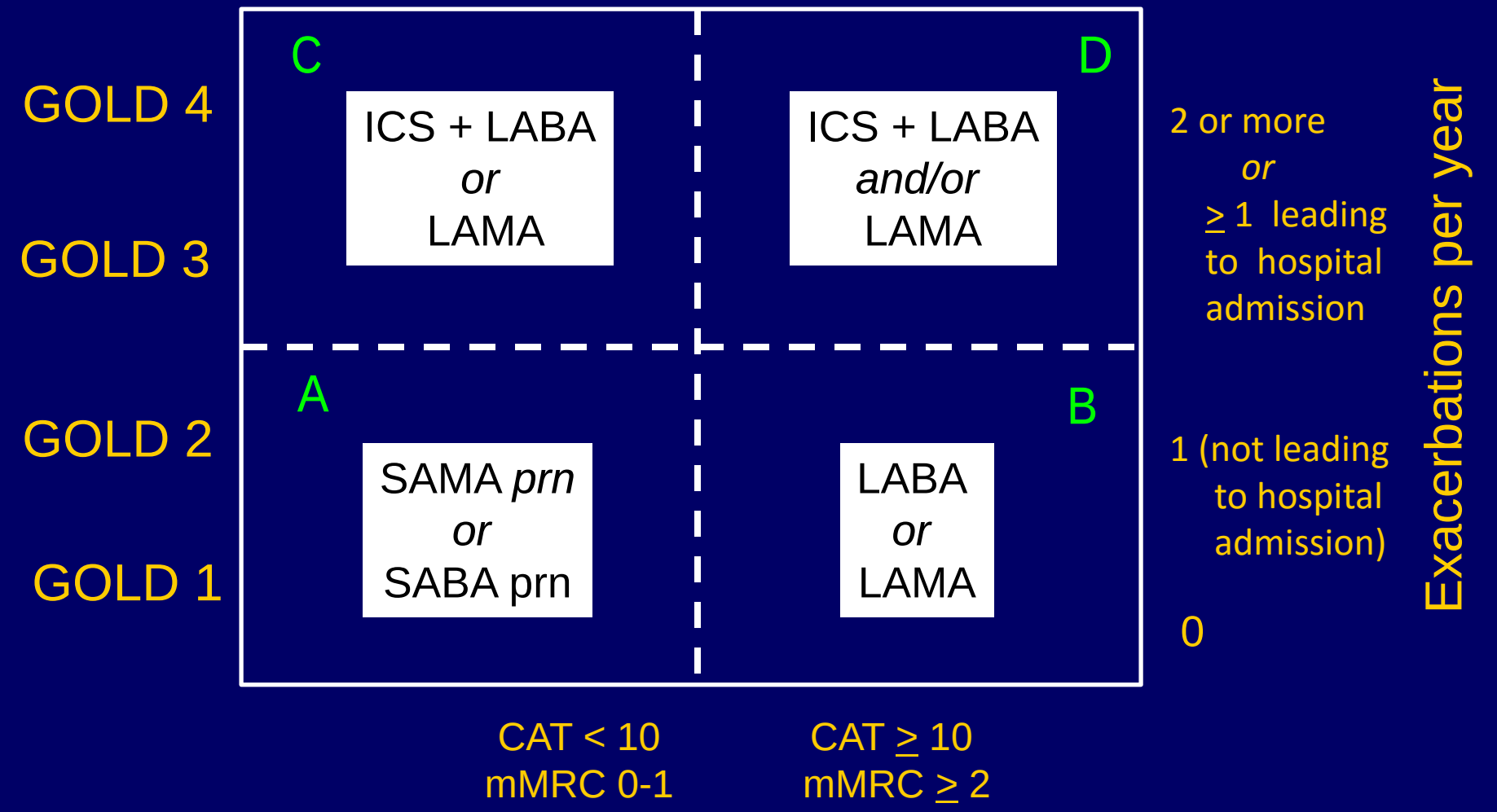
(Medications in each box are mentioned in alphabetical order, and therefore not necessarily in order of preference.)

Patient	Recommended First choice	Alternative choice		Other Possible Treatments
A	**SAMA prn** *or* **SABA prn**	LAMA *or* LABA *or* SABA and SAMA		Theophylline
B	LAMA *or* LABA	LAMA and LABA		SABA *and/or* SAMA Theophylline
C	**ICS + LABA** *or* LAMA	LAMA and LABA *or* LAMA and PDE4-inh. *or* LABA and PDE4-inh.		SABA *and/or* SAMA Theophylline
D	**ICS + LABA** ***and/or*** **LAMA**	ICS + LABA and LAMA *or* ICS+LABA and PDE4-inh. *or* LAMA and LABA *or* LAMA and PDE4-inh.		Carbocysteine *SABA and/or* SAMA Theophylline

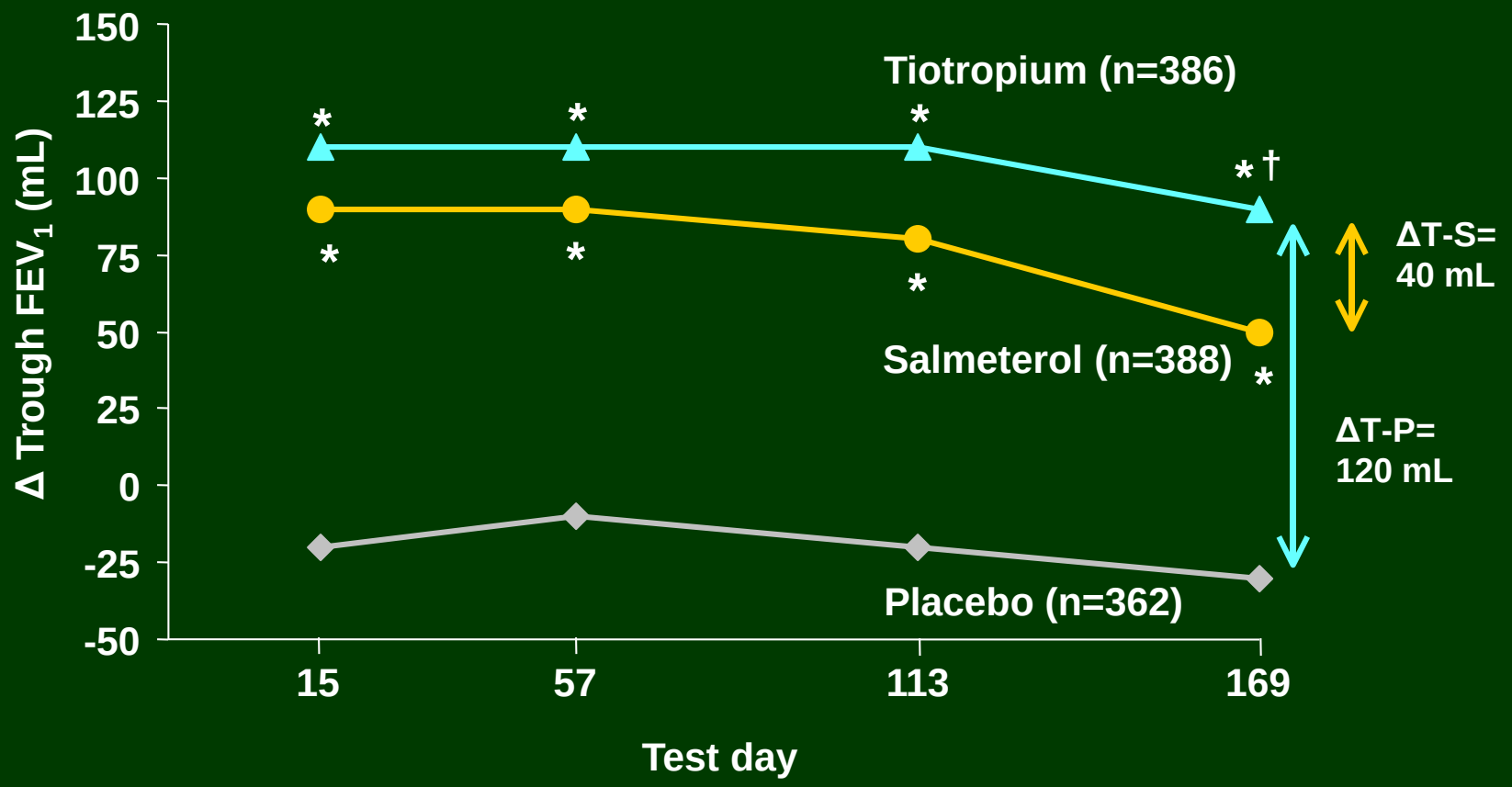
Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Stable COPD: Pharmacologic Therapy

RECOMMENDED FIRST CHOICE

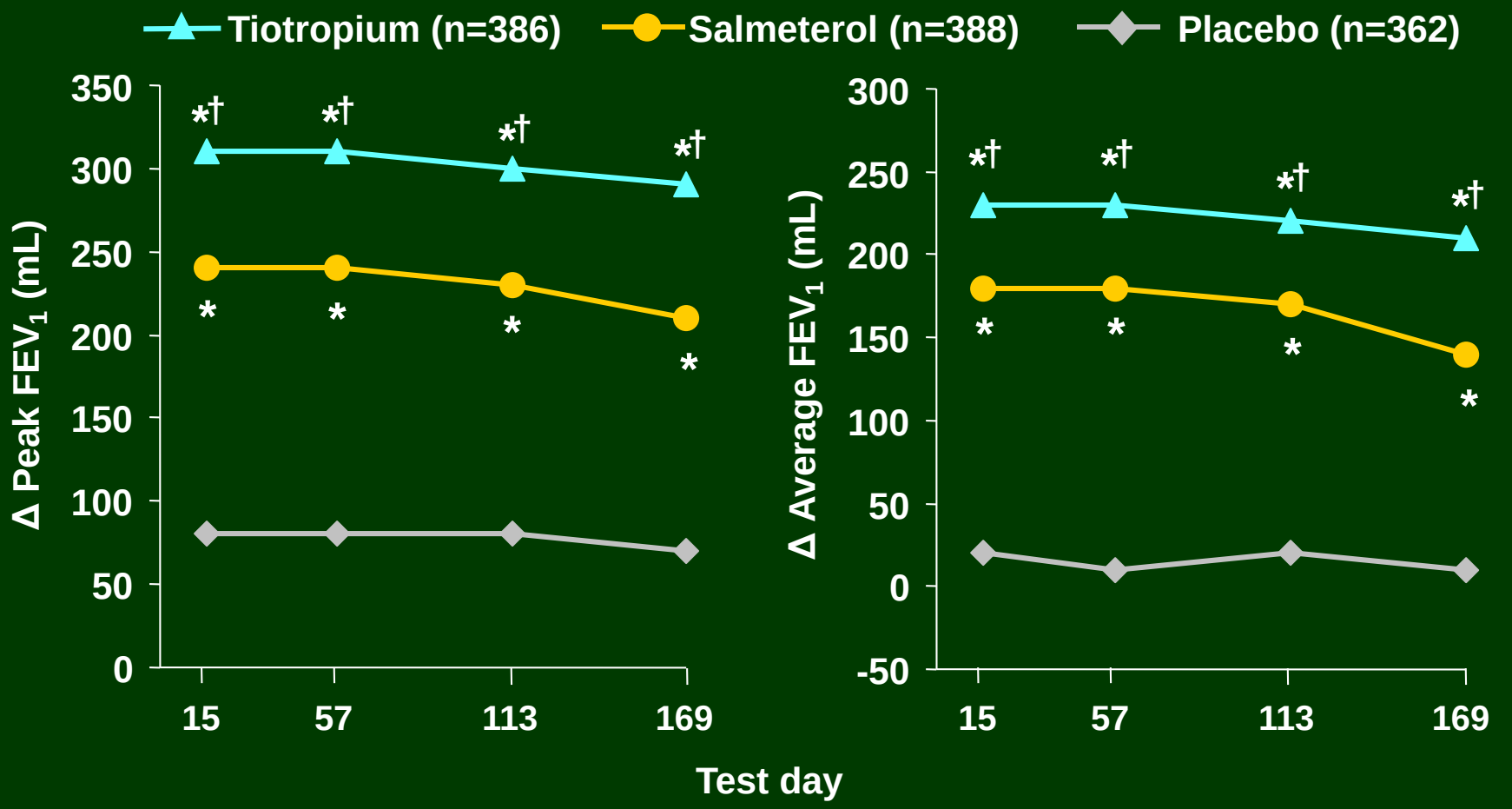


Mean Trough FEV_1 Over 6 Months in Combined Salmeterol Trials



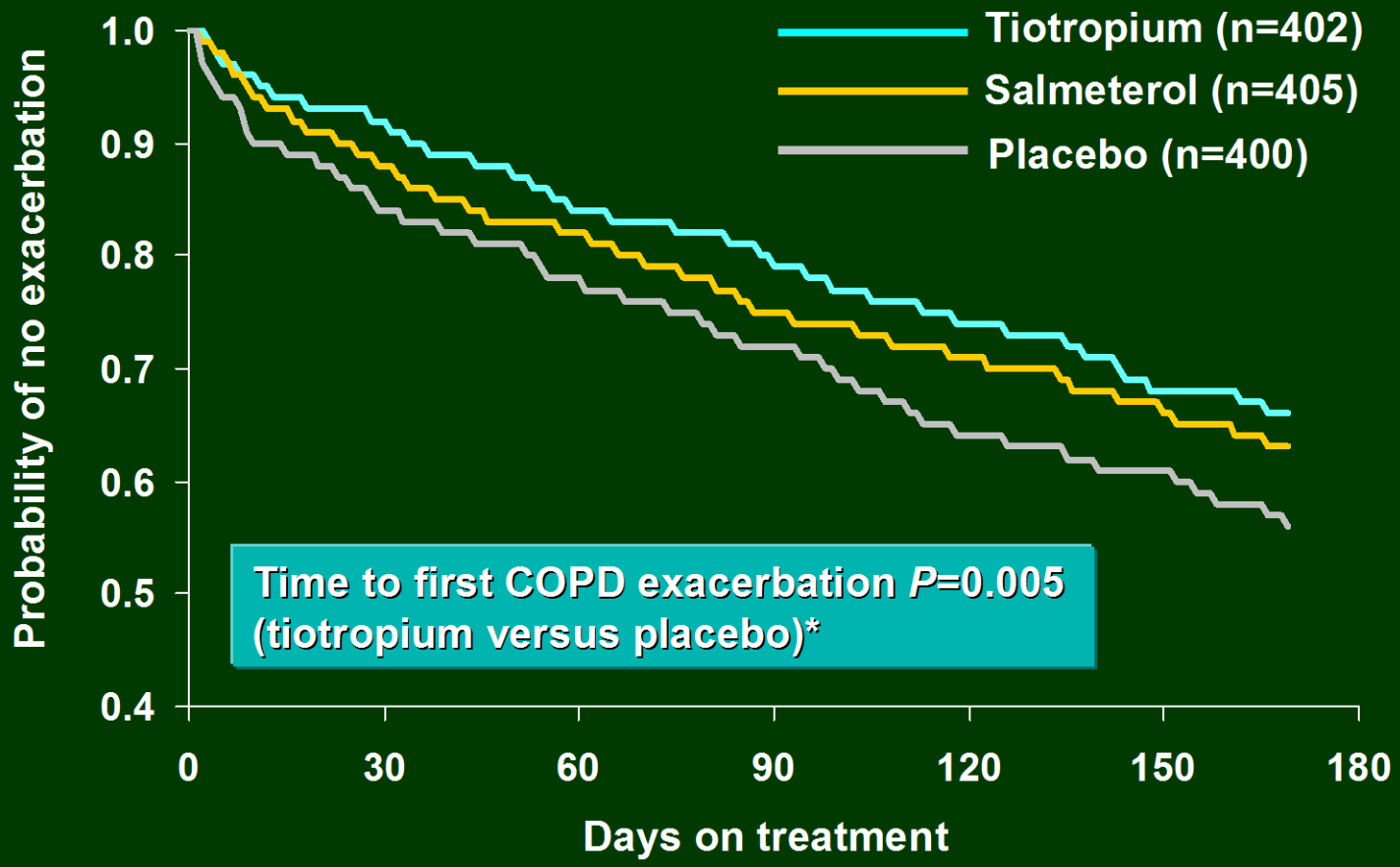
*P<0.0001 versus placebo; †P<0.05 versus salmeterol

Mean Peak and Average (0-3 Hours Postdose) FEV_1 Over 6 Months in Combined Salmeterol Trials



*P<0.0001 versus placebo; †P<0.001 versus salmeterol

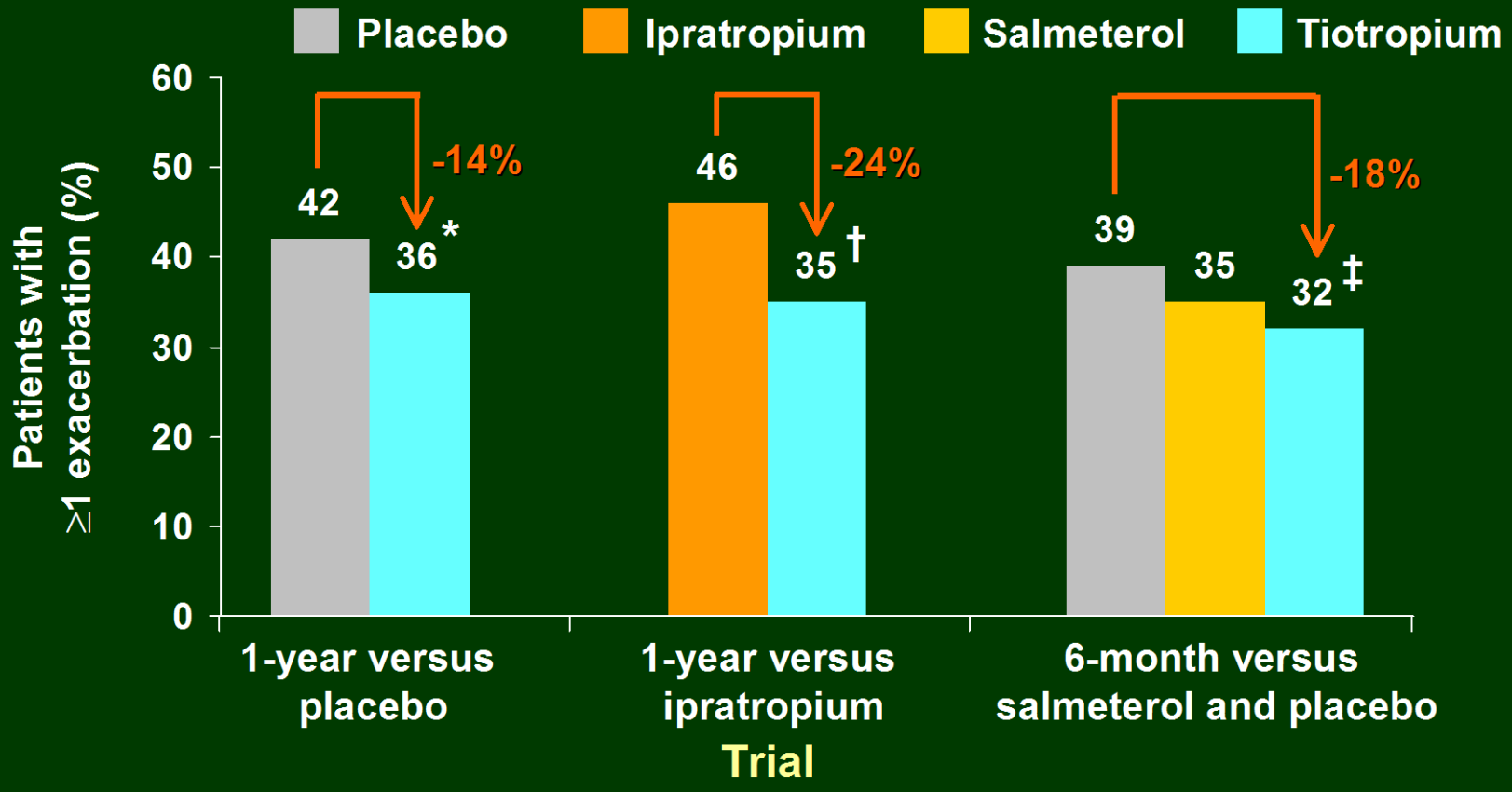
Onset of First COPD Exacerbation (Versus Placebo and Salmeterol)



*Log Rank Test

Brusasco V et al. Thorax (2003)

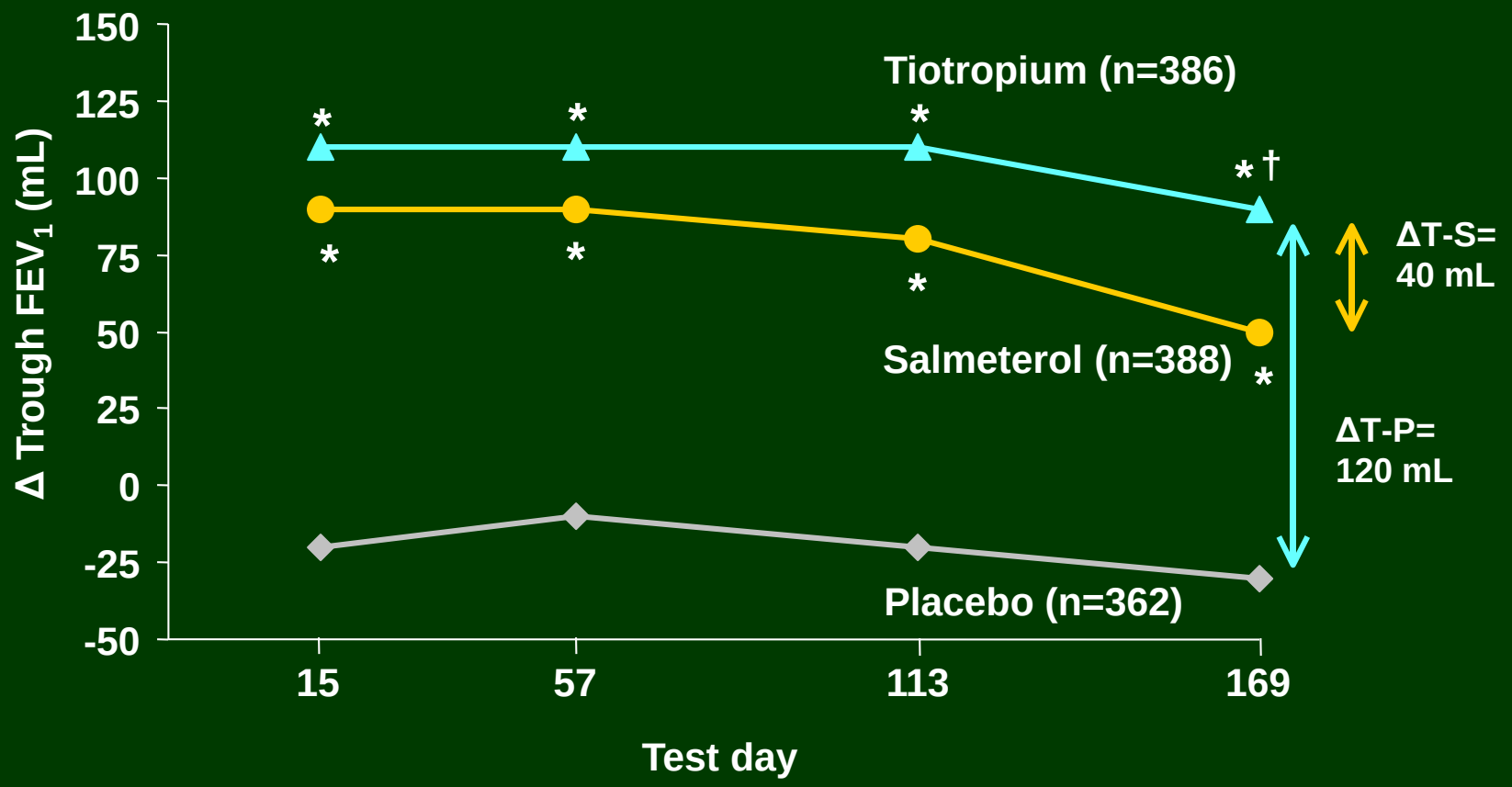
Percentage of Patients with ≥1 COPD Exacerbation in Long-term Trials



*P=0.033 versus placebo
†P=0.014 versus ipratropium
‡P=0.064 versus placebo

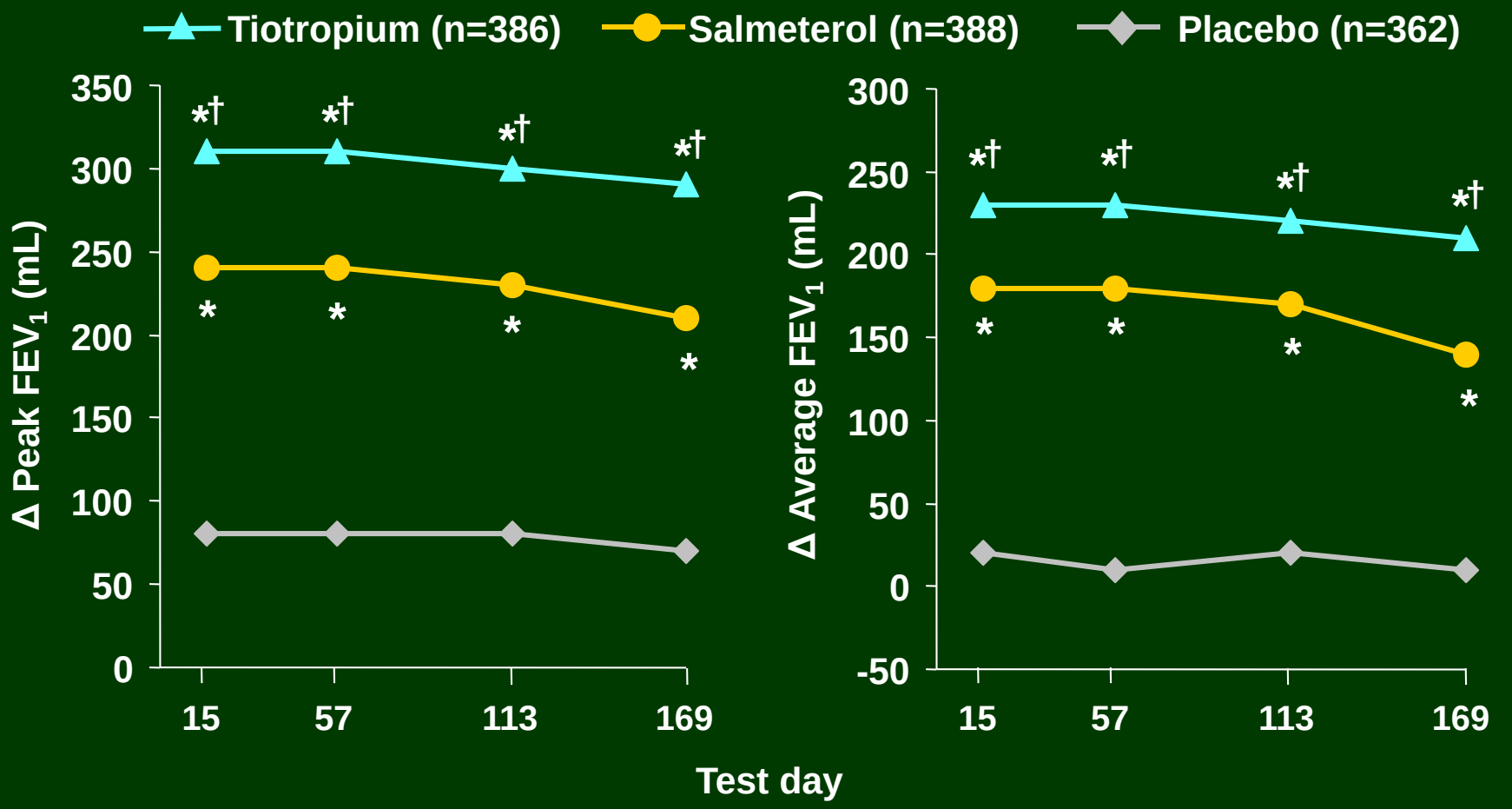
Casaburi R et al. Eur Respir J (2002)
Vincken W et al. Eur Respir J (2002)
Brusasco V et al. Thorax (2003)

Mean Trough FEV_1 Over 6 Months in Combined Salmeterol Trials



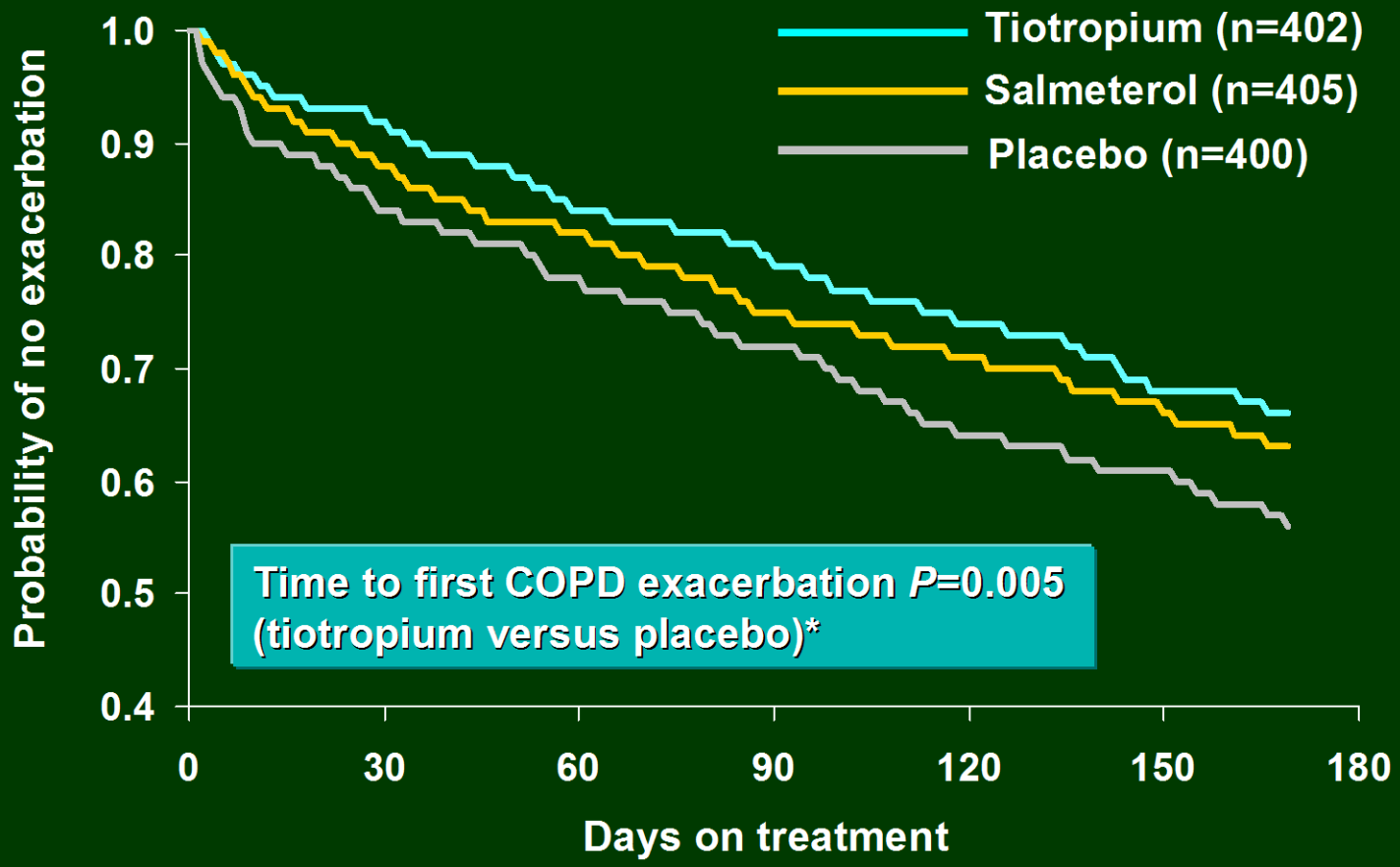
*P<0.0001 versus placebo; †P<0.05 versus salmeterol

Mean Peak and Average (0-3 Hours Postdose) FEV_1 Over 6 Months in Combined Salmeterol Trials



*P<0.0001 versus placebo; †P<0.001 versus salmeterol

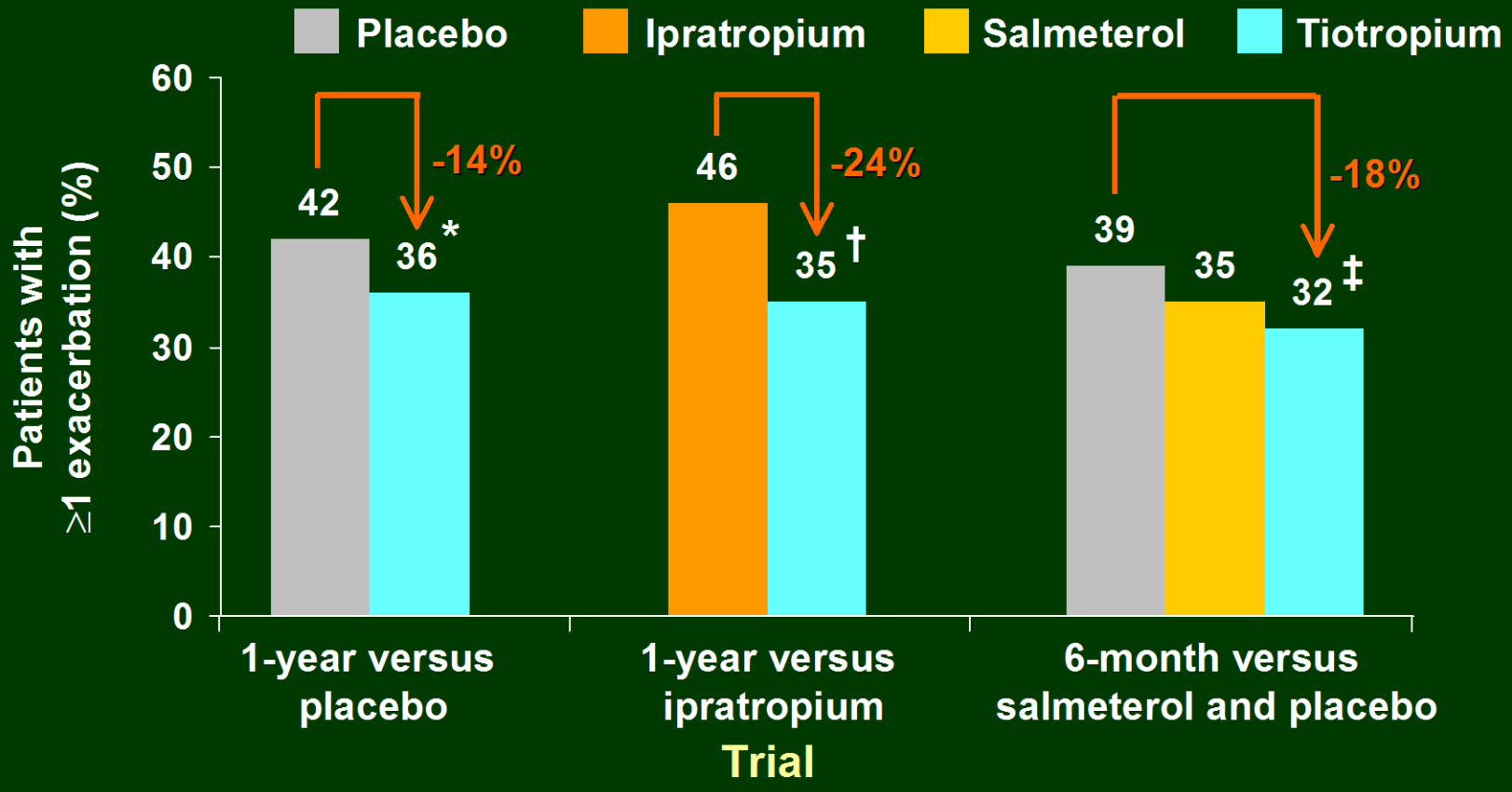
Onset of First COPD Exacerbation (Versus Placebo and Salmeterol)



*Log Rank Test

Brusasco V et al. Thorax (2003)

Percentage of Patients with ≥1 COPD Exacerbation in Long-term Trials



*P=0.033 versus placebo
†P=0.014 versus ipratropium
‡P=0.064 versus placebo

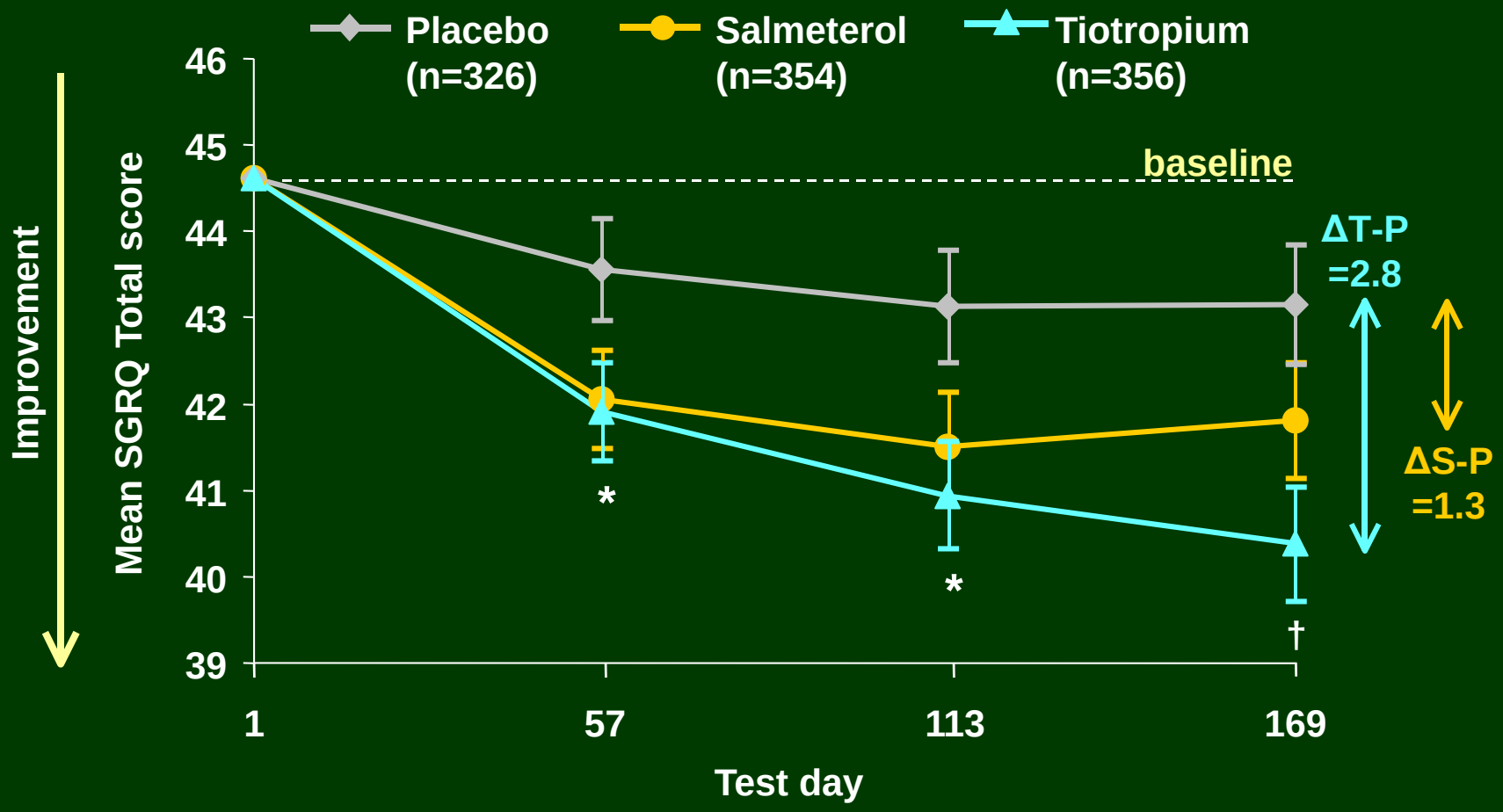
Casaburi R et al. Eur Respir J (2002)
Vincken W et al. Eur Respir J (2002)
Brusasco V et al. Thorax (2003)

Summary: Exacerbations and Hospitalizations Due to COPD Exacerbations

In 1-year trials, compared with placebo and ipratropium, tiotropium:

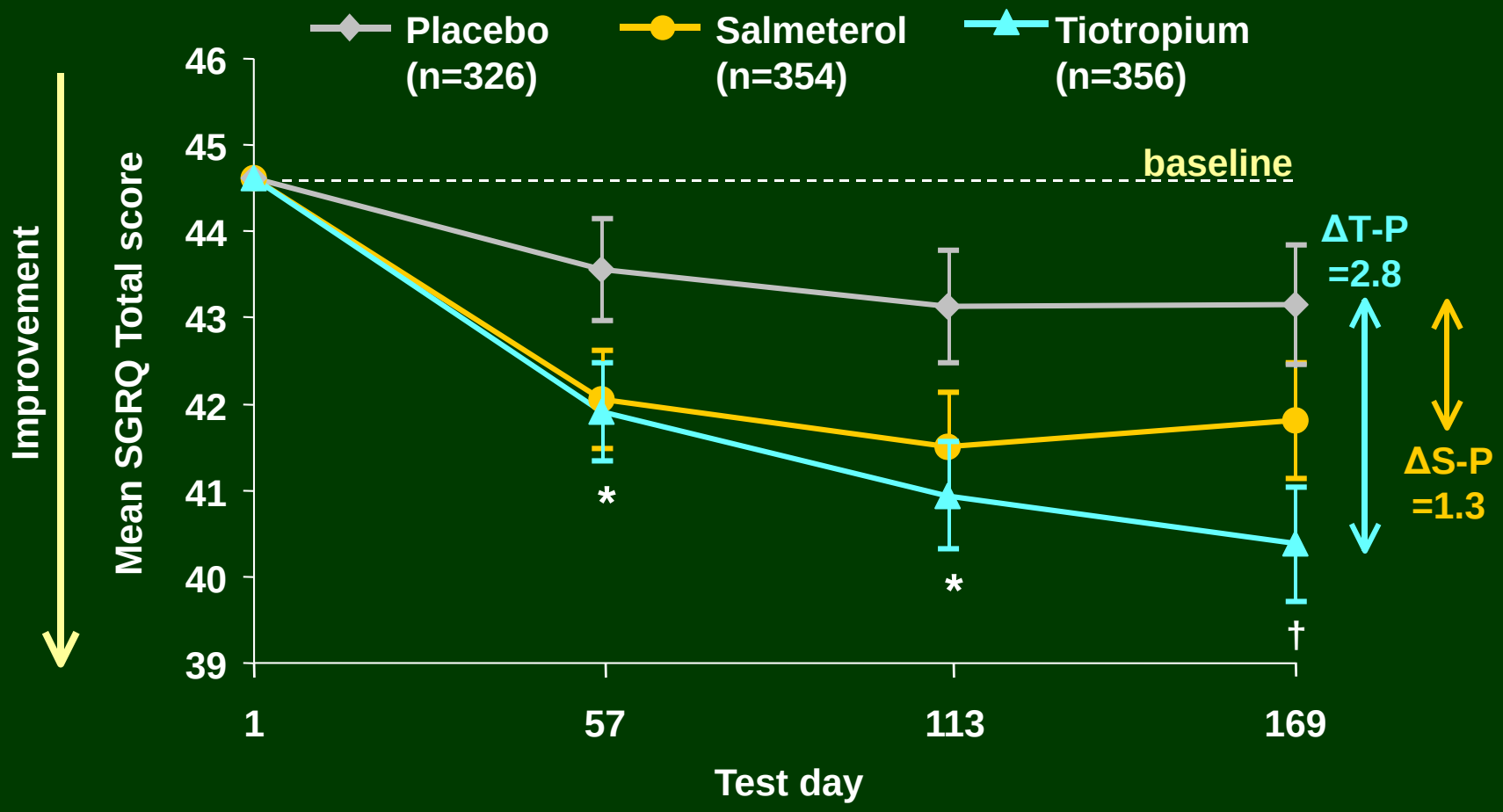
- Reduced the number of patients experiencing exacerbations
- Reduced the number of exacerbations per year in COPD patients
- Delayed the time to first COPD exacerbation
- Reduced the number of hospitalizations due to a COPD exacerbation
- Delayed the time to first hospitalization due to a COPD exacerbation

SGRQ Total Score Over 6 Months (Versus Placebo and Salmeterol)



*P<0.05; †P<0.01 tiotropium versus placebo

SGRQ Total Score Over 6 Months (Versus Placebo and Salmeterol)

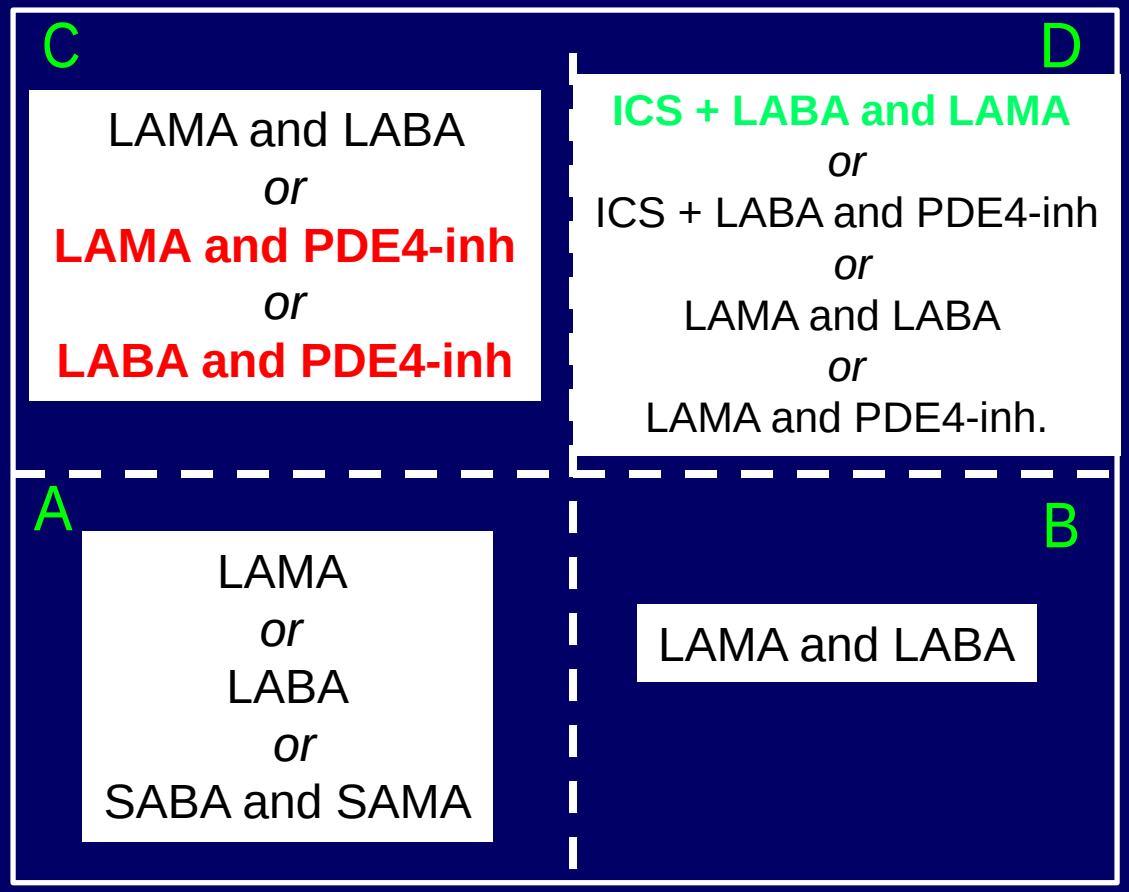


*P<0.05; †P<0.01 tiotropium versus placebo

Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Stable COPD: Pharmacologic Therapy

ALTERNATIVE CHOICE



GOLD 4

GOLD 3

GOLD 2

GOLD 1

2 or more
or
≥ 1 leading to hospital admission

1 (not leading to hospital admission)

0

Exacerbations per year

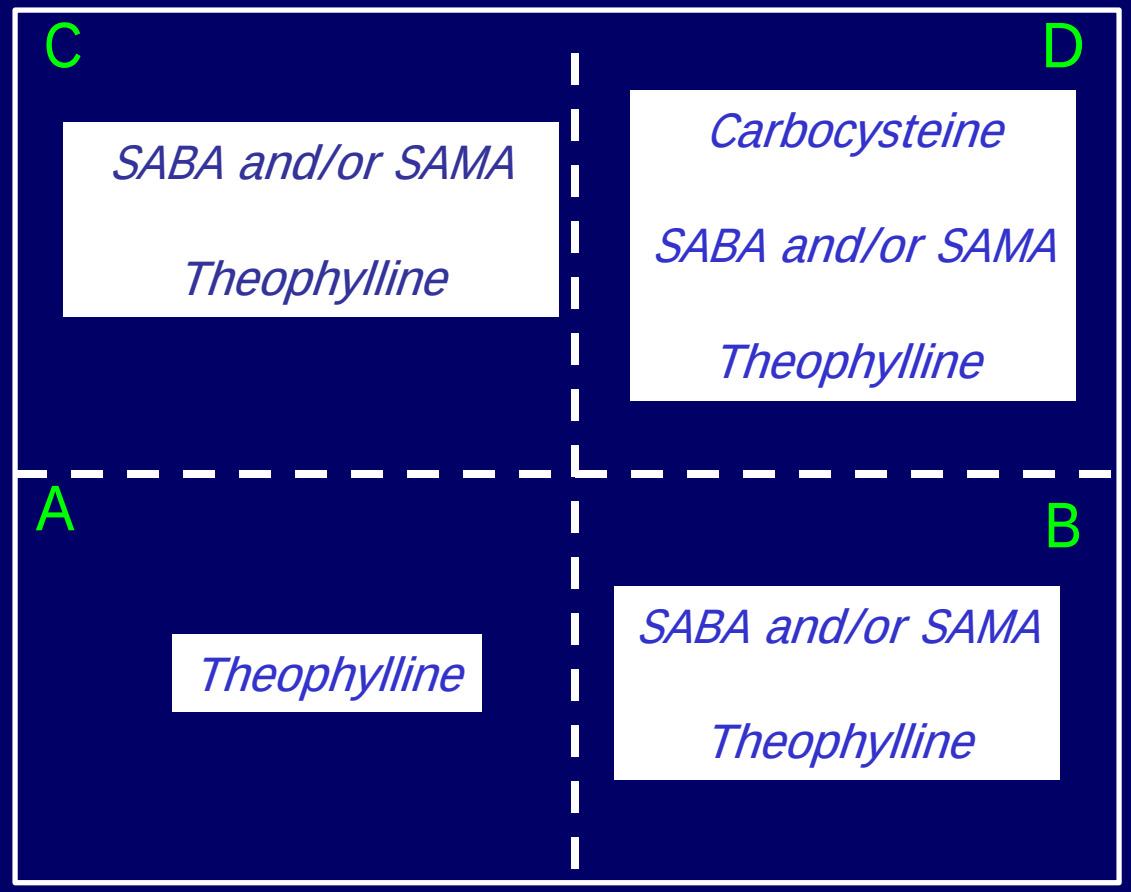
CAT < 10
mMRC 0-1

CAT ≥ 10
mMRC ≥ 2

Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Stable COPD: Pharmacologic Therapy

OTHER POSSIBLE TREATMENTS



GOLD 4

GOLD 3

GOLD 2

GOLD 1

2 or more *or* ≥ 1 leading to hospital admission

1 (not leading to hospital admission)

0

Exacerbations per year

CAT < 10
mMRC 0-1

CAT ≥ 10
mMRC ≥ 2

LABA	LAMA	FDC development phase	Dosing	Inhaler	Company
Vilanterol	Umeclidinium	Approved (Anoro®) in USA, EU	62.5/25 µg once daily	ELLIPTA®	GSK, Theravance
Formoterol	Aclidinium	Positive opinion† (Duaklir®) in EU	400/12 µg twice daily	Genuair®	Almirall, Forest
Olodaterol	Tiotropium	Filed* in EU and USA	5 µg/5 µg once daily	Striverdi	Boehringer Ingelheim
Formoterol	Glycopyrronium	Phase III trials	Twice daily	Pressurized hydrofluoroalkane (HFA MDI)	AstraZeneca

Global Strategy for Diagnosis, Management and Prevention of COPD, 2014: Chapters

- Definition and Overview
- Diagnosis and Assessment
- Therapeutic Options
- Manage Stable COPD
- Manage Exacerbations
- Manage Comorbidities

Manage Exacerbations

'An acute event characterised by a worsening of patient's respiratory symptoms that is beyond normal day-to-day variations, and leads to a change in medications'

Table 1—*Clinical Descriptors Used To Characterize Acute COPD Exacerbations*

Category	Descriptor
Respiratory	Increased shortness of breath
	Increased volume and purulence of sputum
	Increased cough
	Shallow/rapid breathing
Systemic	Increased body temperature
	Increased pulse/heart rate
	Impaired mental status

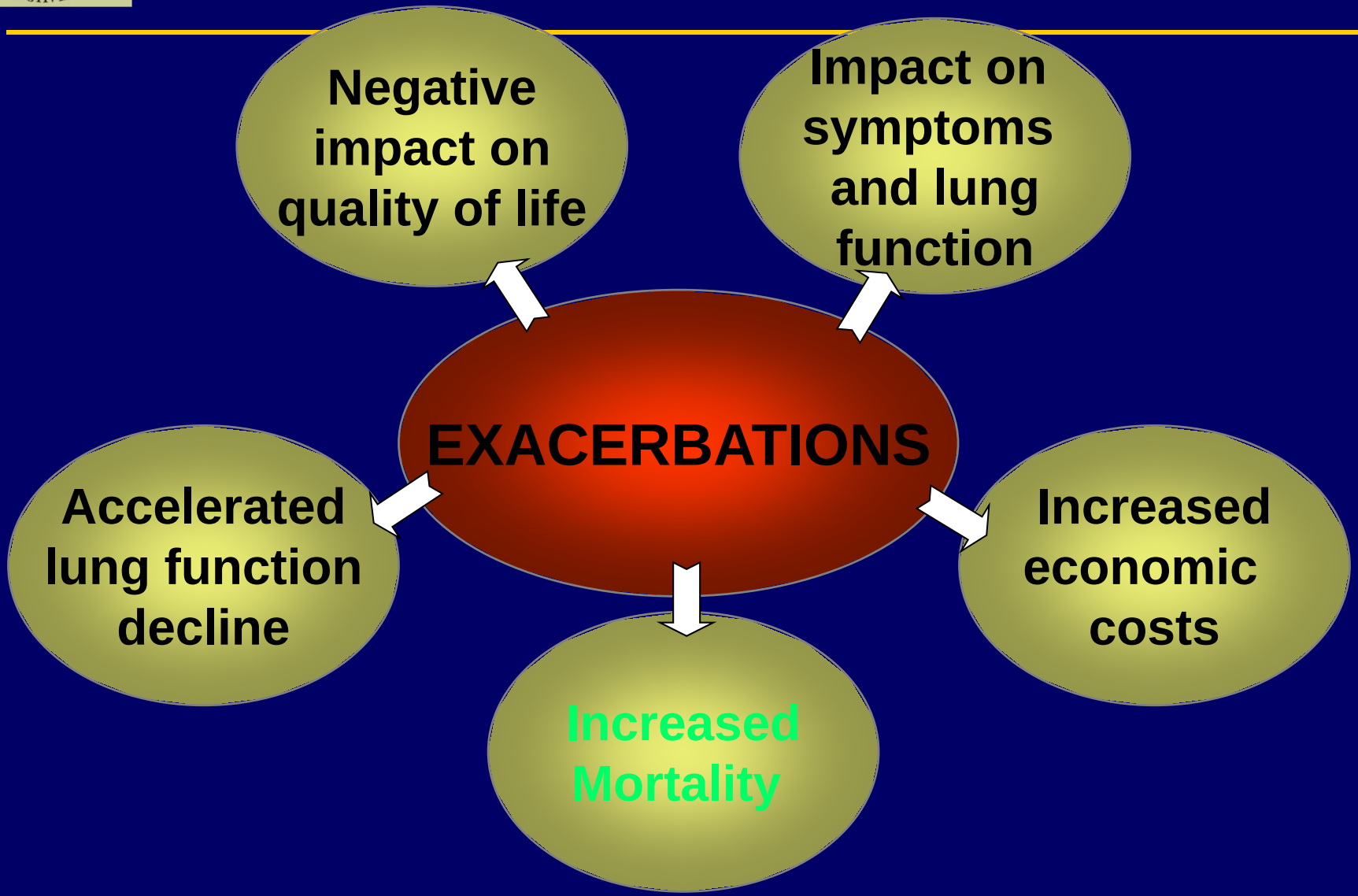
Manage Exacerbations: Key Points

- Most common causes of COPD exacerbations are?
- Treatment goals:
  - minimize the impact of the current exacerbation
  - prevent the development of subsequent exacerbations.

Manage Exacerbations: Key Points

- **Short-acting inhaled beta$_2$-agonists** with or without **short-acting anticholinergics** are usually the preferred bronchodilators for treatment of an exacerbation.
- Systemic corticosteroids and antibiotics can shorten recovery time, improve lung function (FEV_1) and arterial hypoxemia (PaO_2), and reduce the risk of early relapse, treatment failure, and length of hospital stay.
- **COPD exacerbations can often be prevented.**

Consequences Of COPD Exacerbations



C.O.P.D

- Admission to hospital with an **infective exacerbation of COPD** complicated by **hypercapnic** respiratory failure is associated with a **poor prognosis.**
- **A mortality of 11%** during admission and **49% at two years** has been reported in patients with a PaCO2 > 50 mm Hg
- For those with **chronic CO2 retention** (about 25% of those
- admitted with hypercapnic

Manage Exacerbations: Assessments

- *Arterial blood gas measurements*
- *Chest radiograph*
- *ECG*
- *Full blood count*
- *Purulent sputum* during an exacerbation: indication to begin empirical antibiotic treatment.
- *Biochemical tests*
- *Spirometric tests:* not recommended during an exacerbation.

VOCs

- Recently, interest on the potential diagnostic value of **volatile organic compounds (VOCs)**
- **exhaled in human breath** has been increasing.
- The **electronic nose (enose)** constitutes an
- emerging **non-invasive technique** capable of detecting and differentiating VOCs patterns
- **(“smell prints”)** in humans (“breatheomics”).

- Recent studies have shown that the **e-nose** can
- **reliably identify** patients with **bronchial asthma, lung cancer, bacterial pneumonia** and
- bacterial sinusitis, **as well as to identify and classify various bacterial species cultured in**
- **vitro.**

- Among the ECOPD, the e-nose was able to **discriminate breath-prints of infected patients**
- **versus non-infected patients** with a classification success ratio of 75% (p = 0.018), **sensitivity of 88% and specificity of 60%.**
- Additionally, the percentage of success ratio in the **pneumonic subgroup of ECOPD (classification success ratio: 100%, p = 0.014; sensitivity and specificity of 100%)** was further improved.

- Breath-prints from **ECOPD** were
- significantly **distinguishable from stable COPD** ($p < 0.05$).
- Breath-prints from **pneumonic ECOPD** were significantly distinguishable from **stable COPD**.
- Also, breath-prints from **COPD patients** were **significantly distinguished from healthy controls**.

Manage Exacerbations: Treatment Options

Oxygen: titrate to improve the patient's hypoxemia with a target saturation of **88-92%.**

Bronchodilators: Short-acting inhaled beta$_2$-agonists with or without short-acting anticholinergics are preferred.

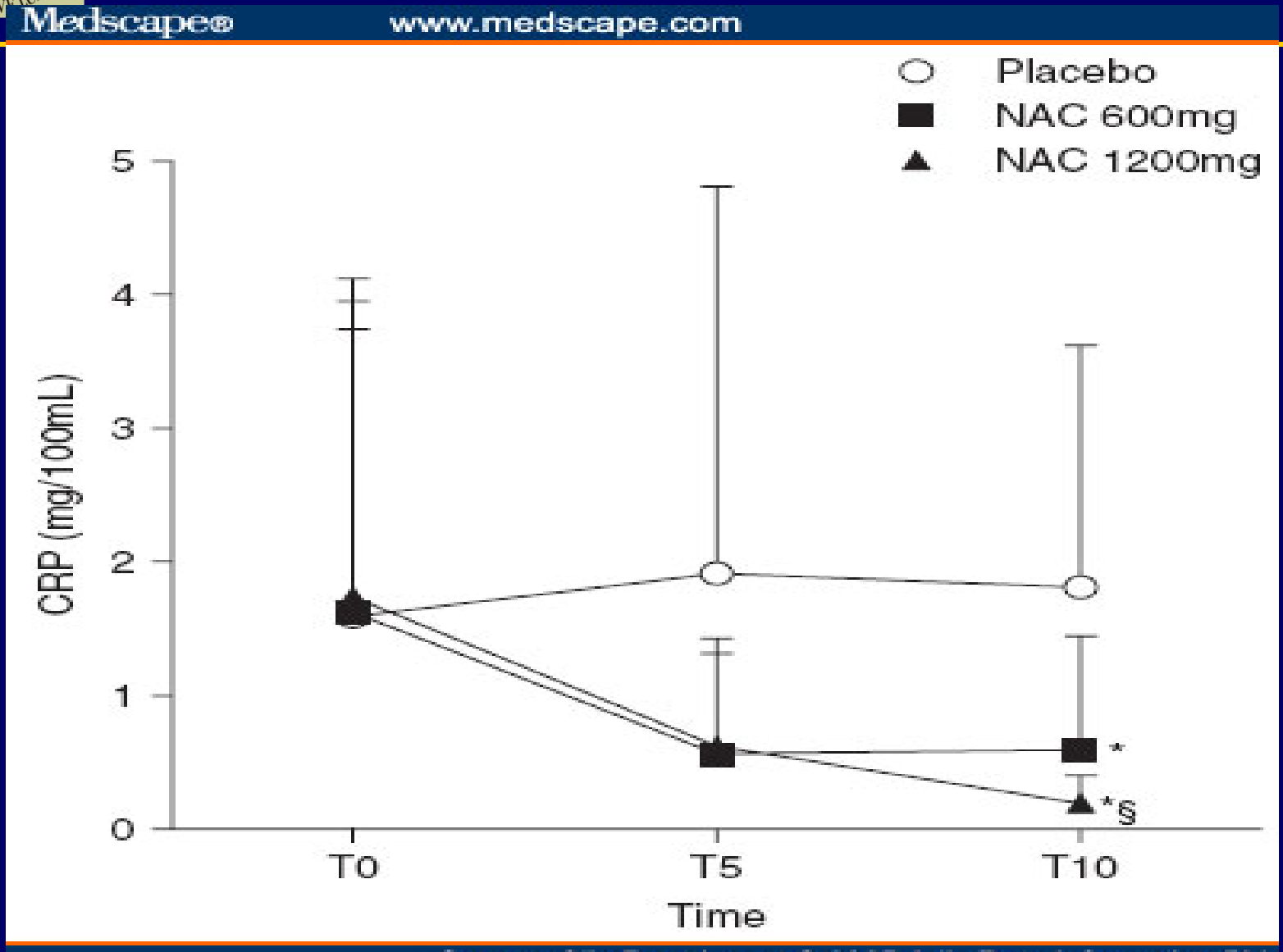
Systemic Corticosteroids: Shorten recovery time, improve lung function (FEV_1) and arterial hypoxemia (PaO_2), and reduce the risk of early relapse, treatment failure, and length of hospital stay. A dose of 40 mg prednisone per day for 5 days is recommended.

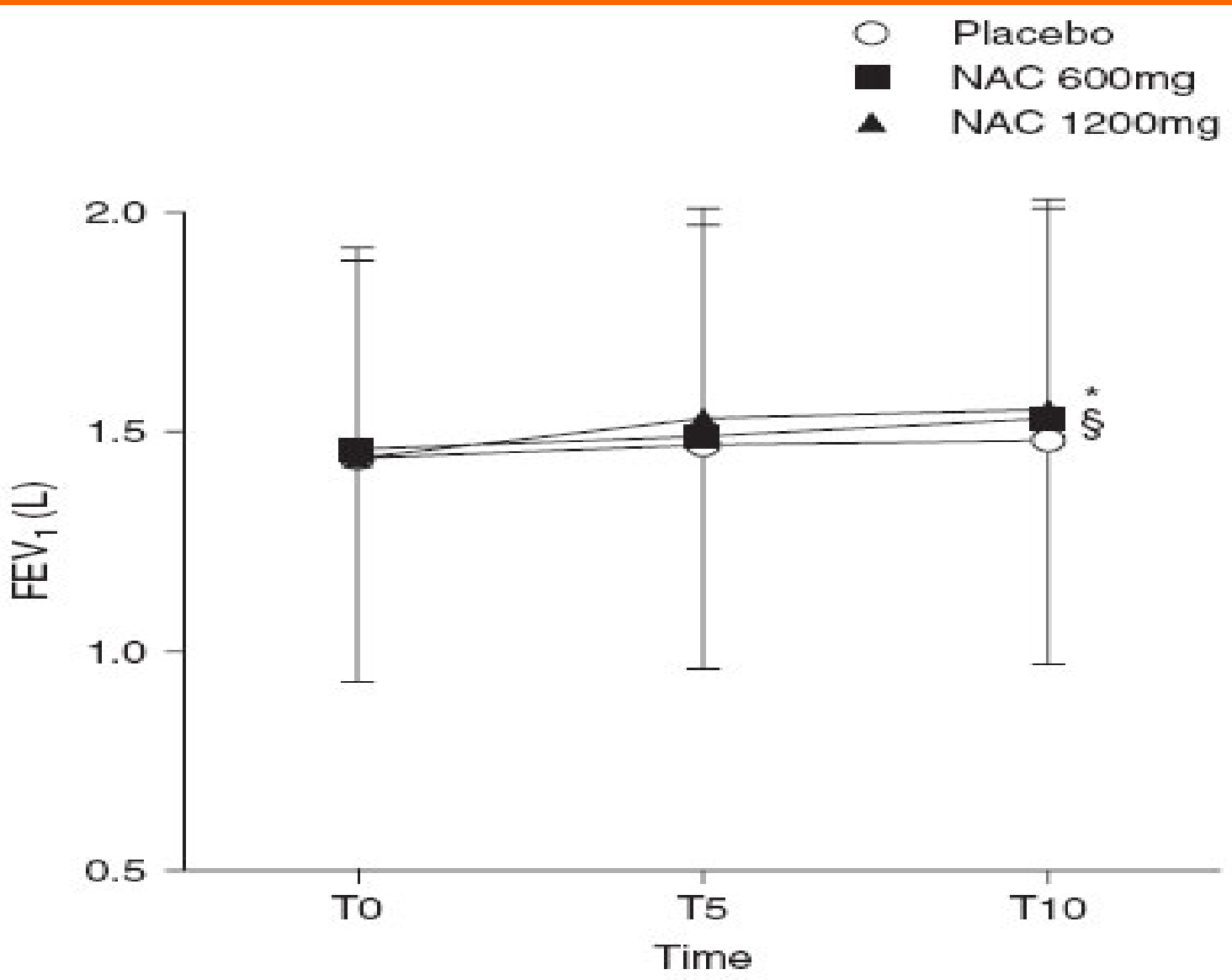
Manage Exacerbations: Treatment Options

Antibiotics should be given to patients with:

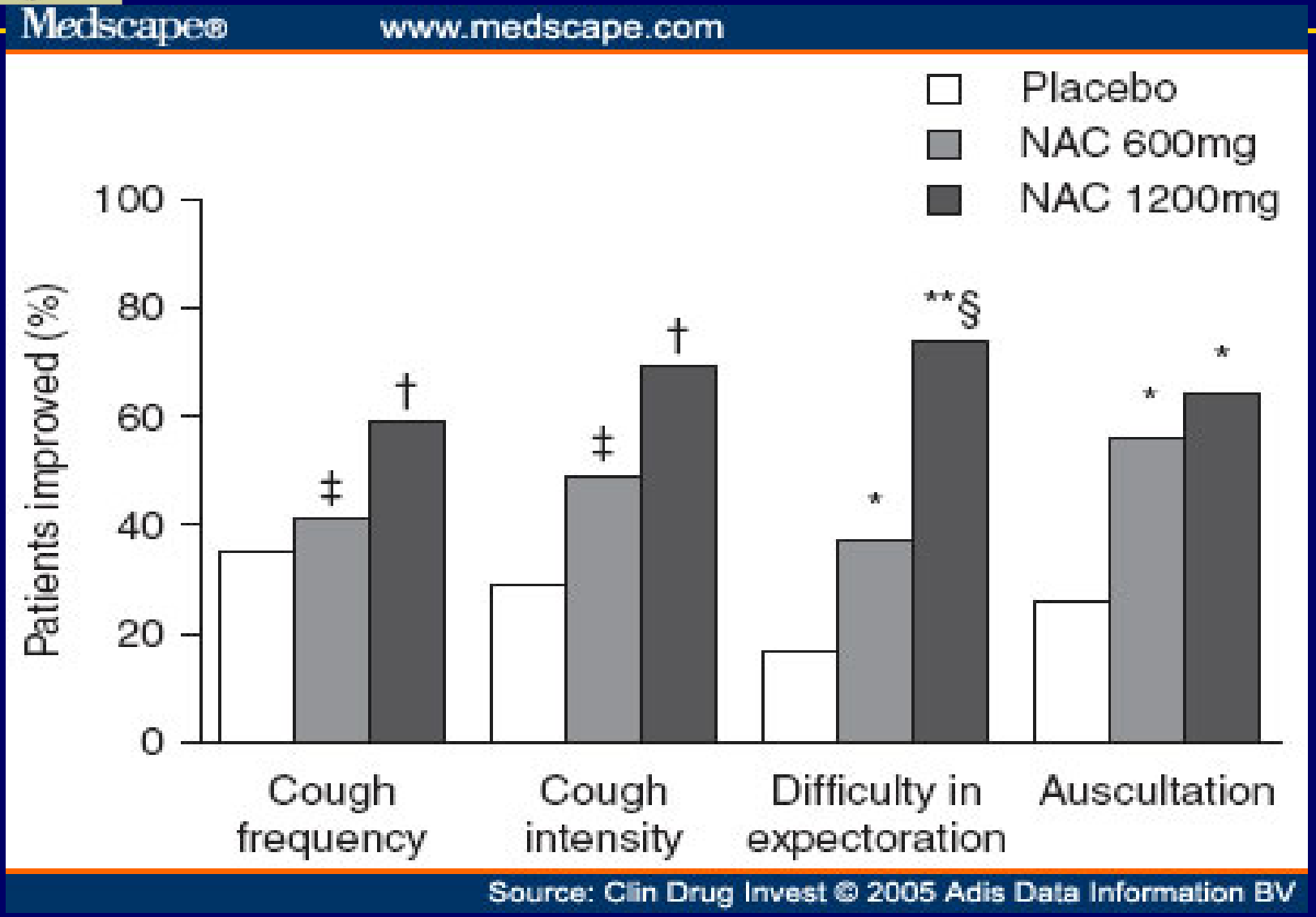
- Three cardinal symptoms:
  - increased **dyspnea,**
  - increased **sputum volume**,
  - and increased **sputum purulence.**
- Who require mechanical ventilation.

NAC / C.R.P


Medscape®
www.medscape.com
Placebo
NAC 600mg
NAC 1200mg
CRP (mg/100mL)
5
4
3
2
1
0
T0
T5
T10
Time
*
*§
Source: Clin Drug Invest © 2005 Adis Data Information BV



NAC


Medscape®
www.medscape.com
Placebo
NAC 600mg
NAC 1200mg
Patients improved (%)
100
80
60
40
20
0
‡
†
‡
†
*
**§
*
*
Cough frequency
Cough intensity
Difficulty in expectoration
Auscultation
Source: Clin Drug Invest © 2005 Adis Data Information BV

Manage Comorbidities

Cardiovascular disease

Osteoporosis

Anxiety/depression: often under-diagnosed and associated with poor health status and prognosis.

Lung cancer.

Serious infections: respiratory infections are **especially frequent.**

Metabolic syndrome and manifest ***diabetes:*** more frequent in COPD

Global Strategy for Diagnosis, Management and Prevention of COPD, 2014: Summary

- Prevent COPD
- Spirometry is *required* to make the diagnosis of COPD; the presence of a post-bronchodilator $FEV_1/FVC < 0.70$ confirms the presence of persistent airflow limitation and thus of COPD
- The beneficial effects of pulmonary rehabilitation and physical activity cannot be overstated

Global Strategy for Diagnosis, Management and Prevention of COPD, 2014: Summary

- Assessment of COPD requires assessment of
  - symptoms,
  - degree of airflow limitation,
  - risk of exacerbations, and
  - comorbidities
- Combined assessment of symptoms and risk of exacerbations is the basis for non-pharmacologic and pharmacologic management of COPD

Global Strategy for Diagnosis, Management and Prevention of COPD, 2014: Summary

- Treat COPD exacerbations
- Look for **co-morbidities** – and if present treat to the same extent as if the patient did not have COPD

A distinctive therapeutic opportunity arises where the treatment of a multitude of diseases may be possible with targeting **three essential enzymes** (**NOX, SOD, and Gpx/Cat**).

These enzymes can either be **inhibited** to reduce their activity (e.g. **NOX inhibitor - apocynin**)

or **amplified/mimicked** to increase their activity (e.g. **Gpxmimetics – ebselen**).

Thus,targeting this **oxidant-dependent mechanisms** that **drive COPD and its co-morbidities** may have great therapeutic potential.


Nature Is Always Giving Us Examples on Why We Should Never Give Up.
PreventDisease.com

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