

Asthma bronchiale (AB)
Chronic Obstructive Pulmonary
Disease(COPD)

Case studies

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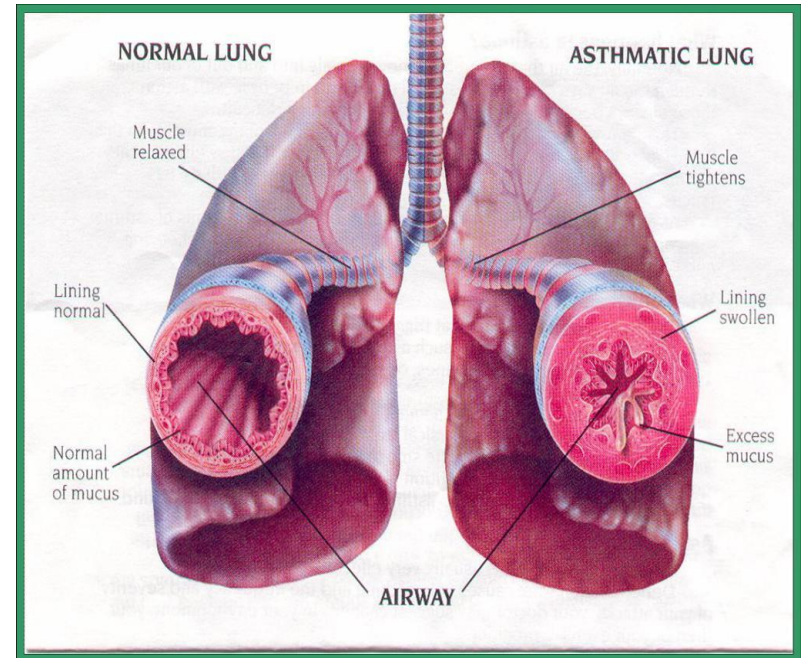
Asthma Bronchiale

- Asthma is one of the most common chronic diseases in the world
- Around 300 million people in the world currently have asthma
- Global prevalence is increasing by 50% each decade
- Considerable economic cost
 - Direct medical costs (hospital admissions, cost of pharmaceuticals etc.)
 - Indirect medical costs (time lost from work and premature death)

What is asthma?

Asthma is a chronic lung-disease

- Underlying inflammation or swelling
- Increased mucus production and
- Contraction of muscles around the airways, or bronchospasm



Inflammation in asthma leads to symptoms

- Chronically **inflamed** airways become **hyperresponsive** to a variety of stimuli and **obstructed** by bronchoconstriction, edema, excess mucus production, and infiltrating inflammatory cells
- The **goal** of asthma treatment is **to suppress airway inflammation**



Asthma symptoms

- Coughing (nighttime or early morning)
- Wheezing
- Chest tightness
- Shortness of breath
- Excessive fatigue

Causes

- The exact cause of asthma is not known, it is thought that a variety of factors interacting with one another
 - Parents with asthma
 - Atopy
 - Childhood respiratory infections
 - Exposure to allergens or infections while the immune system is developing

Asthma Triggers

- A variety of things can cause asthma symptoms to appear



- Allergens
- Irritants – air pollution, chemicals and strong smells
- Food and drinks
- Medicines
- Physical activity
- Upper respiratory infections (viral)
- Strong emotions
- Cold air
- Stress



Diagnosis

Based on:

- Medical history – family history, atopy, symptoms...
- Spirometry - test lung function (FEV1, FVC, PEF)
- Allergy testing – antibody IgE



Asthma Attacks

If one or more of the following symptoms are present

- Coughing or wheezing
- Difficulty breathing, shortness of breath
- Difficulty in talking and walking due to shortness of breath
- Chest tightness

Asthma Management Goals

- tailor to meet individual needs

- Achieve and maintain control of symptoms
- Maintain normal activity levels, including exercise
- Maintain pulmonary function as close to normal levels as possible
- Prevent asthma exacerbations
- Avoid adverse effects from asthma medications
- Prevent asthma mortality

Asthma control

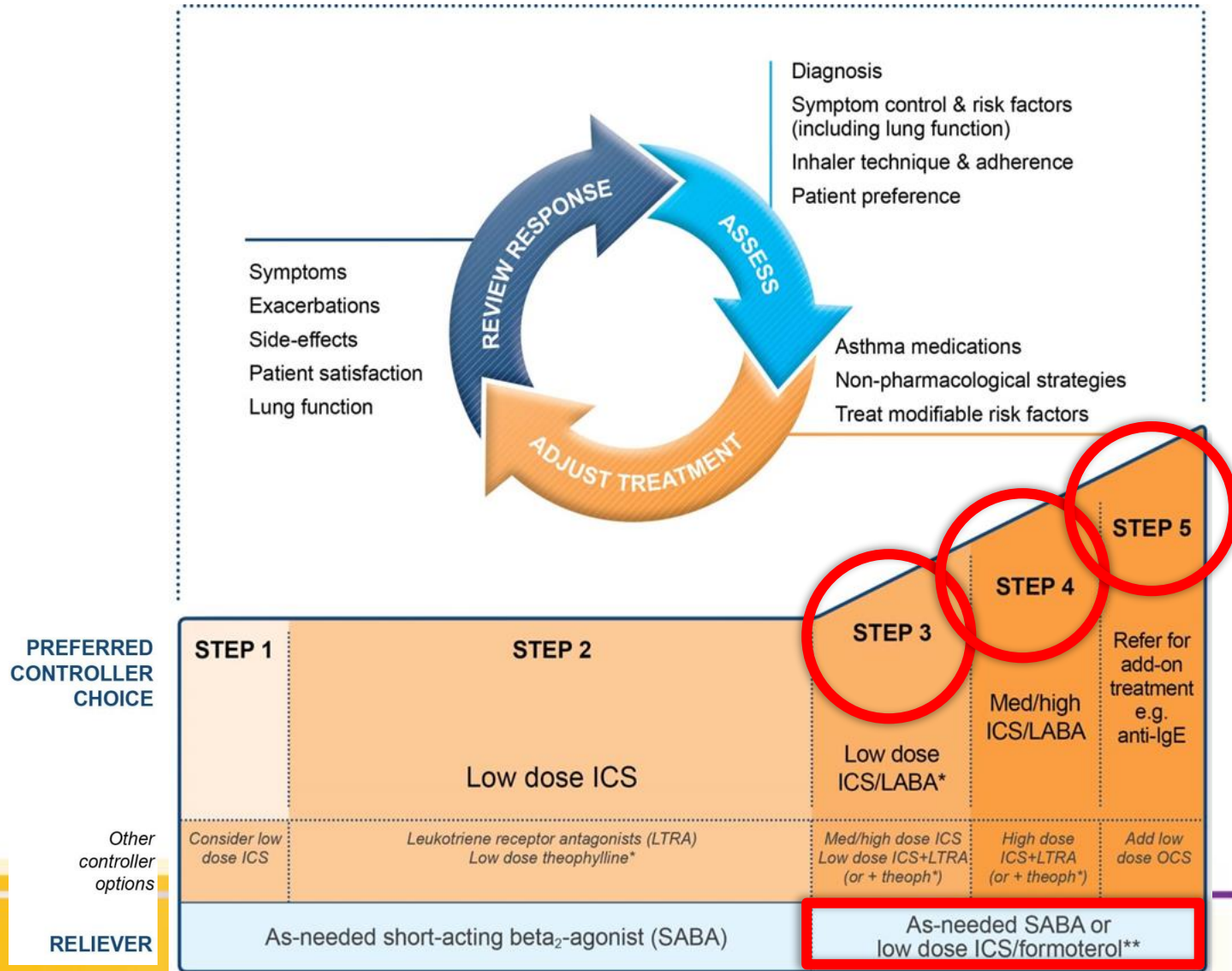
- Despite the availability of effective therapies, asthma control is suboptimal for many patients in Europe
- The majority of patients with asthma continue to experience poor control and significant symptoms
 - About 55 %
- Optimal asthma control depends on many more factors than good medication alone. Compliance plays a crucial part.

Medications to Treat Asthma

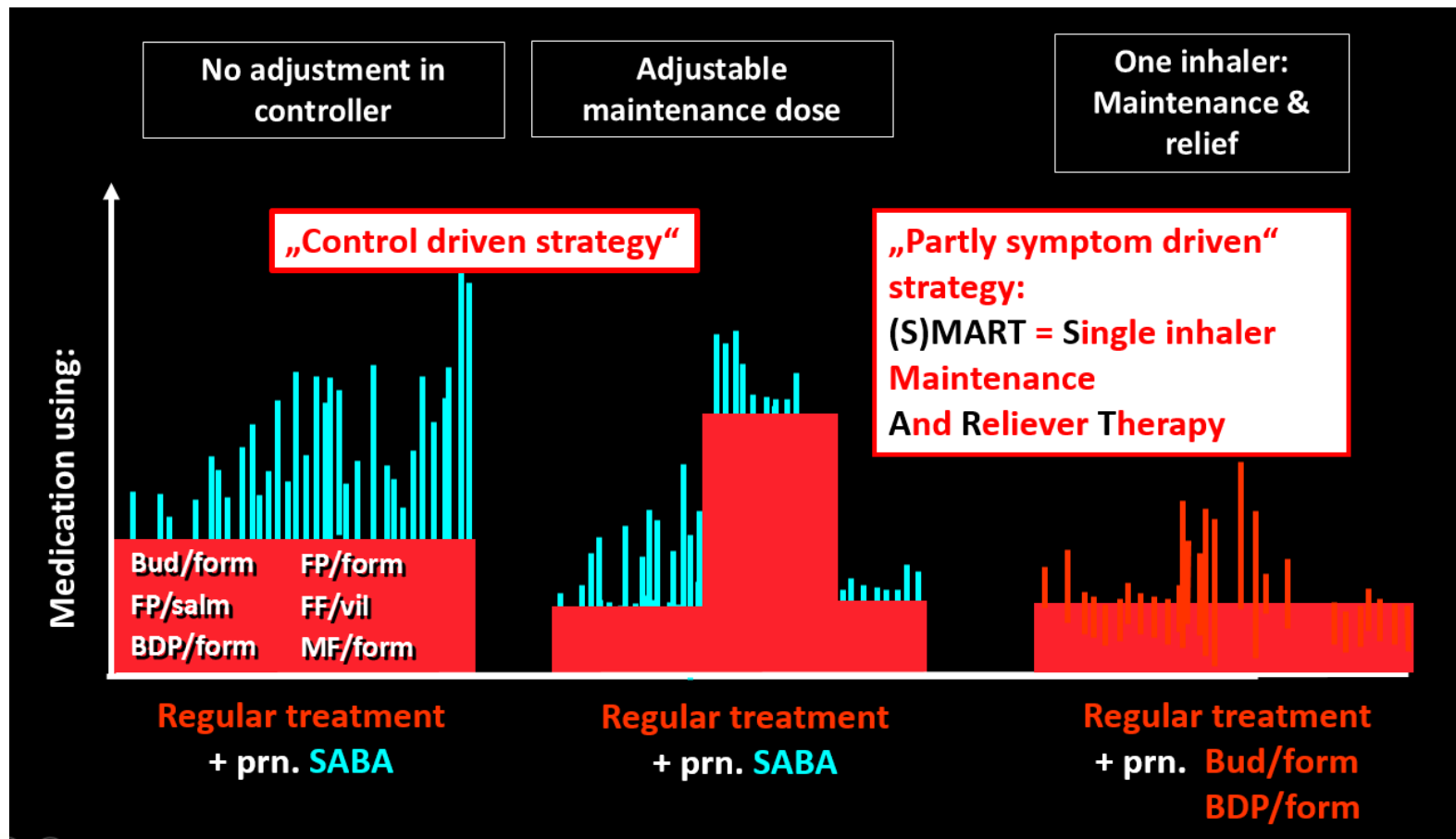
Two major categories of medications are

- Long-term control (called controllers)
 - Taken daily over a long period of time
 - Used to reduce inflammation, relax airway muscles, and improve symptoms and lung function
 - Inhaled corticosteroids (budesonide, fluticasone, ciclesonide, beclomethasone, mometasone)
 - LABA (formoterol, salmeterol, vilanterol)
 - Leukotriene modifiers (montelukast, zafirlucast)
 - Anti IgE (omalizumab)
- Quick relief (called rescue medicines)
 - Used in acute episodes (immediate relief)
 - SABA/SAMA (salbutamol, ipratropium)

Stepwise asthma management



Modern vs traditional asthma treatment with LABA+ICS



Case study – asthma patient

21 year old, atopic patient comes to a general practitioner with breath difficulties and cough.

GP indicates Ventolin inhaler and antibiotics.

Ventolin – what is active substance and the mechanism of action?

Is the approach correct?

Is the GP's approach correct?

What should GP focus on in anamnesis?

Which diseases should be considered?

Which exams can GP provide?

GP suspects asthma bronchiale

Next step of the GP?

- Indication of relief therapy
 - What is the mechanism of action?
- Indication of inhaled corticosteroids
 - Which corticosteroids do you remember?
 - What is their mechanism of action?
- Referral to specialists – pulmonology, allergology

Continuing case study – at the pulmonologist

The pulmonologist diagnosed moderate persistent asthma bronchiale.

How can we diagnose asthma and based on what?

What treatment approach would you suggest?

Continuing case study – at the pulmonologist

... moderate persistent asthma bronchiale

Pulmologist indicated free combination of budesonide 200mcg and formoterol 6 mcg (2-0-2) plus salbutamol

Why did he indicate the therapy?

What does „free combination“ mean?

Continuing case study – at the pulmonologist

...moderate persistent asthma bronchiale

The patient still has uncontrolled asthma despite the treatment...

How is uncontrolled asthma characterised?

Possible reasons?

Is there any other treatment?

Continuing case study – at the pulmonologist

...moderate persistent asthma bronchiale

The pulmonologist changed treatment to a fixed combination of budesonide/formoterol 200/6 in SMART regimen.

What is the product name of the fixed combination?

What is the SMART regimen?

Continuing case study – at the pulmonologist

The patient still has uncontrolled asthma despite the treatment...

What tests would be appropriate to add and why?

Continuing case study – at the pulmonologist

Variant 1:

Pulmonary hypertension was not proved.

Specific anti IgE was detected.

The pulmonologist changed the classification to severe persistent asthma, difficult to treat asthma.

What next step would you suggest?

Continuing case study – at the pulmonologist

Severe persistent asthma, difficult to treat asthma....

The physician added omalizumab to current treatment with Symbicort Turbuhaler 200/6 (2-0-2, SMART).

What is the product name?

What is the mechanism of action?

Who can indicated this treatment?

Continuing case study – at the pulmonologist

Severe persistent asthma, difficult to treat asthma....

Patient is treated with Symbicort Turbuhaler 200/6 (2-0-2, SMART), Xolair 150mg (every fourth week)

...still not under control.

What else can be added?

Continuing case study – at the pulmonologist

Variant 2:

Patient is heavy smoker.

Bronchodilatation test is irreversible.

What can we consider?

Continuing case study – at the pulmonologist

The pulmonologist changed classification of the disease to ACOS (Asthma COPD Overlap Sy).

What treatment would you suggest?

Case study – overlap COPD and asthma (ACOS)

The pulmonologist added tiotropium to the current treatment with Symbicort Turbuhaler 200/6 (2-0-2, SMART).

Why this drug?

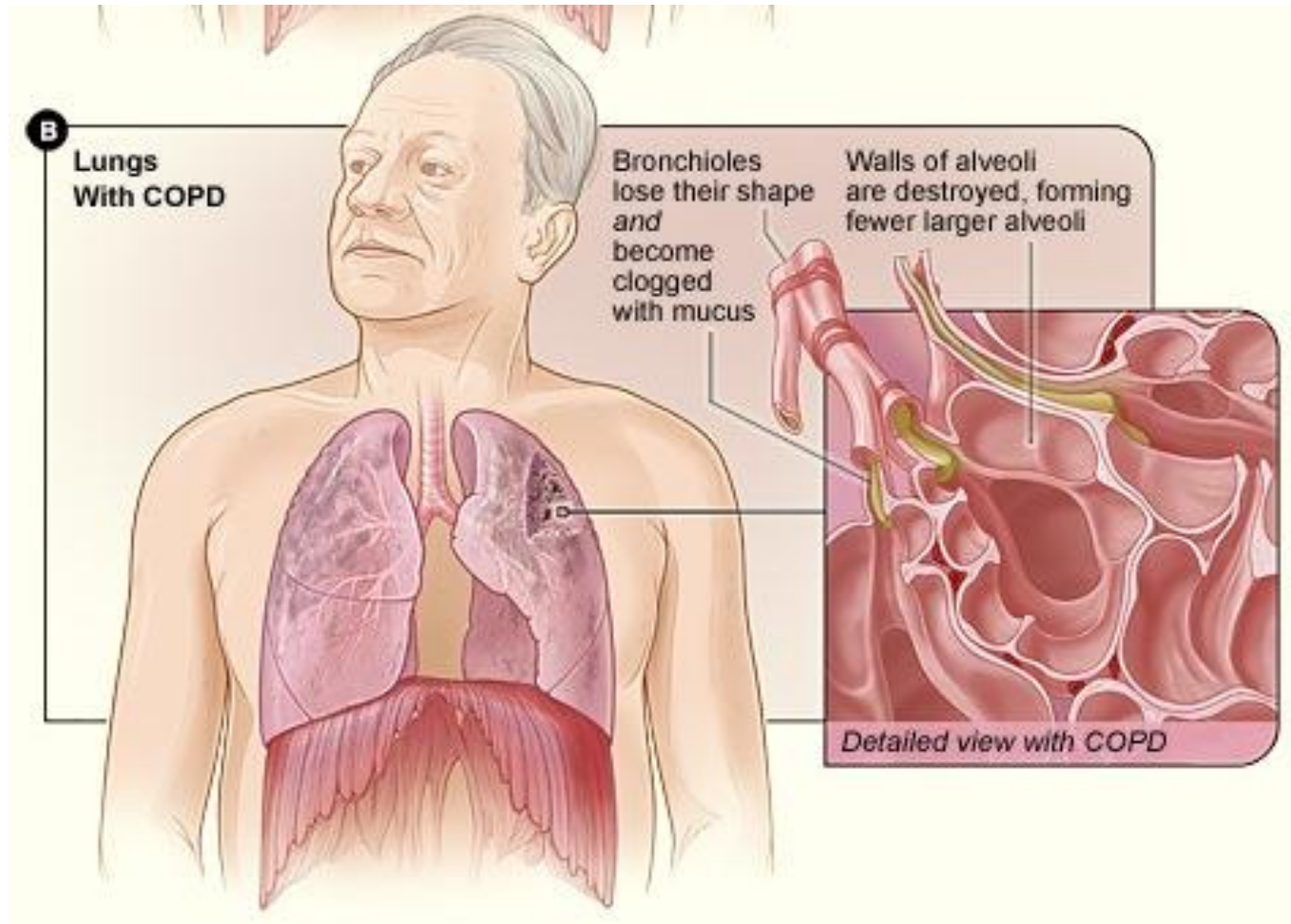
What is the mechanism of action?

What is the product name?

Chronic Obstructive Pulmonary Disease

- A progressive disease that affects the lungs, making it difficult to breathe
- Progressive lung diseases which include:
 - Emphysema
 - Chronic bronchitis
 - Irreversible bronchoconstriction
 - Severe bronchiectasis

Lung with COPD



Definition of COPD

- Chronic Obstructive Pulmonary Disease (COPD) is a **preventable and treatable** disease with some significant extrapulmonary effects that may contribute to the severity in individual patients.
- Its pulmonary component is characterized by airflow limitation that is **not fully reversible**.
- The airflow limitation is **usually progressive** and associated with an abnormal inflammatory response of the lung to noxious particles or gases.

What is COPD?

Common, preventable and treatable disease

AIRFLOW LIMITATION

**CHRONIC
INFLAMMATION**

**Small
airways
disease**

**Parenchymal
destruction**

Comorbidities, Exacerbations and Chronic bronchitis

Causes

Smoke and other noxious particles cause lung inflammation, a normal response that appears to be modified in patients who develop COPD.



**CHRONIC INFLAMMATORY
RESPONSE**

**Parenchymal destruction
EMPHYSEMA**

**Disruption of normal repair
mechanisms
SMALL AIRWAY FIBROSIS**

Prevalence

HIGHER PREVALENCE IN....



SMOKERS than in non-smokers, although prevalence is between 3-11% in never-smokers

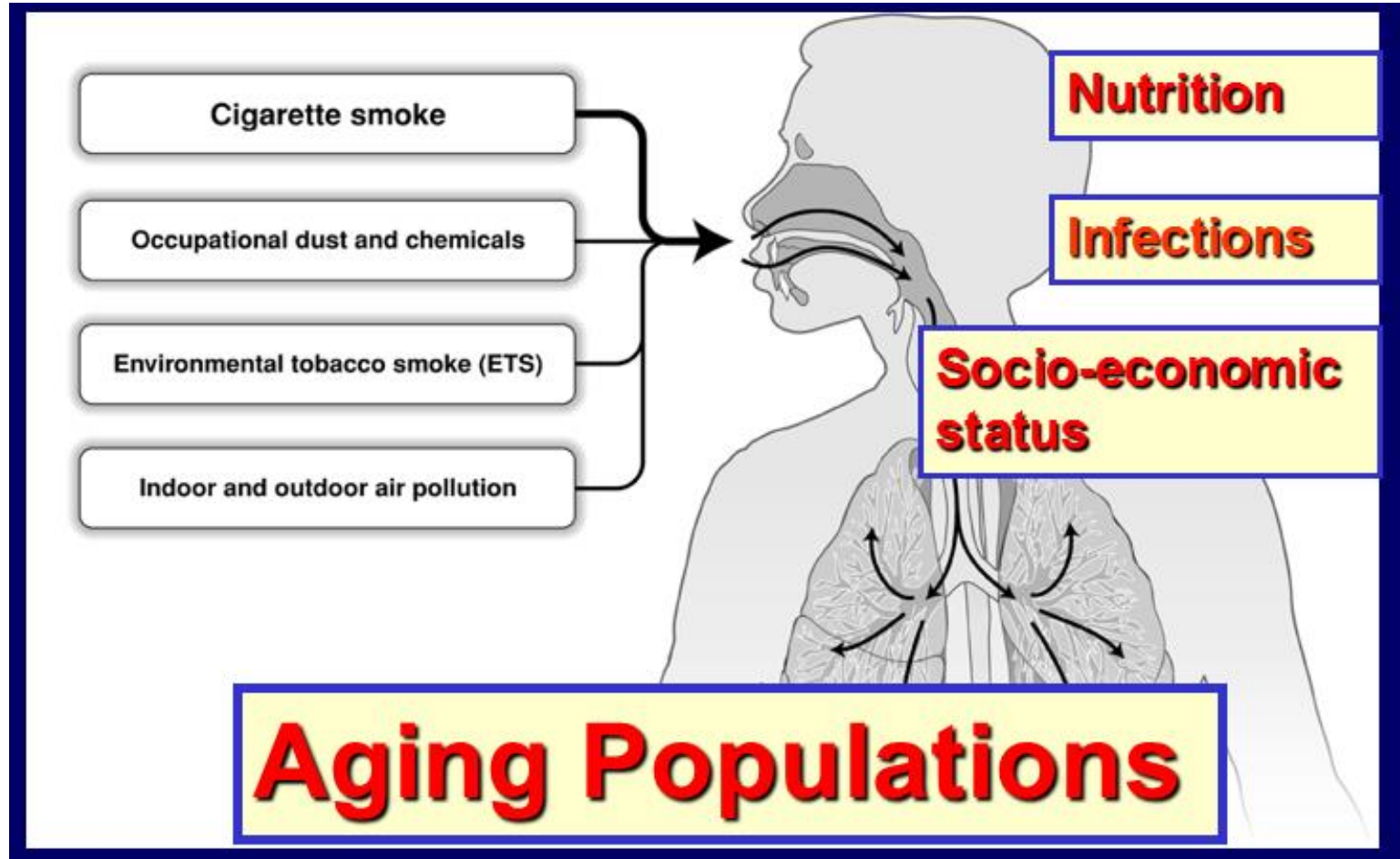


MEN than in women

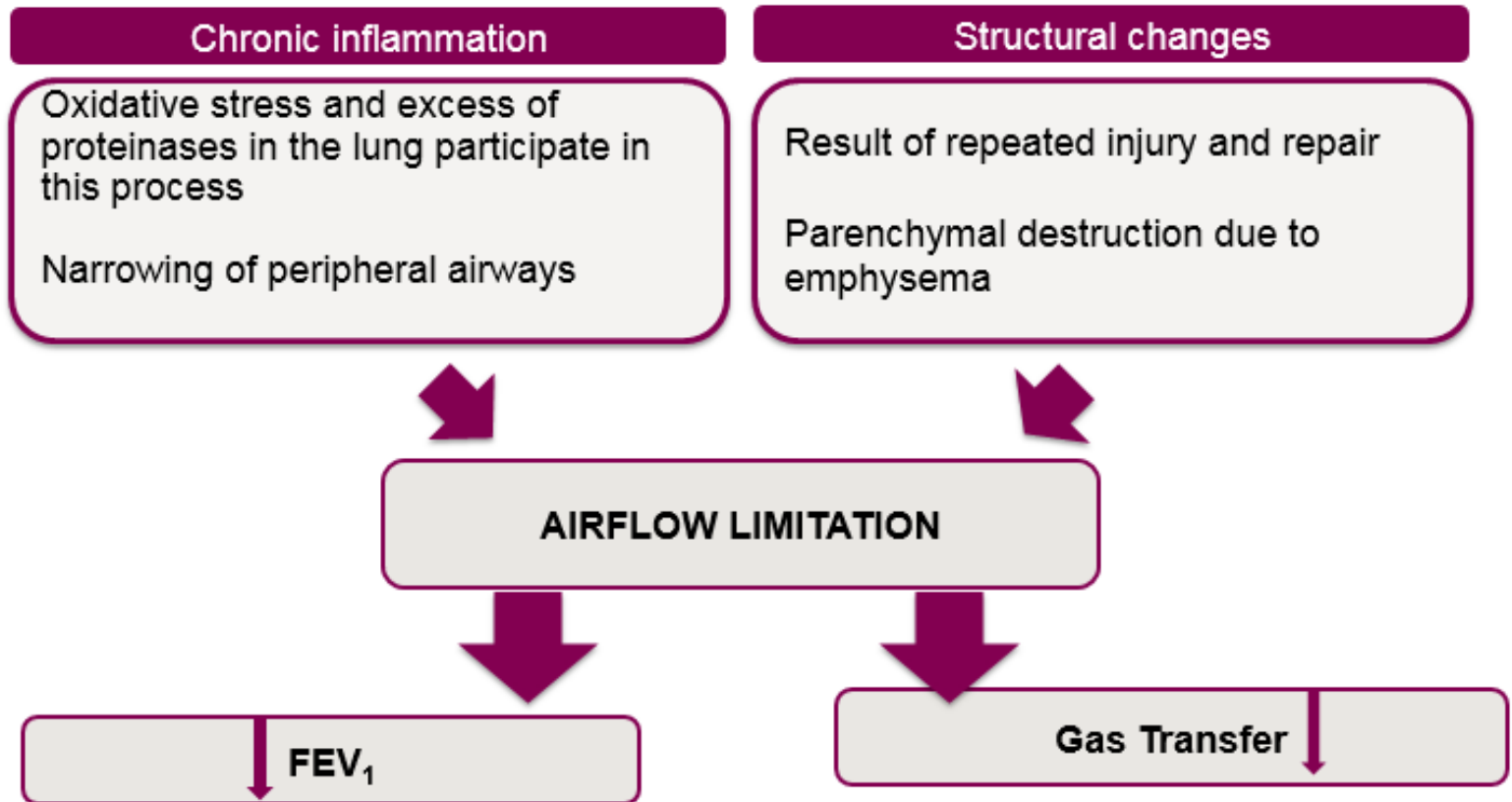


OVER 40 YEARS OLD than in younger people.
Highest prevalence is found among those over the age of 60

Risk factors for COPD



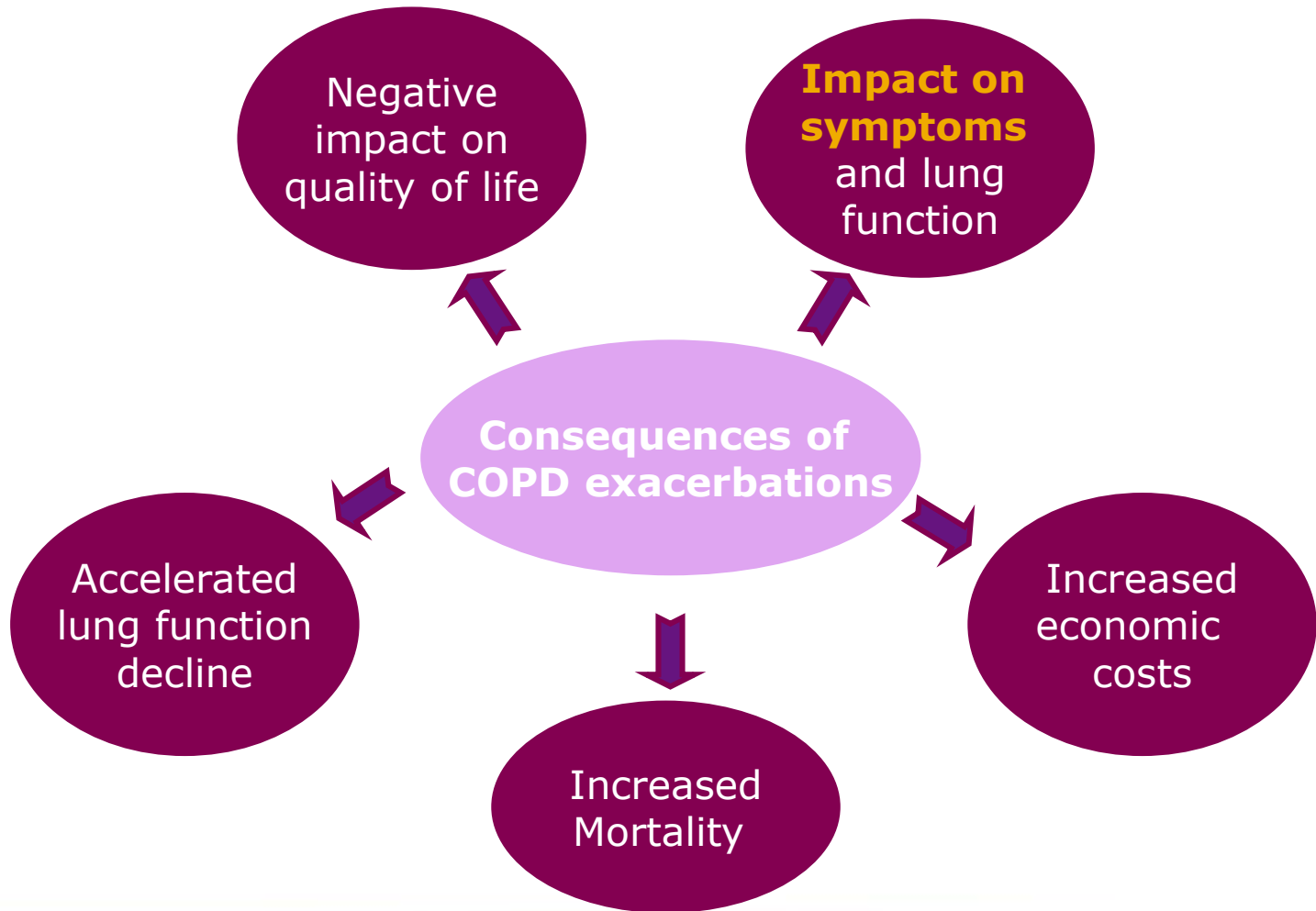
COPD pathophysiology



Symptoms

- Breathlessness
- Abnormal sputum (a mix of saliva and mucus in the airway)
- A chronic cough
- Daily activities can become very difficult as the condition gradually worsens

COPD exacerbations



Goals of therapy

- Relieve symptoms
- Improve exercise tolerance
- Improve health status

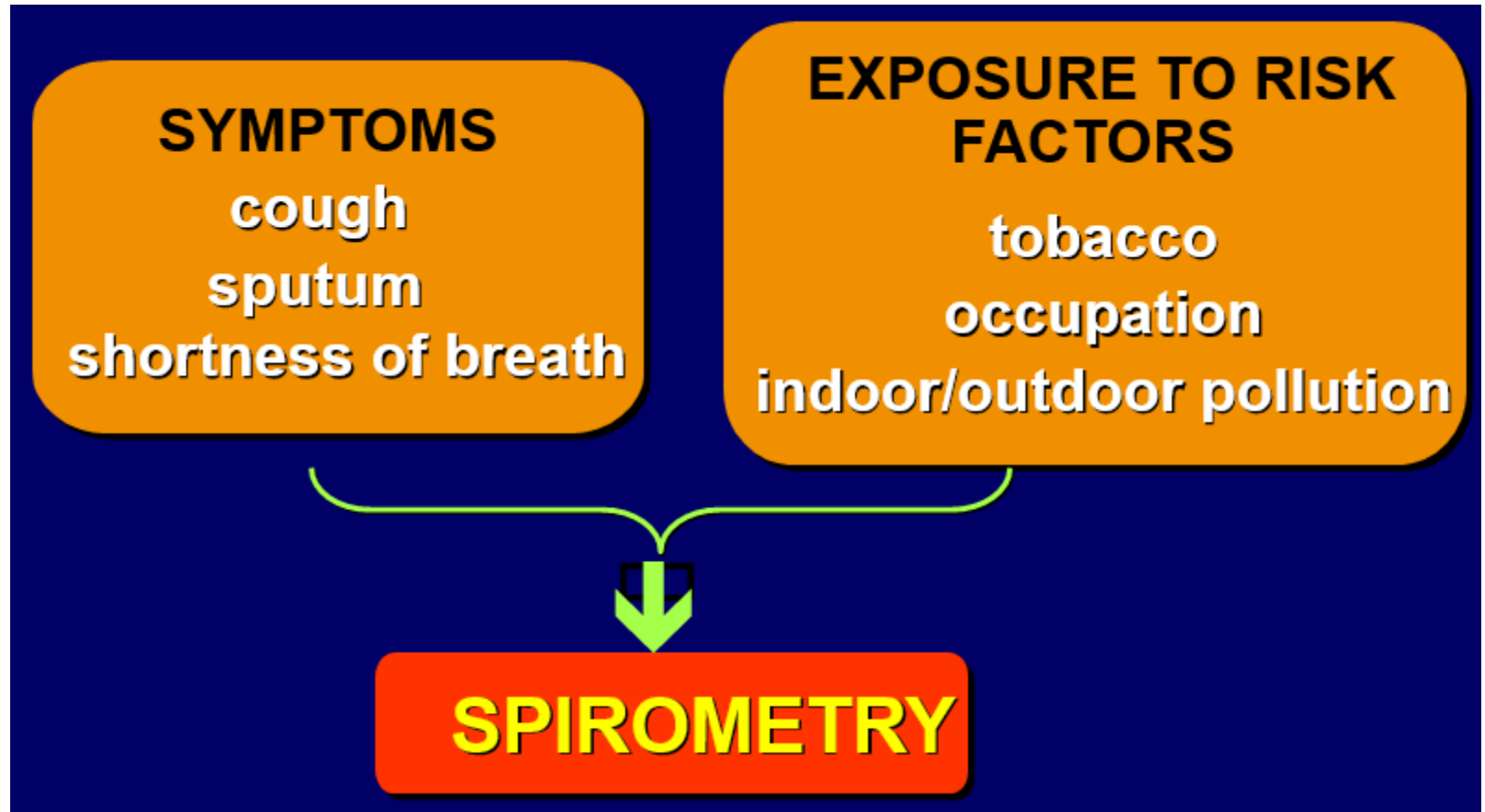
- Prevent disease progression
- Prevent and treat exacerbations
- Reduce mortality

Reduce symptoms

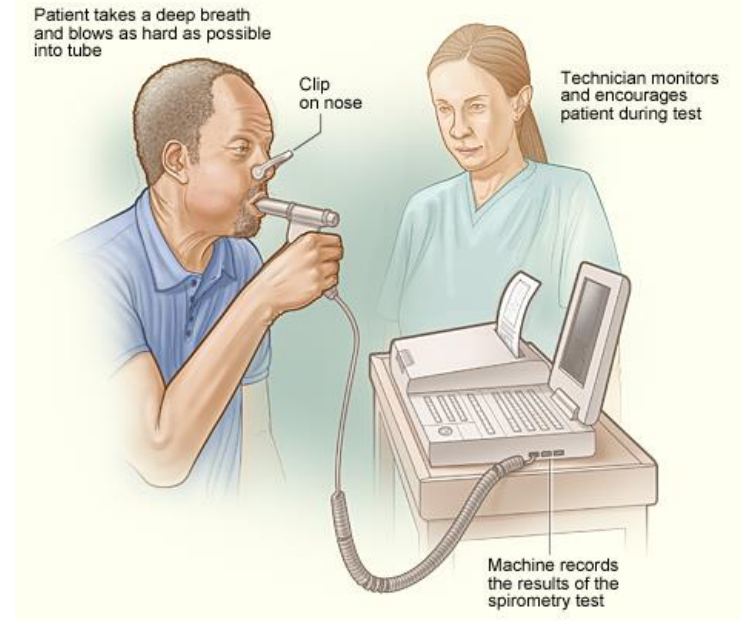
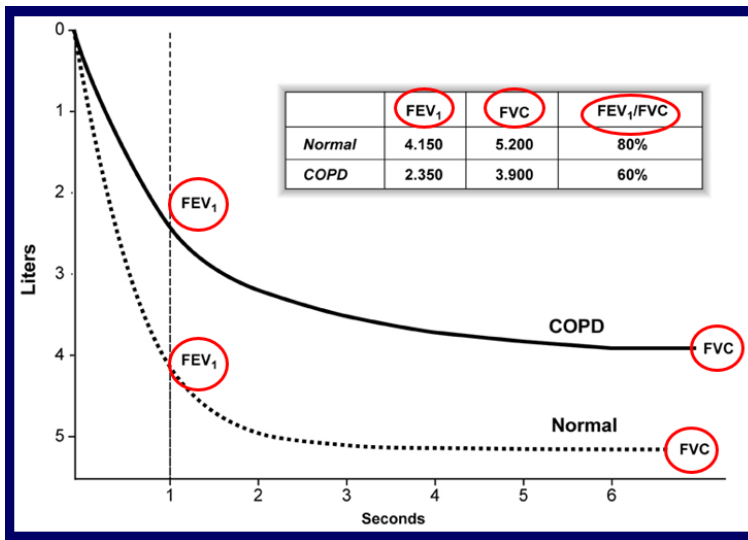
Reduce risk

A major goal is to ensure that COPD burden is minimised, thus giving patients the best possible health-related quality of life

Diagnosis of COPD



Spirometry for COPD Diagnosis and Classification of Severity



Classification of COPD Severity by Spirometry

Stage I: Mild

$FEV_1/FVC < 0.70$

$FEV_1 \geq 80\%$ predicted

Stage II: Moderate

$FEV_1/FVC < 0.70$

$50\% \leq FEV_1 < 80\%$ predicted

Stage III: Severe

$FEV_1/FVC < 0.70$

$30\% \leq FEV_1 < 50\%$ predicted

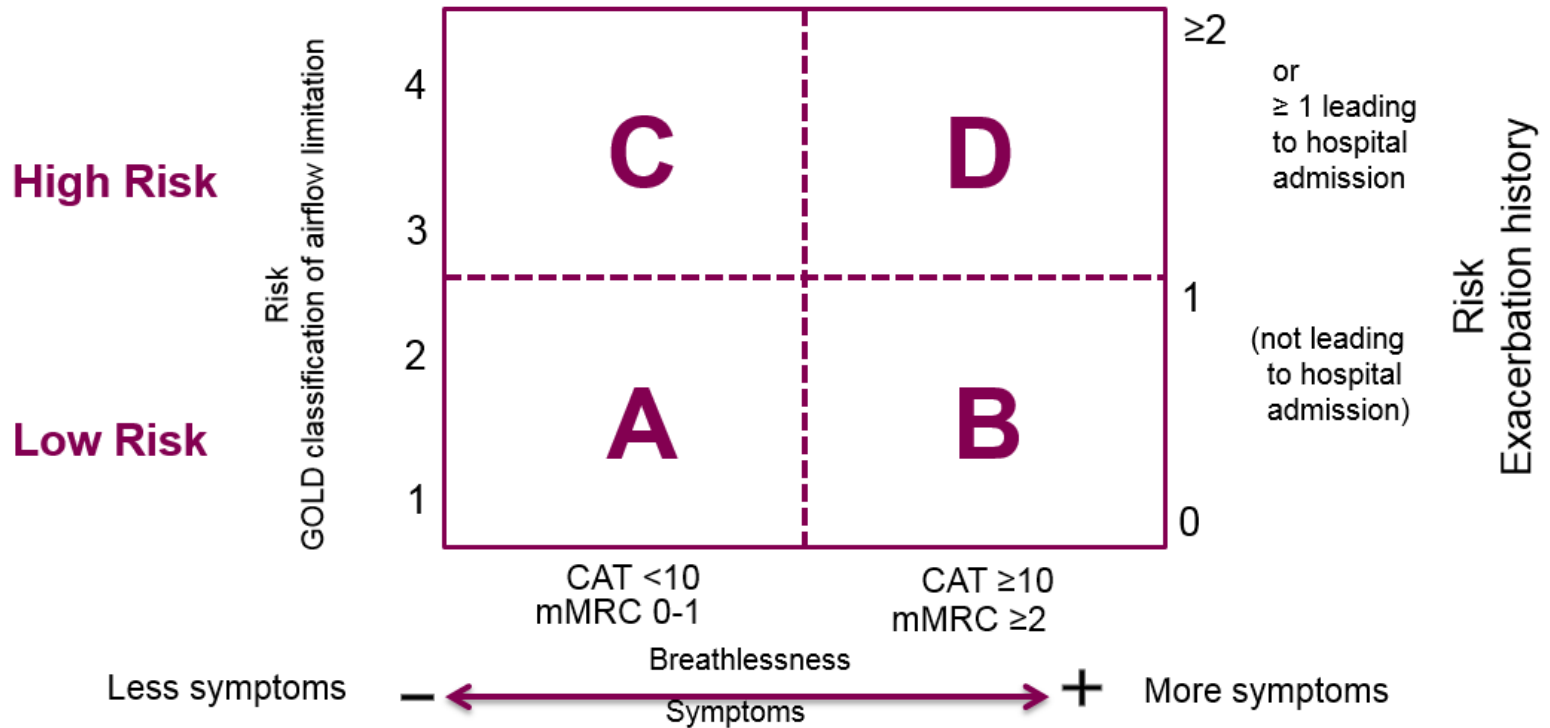
Stage IV: Very Severe

$FEV_1/FVC < 0.70$

$FEV_1 < 30\%$ predicted *or*

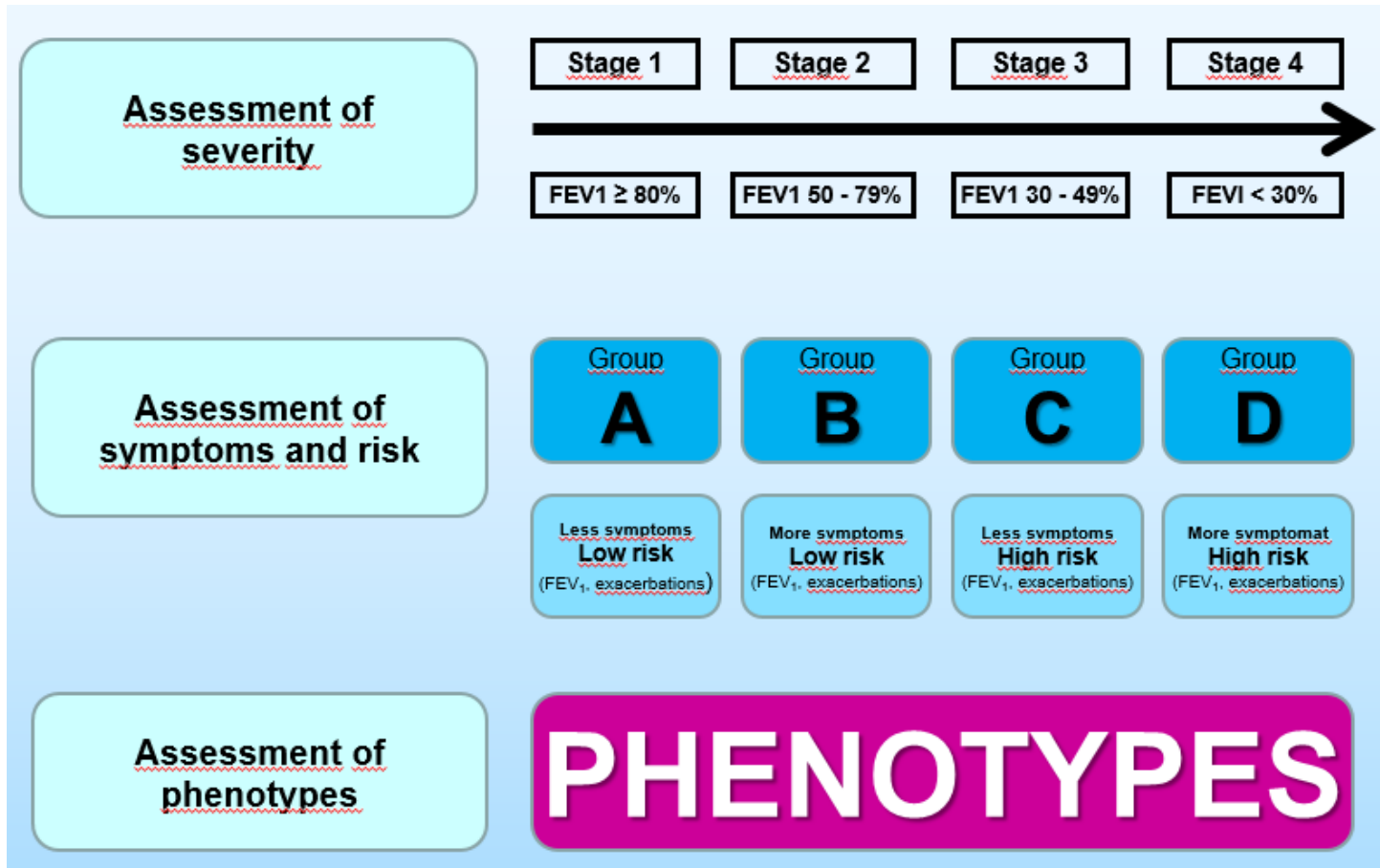
$FEV_1 < 50\%$ predicted *plus*
chronic respiratory failure

Combined COPD assessment



Patients are divided into four groups (A, B, C and D) according to their symptom/risk profile

Assessment of COPD includes



Phenotypes of COPD

Bronchitic phenotype

The presence of productive cough
(≥ 3 months/year in two or more consecutive years)

Emphysematic phenotype

Lifetime absence of productive cough and
clinical signs of pulmonary emphysema (HRCT, DLCO)

Frequent exacerbations phenotype

Presence of frequent exacerbations (≥ 2 /year)
treated with ABT and/or corticosteroids

COPD-asthma overlap (ACOS) phenotype

Two major criteria or One major+two minor criteria,
and definite COPD diagnosis

- Major criteria:
- (a) strong BDT positivity (FEV1 $>15\%$ and > 400 mL),
 - (b) BCT positivity,
 - (c) FeNO ≥ 45 -60 ppb and/or τ_{eo} (sputum) $\geq 3\%$,
 - (d) history of asthma
- Minor criteria:
- (a) mild BDT positivity (FEV1 $> 12\%$ and > 200 mL),
 - (b) \uparrow total IgE, (c) history of atopy

COPD + bronchiectasis Phenotype

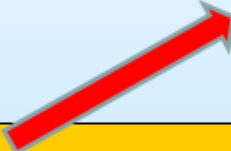
Accented, almost daily, purulent sputum expectoration,
younger age, lower or no smoking burden,
history of prolonged/recurrent respiratory infections,
hemoptysis, HRCT confirmation of bronchiectasis
and definite COPD diagnosis

Pulmonary cachexia phenotype

FFMI < 16 kg/m² (males), FFM < 15 kg/m² (females),
or BMI < 21 (males and females)

Therapy

For all symptomatic patients
regardless of their phenotype



Standard treatment

Inhaled bronchodilators (LABA, LAMA, ultra-LABA, ultra-LAMA)
Pulmonary rehabilitation, Vaccination, Education, Inhalation training, Dietary changes
Comorbidity treatment

Risks elimination

Elimination of smoking, environmental tobacco smoke
occupational risks, home exposures

Therapy

Phenotype specific treatment

Phenotype targeted therapy,
when phenotype(s) occur(s)

Standard treatment

Inhaled bronchodilators (LABA, LAMA, ultra-LABA, ultra-LAMA)
Pulmonary rehabilitation, Vaccination, Education, Inhalation training, Dietary changes
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Elimination of smoking, environmental tobacco smoke
occupational risks, home exposures

Therapy

| | | | | | |
|-------------------------------|--------------------------|--------------------------|--------------------------|--------------------------------|---------------------------|
| Frequent exacerbations | Bronchitic | Emphysematic | ACOS | COPD and bronchiectasis | Pulmonary cachexia |
| phenotype therapy | phenotype therapy | phenotype therapy | phenotype therapy | phenotype therapy | phenotype therapy |

Standard treatment

Inhaled bronchodilators (LABA, LAMA, ultra-LABA, ultra-LAMA)
Pulmonary rehabilitation, Vaccination, Education, Inhalation training, Dietary changes
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Risks elimination

Elimination of smoking, environmental tobacco smoke
occupational risks, home exposures

Therapy

| | | | | | |
|--|---|---|---|---|---|
| <p><u>PDE₄ inhibitors</u></p> <p>ICS+LABA</p> <p><u>Mucoactive drugs</u></p> <p><u>(Antibiotics)</u></p> | <p><u>PDE₄ inhibitors</u></p> <p><u>Mucoactive drugs</u></p> <p><u>(Antibiotics)</u></p> | <p>LVRs (lung volume reduction surgery)</p> <p>BVR (bronchoscopic volume reduction)</p> <p>(bullectomy) (alpha₁-antitrypsin)</p> <p>Teophyllin</p> | <p>ICS+LABA</p> <p>ISC+LABA+LAMA</p> <p><u>Antileukotriens</u></p> | <p><u>PDE₄ inhibitors</u></p> <p><u>Mucoactive drugs</u></p> <p><u>Antibiotics</u></p> <p><u>Physiotherapy</u></p> | <p><u>Nutritional support</u></p> <p><u>Rehabilitation programme</u> (aerobic exercise)</p> |
| <p><u>Frequent exacerbations</u></p> <p><u>phenotype therapy</u></p> | <p><u>Bronchitic</u></p> <p><u>phenotype therapy</u></p> | <p><u>Emphysematic</u></p> <p><u>phenotype therapy</u></p> | <p><u>ACOS</u></p> <p><u>phenotype therapy</u></p> | <p><u>COPD and bronchiectasis</u></p> <p><u>phenotype therapy</u></p> | <p><u>Pulmonary cachexia</u></p> <p><u>phenotype therapy</u></p> |

Standard treatment

Inhaled bronchodilators (LABA, LAMA, ultra-LABA, ultra-LAMA)
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Therapy

Phenotype specific treatment

Phenotype targeted therapy,
when phenotype(s) occur(s)

Standard treatment

Inhaled bronchodilators (LABA, LAMA, ultra-LABA, ultra-LAMA)
Pulmonary rehabilitation, Vaccination, Education, Inhalation training, Dietary changes
Comorbidity treatment

Risks elimination

Elimination of smoking, environmental tobacco smoke
occupational risks, home exposures

Therapy

Respiratory failure and terminal COPD care

Long-term oxygen therapy, High-intensity non-invasive ventilation,
Lung transplantation, Palliative care in terminal COPD

Phenotype specific treatment

Phenotype targeted therapy,
when phenotype(s) occur(s)

Standard treatment

Inhaled bronchodilators (LABA, LAMA, ultra-LABA, ultra-LAMA)
Pulmonary rehabilitation, Vaccination, Education, Inhalation training, Dietary changes
Comorbidity treatment

Risks elimination

Elimination of smoking, environmental tobacco smoke
occupational risks, home exposures

Case study – patient with COPD

Patient comes to a hospital following newspaper advertisement (Is your breathing difficult? Have your lung function tested).

PA: ex-smoker, hypertension

Drugs: Tenormin 100mg OD

CD: Last 3 months cough and increased sputum production. During weather changes and stress he has breathing difficulties. Also he has breathing difficulties when walking up hill.

What tests would you suggest?

Case study – patient with COPD

COPD diagnosed, bronchitic phenotype.

Pulmologist indicated Formovent 12mcg (1-0-1) and combination Atrovent a Ventolin as needed.

What kind of drugs are those? What are their mechanism of action?

Is the suggested treatment satisfactory?

Case study – patient with COPD

Formovent 12mcg (1-0-1) and combination Atrovent a Ventolin as needed.

At bronchitic phenotype is suitable to add mucolytic/expectorant drugs

- Do you know any?
- Why is it not possible to prescribe antitussives?

Can it be appropriate to use other treatment and why?

Case study – patient with COPD

Formovent 12mcg (1-0-1) and combination Atrovent a Ventolin as needed.

Is the suggested treatment suitable for patient with hypertension treated with Tenormin?

- What is the active substance and mechanism of action?

Which interactions of the treatment can be in relation to suggested COPD treatment?

Is there more suitable way of treatment of both diseases?