Chronic Obstructive Pulmonary Disease

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Objectives

Identify	patients with COPD based on symptoms and pulmonary function tests
Classify	COPD stage based on symptoms and risk of exacerbation
Recommend	appropriate treatment options based on the patient's stage of COPD
Counsel	patients regarding the side effects and administration of inhalers and oral therapy
Identify	elements of a monitoring plan for management of chronic COPD.

Guidelines

2019 NHLBI/WHO

- Global Initiative for Chronic Obstructive Lung Disease (GOLD)

2011 ACP/ACCP/ATS/ERS

- Diagnosis and Management of Stable Chronic Obstructive Pulmonary Disease

Definitions

A common preventable and treatable disease, characterized by persistent airflow limitation that is usually progressive and associated with enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients."

Epidemiology

4rd leading cause of death in the U.S.

2nd leading cause of disability in the U.S.

16 million adult report having the diagnosis

15% of Americans currently smoke

Etiology

COMMON OCCUPATIONAL EXPOSURES

GOLD AND COAL MINING

SILICA DUST (GLASS OR CERAMIC INDUSTRY)

COTTON DUST

GRAIN DUST

TOLUENE DIISOCYANATE

ASBESTOS

OPEN COOKING/HEATING FIRES

Pathophysiology Chronic COPD

- Chronic airway inflammation → destructive changes →chronic airflow limitation
- Involvement in airways, pulmonary vasculature and lung parenchyma
- Neutrophilic in nature
- Macrophages
- CD8+ lymphocytes

Pathophysiology Chronic COPD

- Imbalance of oxidants and antioxidants leads to increase in oxidative stress
- Mucus secretion ↑ (early in disease)
- Ciliary motility ↓
- Smooth muscle & connective tissue thickening
- Chronic inflammation cause scaring & fibrosis
- Parenchymal damage causing impaired gas exchange

Pathophysiology Chronic COPD

Chronic airflow obstruction
Thoracic overinflation → dyspnea due to flattening of diaphragm

Thoracic overinflation → increased functional residual capacity (FRC) →↓ inspiratory reserve capacity & inhalation time

Thoracic overinflation responds well to bronchodilators

Pathophysiology

Reversible	Irreversible
Mucus and inflammatory cells and mediators in bronchial secretions	Fibrosis and narrowing of airways
Bronchial smooth muscle contraction in peripheral and central airways	Reduced elastic recoil with loss of alveolar surface area
Dynamic hyperinflation during exercise • Flattening of diaphragm • Increase in functional residual capacity FRC • Decrease in inspiratory reserve capacity IRV	Destruction of alveolar support with reduced patency of small airways

Risk Factors

Exposures: particles inhaled that cause inflammation and cell injury

- Tobacco smoke
- Occupational dusts and chemicals (asbestos, miners)
- Air pollution

Host factors: influence the risk of development

- Deficiency of α_1-antitrypsin (AAT)
- Airway hyperresponsiveness
- Impaired lung growth
- Increasing age
- Female

Risk Factors

Cigarette smoking (85-90% of cases)

85-90% of all cases involve smoking

12-13 times more likely to die than nonsmokers

Mortality dependent on age of starting, total pack-years, and current smoking status

15-20% of smokers develop COPD

Secondhand smoke

E-cigarettes ??

Risk Factors

α_1-antitrypsin (AAT) deficiency

- Autosomal recessive genetic disorder
- Accounts for <1% COPD cases
- Early development (20-50 yo)
- AAT protects lungs from destruction by elastase (released by neutrophils)
- Accelerated decline in lung function

Presentation

Subjective	Objective
Chronic cough	Cyanosis of mucosal membranes
Sputum production	Increased resting respiratory rate
Persistent or progressive dyspnea worse with exercise; progressive over time	Barrel chest and use of accessory muscles
History of exposure to risk factors Tobacco smoke exposure	Spirometry • FEV_1:FVC < 70% • Postbronchodilator FEV_1 < 80% predicted and <12% improvement

Symptoms of COPD

The characteristic symptoms of COPD are chronic and progressive dyspnea, cough, and sputum production.

Dyspnea: Progressive, persistent and characteristically worse with exercise.

Chronic cough: May be intermittent and may be unproductive.

Chronic sputum production: Any patter of sputum my indicate COPD

Symptoms of COPD assessment

Medical History

- Exposure to risk factors Past medical history Family history Symptom development
- Exacerbation/hospitalization history Comorbid conditions
- Impact on QOL and support

Physical Exam

- Not diagnostic in COPD
- Physical signs of airflow limitation are not present until late in the disease progression
- Decreased breathe sounds and other signs are present during exacerbations

COPD Indicators

KEY INDICATORS FOR CONSIDERING A DIAGNOSIS OF COPD

Consider COPD, and perform spirometry, if any of these indicators are present in an individual over age 40. These indicators are not diagnostic themselves, but the presence of multiple key indicators increases the probability of a diagnosis of COPD. Spirometry is required to establish a diagnosis of COPD.

Dyspnea that is:	Progressive over time. Characteristically worse with exercise. Persistent.
Chronic Cough:	May be intermittent and may be unproductive. Recurrent wheeze.
Chronic Sputum Production:	Any pattern of chronic sputum production may indicate COPD.
Recurrent Lower Respiratory Tract Infections	
History of Risk Factors:	Host factors (such as genetic factors, congenital/developmental abnormalities etc.). Tobacco smoke (including popular local preparations). Smoke from home cooking and heating fuels. Occupational dusts, vapors, fumes, gases and other chemicals.
Family History of COPD and/or Childhood Factors:	For example low birthweight, childhood respiratory infections etc.

TABLE 2.1

Diagnosis

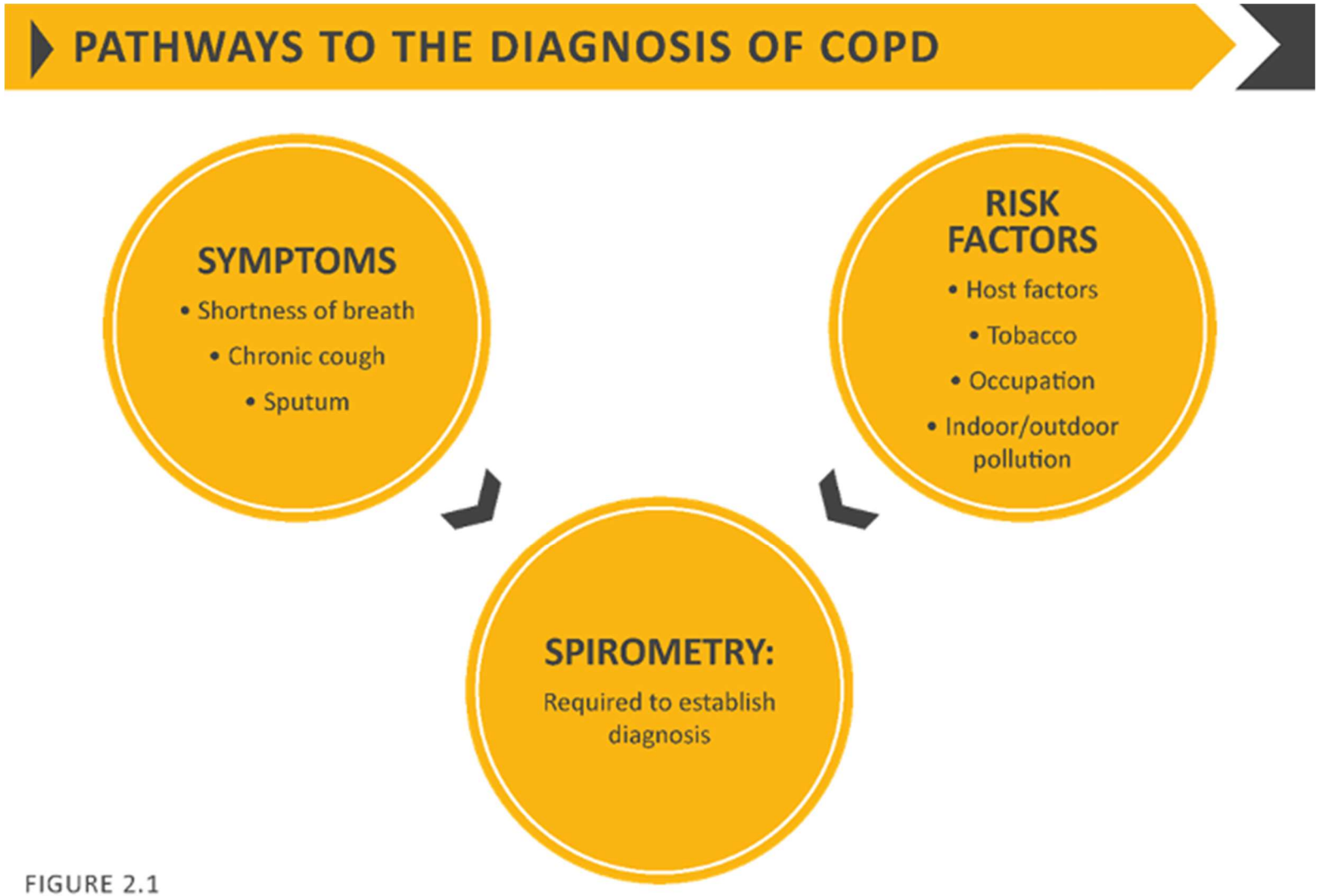


FIGURE 2.1

COPD Diagnosis

Spirometry

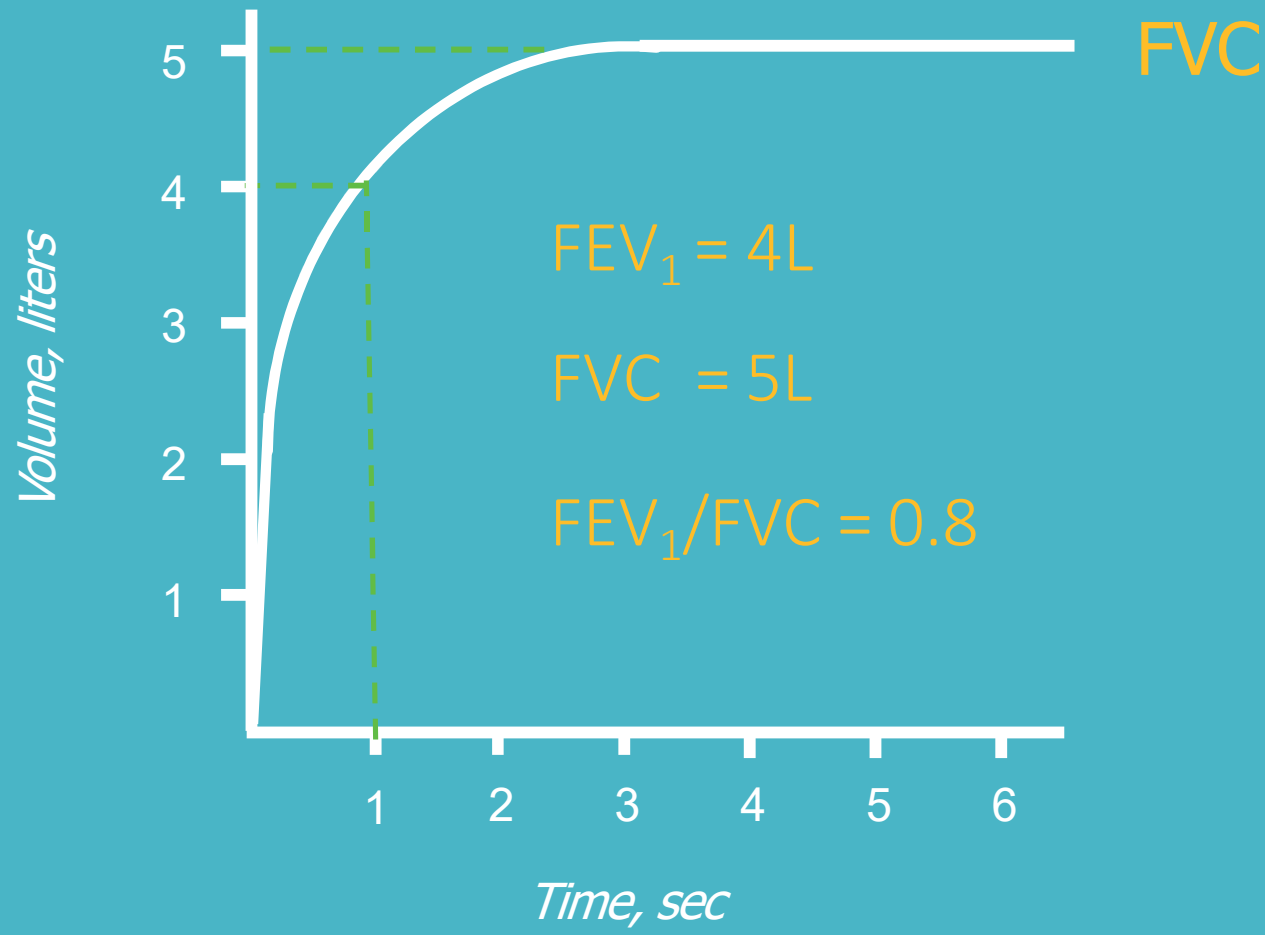
Gold standard for measuring airflow obstruction Most reproducible	Standardized	Objective way of measuring airflow limitation Reversibility testing is NOT recommended

Diagnosis

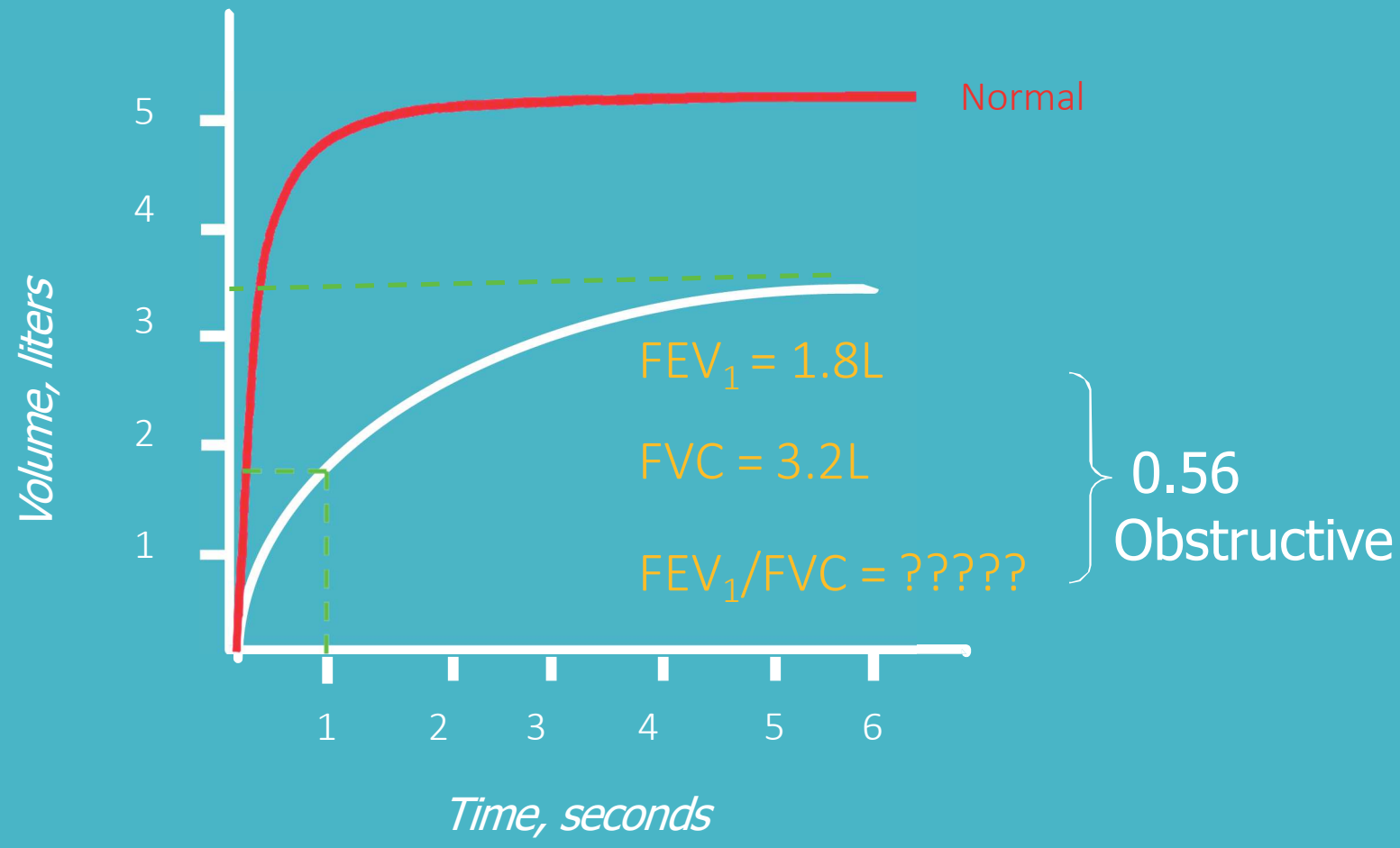
2 important measurements for COPD Forced vital capacity (FVC)	Forced expiratory volume in 1 second (FEV1) Used to determine FEV1/FVC ratio	Cut-off for airflow obstruction = 0.7

Post-bronchodilator FEV1/FVC < 0.70 confirms the presence of airflow limitation that is not fully reversible

Spirometry: Normal Trace Showing FEV_1 and FVC



Spirometry: Obstructive or Restrictive?



Spirometry

Diagnosis

- A post-bronchodilator test
- Fixed ration of $FEV_1/FVC < 0.70$

Severity of airflow obstruction

- See next slide

Follow up assessments

- Usually does not correlate with symptoms
  - Used in some special circumstances
    - Ex.: Lung reduction surgery or transplant
- Monitor progression of the disease

Classification by Spirometry

GOLD Classification	Severity	Post-Bronchodilator FEV_1
1	Mild	≥ 80% predicted
2	Moderate	50-80% predicted
3	Severe	30-49% predicted
4	Very severe	< 30% predicted

Assessment of Symptoms

COPD Assessment Test (CAT): An 8-item measure of health status impairment in COPD

- http://www.catestonline.org

COPD Control Questionnaire (CCQ): A 10-item self-administered questionnaire to assess control

- http://www.ccq.nl/

Symptom Assessment Chronic COPD

COPD Assessment Test (CAT)

- 8-item unidimensional assessment of COPD health status
- Scores range 0-40 (lower scores are better)
  - ≥ 10 indicate symptoms have more impact on health status

Modified medical research council questionnaire for assessing the severity of breathlessness (mMRC)

- Grades 0-4 (lower scores are better)
  - Grade ≥2 indicate breathlessness is more severe

Modified MRC (mMRC) Questionnaire

PLEASE TICK IN THE BOX THAT APPLIES TO YOU
(ONE BOX ONLY)

mMRC Grade 0. I only get breathless with strenuous exercise. ☐

mMRC Grade 1. I get short of breath when hurrying on the level or walking up a slight hill. ☐

mMRC Grade 2. I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level. ☐

mMRC Grade 3. I stop for breath after walking about 100 meters or after a few minutes on the level. ☐

mMRC Grade 4. I am too breathless to leave the house or I am breathless when dressing or undressing. ☐

Differential Diagnosis

Asthma	Congestive heart failure	Tuberculosis
bronchiolitis	Pulmonary fibrosis	Cardiomegaly

Treatment Approach to COPD

1

Reduce symptoms

- Relieve symptoms
- Improve exercise tolerance
- Improve health status

2

Reduce risk

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

Non-pharmacologic Treatment

Smoking cessation

Vaccination

Pulmonary rehabilitation

- Can include exercise training, education, self-management to affect behavior
- Designed to improve physical and psychological condition

Long-term oxygen therapy

Others such as:

- Surgery: lung reduction, transplant
- Palliative care and hospice

Smoking Cessation

- Most important intervention that can be made for COPD
- Only intervention proven to affect long-term decline in FEV_1 and slow the progression of COPD
- Reduces risk of developing COPD
- Ask, Advice, Assess, Assist, Arrange

Oxygen Therapy

Increases survival in patients with severe resting hypoxemia:

- Oxygen use recommended if:
- Resting $PaO_2 \leq 55$ mmHg or $SaO_2 \leq 88\%$
- OR
- Resting PaO_2 55-60 mmHg or $SaO_2 \leq 88\%$ with:
  - Peripheral edema suggesting congestive cardiac failure,
  - Polycythemia, or
  - Pulmonary hypertension
- Then:
- Titrate to keep SaO2 ≥ 90%

Pharmacologic Treatment

Pharmacologic Treatment

Bronchodilators

- β_2-agonists (short- and long-acting)
- Anticholinergics (short- and long-acting)
- Methylxanthines

Inhaled corticosteroids

Phosphodiesterase inhibitors

α_1-antitrypsin replacement therapy

Bronchodilators

Mechanism: relax smooth muscle, improve lung emptying, reduce thoracic hyperinflation

- β_2-agonists (β_2 selective)
- Anticholinergics (M_1, M_2, M_3 non-selective)
- Methylxanthines

β_2-agonists (β_2 selective)

SABA: Short acting (inhaled or nebulized)

- Albuterol (Ventolin, ProAir, Proventil)
- Levalbuterol (Xopenex)

LABA: Long acting β_2 agonists (inhaled)

- Formoterol (Foradil) Q12H
- Arformoterol (Brovana) Q12H
- Salmeterol (Serevent) Q12H
- Indacaterol (Arcapta) Q24H
- Olodaterol (Striverdi) Q24H

Anticholinergic (M_1, M_2, M_3 non-selective)

SAMA: Short acting muscarinic agent

- Ipratropium (Atrovent)

LAMA: Long-acting muscarinic agent

Aclidinium (Tudorza) Q12H

Glycopyrronium (Seebri) Q24H

Tiotropium (Spiriva) Q24H

Umeclidinium (Incruse) Q24H

Methylxanthines

MOA: Inhibit phosphodiesterase, Ca^{2+}, prostaglandins

Theophylline (PO)

Aminophylline (IV)

Inhaled Corticosteroids

Ciclesonide
- Alvesco® (MDI: 80, 160mch/inh.)

Beclomethasone dipropionate
- QVAR® (MDI: 40 & 80mcg/inh.)

Budesonide
- Pulmicort Flexhaler® (DPI: 90, 180mcg/inh.)
- Pulmicort (susp. for neb.)

Flunisolide
- Aerospan (80mcg/inh.)

Fluticasone propionate
- Flovent® HFA (MDI: 44, 110, 220mcg/inh.)
- Flovent® Diskus (DPI: 50, 100, 250mcg/inh)
- Arnuity Elipta (100, 200 mcg/inh.)

Mometasone furoate
- Asmanex® Twisthaler (DPI:110, 220mcg/inh.)
- Asmanex® HFA (100, 200 mcg/inh.)

Inhaled Corticosteroids (ICS)

An ICS combined with a LABA is more effective than the individual agents in reducing exacerbations and improving lung function and symptoms

Regular use of an ICS alone, increases the risk of pneumonia in patients with severe disease

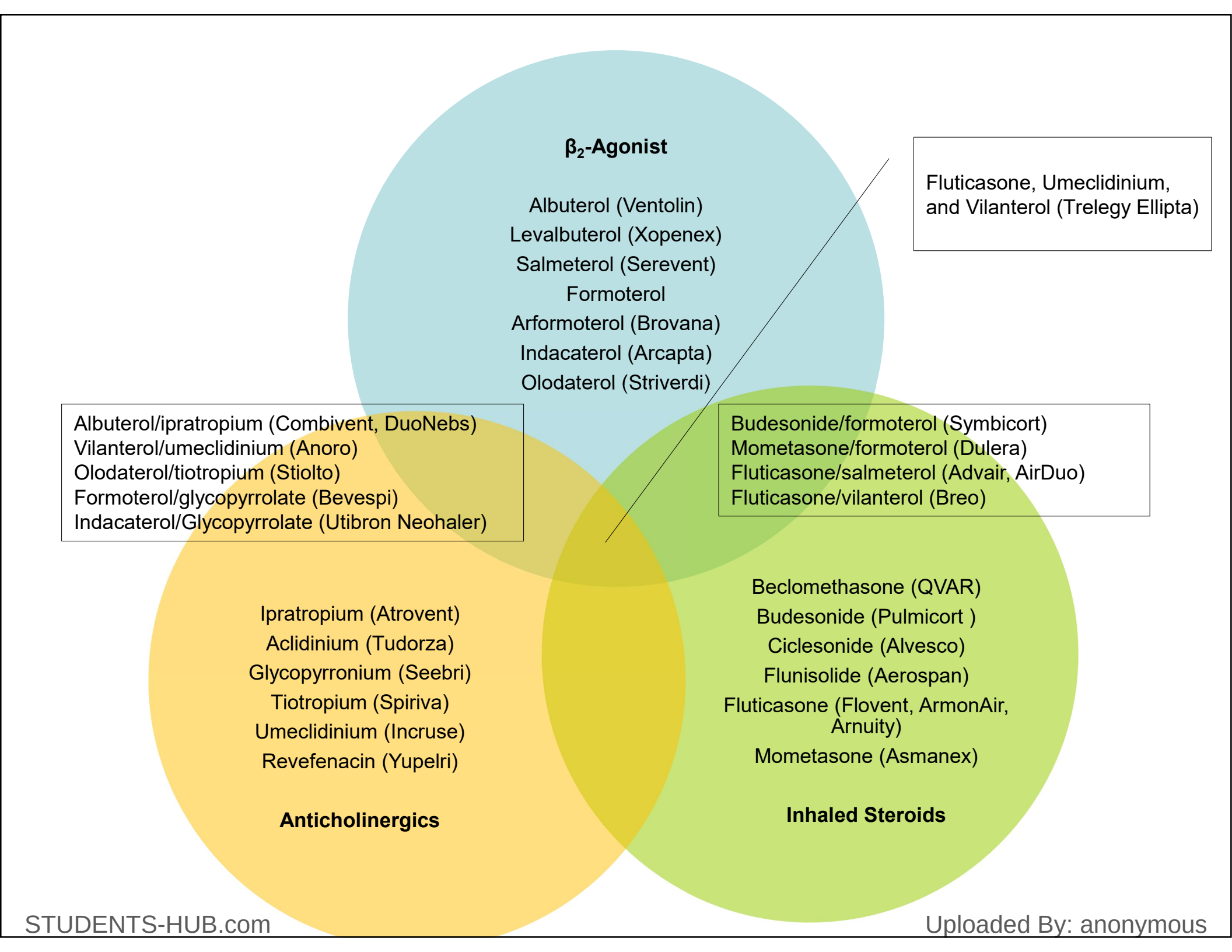
Triple therapy (ICS/LAMA/LABA) improves lung function, symptoms and reduces exacerbations

ICS and Eosinophils

Recent studies have shown correlation between blood eosinophil counts and the effect of ICS on COPD

Blood eosinophil counts can be used to guide therapy with ICS

- Which pts. are most likely to benefit
- < 100 cells/µL: ICS have little effect
- > 300 cells/µL: ICS have greatest effect



COPD Specific Meds

Phosphodiesterase-4 Inhibitor

- **Roflumilast (Daliresp)**
- NOTE: Always use with a long-acting bronchodilator

α_1-antitrypsin Replacement Therapy

- Pooled human AAT (Prolastin-C, Aralast-NP, Zemaira, Glassia)
- Indication: α_1-antitrypsin (AAT) deficiency

Treatment Evidence

Smoking cessation

- Prevents the development and progression of COPD (FEV_1 decline)

Oxygen therapy

- Improves survival in patients with chronic hypoxemia (mortality benefit)

Pharmacologic therapy:

- Reduces symptoms
- Reduces frequency and severity of exacerbations
- Improves health status and exercise tolerance

Specific Treatment Evidence

Long-acting β_2-agonists

- Salmeterol and formoterol reduce treatment and hospitalizations for exacerbations

Long-acting anticholinergics

- Tiotropium reduces exacerbations and related hospitalizations

Corticosteroids

- Long-term safety is unknown
- Effective in patients with FEV_1 < 60% predicted
- Possible association with increased pneumonia
- Can use blood eosinophils to guide tx decisions

Roflumilast

- Improves FEV_1 with salmeterol or tiotropium

Treatment Algorithm

(2019 GOLD Guidelines)

ABCD Assessment Tool

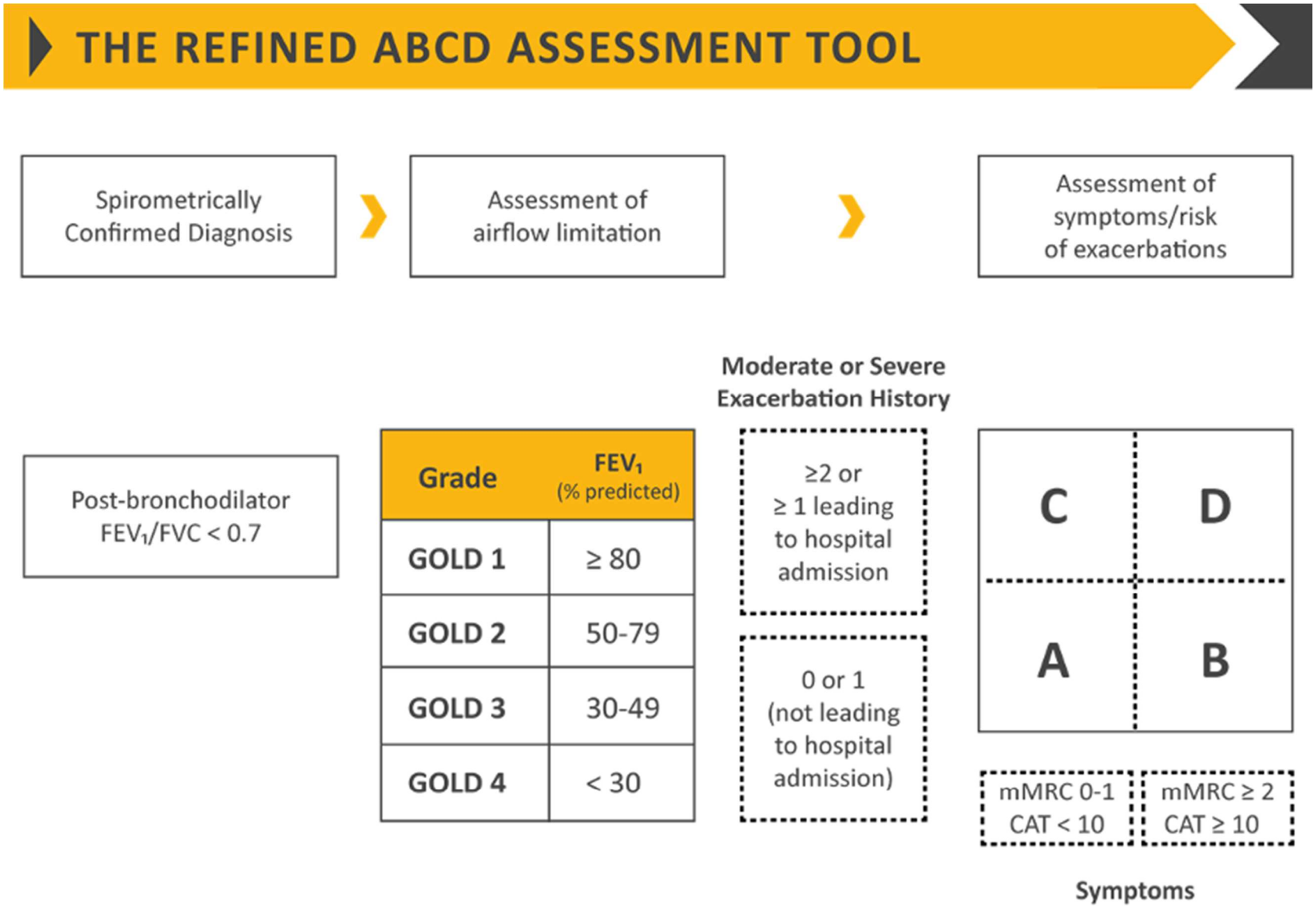
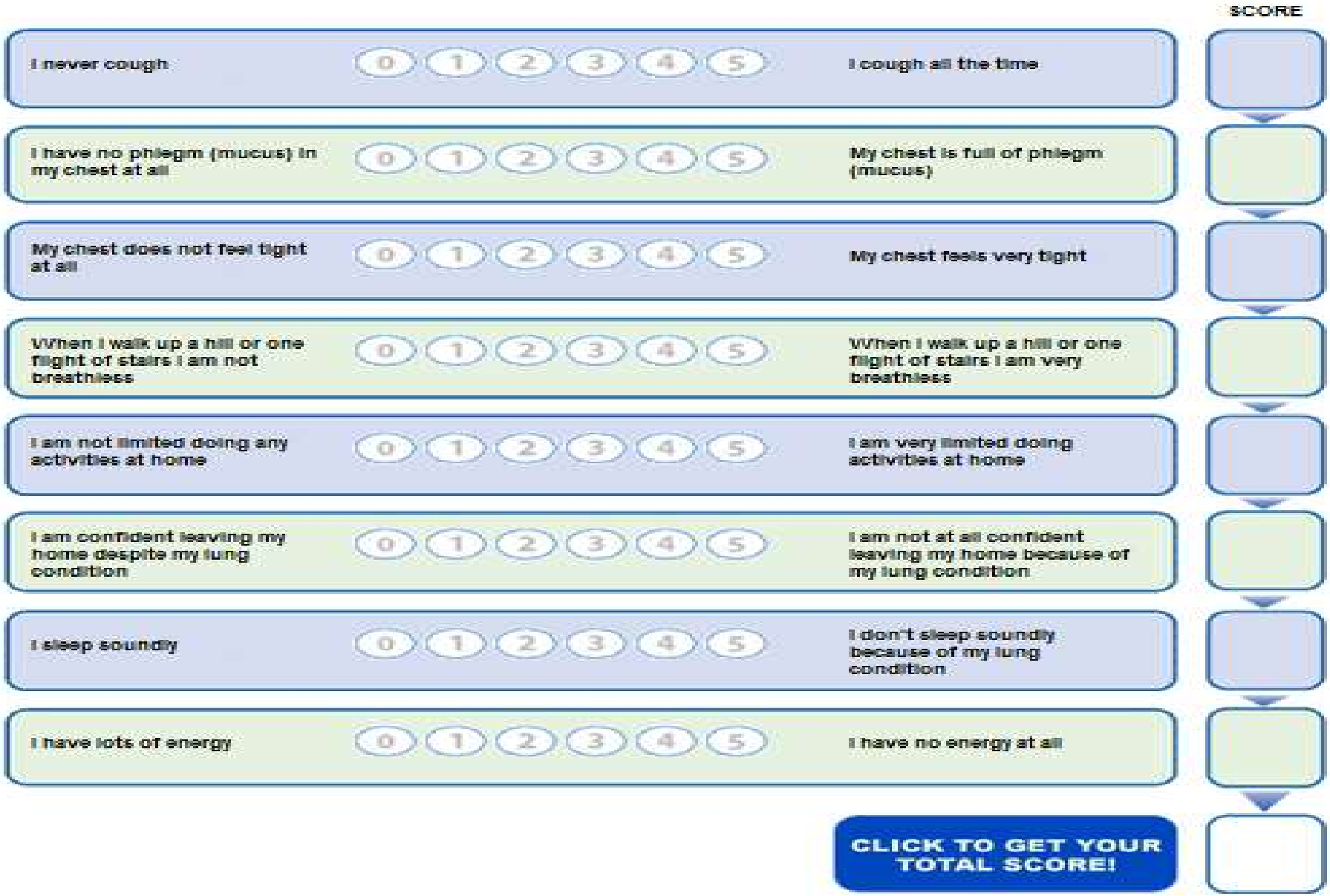


FIGURE 2.4

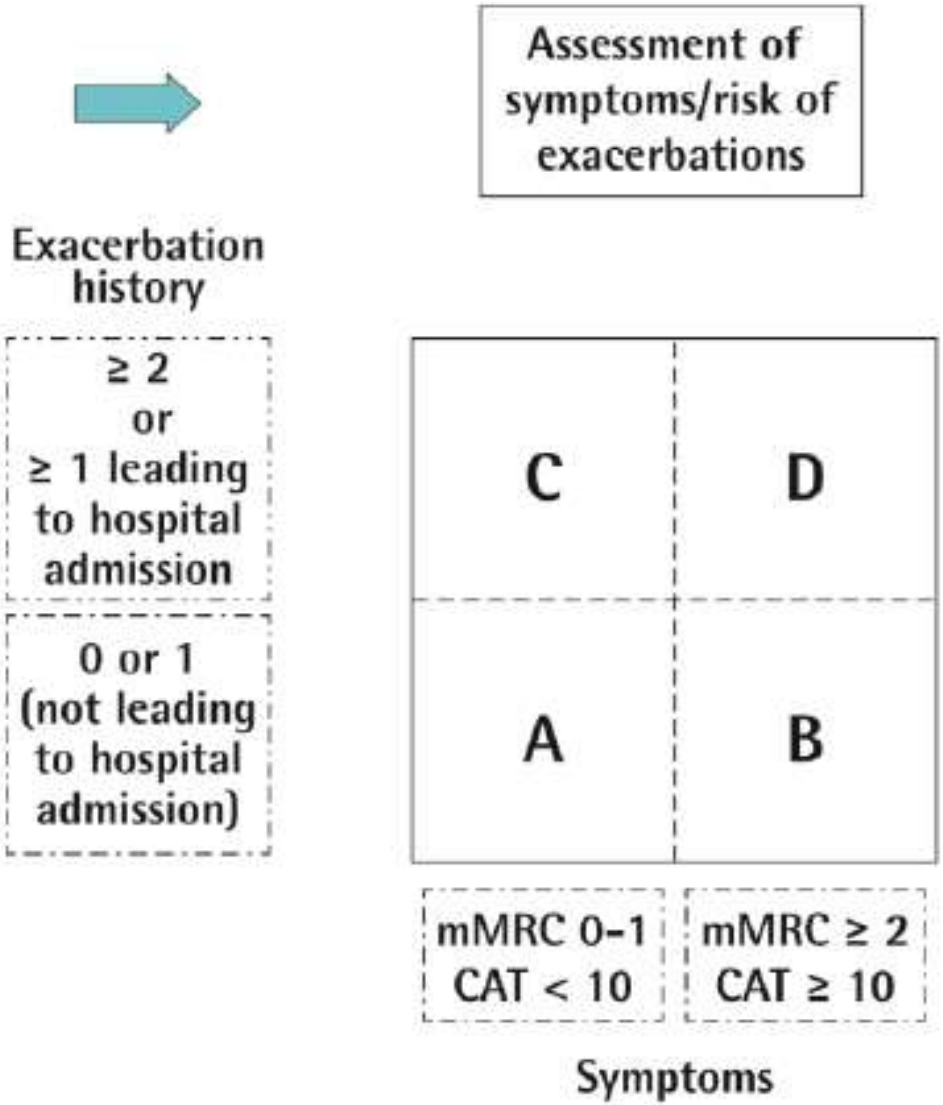
Symptom Assessment: mMRC

0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on the level or walking up a slight hill
2	I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level
3	I stop for breath after walking about 100m or after a few minutes on the level
4	I am too breathless to leave the house, or I am breathless when dressing or undressing

Symptom Assessment: CAT



ABCD Assessment Tool



Assessing Risk of Exacerbation

Exacerbation: acute worsening of COPD symptoms that requires additional therapy

Assessed by history of exacerbations and hospitalizations

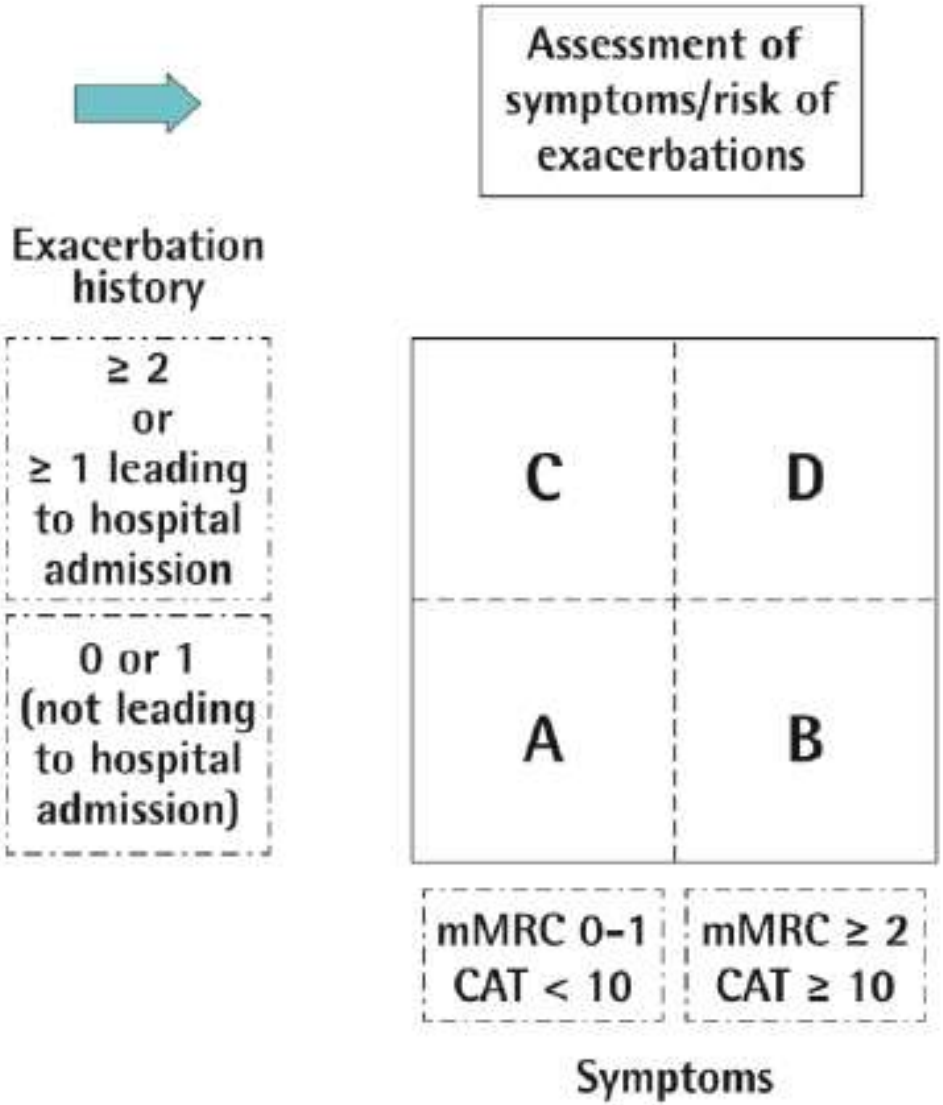
Classified as:

- Mild: treated with SABD (short acting bronchodilator) only
- Moderate: SABD plus antibiotics and/or oral corticosteroids
- Severe: ER visit or hospitalization

Risk: Exacerbation History

History of exacerbations in past year	•0-1 → low risk •≥ 2 → high risk
History of exacerbations requiring hospitalization in past year	•≥ 1 → high risk

ABCD Assessment Tool



GOLD Classification

C Few symptoms, high exacerbation risk	D More symptoms, high exacerbation risk
A Few symptoms, low exacerbation risk	B More symptoms, low exacerbation risk

Non-Pharm Therapy

NON-PHARMACOLOGIC MANAGEMENT OF COPD

PATIENT GROUP	ESSENTIAL	RECOMMENDED	DEPENDING ON LOCAL GUIDELINES
A	Smoking Cessation (can include pharmacologic treatment)	Physical Activity	Flu Vaccination Pneumococcal Vaccination
B-D	Smoking Cessation (can include pharmacologic treatment) Pulmonary Rehabilitation	Physical Activity	Flu Vaccination Pneumococcal Vaccination

TABLE 4.8

INITIAL PHARMACOLOGICAL TREATMENT

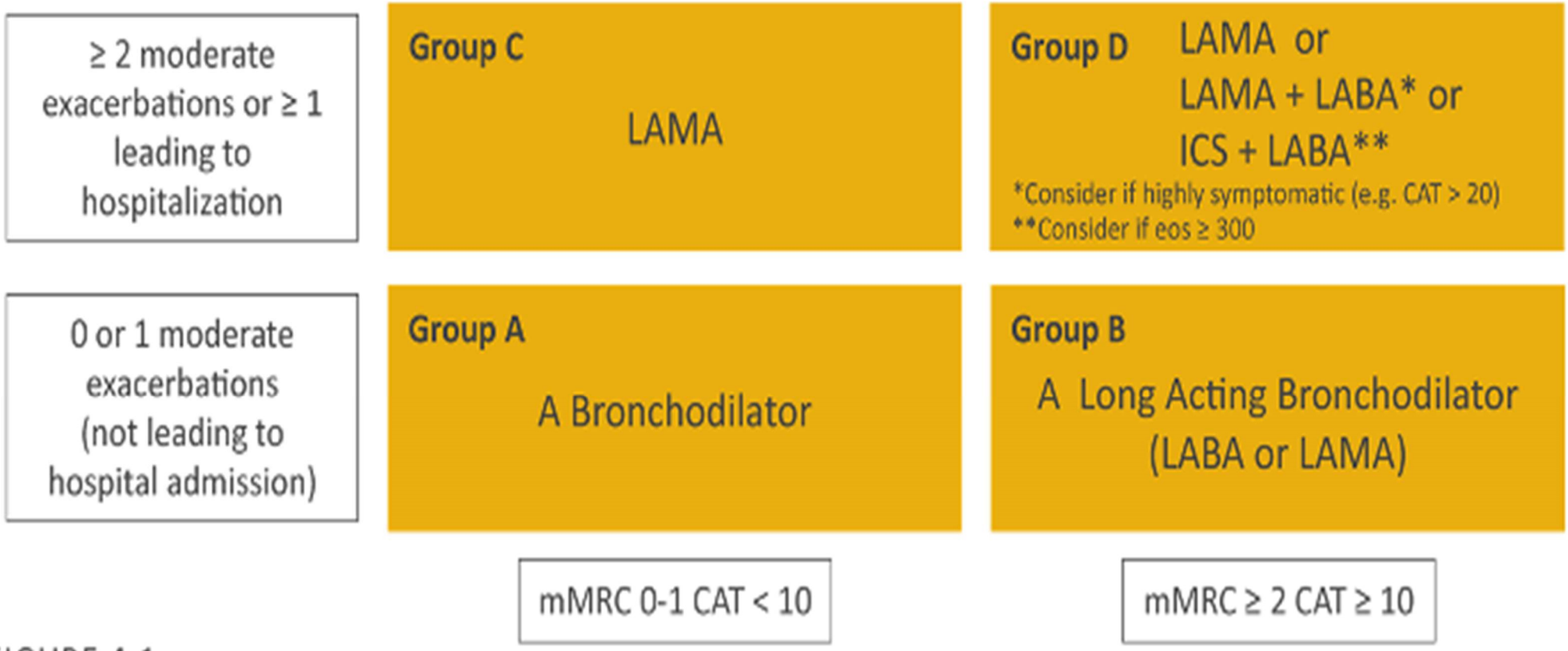


FIGURE 4.1

Definition of abbreviations: eos: blooeosinophil count in cells per microliter; mMRC: modified Medical Research Council dyspnea questionnaire; CAT™: COPD Assessment Test™.

MANAGEMENT CYCLE

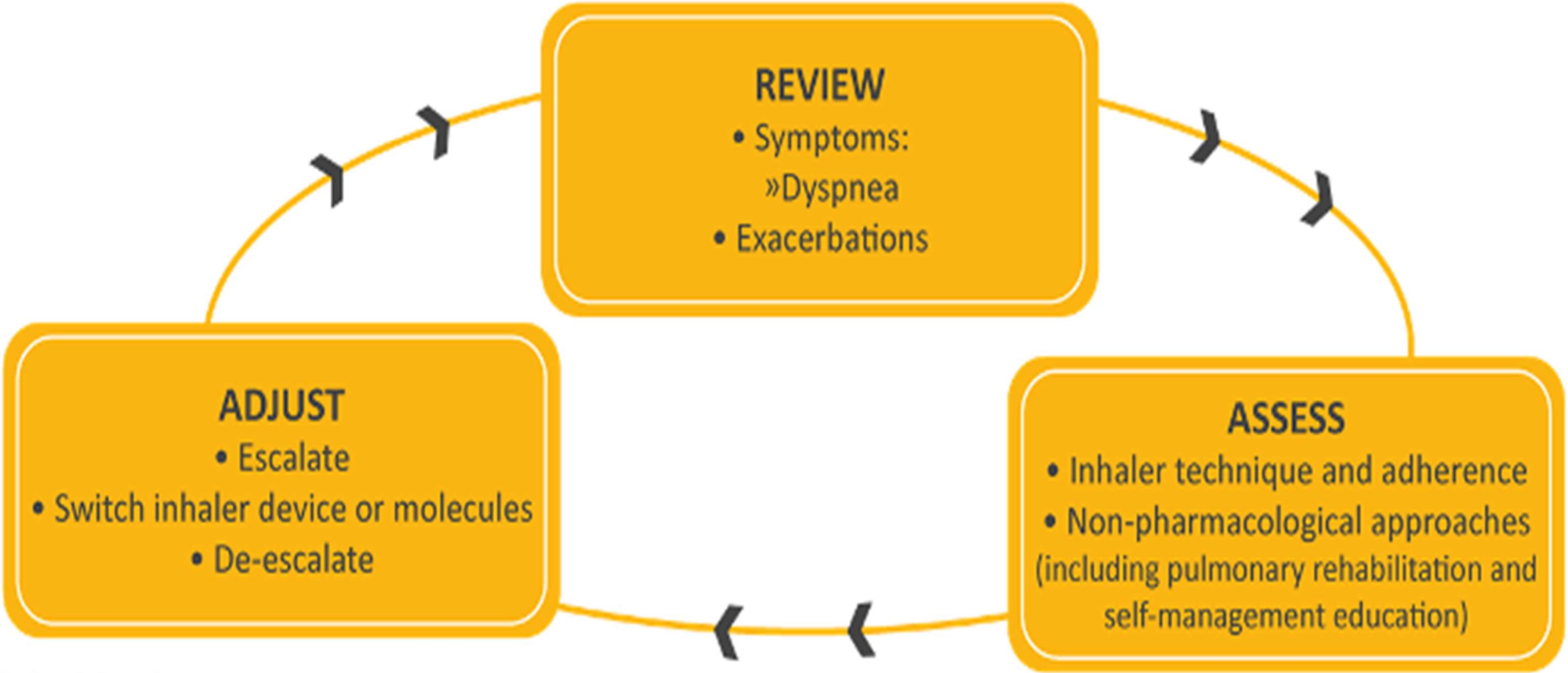


FIGURE 4.2

Monitoring Treatment Efficacy and Safety

Lung function will decline over time.

Optimal follow-up time after treatment initiation or adjustment not identified.

- CAT can be repeated every 2-3 months (trends of symptom scores more helpful than singular assessment)
- Spirometry should be assessed at least once/yr
- Smoking status – evaluate at every opportunity

Monitoring Treatment Efficacy and Safety

- Symptom control (cough, sputum production, dyspnea, fatigue, limitations to activity, sleep disturbances)
- Exacerbation history and risk
- Inhaler technique!!!
- Treatment adherence
- Side effects
- Treatment affordability

Evidence

Patients with a high risk of exacerbations tend to have severe or very severe airflow limitation

Higher exacerbation rates are associated with faster decline of FEV_1 and worsening of health status

Hospitalization for COPD exacerbation is associated with poor prognosis

CAT scores ≥ 10 are associated with significantly impaired health status

COPD Exacerbation

COPD Exacerbation

A change in the patient's baseline symptoms beyond day-to-day variability sufficient to warrant a change in management

- Hypoxemia and hypercapnia
- Respiratory acidosis and respiratory failure

Can be caused by several factors

- Most common cause are infections

Management of COPD Exacerbations – Outpatient

Bronchodilators

- SABA + SAMA (use spacer or nebulizer)

Oral corticosteroids

- ↓ recovery time
- ↑ lung function (FEV1) & PaO2
- ↓ relapse risk, treatment failure, length of hospital stay
- 40 mg prednisone daily x 5 days

Antibiotics (high suspicion for bacterial infection)

- ↑ dyspnea
- ↑ sputum production (volume)
- ↑ sputum purulence

COPD Exacerbations Indications for Hospitalization

- Marked increase in symptom severity
- Severe COPD
- New physical signs (e.g. cyanosis, peripheral edema)
- Failure to respond to outpatient treatment
- Serious co-morbidities (e.g. heart failure, arrhythmias)
- Frequent exacerbations (≥2/yr)
- Advanced age
- Insufficient home support

Management of COPD Exacerbations - Hospitalization

Oxygen, target saturation of 88-92%

Bronchodilators

- SABA + SAMA (use spacer or nebulizer)

Oral or IV corticosteroids

Antibiotics (high suspicion for bacterial infection)

- ↑ dyspnea
- ↑ sputum production (volume)
- ↑ sputum purulence

Antibiotics

Should be given to patients with ≥ 2 cardinal symptoms

- Increase in sputum purulence AND
- Increase in sputum production AND/OR
- Worsening of dyspnea

Given automatically if the patient requires mechanical ventilation

Frequent exacerbations may require sputum culture

Duration: 5-7 days

Antibiotics

When used appropriately, they can:

Shorten recovery time

Reduce risk of early relapse

Reduce risk of treatment failure

Reduce time in hospital

Antibiotic Selection for COPD Exacerbations

Patient Characteristics	Likely Pathogen	Recommended Therapy
Uncomplicated exacerbation <4 exacerbations/yr No comorbid illness -FEV1 35-50% predicted	S. Pneumoniae H. Influenzae M. catarrhalis H. Parainfluenzae (bacterial resistance is uncommon)	Macrolide (azithromycin, clarithromycin) 2nd or 3rd gen cephalosporin Doxycycline
Complicated exacerbation -Age ≥ 65 yrs + >4 exacerbations/yr -FEV1 35-50% predicted	Above pathogens + Drug resistant pneumococci β-lactamase producing H. influenza and M. catarrhalis	Amoxicillin/clavulanate Levofloxacin or moxifloxacin

Antibiotics

Choice of antibiotic depends on local infections patterns

- Aminopenicillin ± clavulanic acid
  - Amoxicillin
  - Amoxicillin/clavulanate
- Macrolide
  - Azithromycin
  - Clarithromycin
- Tetracycline
  - Doxycycline
  - Minocycline

Asthma-COPD Overlap Syndrome (ACOS)

Pts with both Asthma and COPD

Difficult to differentiate in adults with smoking history

Clinical outcomes are worse than with asthma or COPD alone

Referral to specialist if:

- Persistent symptoms/exacerbations despite treatment
- Unsure of accurate diagnosis
- Comorbidities that may interfere with assessment and management

Asthma-COPD Overlap Syndrome (ACOS)

Treatment should focus on asthma management first

ICS – improve morbidity and mortality in asthma

LABA is reasonable 2nd agent to add to regimen as they are indicated in both asthma and COPD, but should NOT be used as monotherapy

Asthma-COPD Overlap Syndrome

Asthma features

- Inhaled corticosteroids
- Not long-acting bronchodilator monotherapy

COPD

- Bronchodilators (or combination therapy)
- Not inhaled corticosteroid monotherapy

Overall Key Points

COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease

Spirometry is required to make the diagnosis; the presence of a post-bronchodilator FEV1/FVC < 0.70 confirms the presence of persistent airflow limitation

The goals of COPD assessment are to determine the level of airflow limitation, the impact of disease on the patient's health status, and the risk of future events, in order to guide therapy

Concomitant chronic disease occur frequently in COPD patients

Summary

Smoking is significant risk factor for COPD

Smoking cessation is only intervention to slow the decline in lung function

Use the ABCD assessment tool to determine initial therapy

Then reassess patients and change therapy depending on if they are having continued dyspnea or exacerbations