Asthma and Chronic Obstructive Pulmonary Disease (COPD)

Diagnostic and management fundamentals

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Learning Objectives

- Contrast pathophysiology of asthma and COPD
- Recite diagnostic criteria for asthma and COPD
- Create a management plan for a patient with asthma, COPD or asthma-COPD overlap syndrome
- Identify the interventions associated with improved or worsened mortality in those with asthma or COPD

Overall, Things are Better Today than in the Past

- Preventable deaths decreasing!
- Extreme poverty decreasing!
  - More manufacturing, roads, cars
    - But with these, more pollution

COPD: It's Even Worse than I Thought

- Year 2000, COPD 4th leading cause of death
- Year 2016: COPD 3rd leading cause of death
  - > 3 million COPD deaths globally
- In all but low-income countries, now a leading cause of death

Source: WHO

Pathophysiology of Asthma

- Bronchial inflammation
  - Generally, the cells involved in allergic response
- Bronchial hyper-responsiveness
  - Inhaled stimuli and cell-based mediators (e.g. histamine)
  - Dust, fumes, allergens, exercise, extreme temperatures, respiratory infections
- Result: airflow limitation, most pronounced in expiration, generally with high degree of reversibility with bronchodilators
  - Plus, 12-fold risk of developing COPD

Source: GINA, GOLD

Pathophysiology of COPD

- Repetitive or chronic insults
  - Inhalational exposure (e.g. cigarette smoke)
  - Chronic inflammation
  - Protease activity (e.g. alpha 1-antitrypsin deficiency)
- Causing some mixture of
  - Airway fibrosis and narrowing
  - Alveolar wall destruction
  - Goblet cell hyperplasia
  - Ciliary impairment
- Resulting in airflow limitation poorly responsive to bronchodilators
  - +/- hypoxia, hypercapnia, or increased pulmonary vascular resistance

Source: GOLD

Clinical Presentation of Asthma or COPD

- Chronic cough
- Wheeze
- Dyspnea, especially on exertion
- Recurrent lower respiratory tract infections (COPD > asthma)
- Increased perceived severity of respiratory tract infections
- Variability in symptom severity (asthma >> COPD)

Diagnosis of Asthma and COPD

Spirometric diagnosis with symptoms

There is no substitute

…but let us try to find one!

Can Airflow Limitation be Diagnosed Without Spirometry? (1/2)

Scenario	Likelihood of Airflow Limitation
Well 54-year-old US man with wheezing	21%
Well 54-year-old US man with 19 pack-years of cigarette smoking	6%
Well 54-year-old US man, 41 pack-years of cigarette smoking, in the US	60%
As above, but in Southeast Asia*	55%
As above, but in Africa*	68%
70-year-old wheezing man with 55 years of cigarette smoking and maximum laryngeal height of 3.8 cm	99%

Note: establishing presence of airflow limitation is only the first step
Plus, even among heavy smokers, < 50% will develop COPD

Can Airflow Limitation be Diagnosed Without Spirometry? (2/2)

Single Best Findings That Are the Easiest to Measure	Likelihood Ratio
Smoking status, > 40 pack-years	12
Auscultated wheezing or laryngeal height ≤ 4 cm	×4
To "Rule In" Obstructive Disease, Must Use a Multivariate Model[a]	**Posterior Odds of Disease, Probability (%)**
Smoking > 55 y and wheezing symptoms and auscultated wheezing	156 (99)
History of OAD and smoking > 40 pack-years and age ≥ 45 y and laryngeal height ≤ 4 cm	220 (99)
To "Rule Out" Obstructive Disease, Must Use a Multivariate Model[a]	**Posterior Odds of Disease, Probability (%)**
Smoking < 30 y and no wheezing symptoms and no auscultated wheezing	0.02 (1.5)
No history of OAD and smoking < 40 pack-years and age < 45 y and laryngeal height > 4 cm	0.03 (3)

Note: establishing presence of airflow limitation is only the first step

Simel DL and Keitz S (2009)

Diagnosis of Asthma and COPD

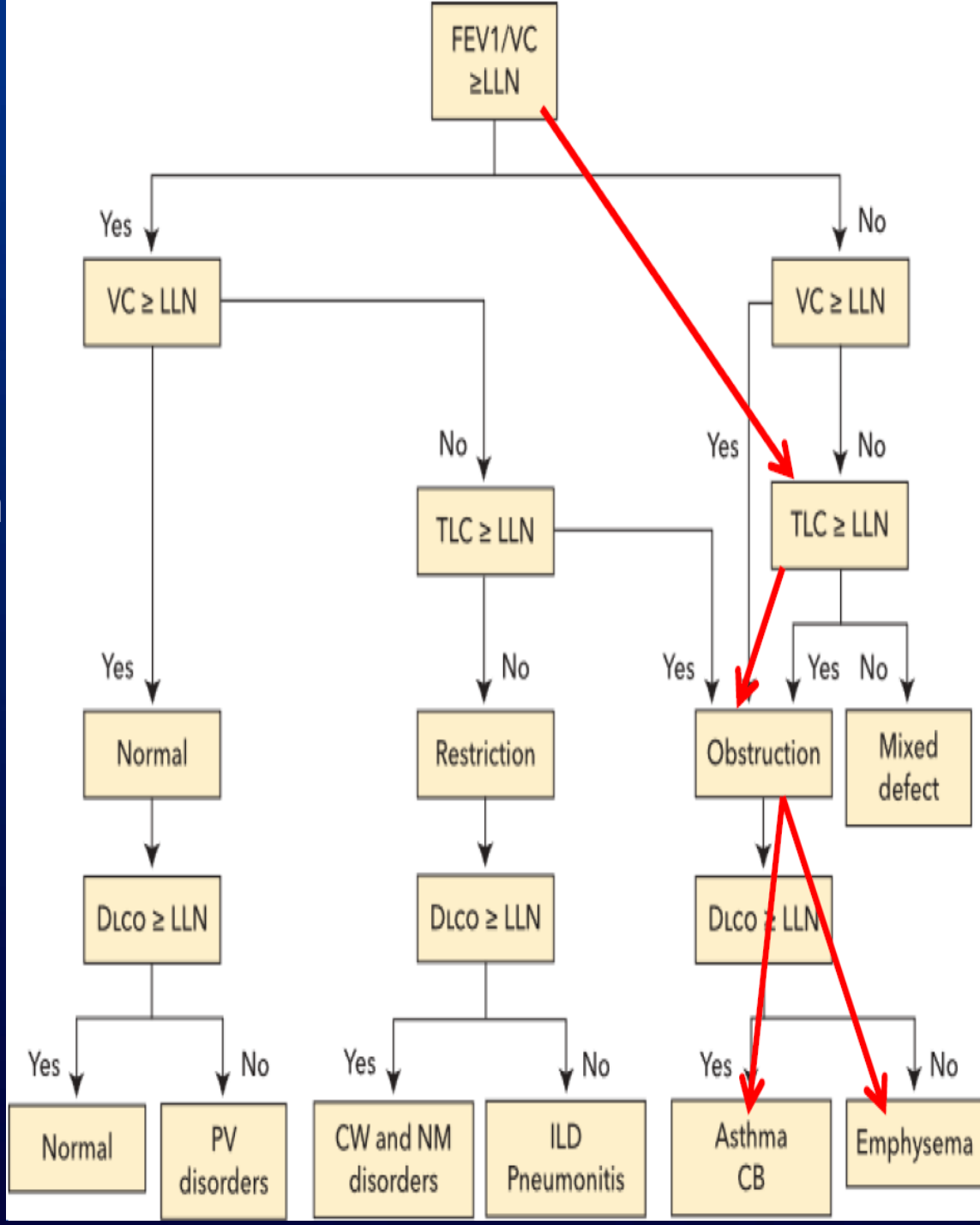
- Consider other causes of similar symptoms
  - Lung cancer
  - Chronic infections (e.g. tuberculosis)
  - Congestive heart failure
  - Interstitial lung disease
  - For cough, upper airway cough syndrome, gastroesophageal reflux disease or medications
- Spirometry for chronic, bothersome symptoms
  - No role for spirometry if no symptoms!

Diagnosing Asthma or COPD

- FEV1/FVC ratio < 70% of predicted = airflow obstruction
  - Forced expiratory volume over 1 second (FEV_1)
  - Forced vital capacity (FVC)
  - Reference values by age, height, sex, race
  - Persistent limitation after bronchodilator: COPD
  - FEV_1 improves ≥12% and ≥ 200 mL after bronchodilator: asthma

Pitfalls

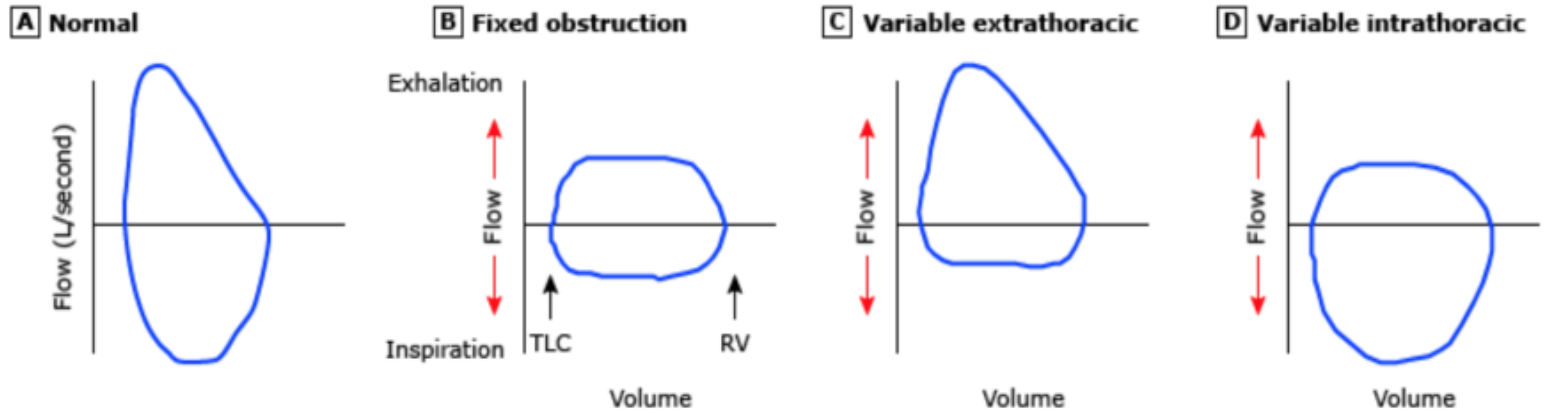
- Restrictive disease
- Poor quality study
- Intermittent obstruction



Source: MKSAP 18

Notes on Airway Obstruction

Flow-volume loops in upper airway obstruction



(A) Normal flow-volume loop: the expiratory portion of the flow-volume curve is characterized by a rapid rise to the peak flow rate, followed by a nearly linear fall in flow. The inspiratory curve is a relatively symmetrical, saddle-shaped curve.
(B) Fixed upper airway obstruction (can be intrathoracic or extrathoracic): flow limitation and flattening are noted in both the inspiratory and expiratory limbs of the flow-volume loop.
(C) Dynamic (or variable, nonfixed) extrathoracic obstruction: with flow limitation and flattening are noted on the inspiratory limb of the loop.
(D) Dynamic (or variable, nonfixed) intrathoracic obstruction: flow limitation and flattening are noted on the expiratory limb of the loop.

Aboussouan LS and Stoller JK. “Flow-volume loops.” In: UpToDate, Barnes PJ and Wood RA (Eds), UpToDate, Waltham, MA, 2019.

Special Asthma Variants

- Allergic variant: high sputum eosinophils, high exhaled nitric oxide
  - If refractory, anti-IgE, anti-IL4 or anti-IL5 treatment may be considered
- Cough variant asthma
- Exercise-induced asthma
  - Give β_2-agonists prior to exercise
- Occupational asthma
- Aspirin-exacerbated respiratory disease
- Reactive airways dysfunction syndrome
  - New, persistent (3 months or longer) asthma symptoms after intense inhalational exposure
- Allergic bronchopulminary aspergillosis
  - High IgE, Aspergillus hypersensitivity, imaging findings
  - Treat with steroids ± antifungals

Chronic Cough with Normal Spirometry

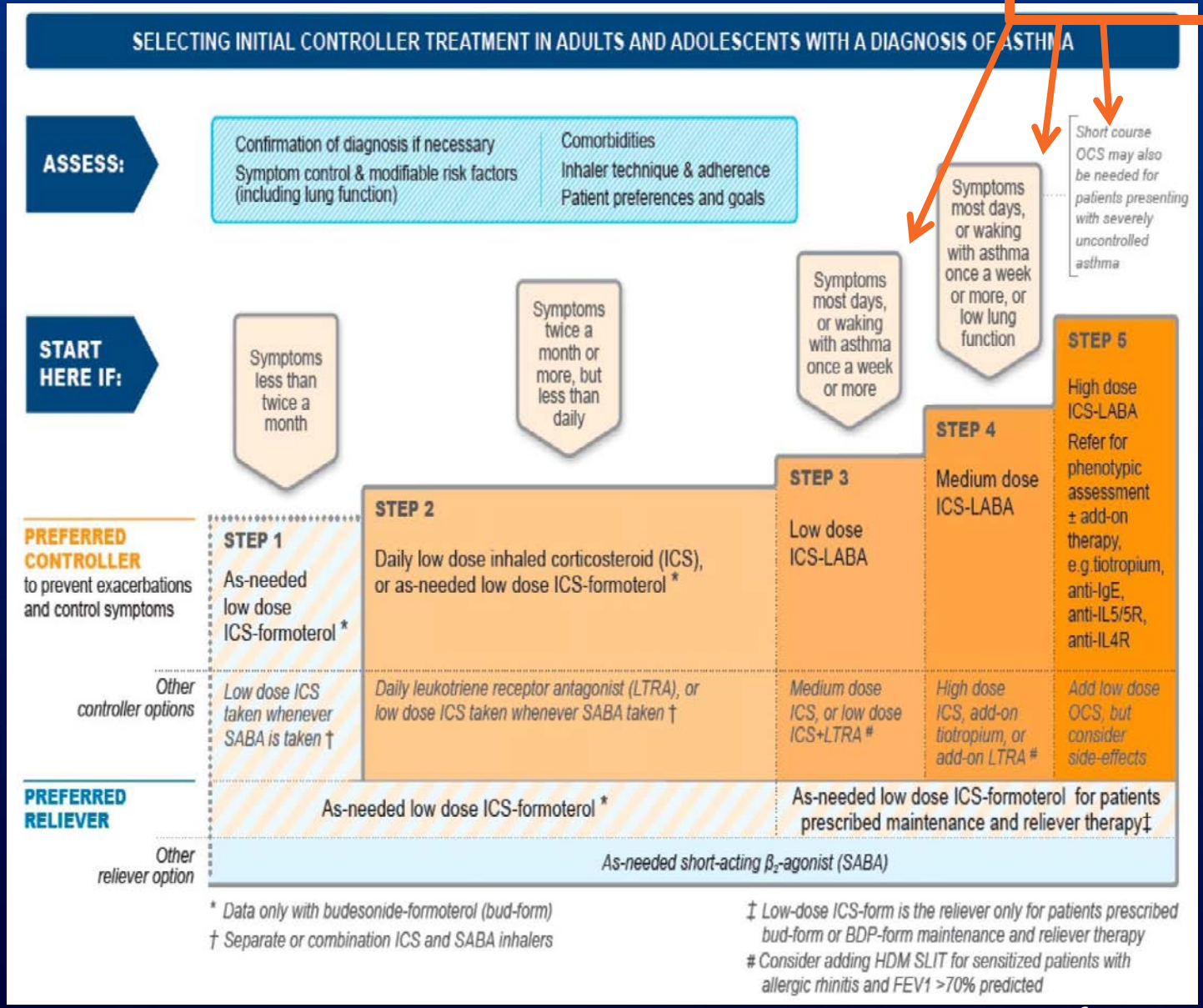
- Spirometry after “provoking” with exercise, cold air, or methacholine (known as “bronchoprovocation”)
- Chest radiograph, especially if at risk for lung cancer or indolent infection (e.g. TB)
- Exclude medication side effect (e.g. ACE inhibitors)
- Consider empiric, stepwise treatment
  - Upper airway cough syndrome: nasal corticosteroid
  - Gastroesophageal reflux disease: PPI or H_2 blocker
  - If no bronchoprovocation, could trial asthma treatment

Asthma/COPD Pharmacotherapy Acronyms

- SABA = short-acting β_2-agonist (e.g. albuterol)
- SAMA = short-acting muscarinic antagonist (e.g. ipratroium)
- LABA = long-acting β_2-agonist (e.g. salmeterol)
- LAMA = long-acting muscarinic antagonist (e.g. tiotropium)
- LTRA = leukotriene receptor antagonist (e.g. montelukast)
- ICS = inhaled corticosteroid (e.g. beclomethasone)
- OCS = oral corticosteroid (e.g. prednisone)

Asthma Treatment

+LAMA?



Most adults and adolescents start at step 2

Reference: GINA

Special Note

- Don’t use LABA without concomitant ICS
  - Associated with higher risk of asthma-related death

GINA Questionnaire to Assess Asthma Control

- In the past 4 weeks, as the patient had:
  - Daytime symptoms more than 2x/week?
  - Any night waking due to asthma?
  - SABA reliever needed more than 2x/wk?
  - Any activity limitation due to asthma?
- None of these: well controlled
- 1-2 of these: partly controlled
- 3-4 of these: uncontrolled

Evaluation of Uncontrolled Asthma

- First, verify inhaler technique
- Next, evaluate for triggers – "AIR-SMOG"
  - **A**llergens
  - **I**rritants/infection
  - **R**hinitis/sinusitis
  - **S**moking/sleep apnea/stress
  - **M**edications (β-blockers, NSAIDs)
  - **O**ccupational exposure
  - **G**astroesophageal reflux disease

Step Up Asthma Treatment if Truly Uncontrolled

- First, verify inhaler technique and adherence
- Next, control triggers
- Next, step up therapy
  - If symptoms are severe, step up therapy while addressing the other components

Asthma Action Plan for Exacerbations

- Early and mild:
  - Increase use of reliever (e.g. albuterol)
  - Increase controller (quadruple dose)
  - Review response

Asthma Action Plan for Exacerbations

- Late or moderate
  - Peak expiratory flow or FEV1 < 60% of patient's best
  - No improvement after 48 hours
  - Steps:
    - Continue reliever
    - Continue controller
    - Add prednisone or prednisolone 40-50 mg daily (adults; weight-based in children)
    - Evaluation by clinician

Treating Asthma Exacerbations in Clinic

- No tachypnea, hypoxia, increased work of breathing
  - Administer 4-10 puffs of short-acting β_2-agonist by metered dose inhaler+spacer, or nebulizer
    - If improving, can return home with close follow-up
    - If not improving, transfer to acute care facility

Treating Severe Asthma Exacerbations

- Tachypnea, hypoxia, increased work of breathing or decreased level of consciousness
  - Transfer to acute care facility
    - Nebulized bronchodilators, systemic corticosteroid, possibly IV magnesium sulfate, intensive care interventions if indicated

Asthma Treatments in Pregnancy

- Oral and inhaled corticosteroids
- Short- and long-acting β_2-agonists
- Leukotriene receptor antagonists

- No evidence of fetal harm for any of above

Principles of COPD Management

- Smoking cessation
- Minimization of particulate exposure
  - Indoor open fires, poorly functioning stove
  - Occupational dusts or fumes
- Protect from infections
  - Influenza virus, pneumococcus (PPSV-23 ± PCV-13)
- Treatment intensity depends on symptoms, risk of exacerbations
- Pulmonary rehabilitation, if available
- Supplemental oxygen, if candidate

Address Smoking at Each Visit

- One study in Nigeria
  - 70% of patients with COPD were smoking
  - 32% were counseled on smoking cessation

Desalu et al (2013)

- Counseling improves quit rates
- Use nicotine replacement therapy, pharmacotherapy or a combination
  - Varenicline, bupropion are main medications

GOLD Grading: Spirometry

If FEV1/FVC <0.7	
FEV1 ≥ 80%	Mild
FEV1 <80% and ≥ 50%	Moderate
FEV1 <50% and ≥ 30%	Severe
FEV1 <30%	Very Severe

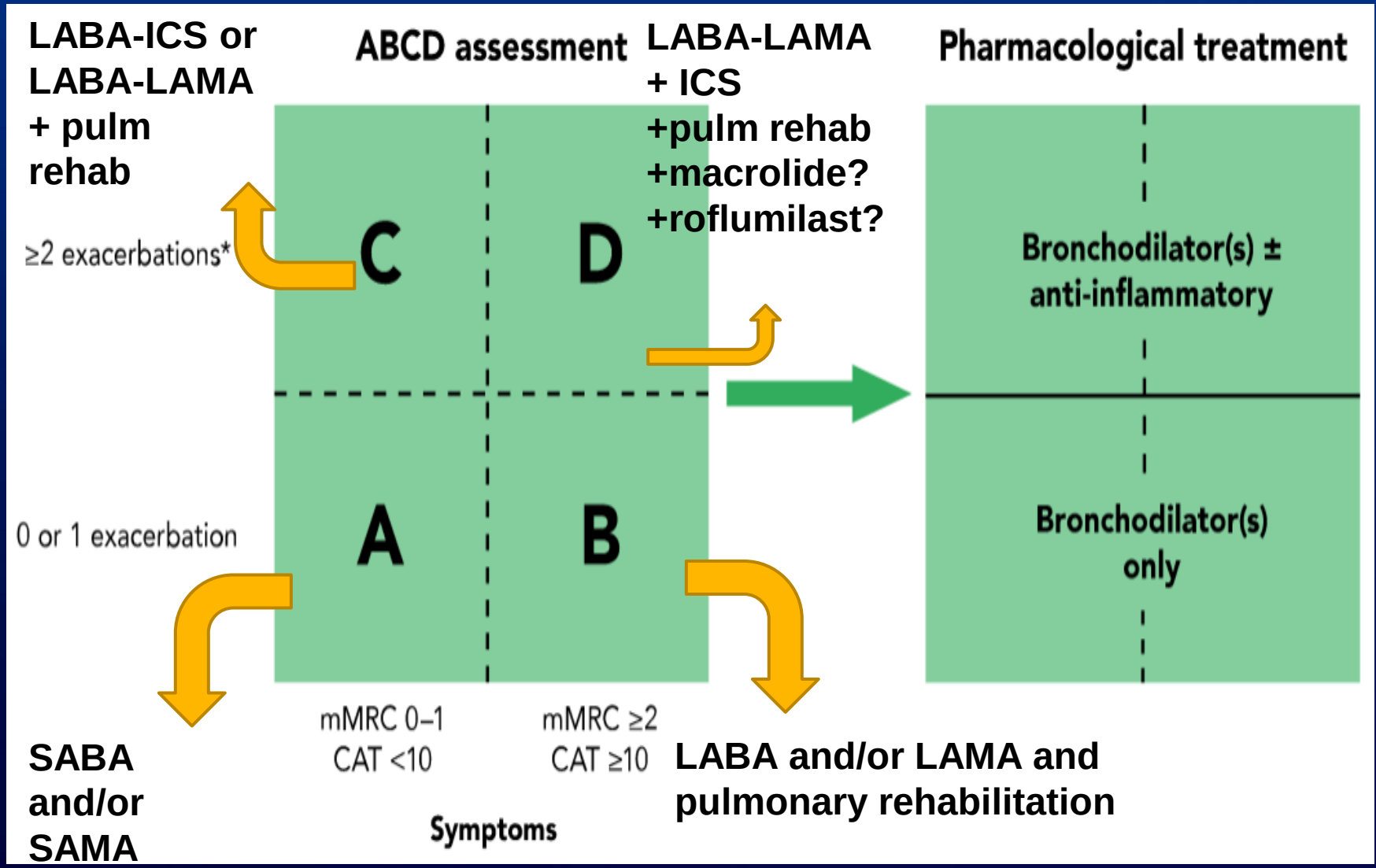
A single FEV1 has low predictive value for exacerbations
A decreasing FEV1 has more predictive value

GOLD Staging: Symptoms and Exacerbations

- mMRC 0: breathless with strenuous exercise only
- mMRC 1: breathless when hurrying on level ground, or when walking up slight incline
- mMRC 2: must walk more slowly than peers, or breathless walking at own pace
- mMRC 3: breathless walking 100 m
- mMRC 4: breathless dressing

- Low risk: 0-1 exacerbation in one year
- High risk: 2+ exacerbations in one year

Pharmacotherapy for Stable COPD



ICS risky if frequent infections or history of mycobacterial infection

Reference: GOLD

COPD Medications that Reduce Mortality?

- Just one, but only for some

- Supplemental oxygen indications:
  - Resting SpO2 < 90% with right heart failure or erythrocytosis, or
  - Resting SpO2 < 89% without right heart failure
    - Mortality benefit really for those with resting SpO2 < 81%

Treatment of COPD Exacerbation

- Nonsevere: bothersome symptoms without decompensation
  - Alert
  - Minimal if any tachypnea
  - Minimal change in SpO2 from baseline
  - Any one of these:
    - Increased dyspnea
    - Increased sputum volume
    - Increased sputum production
- Treat nonsevere exacerbations at home (or possibly hospital)
  - SABA ± SAMA every 4-6 hours and as needed
  - Steroids: 5 days of prednisone 40 mg daily
  - Antibiotics: only if evidence of pneumonia

Treatment of COPD Exacerbation

- Severe: respiratory failure, or any two of
  - Increased dyspnea
  - Increased volume of sputum
  - Increased purulence of sputum
- Treat severe exacerbations in hospital:
  - SABA ± SAMA every 4-6 hours and as needed
  - Steroids: 5 days of prednisone 40 mg daily
    - Occasionally (but not often) longer and more
  - Antibiotics: ceftriaxone or levofloxacin
    - Cefepime or piperacillin-tazobactam if risk of drug-resistant organisms
  - Respiratory failure
    - CPAP or BiPAP if awake
    - Intubation and mechanical ventilation if obtunded
  - Nonresolving: consider pulmonary embolism

Asthma-COPD Overlap Syndrome (ACOS)

- **Major Criteria (need 2)**
  - **Positive bronchodilator response (FEV1 ≥15% and ≥400 ml)**
  - **Sputum eosinophilia**
  - **Personal history of asthma**
- **Minor Criteria (need 2)**
  - **High total IgE**
  - **Personal history of atopy**
  - **Positive bronchodilator (FEV1 ≥12% and ≥200 ml)**
- **Reach for ICS earlier here than for those with COPD alone**

Soler-Cataluna et al. Archivos de Bronconeumologia 2012; 48(9).

Advanced COPD

- Severe symptoms despite optimal medications
- Numerous exacerbations despite optimal medications
- Consider procedural treatments, if available
- Consider specialty palliative care ± hospice, if available
  - Opioids may be used for dyspnea

Procedural Treatment Options for Severe Disease

- Bronchial thermoplasty for severe, refractory asthma
  - Radiofrequency ablation of airway smooth muscle
  - Only if $FEV_1 > 60\%$
  - Recommended in context of clinical trial
  - Quality of life purposes
- Lung volume reduction surgery for some with severe, refractory COPD
  - Only for very carefully selected patients
  - Quality of life purposes
- Lung transplantation
  - Only for very carefully selected patients
  - Potential to improve quality and length of life

Summary

Diagnosing Asthma or COPD

- FEV1/FVC ratio < 70% of predicted = airflow obstruction
  - Forced expiratory volume over 1 second (FEV_1)
  - Forced vital capacity (FVC)
  - Reference values by age, height, sex, race
  - Persistent limitation after bronchodilator: COPD
  - FEV_1 improves ≥12% and ≥ 200 mL after bronchodilator: asthma

Asthma Treatment

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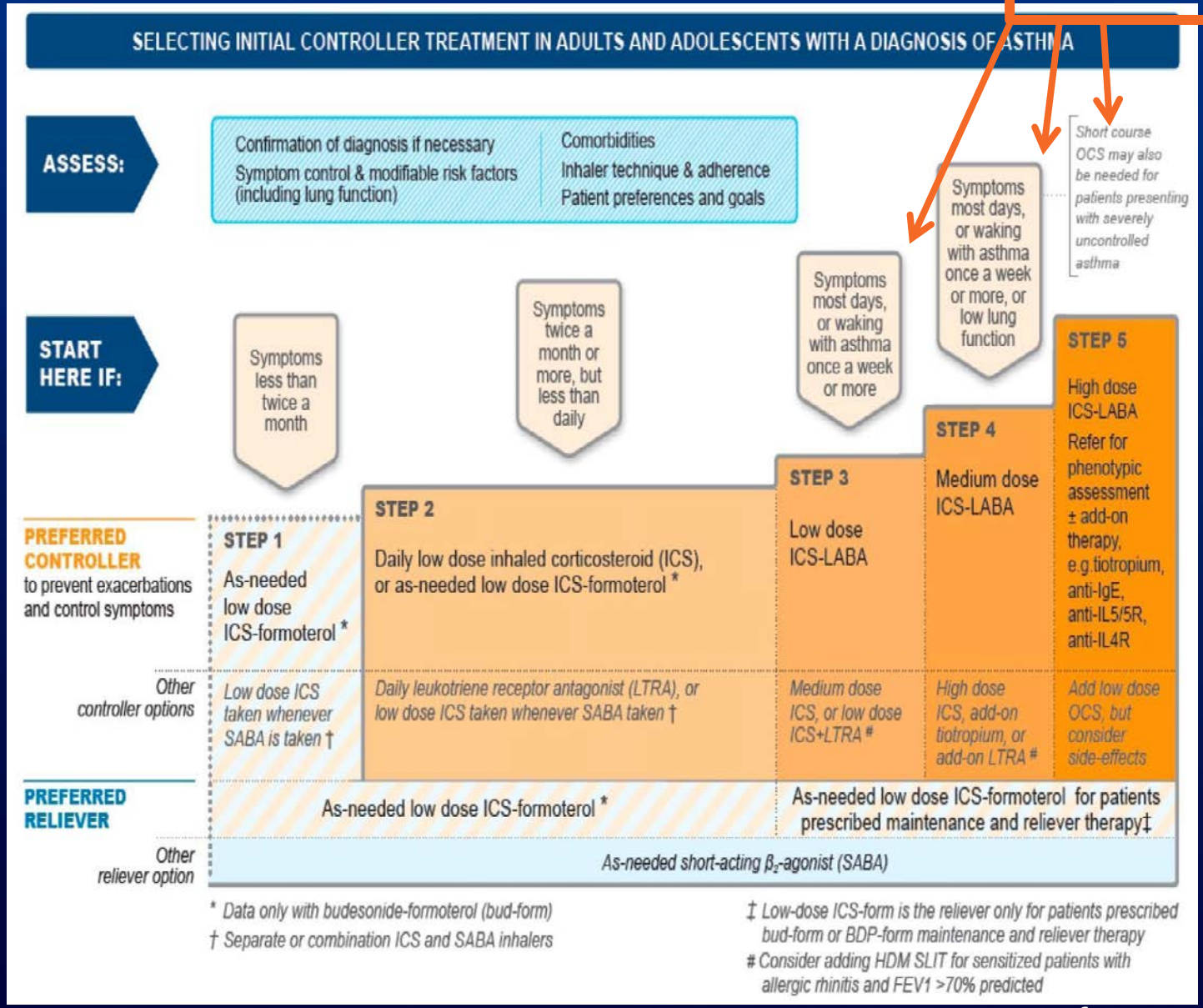

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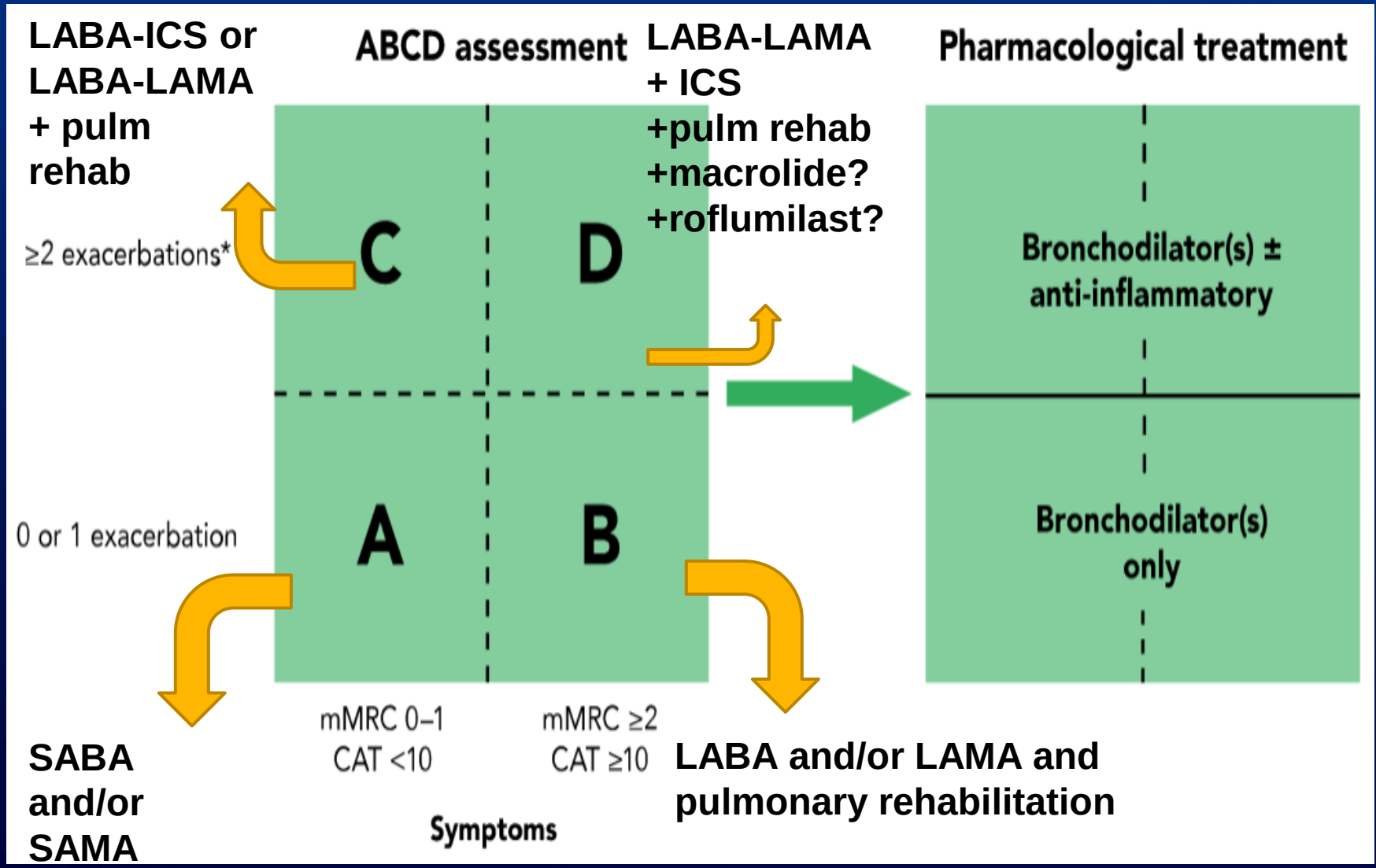

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Asthma Action Plan for Exacerbations

- Increase use of reliever (e.g. albuterol)
- Quadruple dose of controller
- Add oral corticosteroids if no improvement, or if severe
  - Prednisone 40 mg daily reasonable to start
  - Duration less clear than in COPD, and based on symptoms
    - 5-14 days, typically

Treatment of COPD Exacerbation

- Nonsevere: bothersome symptoms without decompensation
- Severe: two cardinal manifestations or clinical decompensation
- Treat nonsevere exacerbations at home (or possibly hospital)
- SABA ± SAMA every 4-6 hours and as needed
- Steroids: 5 days of prednisone 40 mg daily
- Antibiotics:
  - Nonsevere exacerbation: only if evidence of pneumonia
  - Any severe exacerbation
- CPAP or BiPAP if awake with respiratory failure
- Intubation with mechanical ventilation if respiratory failure and obtunded

References (1/2)

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- Desalu OO, Onyedum CC, Adeoti AO et al. Guideline-based COPD management in a resource-limited setting - physicians' understanding, adherence and barriers: a cross-sectional survey of internal and family medicine hospital-based physicians in Nigeria. Prim Care Respir J. 2013 Mar;22(1):79-85. doi: 10.4104/pcrj.2013.00014.

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