

بنام خداوند جان و خرد

COPD MANAGMENT

Dr Akbar Sharifi, Pulmonologist

Pathogenesis

Biomarkers

Treatable
traits

Mortality

COPD MANGMENT

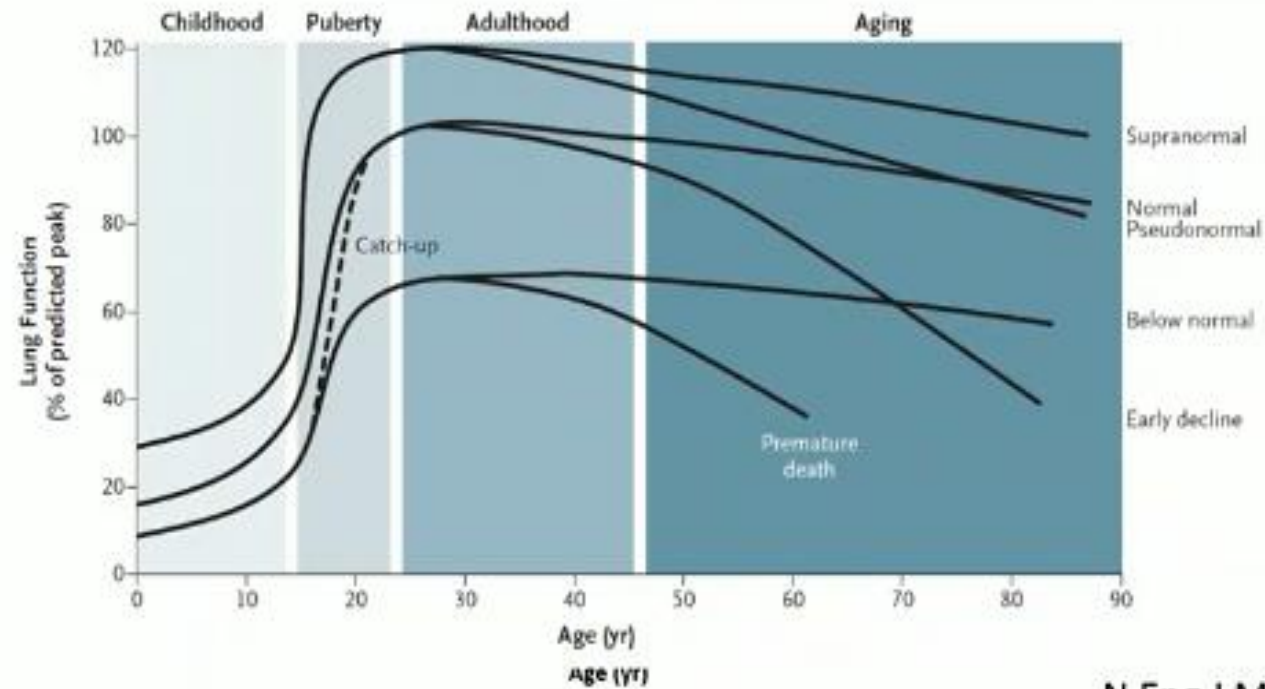


REVIEW ARTICLE

Jeffrey M. Drazen, M.D., Editor

Update on the Pathogenesis of Chronic Obstructive Pulmonary Disease

Alvar Agustí, M.D., Ph.D., and James C. Hogg, M.D., Ph.D.



N Eng J Med 2019; 381: 1248-56



EDITORIAL
COPD



Time for a change: anticipating the diagnosis and treatment of COPD

Alvar Agusti^{1,2}, Bernardino Alcazar^{2,3}, Borja Cosio^{2,4}, Jose Maria Echave⁵, Rosa Faner², Jose Luis Izquierdo^{6,7}, Jose Maria Marin^{2,8}, Juan Jose Soler-Cataluña⁹ and Bartolome Celli¹⁰, on behalf of the Scientific Committee of the ANTES programme

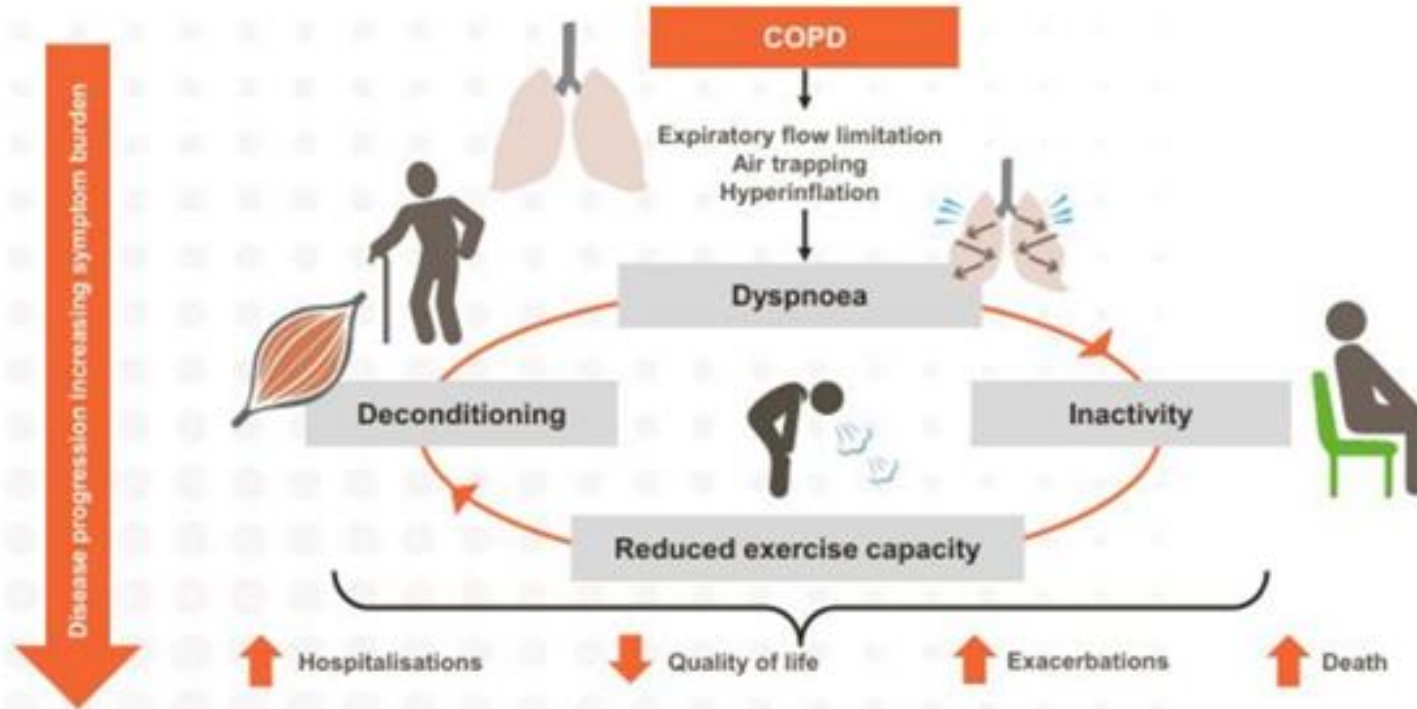


Eur Respir J 2020; 56; 2002104

The central role of airflow limitation leads to the key symptoms in COPD¹



- Dynamic hyperinflation results in a cycle of deconditioning, and a decrease in quality of life and health status²



1. Barnes PJ et al. Nat Rev Dis Primers. 2015;1:15076; 2. Cooper CB. Respir Med. 2009;103:325–34

What are the goals of assessing COPD?



The level of airflow limitation



The impact of disease on the health status of the patient



The risk of future events (such as exacerbations, hospital admissions, or death)



All of these are required to guide therapy.¹

Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of COPD 2021 Report

It should be noted that there is only a **weak correlation between FEV1**, symptoms and impairment of a patient's health status.

For this reason, formal symptomatic assessment is required.

In the past, COPD was viewed as a disease largely characterized by breathlessness.

A simple measure of breathlessness such as the Modified British Medical Research Council (**mMRC**) Questionnaire and COPD Assessment Test (**CAT**)

Table 64.1 The BODE Index: Four Variables Predictive of Survival in Patients with COPD

Variable	POINTS ON THE BODE INDEX			
	0	1	2	3
B: Body mass index (kg/m ²)*	>21	≤21	—	—
O: FEV ₁ (% of predicted) [†]	≥65	50–64	36–49	≤35
D: Distance walked in 6 min (m)	≥350	250–349	150–249	≤149
E: mMRC dyspnea scale (score)	0–1	2	3	4

Values (0-3) are assigned to each variable and summed, providing a score from 0 to 10.

*Values for body mass index are 0 or 1 owing to the inflection point in the inverse relationship between survival and body mass index at a value of 21 kg/m².

[†]FEV₁ categories are based upon stages identified by the American Thoracic Society.

FEV₁, forced expiratory volume in 1 second; mMRC, modified Medical Research Council.

From Celli B, Goldstein R, Jardim J, Knobil K. Future perspectives in COPD. *Respir Med.* 2005;99:541–548.

Table 64.2 Estimates of Mortality Based on BODE Index

BODE Index Score	MORTALITY RATE (%)		
	12 Months	24 Months	52 Months
0–2	2	6	19
3–4	2	8	32
5–6	2	14	40
7–10	5	31	80

Index score is used to predict mortality at different times.

Data from Celli BR, Cote CG, Marin JM, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med.* 2004;350(10):1005–1012.

Tools to assess symptoms: mMRC dyspnoea scale



- The **mMRC** dyspnoea scale provides a simple measure of **breathlessness**^{1,2}
- It correlates well with other measures of health status and predicts overall mortality risk.^{1,2}
- An mMRC score > 2 is the threshold for separating less breathlessness (scores of < 2) from more breathlessness (scores of ≥ 2)¹

Modified MRC dyspnoea scale

Please tick only 1 box that applies to you (ONE BOX ONLY) (Grade 0-4)

mMRC Grade 0	I only get breathless with strenuous exercise	<input type="checkbox"/>
mMRC Grade 1	I get short of breath when hurrying on the level or walking up a slight hill	<input type="checkbox"/>
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	<input type="checkbox"/>
mMRC Grade 3	I stop for breath after walking about 100 metres or after a few minutes on the level	<input type="checkbox"/>
mMRC Grade 4	I am too breathless to leave the house or I am breathless when dressing or undressing	<input type="checkbox"/>

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of COPD 2021 Report

2. Bestall JC et al. Thorax. 1999;54:581-86

Assessing health status in COPD patients: CAT and SGRQ tools



- Several detailed questionnaires are available for assessing health status in COPD patients, these include the COPD Assessment Test (CAT) and the St George's Respiratory Questionnaire (SGRQ)^{1,2}

The CAT is an 8-item measure of health status impairment in COPD. Scores > 10 signify that regular treatment for COPD is required^{1,3}

CAT Assessment			Score
For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.			
Example: I am very happy <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> I am very sad			
I never cough	<input type="radio"/> <input type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	I cough all the time	
I have no phlegm (mucus) in my chest at all	<input type="radio"/> <input type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	<input type="radio"/> <input type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	<input type="radio"/> <input type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	<input type="radio"/> <input type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	<input type="radio"/> <input type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	<input type="radio"/> <input type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	I don't sleep soundly because of my lung condition	
I have lots of energy	<input type="radio"/> <input type="radio"/> <input checked="" type="radio"/> <input type="radio"/> <input type="radio"/>	I have no energy at all	
Total Score			

The SGRQ is the most widely documented comprehensive measure; scores <25 are uncommon in diagnosed COPD patients, and scores ≥ 25 should be considered the threshold for considering regular treatment for COPD symptoms^{1,4,5}

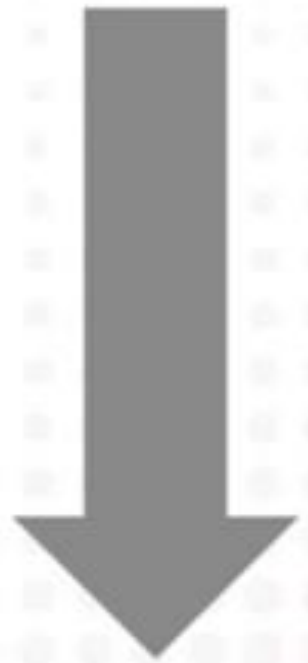
Questions about how much chest trouble you have had over the past 3 months					
	Please tick (✓) one box for each question:				
	most days a week	several days a week	a few days a month	only with chest infections	not at all
1. Over the past 3 months, I have coughed:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Over the past 3 months I have brought up phlegm (sputum):	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Over the past 3 months, I have had shortness of breath:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Over the past 3 months, I have had attacks of wheezing:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. During the past 3 months how many severe or very unpleasant attacks of chest troubles have you had?	Please tick (✓) one: more than 3 attacks <input type="checkbox"/> 3 attacks <input type="checkbox"/> 2 attacks <input type="checkbox"/> 1 attack <input type="checkbox"/> no attacks <input type="checkbox"/>				

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of COPD 2021 Report
2. Bestall JC et al. Thorax. 1999;54:581-86; 3. Jones PW et al. Eur Resp J 2009;34: 648-654; 4. Jones PW et al. Am Rev Resp Dis 1992;145:1321-1327; 5. SGRQ, original version.

Maintenance therapy for stable COPD: Where do we stand today?



We have clear treatment goals



Reduce symptoms

- Relieve symptoms
- Improve exercise tolerance
- Improve health status



Reduce risk

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

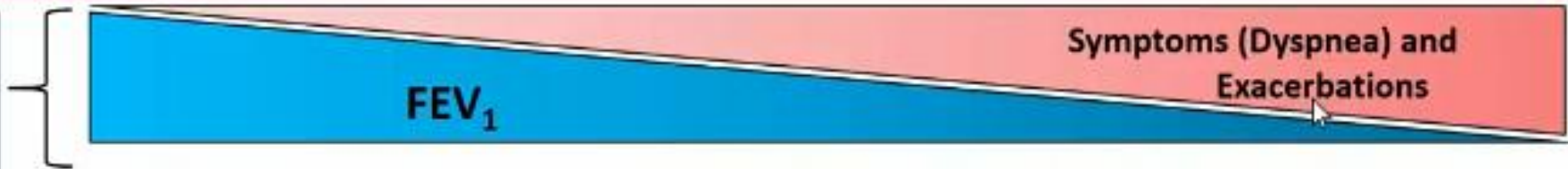
These goals should be achieved with minimal side effects

DRUGS

- Bronchodilators : long acting Beta2-agonists(LABA), SABA
- Antimuscarinic drugs(LAMAs , SAMAs)
- Inhaled corticosteroids (ICS)
- Methylxanthines
- Roflumilast
- Anti-inflammatory agents

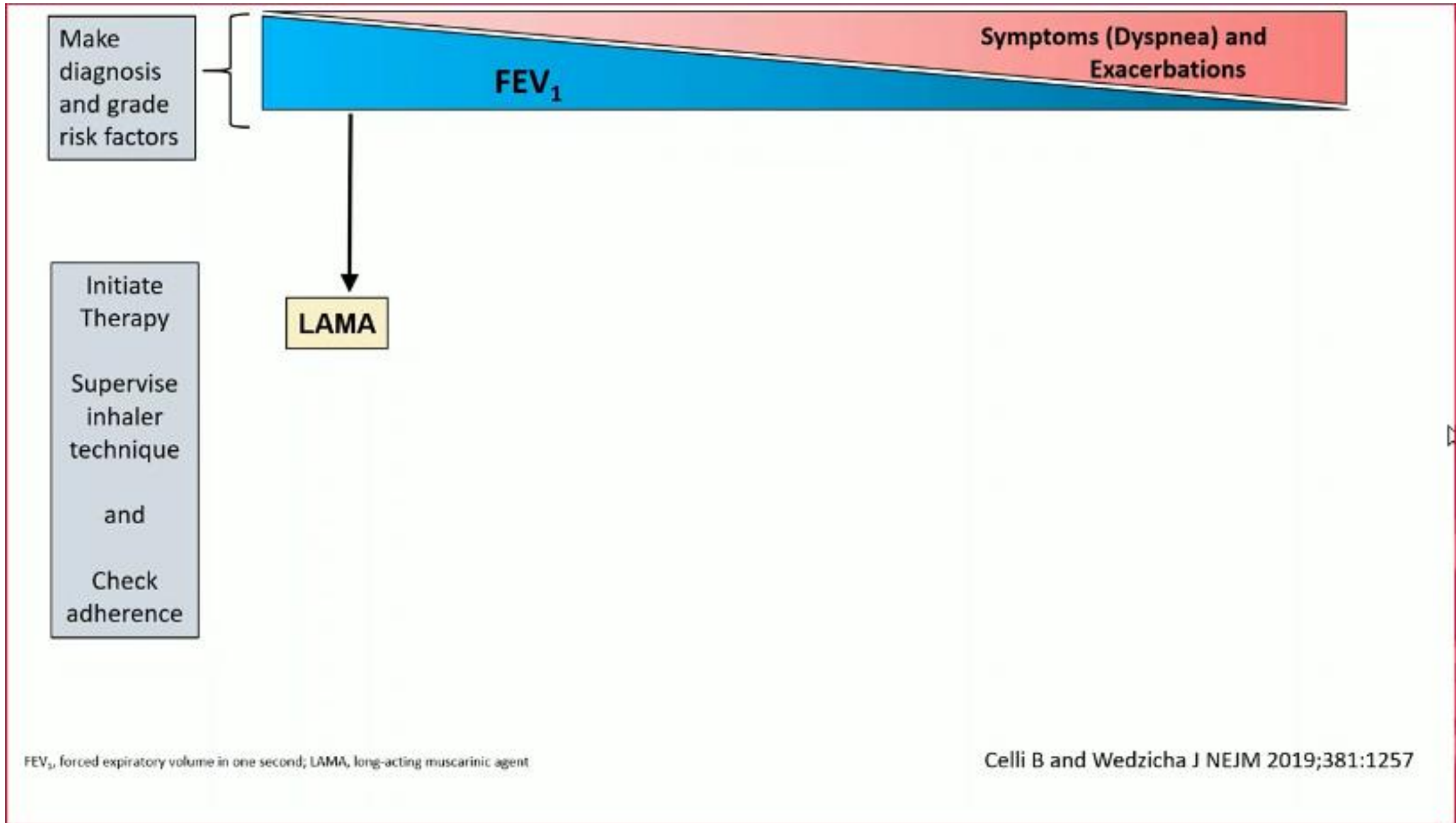
- Bronchodilators are the cornerstone of COPD pharmacotherapy
- In patients with milder COPD, LAMA may suffice
- LAMA/LABA combinations bronchodilate more than single agents and numerically improve other outcomes
- They are well tolerated at the right dose
- We should start therapy earlier in the course of the disease

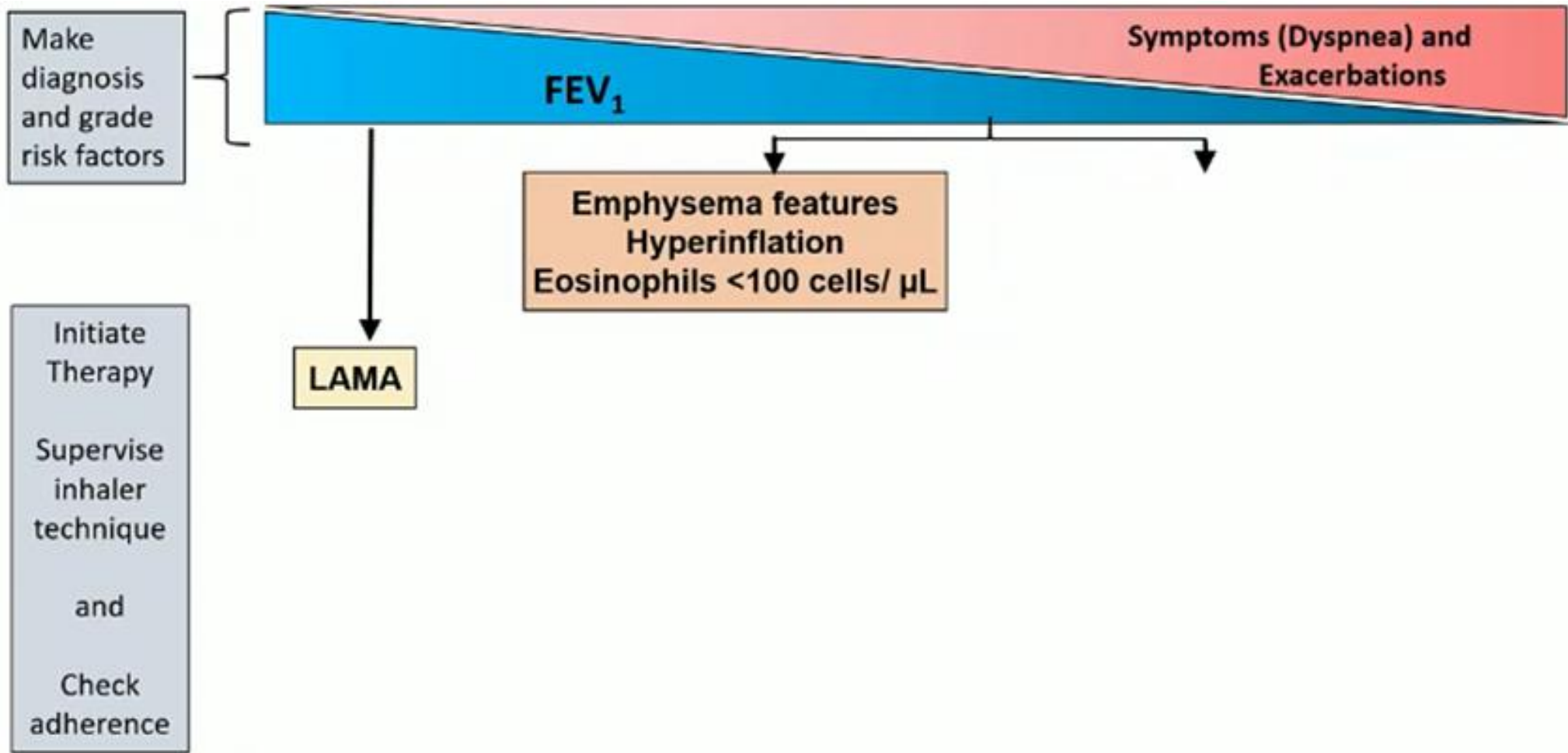
Make diagnosis and grade risk factors



FEV_1 , forced expiratory volume in one second; LAMA, long-acting muscarinic agent

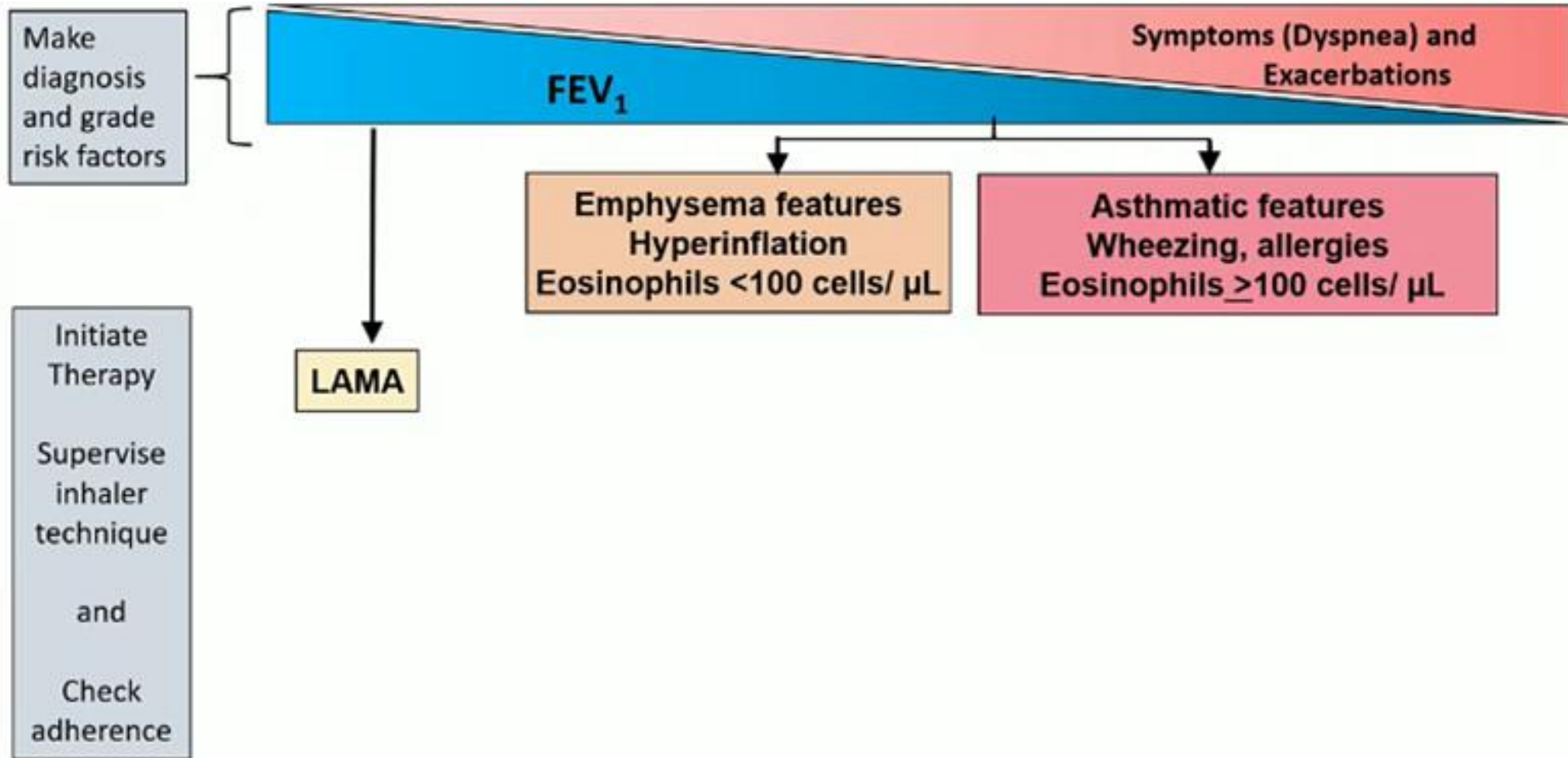
Celli B and Wedzicha J NEJM 2019;381:1257





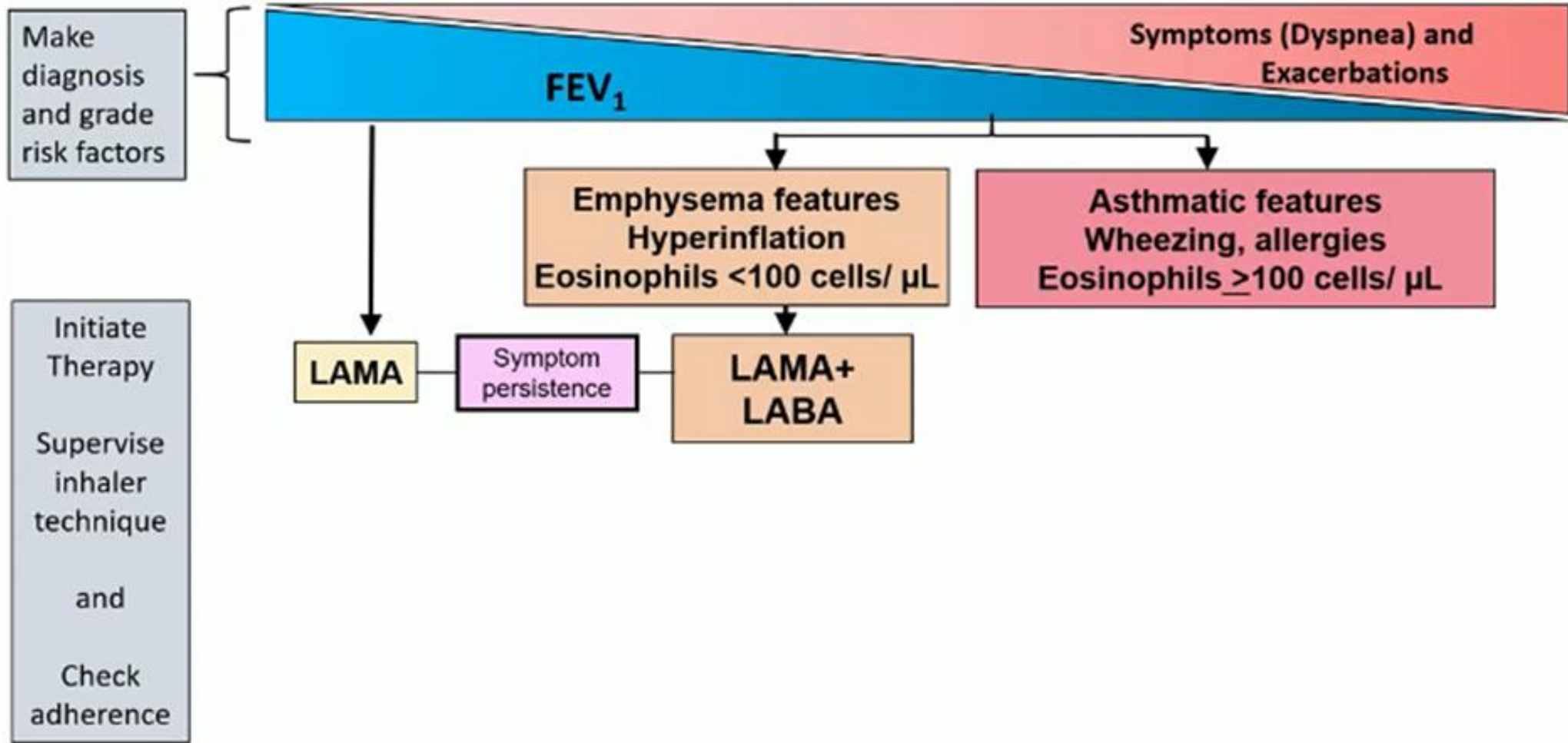
FEV₁, forced expiratory volume in one second; LAMA, long-acting muscarinic agent

Celli B and Wedzicha J NEJM 2019;381:1257



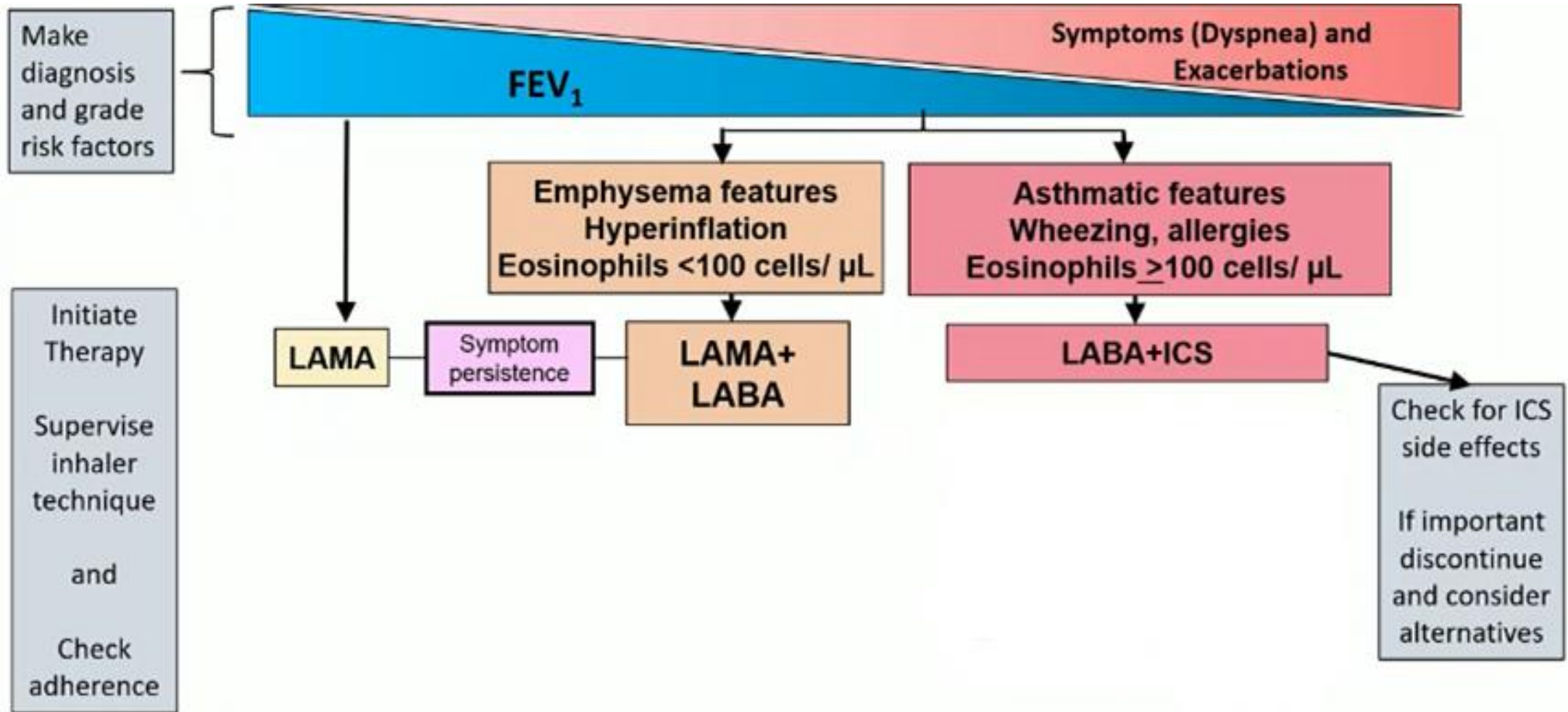
FEV₁, forced expiratory volume in one second; LAMA, long-acting muscarinic agent

Celli B and Wedzicha J NEJM 2019;381:1257



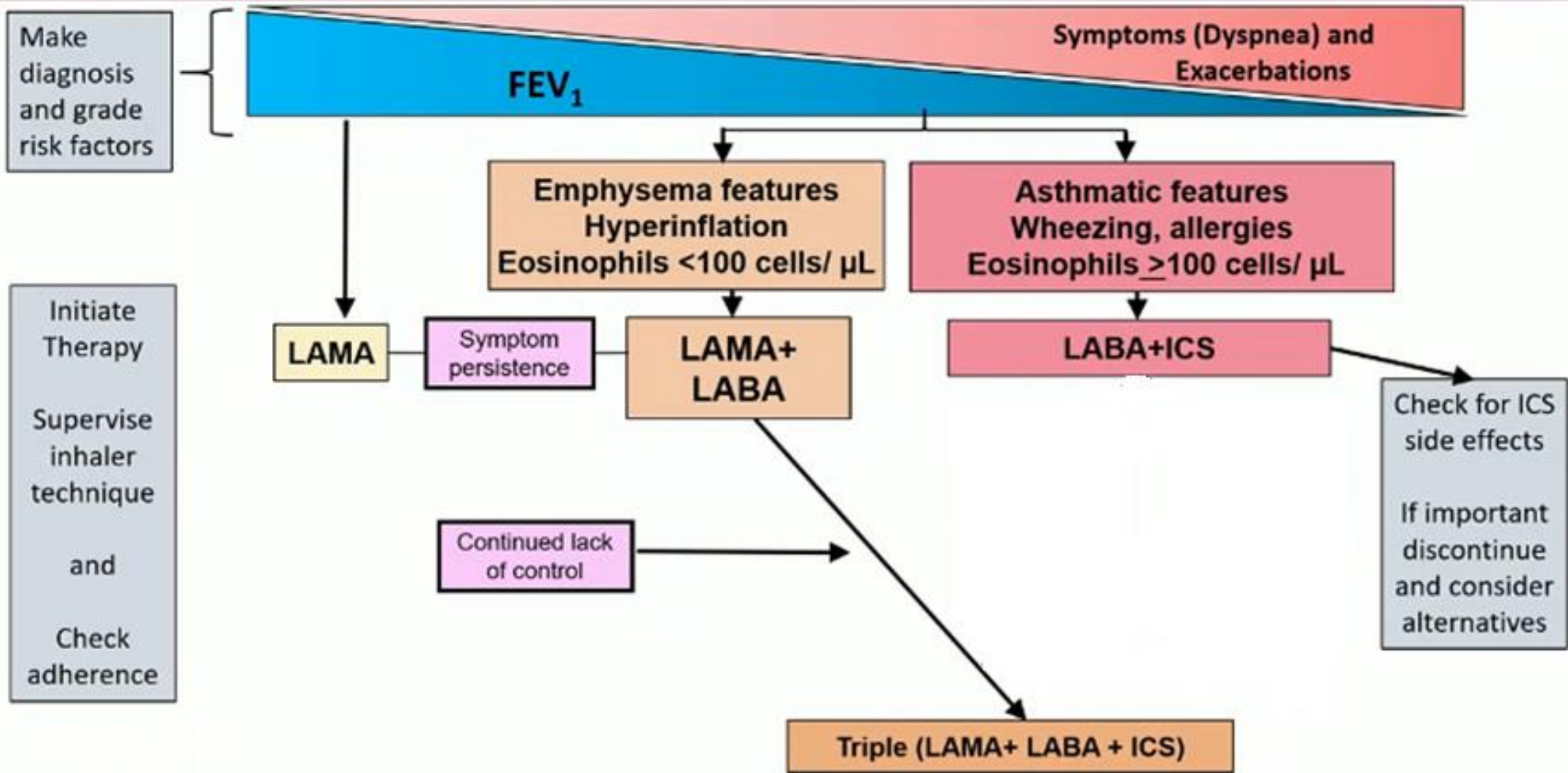
FEV₁, forced expiratory volume in one second; LAMA, long-acting muscarinic agent; LABA, long-acting beta-agonist

Celli B and Wedzicha J NEJM 2019;381:1257



FEV₁, forced expiratory volume in one second; LAMA, long-acting muscarinic agent; LABA, long-acting beta-agonist; ICS, inhaled corticosteroid;

Celli B and Wedzicha J NEJM 2019;381:1257



FEV₁, forced expiratory volume in one second; LAMA, long-acting muscarinic agent; LABA, long-acting beta-agonist; ICS, inhaled corticosteroid;

Celli B and Wedzicha J NEJM 2019;381:1257

Assessing COPD severity



- GOLD advocates a holistic approach to assess severity which includes:¹
 - **Symptomatic assessment**
 - **Spirometric classification of severity**
 - **Risk of exacerbations**



- This provides an overall understanding of the impact of COPD on an individual patient, and importantly helps to guide therapy.¹
- Assessment of COPD severity should be carried out regularly (at least annually, and more frequently for severe disease) to monitor disease progression, help determine prognosis and inform management strategies²

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of COPD 2021 Report
2. Gruffydd-Jones K. (2016). Assessment of COPD in Primary Care. In: Primary Care Respiratory Academy. PCRS UK, pp. 17-9

COPD treatment should be individualised based on symptoms and exacerbation risk



For Group B patients with persistent SYMPTOMS



Symptomatic despite as-needed SABA/SAMA

LAMA/LABA

Maximal bronchodilation

For SYMPTOMATIC patients on COPD maintenance therapy and AT RISK OF EXACERBATIONS



Symptomatic despite COPD maintenance therapy and history of COPD exacerbations

LAMA/LABA

or

ICS/LABA

Group C or D patients

LAMA

+

ICS/LABA

Group D patients

Triple Therapy

- LABA, long-acting β 2-agonist; LAMA, long-acting muscarinic antagonist; SABA, short-acting β 2-agonist; SAMA, short-acting muscarinic agonist

Initial Pharmacological Treatment



When do I start ICS?

- **Concomitant Asthma**
- After maximal bronchodilation
 - 2 or more exacerbations/yr
 - Hospitalization for an exacerbation
 - Unacceptable symptoms

- **Unsure**
 - Blood eosinophil count
 - Measure efficacy

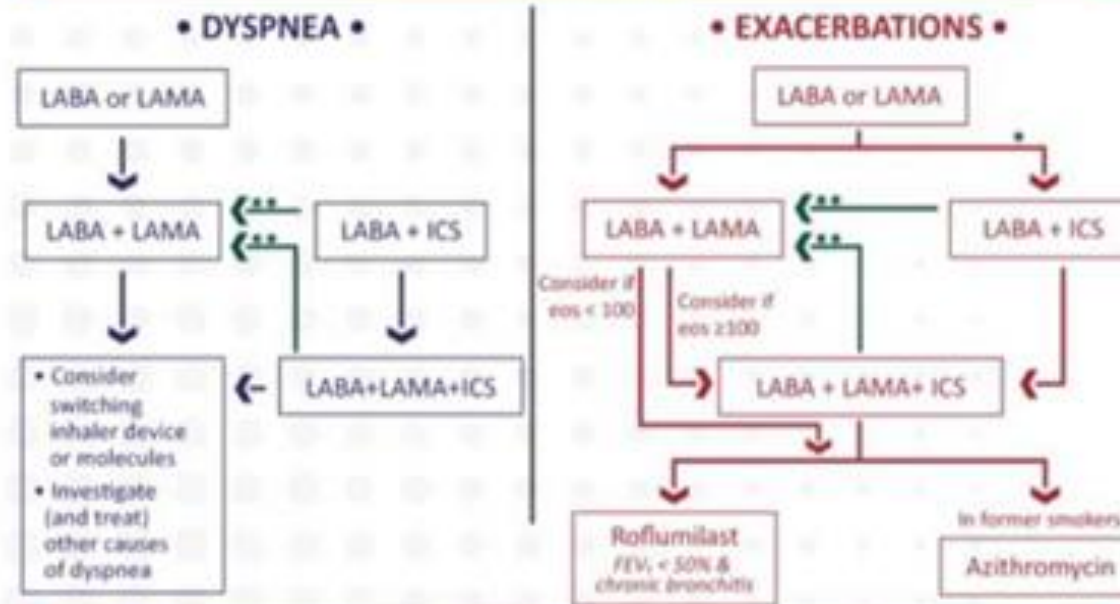
When do I stop ICS?

- Cannot find a good reason why they were started
- **Unacceptable Adverse Effects**
 - Second documented pneumonia while on treatment
 - Recurrent oral candidiasis

GOLD guidelines advocate individualised therapy based on symptoms and exacerbation risk

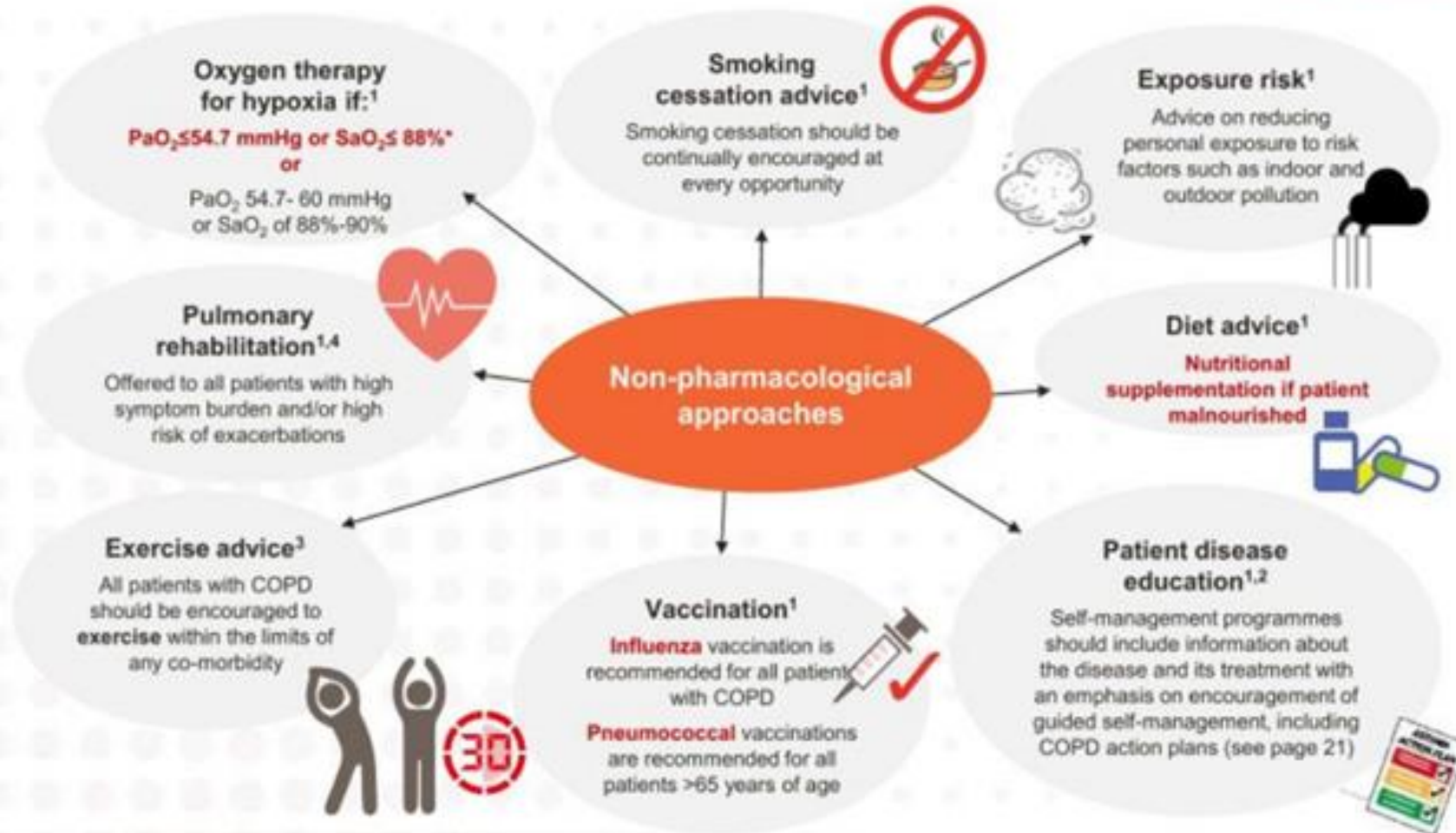


- IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT.
- IF NOT:
 - ✓ Consider the predominant treatable trait to target (dyspnea or exacerbations)
 - Use exacerbation pathway if both exacerbations and dyspnea need to be targeted
 - ✓ Place patient in box corresponding to current treatment & follow indications
 - ✓ Assess response, adjust and review
 - ✓ These recommendations do not depend on the ABCD assessment at diagnosis



eos = blood eosinophil count (cells/ μ L)
 * Consider if eos \geq 300 or eos \geq 100 AND \geq 2 moderate exacerbations / 1 hospitalization
 ** Consider de-escalation of ICS or switch if pneumonia, inappropriate original indication or lack of response to ICS

Other non-pharmacological strategies are important for good COPD management



*With or without hypercapnia confirmed twice over a three week period

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of COPD 2021 Report
 2. Gruffydd-Jones K. *PCRS UK*, 2016; pp. 17-9; 3. Gruffydd-Jones K. *PCRS UK*, 2016; pp. 20-7; 4. British Lung Foundation. Your COPD self-management plan

Self-management COPD plans encourage patients to better manage their disease

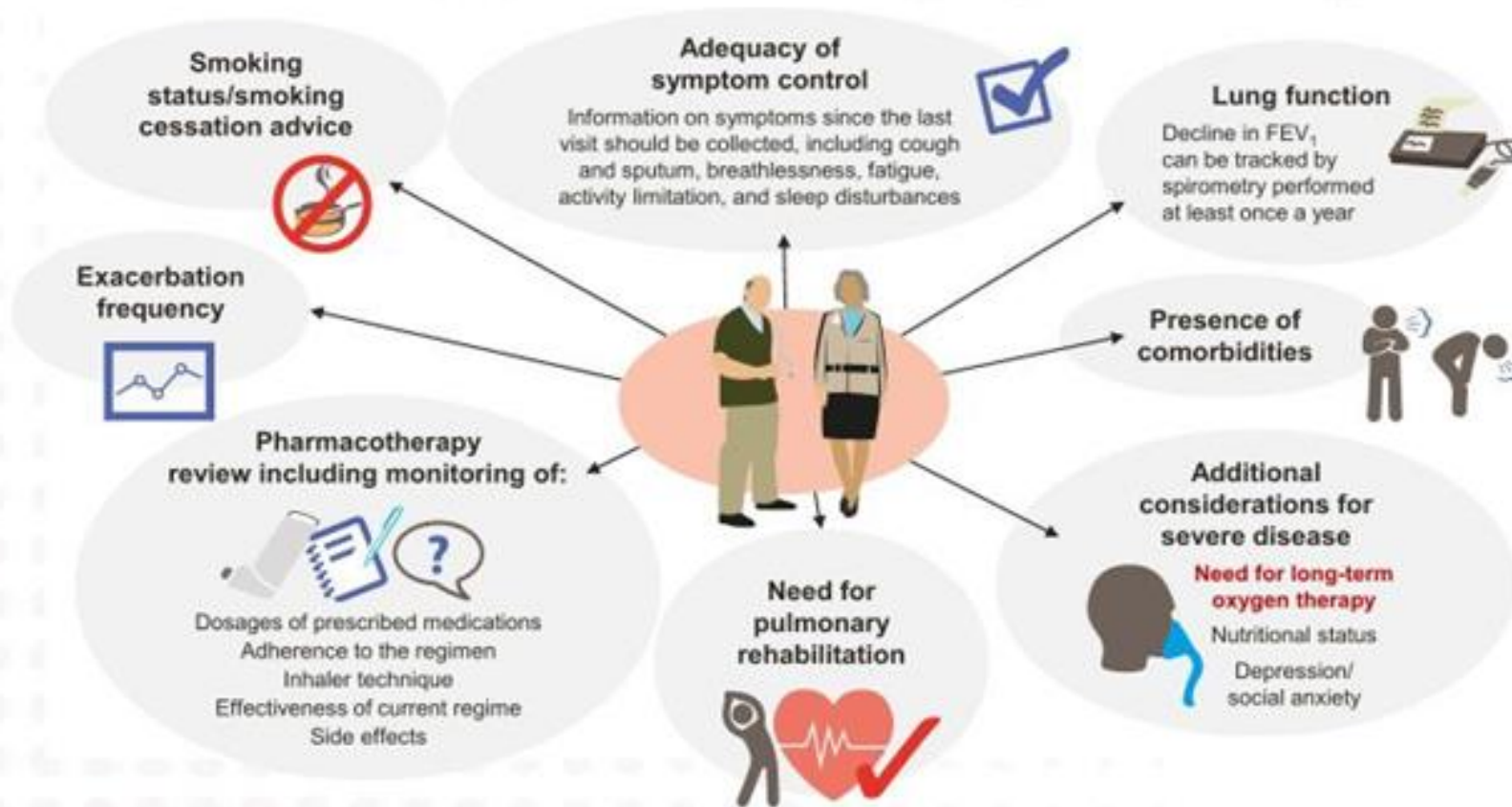


GROUP D	GROUP C
<ul style="list-style-type: none"> - Smoking cessation - Avoiding other risk factors - Maintaining/increasing physical activity - Ensuring adequate sleep and healthy diet - Self-managing breathlessness - Energy conservation techniques - Stress management strategies - Monitoring/managing worsening symptoms - Action plan for exacerbations - Maintaining regular contact with their healthcare professional - Discussing palliative /advance care strategies with their healthcare professional 	<ul style="list-style-type: none"> - Smoking cessation - Avoiding other risk factors - Maintaining/increasing physical activity - Ensuring adequate sleep and healthy diet - Monitoring/managing worsening symptoms - Action plan for exacerbations - Maintaining regular contact with their healthcare professional 
GROUP A	GROUP B
<ul style="list-style-type: none"> - Smoking cessation - Avoiding other risk factors - Maintaining/increasing physical activity - Ensuring adequate sleep and healthy diet 	<ul style="list-style-type: none"> - Smoking cessation - Avoiding other risk factors - Maintaining/increasing physical activity - Ensuring adequate sleep and healthy diet - Self-managing breathlessness - Energy conservation techniques - Stress management strategies 

A regular clinical review provides the opportunity to adjust treatment if necessary



A routine follow up of patients with COPD should typically contain the following:¹⁻³



Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of COPD 2021 Report
 2. PCRS UK. Opinion Sheet 19: Reviewing people with COPD. December 2013; 3. PCRS UK. The building blocks of a good asthma or COPD review

Effect of smoking cessation on FEV₁ in patients with COPD

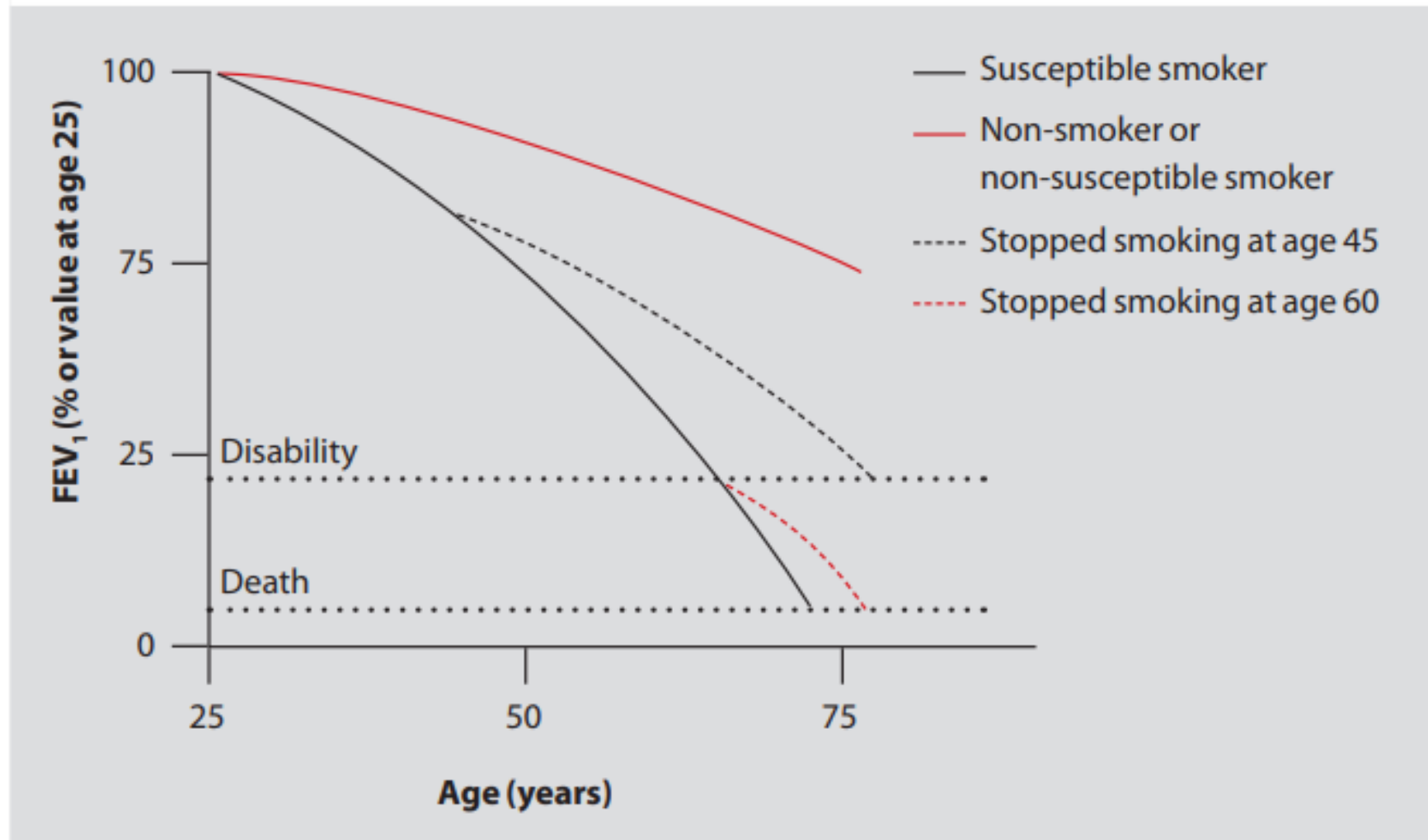


Figure 4.3 Effect of smoking cessation on FEV₁ in patients with COPD. FEV₁, forced expiratory volume in 1 second. Reproduced with permission from [3].

Summary



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



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** (such as exacerbations, hospital admissions, or death), in order to guide therapy



Concomitant chronic diseases occur frequently in COPD patients. These **comorbidities** should be actively sought and treated appropriately when present as they can influence mortality and hospitalisations independently.



The 'ABCD' assessment tool combines the patient's **symptomatic assessment and degree of airflow limitation with exacerbation risk**. This approach highlights the importance of patient reported outcomes e.g. symptoms and exacerbation risks in guiding therapy for COPD