State of the Art: COPD in 2020

Bartolome R. Celli, M.D., FCCP
Professor of Medicine
Harvard Medical School

CHEST Congress 2020

ITALY
Bologna | 25-27 June

Universita di Bologna Founded 1088

B. Celli Disclaimer

No stocks or ownership in any company.

No Tobacco funds

Advisory boards: *GSK, B.I., Astra Zeneca, Novartis, Pulmonx, Chiesi, Menarini.*

Member of the Scientific and Executive Committee of GOLD

Agenda

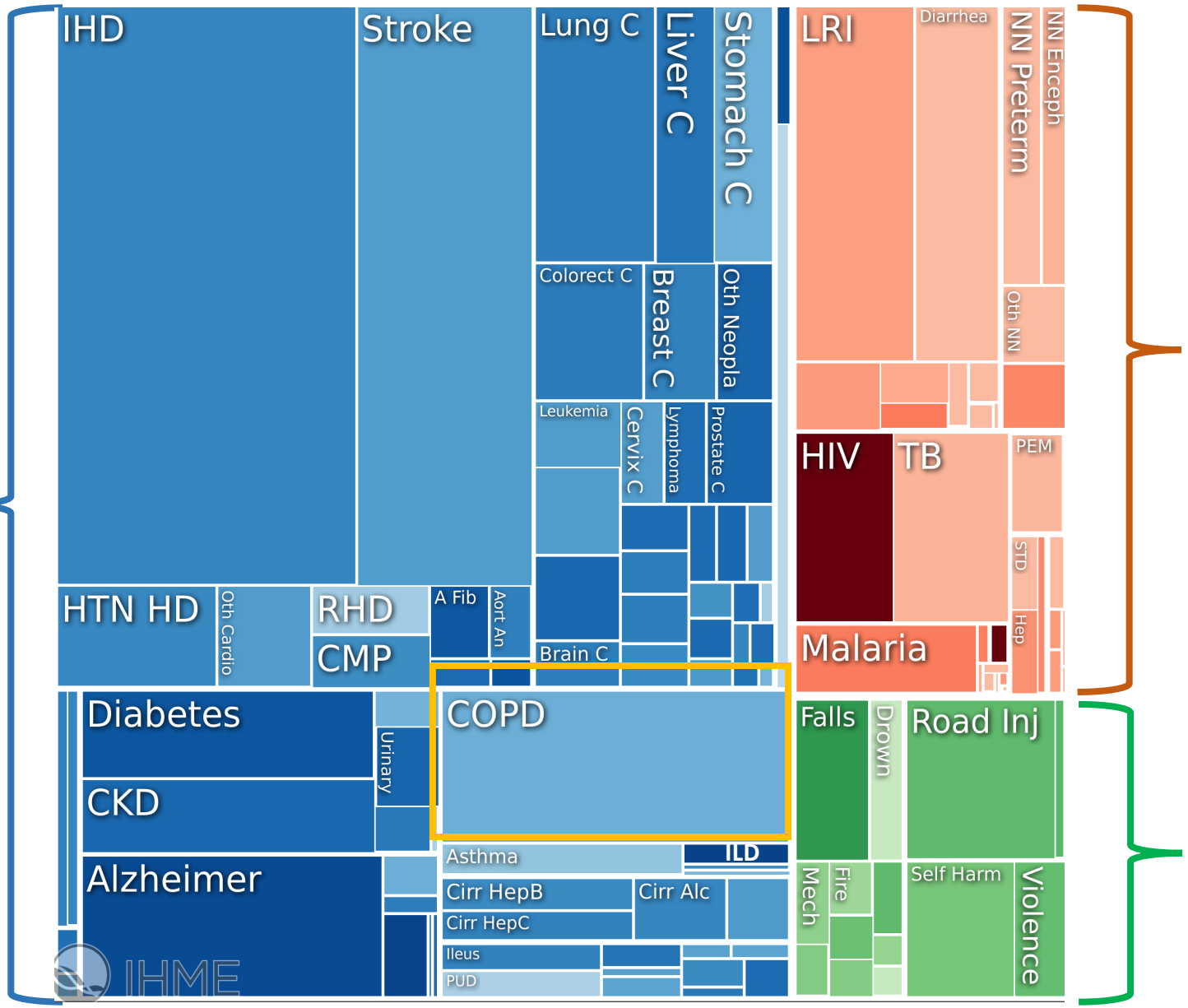
- Describe the COPD landscape in the World
- There are several “natural courses” to develop COPD
- Provide a practical approach to initiate and modify pharmacotherapy in patients with COPD.
- Review the tools available for patients on maximal therapy who remain functionally impaired
- Conclusions

Agenda

- Describe the COPD landscape in the World

www.GBD
Accessed
2/2020

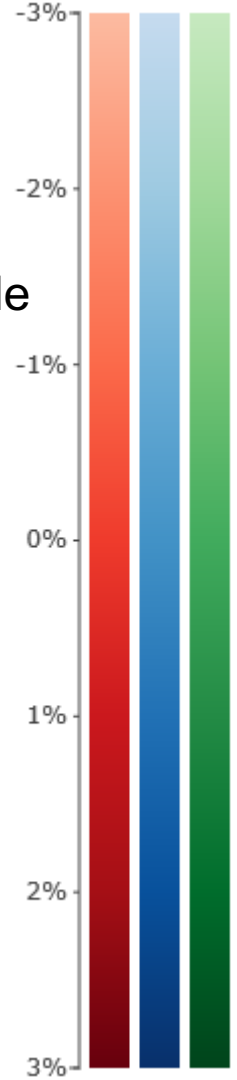
Non
Communicable



Communicable

Injuries

Annual % change 1990-2013 Death 100K persons



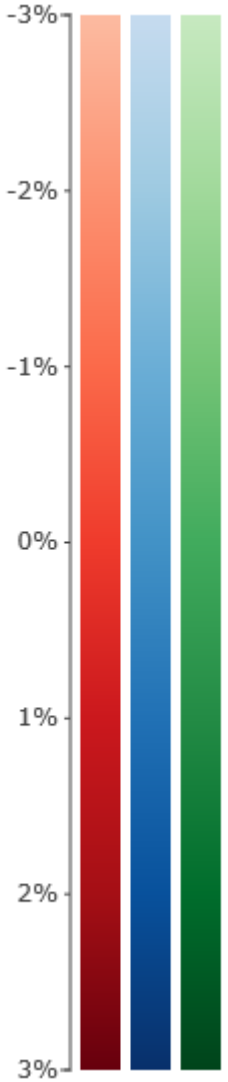
www.GBD
Accessed
2/2020

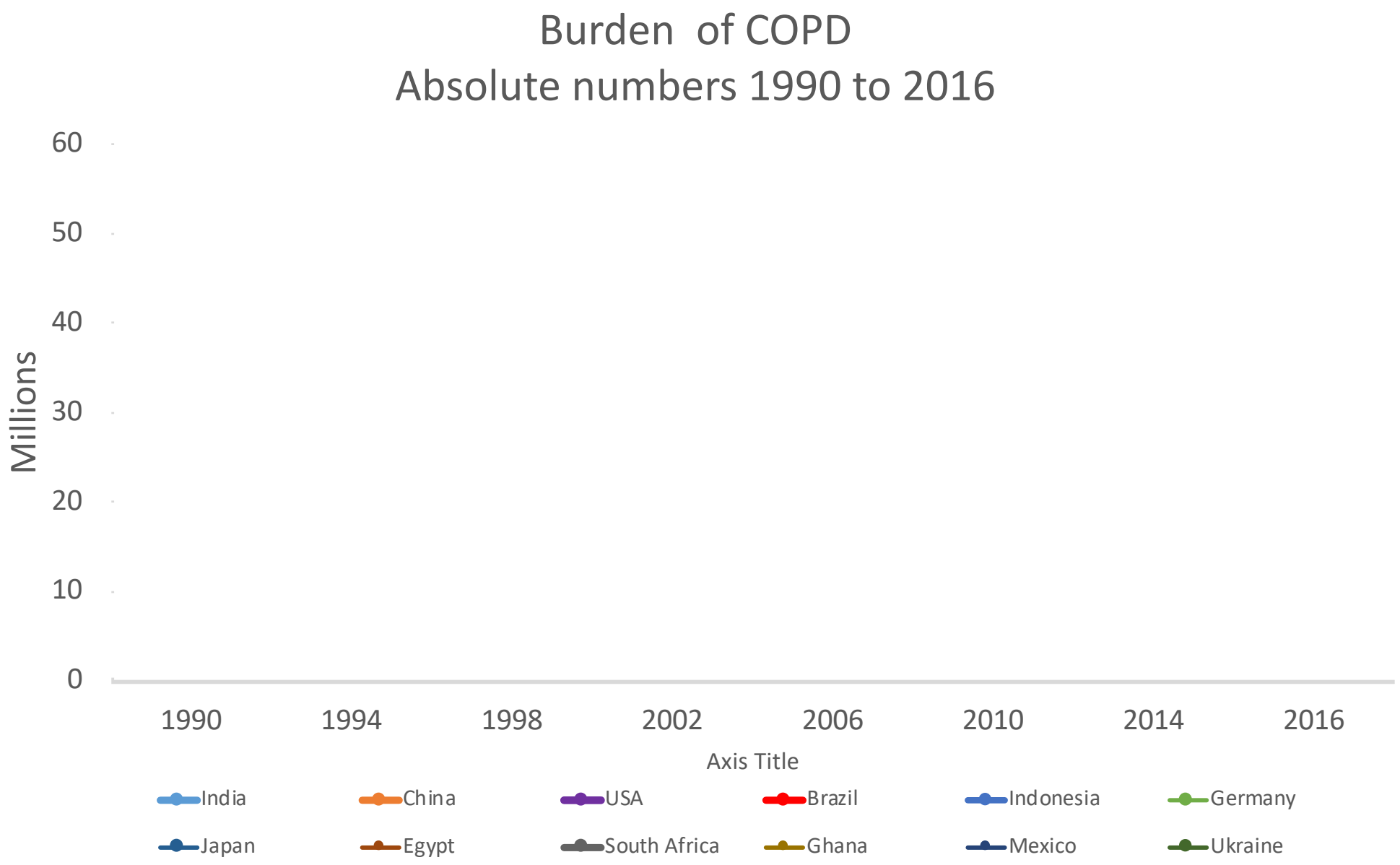
COPD

Percent of deaths: 5.36

Annual % change = - 1.01

Annual % change
1990-2013
Death 100K persons





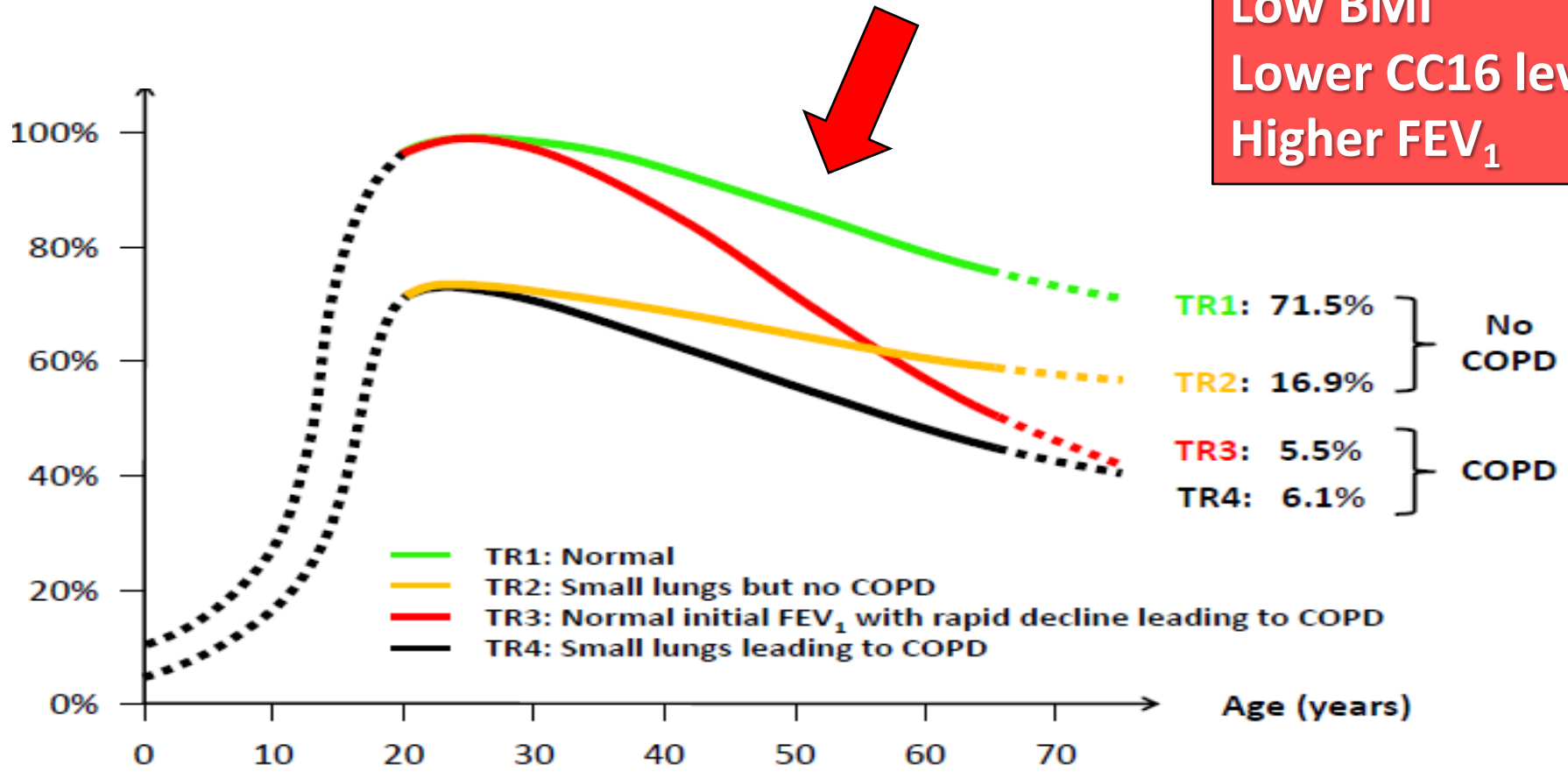
WWW.GBD. Accessed July 2019 (Courtesy Dr. Sundeep Salvi)

Agenda

- There are several “natural courses” to develop COPD

Course of Lung Function

Determinants of loss



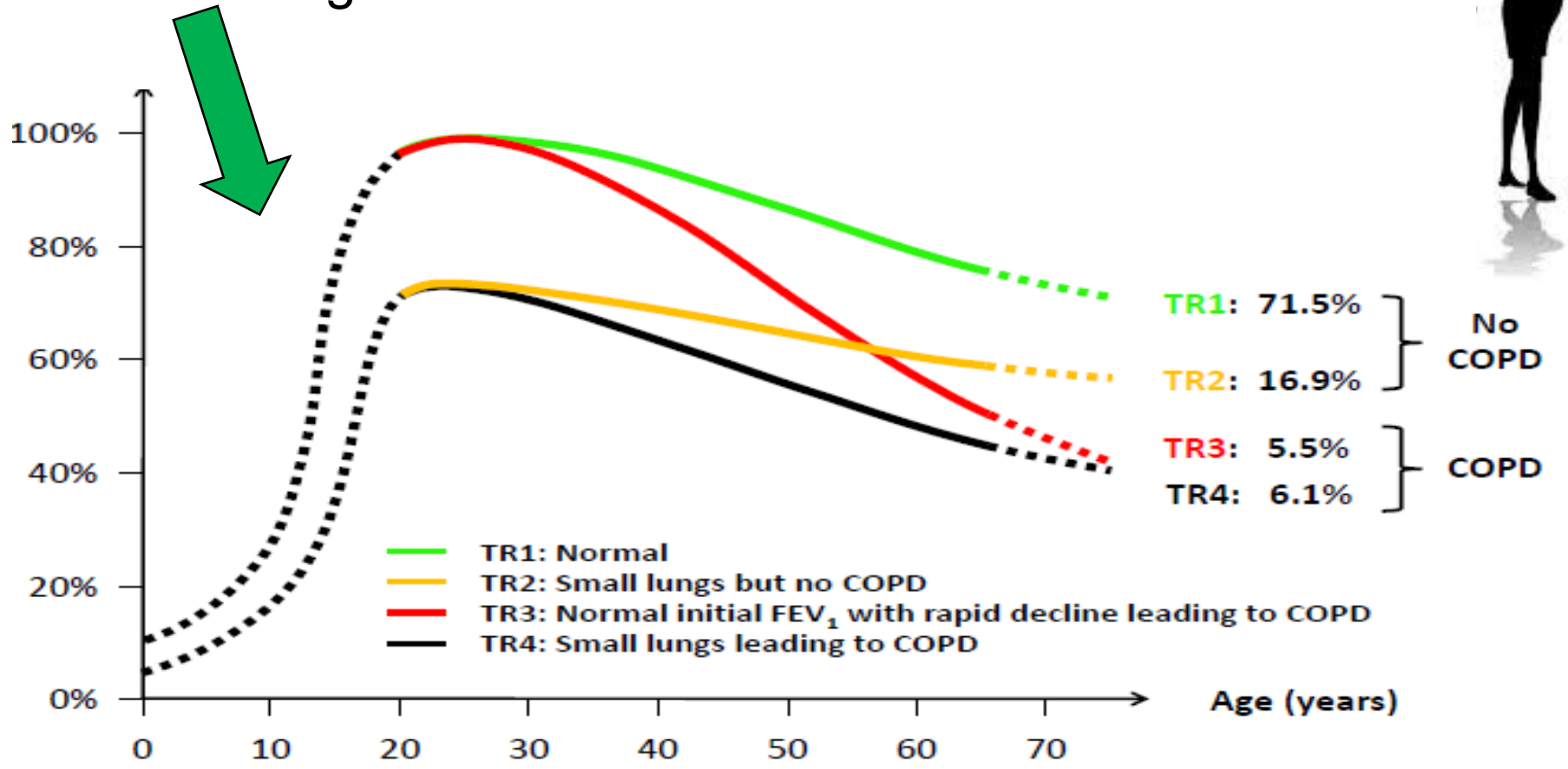
Current smoking
Male
Emphysema
Low BMI
Lower CC16 levels
Higher FEV_1

No pharmacological therapy
Exacerbations
Pollution
Poverty

Lange P et al NEJM 2015;372:2

Course of Lung Function

Determinants of gain

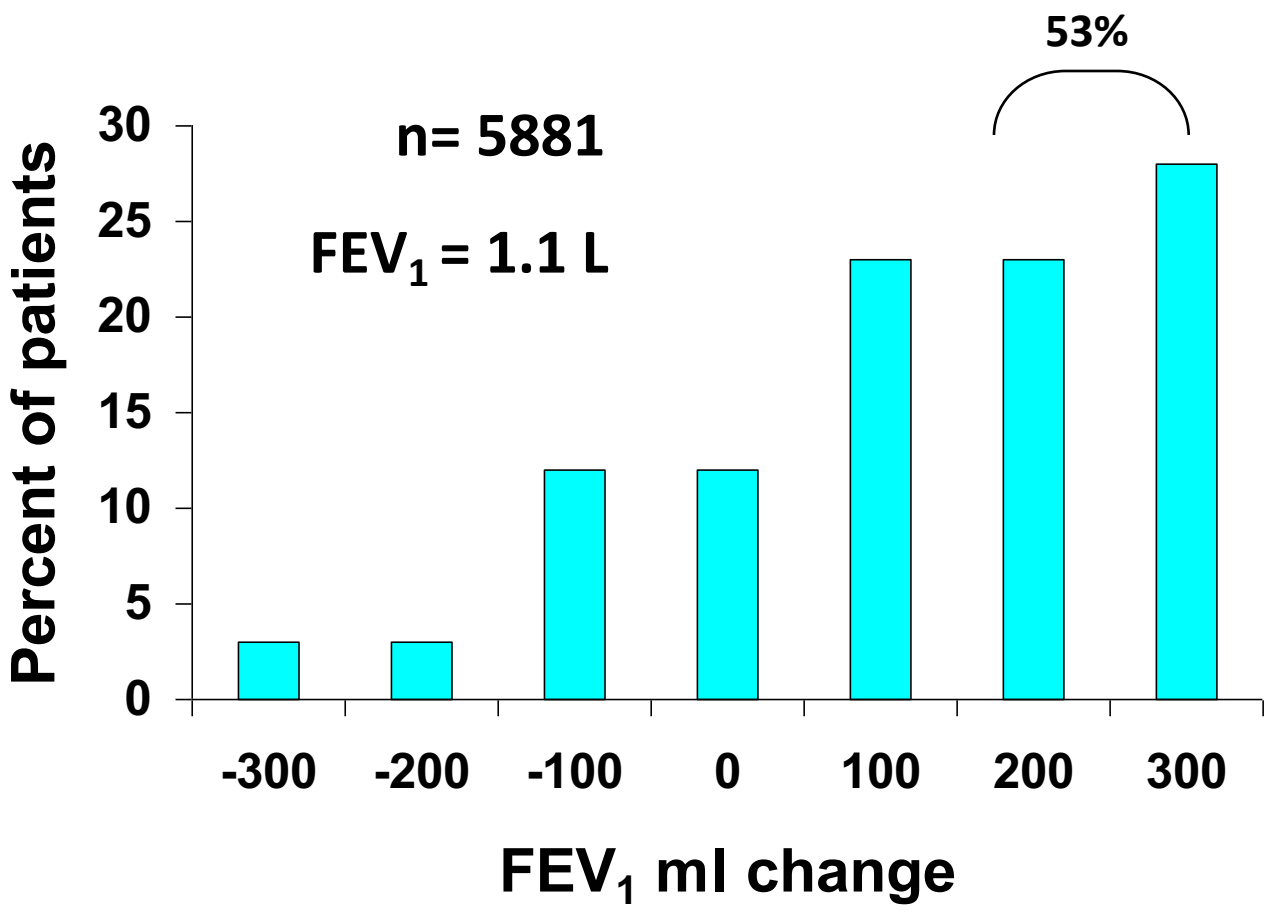


Lange P et al NEJM 2015;372:2

Agenda

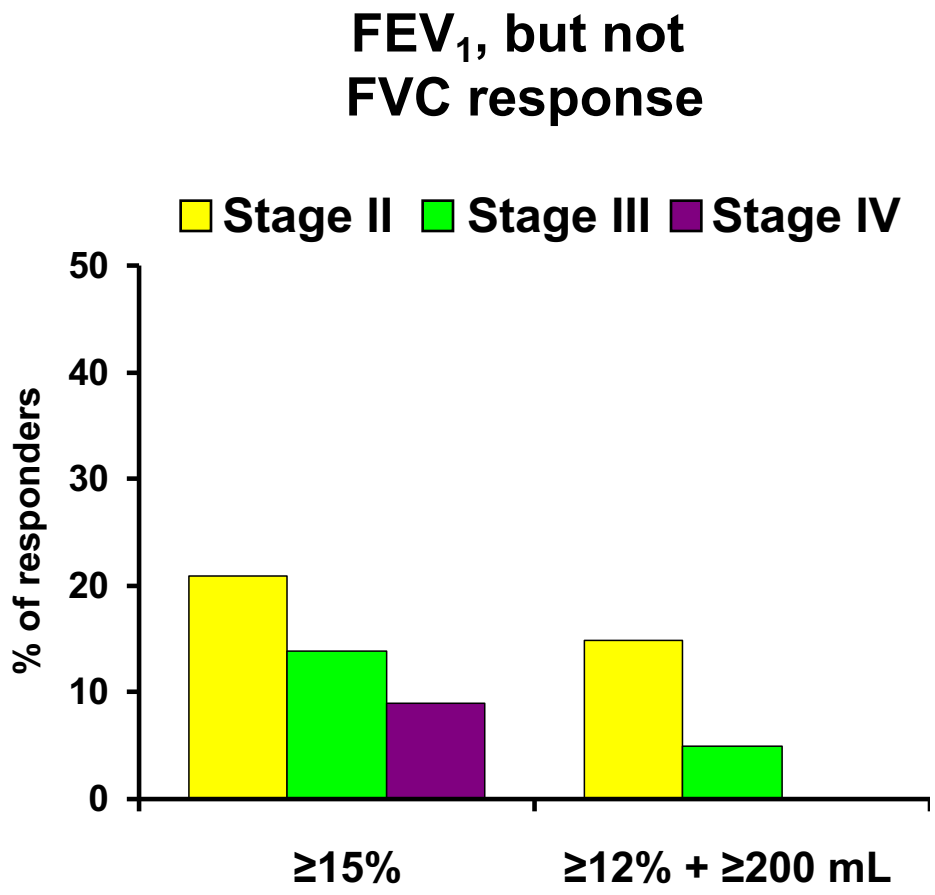
- Provide a practical approach to initiate and modify pharmacotherapy in patients with COPD.

Bronchodilator responsiveness in COPD



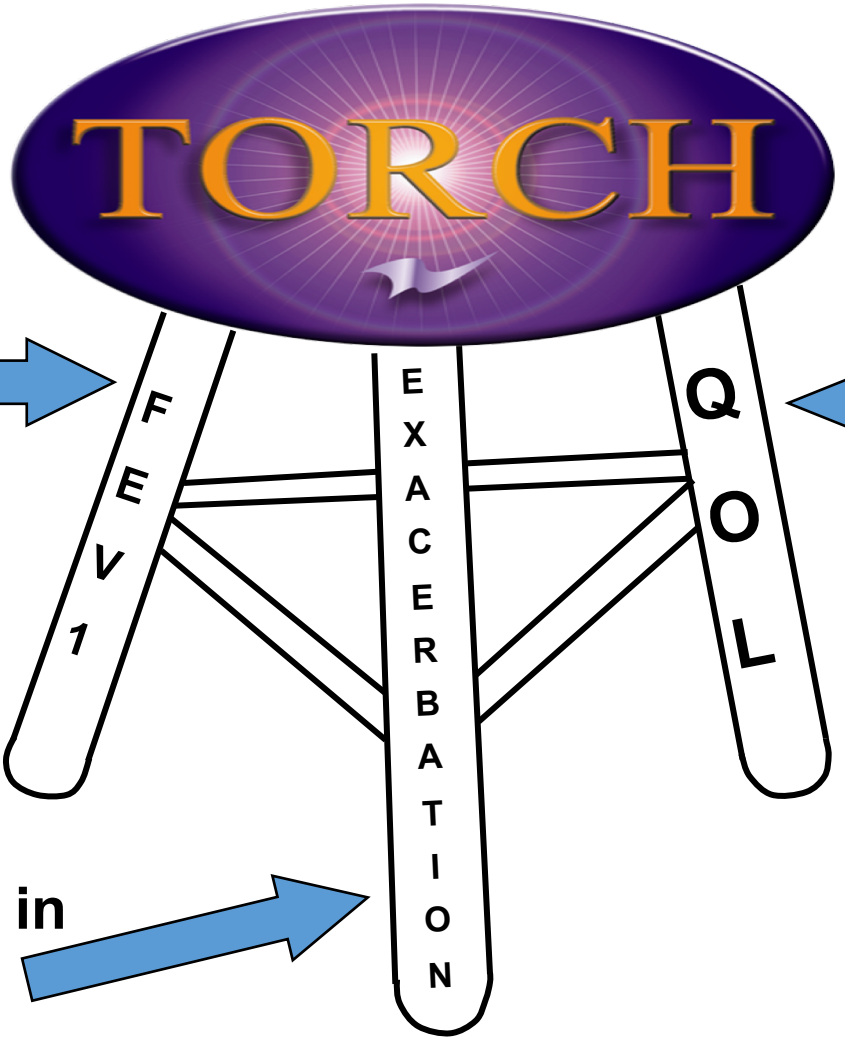
Tashkin D et al ERJ 2008;31:742

Bronchodilator responsiveness in COPD



Tashkin D et al ERJ 2008;31:742

TORCH: DB, R, PC, 3 year trial. 6000 patients comparing F, S, SF, P
Outcome: Primary: Mortality Secondary: FEV1, QoL, Exacerbations



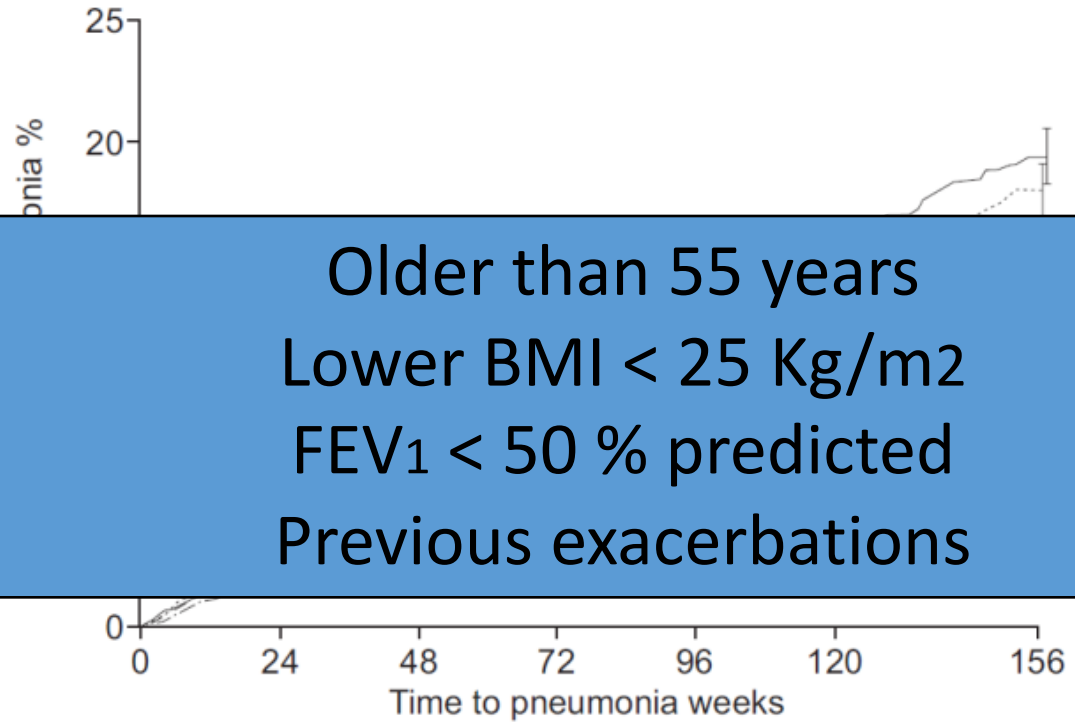
92 ml difference from placebo

St George's is 3.1 better than placebo and better than baseline

25% reduction in exacerbations

Calverley P et al NEJM 2007;22:356

Pneumonia Risk in TORCH



Older than 55 years

Lower BMI < 25 Kg/m2

FEV_1 < 50 % predicted

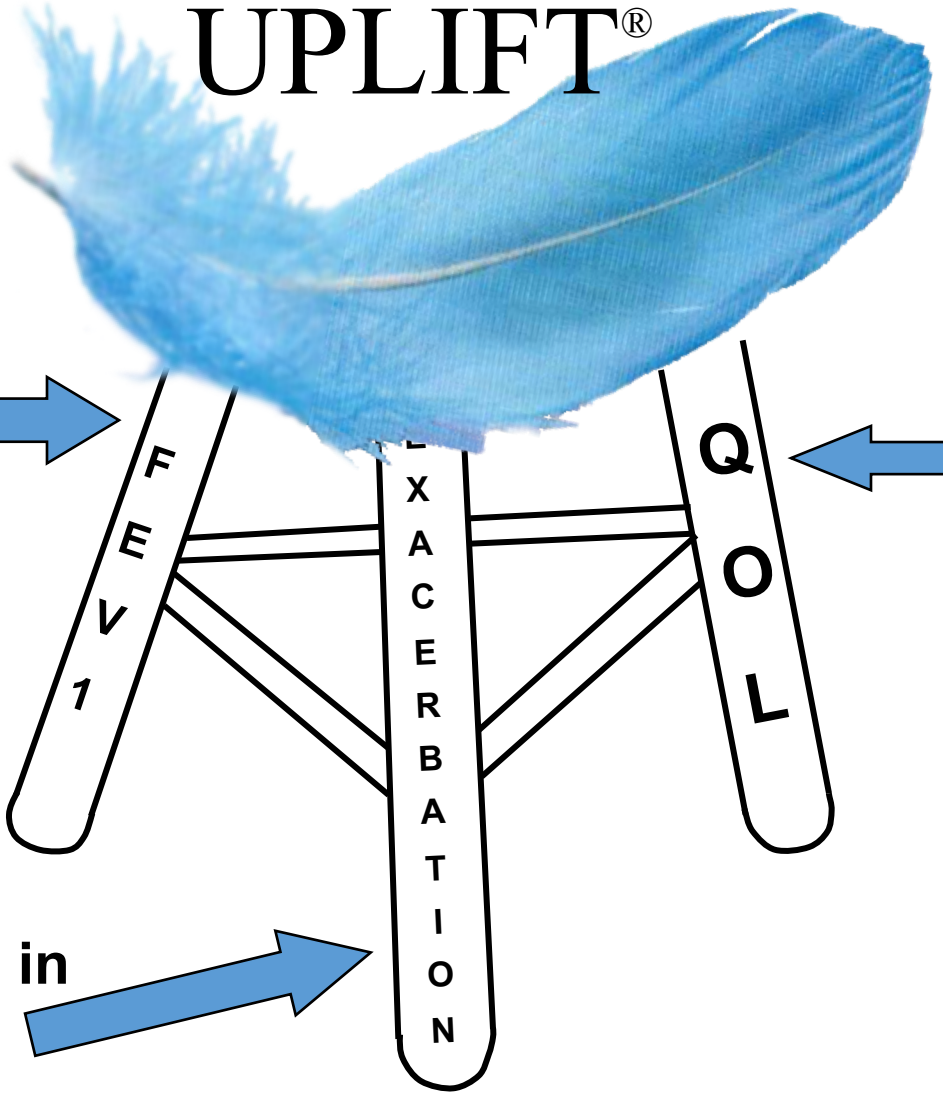
Previous exacerbations

Patients n				
SFC	1546	1231	1034	631
FP	1552	1189	992	574
SAL	1542	1214	1024	645
P	1544	1117	947	587

Crim C et al ERJ 2009;34:341

UPLIFT: DB, R, PC, 4 year trial. 6000 patients. Tio vs Usual care
Outcome: Primary: FEV1 decline Secondary: QoL, AE, Mortality

UPLIFT®



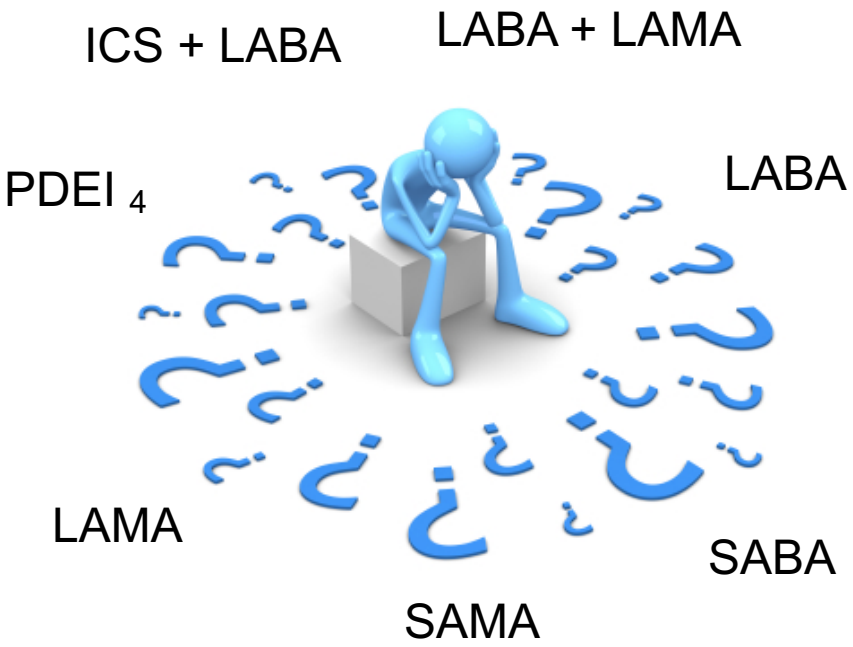
110 ml difference from placebo

St George's is 3.3 units better than placebo and better than baseline

16% reduction in exacerbations

Tashkin D et al NEJM 2008;359:1543

How to approach?



GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE™

Diagnosis → **Assessment of airflow limitation**

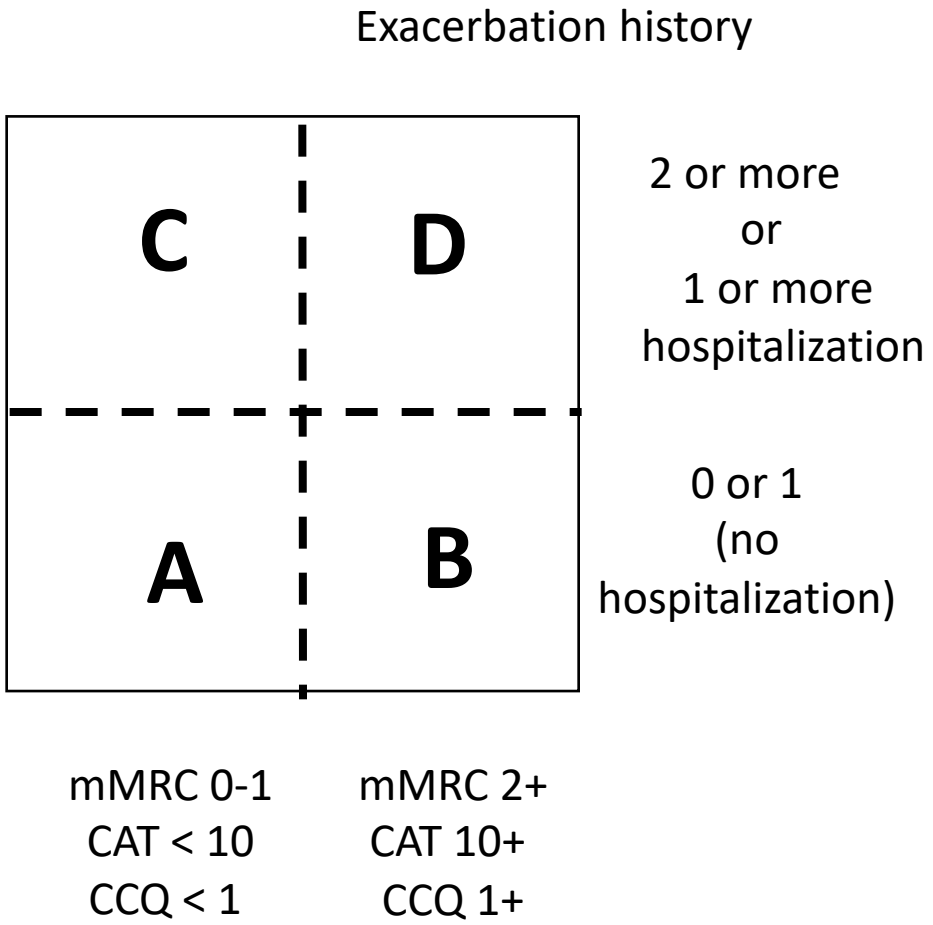
$FEV_1/FVC<0.7$

Grade	FEV_1 (% pred.)
1	≥80
2	50-79
3	30-49
4	<30

Diagnosis → **Assessment of airflow limitation** → **Assessment of symptoms/risk of exacerbations**

$FEV_1/FVC<0.7$

Grade	FEV_1 (% pred.)
1	≥80
2	50-79
3	30-49
4	<30



GOLD 2019: Initial Pharmacological Treatment

INITIAL PHARMACOLOGICAL TREATMENT

≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization	**Group C** LAMA	**Group D** LAMA or LAMA + LABA* or ICS + LABA†
0 or 1 moderate exacerbation (not leading to hospital admission)	**Group A** A Bronchodilator	**Group B** A Long-acting Bronchodilator (LABA or LAMA)
	mMRC 0-1 CAT < 10	mMRC ≥ 2 CAT ≥ 10

ICS=inhaled corticosteroid; LABA=long-acting beta$_2$-adrenergic agonist; LAMA=long-acting muscarinic antagonist.
*Consider if highly symptomatic (eg, CAT > 20)

†Consider if eosinophils ≥ 300

GOLD 2019: FOLLOW-UP PHARMACOLOGICAL TREATMENT

1. IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT.

2. 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 and follow indications
- ✓ Assess response, adjust, and review
- ✓ These recommendations do not depend on the ABCD assessment at diagnosis

DYSPNEA

EXACERBATIONS

*Consider if eosinophils ≥ 300 cells/µL or ≥ 100 cells/µL + ≥ 2 moderate exacerbations or 1 hospitalized exacerbation.

†Consider de-escalation of ICS or switch if pneumonia, inappropriate original indication, or lack of response.

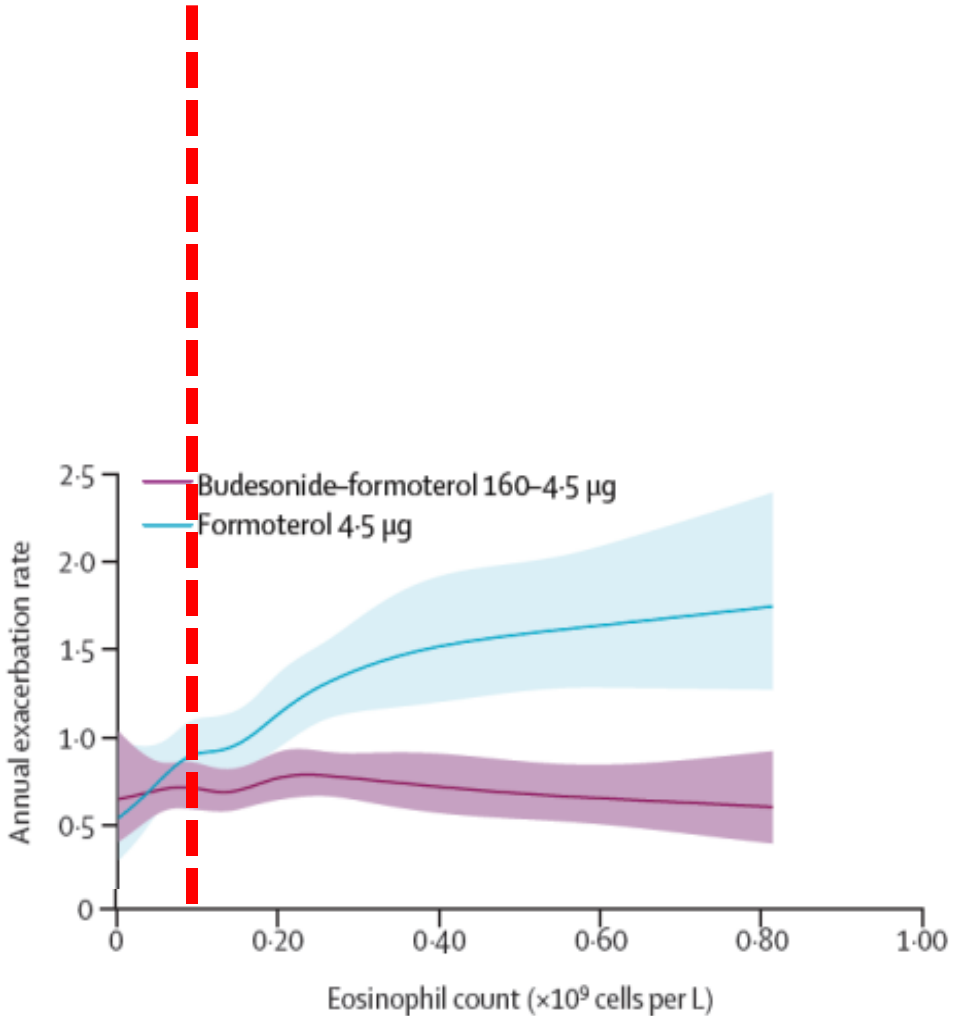
Exacerbations predictors: Post hoc analysis of budesonide in 3 RC COPD trials

Data from 3 RC trials of:
B/F versus F alone who
had eosinophils measured

N = 4153 patients

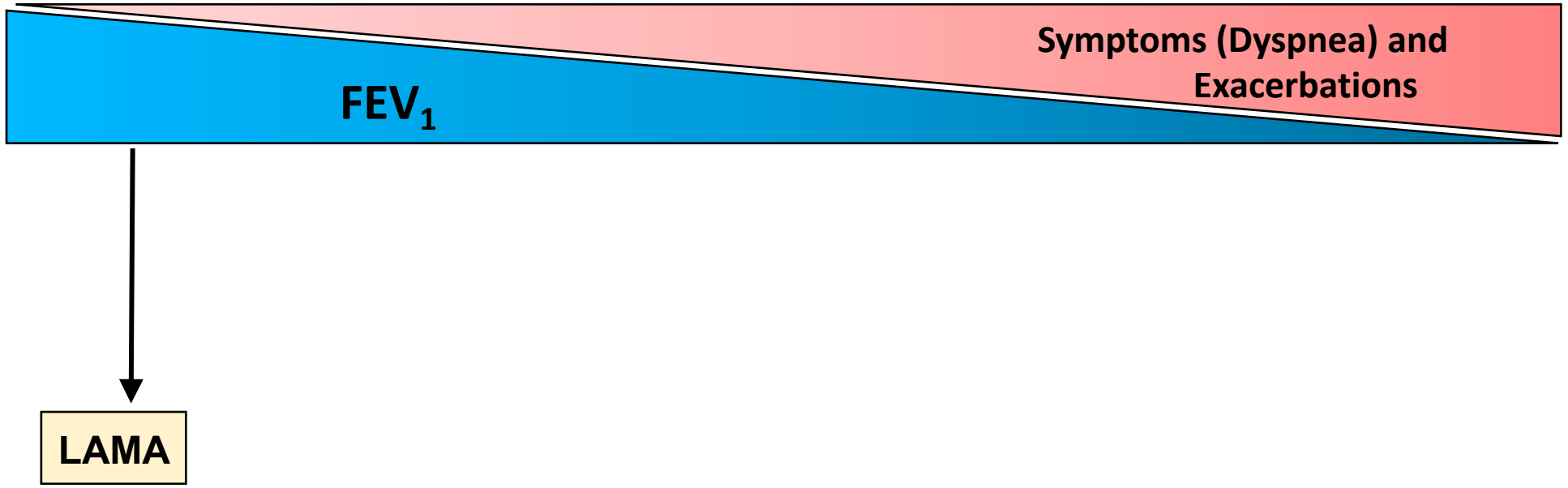
FEV_1 = 1 L 38% pred

Outcomes:
Exacerbations
FEV_1
QoL



Bafadhel M et al Lancet RM 2018;6:117

Make diagnosis and grade risk factors



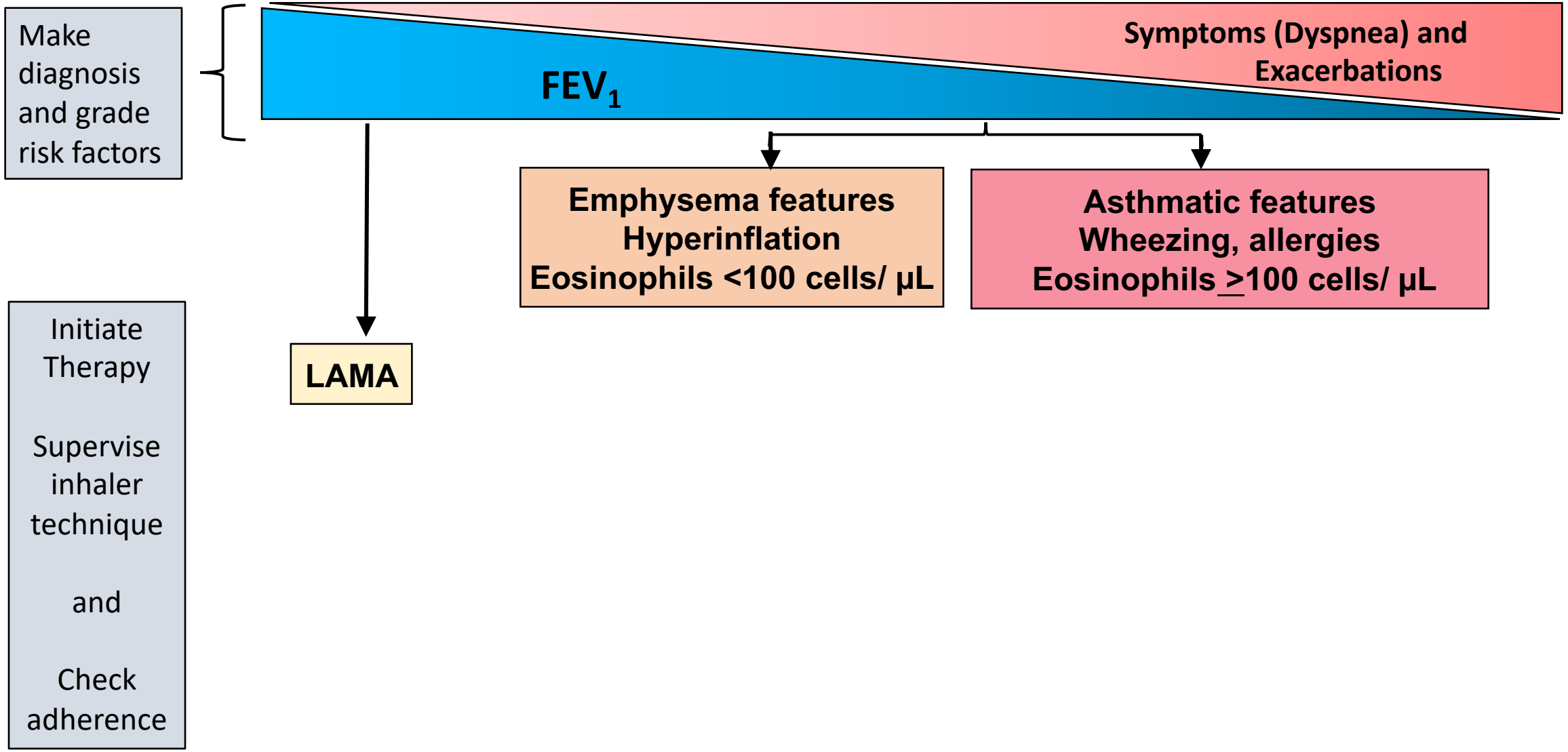
Initiate Therapy

Supervise inhaler technique

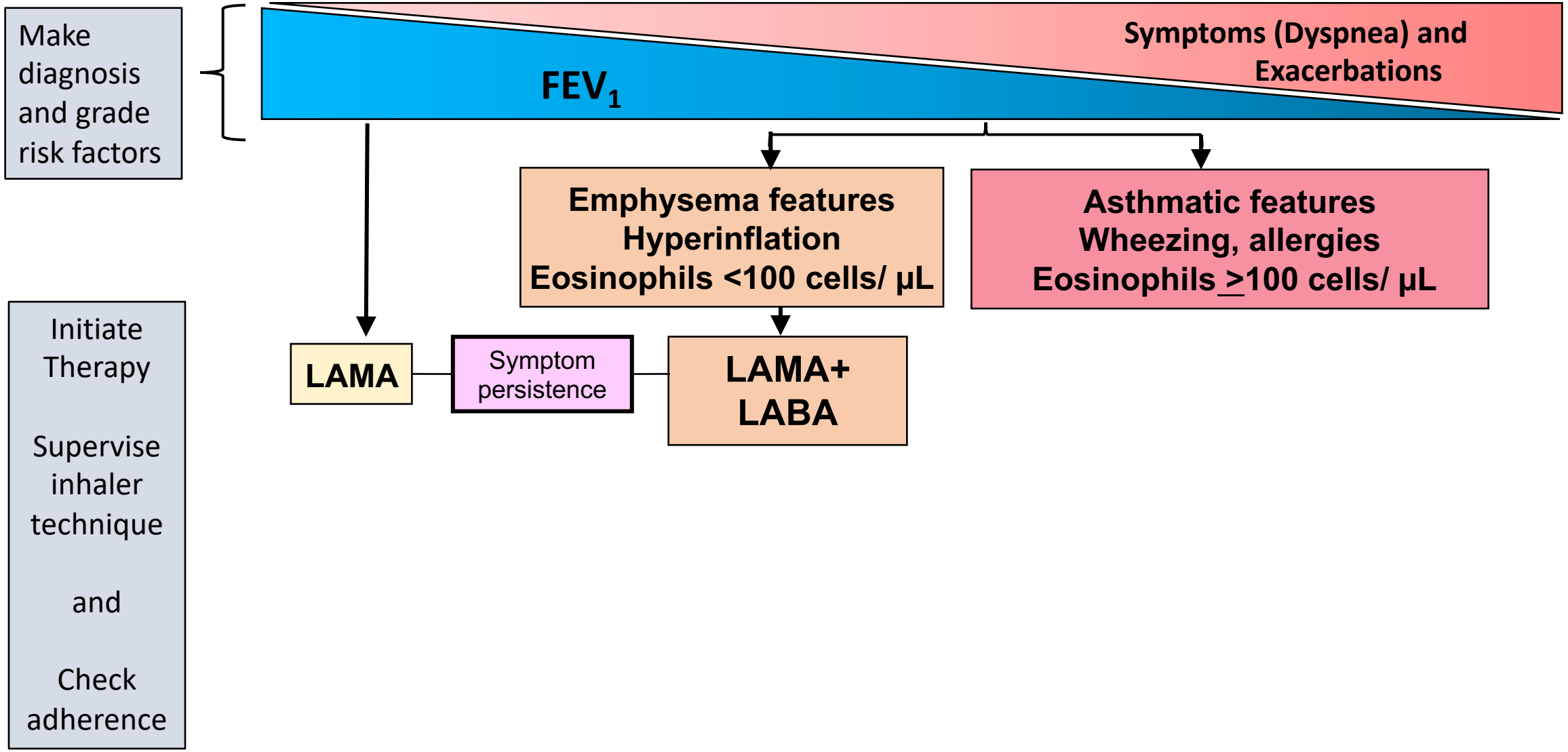
and

Check adherence

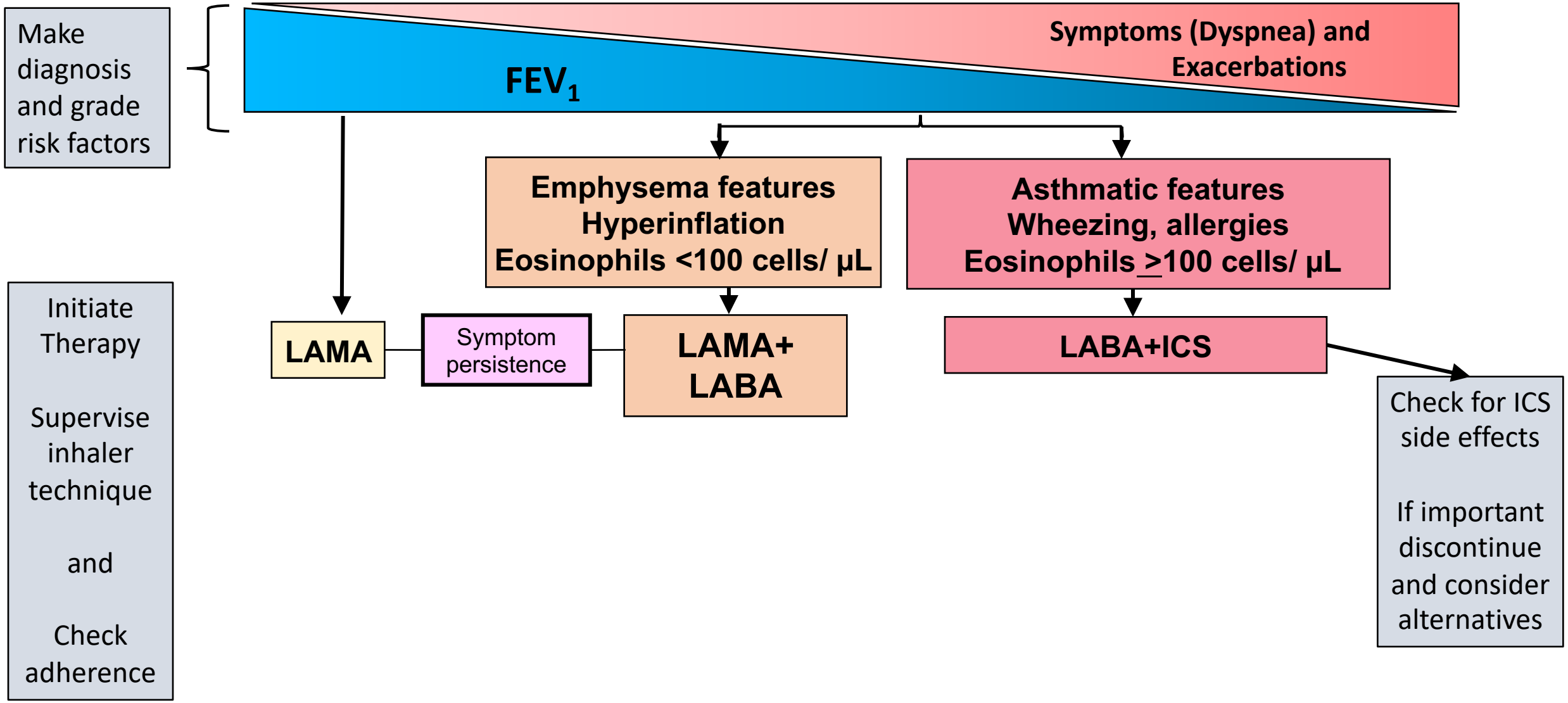
Celli B and Wedzicha J NEJM 2019;381:1257



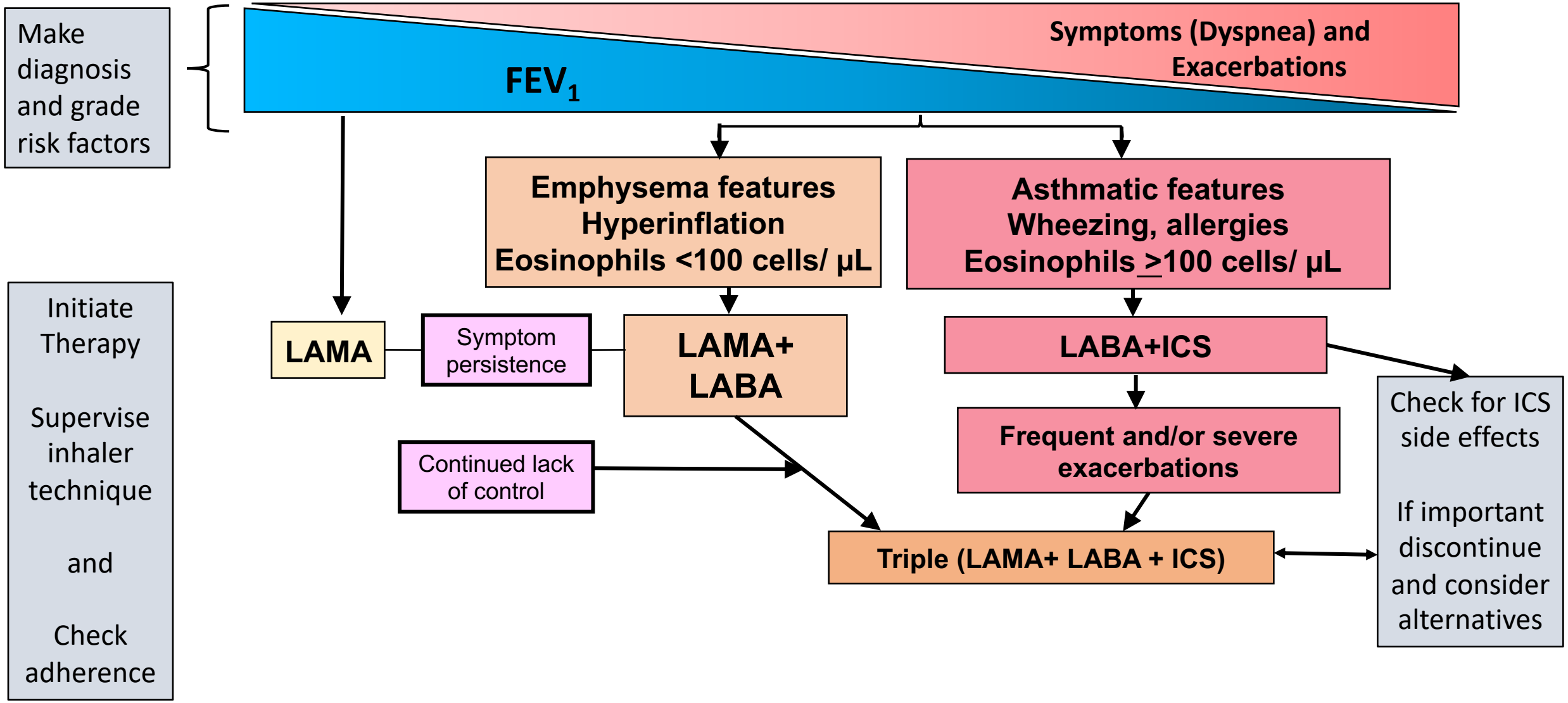
Celli B and Wedzicha J NEJM 2019;381:1257



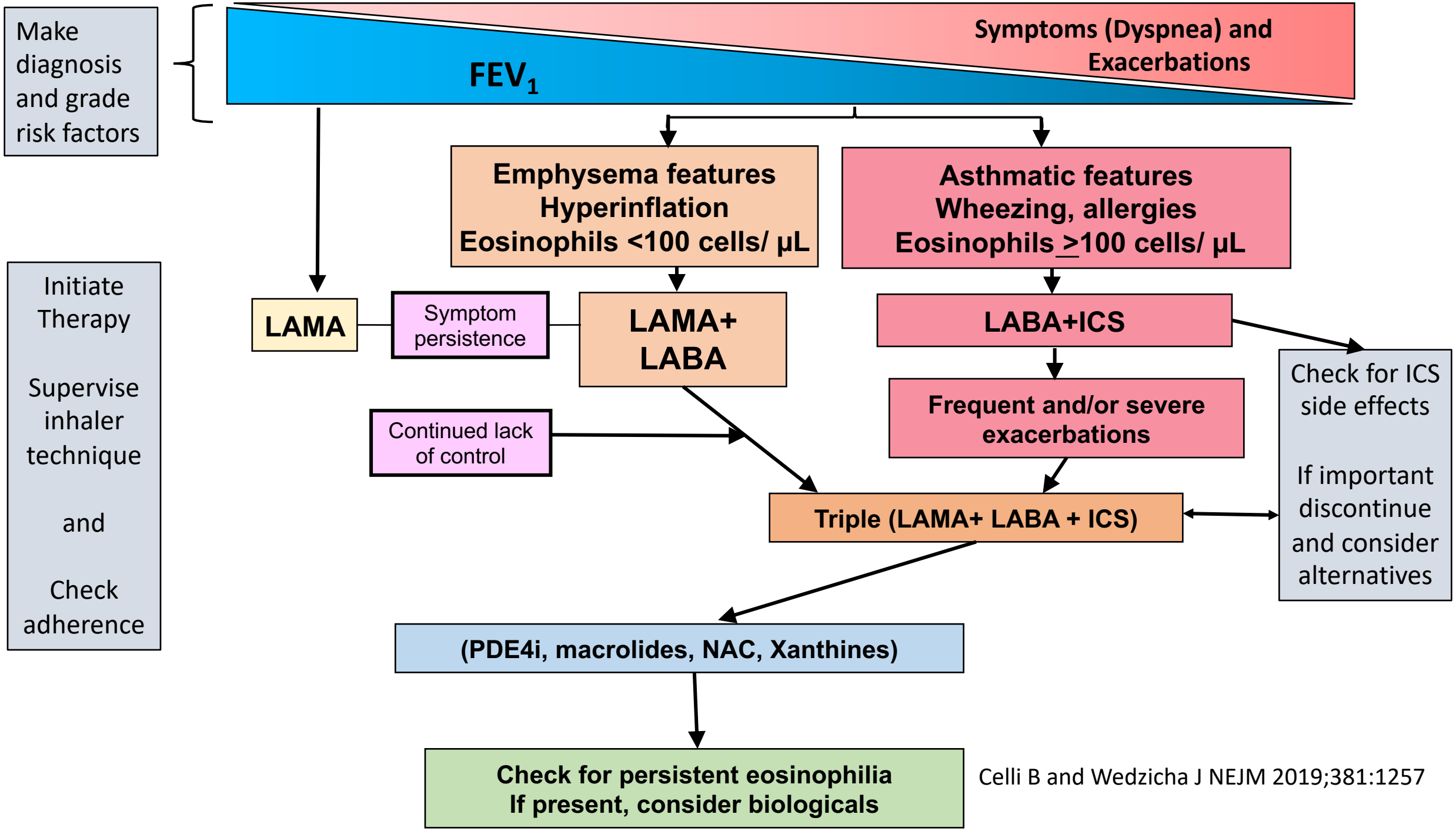
Celli B and Wedzicha J NEJM 2019;381:1257



Celli B and Wedzicha J NEJM 2019;381:1257



Celli B and Wedzicha J NEJM 2019;381:1257



Celli B and Wedzicha J NEJM 2019;381:1257

Agenda

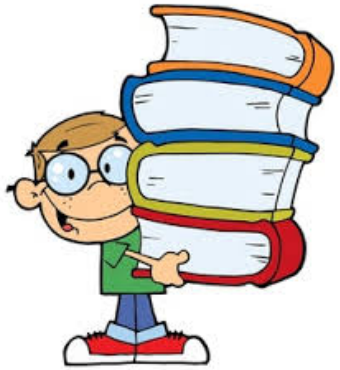
- Review the tools available for patients on maximal therapy who remain functionally impaired

Pulmonary rehabilitation for chronic obstructive pulmonary disease (Review)

McCarthy B, Casey D, Devane D, Murphy K, Murphy E, Lacasse Y

Cochrane

Along with 31 RCT's included in the 2006 Cochrane Review, the authors included 34 additional RCT's with a grand total of 3,822 participants

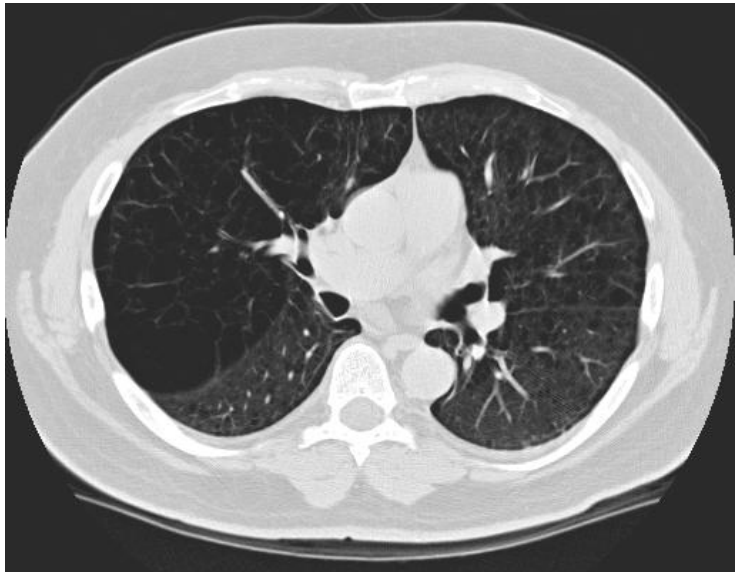


Conclusions

"We found statistically and clinically significant improvements in important domains of health related quality of life, including dyspnea, fatigue, emotional function and mastery as well as in the 6 MWD, a test of functional capacity"

Cochrane Database of Systematic Reviews 2015, Issue 2. Art. No.: CD003793.
DOI: 10.1002/14651858.CD003793.pub3.

Hyperinflation in a 63 year old man with mMRC dyspnea of 3



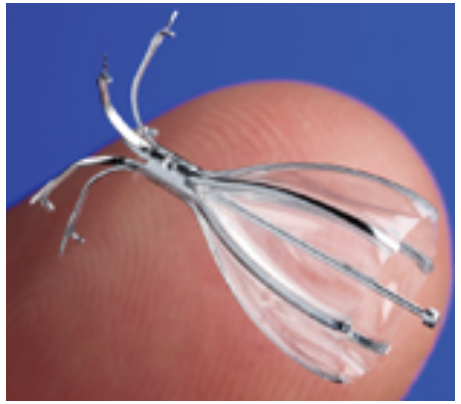
FEV_1 = 32 %

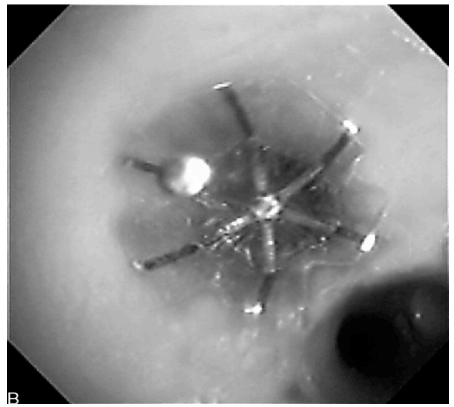
FRC = 192 %

DLCO = 49 %

Endobronchial Valves (EBV)

- Zephyr (Pulmonx)
  - silicone based mounted in a nitinol stent one way valve
- Spiration (Olympus)
  - 6 Nitinol struts and polyurethane umbrella shape unidirectional valve





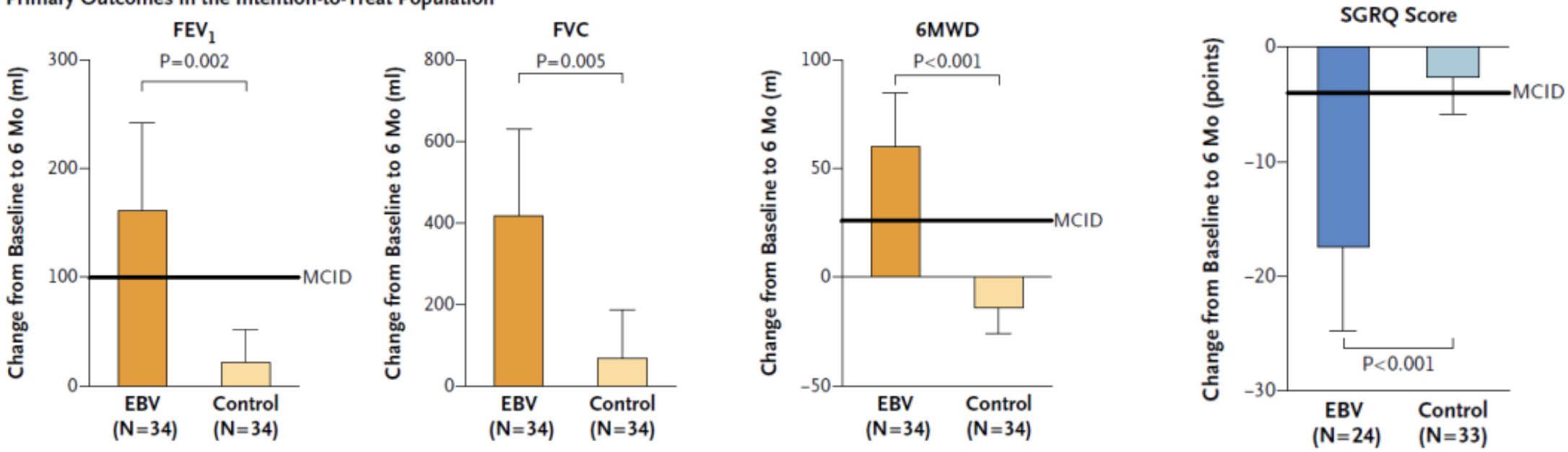
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Endobronchial Valves for Emphysema without Interlobar Collateral Ventilation

Karin Klooster, Nick H.T. ten Hacken, M.D., Ph.D., Jorine E. Hartman, Ph.D., Huib A.M. Kerstjens, M.D., Ph.D., Eva M. van Rikxoort, Ph.D., and Dirk-Jan Slebos, M.D., Ph.D.

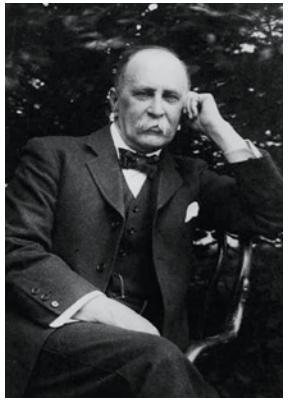
A Primary Outcomes in the Intention-to-Treat Population



Conclusions

- COPD is an important health problem worldwide
- Although cigarettes remain the most important cause, this is not so for the majority of countries in the world
- Well applied pharmacotherapy works
- In patients with persistent symptoms consider rehabilitation
- Check for emphysema and hyperinflation for potential LVR
- A nihilistic approach is not justified!

"If it were not for the great variability among individuals,medicine might as well be a science and not an art"



William Osler