ΑΘΗΝΑΪΚΟ ΠΝΕΥΜΟΝΟΛΟΓΙΚΟ ΙΝΣΤΙΤΟΥΤΟ

METROPOLITAN HOSPITAL
ΘΕΡΑΠΕΥΤΗΡΙΟ METROPOLITAN

GOLD 2019
ΚΡΙΤΙΚΗ

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Δ/ντής Πνευμον. Κλινικής ΠΝΟΗ Νοσοκ. Metropolitan


ΤΟ ΠΡΟΒΛΗΜΑ ΜΕ ΤΟΝ ΚΟΣΜΟ
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ΕΙΝΑΙ ΓΕΜΑΤΟΙ ΑΜΦΙΒΟΛΙΕΣ, ΕΝΩ
ΟΙ ΗΛΙΘΙΟΙ ΕΙΝΑΙ ΓΕΜΑΤΟΙ
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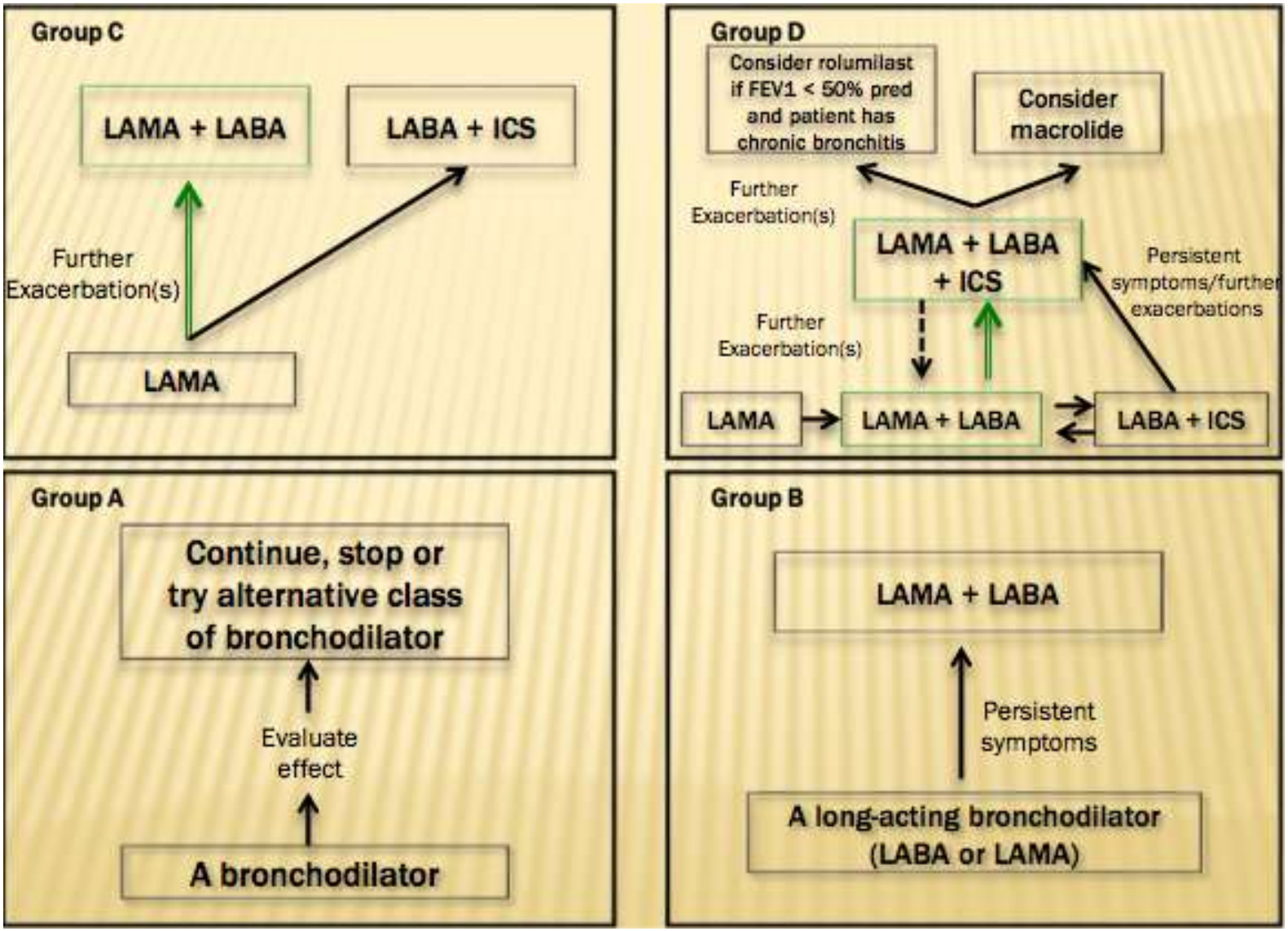
Τσαρλς Μπουκόφσκι

GOLD 2018



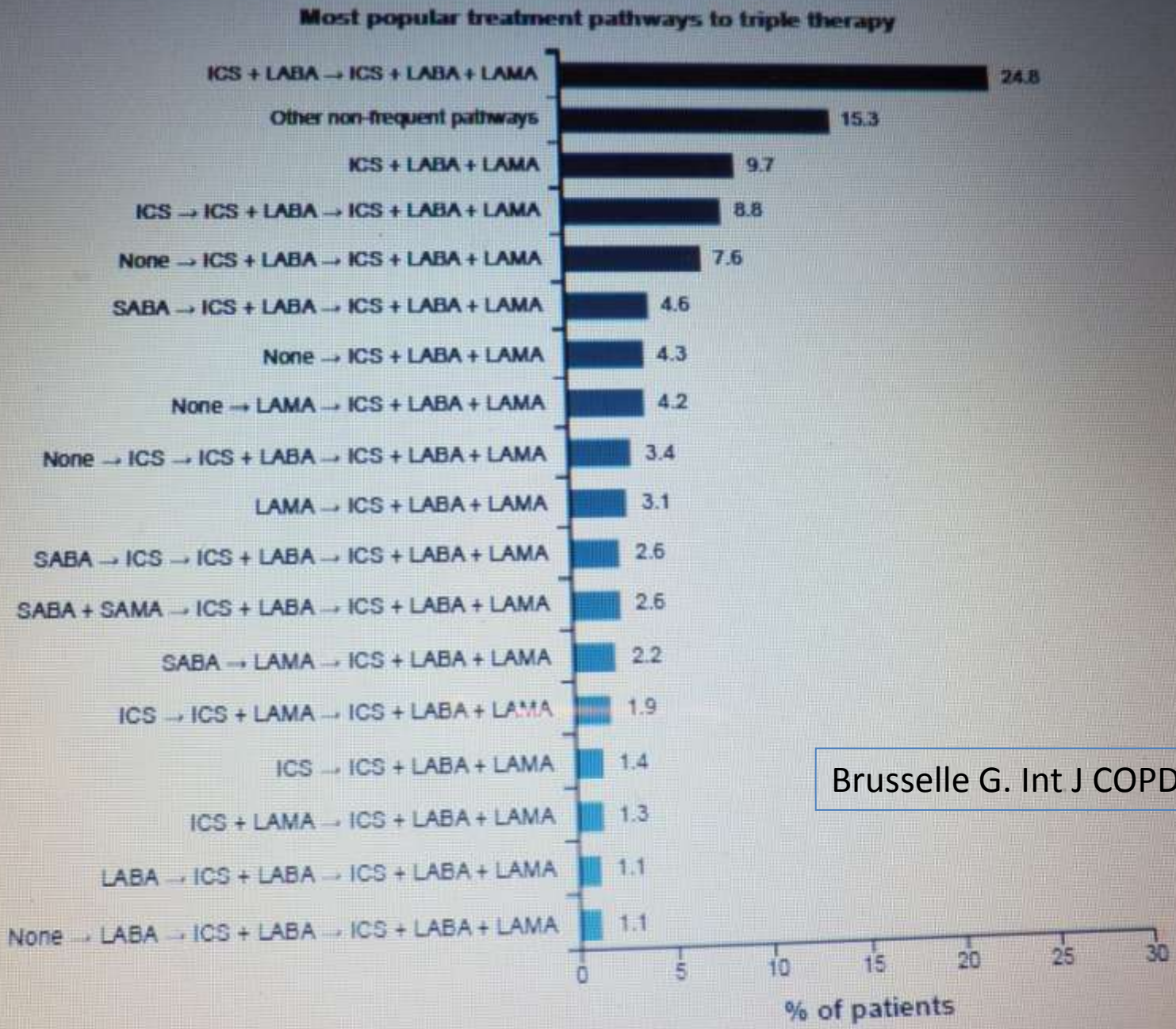
From the Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017. Available from: http://goldcopd.org.

Η ΔΙΑΦΟΡΕΤΙΚΗ ΠΡΑΓΜΑΤΙΚΟΤΗΤΑ…

Brusselle G et al. The inevitable drift to triple therapy in COPD. Int J COPD 2015

Methods: This was a historical analysis of COPD patients without asthma from the Optimum Patient Care Research Database (387 primary-care practices across the UK) from 2002 to 2010. Patient disease severity was classified using GOLD 2013 criteria. Data were analyzed to determine prescribing of TT before, at, and after COPD diagnosis; the average time taken to receive TT; and the impact of lung function grade, modified Medical Research Council dyspnea score, and exacerbation history on the pathway to TT.

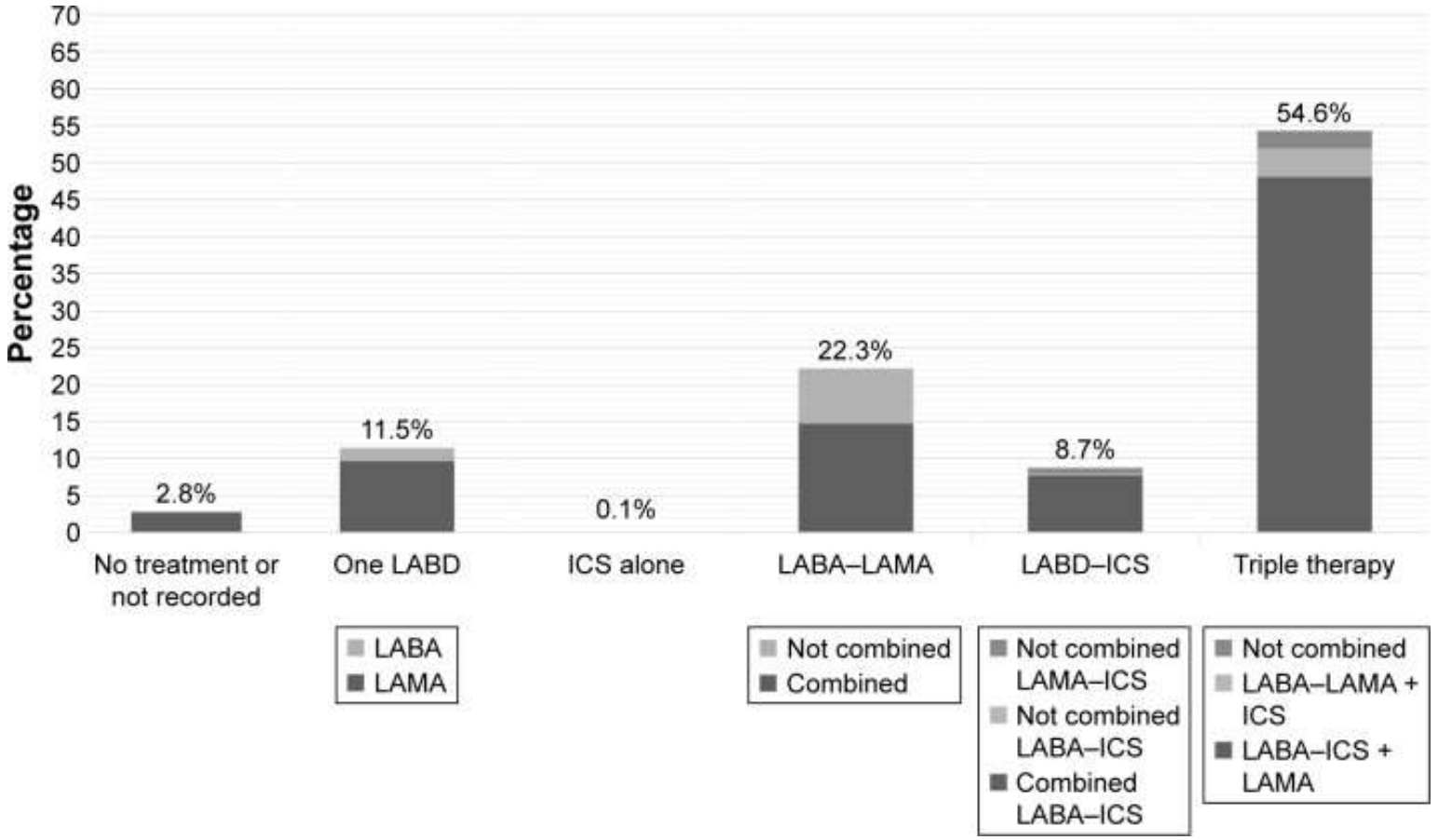
Results: During the study period, **32%** of patients received TT. Of these, **19%, 28%, 37%**, and 46% of patients classified as **GOLD A, B, C**, and D, respectively, progressed to TT after diagnosis (*P*,0.001). Of all patients prescribed TT, 25% were prescribed TT within 1 year of diagnosis, irrespective of GOLD classification (*P*=0.065). **The most common prescription pathway to TT was LABA plus ICS**. It was observed that **exacerbation history** did influence the pathway of LABA plus ICS to TT.



Brusselle G. Int J COPD 2015

of different treatment pathways leading to triple therapy (ICS plus LABA plus LAMA), identified from total triple therapy population (n=3,505).

Lopez-Campos JL. Determinants of medical prescriptions for COPD care: an analysis of the EPOCONSUL clinical audit.



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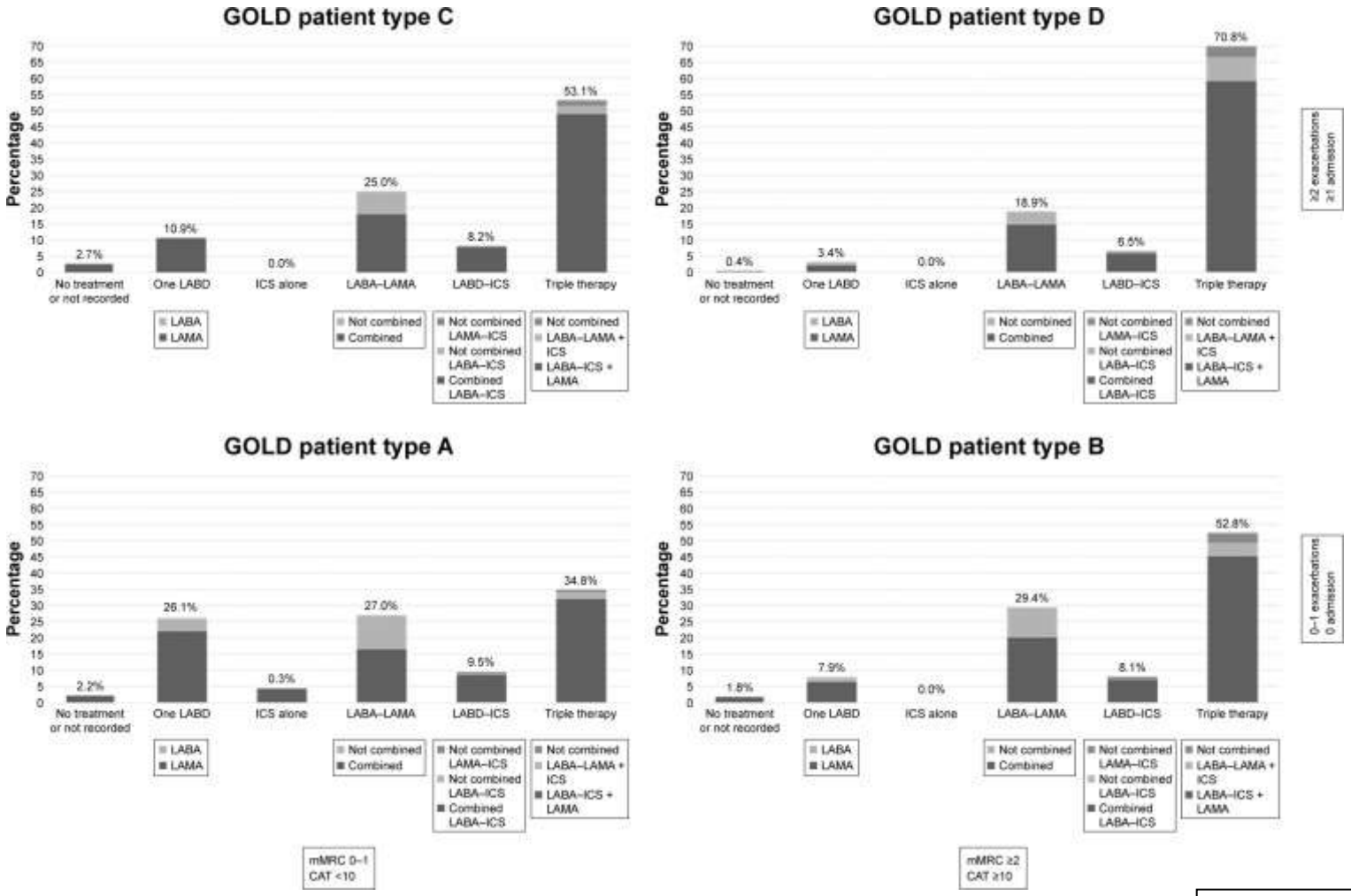
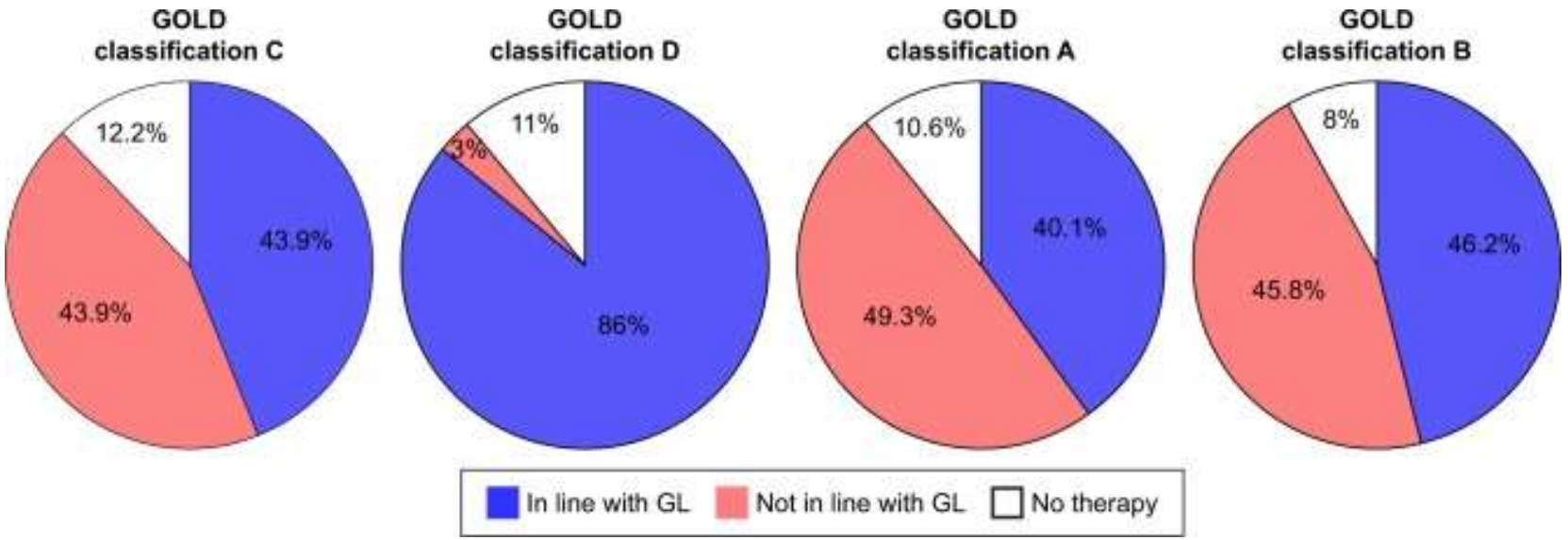


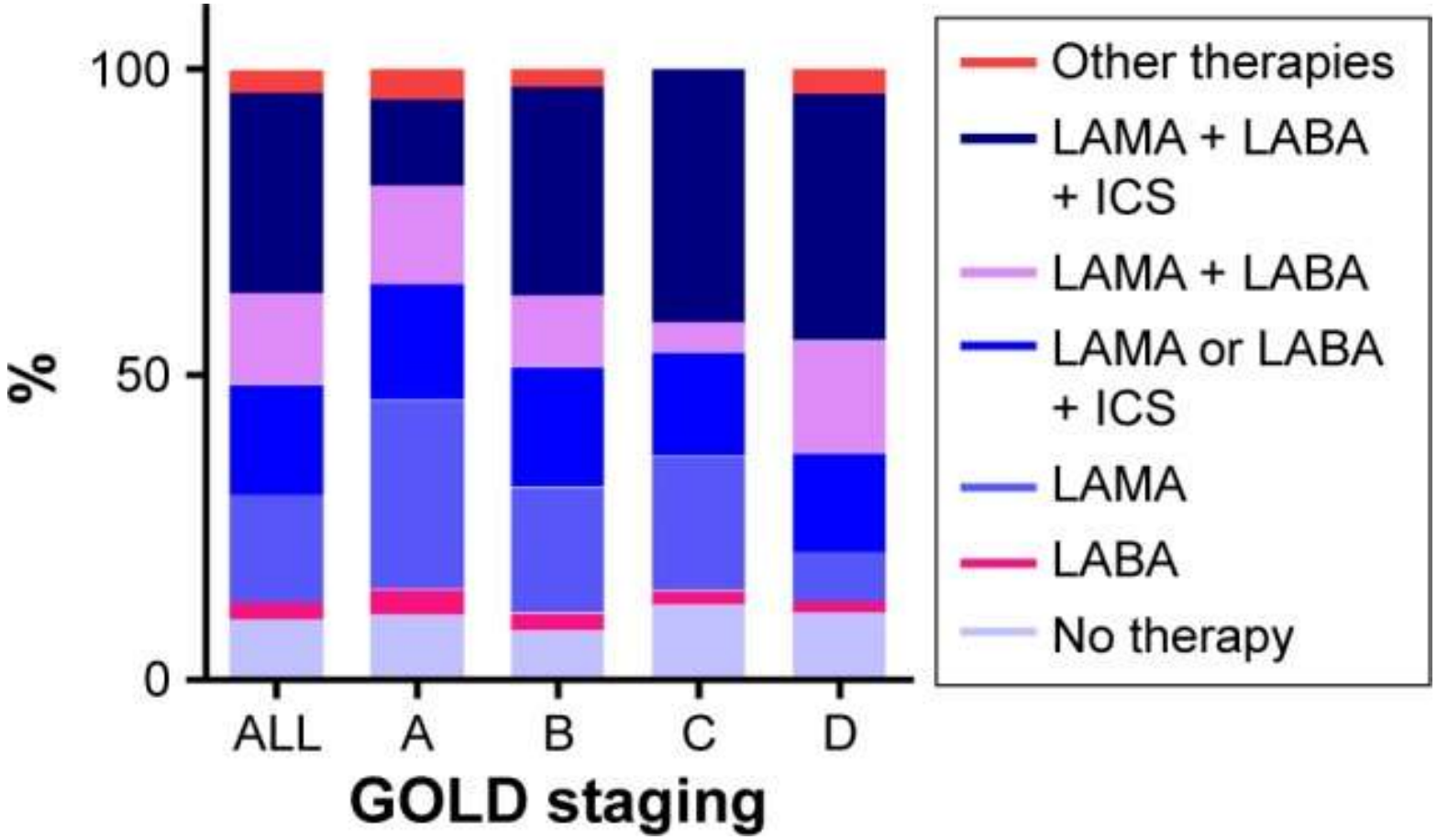
Int J COPD 2018

Palmiotti GA. Adherence to GOLD guidelines in real-life COPD management in the Puglia region of Italy.



Int J COPD 2018

Palmiotti GA. Adherence to GOLD guidelines in real-life COPD management in the Puglia region of Italy.



Int J COPD 2018

Global Initiative for Chronic
Obstructive
Lung
Disease

GLOBAL STRATEGY FOR THE DIAGNOSIS, MANAGEMENT, AND PREVENTION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

COPD Definition

- Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.

Inflammation (local-systemic) ?

Smoking ?

Exacerbations - Morbidity ?

Progression in natural history ?

COPD: Risk factor for comorbidities ?

ABCD assessment tool

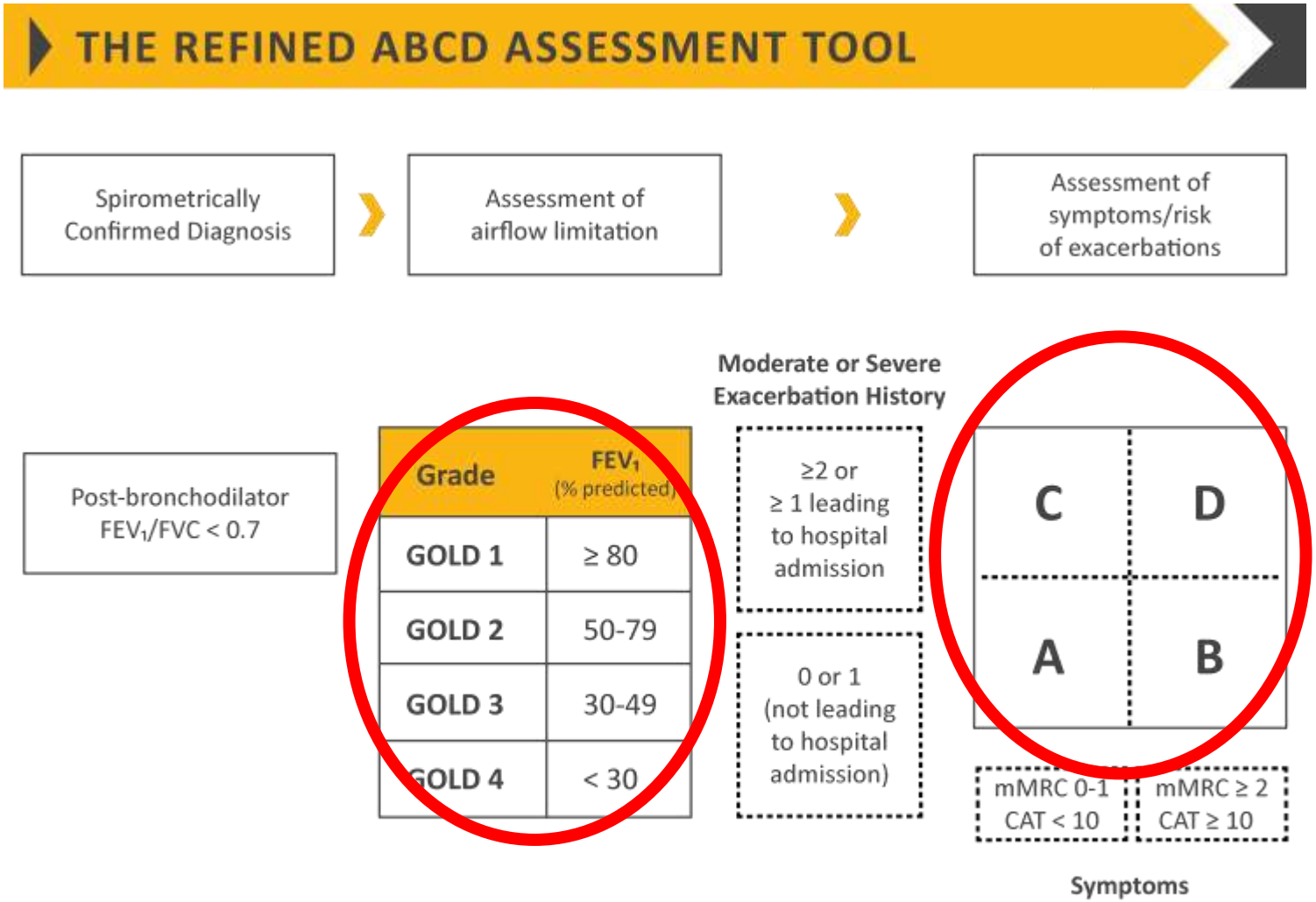


FIGURE 2.4

ABCD Assessment Tool

Example

- Consider two patients:
  - Both patients with FEV_1 < 30% of predicted
  - Both with CAT scores of 18
  - But, one with **0 exacerbations** in the past year and the other with **3 exacerbations** in the past year.

- Both would have been labelled **GOLD D** in the prior classification scheme.
- With the new proposed scheme, the subject with 3 exacerbations in the past year would be labelled **GOLD grade 4, group D**.
- The other patient, who has had no exacerbations, would be classified as **GOLD grade 4, group B**.

Summary

ROLE OF SPIROMETRY

- **Diagnosis**
- **Assessment of severity of airflow obstruction (for prognosis)**
- **Follow-up assessment**
  - » Therapeutic decisions.
    - – Pharmacological in selected circumstances (e.g., discrepancy between spirometry and level of symptoms).
    - – Consider alternative diagnoses when symptoms are disproportionate to degree of airflow obstruction.
    - – Non-pharmacological (e.g., interventional procedures).
  - » Identification of rapid decline.

TABLE 2.6

Management of Stable COPD

- Once COPD has been diagnosed, effective management should be based on an individualized assessment to reduce both current symptoms and future risks of exacerbations.

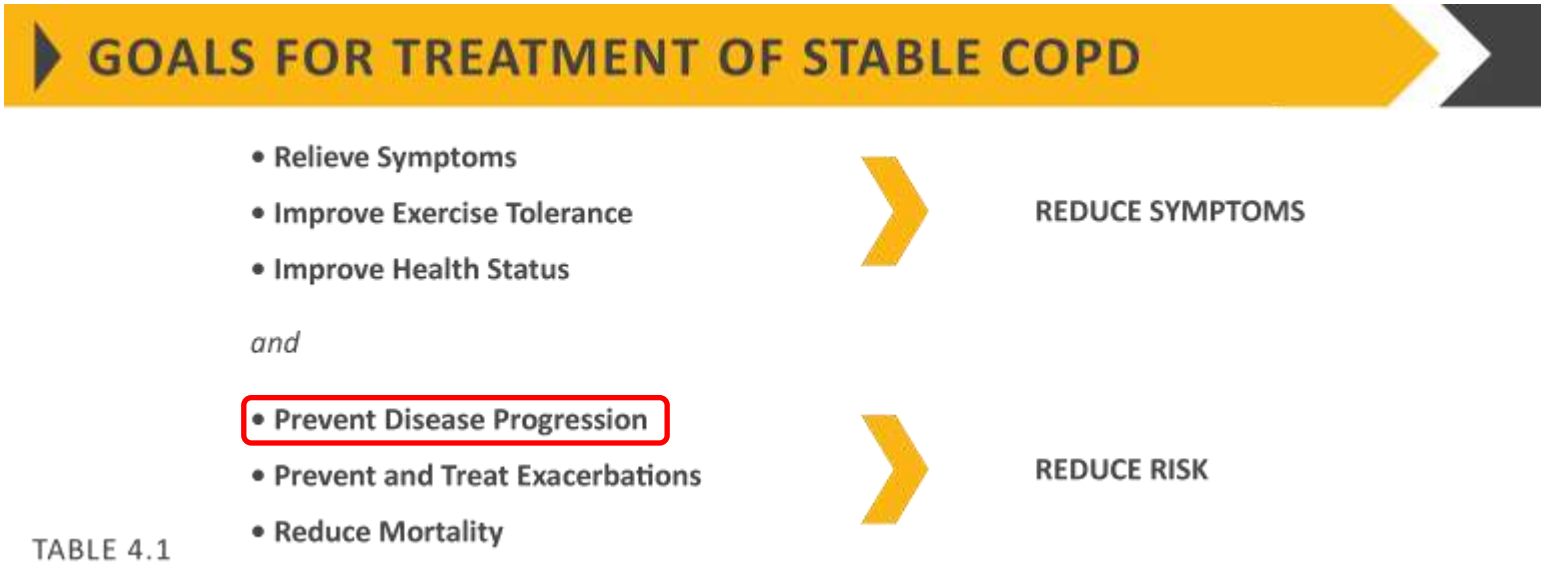
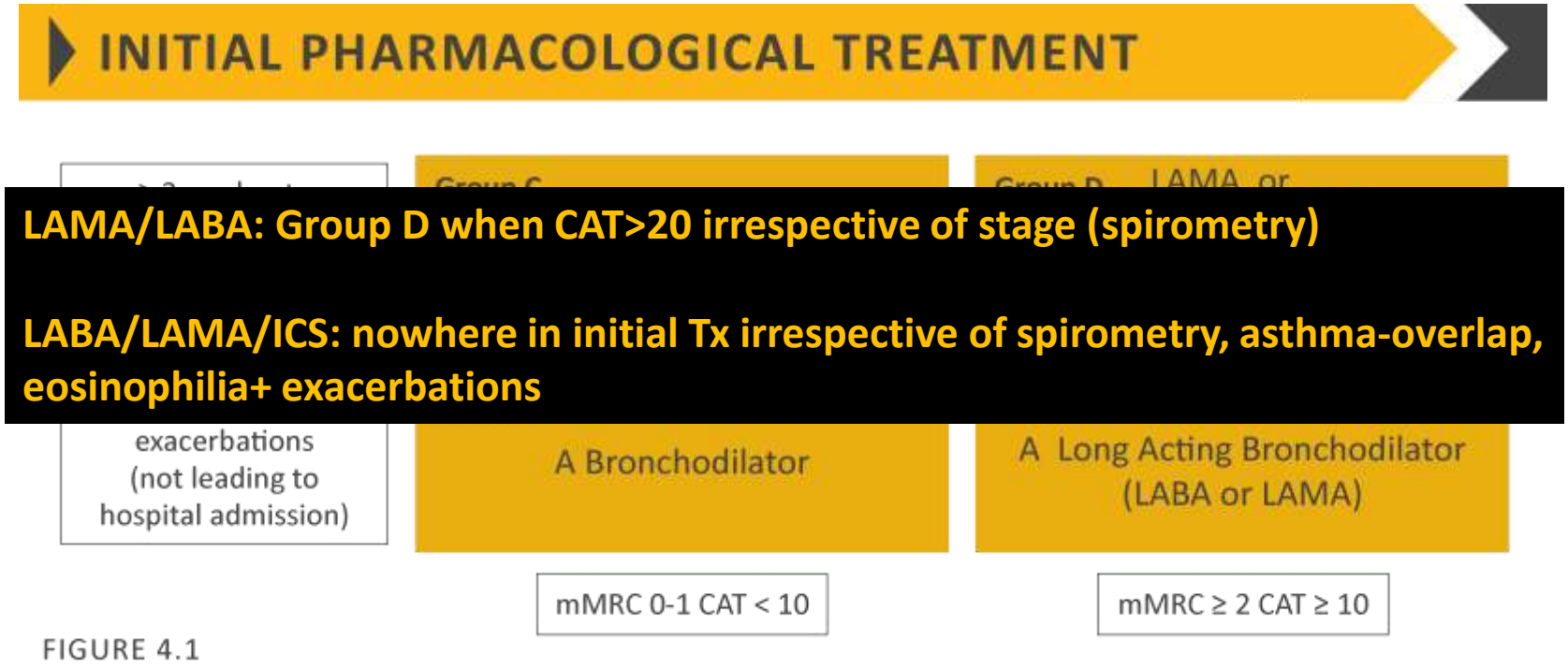


TABLE 4.1

ΘΕΡΑΠΕΙΑ ΣΤΑΘΕΡΗΣ ΧΑΠ
Αρχική Φαρμακοθεραπεία



LAMA/LABA: Group D when CAT>20 irrespective of stage (spirometry)

LABA/LAMA/ICS: nowhere in initial Tx irrespective of spirometry, asthma-overlap, eosinophilia+ exacerbations

FIGURE 4.1

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

Group B

- Initial therapy should consist of a long acting bronchodilator (**LABA** or **LAMA**).
- Long-acting inhaled bronchodilators are superior to short-acting bronchodilators taken as needed i.e., *pro re nata* (prn) and are therefore recommended.

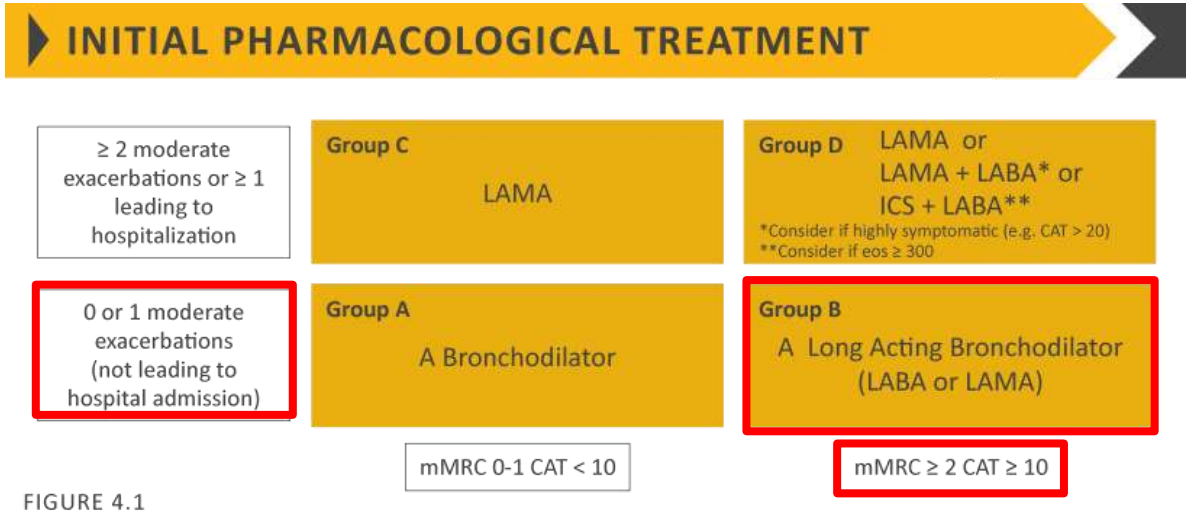


FIGURE 4.1

Group B

- There is no evidence to recommend one class of long-acting bronchodilators over another for initial relief of symptoms in this group of patients.
- In the individual patient, the choice should depend on the patient's perception of symptom relief.
- For patients with severe breathlessness initial therapy with two bronchodilators may be considered.
- **Group B** patients are likely to have comorbidities that may add to their symptomatology and impact their prognosis, and these possibilities should be investigated.

Modified MRC dyspnea scale

MODIFIED MRC DYSPNEA SCALE[a]

PLEASE TICK IN THE BOX THAT APPLIES TO YOU | ONE BOX ONLY | Grades 0 - 4

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.	☐

[a] Fletcher CM. BMJ 1960; 2: 1662.

TABLE 2.5

Group D

- In general, therapy can be started with a LAMA as it has effects on both breathlessness and exacerbations.
- For patients with more severe symptoms (order of magnitude of CAT™ ≥ 20), especially driven by greater dyspnea and/or exercise limitation, LAMA/LABA may be chosen as initial treatment based on studies with patient reported outcomes as the primary endpoint where LABA/LAMA combinations showed superior results compared to the single substances.
- An advantage of LABA/LAMA over LAMA for exacerbation prevention has not been consistently demonstrated, so the decision to use LABA/LAMA as initial treatment should be guided by the level of symptoms.

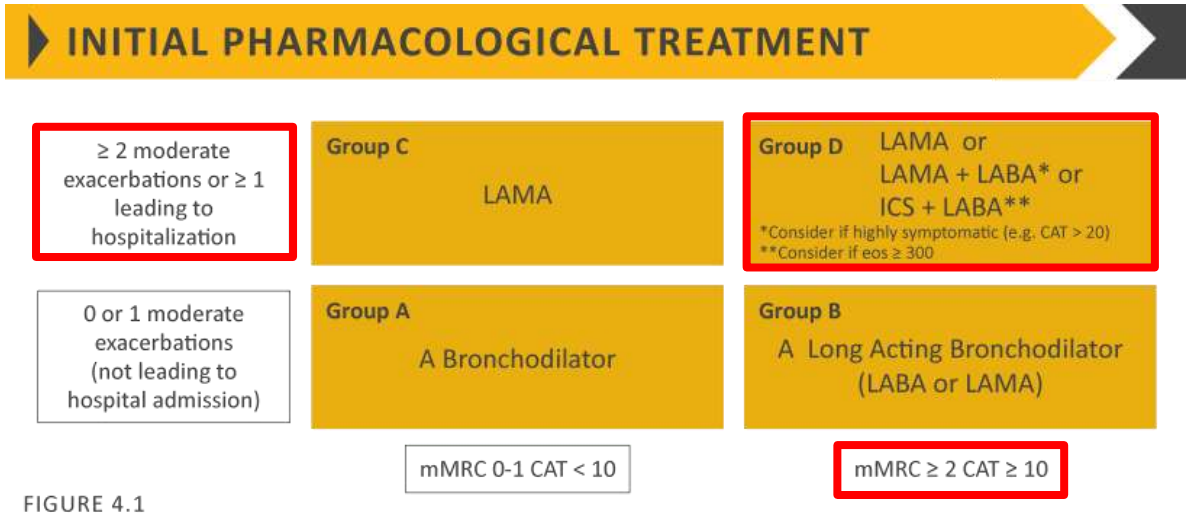


FIGURE 4.1

Group D

- In some patients, initial therapy with LABA/ICS may be the first choice.
- This treatment has the greatest likelihood of reducing exacerbations in patients with blood eosinophil counts ≥ 300 cells/µL.
- LABA/ICS may also be first choice in COPD patients with a history of asthma.
- ICS may cause side effects such as pneumonia, so should be used as initial therapy only after the possible clinical benefits versus risks have been considered.

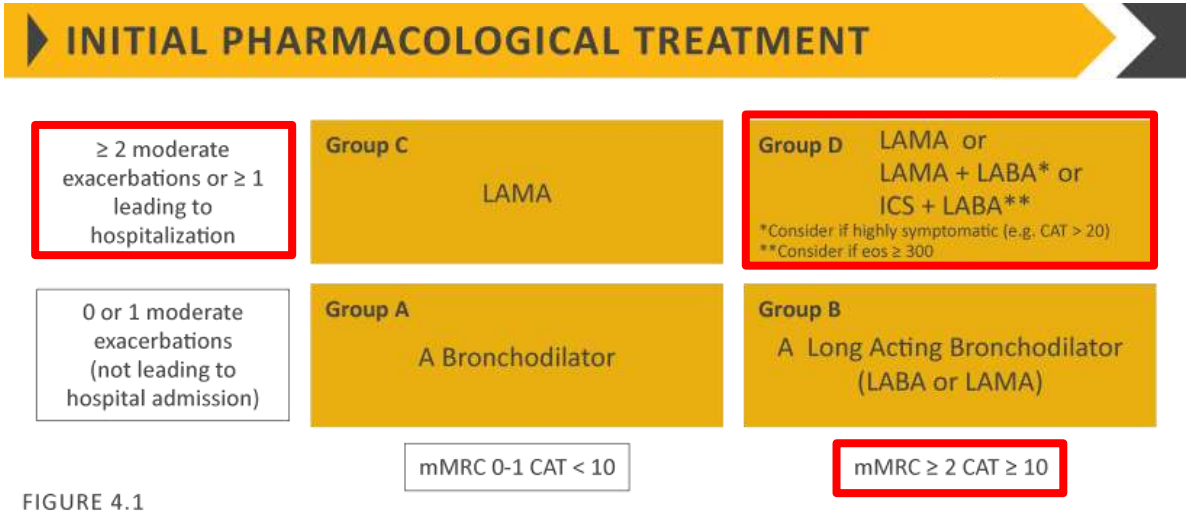
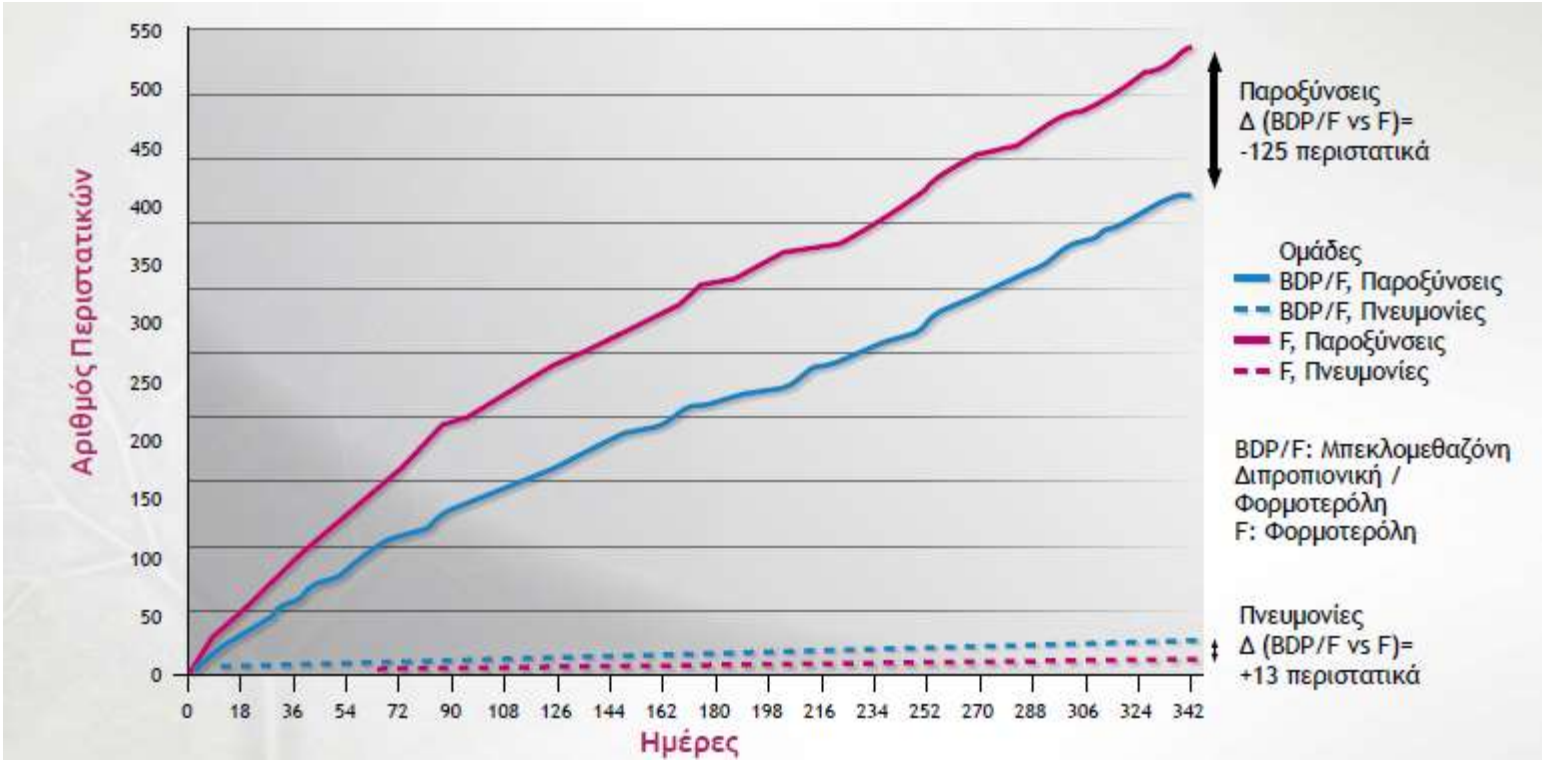


FIGURE 4.1

Το όφελος από τη μείωση των παροξύνσεων υπερισχύει της εμφάνισης πνευμονιών



Ασφάλεια και ανεκτικότητα

Το **«ισοζύγιο» αποτελεσματικότητα/ ασφάλεια** με τη χορήγηση Τριπλής Θεραπείας FF/UMEC/VI **(NNT):**

Αποτρέπεται
1 παρόξυνση ΧΑΠ
επιπλέον ανά έτος για κάθε
4 ασθενείς υπό θεραπεία

Υπάρχει κίνδυνος
1 πνευμονίας
επιπλέον ανά έτος για κάθε
33 ασθενείς υπό θεραπεία

Επιπλέον, αν παρακολουθούσαμε **1.000 ασθενείς για 1 έτος** (1.000 patient-years) αναμένουμε να δούμε:

	Τριπλή Θεραπεία	UMEC / VI
Μέτριες/ σοβαρές παροξύνσεις *(ανά 1000 patient-years)*	**922,8**	**1147,6**
Πνευμονίες *(ανά 1000 patient-years)*	**95,8**	**61,2**

- **σημαντικό όφελος** με περίπου **225 λιγότερες παροξύνσεις**
- στον αντίποδα, ένα αποδεκτό ρίσκο για **επιπλέον 35 πνευμονίες**

AESI: ανεπιθύμητο συμβάν ειδικού ενδιαφέροντος, LRTI: λοίμωξη του κατώτερου αναπνευστικού, SAE: σοβαρό ανεπιθύμητο συμβάν, URTI: λοίμωξη του ανώτερου αναπνευστικού

1. Lipson DA et al. NEJM 2018; doi: 10.1056/NEJMoa1713901 2. Lipson DA et al. NEJM 2018; doi: 10.1056/NEJMoa1713901 (supplementary).

ΘΕΡΑΠΕΙΑ ΣΤΑΘΕΡΗΣ ΧΑΠ
Μοντέλο παρακολούθησης

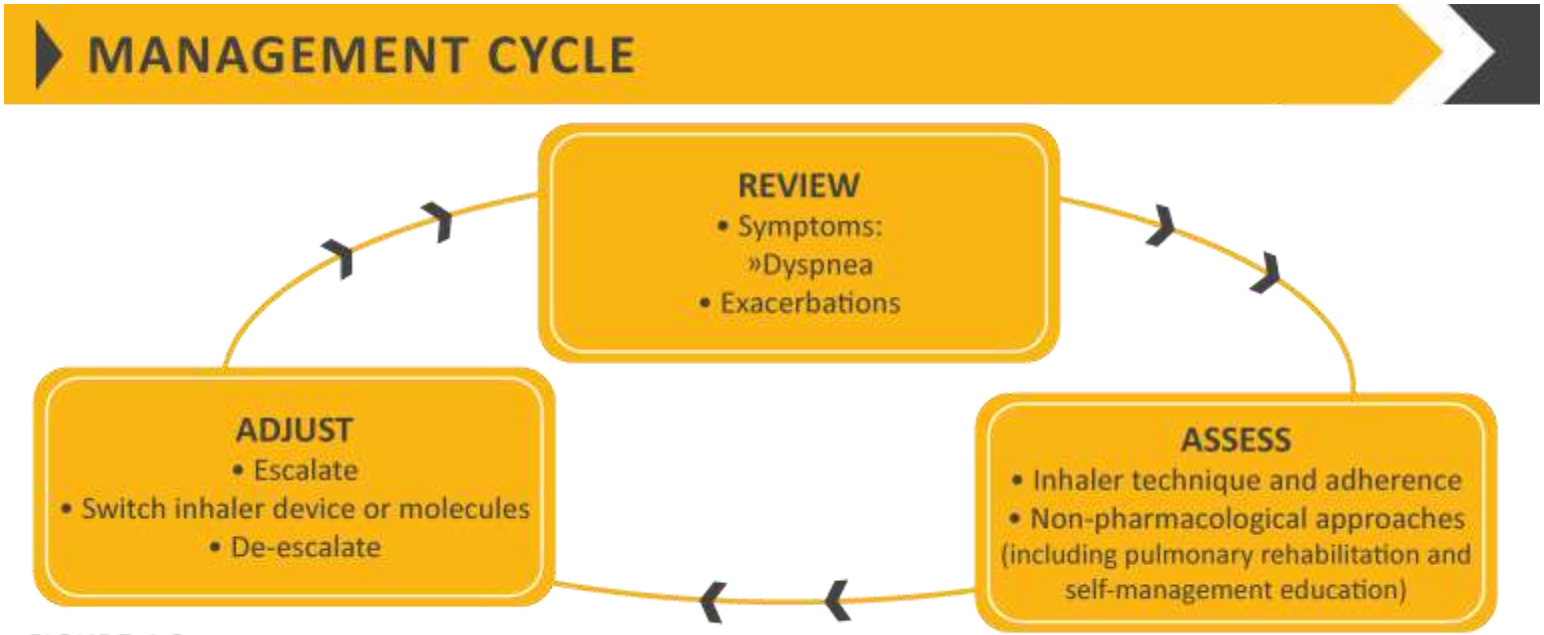
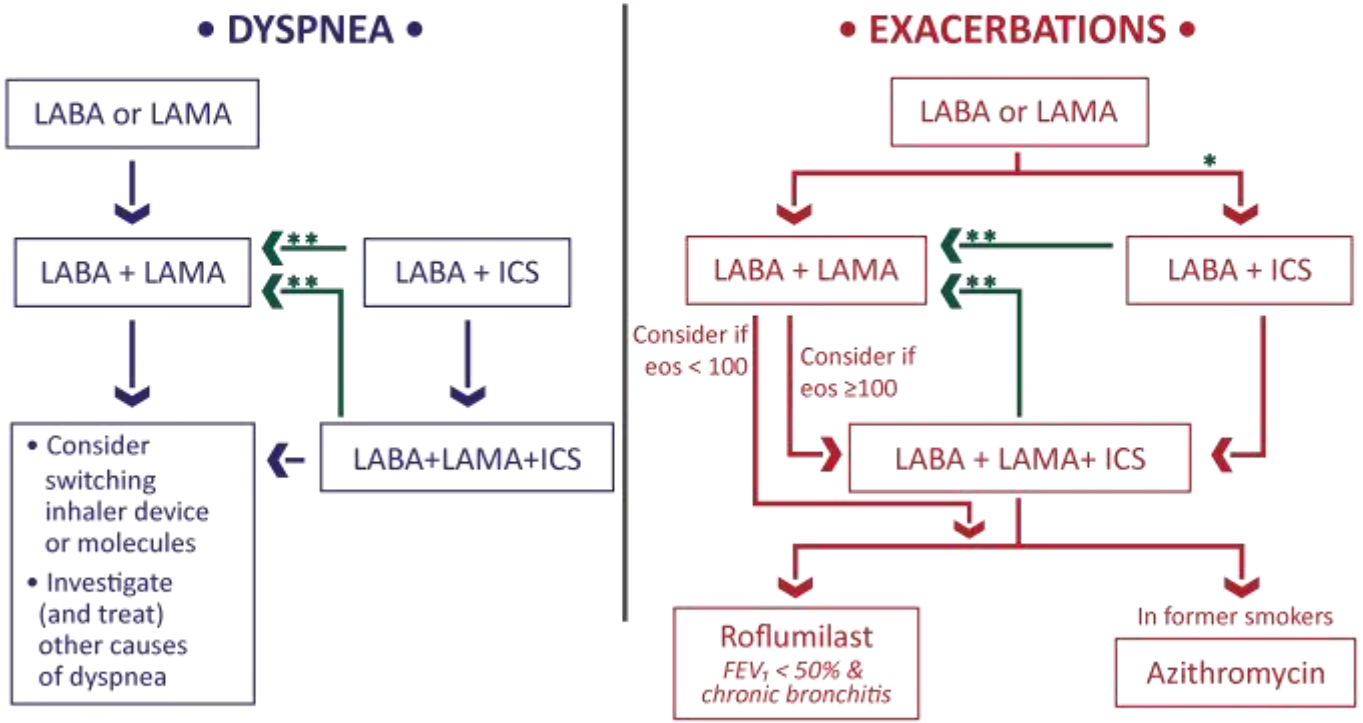


FIGURE 4.2

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



eos = blood eosinophil count (cells/µL)

** Consider if eos ≥ 300 or eos ≥ 100 AND ≥2 moderate exacerbations / 1 hospitalization*

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

FIGURE 4.3

Treatment of stable COPD

- **Figure 4.3** suggests escalation and de-escalation strategies based on available efficacy as well as safety data.
- The response to treatment escalation should always be reviewed, and de-escalation should be considered if there is a lack of clinical benefit and/or side effects occur.
- De-escalation may also be considered in COPD patients receiving treatment who return with resolution of some symptoms that subsequently may require less therapy.
- Patients, in whom treatment modification is considered, in particular de-escalation, should be undertaken under close medical supervision.
- We are fully aware that treatment escalation has not been systematically tested; trials of de-escalation are also limited and only include ICS.

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Inhaled Corticosteroids in COPD: Friend or Foe ?

Agusti A, Fabbri L, Singh D, Vestbo J, Celli B, Franssen F, Rabe KF, Papi A.

STRONG SUPPORT	CONSIDER USE	AVOID USE
History of hospitalisation(s) for ECOPD*		Repeated pneumonia events
≥2 moderate ECOPD/year*	1 moderate ECOPD/year*	
Blood eosinophils >300 cells/μL	Blood eosinophils 100–300 cells/μL	Blood eosinophils <100 cells/μL
History of, or concomitant, asthma		History of mycobacterial infection

*despite appropriate long-acting bronchodilator maintenance therapy

Abbreviations: ICS, inhaled corticosteroid; COPD, chronic obstructive pulmonary disease; ECOPD, COPD exacerbation.

Eur Respir J 2018

Assessment of Exacerbation Risk

- COPD exacerbations are defined as an acute worsening of respiratory symptoms that result in additional therapy.

- Classified as:
  - **Mild** (treated with SABDs only)
  - **Moderate** (treated with SABDs plus antibiotics and/or oral corticosteroids) or
  - **Severe** (patient requires hospitalization or visits the emergency room). Severe exacerbations may also be associated with acute respiratory failure.

- Blood eosinophil count may also predict exacerbation rates (in patients treated with LABA without ICS).

Βασικά σημεία κριτικής GOLD 2019

- **Απόκρυψη της προοδευτικής συν τω χρόνω επιδείνωσης της νόσου και της αναπόφευκτης φυσικής πορείας της.**
- **Υποβάθμιση της σπιρομέτρησης σε εργαλείο διάγνωσης μόνο & σε μέσο αξιολόγησης-προβληματισμού εάν είναι δυσανάλογη των συμπτωμάτων – Δεν συμπεριλαμβάνεται ούτε σαν παράμετρος στην αρχική θεραπεία, ούτε σαν παράμετρος παρακολούθησης, ούτε σαν παράμετρος τροποποίησης της θεραπείας.**
- **Ίσως θα έπρεπε να γίνεται μεγαλύτερη εκμετάλλευση της σπιρομέτρησης και σε άλλες παραμέτρους (FVC, IC, SVC, SAD)**
- **Σωστή η συναξιολόγηση του <u>σταδίου σοβαρότητας</u> (FEV1-pb %pred) και του <u>επιπέδου ελέγχου της νόσου</u> (ABCD) . Όχι μόνο ABCD.**
- **Στην αρχική θεραπεία, μετά την ακύρωση της σπιρομέτρησης, ουσιαστικά καταργείται και το ABCD, δεδομένου ότι η πρώτη επιλογή παντού είναι LAMA (και σε ασθενή με FEV1 65%, δύσπνοια 2 και 0 παροξύνσεις (B) και σε ασθενή με FEV1 35%, δύσπνοια 4, CAT 18, Eos 150 και 4 παροξύνσεις + 2 νοσηλείες(D)).**
- **mMRC = 2 είναι σοβαρή δύσπνοια**
- **Πουθενά στην αρχική θεραπεία τα LAMA/LABA εκτός από D με CAT>20.**
- **Πουθενά στην αρχική θεραπεία τα LAMA/LABA/ICS (ACO ??, παροξύνσεις σε ηωσινοφιλική ΧΑΠ ??)**

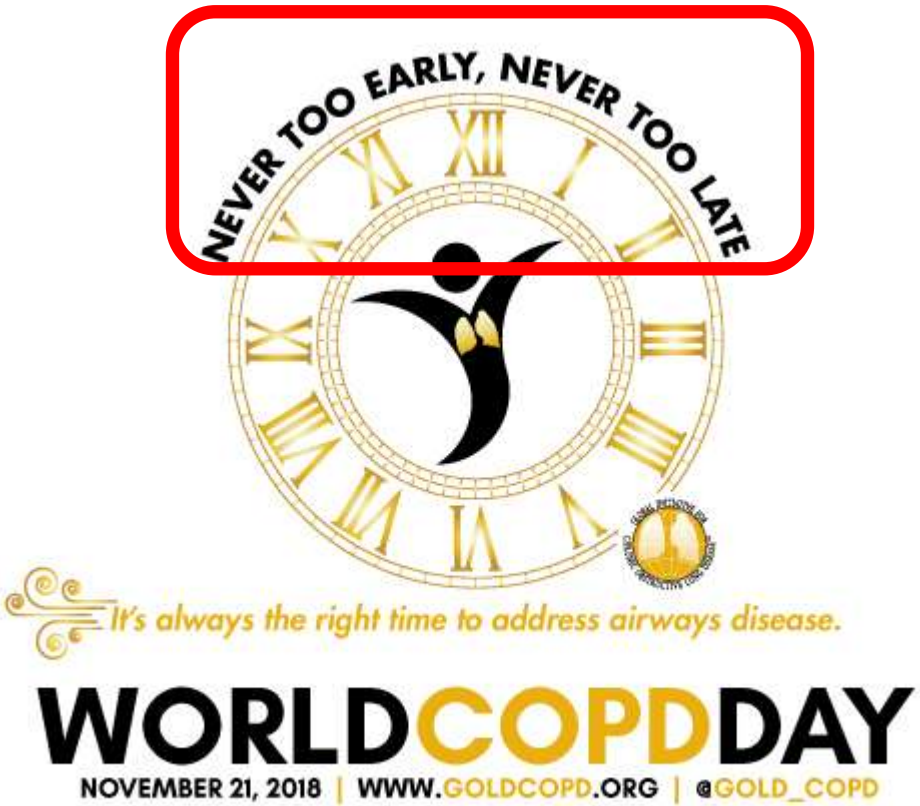
Βασικά σημεία κριτικής GOLD 2019

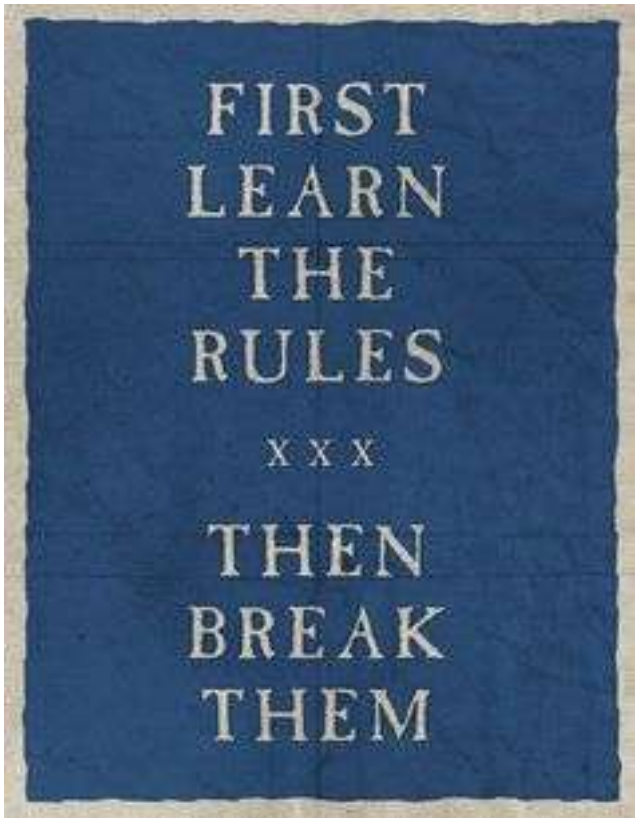
- Πότε θα γίνεται ο επανέλεγχος ?
- Στον επανέλεγχο καταργείται επίσημα το ABCD
- Ακόμα και εάν στον επανέλεγχο στοχεύουμε και σε επιμένουσα δύσπνοια και σε επιμένουσες παροξύνσεις, από LAMA (ή LABA) πάμε σε LABA/ICS εάν τα Eos>300, στερώντας το 2^{ο} βρογχοδιασταλτικό από τον επίμονα δυσπνοϊκό άσθενή.
- Αποκλιμάκωση (ICS) μόνο σε πνευμονία & σοβαρές παρενέργειες, μη ανταπόκριση, εξαρχής μη αναγκαία χορήγηση. ΌΧΙ αποκλιμάκωση εάν ο ασθενής πληροί τις προυποθέσεις για ICS και βελτιώνεται.
- Υπάρχουν πολλές μελέτες αποκλιμάκωσης (COSMIC, GLUKOLD, WISDOM, SUNSET κλπ) που δείχνουν υποτροπή της φλεγμονής, υποτροπή των παροξύνσεων, ταχύτερη απώλεια FEV1 κυρίως σε ηωσινοφιλικούς ασθενείς.
- Υπάρχει σήμα πνευμονίας αλλά δεν είναι σε καμμία μελέτη πιο σημαντικό από το σήμα μείωσης των παροξύνσεων. Επιπλέον, σε αρκετές μελέτες δεν φαίνεται περισσότερη πνευμονία με την χρήση ICS.
- Μέτρια παρόξυνση και με χρήση αντιβιοτικών (πολλές φορές με αυτοδιαχείριση του ασθενούς ή τηλεφωνικά) και με χρήση OCS ??
- Μία μέτρια ή σοβαρή παρόξυνση βιώνεται το ίδιο, έχει την ίδια επίπτωση στην ποιότητα ζωής και έχει την ίδια έκβαση σε ασθενή με FEV1 30% ή με 60% ??

Γενικά σημεία κριτικής

- Όχι στην υπεραπλούστευση - Όχι στην υπεργενίκευση μιάς χρόνιας, προοδευτικά εξελισσόμενης αναπνευστικής νόσου με πολλαπλά πρόσωπα (φαινότυπους – ενδότυπους), που μπορεί να είναι ανίατη αλλά είναι αποτελεσματικά αντιμετωπίσιμη και με δυνατότητες τροποποίησης της φυσικής πορείας της (ταχύτητα επιδείνωσης – ποιότητα ζωής – παροξύνσεις – θνητότητα).
- Όχι minimal αντιμετώπιση – Ναι στην maximal αντιμετώπιση βάσει φαινο- ενδο-τύπων (η κατάλληλη αγωγή στον κατάλληλο ασθενή).
- Όχι σε ένα σύστημα ταξινόμησης, θεραπείας και παρακολούθησης που αφορά τον ειδικό γιατρό μόνο στην διάγνωση ενώ μετά να μπορεί να την διαχειρίζεται ο οποιοσδήποτε.

COPD




FIRST
LEARN
THE
RULES
XXX
THEN
BREAK
THEM


"LEARN THE
RULES LIKE
A PRO SO
YOU CAN
BREAK THEM
LIKE AN
ARTIST"
-Pablo Picasso