



UPDATE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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- No disclosures

Objectives

- Review GOLD classification by symptom and its guidance for treatment
- Explore new studies released on triple inhaler therapy
- Review newest data on chronic azithromycin and roflumilast

We have more than inhalers!



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Diagnostic considerations

<u>GOLD</u>	<u>ATS</u>
FEV1/FVC ratio < 70	FEV1/FVC ratio < 5 th percentile of predicted value or LLN

In patients with FEV₁/FVC < 0.70:

GOLD 1:	Mild	FEV ₁ ≥ 80% predicted
GOLD 2:	Moderate	50% ≤ FEV ₁ < 80% predicted
GOLD 3:	Severe	30% ≤ FEV ₁ < 50% predicted
GOLD 4:	Very Severe	FEV ₁ < 30% predicted

Your name:

Today's date:



How is your COPD? Take the COPD assessment test™ (CAT)

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your well being and daily life. Your answers, and test score, can be used by you or your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

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 (0) (1) (2) (3) (4) (5) I am very sad

		Score
I never cough	(0) (1) (2) (3) (4) (5) I cough all the time	<input type="text"/>
I have no phlegm (mucus) in my chest at all	(0) (1) (2) (3) (4) (5) My chest is completely full of phlegm (mucus)	<input type="text"/>
My chest does not feel tight at all	(0) (1) (2) (3) (4) (5) My chest feels very tight	<input type="text"/>
When I walk up a hill or one flight of stairs I am not breathless	(0) (1) (2) (3) (4) (5) When I walk up a hill or one flight of stairs I am very breathless	<input type="text"/>
I am not limited doing any activities at home	(0) (1) (2) (3) (4) (5) I am very limited doing activities at home	<input type="text"/>
I am confident leaving my home despite my lung condition	(0) (1) (2) (3) (4) (5) I am not at all confident leaving my home because of my lung condition	<input type="text"/>
I sleep soundly	(0) (1) (2) (3) (4) (5) I don't sleep soundly because of my lung condition	<input type="text"/>
I have lots of energy	(0) (1) (2) (3) (4) (5) I have no energy at all	<input type="text"/>
Total score		<input type="text"/>

The MRC Breathlessness Scale

Grade	Degree of breathlessness related to activities
1	Not troubled by breathlessness except on strenuous exercise
2	Short of breath when hurrying on the level or walking up a slight hill
3	Walks slower than most people on the level, stops after a mile or so, or stops after 15 minutes walking at own pace
4	Stops for breath after walking about 100 yds or after a few minutes on level ground
5	Too breathless to leave the house, or breathless when undressing

Vogelmeier C, Criner G, Martinez F, et al. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2017 Report. GOLD Executive Summary. *Am J Respir Crit Care Med.* 2017 Mar 1;195(5):557-582.

Exacerbation risk

Low risk

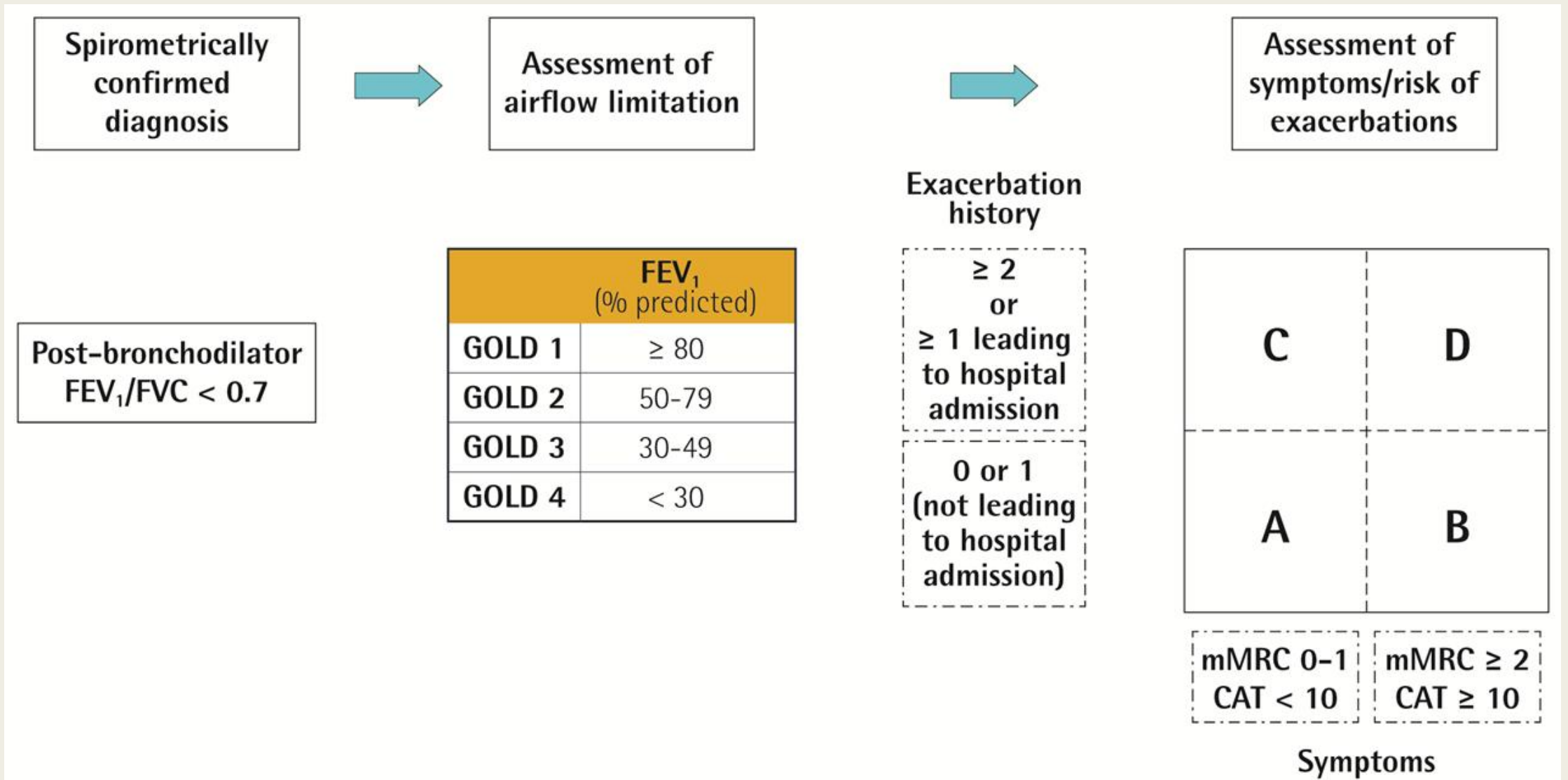
0 to 1 exacerbations
(no hospitalizations)

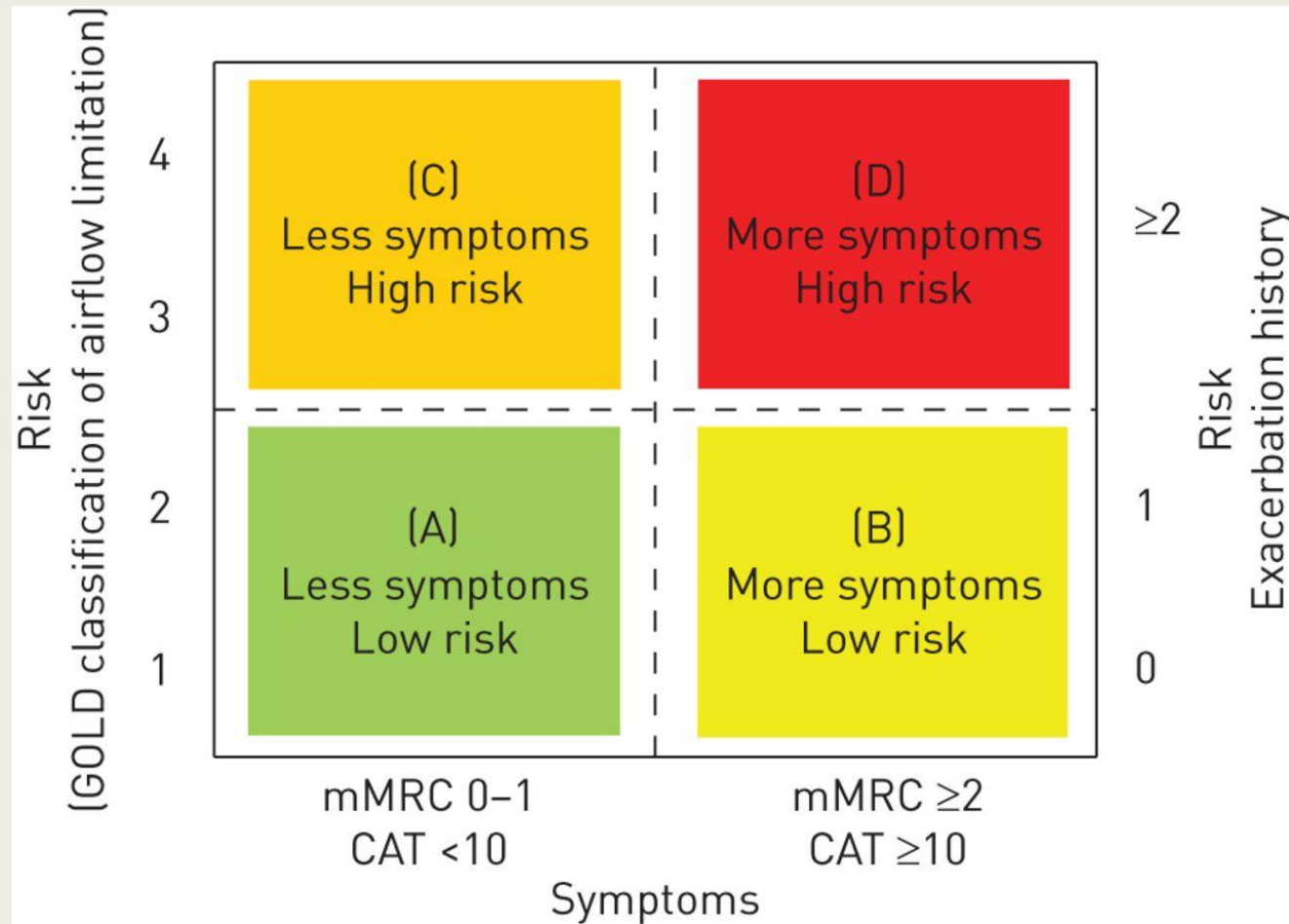
High risk

2 exacerbation

or

>1 exacerbation
leading to
hospitalization

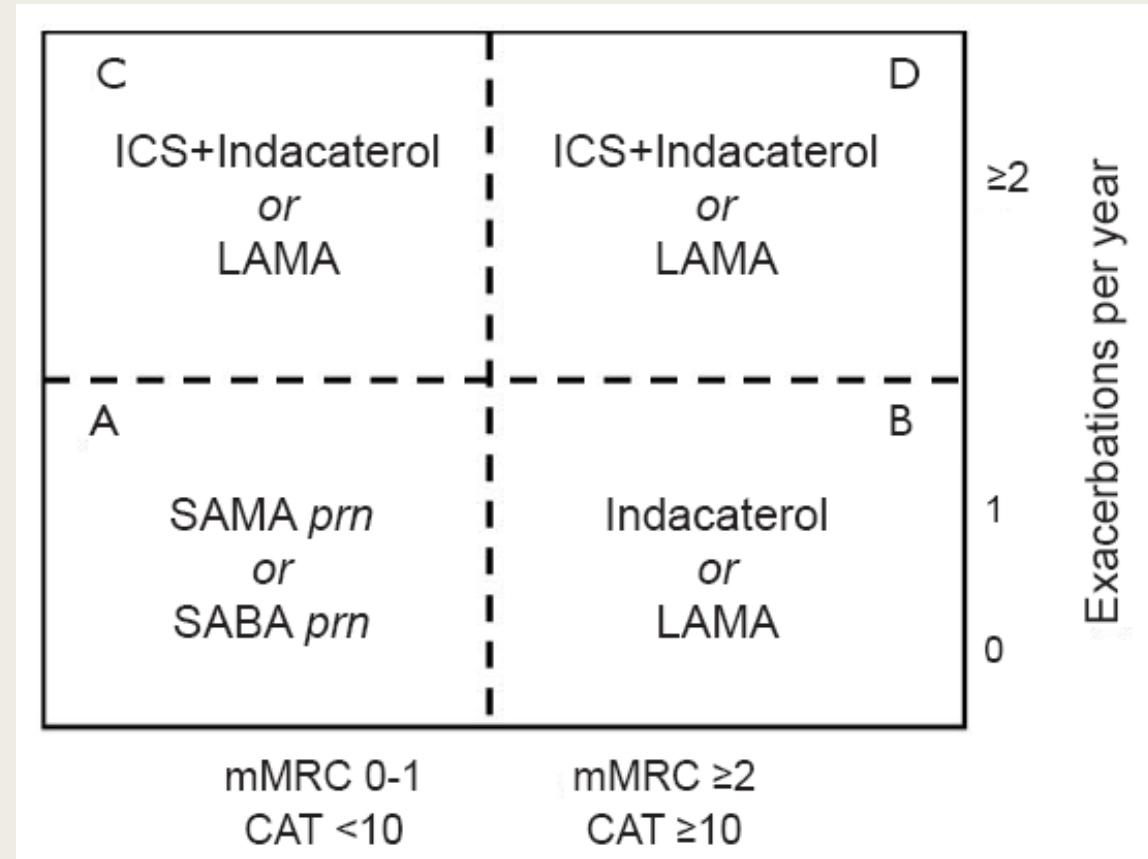




What's the point?



Treatment guidance



Prediction of risk of exacerbation?

Table 4 Annual rate of exacerbations (95% confidence interval), per GOLD

Old stage		P-value*	New stage		P-value*	Substage		P-value*
2	0.53 (0.50 - 0.55)	-	A	0.35 (0.29 - 0.41)	-	C1	0.47 (0.39 - 0.57)	-
3	0.72 (0.69 - 0.76)	<0.001	B	0.45 (0.42 - 0.48)	0.001	C2	0.55 (0.41-0.71)	0.37
4	0.80 (0.72 - 0.89)	0.09	C	0.58 (0.51 - 0.68)	0.001	C3	0.96 (0.70-1.24)	0.06
			D	0.74 (0.71 - 0.77)	0.001	D1	0.56 (0.53-0.60)	-
						D2	0.75 (0.69-0.81)	<0.001
						D3	0.97 (0.92-1.04)	<0.001
AIC	22,697.09			22,571.27			22,417.35	

Mortality prediction?

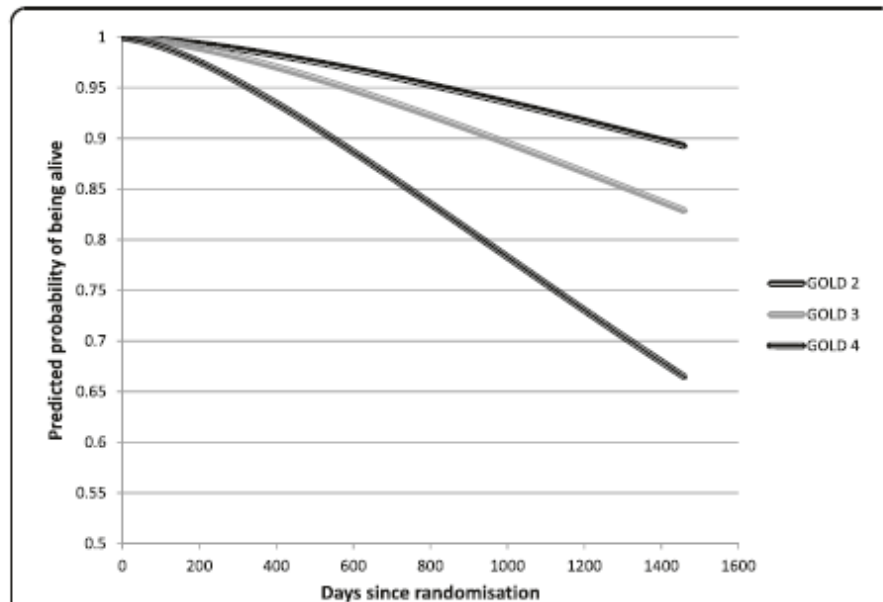


Figure 1 Model-based adjusted survival curves, per GOLD stage 2, 3 and 4.

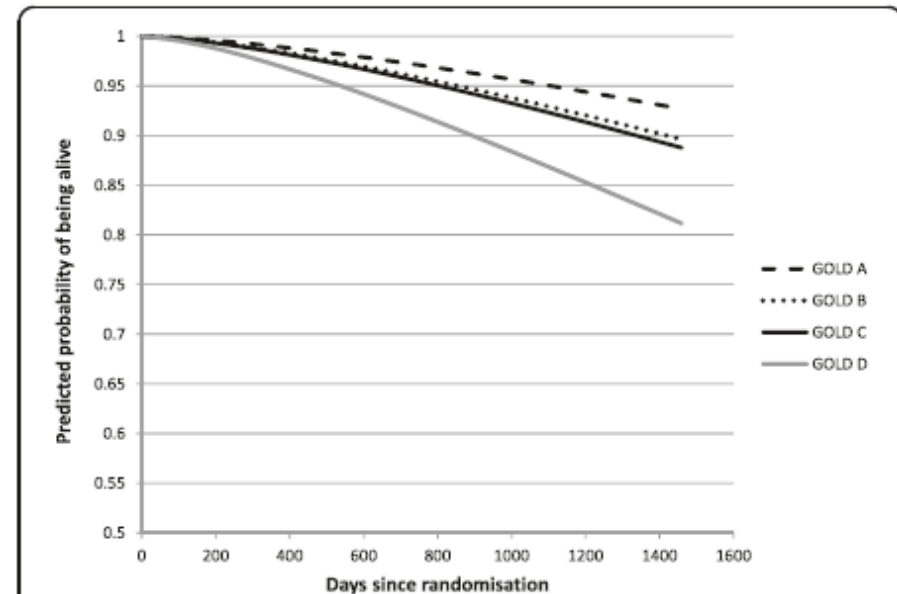


Figure 2 Model-based adjusted survival curves, per GOLD stage A, B, C and D.

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Respiratory Inhalers

At a Glance 2016

Allergy & Asthma Network is a national nonprofit organization dedicated to ending needless death and suffering due to asthma, allergies and related conditions through outreach, education, advocacy and research.



AllergyAsthmaNetwork.org

800.878.4403

Short-acting beta₂-agonist bronchodilators relax tight muscles in airways and offer quick relief of symptoms such as coughing, wheezing and shortness of breath for 3-6 hours

ProAir® HFA
albuterol sulfate
[D2B] A



ProAir® RespiClick
albuterol sulfate inhalation powder
[D2B] A



Proventil® HFA
albuterol sulfate
A



Ventolin® HFA
albuterol sulfate
[D2B] A



Xopenex HFA®
levalbuterol tartrate
A



Long-acting beta₂-agonist bronchodilators relax tight muscles in airways and offer lasting relief of symptoms such as coughing, wheezing and shortness of breath for at least 12 hours

Arcapta® Neohaler™
indacaterol inhalation powder
C



Serevent® Diskus®
salmeterol xinafoate inhalation powder
[D2B] A C



Striverdi® RespiMat®
olodaterol hydrochloride
[D2B] C



Inhaled corticosteroids reduce and prevent swelling of airway tissue; they do not relieve sudden symptoms of coughing, wheezing or shortness of breath

Aerospan®
80 mcg flunisolide
★ A



Alvesco® HFA
80 mcg, 160 mcg ciclesonide
[D2B] A



Arnuity® Ellipta®
100 mcg, 200 mcg fluticasone furoate inhalation powder
[D2B] A



Asmanex® HFA
mometasone furoate
[D2B] A



Asmanex® Twisthaler®
110 mcg, 220 mcg mometasone furoate inhalation powder
[D2B] A



Flovent® Diskus®
50 mcg, 100 mcg, 250 mcg fluticasone propionate inhalation powder
[D2B] A



Flovent® HFA
44 mcg, 110 mcg, 220 mcg fluticasone propionate
[D2B] A



Pulmicort Flexhaler®
80 mcg, 160 mcg budesonide inhalation powder
[D2B] A



QVAR® (HFA)
40 mcg, 80 mcg beclomethasone dipropionate
[D2B] A



Combination medications contain both inhaled corticosteroid and long-acting beta₂-agonist (LABA)

Advair Diskus®
100/50, 250/50, 500/50 fluticasone propionate and salmeterol inhalation powder
[D2B] A C



Advair® HFA
45/21, 115/21, 230/21 fluticasone propionate and salmeterol xinafoate
[D2B] A



Breo® Ellipta®
100/25 mcg, 200/25 mcg fluticasone furoate and vilanterol inhalation powder
[D2B] A C



Dulera®
100/5, 200/5 mometasone furoate and formoterol fumarate dihydrate
[D2B] A



Symbicort® (HFA)
80/4.5, 160/4.5 budesonide and formoterol fumarate dihydrate
[D2B] A C



contain both long-acting muscarinic antagonist (LAMA) and long-acting beta₂-agonist (LABA)

Anoro® Ellipta®
umeclidinium and vilanterol inhalation powder
[D2B] C



Stiolto® RespiMat®
tiotropium bromide and olodaterol
[D2B] C



Utibron® Neohaler®
glycopyrrolate and indacaterol inhalation powder
[D2B] C



Muscarinic antagonist (anticholinergic) bronchodilators relieve cough, sputum production, wheeze and chest tightness associated with chronic lung diseases

Short-acting
Atrovent® HFA
ipratropium bromide
[D2B] C



Long-acting
Seebri™ Neohaler®
glycopyrrolate inhalation powder
C



Incruse® Ellipta®
umeclidinium inhalation powder
[D2B] C



Spiriva® HandiHaler®
tiotropium bromide inhalation powder
C



Spiriva® RespiMat®
1.25, 2.5 mcg tiotropium bromide
[D2B] A C



Tunorza™ Pressair™
acridinium bromide inhalation powder
C

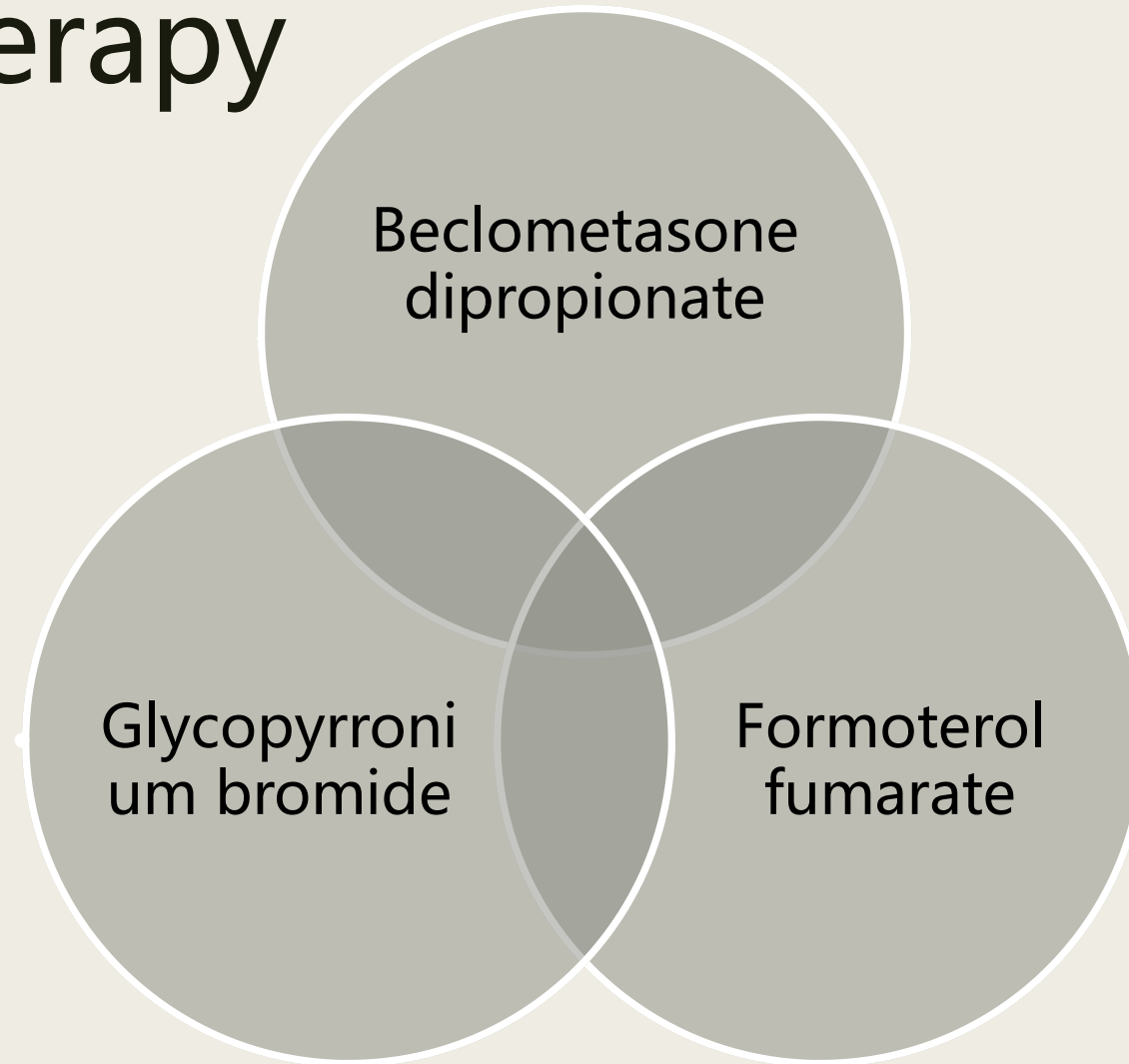


Combination anticholinergic and beta₂-agonist Short-acting

Combivent® RespiMat®
ipratropium bromide and albuterol
[D2B] C



Triple therapy

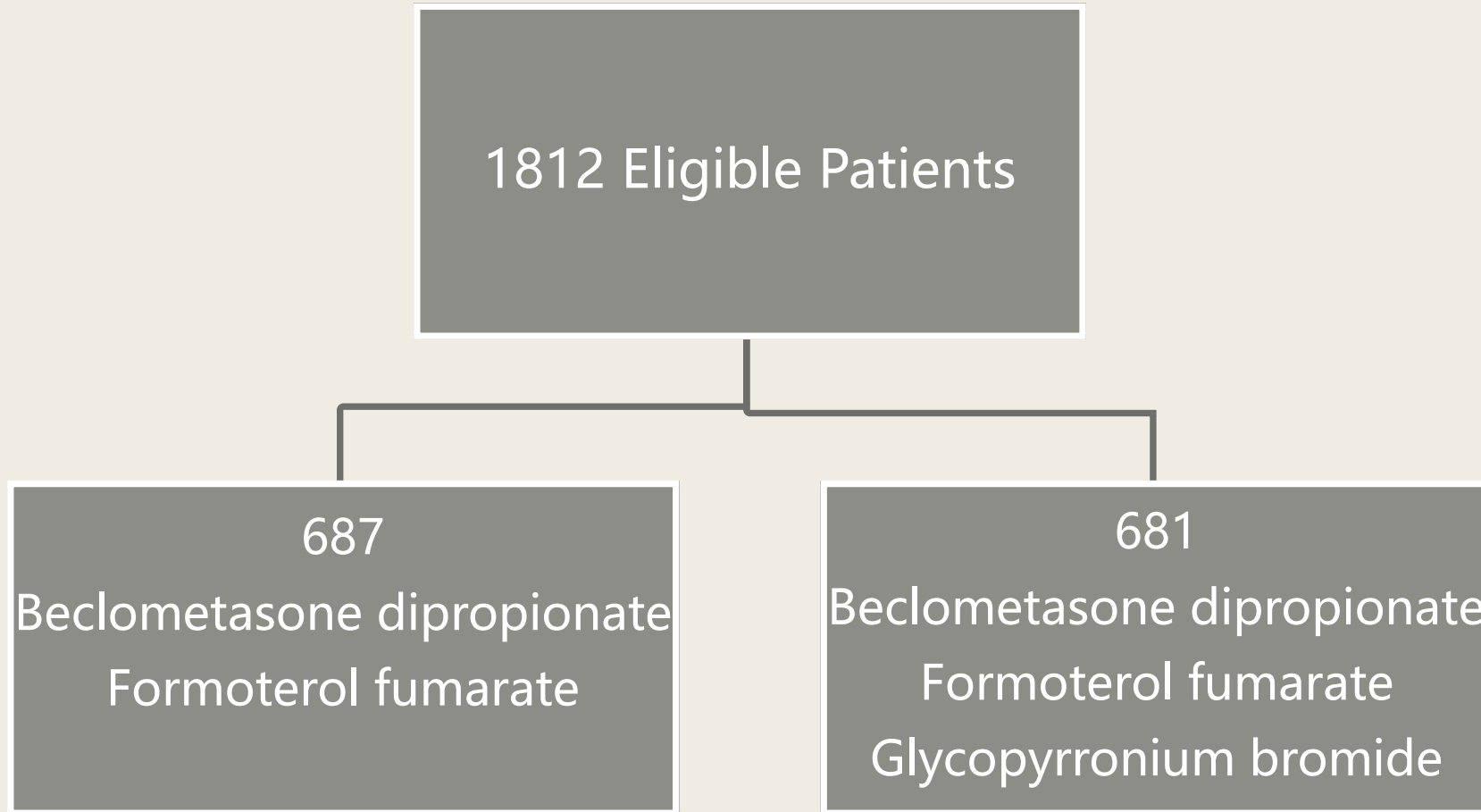


Inclusion Criteria

- Age > 40 years
- FEV1/FVC ratio < 70%, FEV1 < 50%
- Long acting therapy for 2 months
- Symptomatic

Exclusion Criteria

- COPD exacerbation in last 4 weeks
- Allergy or atopy
- Severe cardiac disease



Main outcomes

- Triple therapy had more effect on 2 hour post dose FEV1
- 23% lower rate of exacerbation with triple therapy
- No difference in breathlessness
- Improvement in QOL

Problems

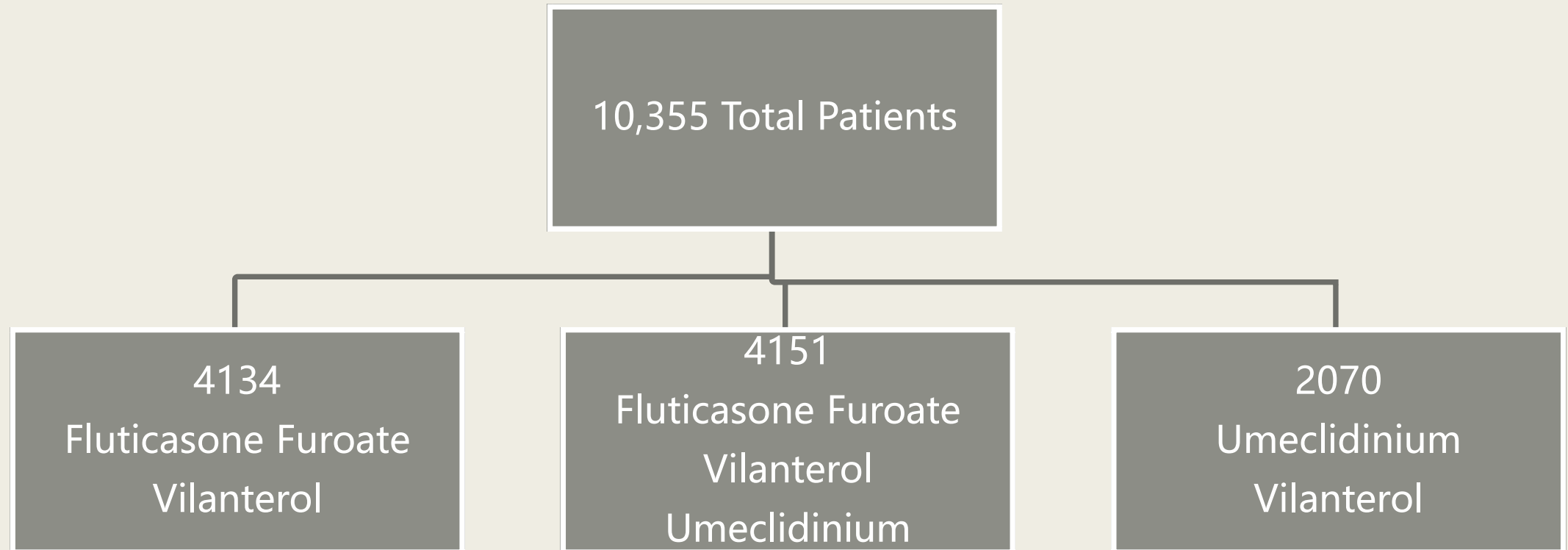
- Didn't address LABA and LAMA combination
- Low baseline exacerbation rate
- Do you need a triple inhaler or triple therapy

What about pneumonia during ICS use?



“THE BAD NEWS IS, THERE IS NO CURE FOR THE COMMON COLD. THE GOOD NEWS IS, I THINK YOU HAVE PNEUMONIA.”

IMPACT trial



Outcomes

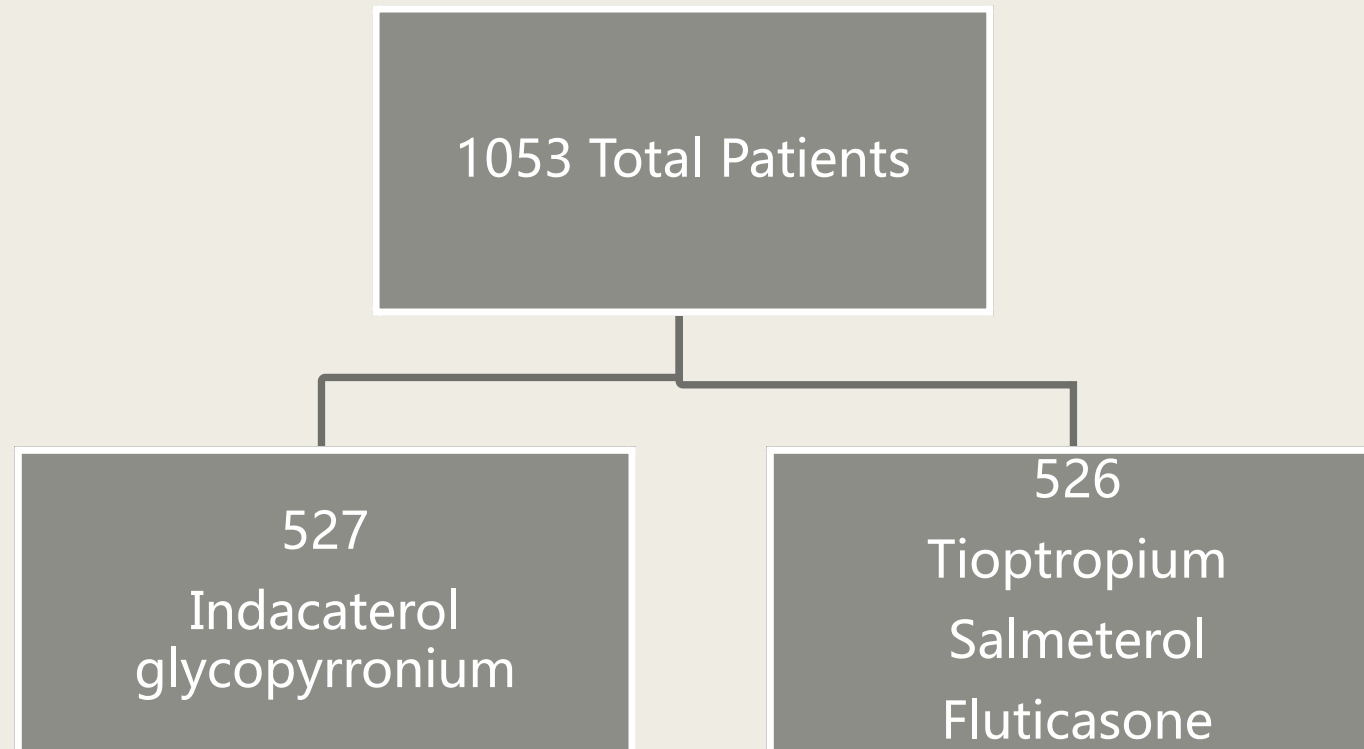
- Significantly lower rates of moderate or severe COPD exacerbations, better lung function, QOL than any other dual therapy
- ICS-LABA combination superior with rates of exacerbations compared to LABA-LAMA, contrast to FLAME trial.
- All cause mortality?



SUNSET Trial

Can you safely withdraw ICS in patient on long-term triple therapy without frequent exacerbations?

SUNSET Trial



Sunset Trial - Outcomes

- Significant decrease in FEV1
- No difference in moderate to severe COPD exacerbation except in patient group with > 300 eosinophils.



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Do macrolides truly reduce the risk
of exacerbations?

2011
NEJM

- Compared azithromycin 250mg daily to placebo
- Less exacerbations and increased QOL

2015
PLOS ONE

- Meta-analysis
- Could reduce exacerbations
- Could increase macrolide resistance

2018
CHEST

- Long term efficacy and safety
- Retrospective analysis
- Reduction in exacerbations
- Increase in resistant infection and pseudomonas infections

Roflumilast

Roflumilast



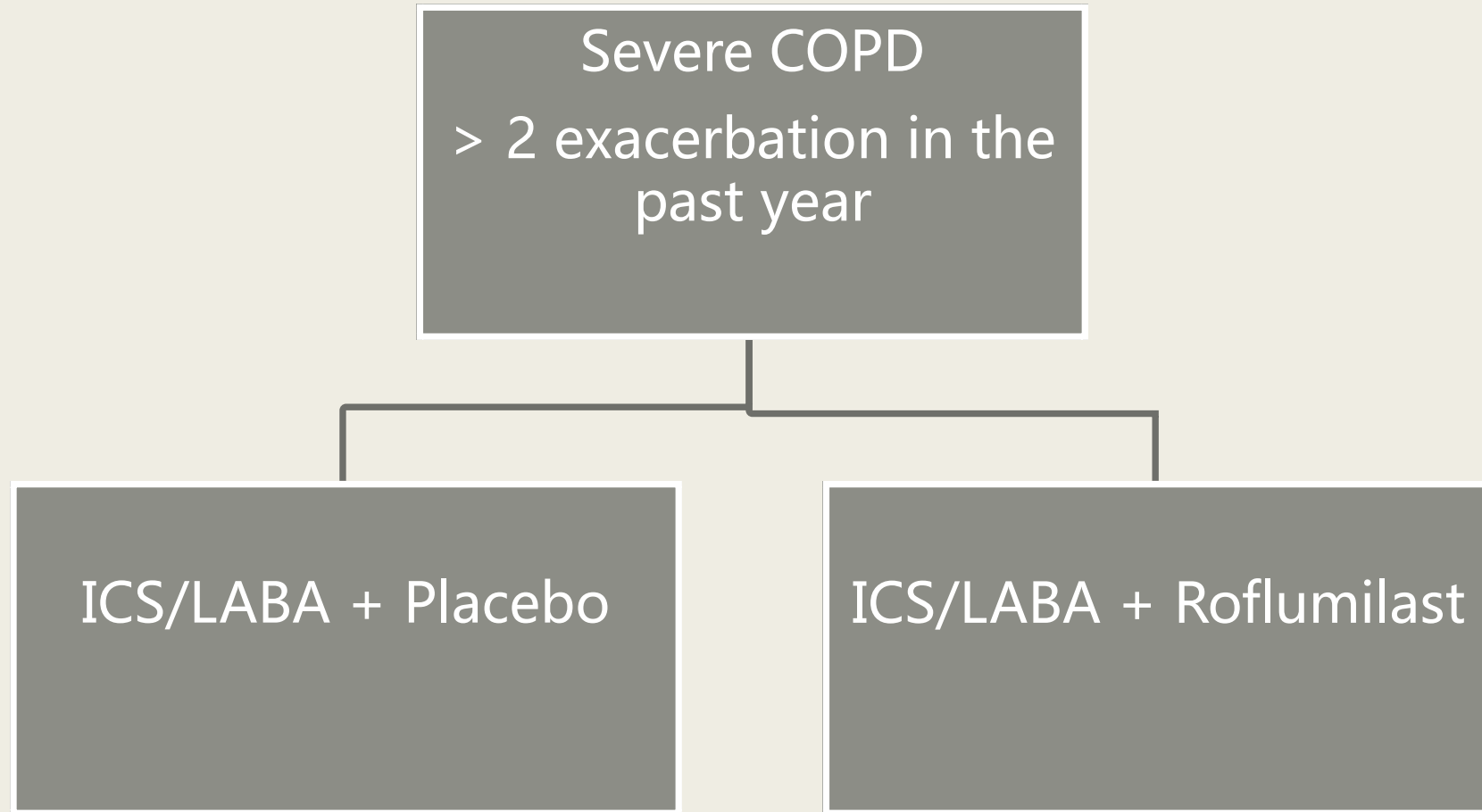
REACT Trial

- First large trial with roflumilast
- Compared patients with severe COPD using roflumilast versus placebo
- 14.2% decrease in moderate to severe exacerbation in 1 year of use

When do you add on roflumilast?

- Maximal inhaler therapy
- History of multiple exacerbations
- Chronic systemic corticosteroids
- Caution side effects

What's new with roflumilast?



Main outcomes

Decreased
overall
exacerbations

Greatest
decrease in
hospitalized
patients

Decrease in
death and
hospitalization
related to
severe
exacerbations

Summary

- Consider using symptoms based model for classification and treatment guidance
- New triple inhaler therapy trials show a reduction in COPD exacerbation rates
- Inhaler therapy can be de-escalated safely in patients on triple therapy with good control
- Newer data on chronic azithromycin in COPD suggests that there is long term reduction in exacerbations but increased rates of infection
- Newer data on roflumilast suggests that patients who have been hospitalized for COPD exacerbation have the greatest decrease in rates of exacerbation

References

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