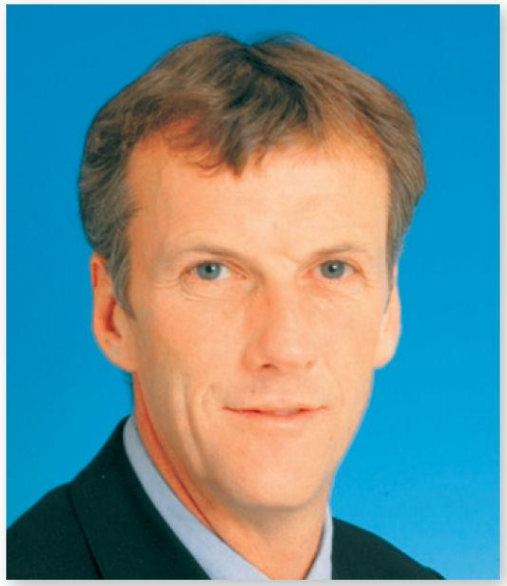

Adjunct Associate Professor Robert Young

General Physician

Auckland City Hospital

Saturday, June 10, 2017

7:00 - 7:55 GlaxoSmithKline Breakfast Session - COPD

New approaches in the management of COPD

Dr Robert Young
BMedSc MBChB DPhil (Oxon) FRACP FRCP
Associate Professor
Consultant Physician

Disclosures and disclaimer

- I am not being paid an honorarium for this presentation
- I am not a GSK employee and do not hold shares in GSK
- No part of this presentation can be copied, retrieved, photographed or downloaded without permission from GSK and Assoc Prof Rob Young
- I have previously received honoraria for presentations sponsored by GlaxoSmithKline and Astra Zeneca on topics related to COPD and it's management
- I received honoraria for participation on an advisory board for GSK

Commonly asked questions from New Zealand GP's about COPD

- ✓ What are **the new types of inhaler devices** now available?
- ✓ Can we have clarification around **Special Authority criteria** for the dual bronchodilators; duration of assessment of mono bronchodilator before adding a dual bronchodilator?
- ✓ What are the changes to the **new 2017 GOLD Strategy Update?:**
  - Is the 2017 GOLD Strategy saying I should be managing my patients with co-morbid asthma with a **LAMA/LABA** (rather than treating as asthma)?
  - **Eosinophils** are not generally recommended as a biomarker in clinical practice. Why do you think this is?
  - Do you have any recommendations on if/how to withdraw **ICS/LABA**?

New Approaches in COPD management: Agenda

1. Overview of treatments available for COPD in NZ

2. The changing landscape of COPD

- Summary of changes to the 2017 GOLD strategy update
- FEV_1 for diagnosis and prognosis
- Pharmacologic treatment updates including new place for LAMA/LABA
- Patients most suitable for ICS/LABA
- Importance of inhaler delivery

3. Non-pharmacological treatment for COPD

Burden of COPD in New Zealand - Key Statistics

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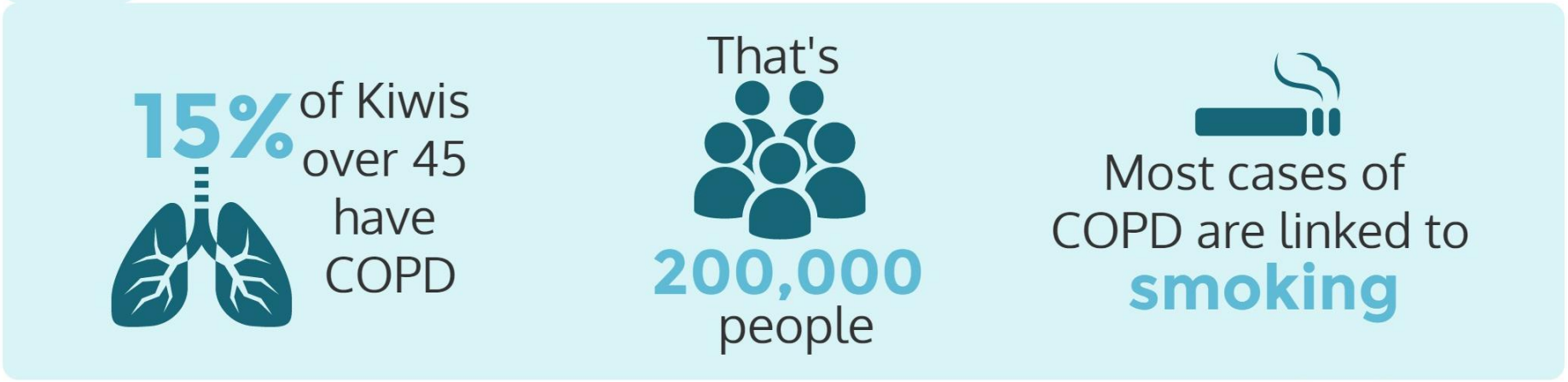
- per year (3



- **Approximately 87 per 100,000 people with a new diagnosis per year = 3,500 new cases per year**
- **However studies show that as much as 70% of patients with COPD go undiagnosed**

https://www.asthmafoundation.org.nz/research/key-statistics (accessed 20/03/2017)
http://asthmafoundation.org.nz/wp-content/uploads/2012/08/2015-Respiratory-Impact-Report.pdf (accessed 20/03/2017)

Overview of treatments available for COPD in NZ

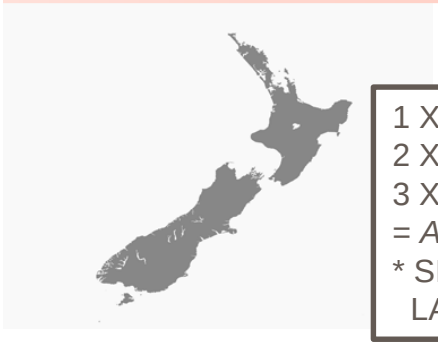
The changing landscape of COPD treatments in NZ

Introduction of new COPD therapies

Changes to 2017 GOLD Strategy Update

GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE

2016 — March — November



1 X new ICS/LABA = *Breo Ellipta*
2 X new LAMA = *Incruse Ellipta and Spiriva in Respimat*
3 X new dual bronchodilators*
= *Anoro Ellipta, Spiolto Respimat, Ultibro Breezhaler*
* SPECIAL AUTHORITY REQUIREMENTS:
LAMA monotherapy prior to LAMA/LABA

LABAs have been left out to simplify schematic
ICS = inhaled corticosteroid; LABA = long acting beta2 agonist; LAMA = long acting muscarinic antagonist

Overview of inhalers available for COPD in NZ

Adapted from http://ccn.health.nz/FocusAreas/ServiceLevelAlliances/Pharmacy/tabid/1347/ArticleID/1307/Funded-Inhalers-in-New-Zealand-2016.aspx (accessed 20/03/2017) ICS = inhaled corticosteroid; LABA = long acting beta2 agonist; LAMA = long acting muscarinic antagonist

The changing landscape of COPD

Summary of changes to the 2017 GOLD strategy update

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

We have clear treatment goals **that have not changed**

These goals should be achieved with minimal side effects

* To date, no pharmacotherapy has been proven to prevent disease progression or reduce mortality in COPD

Reference: GOLD 2015. p32. http://www.goldcopd.org/Guidelines/guidelines-resources.html; Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2017.

Summary of changes to the 2017 GOLD strategy update - 1

- Lung function is no longer included in the treatment classification grid, but remains important for diagnosis and prognosis
- Greater emphasis on individualised treatment and individualised treatment choices (co-existing asthma)
- Greater guidance on treatment options, with escalation (and de-escalation) strategies now suggested
- Greater emphasis on the use of LAMA/LABA for appropriate patients

Summary of changes to the 2017 GOLD strategy update - 2

- Triple Therapy is recommended for patients who have a high burden of symptoms and/or exacerbations despite initial maintenance therapy
- ICS/LABAs are recommended for patients (1) with co-existing asthma or ACOS, (2) with a higher blood eosinophil count, and (3) where patients are unable to access newer treatment classes
- There is a significant relationship between poor inhaler technique and symptom control in patients with COPD; therefore, inhaler technique needs to be assessed regularly

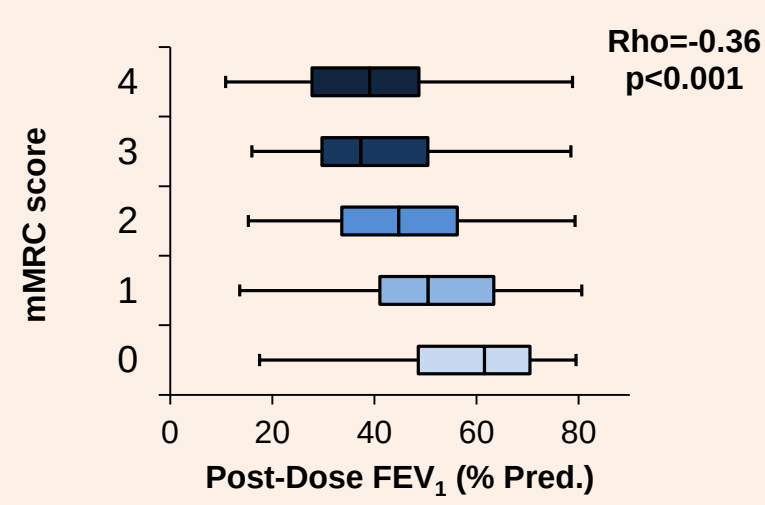
Reference: 1. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2017.

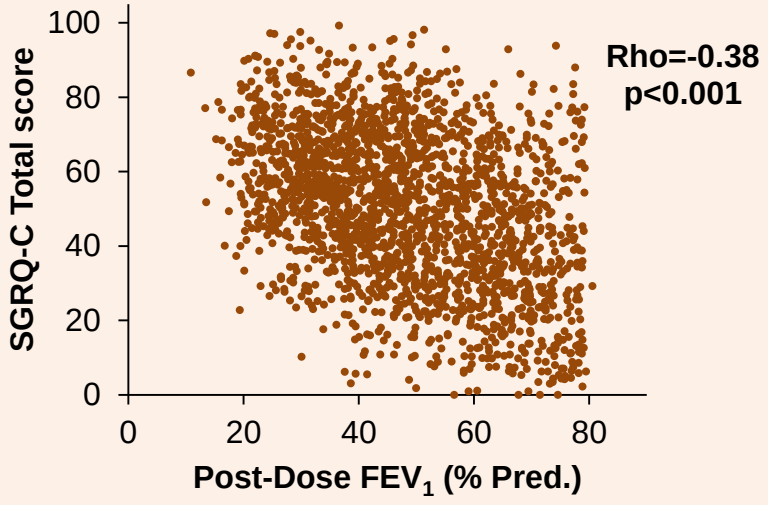
The changing landscape of COPD

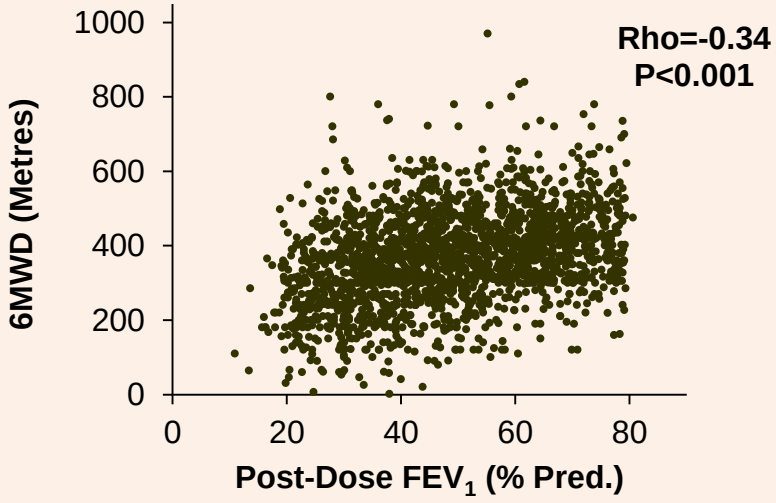
FEV_1 for diagnosis and prognosis

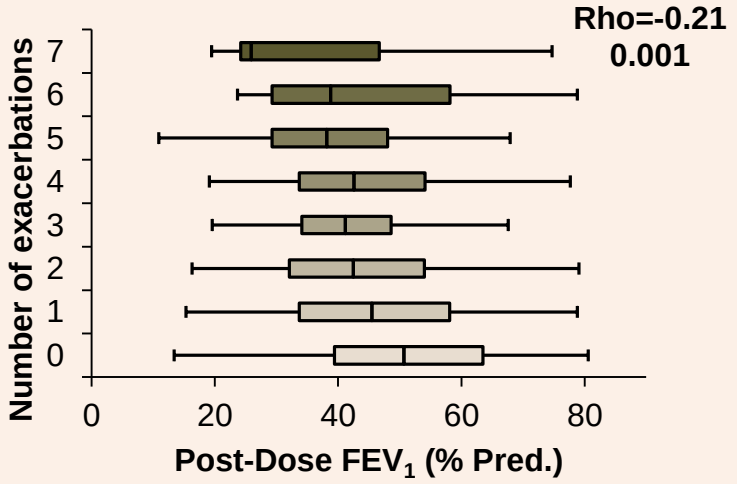
FEV_1 is a poor predictor of individual disease severity

Weak correlation between disease outcome parameters and FEV_1





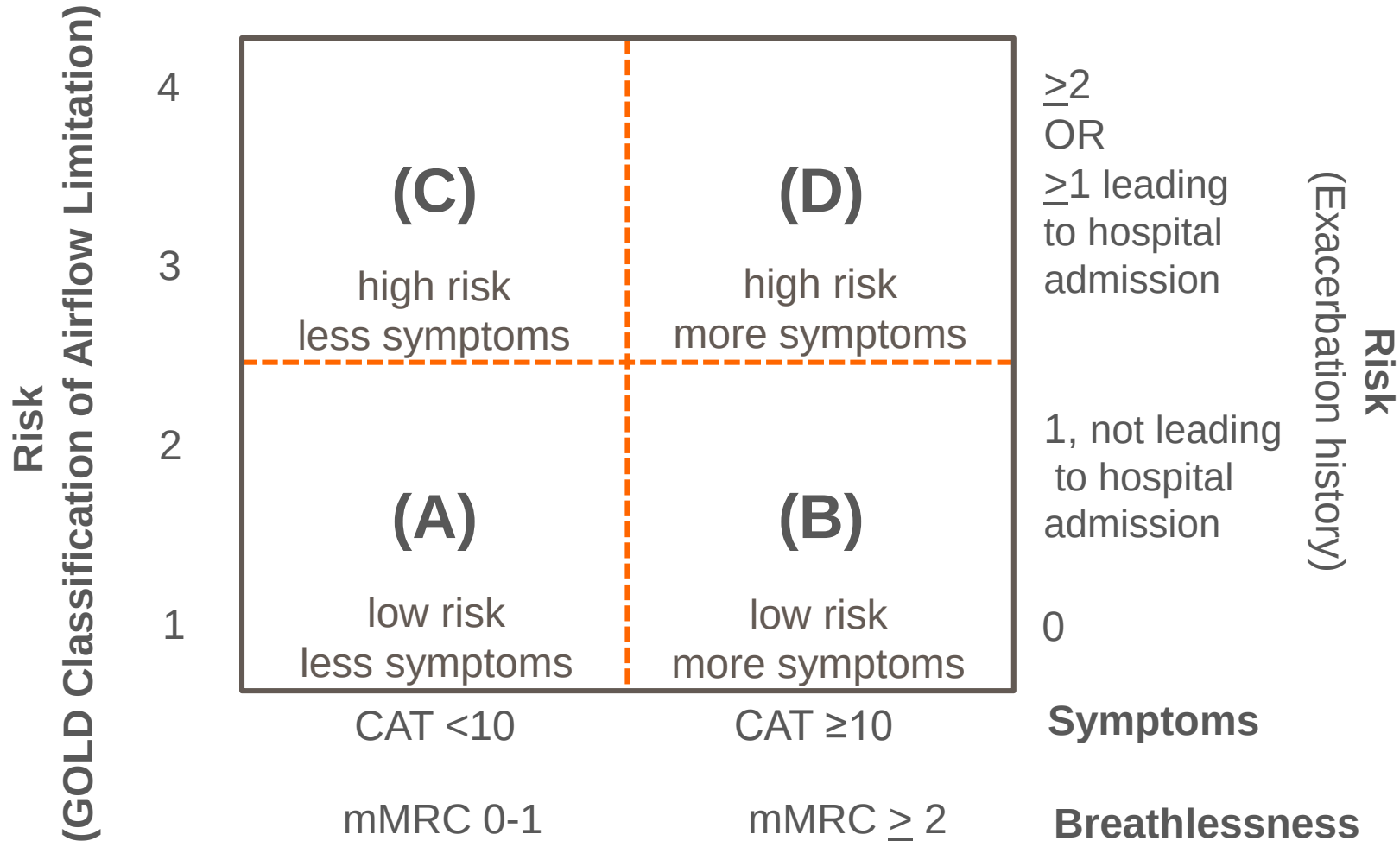




Agusti A, et al. Respir Res 2010; 11: 122.

GOLD 2011-2016: Patients stratified based on risk (airflow limitation + exacerbation history) and symptoms

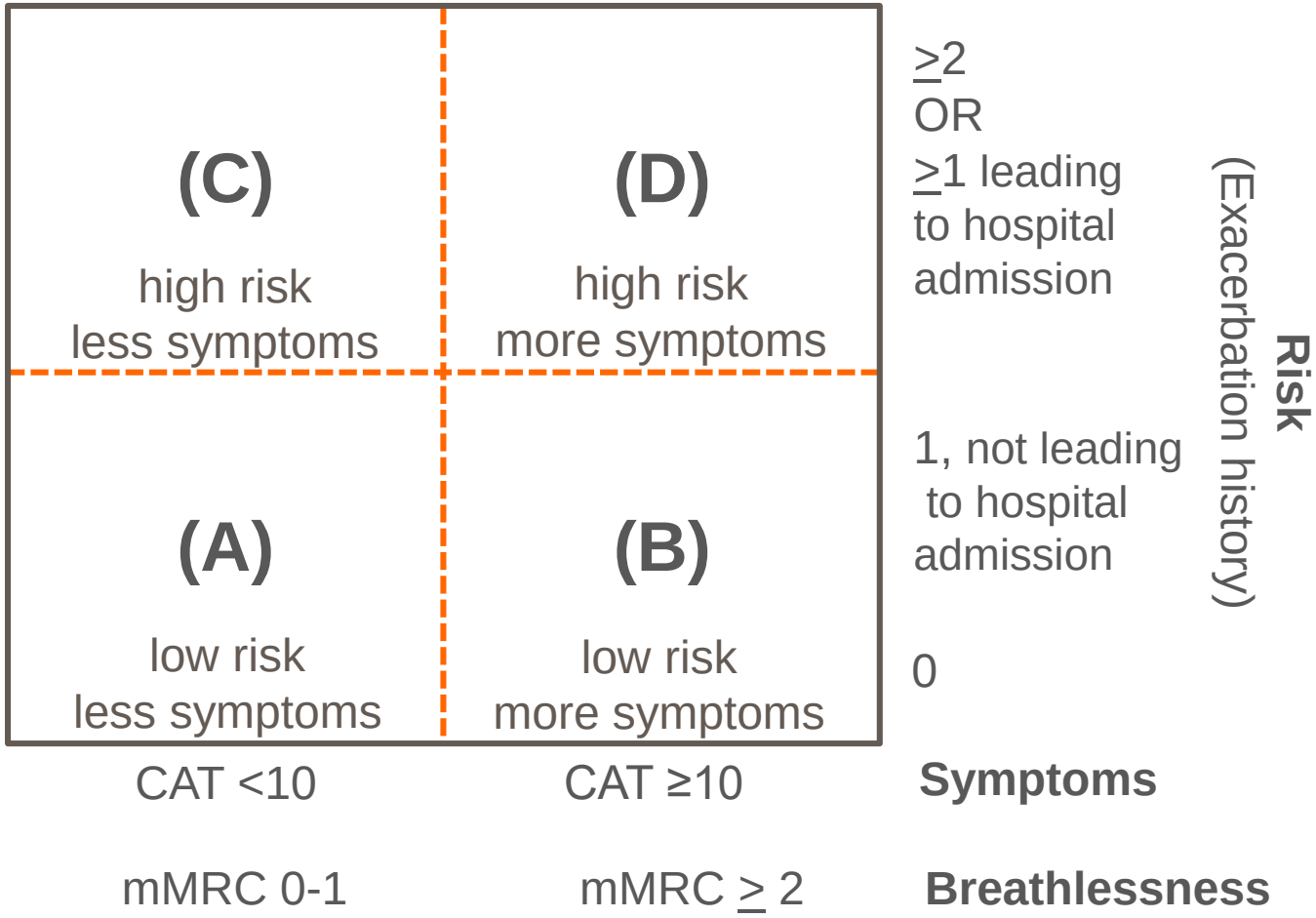
Stratification to guide pharmacologic treatment algorithm



Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2016.

NEW GOLD 2017: Patients stratified based on risk (exacerbation history) and symptoms

Stratification to guide pharmacologic treatment algorithm



Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2017.

NEW 2017 GOLD: FEV_1 informs diagnosis and prognosis

Diagnosis → **Assessment of airflow limitation (severity + prognosis)**

$FEV_1/FVC<0.7$

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

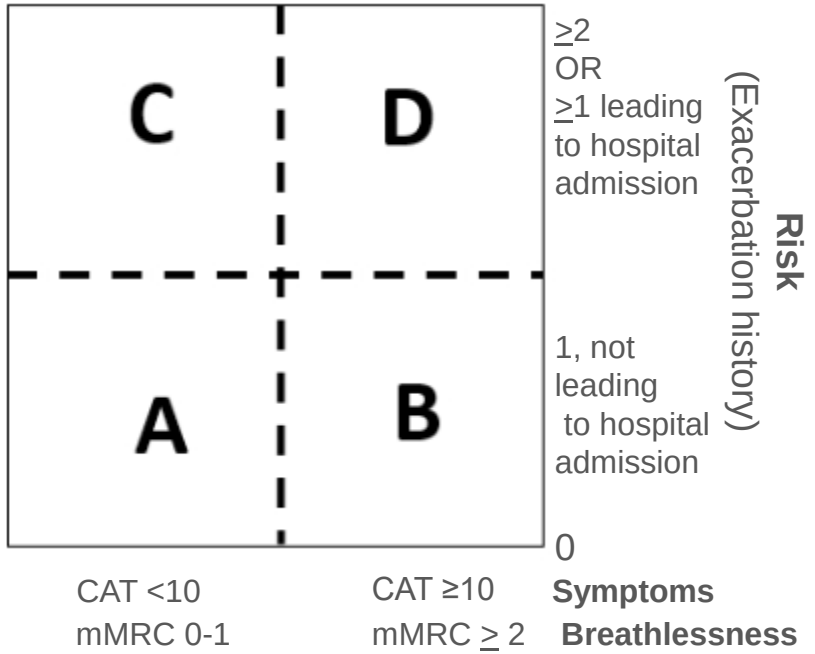
Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2017.

NEW 2017 GOLD: FEV_1 informs diagnosis and prognosis but not treatment recommendations

Diagnosis → **Assessment of airflow limitation (severity + prognosis)** → **Assessment of symptoms/risk of exacerbation**

$FEV_1/FVC<0.7$

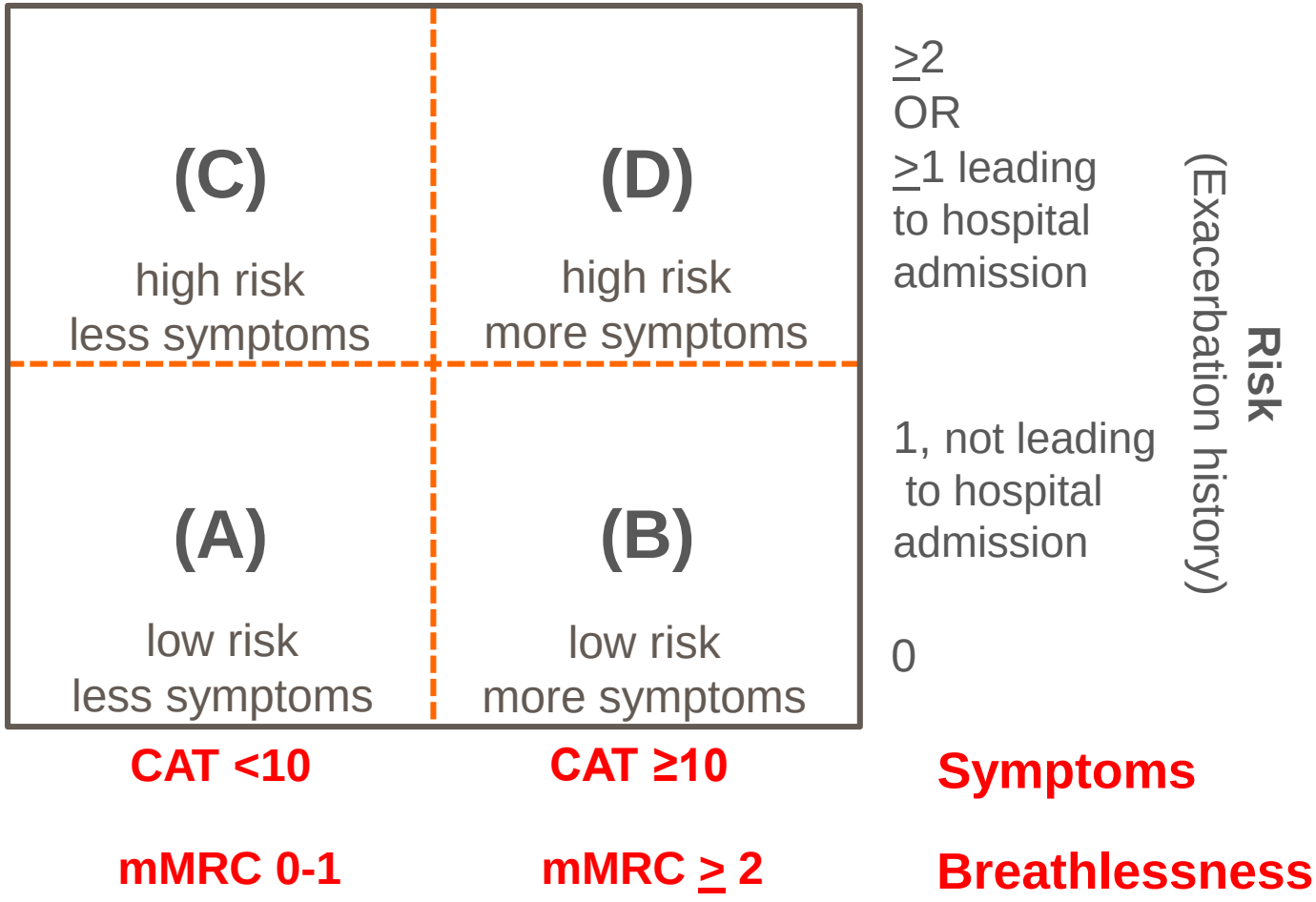
Grade	FEV_1 (% pred.)
1	≥80
2	50-79
3	30-49
4	<30



Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2017.

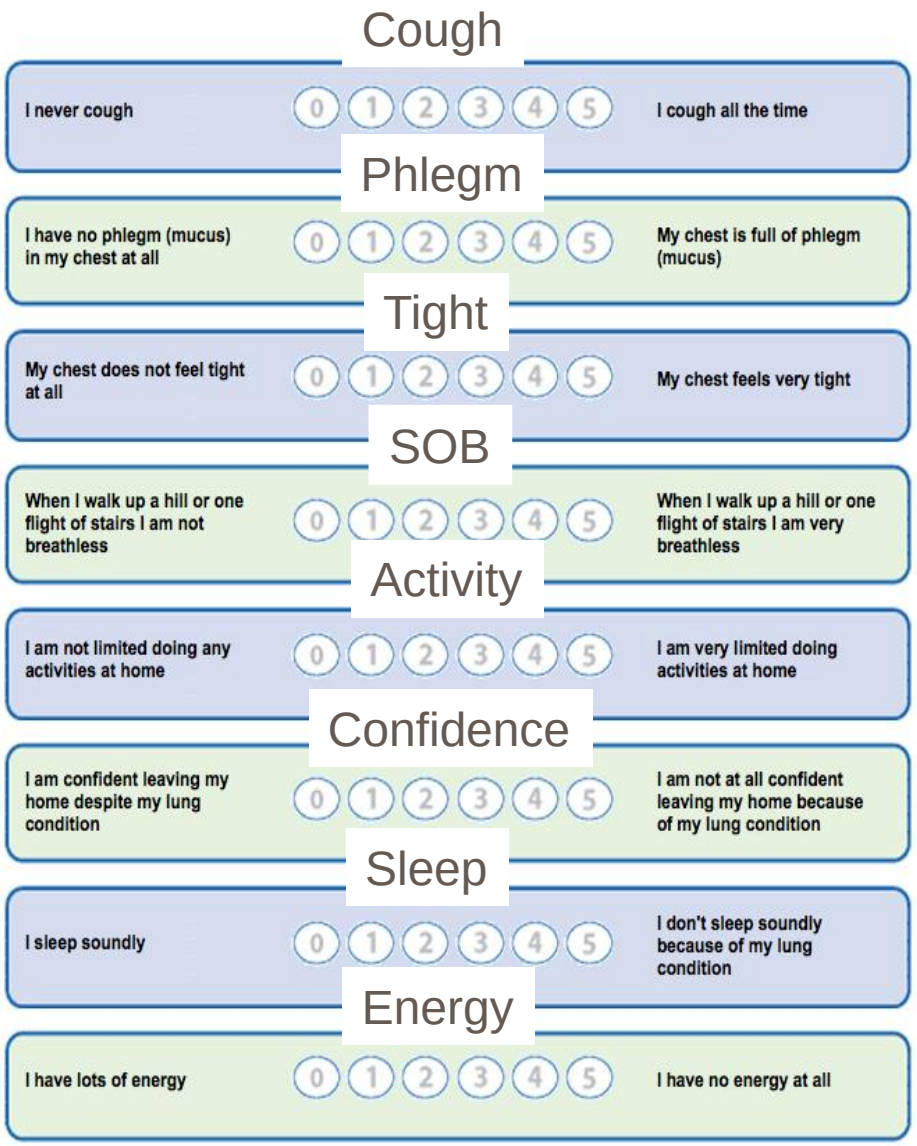
NEW 2017 GOLD: Patients stratified based on risk (exacerbation history) and symptoms

Stratification to guide pharmacologic treatment algorithm



Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2017.

Assessment of symptoms: The CAT questionnaire (www.catestonline.org)



COPD Self Assessment Test

Score/40
- mild 0-10
- mod 10-15
- severe 15-25
- very severe 25-40

High Symptoms

Basis on which to establish
- overall disability
- specific disabilities and
- response to treatments

Assessment of symptoms: Modified MRC Breathlessness Score

Grade	Description of Breathlessness
0	I only get breathless with strenuous exercise.
1	I get short of breath when hurrying on level ground or walking up a slight hill.
2	On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace.
3	I stop for breath after walking about 100 yards or after a few minutes on level ground.
4	I am too breathless to leave the house or I am breathless when dressing.

High Symptoms

Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2017.

Exercise, exercise tolerance and COPD

Regular exercise programme:

- Improve muscle conditioning and efficiency
- Reduce hyperinflation
- Anti-inflammatory effect
- Psychological wellbeing

Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2017.

The changing landscape of COPD

Pharmacologic treatment updates including new place for LAMA/LABA

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

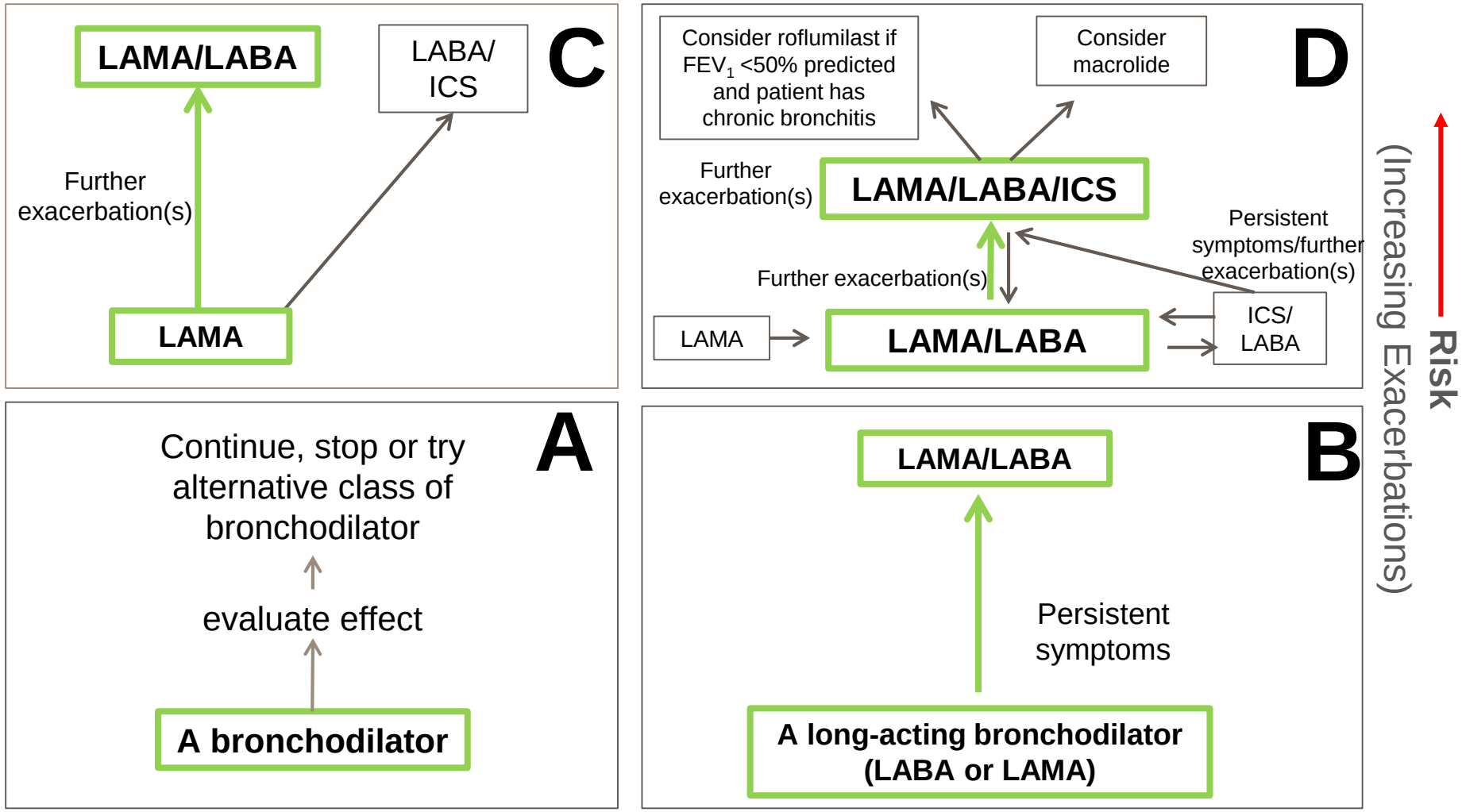
We have clear treatment goals **that have not changed**

These goals should be achieved with minimal side effects

* To date, no pharmacotherapy has been proven to prevent disease progression or reduce mortality in COPD

Reference: GOLD 2015. p32. http://www.goldcopd.org/Guidelines/guidelines-resources.html; Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2017.

Changes for Management of Stable COPD:
Summary of new pharmacologic treatment algorithms by 2017 GOLD Update

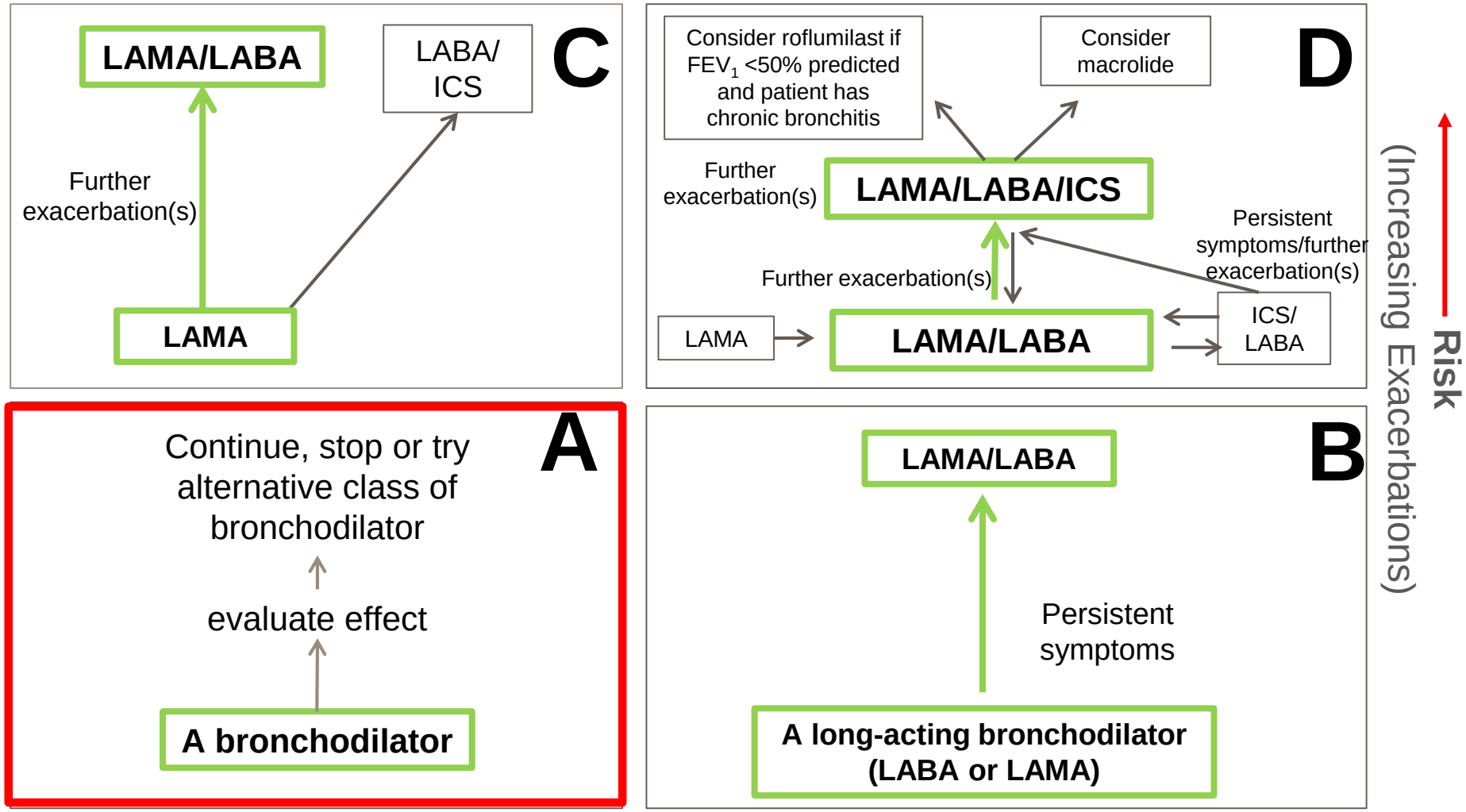


Preferred treatment pathway= →

Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2017.

The 2017 GOLD strategy update
Group A: Low level of symptoms and low risk of exacerbation

Stratification to guide pharmacologic treatment algorithm

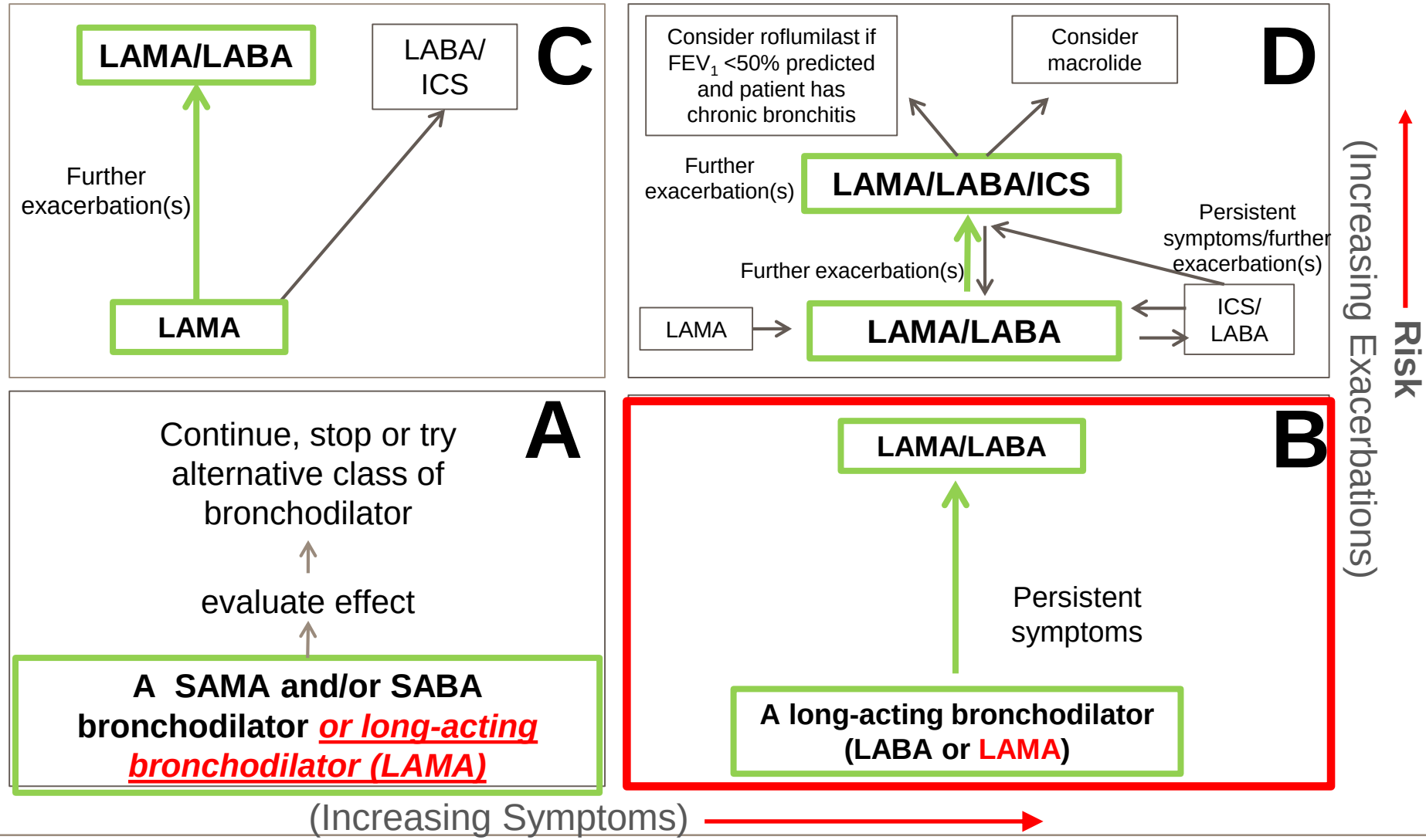


Preferred treatment pathway= →

Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2017.

The 2017 GOLD strategy update
Group B: High level of symptoms and low risk of exacerbation

Stratification to guide pharmacologic treatment algorithm

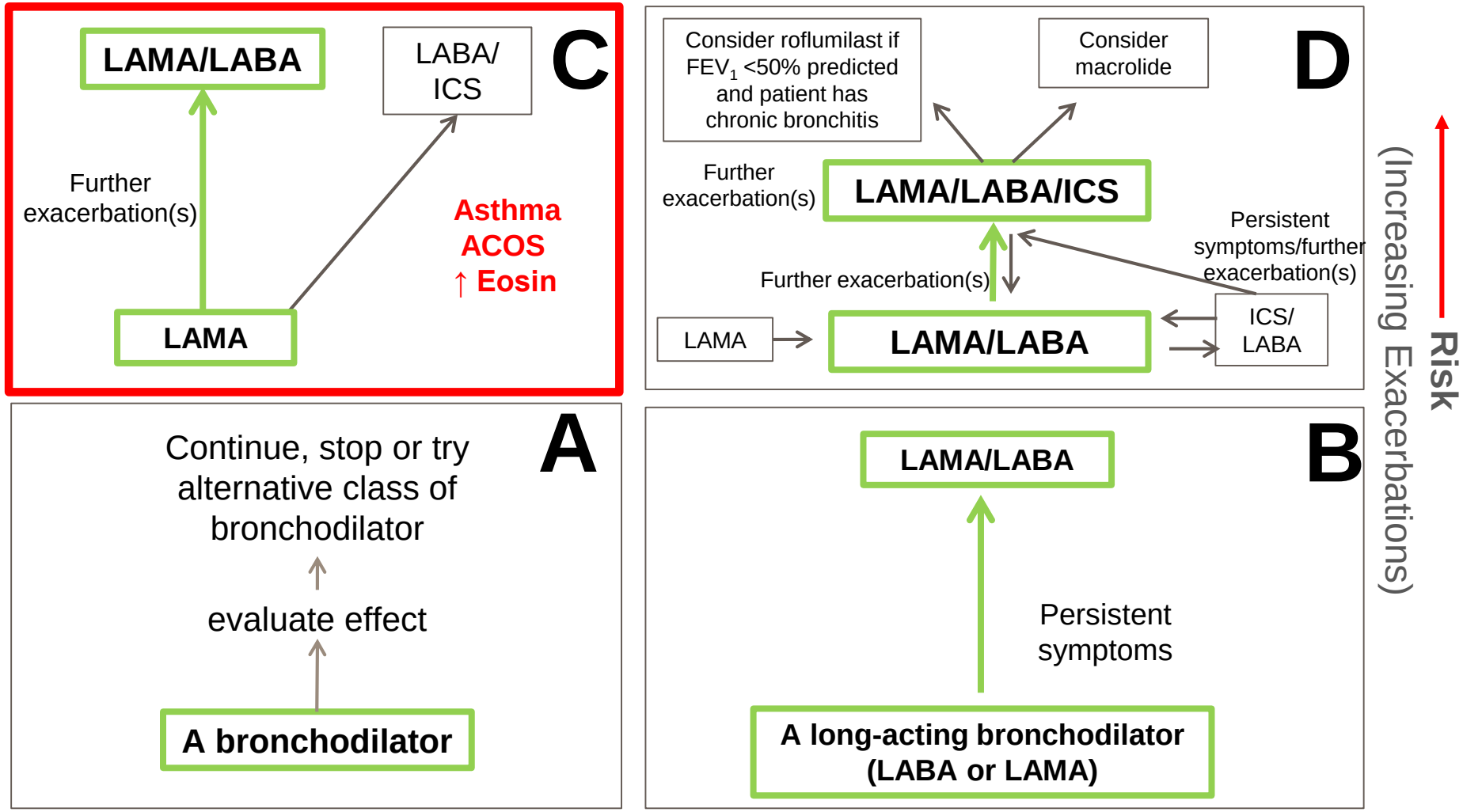


Preferred treatment pathway= →

Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2017.

The 2017 GOLD strategy update
Group C: Low level of symptoms and high risk of exacerbation

Stratification to guide pharmacologic treatment algorithm

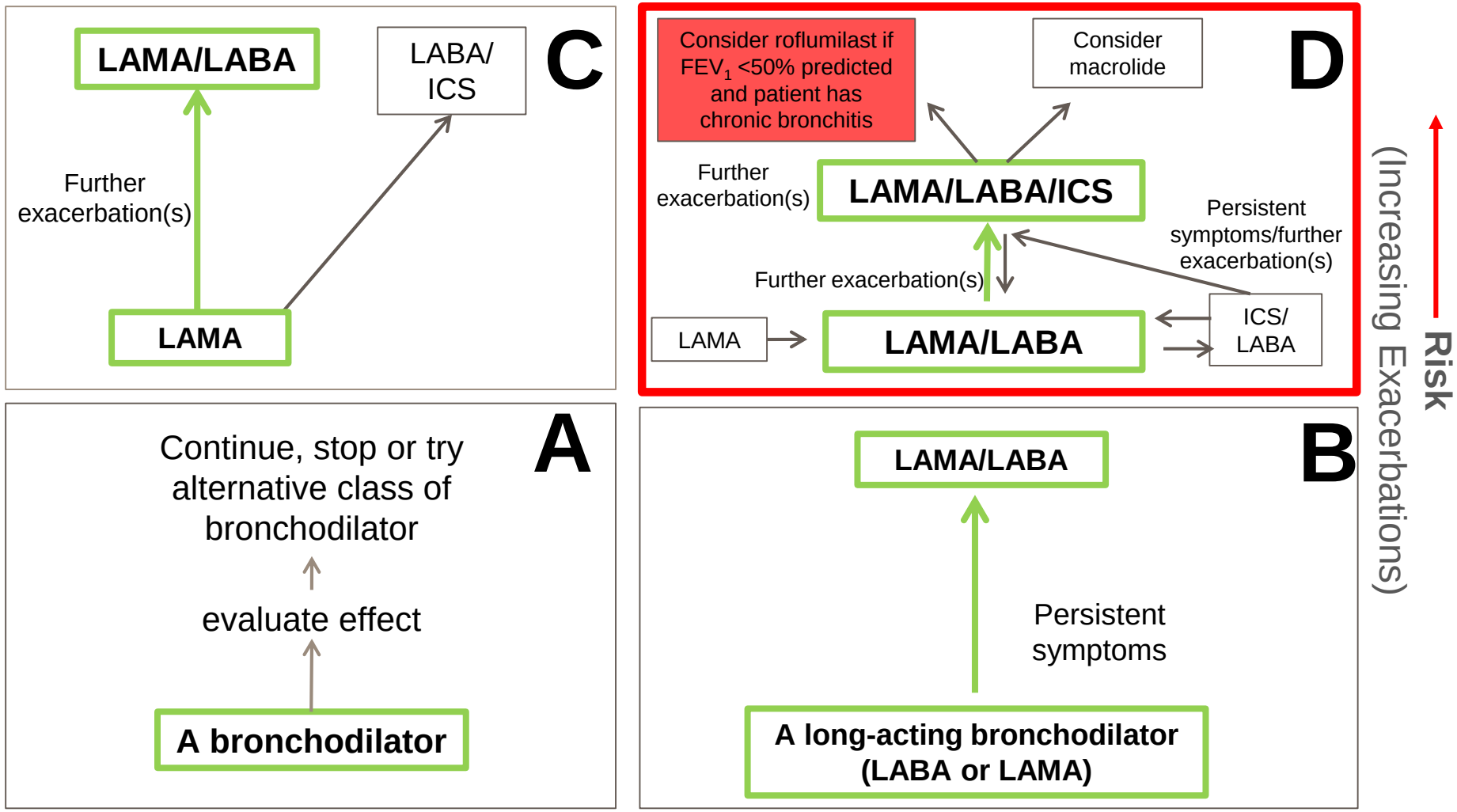


Preferred treatment pathway= →

Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2017.

The 2017 GOLD strategy update
Group D: High level of symptoms and high risk of exacerbation

Stratification to guide pharmacologic treatment algorithm



Preferred treatment pathway= →

Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2017.

Changes for Management of Stable COPD:
Summary of new pharmacologic treatment algorithms in 2017 GOLD

Group A: SABA and/or SAMA or LAMA (or LABA)*

Group B: Initial therapy should consist of LAMA or LABA progressing to LAMA/LABA if patient has persistent symptoms

Group C: Initial therapy should consist of LAMA, progressing to LAMA/LABA (preferred) or ICS/LABA (alternative) if patient has persistent exacerbations

Group D:

- Initial therapy should consist of LAMA/LABA (preferred) or ICS/LABA in ACOS patients or those with high EOS
- If patient develops further exacerbations, LAMA/LABA/ICS is recommended
- If patient develops further exacerbations, roflumilast (not registered in NZ), macrolide or stopping ICS could be considered in certain patients

*Gold states that long acting bronchodilators are preferred over short acting alternatives, with the exception being when patients only have occasional dyspnoea.

Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2017.

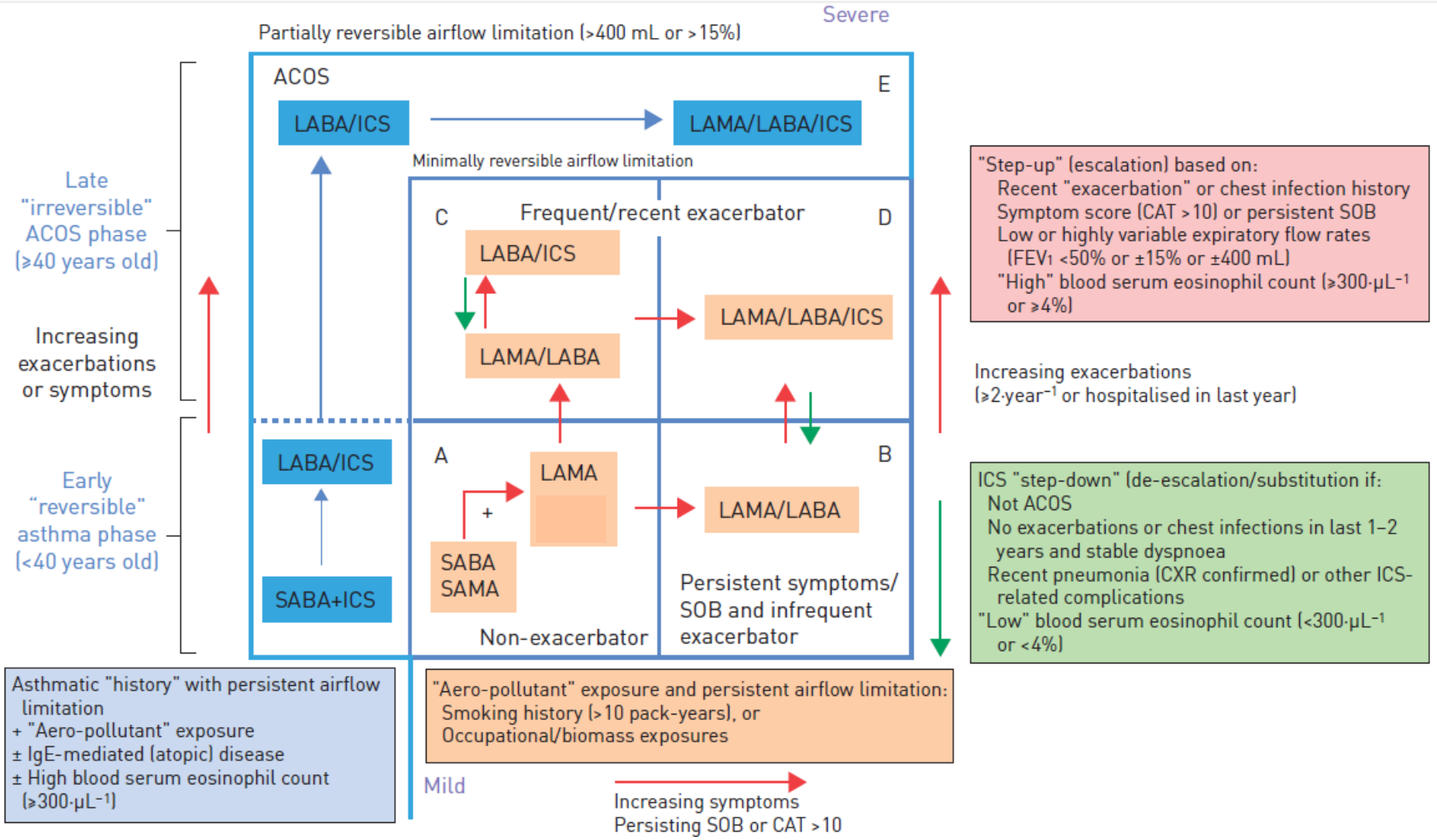
The 2017 GOLD strategy update
Group C and D: High risk of exacerbation

GOLD C and D Patients

*'It should be noted that there is a **lack of direct evidence** supporting therapeutic recommendations for patients in groups C and D. These recommendations will be **re-evaluated as additional data become available**.'*

Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2017.

‘Distilling’ the 2017 GOLD strategy update – NZ context



Young RP, Hopkins RJ. A new alphabet for COPD care: where “E” stands for España. Eur Respir J 2017; 49: 1601970

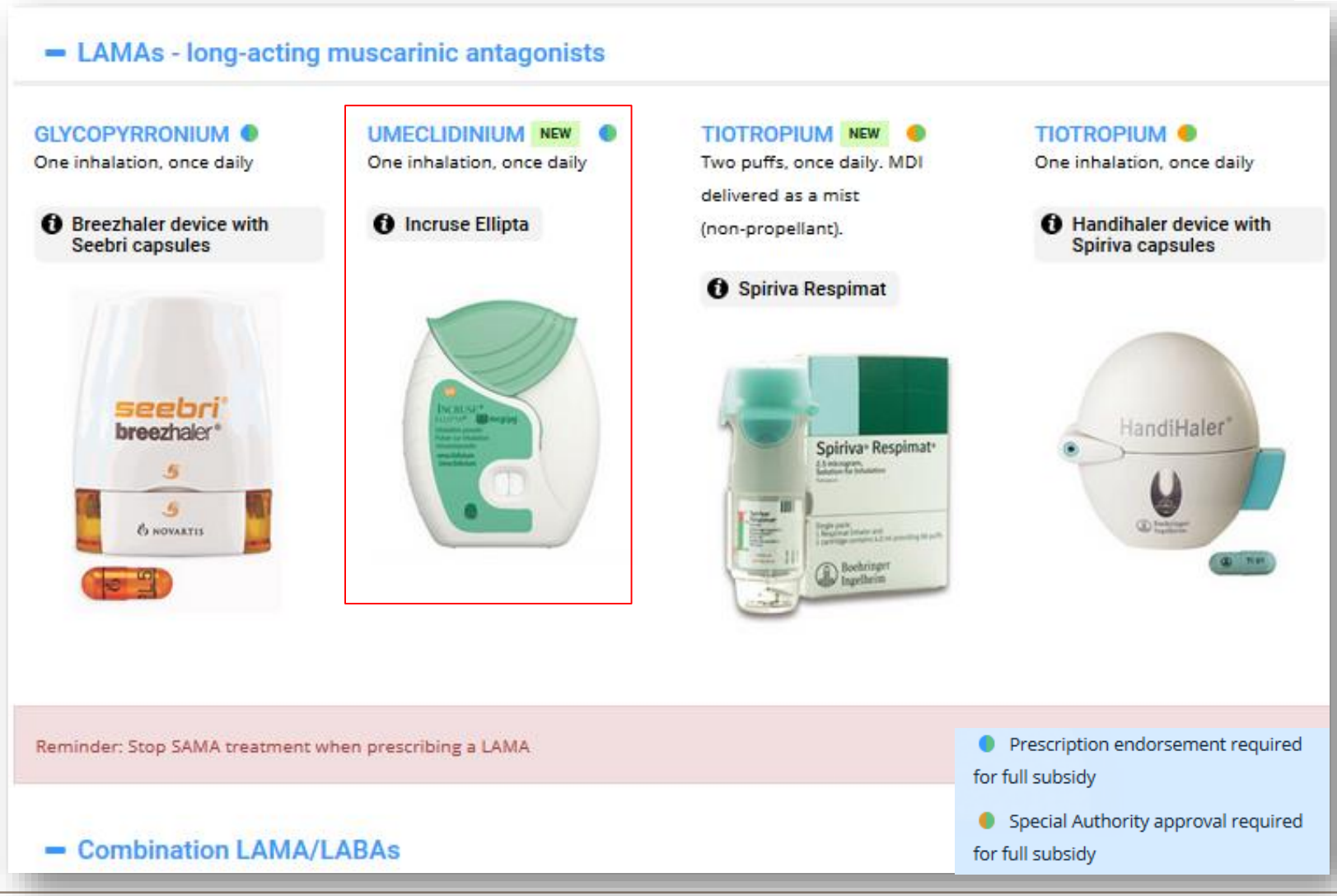
Group A: Low symptom level and low risk of exacerbation

Short-acting and long-acting mono-bronchodilators available in NZ

Adapted from http://ccn.health.nz/FocusAreas/ServiceLevelAlliances/Pharmacy/tabid/1347/ArticleID/1307/Funded-Inhalers-in-New-Zealand-2016.aspx (accessed 20/03/2017) ICS = inhaled corticosteroid; LABA = long acting beta2 agonist; LAMA = long acting muscarinic antagonist

Long acting muscarinic antagonists (LAMAs) available in New Zealand

http://www.bpac.org.nz/2016/copd-tool

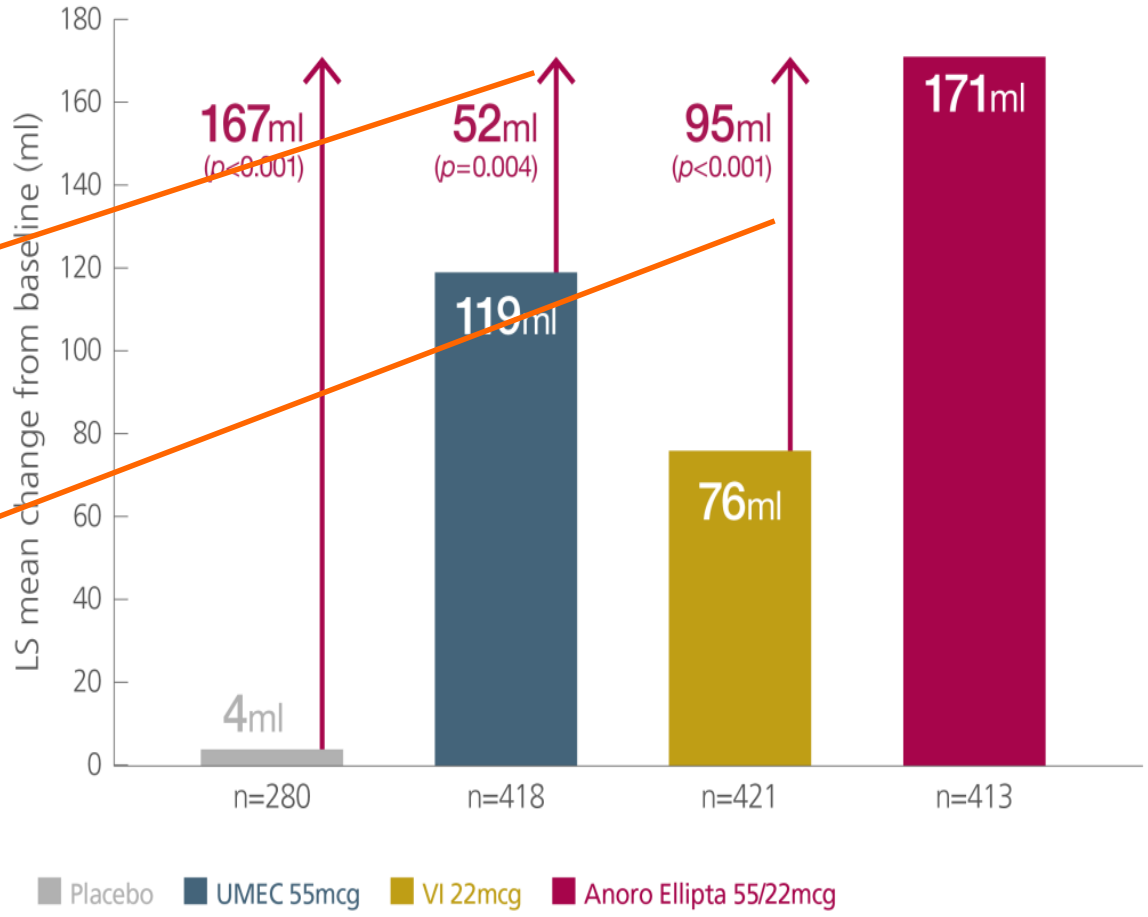


The prescriber must provide written endorsement that the patient has been diagnosed as having COPD using spirometry to access subsidy.

Anoro Ellipta demonstrates significant improvement of trough FEV_1 compared with monotherapy and placebo

Benefit of LABA when added to LAMA

Benefit of LAMA when added to LABA

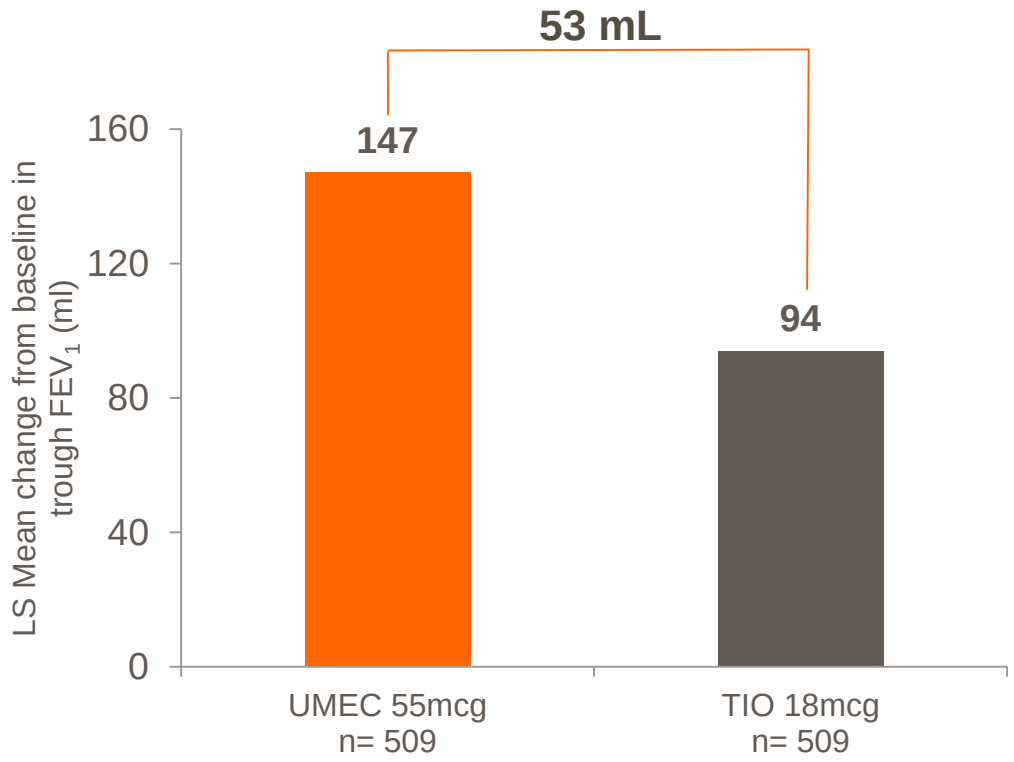


Vilanterol mono-therapy is unlicensed in COPD

Adapted from Donohue JF, *et al. Respir Med* 2013; 107: 1538–1546.

Incruse Ellipta (umeclidinium) offers improvements in lung function vs tiotropium

LS mean change from baseline in trough FEV_1 at Day 85



Difference = 53 mL [95% CI: 25, 81 mL], p<0.001); Intention to Treat Population

Feldman et al. Int J Chron Obstruct Pulmon Dis 2016;11:719-30

Combination LAMA/LABAs available in New Zealand

http://www.bpac.org.nz/2016/copd-tool

Combination LAMA/LABAs

GLYCOPYRRONIUM + INDACATEROL NEW
One inhalation, once daily

Breezhaler device with Ultibro capsule

UMECLIDINIUM + VILANTEROL NEW
One inhalation, once daily

Anoro Ellipta

OLODATEROL + TIOTROPIUM NEW
Two puffs, once daily. MDI delivered as a mist (non-propellant).

Spiolto Respimat

Special Authority Criteria[1]

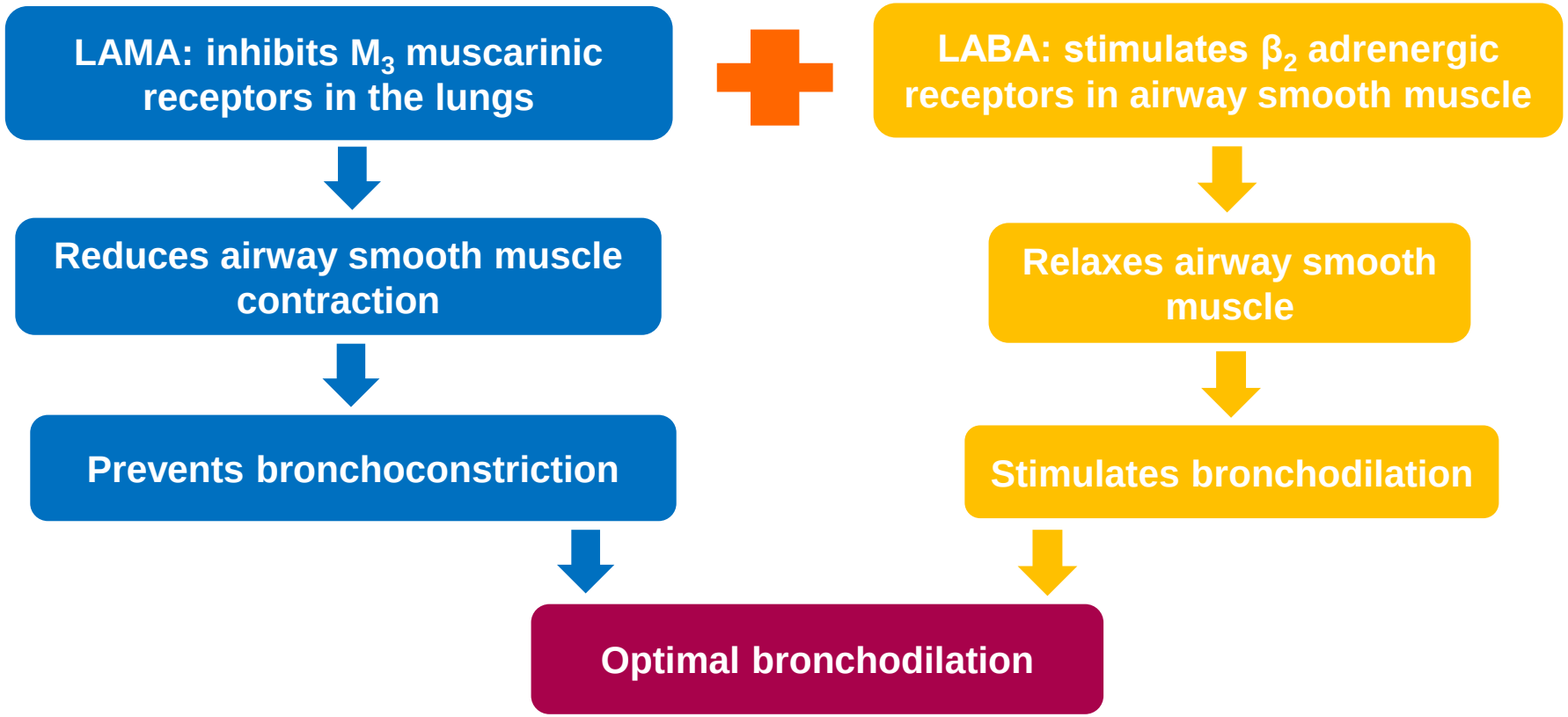
INITIAL APPLICATION:

- **Patient has been stabilised on a LAMA**
- Prescriber considers that patient would receive additional benefit from switching to a combination product

Special Authority approval required for full subsidy

LAMA = long-acting muscarinic antagonists; LABA = long-acting beta$_2$ agonists

Dual bronchodilators may provide optimal bronchodilation through complementary mechanisms[1,2]



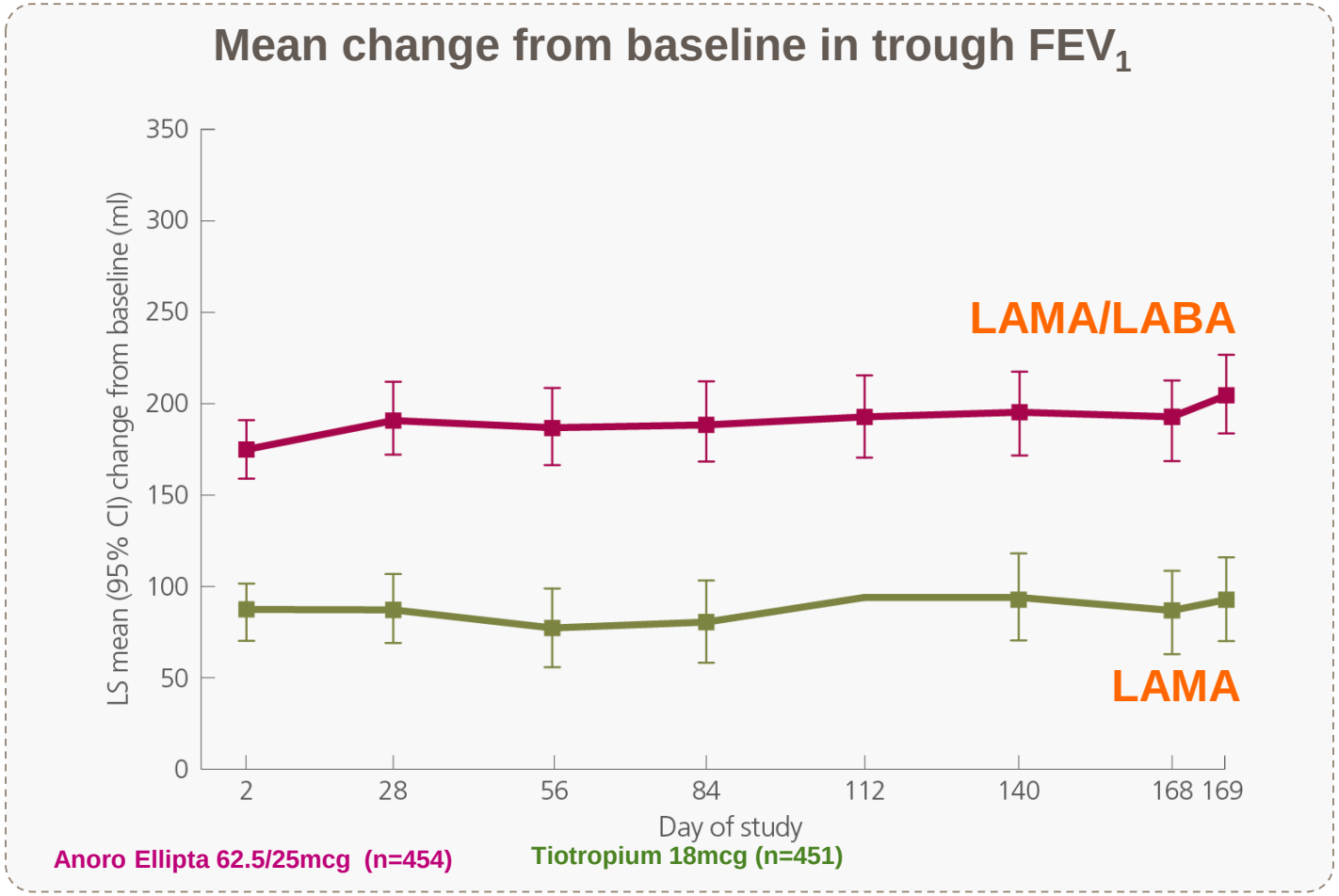
"Combining bronchodilators with different mechanisms and durations of action may increase the degree of bronchodilation with a lower risk of side effects compared to increasing the dose of a single bronchodilator"

- GOLD 2017[3]

References: 1. Cazzola M & Molimard M. Pulm Pharmacol Ther 2010; 23:257–267. 2. Jones R & Østrem A. Prim Care Respir J 2011; 20:33–45. 3. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary.

Anoro Ellipta significantly improved trough FEV_1 compared with tiotropium

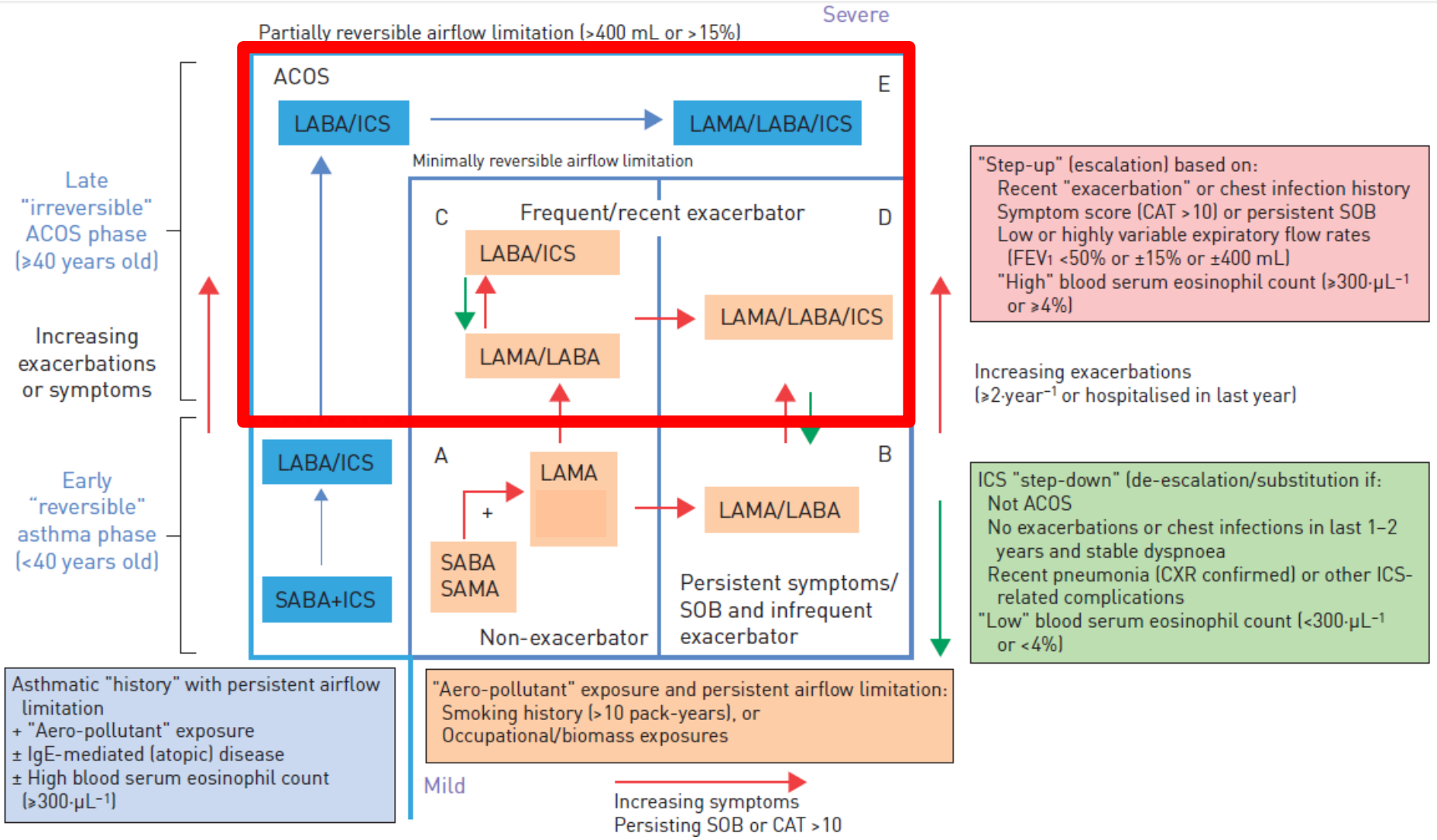
Immediate, sustained, significant improvement in trough FEV_1



Results of 24-week, randomised, double-dummy, active-controlled, blinded, multi-centre, parallel-group studies that compared the efficacy and safety of Anoro Ellipta with tiotropium in subjects with COPD.

Reference: Maleki-Yazdi M *et al. Respir Med* 2014; 108:1752–1760

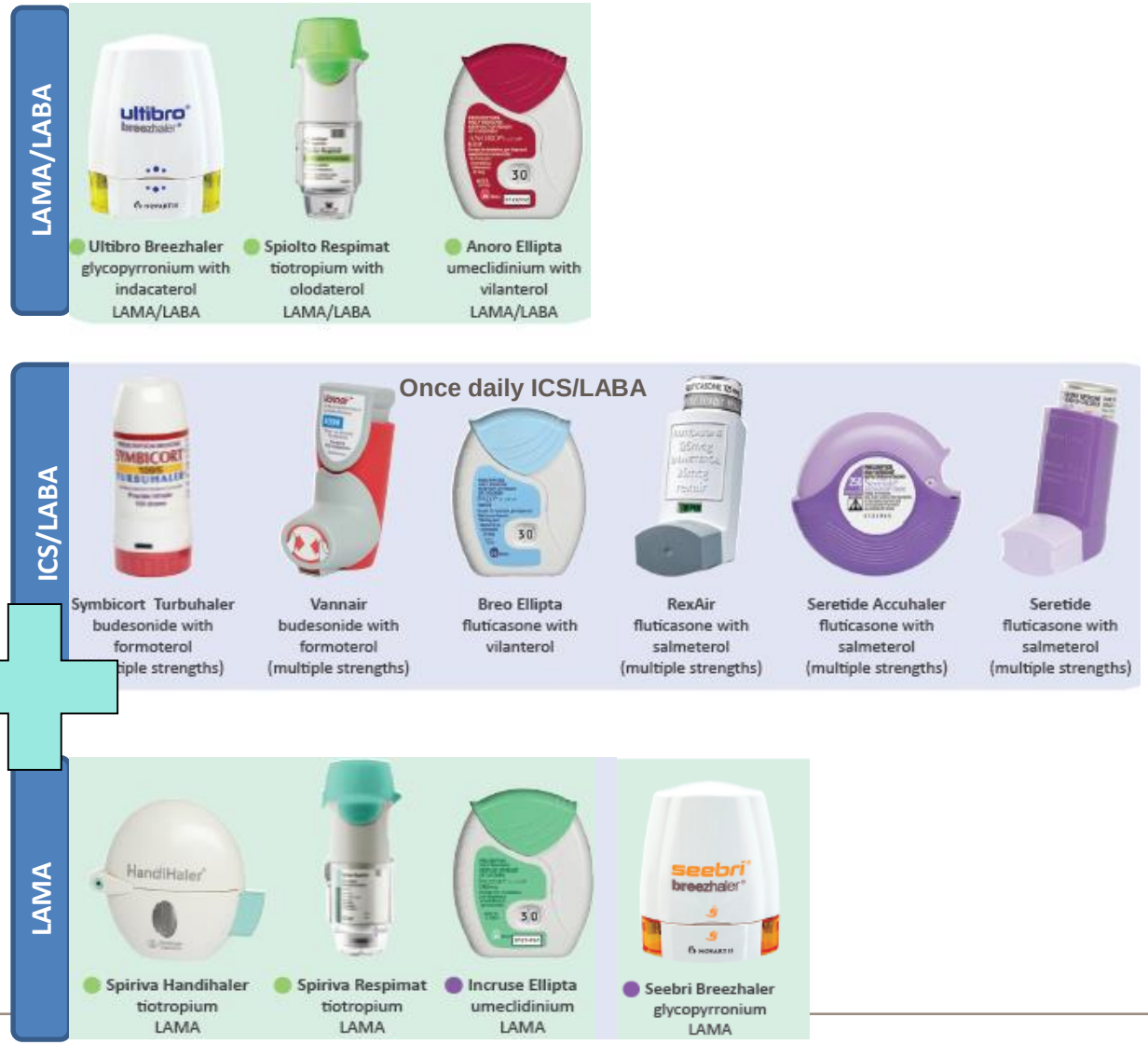
‘Distilling’ the 2017 GOLD strategy update



Young RP, Hopkins RJ. A new alphabet for COPD care: where “E” stands for España. Eur Respir J 2017; 49: 1601970

Group C, D and E (ACOS)

LAMA/LABA, ICS/LABA and/or LAMA



The changing landscape of COPD

Patients most suitable for ICS/LABA

Which of my COPD patients would benefit from an ICS?

GOLD 2017 recommendations:

In GOLD D patients, ICS/LABA as initial therapy may be the first choice in:

- Those patients who may co-existing asthma or a history and/or findings that are suggestive of asthma-COPD overlap syndrome
- Patients with high eosinophil counts may also be considered as a parameter to support the use of ICS-containing therapy

Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2017.

ACOS subgroup of COPD spectrum

- Recommendations are based on expert opinion and not RCTs (ACOS usually excluded from COPD trials)

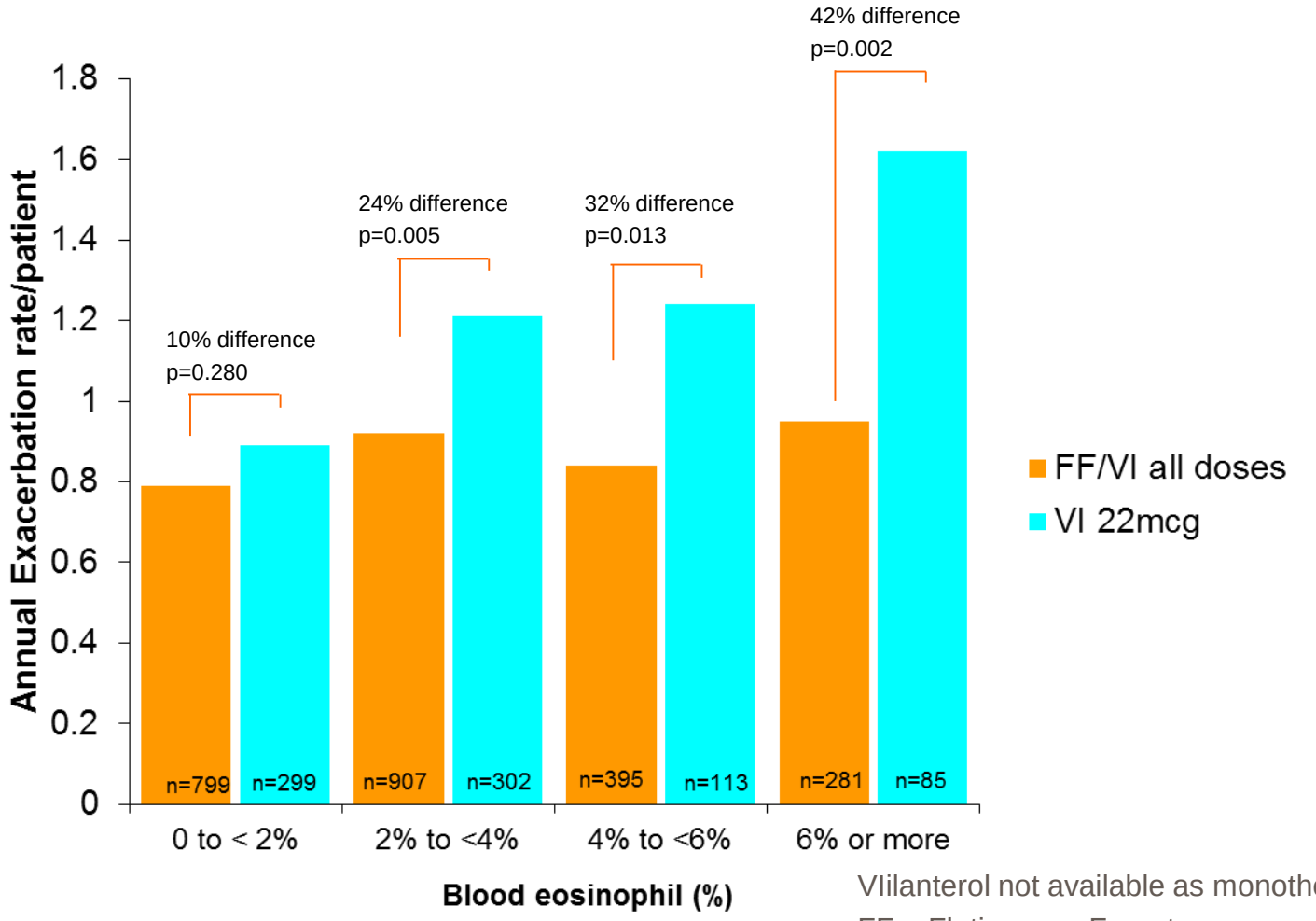
- Features of ACOS
  - History of asthma (childhood or 20+ years of asthma) and smoking
  - History of atopy, allergic rhinitis or high IgE
  - High serum eosinophilia (>2%)
  - Highly variable PEFR or FEV_1 (>15% variability)

- About 20% of all COPD cohorts, suffer frequent exacerbations, moderate-severe GOLD grade (GOLD phenotype C and D)

- Assumed to
  - Gain greater benefit from ICS use with reduction in exacerbations
  - Have greater responsiveness to ICS with regards bronchodilator benefits

http://www.goldcopd.org/uploads/users/files/AsthmaCOPDOverlap.pdf

The effect of adding fluticasone furoate to vilanterol (Breo Ellipta) by blood eosinophils



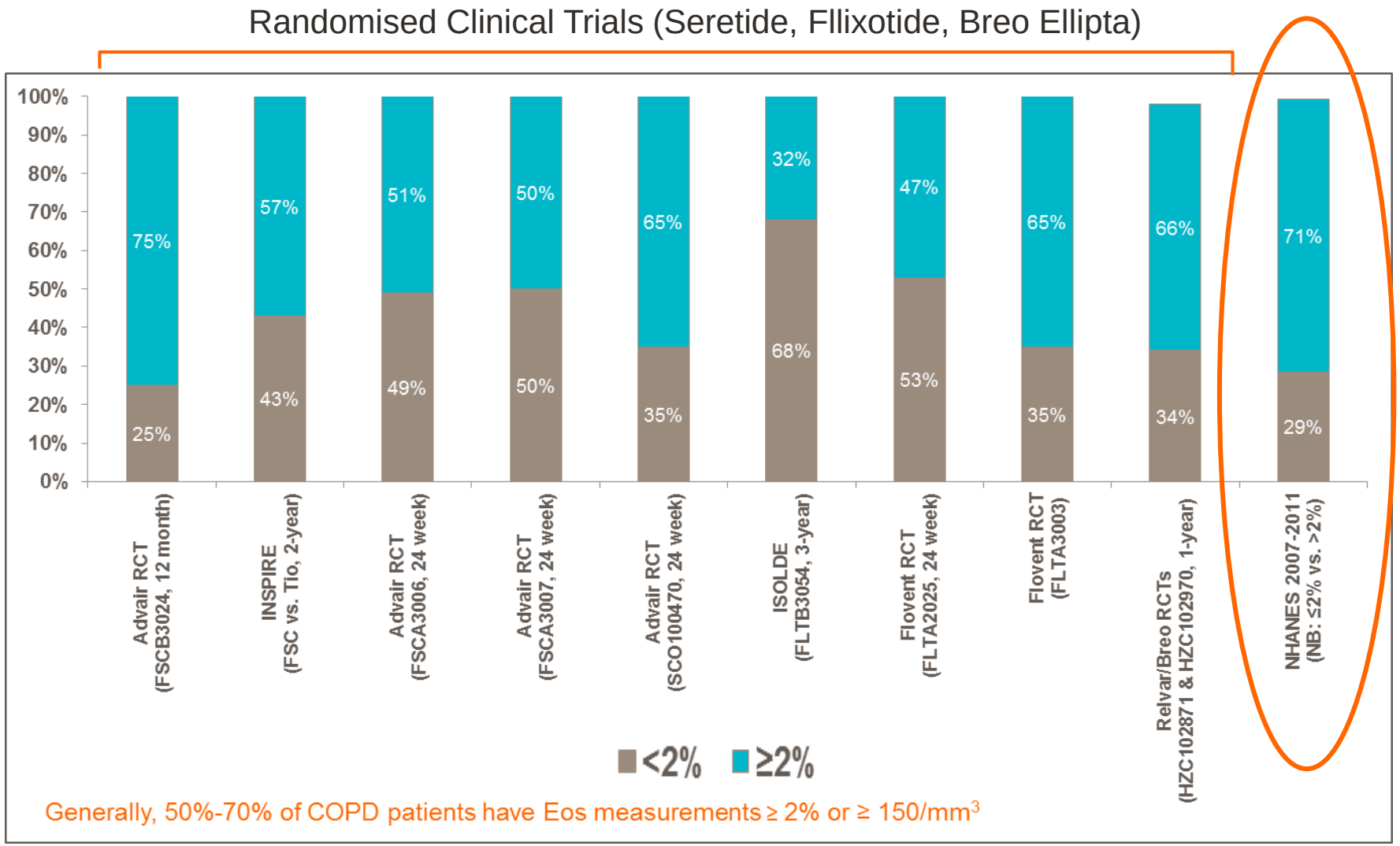
VIilanterol not available as monotherapy

FF = Fluticasone Furoate

VI = Vilanterol

Pascoe et al. *Lancet Respir Med* 2015; 3: 435–42

Distribution of patients by a 2% eosinophil cut-off point

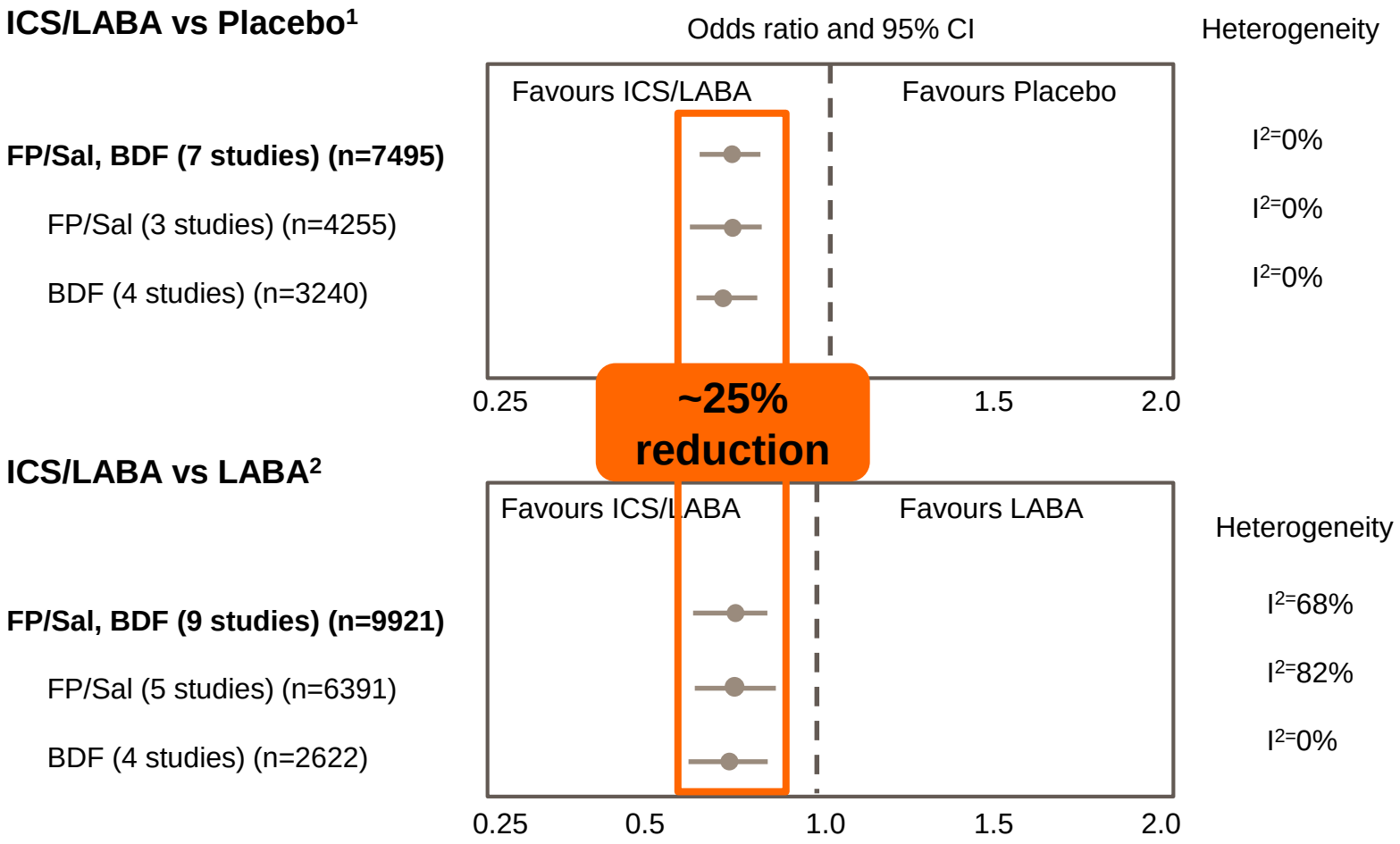


Di Santostefano et al;.*AJRCCM* 2015;192; A2868 (poster presentation); NHANES; http://www.cdc.gov/nchs/nhanes/about_nhanes.htm ;

Pascoe et al. *Lancet Respir Med* 2015; 3: 435–42

ICS/LABA therapy significantly reduces the exacerbation risk

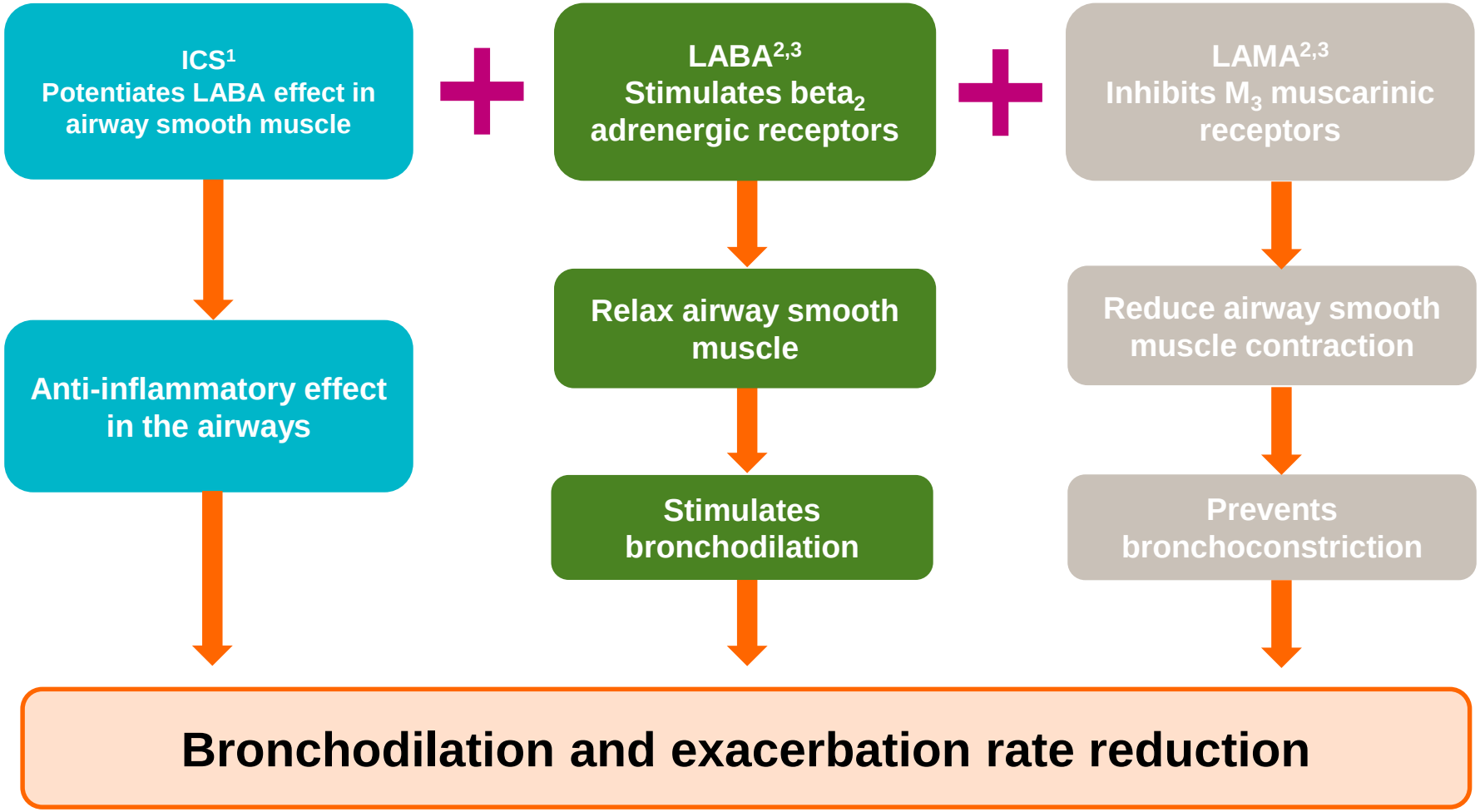
Results of two large Cochrane meta-analyses



BDF, budesonide/formoterol; CI, confidence intervals; FP, fluticasone propionate; ICS, inhaled corticosteroid; LABA, long-acting beta$_2$ agonist; Sal, salmeterol

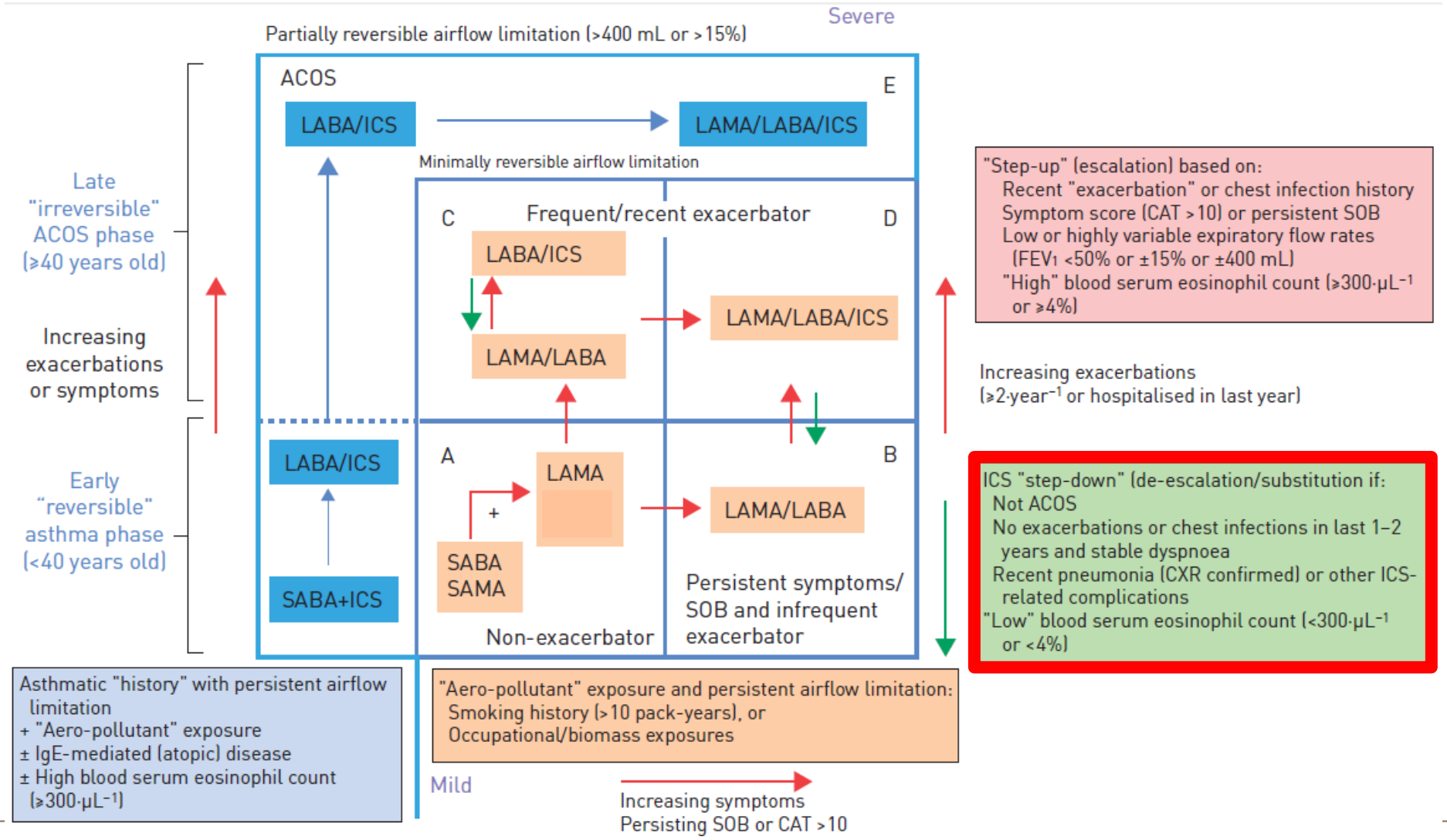
1. Nannini et.al. Combined corticosteroid and long-acting B-agonist in one inhaler vs placebo for COPD (Review). Cochrane. 2013.
2. Nannini et.al. Combined corticosteroid and long-acting B-agonist in one inhaler vs LABA for COPD (Review). Cochrane 2012

Combining ICS/LABA and LAMA therapy provides dual bronchodilation while maintaining exacerbation control[1–3]



1. Johnson M. *Proc Am Thorac Soc* 2005;2:320–325; 2. Cazzola M, Molimard M. *Pulm Pharmacol Ther* 2010;23:257–267;
3. Jones R, Østrem A. *Prim Care Respir J.* 2011;20:33–45

When would you consider withdrawing an ICS?



Importance of inhaler delivery

Summary of Changes

Inhaler delivery

GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE

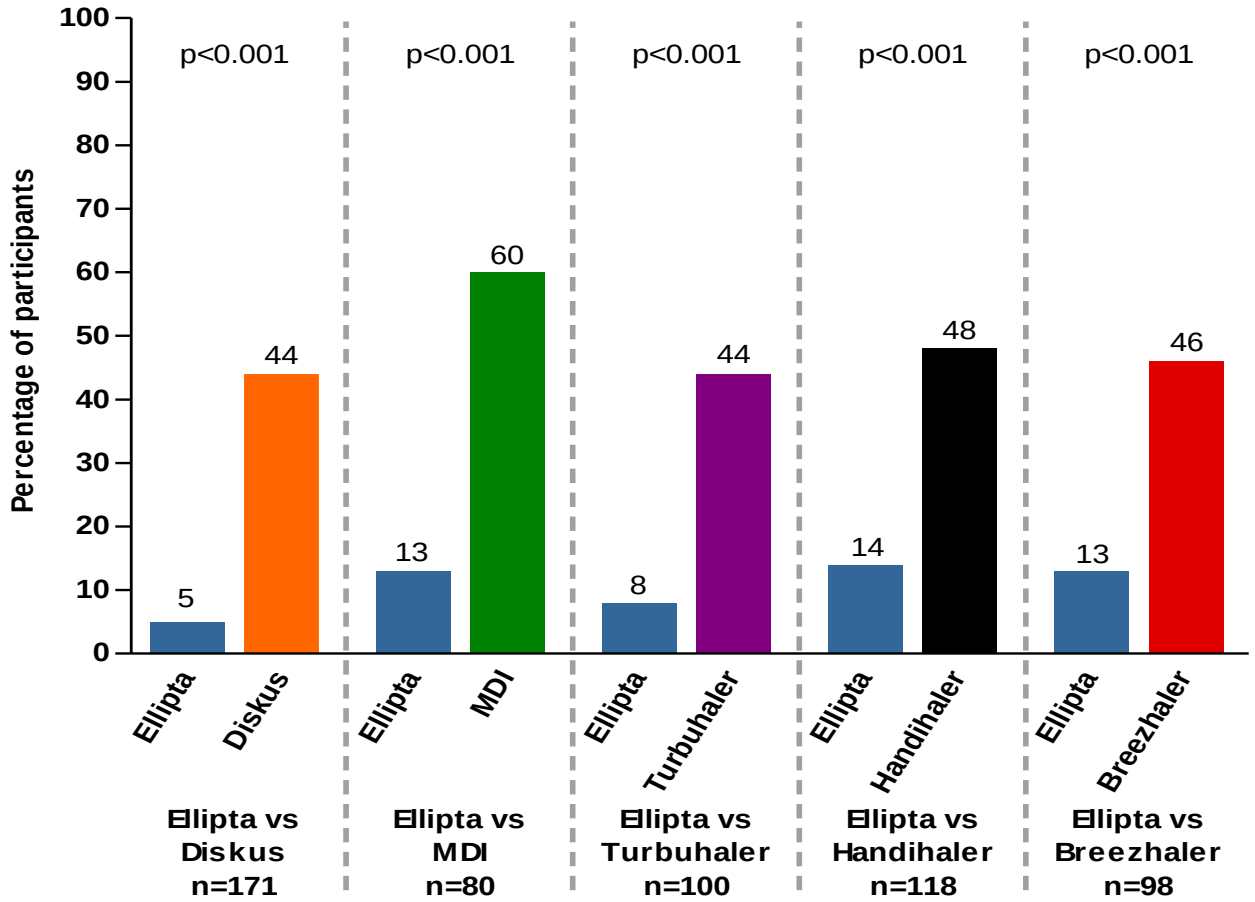
gsk

2107 GOLD Update states:

- On average more than two thirds of patients make at least one error in using an inhalation device
- Observational studies have shown a significant relationship between poor inhaler use and symptom control in patients with COPD
- Key determinants of poor inhaler technique include use of multiple devices, older age and lack of previous education on inhaler technique
- GOLD recognise the importance of education and training in inhaler technique

Significantly fewer COPD patients made inhaler errors after reading the patient information leaflet

Proportion of participants who made at least one critical error after reading the patient information leaflet



Van der Palen et al. Primary Care Respir Med 26: 16079 (2016)

Non-pharmacological treatment for COPD

Non-pharmacological treatment for COPD

- Vaccinations – Influenza and pneumococcal
- Regular Exercise – optimise physical “fitness” or condition (anti-inflammatory)
- Pulmonary rehabilitation (post hospital discharge or after significant exacerbation) – physical conditioning, confidence and inhaler optimisation
- Diet – Diet high in fruit, vegetables and fibre (Mediterranean Diet)
- Treat underlying **Coronary Artery Disease** risk factors

Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2014

Questions Welcomed!

Chairperson: Other questions being asked by GPs

- Do you have any potential safety concerns with the introduction of the new medicines?

- Is there any difference between the different ICS available in NZ and the risk of pneumonia?

- What is the definition of severe breathlessness?

- Sometimes it's hard to know when to refer patients with COPD. At what stage would you like to see COPD patients in your respiratory clinic?

Anoro® Ellipta® (umeclidinium bromide/vilanterol trifenatate inhaler 62.5/25mcg per inhalation) **is a fully funded medicine; Special Authority criteria apply. Maximum Daily Dose:** One inhalation once daily. **Prescription Medicine** for long-term regular treatment to relieve symptoms in adult patients with Chronic Obstructive Pulmonary Disease (COPD). This medicine has risks and benefits.

Warnings and Precautions: Not recommended for use in patients with asthma or for relief of acute symptoms or an acute exacerbation. Use care when co-administering with strong CYP3A4 inhibitors (e.g. ketoconazole), beta-blockers and in patients with severe cardiovascular disease, narrow-angle glaucoma or urinary retention. **Common Side Effects:** Nasopharyngitis, oropharyngeal pain, sinusitis, pharyngitis, cough, urinary tract infection, constipation, dry mouth, hypertension. Paradoxical bronchospasm may occur. Before prescribing *Anoro Ellipta,* please review the Data Sheet at www.medsafe.govt.nz.

***Incruse® Ellipta®*:** In addition to the *Anoro Ellipta* information above which also applies to *Incruse Ellipta* (umeclidinium bromide), *Incruse* is available in a 62.5mcg per inhalation in the *Ellipta* device. *Incruse Ellipta* **is a fully funded medicine**. The prescriber must provide written endorsement that the patient has been diagnosed as having COPD using spirometry to access subsidy. Before prescribing *Incruse Ellipta,* please review the Data Sheet at www.medsafe.govt.nz.

Incruse® Ellipta® (umeclidinium bromide inhaler 62.5mcg per inhalation) is a **Prescription Medicine.** Incruse Ellipta is indicated as a long-term maintenance bronchodilator treatment to relieve symptoms in adult patients with Chronic Obstructive Pulmonary Disease (COPD). Incruse Ellipta is a fully funded medicine. The prescriber must provide written endorsement that the patient has been diagnosed as having COPD using spirometry to access subsidy. ***Maximum Daily Dose:*** One inhalation once daily. Contraindications: Patients with severe milk-protein allergy or those who have hypersensitivity to umeclidinium or any excipients. ***Side Effects:*** Urinary tract infection, tachycardia, upper respiratory tract infection, nasopharyngitis, sinusitis, cough, dysgeusia. ***Warnings and Precautions:*** Not recommended for use in patients with asthma or for relief of acute symptoms or an acute exacerbation. Use care in patients with severe cardiovascular disease (particularly cardiac arrhythmias), narrow-angle glaucoma or urinary retention. Paradoxical bronchospasm may occur. Before prescribing Incruse Ellipta, please review the Data Sheet at www.medsafe.govt.nz.

***Breo*® *Ellipta*®** (fluticasone furoate/vilanterol trifenatate inhaler 100/25mcg per inhalation) **is a fully funded medicine. *Breo Ellipta* 200/25mcg is a private purchase medicine (dose indicated in asthma only); a prescription charge will apply. Maximum Daily Dose:** One inhalation once daily. **Maintenance Dose:** Titrate to lowest effective dose. **Prescription Medicine** for the regular treatment of asthma (12 years of age and older) (100/25 and 200/25mcg) and/or COPD (100/25mcg) with a FEV1<70% predicted normal (post-bronchodilator) in patients with an exacerbation history. This medicine has risks and benefits. **Warnings and Precautions:** Not for relief of acute symptoms or an acute exacerbation. Do not discontinue abruptly. Use care when co-administering with strong CYP3A4 inhibitors (e.g. ketoconazole, ritonavir) or in patients with hepatic impairment, severe cardiovascular disease, pulmonary tuberculosis or chronic or untreated infections. **Common Side Effects:** Candidiasis of mouth and throat, headache, nasopharyngitis, oropharyngeal pain, sinusitis, pharyngitis, rhinitis, cough, dysphonia, upper respiratory tract infection, bronchitis, influenza, abdominal pain, arthralgia, back pain, pyrexia. Paradoxical bronchospasm may occur. Physicians should remain vigilant for the possible development of pneumonia in patients with COPD as the clinical features of such infections overlap with the symptoms of COPD exacerbations. The incidence of pneumonia in patients with asthma was uncommon. Avoid beta-blockers if possible. Before prescribing *Breo Ellipta,* please review the Data Sheet at www.medsafe.govt.nz.

Seretide® (fluticasone propionate/salmeterol xinafoate inhaler 50/25 or 125/25mcg per actuation and *Accuhaler*® 100/50, 250/50mcg per actuation) is a **fully funded medicine. *Seretide* 250/25mcg inhaler is a private purchase medicine; a prescription charge will apply. Maximum Daily Dose:** MDI 2 puffs twice daily, *Accuhaler* 1 inhalation twice daily. **Maintenance Dose:** Titrate to lowest effective dose 1-2 times daily. **Prescription Medicine** for the treatment of reversible obstructive airway disease (ROAD) including asthma, and for the treatment of chronic obstructive pulmonary disease (COPD). This medicine has risks and benefits. **Warnings and Precautions:** Not for relief of acute symptoms. Do not discontinue abruptly. Use care when co-administering strong CYP3A4 inhibitors (e.g. ketoconazole) or in patients with pulmonary tuberculosis or thyrotoxicosis. **Common Side Effects:** Hoarseness/dysphonia, throat irritation, headache, oral candidiasis and palpitations. Paradoxical bronchospasm may occur. Avoid beta-blockers if possible. Before prescribing *Seretide*, please review the Data Sheet at www.medsafe.govt.nz. *Seretide* and *Accuhaler* are registered trade marks of the GlaxoSmithKline group of companies. Marketed by GlaxoSmithKline NZ Limited, Auckland. **Adverse events involving GlaxoSmithKline products should be reported to GSK Medical Information on 0800 808 500.**