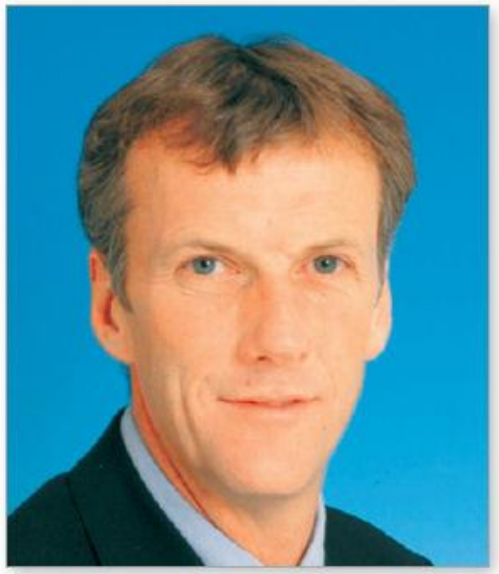


Associate Professor Rob Young

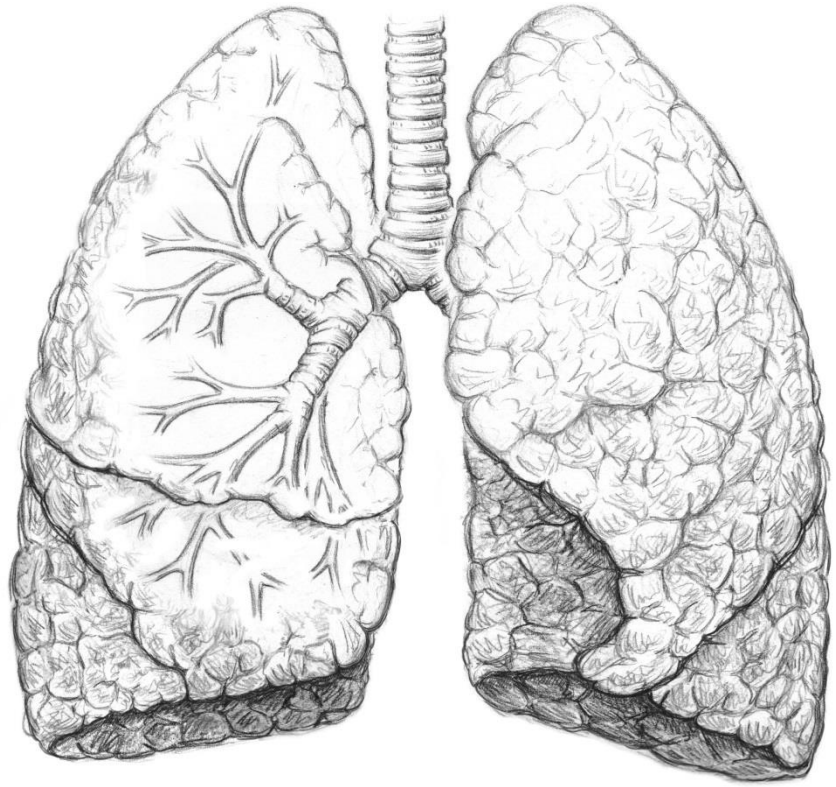
General Physician

Auckland City Hospital

Saturday, August 10, 2019

(Room 5)

7:00 - 7:55 GSK Breakfast Session - Simplifying COPD Treatment



Simplifying COPD Treatment

Associate Professor Robert Young
GPCME South , August 2019
BMedSc MBChB DPhil (Oxon) FRACP FRCP
Associate Professor
Consultant Physician

TAP DA1924JB-PM-NZ-UCV-PPT-190002

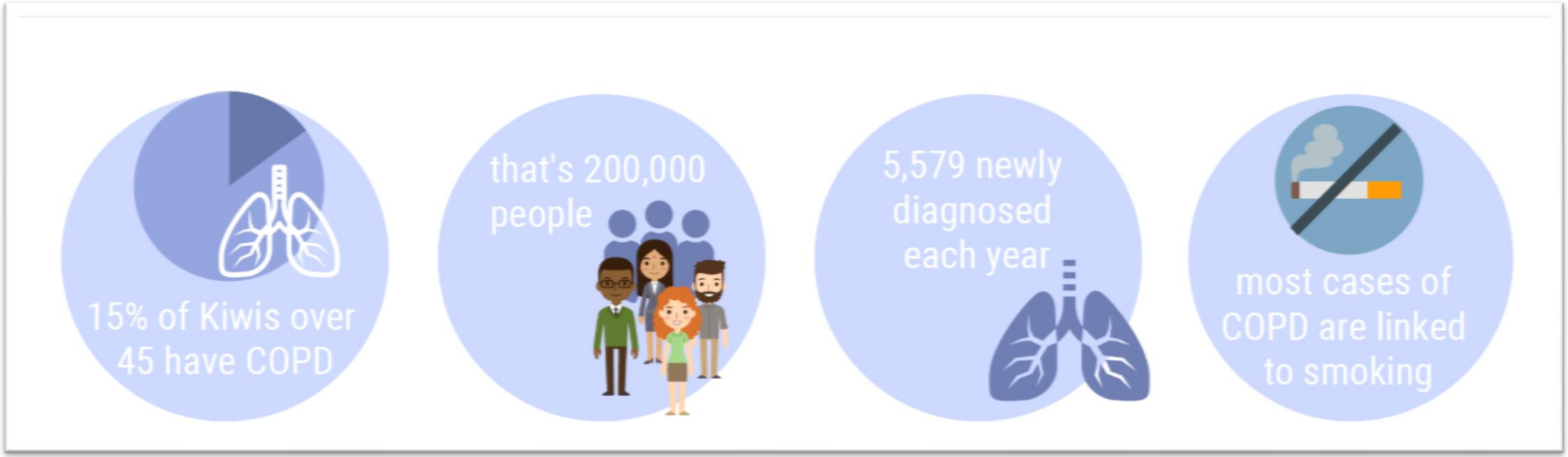
Disclosures and disclaimer

- I have been paid an honorarium for this presentation
- I am a not 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 received honoraria for participation on an advisory board for GSK

Agenda

- An overview of the disease and funded treatments in New Zealand
- Diagnosis of COPD (spirometry) and symptom assessment (CAT)
- Simplifying treatments, the New Zealand context (“treatable traits”)
- The benefits of dual bronchodilation (role of LAMA/LABA)
- The place of Inhaled Corticosteroids (“ICS responsive” COPD)
- Non-pharmacological treatment
- Summary

COPD has a high social and economic burden in NZ

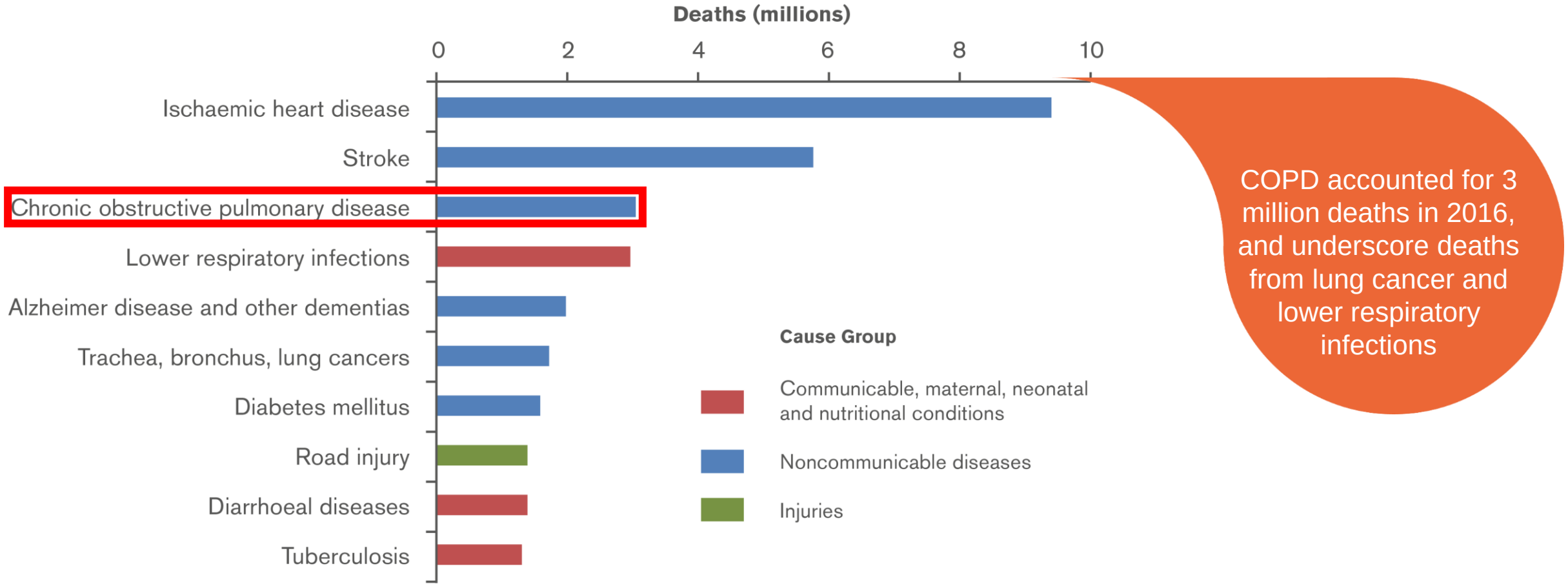


High & **disproportionate burden of disease** for Maori and Pacific Peoples.

COPD remains a disease that is under-diagnosed and under-treated.

Reference: Asthma and Respiratory Foundation: https://s3-ap-southeast-2.amazonaws.com/assets.asthmafoundation.org.nz/images/documents/Impact-of-Respiratory-disease_FINAL.pdf

COPD is the third leading cause of death globally



COPD accounted for 3 million deaths in 2016, and underscore deaths from lung cancer and lower respiratory infections

Source: Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2016. Geneva, World Health Organization; 2018.

Reference: 1. World Health Organization. Global health estimates 2016. Available at: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death

HIV, human immunodeficiency virus

What are the funded long acting inhalers for COPD in New Zealand?

Funded inhaled maintenance treatments for COPD in New Zealand

LAMA
No Special Authority*

Incruse Ellipta
UMECLIDINIUM[2]

Seebri® Breezhaler ®
GLYCOPYRRONIUM[3]

Spiriva® Respimat® +
Handihaler ®
TIOTROPIUM[3]

LAMA/LABA‡
Special Authority Required[1]

Anoro Ellipta
UMECLIDINIUM/
VILANTEROL[5]

Ultibro®
Breezhaler ®
GLYCOPYRRONIUM
INDACATEROL[6]

Spiolto®
Respimat®
TIOTROPIUM/
OLODATEROL[7]

ICS/LABA

Breo Ellipta
FLUTICASONE
FUROATE/
VILANTEROL[8]

FLUTICASONE
PROPIONATE/
SALMETEROL[9]
Seretide/Rexair

Symbicort®
Turbuhaler® /Vannair®
BUDESONIDE/
EFORMOTEROL[10]

‡ SPECIAL AUTHORITY REQUIREMENTS: Patient must be stabilised on a LAMA monotherapy prior to LAMA/LABA
* The prescriber must provide written endorsement that the patient has been diagnosed as having COPD using spirometry to access subsidy
ICS = Inhaled Corticosteroid; LABA = Long Acting Beta$_2$ Agonist; LAMA = Long Acting Muscarinic Antagonist

References: 1. Pharmaceutical Schedule, PHARMAC, July 2019. 2. Incruse Ellipta Data Sheet, GSK New Zealand, 2019 3. Seebri Breezhaler Data Sheet, Novartis New Zealand, 2019; 4. Spiriva Data Sheet, BI New Zealand, 2019; 5. Anoro Ellipta Data Sheet, GSK New Zealand, 2019. 6. Ultibro Breezhaler Data Sheet, Novartis New Zealand, 2019 7. Spiolto Data Sheet, BI New Zealand, 2019; 8. Breo Ellipta Data Sheet, GSK New Zealand, 2015 9. Seretide Data Sheet, GSK New Zealand, 2019 10, Symbicort Turbuhaler Data Sheet, AZ New Zealand, 2015; 1. Pharmaceutical Schedule, PHARMAC, May 2017.

How do I diagnose and assess symptoms in my COPD patients?

Key indicators for considering COPD diagnosis in your patients (> 40 yo)

Dyspnoea/breathlessness that is:	• Progressive over time • Characteristically worse with exercise • Persistent
Chronic cough:	• May be intermittent and may be unproductive • Recurrent wheeze
Sputum production:	• Any pattern of chronic sputum production may indicate COPD • Bouts of productive cough with breathlessness and/or wheeze (LRTI)
Recurrent lower Respiratory tract infections	
Host of risk factors:	• Host factors (such as congenital/developmental abnormalities etc.) • Tobacco smoke • Smoke from home cooking and heating fuels • Occupational dust, vapours, gases, other chemicals
Family history of COPD and/or childhood factors	• For example low birthweight, childhood respiratory infections etc.

Reference: Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2019.

FEV1 informs diagnosis and prognosis but not treatment recommendations

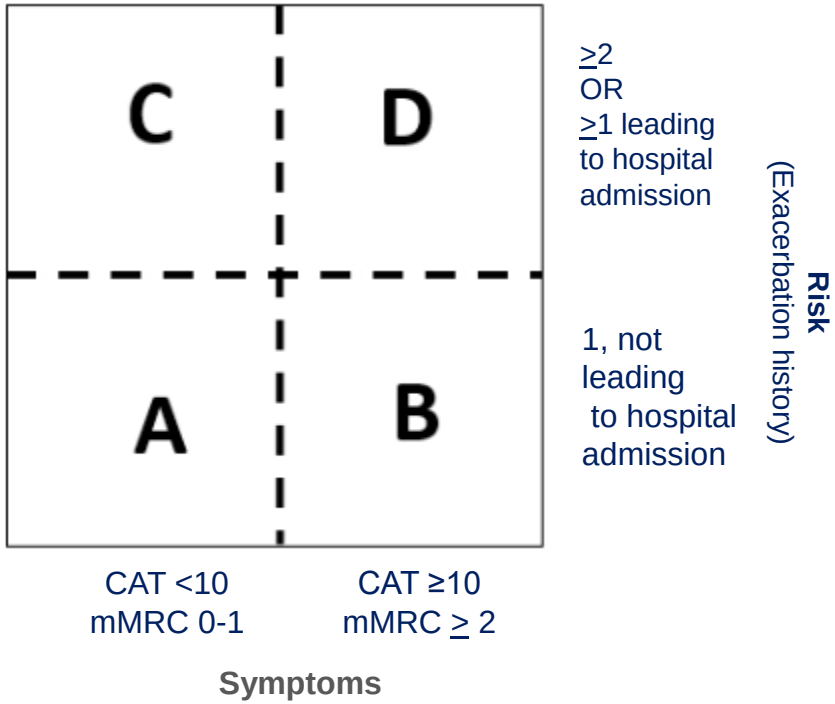
Diagnosis

$FEV_1/FVC<0.7$

Assessment of airflow limitation (severity + prognosis)

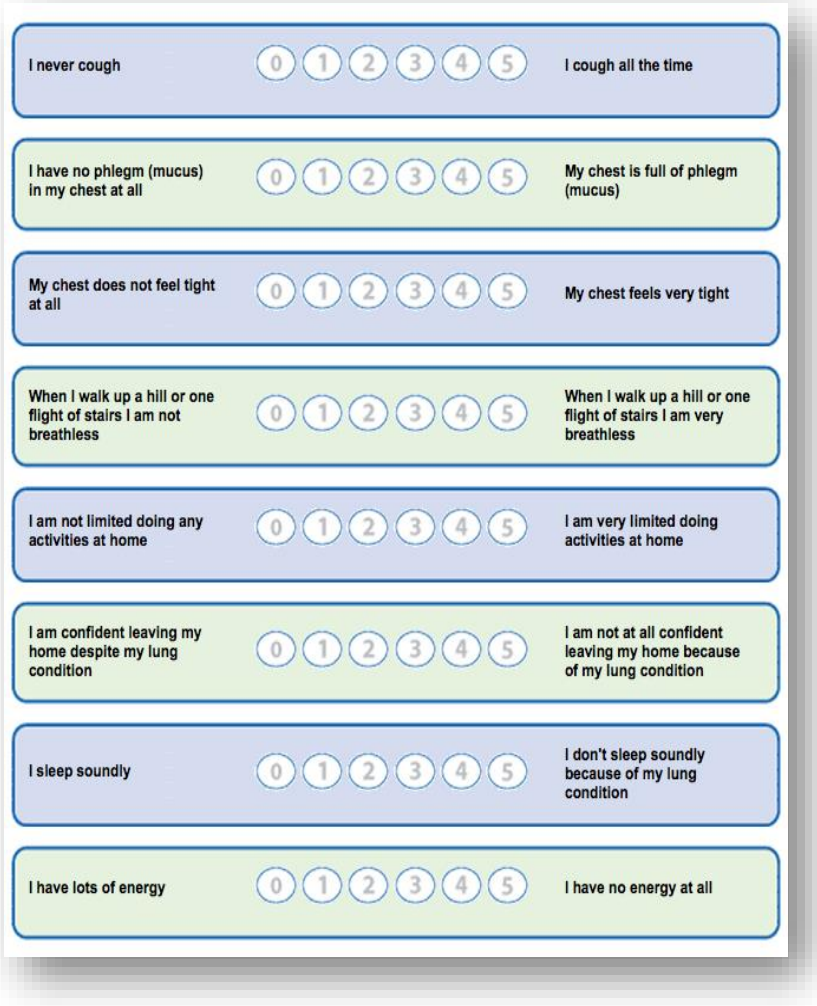
Grade	FEV_1 (% pred.)
1	≥80
2	50-79
3	30-49
4	<30

Assessment of symptoms/risk of exacerbation



Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2019.

The CAT (COPD Assessment Test)



Cough

Phlegm

Tight

SOB

Activity

Confidence

Sleep

Energy

<u>Score out of 40</u>

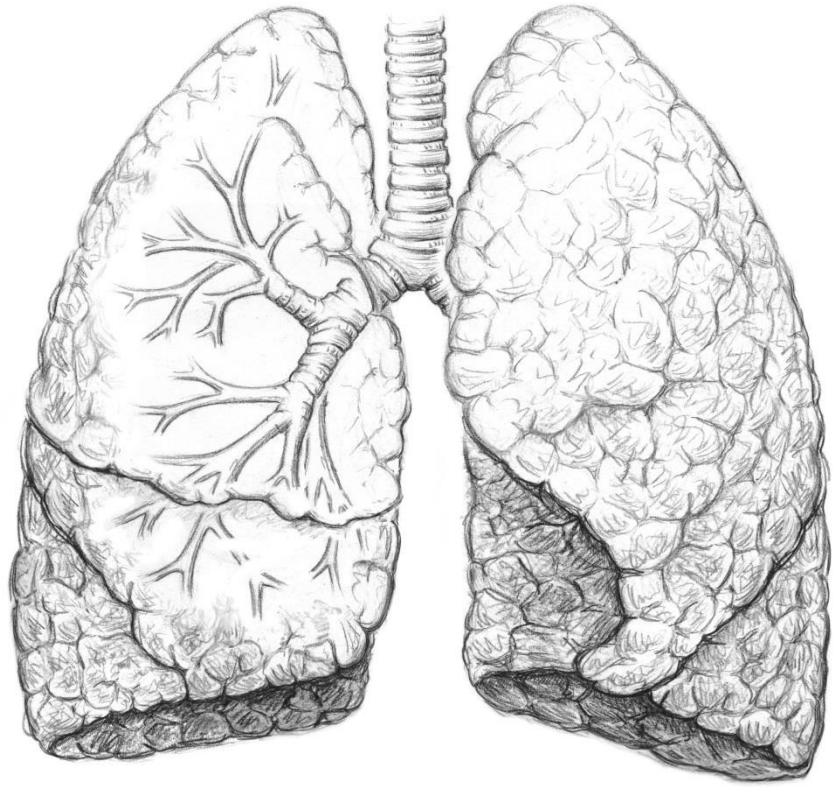
Mild: 0-10
Moderate: 10-15
Severe: 15-25
Very severe: 25-40

Basis on which to establish
Overall disability
Specific disabilities and response to treatments

Modified MRC Breathlessness Score

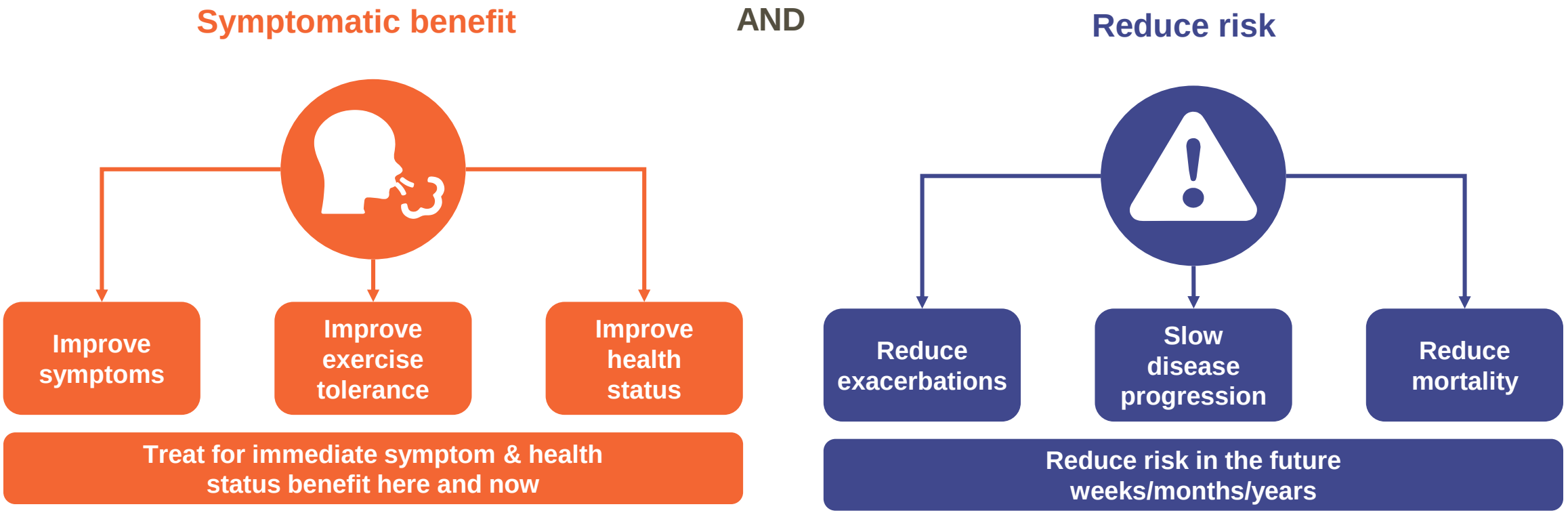
Grade	Description of Breathlessness
0	I only get breathless with strenuous exercise.
1	I get short of breath when hurrying on level ground or walking up a slight hill.
2	On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my 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.

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



Simplifying COPD:
COPD in the NZ context

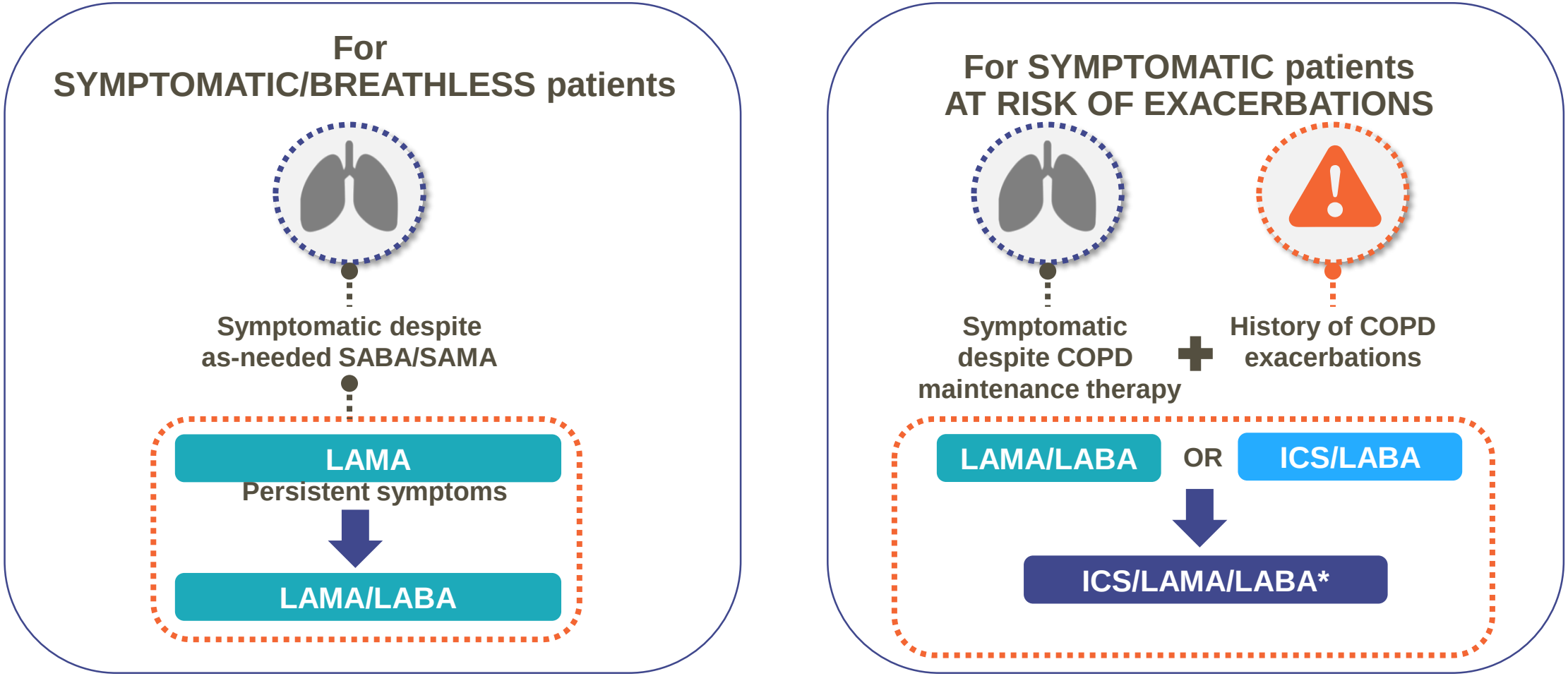
Reducing symptoms and risk of exacerbations are key objectives of COPD treatment



Routine follow-up of COPD patients is essential

GOLD. Global Strategy for the Diagnosis, Management and Prevention of COPD. 2018. Available from: http://goldcopd.org (accessed August 2018)

Simplifying COPD: COPD treatment should be individualised based on symptoms and exacerbation risk

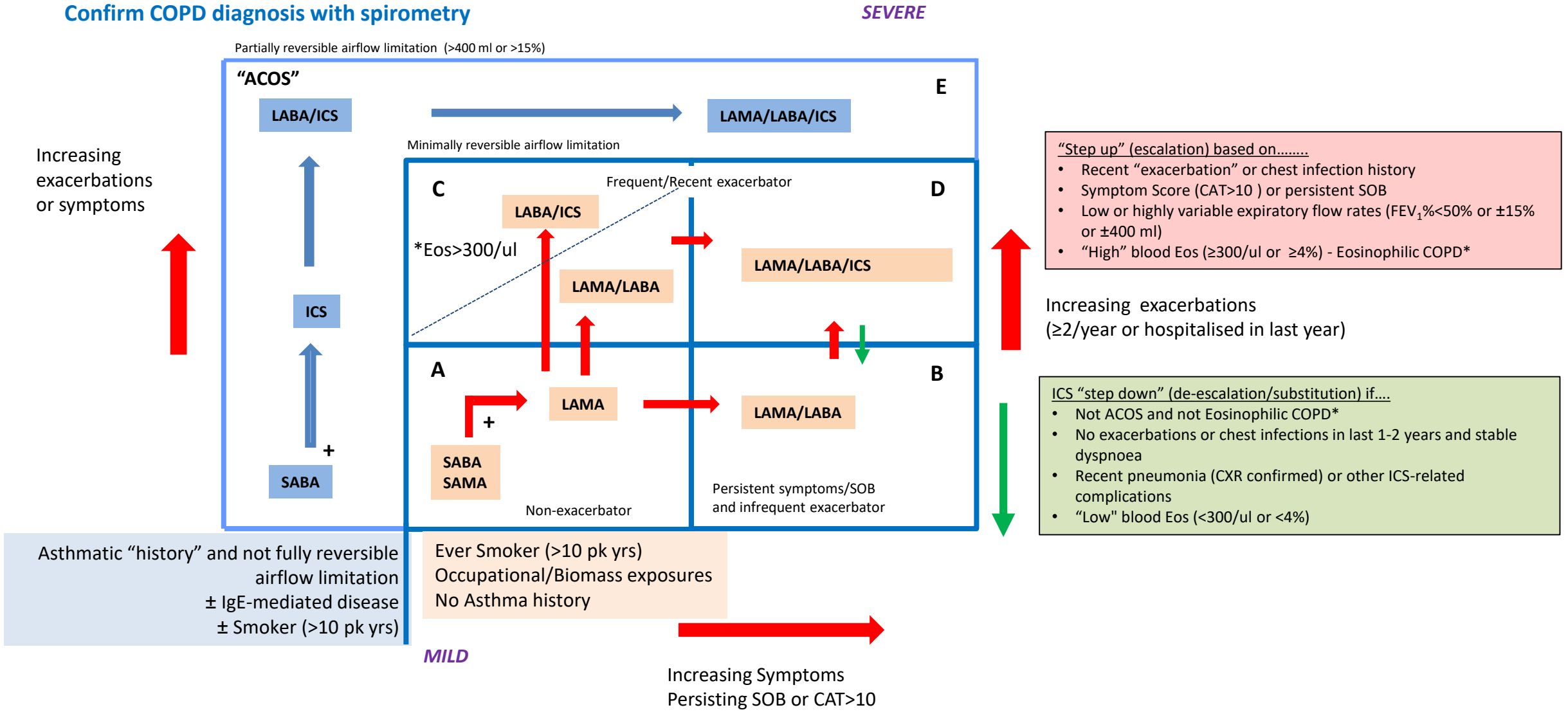


… however, GOLD acknowledges that there is a **lack of robust evidence** to inform selection of the **most appropriate treatment** for patients with COPD who are symptomatic and at risk of exacerbation[1]

* LAMA/LABA/ICS single inhaler triple therapies are not yet registered in New Zealand.; Global Strategy for the Diagnosis, Management and Prevention of COPD (GOLD) report 2017. (http://goldcopd.org)

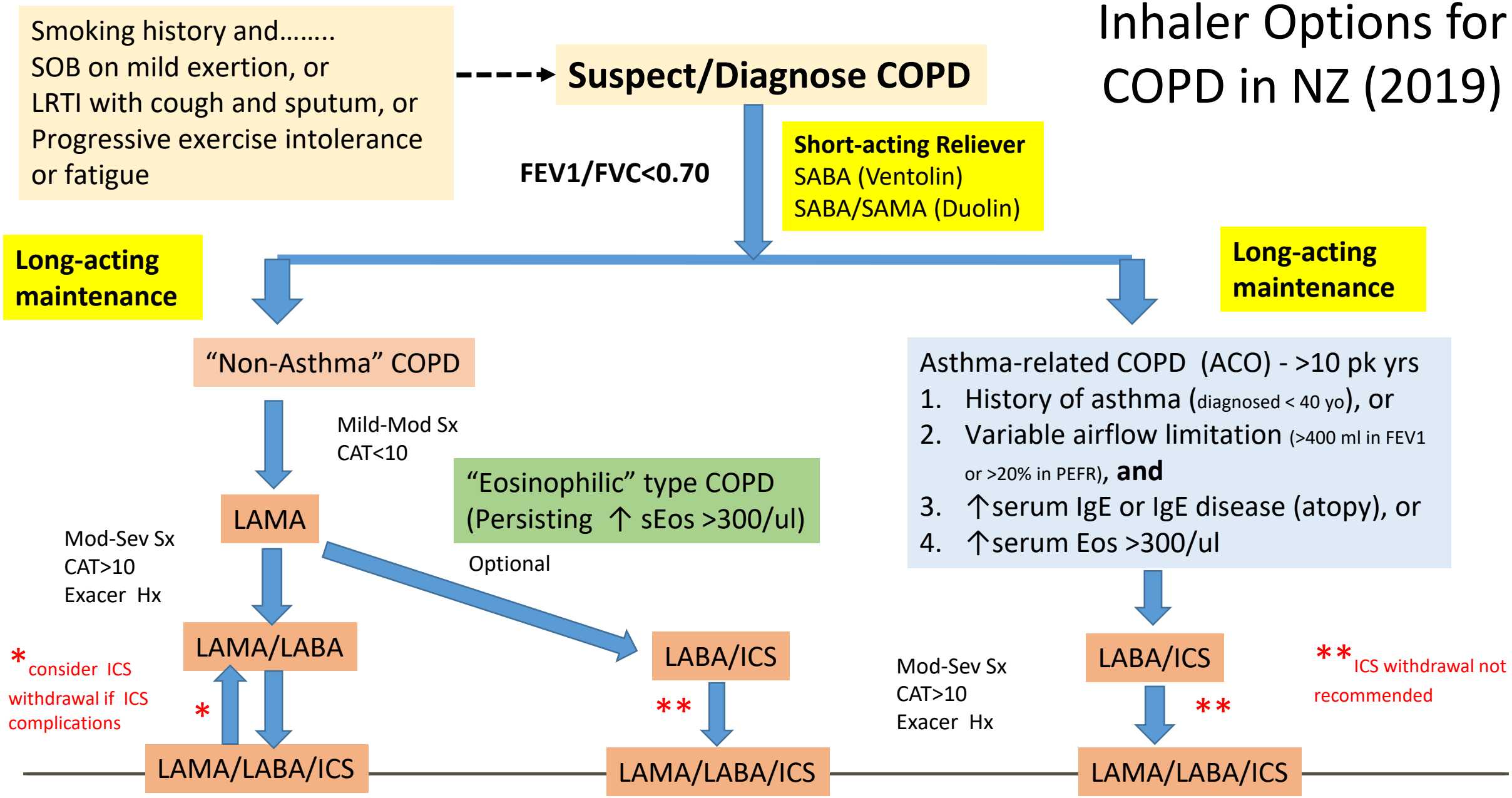
Simplifying COPD: NZ context 2018

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



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

Inhaler Options for COPD in NZ (2019)



What are the benefits of dual bronchodilation in my COPD patient?

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]

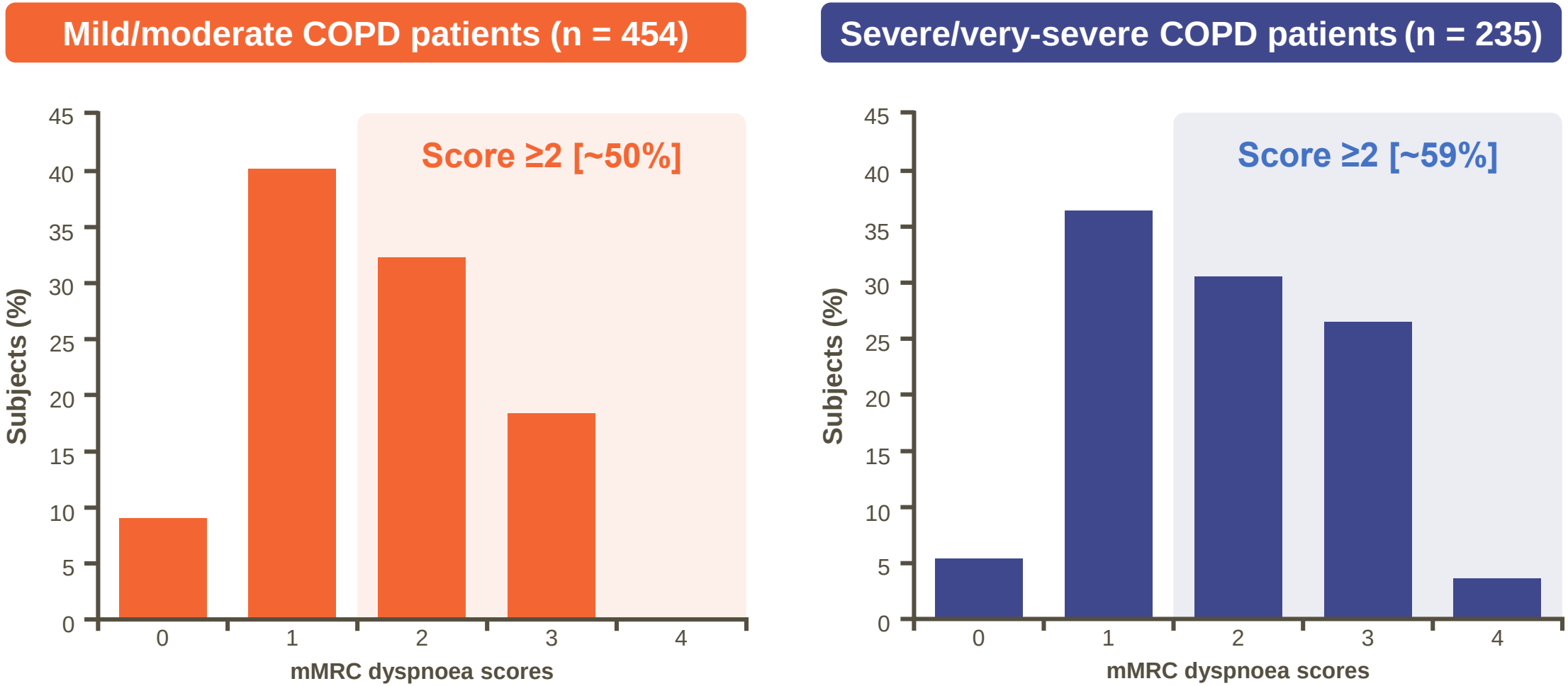
INITIAL APPLICATION:

- **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

A high symptom burden persists in most patients when using a mono bronchodilator



The figure is reproduced with the permission of Elsevier. It was first published in *Prim Care Respir J.*
* Mild/moderate and severe/very severe were defined according to GOLD 2006 staging (based on post-bronchodilator FEV_1).

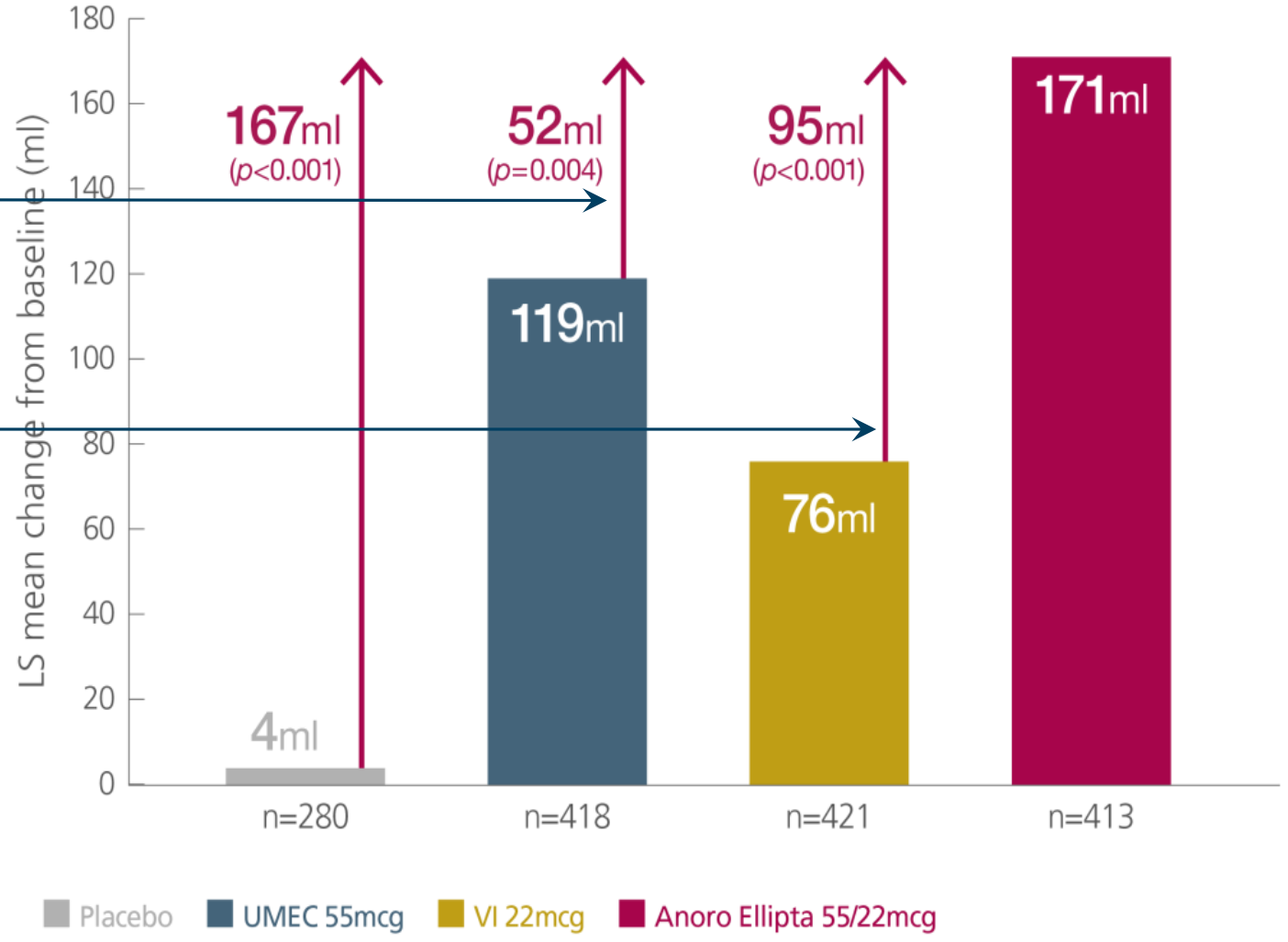
Dransfield MT, et al. *Prim Care Respir J*. 2011;20:46–53.

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

LAMA/LABA vs LABA and LAMA

Benefit of LABA when added to LAMA

Benefit of LAMA when added to LABA



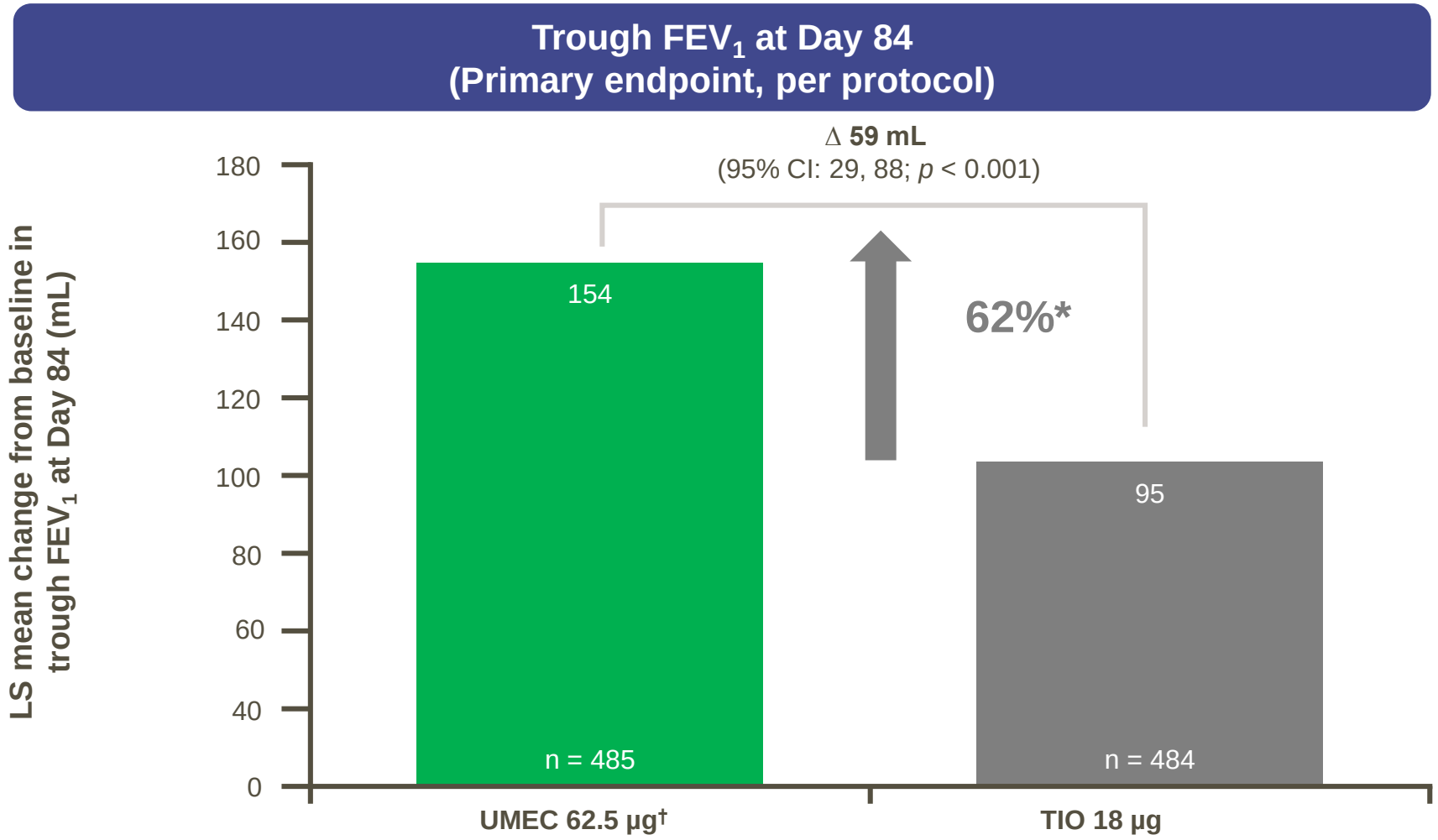
Vilanterol monotherapy is unlicensed in COPD

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

Are there data that compares bronchodilator products?

Greater improvement in FEV_1 with Incruse (umeclidinium) compared with Spiriva Handihaler (tiotropium)

LAMA Monotherapy



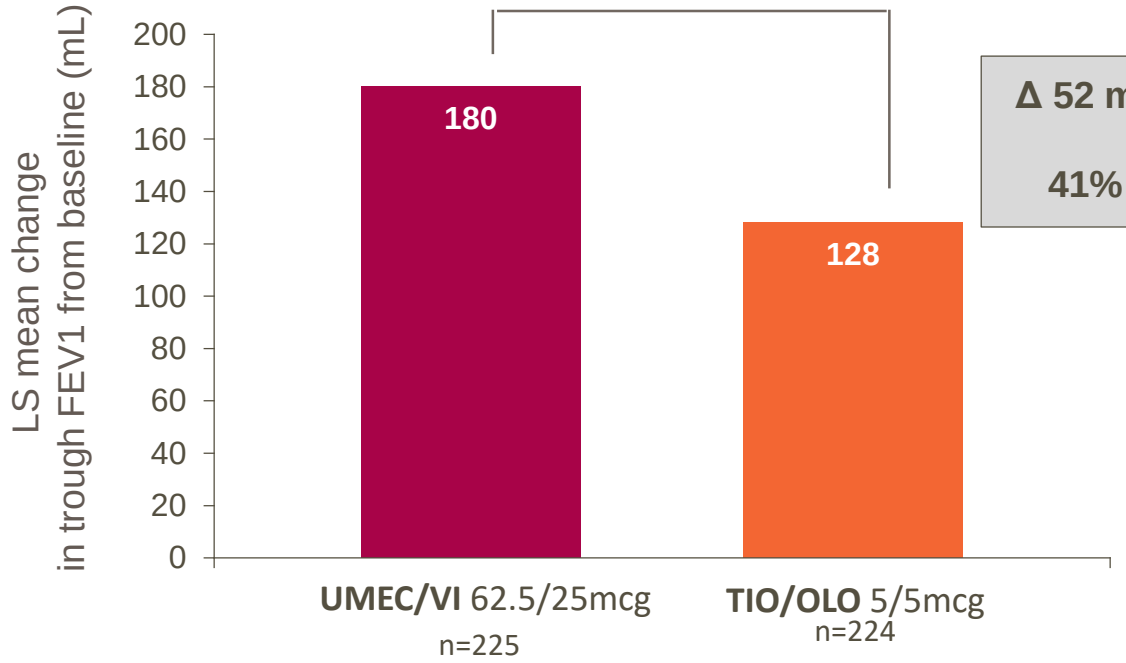
* Estimated calculation only; † Delivered dose 55 µg. TIO, tiotropium; UMEC, umeclidinium.

Feldman G, et al. *Int J Chron Obstruct Pulmon Dis.* 2016;11:719–730.

Greater improvement in lung function with Anoro (umeclidinium/vilanterol) over Spiolto (tiotropium/olodaterol)

LAMA/LABA dual therapy

Trough FEV_1 at Week 8*



Δ 52 mL (95% CI: 28, 77)
p < 0.001
41% improvement***

UMEC = umeclidinium
VI = vilanterol
TIO = tiotropium
OLO = olodaterol

Anoro demonstrated superior lung function (trough FEV1) vs. Spiolto

*8-week open label, crossover trial in symptomatic patients with moderate COPD not receiving ICS in intention to treat population

Change from baseline in the non inferiority primary analysis in per protocol population (53mL, 95% CI 26,80; P<0.001)

Adapted from Feldman G.J et al. Adv Ther 2017; 34:2518-2533

Which of my patients would benefit from an ICS?

How should I manage my COPD patients with a previous diagnosis of asthma?

Which of my COPD patients would benefit from an ICS?

GOLD 2019 recommends:

- For patients with persistent exacerbations on long acting bronchodilator monotherapy, escalation to ICS/LABA or LAMA/LABA is recommended.
- ICS/LABA may be preferred for patients with a history or finding suggestive of asthma
- Blood eosinophils may identify patients with a greater likelihood of a beneficial response to ICS

Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2019.

Asthma COPD Overlap (ACOS) subgroup of COPD spectrum

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% or 300/ul)
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)

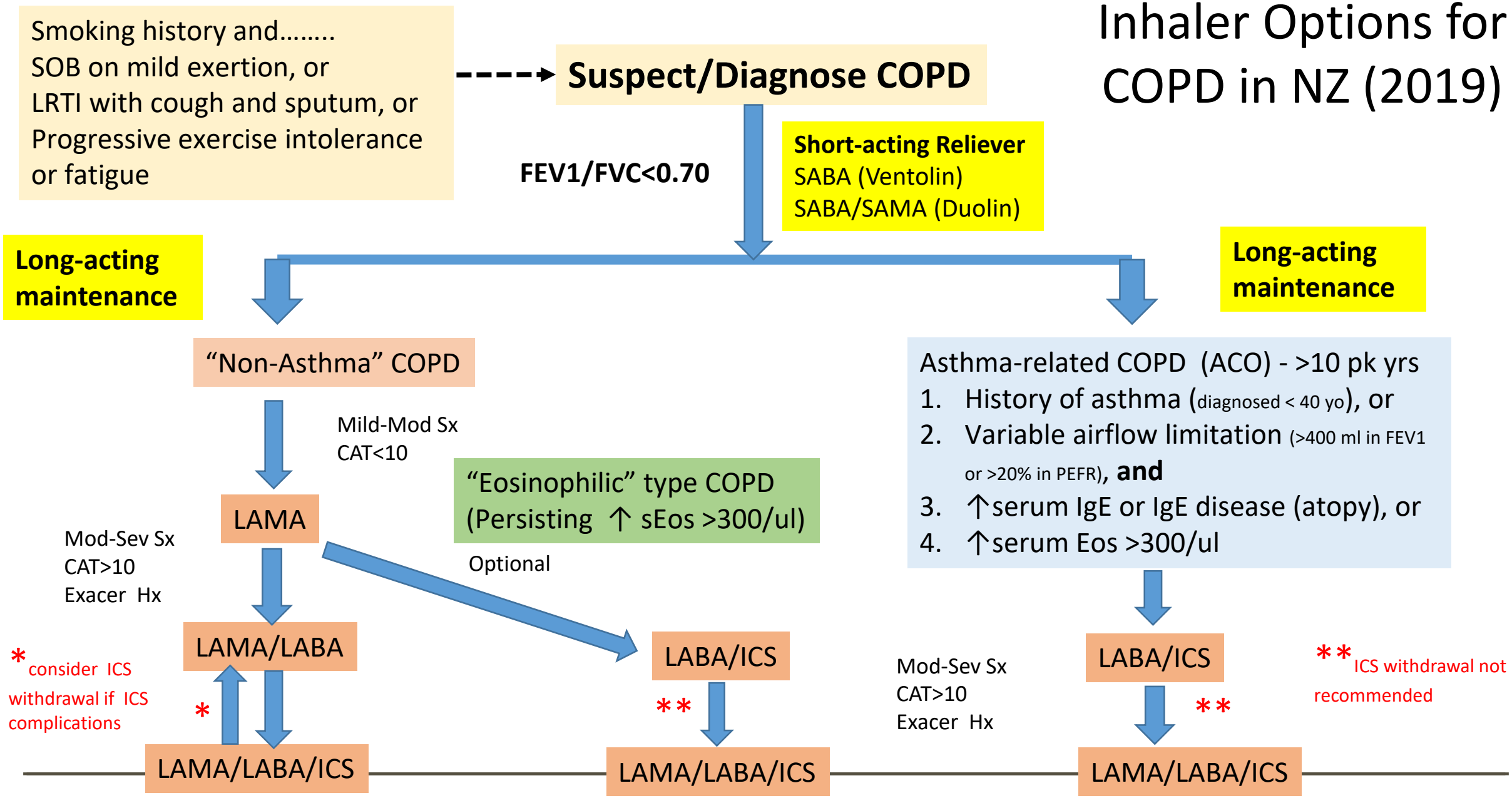
Assumed to:

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

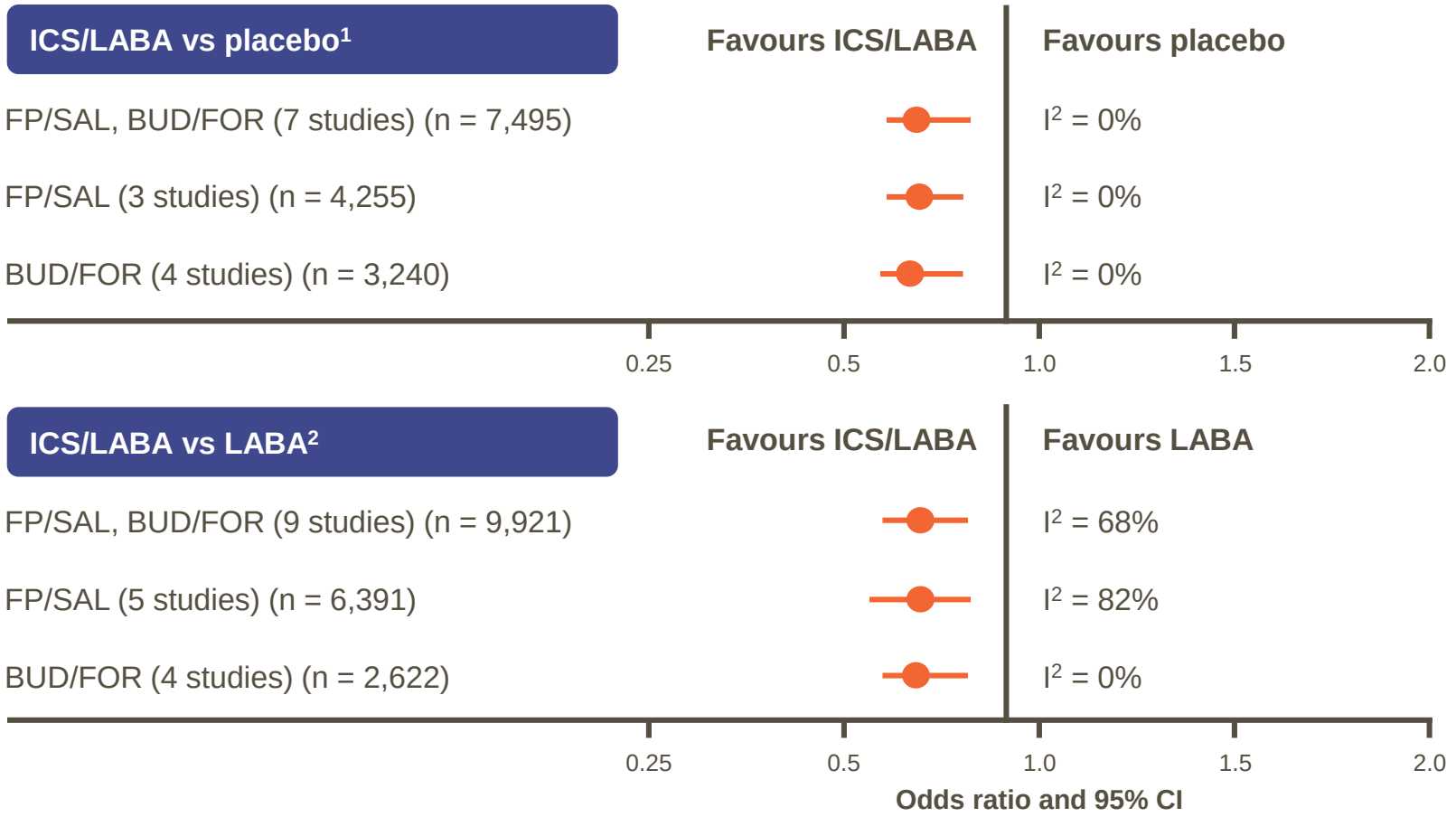
Recommendations are based on expert opinion and not RCTs
(ACOS usually excluded from COPD trials)

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

Inhaler Options for COPD in NZ (2019)



ICS/LABA reduces exacerbations in COPD



Two large independent Cochrane meta-analyses have confirmed significant reductions in the rate of exacerbations (~25%) with ICS/LABA treatments compared with placebo, and compared with LABA alone

LAMA better than LABA alone

ICS/LABA vs LAMA/LABA **depends on the COPD phenotype**

The graph has been independently created by GSK from the original data. BUD, budesonide; FOR, formoterol; FP, fluticasone propionate; SAL, salmeterol.

1. Nannini LJ, et al. *Cochrane Database Syst Rev.* 2013;11:CD003794; 2. Nannini LJ, et al. *Cochrane Database Syst Rev*. 2012;9:CD006829.

When would you consider withdrawing an ICS?

Benefits and risks of ICS-containing therapy in COPD

Benefits[1,2]

- Well established
- Recommended as a treatment option for patients with a history of exacerbations
- Reduces number of exacerbations*
- Improves lung function*
- Improves QoL*

Risks[3–5]

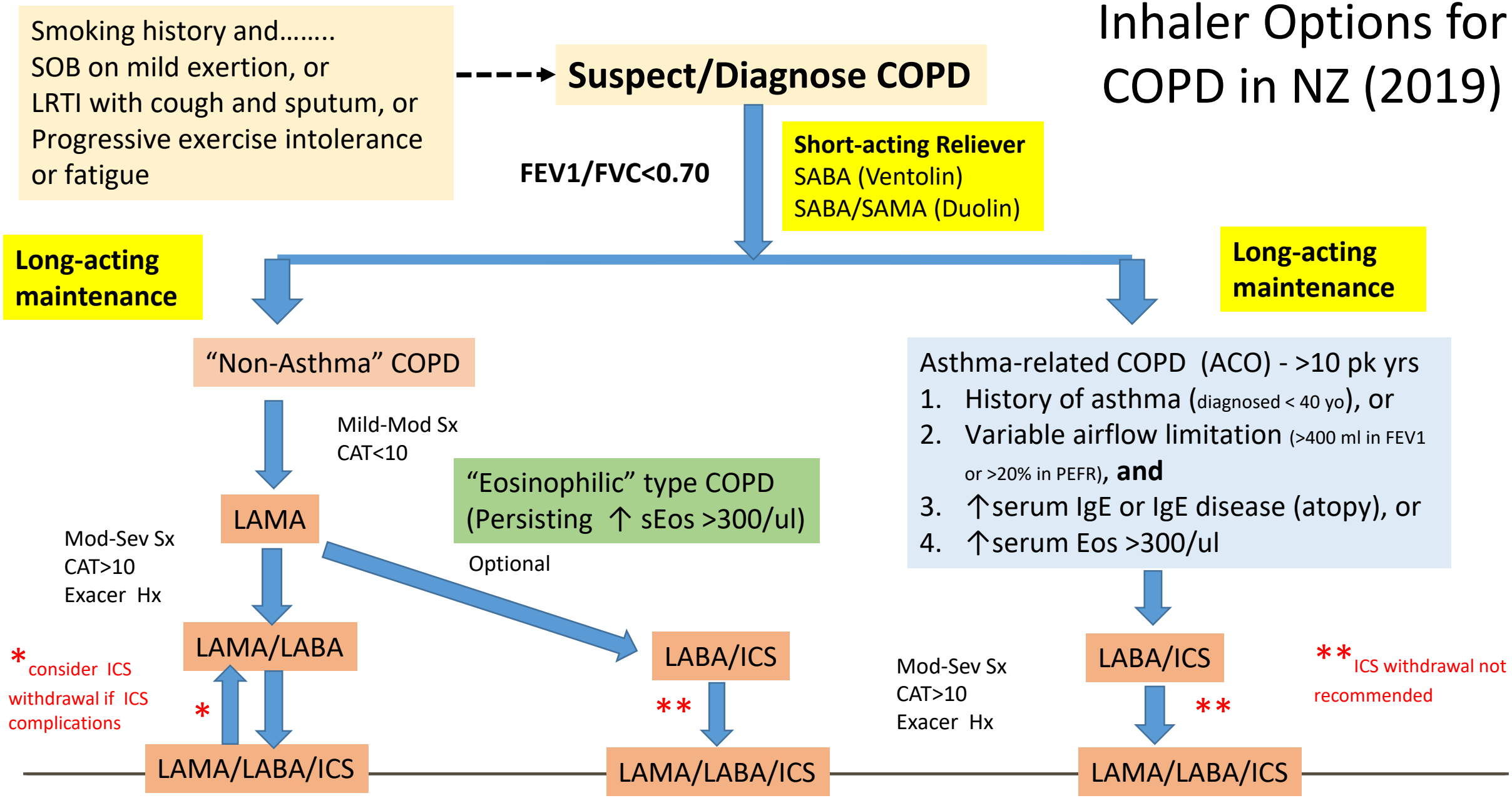
Adverse events, including increased risk of pneumonia in patients:

- With history of pneumonia or exacerbations
- Current smokers
- ≥55 years of age
- With poor lung function
- With low body mass index
- With multiple comorbid diseases

ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; QoL, quality of life
*Compared to placebo or LABA alone

References 1. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD), 2019. 2. Nannini L *et al. Cochrane Database Syst Rev* 2013; CD006829. 3. Kew K *et al. Cochrane Database Syst Rev* 2014; CD010115. 4. Mullerova H *et al. Respir Med* 2012; 106:1124–1133. 5. DiSantostefano RL *et al. Int J Chron Obstruct Pulmon Dis* 2014; 9:457–468.

Inhaler Options for COPD in NZ (2019)

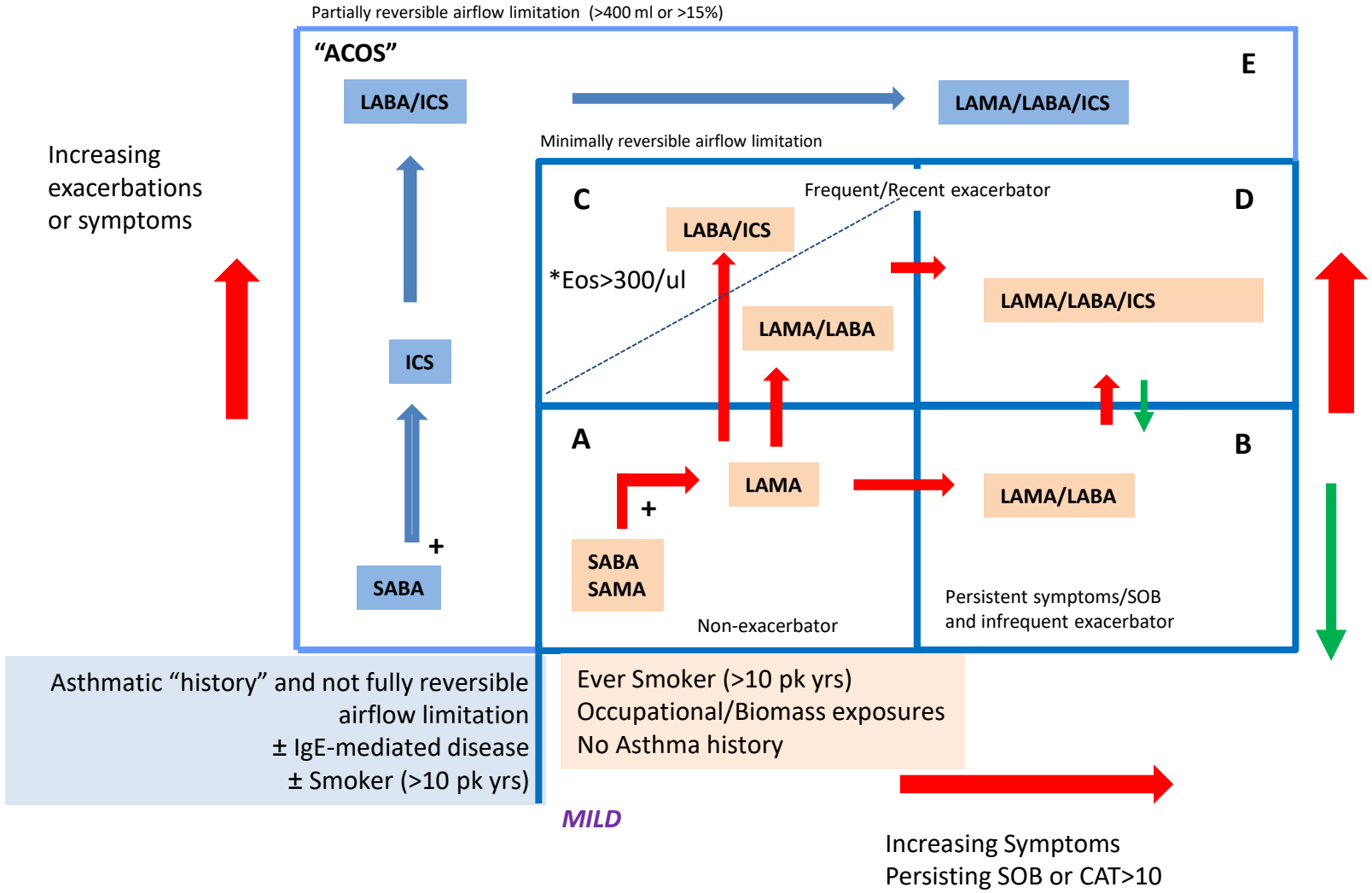


Simplifying COPD: NZ context 2018

Confirm COPD diagnosis with spirometry

SEVERE

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



"Step up" (escalation) based on……..

- Recent "exacerbation" or chest infection history
- Symptom Score (CAT>10) or persistent SOB
- Low or highly variable expiratory flow rates (FEV_1%<50% or ±15% or ±400 ml)
- "High" blood Eos (≥300/ulf or ≥4%) - Eosinophilic COPD*

Increasing exacerbations
(≥2/year or hospitalised in last year)

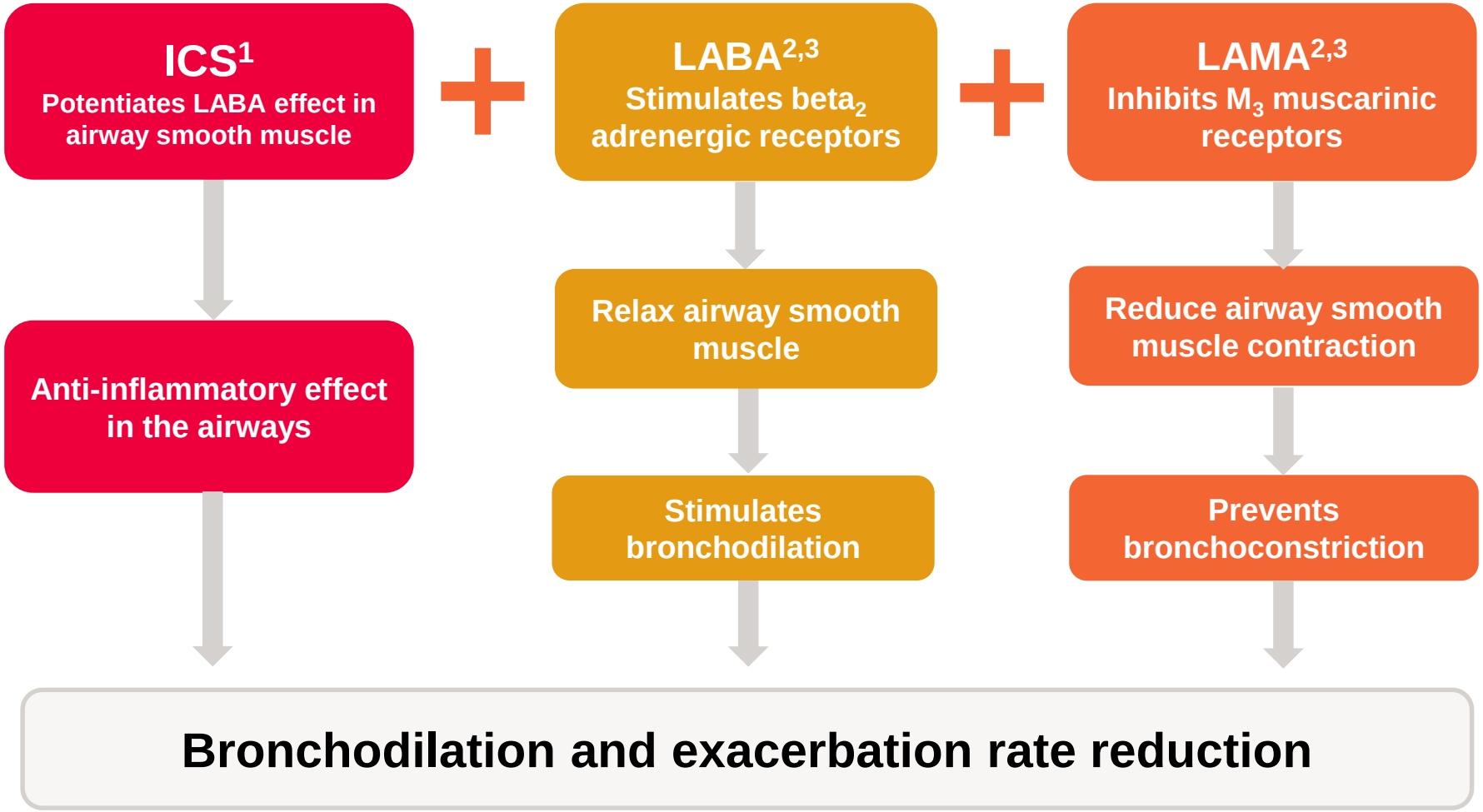
ICS "step down" (de-escalation/substitution) if….

- Not ACOS and not Eosinophilic COPD*
- No exacerbations or chest infections in last 1-2 years and stable dyspnoea
- Recent pneumonia (CXR confirmed) or other ICS-related complications
- "Low" blood Eos (<300/ul or <4%)

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

What about ICS+LABA+LAMA?

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

IMPACT: A landmark trial in symptomatic patients with COPD and a history of exacerbations[1,2]

First study to compare single inhaler Triple Therapy TRELEGY Ellipta (**ICS/LAMA/LABA**) with ANORO (**LAMA/LABA**) and with BREO (**ICS/LABA**)

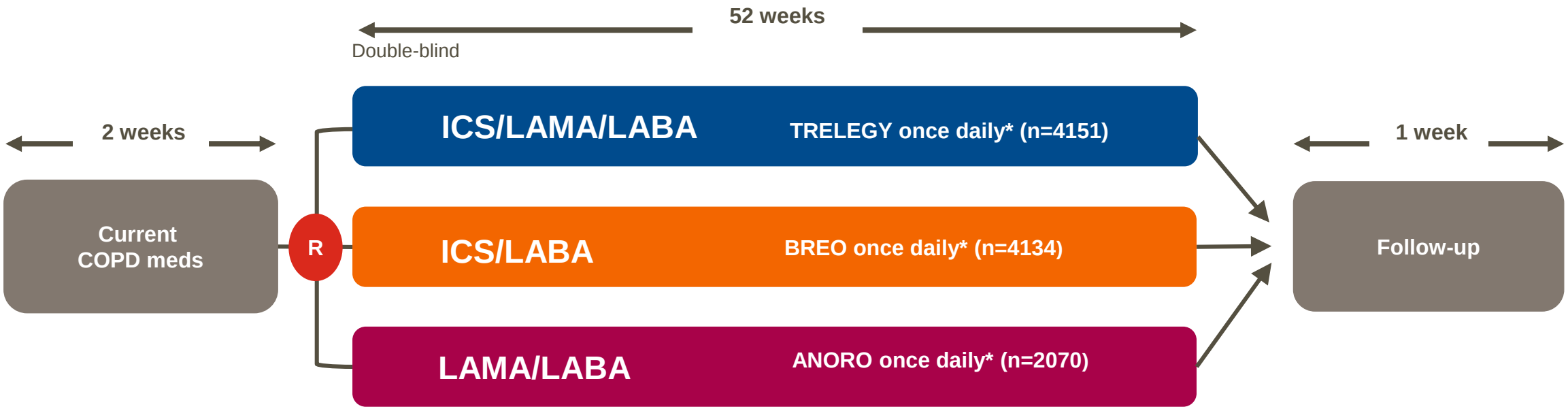
- IMPACT studied *a broad and generalisable population* of COPD patients with a history of ≥1 moderate/severe exacerbations in the past 12 months, who were receiving maintenance treatment
- According to cohort studies, the percentage of patients with COPD who are on maintenance therapy and have experienced ≥1 exacerbation over 12 months is approximately 50%[3]

FF: fluticasone furoate; UMEC:umelidinium;VI: vilanterol

References: 1. Pascoe SJ, et al. Eur Respir J. 2016;48:320–330; 2. Lipson DA, et al. N Engl J Med. 2018;378:1671–1680; 3. DOF RF/CPD/0003/18

*Trelegy (FF/UMEC/VI) is not funded in New Zealand

IMPACT: TRELEGY* (ICS/LABA/LAMA) vs BREO (ICS/LABA) and ANORO (LAMA/LABA), delivered in the ELLIPTA inhaler



Co-primary treatment comparisons (ITT population)

- Annual rate of moderate/severe exacerbations comparing:
  - ICS/LABA/LAMA with ICS/LABA
  - ICS/LABA/LAMA with LAMA/LABA

For all combinations, delivered doses were as follows: FF (100 µg), UMEC (62.5 µg) and VI (25 µg); all treatments were administered via the ELLIPTA inhaler
TRELEGY 100/62.5/25µg; BREO 100/62.5/25µg; ANORO 62.5/25µg

References: 1. Lipson DA, et al. N Engl J Med. 2018;378:1671–1680; 2. Lipson DA, et al. N Engl J Med. 2018;378:1671–1680 (Supplementary Appendix).

*Trelegy (FF/UMEC/VI) is not funded in New Zealand

The IMPACT Study: Baseline demographics[1]

Mostly GOLD Group D

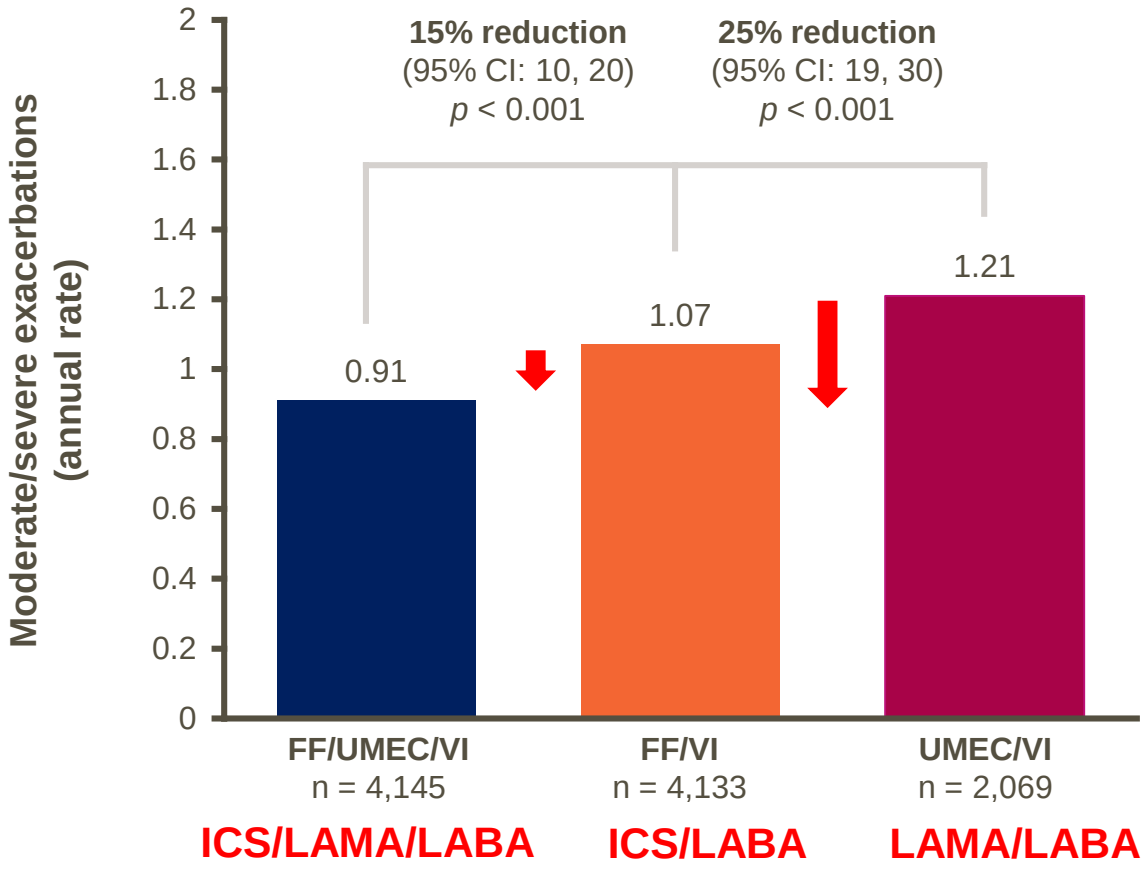
	ICS/LABA/LAMA TRELEGY Ellipta (100/62.5/25 mcg) n=4151	ICS/LABA BREO (100/25 mcg) n=4134	LABA/LAMA ANORO (62.5/25 mcg) n=2070	Overall (N=10355)
Age (y), Mean (SD)	65.3 (8.2)	65.3 (8.3)	65.2 (8.3)	65.3 (8.3)
Sex (% male)	67%	66%	66%	66%
Former smoker n, (%)	2715 (65%)	2711 (66%)	1342 (65%)	6768 (65%)
Post-bronchodilator FEV_1 % predicted, Mean (SD)	45.7 (15.0)	45.5 (14.8)	45.4 (14.7)	45.5 (14.8)
COPD exacerbations in prior year, n (%)				
1 moderate and no severe[2]	1198 (29%)	1242 (30%)	616 (30%)	3056 (30%)
≥2 moderate or ≥1 severe	2953 (71%)	2892 (70%)	1454 (70%)	7299 (70%)
≥1 severe	1087 (26%)	1069 (26%)	515 (25%)	2671 (26%)
Baseline COPD medications,[2] n (%)				
ICS + LABA + LAMA	1581 (38%)	1563 (38%)	826 (40%)	3970 (38%)
ICS + LABA	1220 (29%)	1177 (28%)	576 (28%)	2973 (29%)
LABA + LAMA	361 (9%)	331 (8%)	187 (9%)	879 (8%)
LAMA	288 (7%)	346 (8%)	146 (7%)	780 (8%)

References: 1. Lipson DA, et al. N Engl J Med. 2018;378:1671–1680]; 2. Lipson DA, et al. N Engl J Med. 2018;378:1671–1680 (Supplemental Appendix)

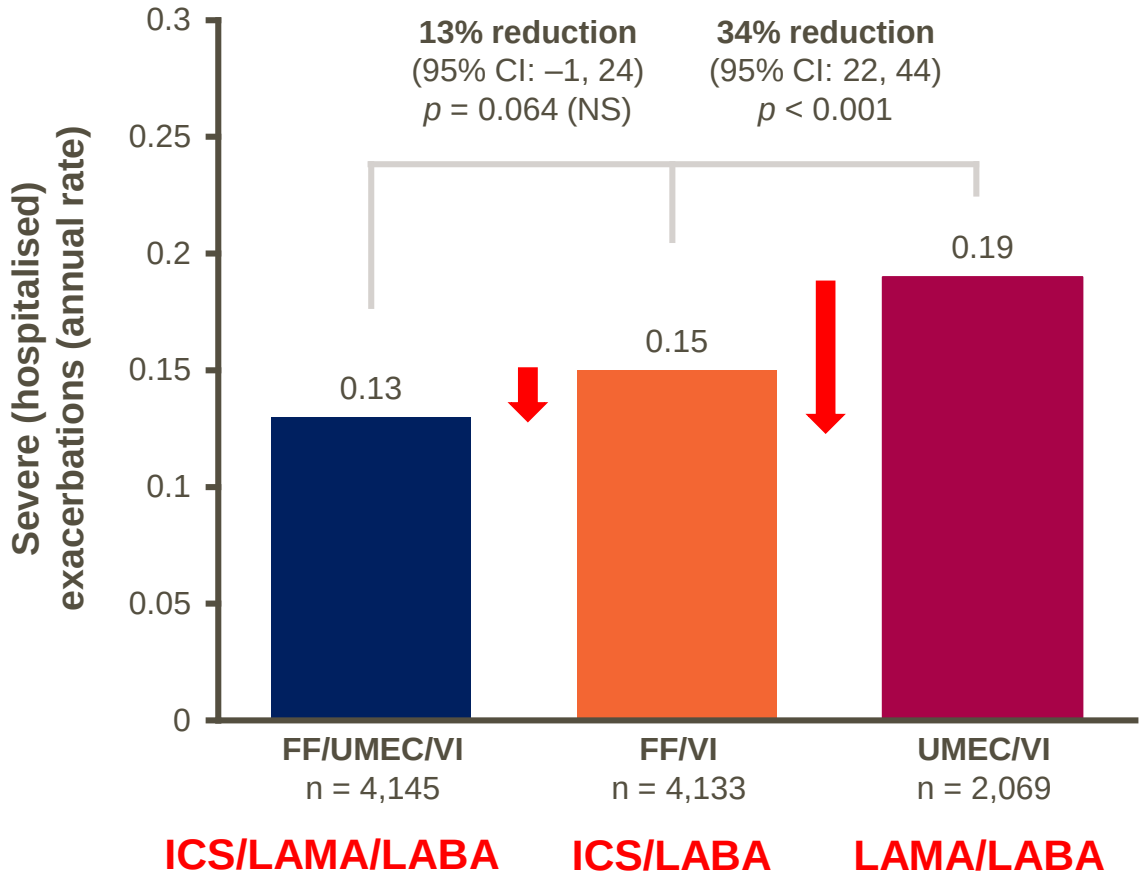
*Trelegy (FF/UMEC/VI) is not funded in New Zealand

IMPACT: Significant reduction in moderate/severe exacerbations and reduction in severe (hospitalised) exacerbations

Moderate/severe exacerbations



Severe (hospitalised) exacerbations



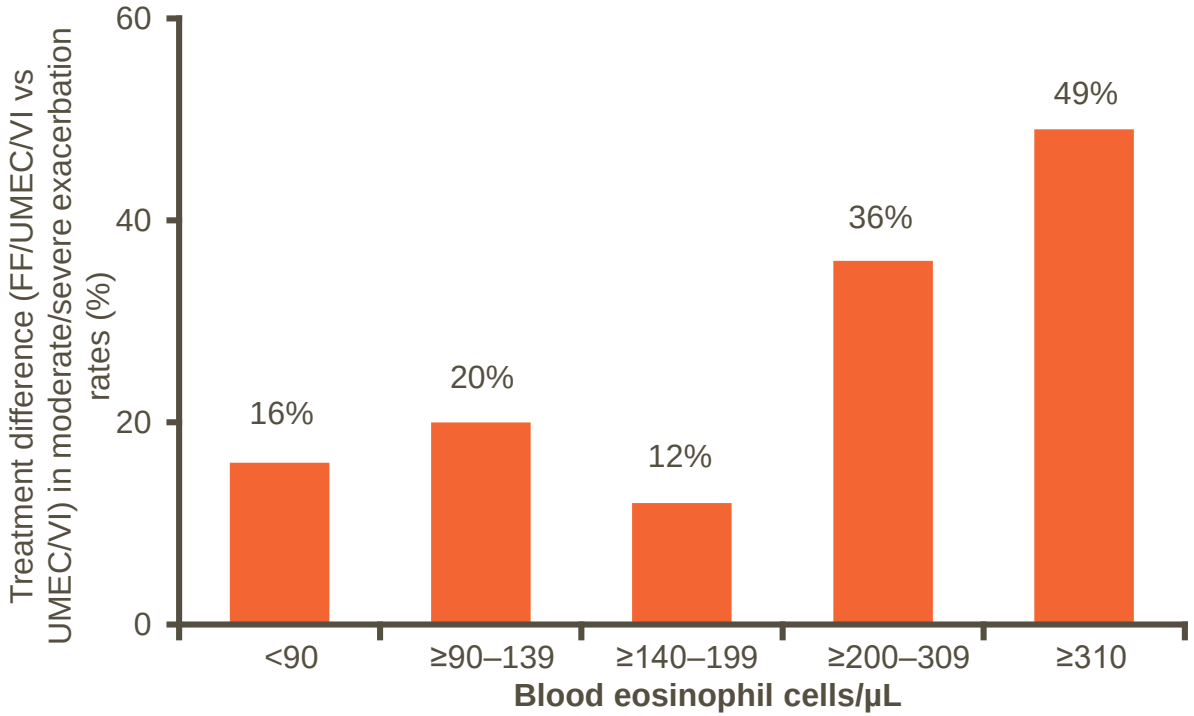
Lipson DA, et al. *N Engl J Med*. 2018;378:1671–1680.

The graphs have been independently created by GSK from the original data. Note: The n reflects the number of patients included in each analysis from the ITT population. Patients were excluded if they had predefined data missing; this varied according to the analysis. The ITT population comprised: 4,151 patients treated with FF/UMEC/VI, 4,134 patients treated with FF/VI and 2,070 patients treated with UMEC/VI.
FF, fluticasone furoate; NS, not statistically significant; UMEC, umeclidinium; VI, vilanterol.

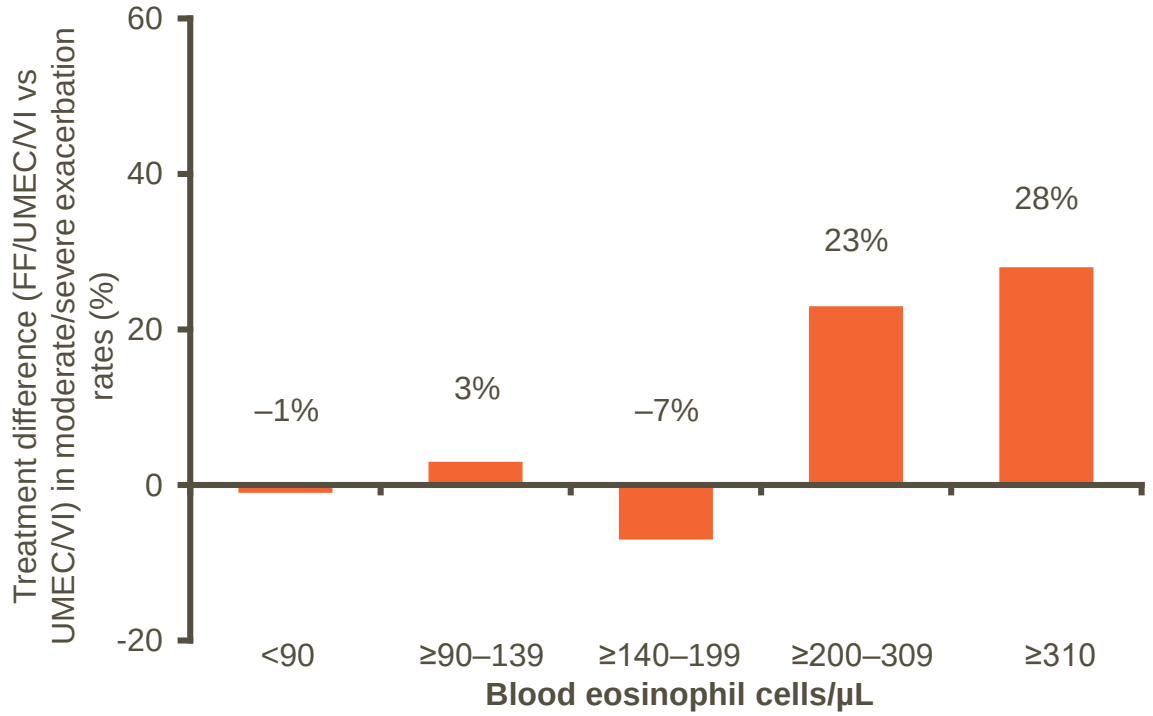
*Trelegy (FF/UMEC/VI) is not funded in New Zealand

Post hoc analysis of IMPACT: Interaction between smoking status and blood eosinophil count in moderate/severe exacerbations – the "ICS Effect"

Former smokers (ICS/LAMA/LABA vs LAMA/LABA)



Current smokers (ICS/LAMA/LABA vs LAMA/LABA)



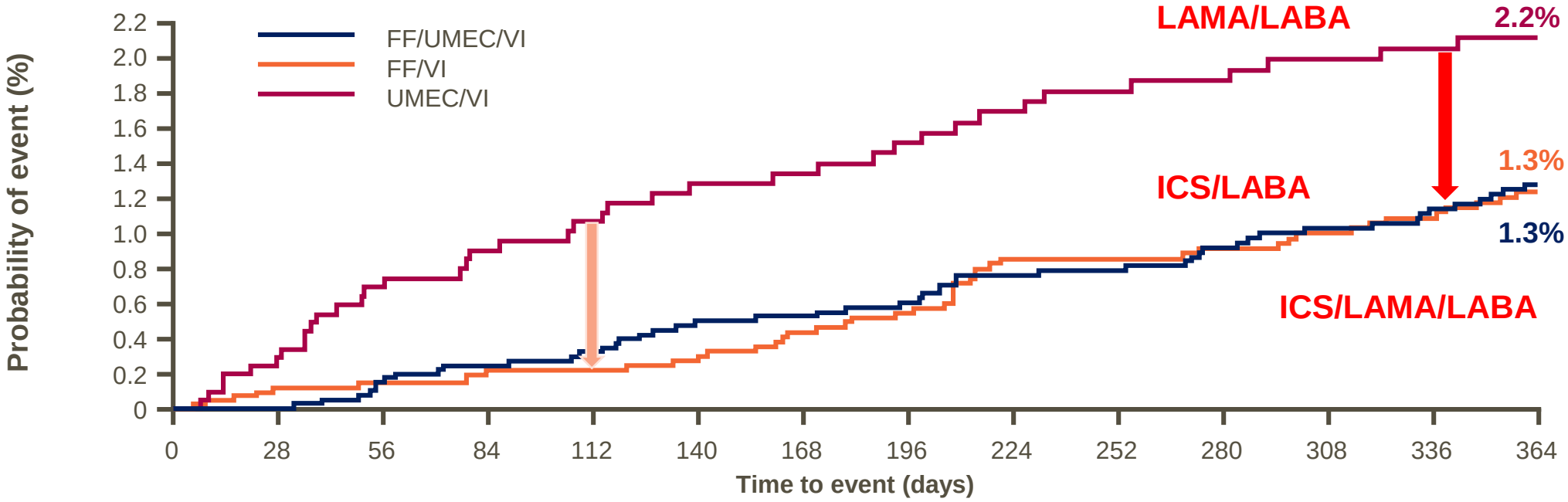
- In former smokers, regardless of blood eosinophil counts, triple therapy show greater clinical benefit than LAMA/LABA in terms of exacerbation reduction and other endpoints
- As the blood eosinophils increase, the benefit further increases[1]

FF, fluticasone furoate; UMEC, umeclidinium; VI, vilanterol.

1. Pascoe S, et al. ERS 2018. #OA2127; 2. Bafadhel M, et al. *Lancet Respir Med*. 2018;6:117–126; 3. Siddiqui SH, et al. *Am J Respir Crit Care Med*. 2015;192:523–525.

*Trelegy (FF/UMEC/VI) is not funded in New Zealand

IMPACT: Reduction in the risk of on-treatment all-cause mortality



No. of subjects at risk

FF/UMEC/VI	4,151	4,082	3,968	3,898	3,838	3,752	3,714	3,690	3,613	3,581	3,545	3,486	3,454	3,346
FF/VI	4,134	3,984	3,798	3,694	3,619	3,496	3,443	3,391	3,291	3,258	3,230	3,182	3,152	3,044
UMEC/VI	2,070	1,993	1,880	1,820	1,769	1,713	1,685	1,656	1,612	1,595	1,578	1,548	1,531	1,485

Relative risk reduction:

FF/UMEC/VI vs UMEC/VI

42.1%

HR 0.58
(95% CI: 0.38, 0.88)
p = 0.011

FF/VI vs UMEC/VI

38.7%

HR 0.61
(95% CI: 0.40, 0.93)
p = 0.022

- **The IMPACT study was not designed to study all-cause mortality as a primary outcome, however, all-cause mortality was a pre-specified endpoint**
- **On-treatment refers to data derived from patients who died whilst on study treatment or within 7 days of stopping their study treatment**
- **In the on- and off-treatment analyses, 6% of patients were censored at 52 weeks, hence further analyses are ongoing**

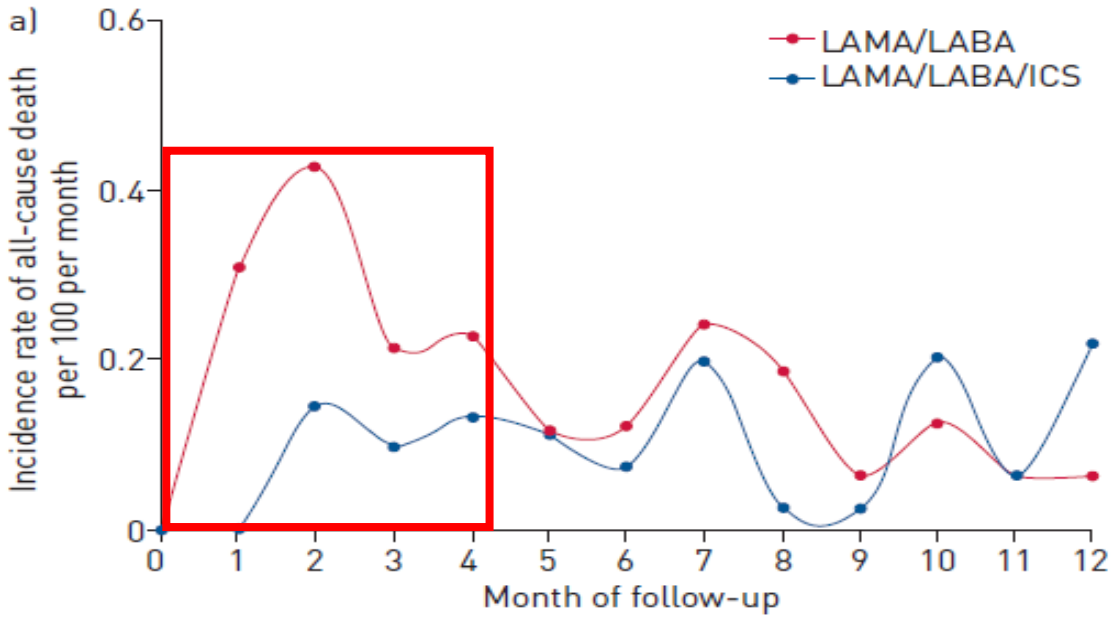
The graphs have been independently created by GSK from the original data. FF, fluticasone furoate; UMEC, umeclidinium; VI, vilanterol.

1. Lipson DA, et al. *N Engl J Med*. 2018;378:1671–1680; 2. GlaxoSmithKline. Data on file. RF/TLY/0096/17(1); 3. Lipson DA, et al. ATS 2018. #A1015.

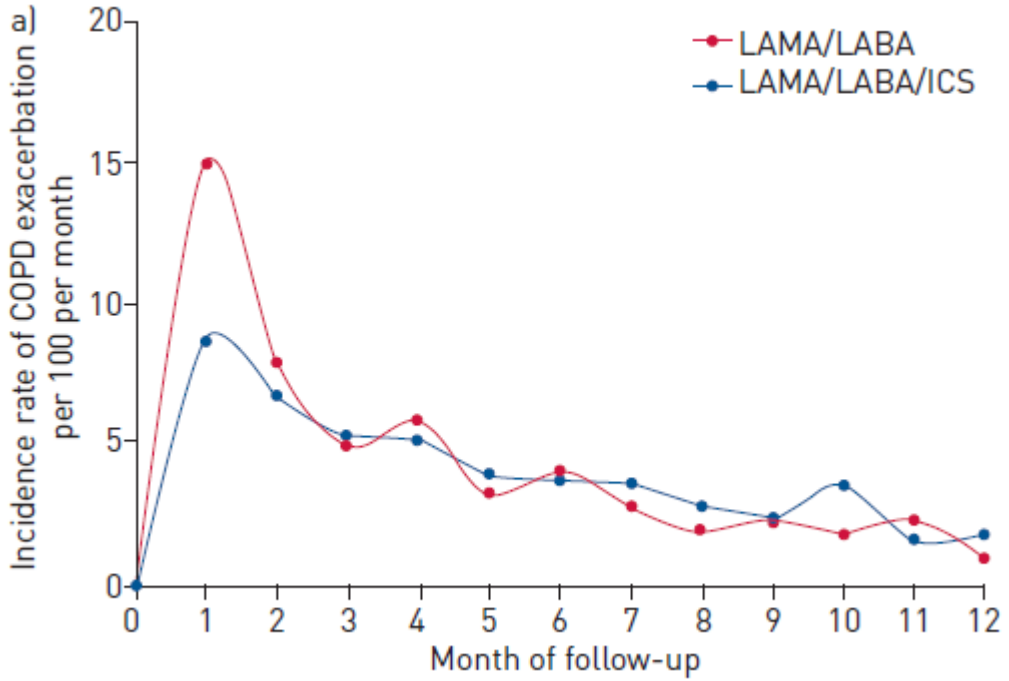
*Trelegy (FF/UMEC/VI) is not funded in New Zealand

IMPACT: Reduction in the risk of on-treatment all-cause mortality

Re-appraisal of IMPACT, Suissa S, et al. Eur Respir J 2018



Excess Deaths – ICS withdrawal effect?



Exacerbations

- **The IMPACT study was not designed to study all-cause mortality as a primary outcome, however, all-cause mortality was a pre-specified endpoint**
- **On-treatment refers to data derived from patients who died whilst on study treatment or within 7 days of stopping their study treatment**
- **In the on- and off-treatment analyses, 6% of patients were censored at 52 weeks, hence further analyses are ongoing**

The graphs have been independently created by GSK from the original data. FF, fluticasone furoate; UMEC, umeclidinium; VI, vilanterol.

1. Lipson DA, et al. *N Engl J Med*. 2018;378:1671–1680; 2. GlaxoSmithKline. Data on file. RF/TLY/0096/17(1); 3. Lipson DA, et al. ATS 2018. #A1015.

*Trelegy (FF/UMEC/VI) is not funded in New Zealand

The IMPACT Study: Baseline demographics[1]

Mostly GOLD Group D

	ICS/LABA/LAMA TRELEGY Ellipta (100/62.5/25 mcg) n=4151	ICS/LABA BREO (100/25 mcg) n=4134	LABA/LAMA ANORO (62.5/25 mcg) n=2070	Overall (N=10355)
Age (y), Mean (SD)	65.3 (8.2)	65.3 (8.3)	65.2 (8.3)	65.3 (8.3)
Sex (% male)	67%	66%	66%	66%
Former smoker n, (%)	2715 (65%)	2711 (66%)	1342 (65%)	6768 (65%)
Post-bronchodilator FEV_1 % predicted, Mean (SD)	45.7 (15.0)	45.5 (14.8)	45.4 (14.7)	45.5 (14.8)
COPD exacerbations in prior year, n (%)				
1 moderate and no severe[2]	1198 (29%)	1242 (30%)	616 (30%)	3056 (30%)
≥2 moderate or ≥1 severe	2953 (71%)	2892 (70%)	1454 (70%)	7299 (70%)
≥1 severe	1087 (26%)	1069 (26%)	515 (25%)	2671 (26%)
Baseline COPD medications,[2] n (%)				
ICS + LABA + LAMA	1581 (38%)	1563 (38%)	826 (40%)	3970 (38%)
ICS + LABA	1220 (29%)	1177 (28%)	576 (28%)	2973 (29%)
LABA + LAMA	361 (9%)	331 (8%)	187 (9%)	879 (8%)
LAMA	288 (7%)	346 (8%)	146 (7%)	780 (8%)

ICS baseline use 67% | 66% | 68%

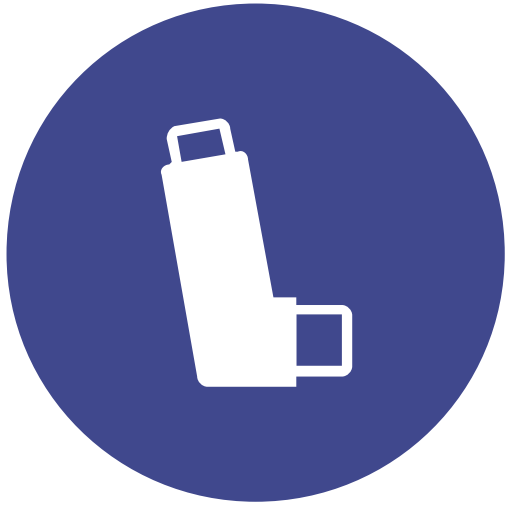
Study ICS use 100% | 100% | 0%

References: 1. Lipson DA, et al. N Engl J Med. 2018;378:1671–1680]; 2. Lipson DA, et al. N Engl J Med. 2018;378:1671–1680 (Supplemental Appendix)

*Trelegy (FF/UMEC/VI) is not funded in New Zealand

What is the importance of device?

Poor inhaler technique is associated with worsening outcomes



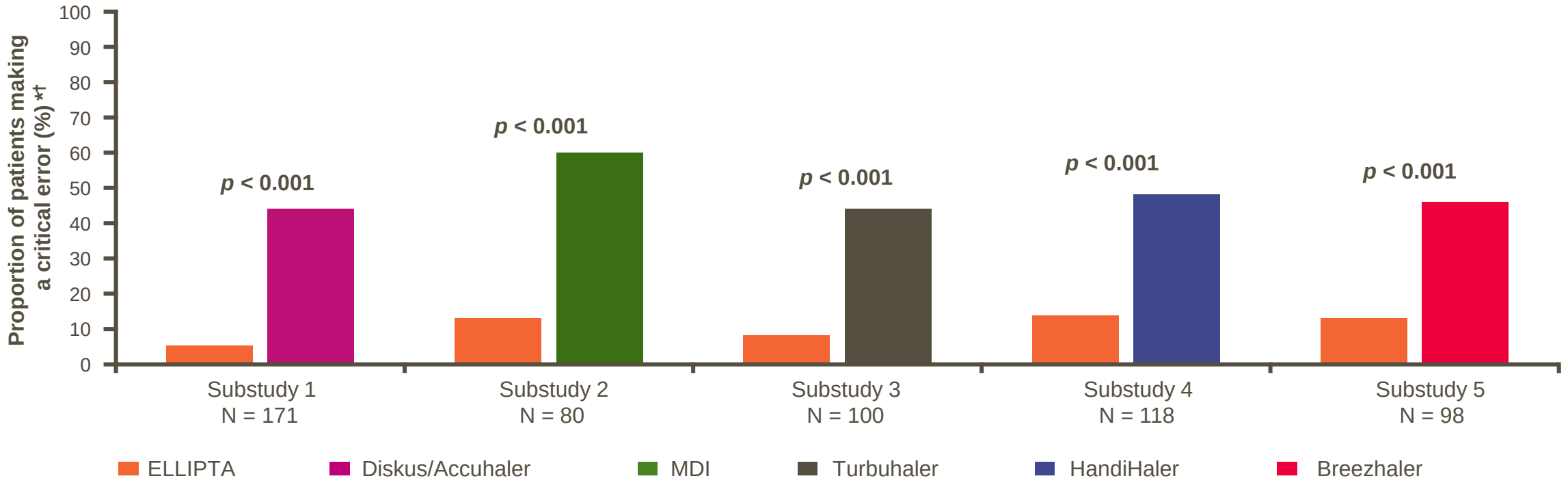
- Large observational study (N = 1,664)
- COPD 52%; asthma 42%
- MDI: n = 843; DPI: n = 1,113
- Inhaler misuse associated with increased risk of:
  - Hospitalisation (OR: 1.47; $p = 0.001$)
  - Emergency room visits (OR: 1.62; $p < 0.001$)
  - Oral corticosteroid use (OR: 1.50; $p < 0.001$)
  - Antimicrobial use (OR: 1.54; $p < 0.001$)

COPD, chronic obstructive pulmonary disease; MDI, metered dose inhaler; OR, odds ratio

Reference: Melani AS, et al. *Respir Med.* 2011;105:930–938.

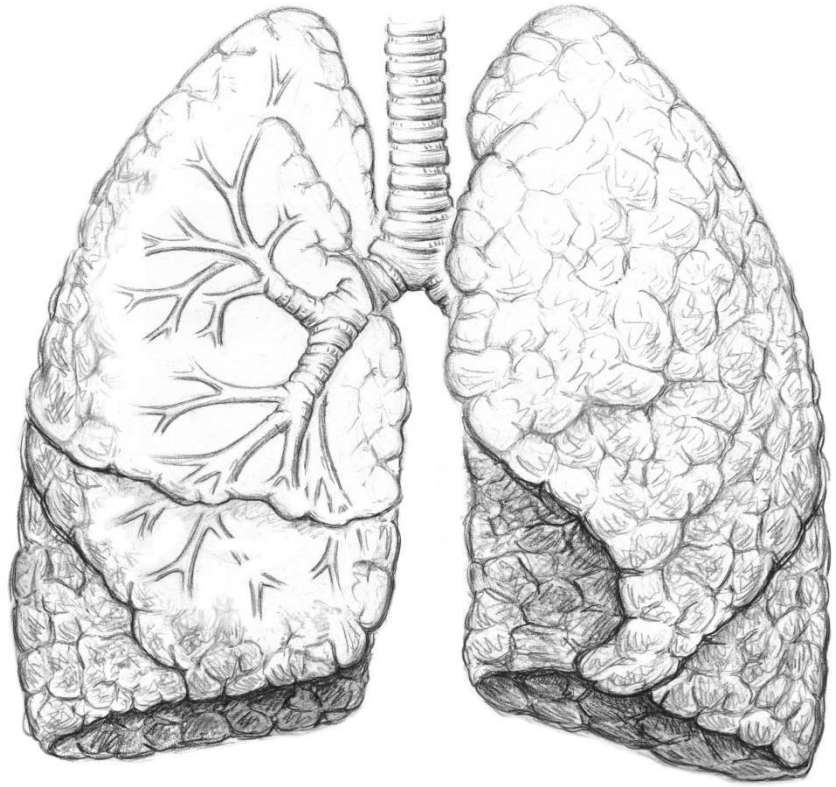
Are there differences across COPD inhalers?

Fewer patients demonstrated critical errors with the use of ELLIPTA vs other commonly used inhalers



* Errors were considered critical if they could have substantially affected dose delivery to the lungs; † In patients with COPD (N = 567).

van der Palen J, et al. *NPJ Prim Care Respir Med*. 2016; 26:16079.



Non-pharmacological treatments for COPD

Non-pharmacological treatments and comorbid diseases

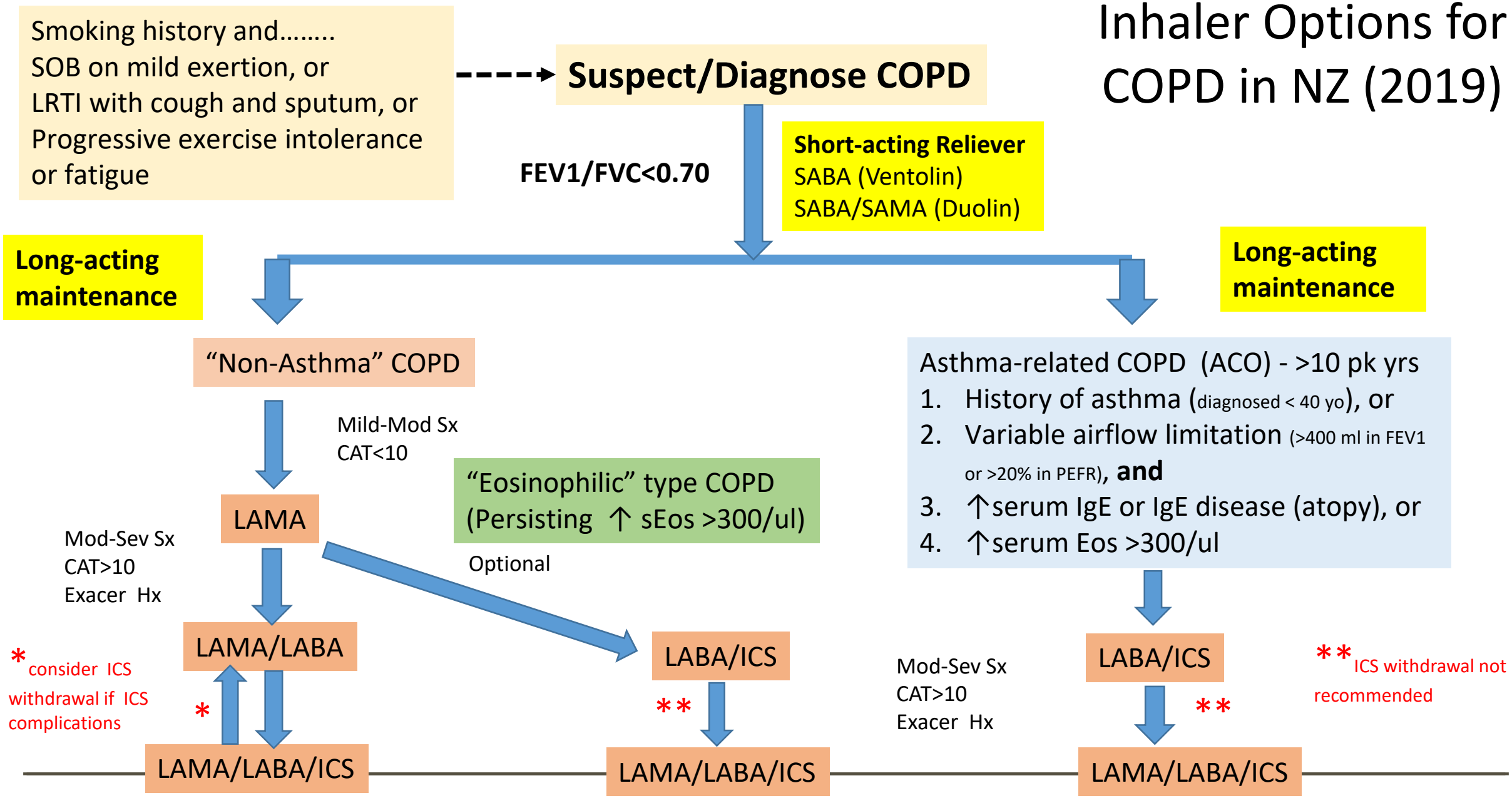
- **Smoking cessation** is key
- **Pulmonary rehabilitation** (referral after hospital discharge or significant exacerbation) – physical conditioning, confidence and inhaler optimisation, initiation of a home-based exercise programme
  Regular exercise: optimise physical "fitness" (anti-inflammatory, improved muscle conditioning, reduce hyperinflation), Physical activity counselling recommended by COPD X. Any exercise is better than none – aim for 10-15 mins/day
- **Vaccinations** – influenza (and pneumococcal in high risk)
- **Diet** high in fruit, vegetables and fibre ("Mediterranean diet"), high protein in cachectic patients
- **Optimise inhaler technique** regularly
- Recognise and **manage comorbid diseases**

  Treat underlying **Coronary Artery Disease** risk factors
  Exacerbations increase risk of cardiovascular deaths, especially in hospitalised patients and within first 30 days after exacerbation. Consider primary prevention in those with other CVS risk factors (smoking, hypertension, diabetes etc).

  Identify **lung cancer** symptomatology early
  Consider imaging in patients with persistent cough or chest pain unresponsive to treatment (CXR and/or CT). Red flags of haemoptysis, weight loss and night sweats.

Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) 2019; COPD-X Summary of Changes V2.52, December 2017; Kunisaki et al. AJRCCM Articles in Press./rccm.201711-2239OC

Inhaler Options for COPD in NZ (2019)



Mandatory Information

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® **(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 .**

Mandatory Information

***Trelegy*® *Ellipta*®** **(fluticasone furoate/umeclidinium bromide/vilanterol trifenatate inhaler 100/62.5/25mcg per inhalation) is a Prescription Medicine. *Trelegy Ellipta* is indicated for the maintenance treatment of adults with moderate to severe chronic obstructive pulmonary disease (COPD) who require treatment with a long-acting muscarinic receptor antagonist (LAMA) + long-acting beta2-receptor agonist (LABA) + inhaled corticosteroid (ICS). *Trelegy Ellipta* is not yet funded in New Zealand. Dosage: one inhalation once daily. After inhalation, rinse mouth with water without swallowing. Contraindications: Patients with severe milk-protein allergy or those who have hypersensitivity to fluticasone furoate, umeclidinium, vilanterol or any excipients. Side Effects: nasopharyngitis, headache, cough, oropharyngeal pain, pneumonia, upper respiratory tract infection, influenza, pharyngitis, rhinitis, arthalgia, back pain, constipation, sinusitis, bronchitis, urinary tract infection, candidiasis of mouth and throat. Warnings and precautions: Treatment in accordance with clinical guidelines. Not indicated for asthma. Treatment re-evaluated if pneumonia occurs. 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. Paradoxical bronchospasm, unstable cardiac disease, hepatic impairment, active or quiescent TB, systemic fungal, bacteria, viral or parasitic infections or ocular herpes simples. Narrow angle glaucoma, urinary retention. Pregnancy: There are insufficient data from the use of fluticasone furoate/umeclidinium/vilanterol in pregnant women. Should be used during pregnancy only if the expected benefit to the mother justifies the potential risk to the fetus. Interactions: Beta-blockers, strong CYP3A4 inhibitors, sympathomimetics, monoamine oxidase inhibitors, tricyclic antidepressants and other long-acting muscarinic antagonists and long-acting ß2-agonists. Before prescribing *Trelegy Ellipta*, please review the Data Sheet at www.medsafe.govt.nz.**

Mandatory Information

***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.**

Mandatory Information

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.**