

CLARITY
CERTAINTY
CONFIDENCE

Revealing proven treatment
pathways in COPD





Faculty/Presenter Disclosure

- Faculty: **Lawrence Homik MD FRCP(C)**
- Relationships with commercial interests:
 - Research/Clinical Trials: **AZ, BI, GSK, Roche**
 - Speakers Bureau/Honoraria: **AZ, BI, Merck, Pfizer, Roche**
 - Advisory Boards: **BI, Roche**



Mitigating Potential Bias

Potential sources of bias identified in the preceding slide has been mitigated as follows:

- Information presented is evidence-based
- Recommendations made are evidence or guideline based rather than personal recommendations of the presenter



Key Message

COPD Definition:

“Chronic obstructive pulmonary disease (COPD) is a respiratory disorder largely caused by smoking, and is characterized by progressive, partially reversible airway obstruction and lung hyperinflation, systemic manifestations, and increasing frequency and severity of exacerbations.”





Learning Objectives

At the end of this program, participants will be able to:

1

The Basics of Dyspnea

2

Recognition and Significance of AECOPD

3

Optimize therapy in High Risk patients

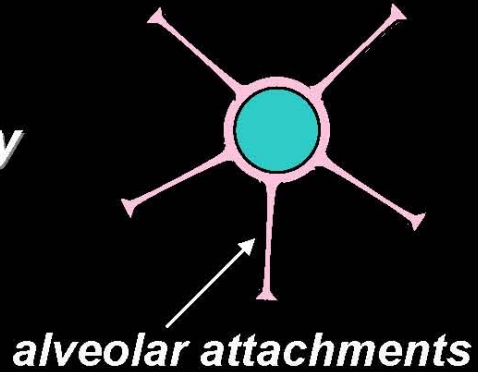
AIR TRAPPING IN COPD

Normal

COPD

Inspiration

*small
airway*

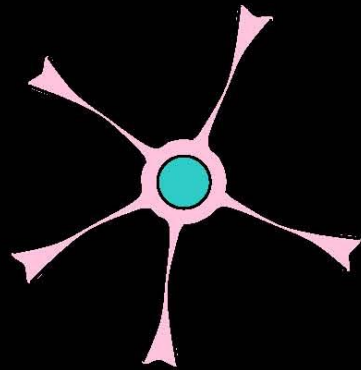


Inflammation

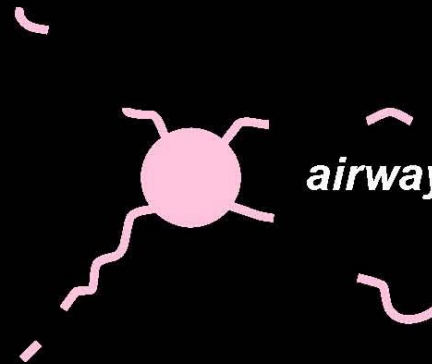


*loss of alveolar attachments
loss of elasticity (emphysema)*

Expiration



airway closure



Air Trapping and Hyperinflation Respiratory Adjustments Over Time

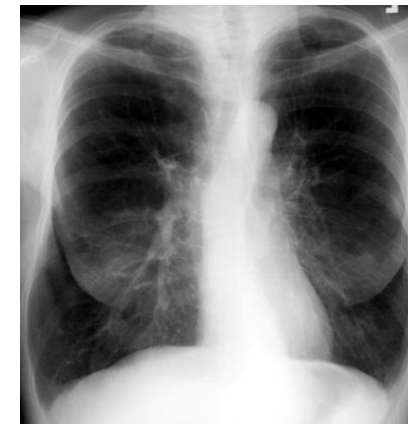
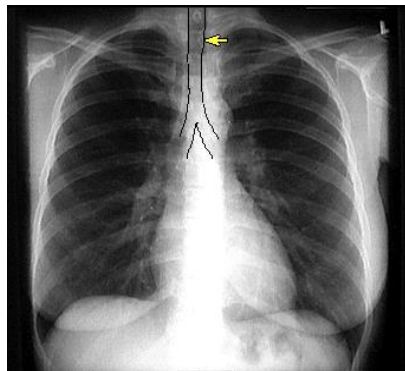


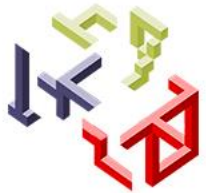
age 40-50

50-55

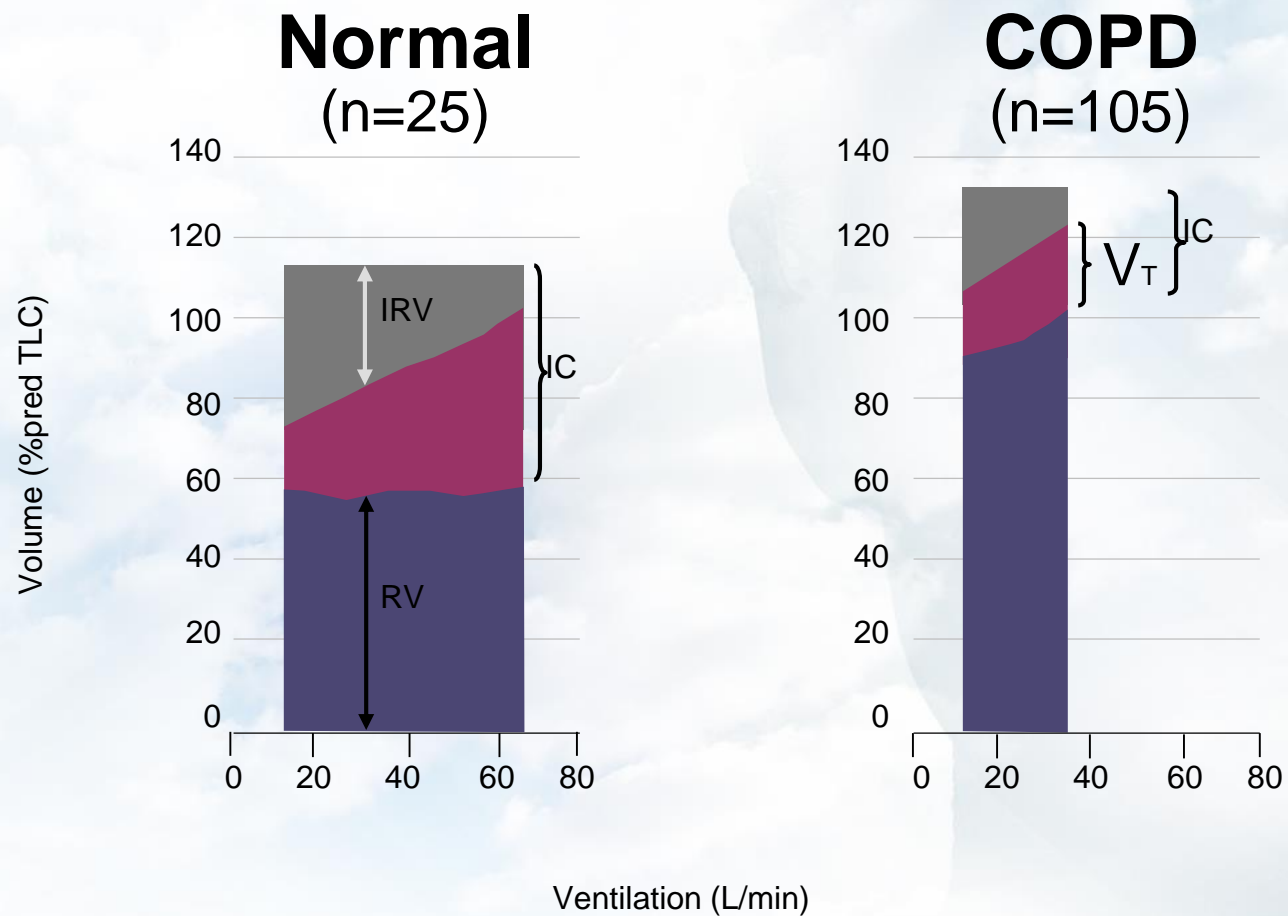
55-60

60-70



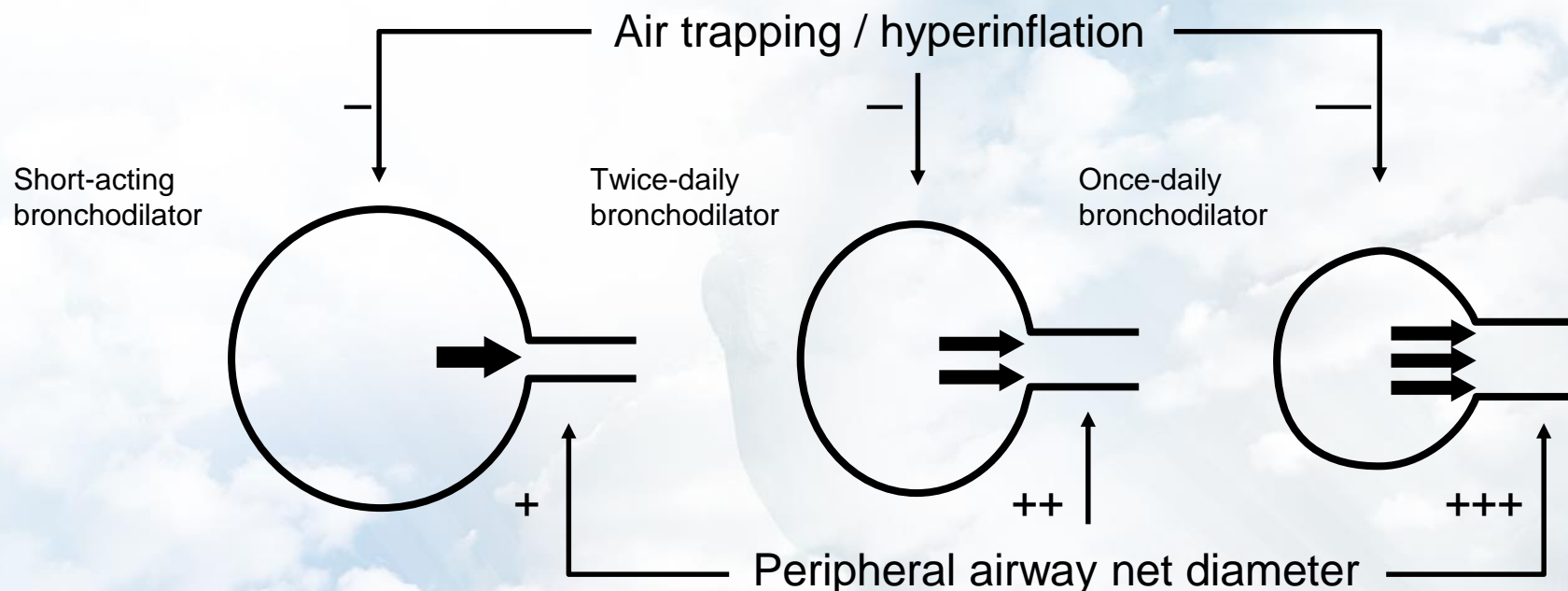


Rationale for Bronchodilator Use in COPD: Improving Dynamic Lung Hyperinflation



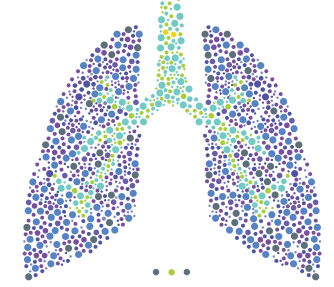


Hypothetical Model of Lung Deflation with Bronchodilator Therapy



Hypothetical model of lung deflation with increased net (area under curve over 24 h) airway calibre. As airway patency over time increases with longer duration of bronchodilator action, emptying of peripheral airways with trapped air is facilitated, thus reducing hyperinflation and improving breathing mechanics ("pharmacological lung volume reduction").

Combination LABA/LAMA reduces rescue medication use vs. monotherapies



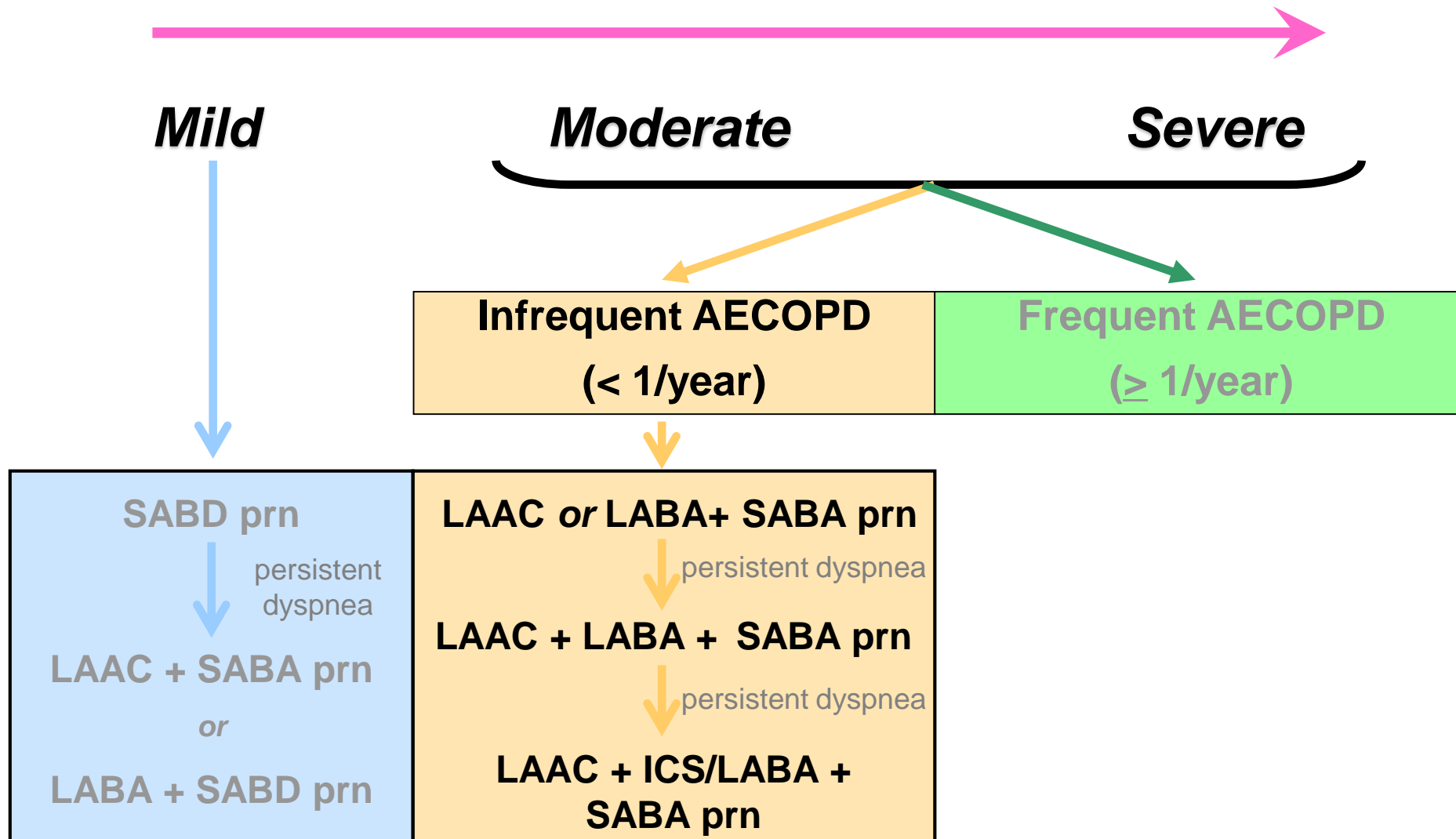
LABA/LAMA FDC	REDUCTION IN DAILY RESCUE MEDICATION WITH FDC VS. MONOTHERAPY	N
Vilanterol/umeclidinium ¹	Umeclidinium ($P < 0.001$) Vilanterol ($P < 0.001$)	2144
Indacaterol/glycopyrronium ²	Indacaterol ($P < 0.05$) Glycopyrronium ($P < 0.001$) Tiotropium ($P < 0.05$)	1532
Olodaterol/tiotropium ³	Olodaterol ($P < 0.05$) Tiotropium ($P < 0.001$)	5162
Formoterol/acclidinium ⁴	Formoterol (NS) Acclidinium ($P < 0.01$)	1692

FDC, fixed-dose combination; LABA, long-acting beta₂ agonist; LAMA, long-acting muscarinic antagonist.

1. Bateman ED, et al. *Eur Respir J* 2013;42:1484-1494.
2. Donohue JF, et al. *Respir Med* 2013;107:1538-1546.
3. CHEST Annual Meeting 2015. Abstract 731A.
4. D'Urzo AD, et al. *Respir Res* 2014;15:123-141.



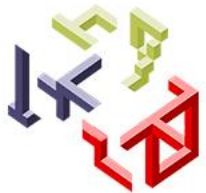
Increasing Disability and Lung Function Impairment





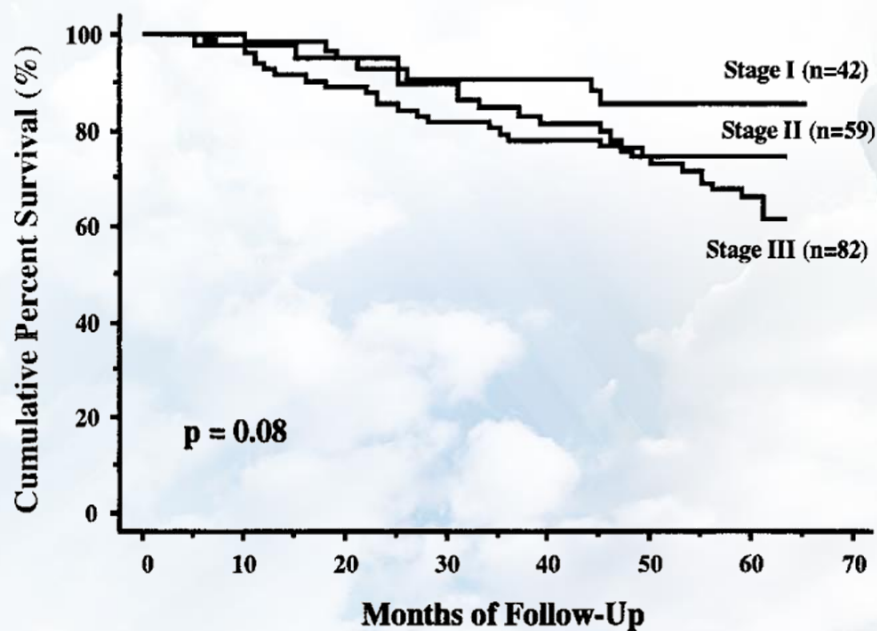
Assessing Disability in COPD – MRC Dyspnea Scale





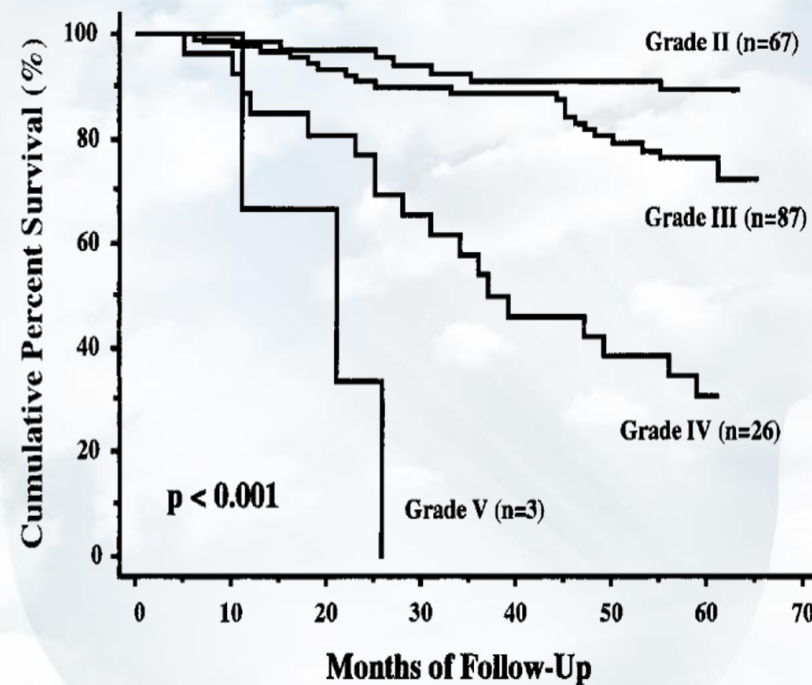
Survival in COPD

FEV₁



5-Year survival according to staging as defined by the ATS Guidelines (% predicted FEV₁)

Symptoms



5-Year survival according to the level of dyspnea as evaluated by the MRC



Exacerbations in COPD Defined

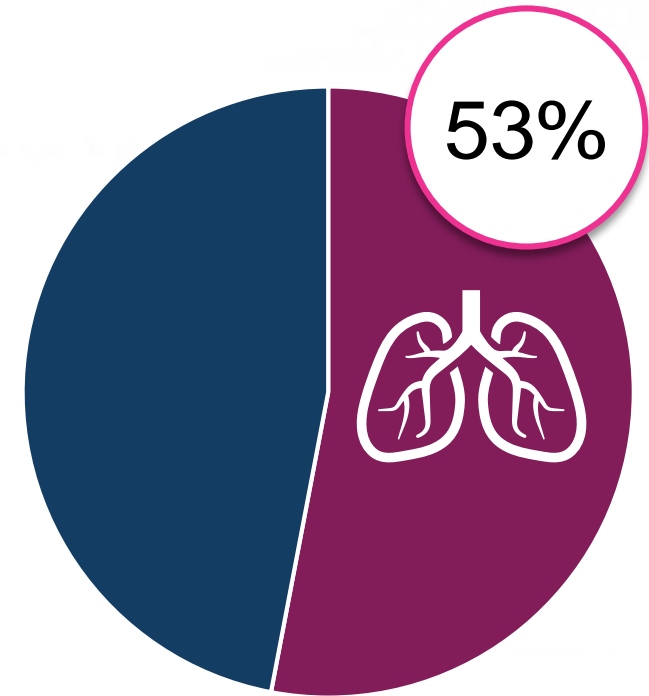
An exacerbation in COPD is defined as an acute worsening of respiratory symptoms (i.e., dyspnea, cough, and sputum) resulting in the need for additional medication^{1,2}

References: 1. Criner GJ, et al. *Chest* 2015;147:894-942; 2. 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>. Accessed July 5, 2017.



Exacerbations in COPD

- Over half (53%) of patients with COPD have had ≥ 1 acute exacerbation, with over half of those reporting that one occurred before they started taking medication^{*1}
- A significant proportion of exacerbations go unnoticed and are not reported^{2,3}

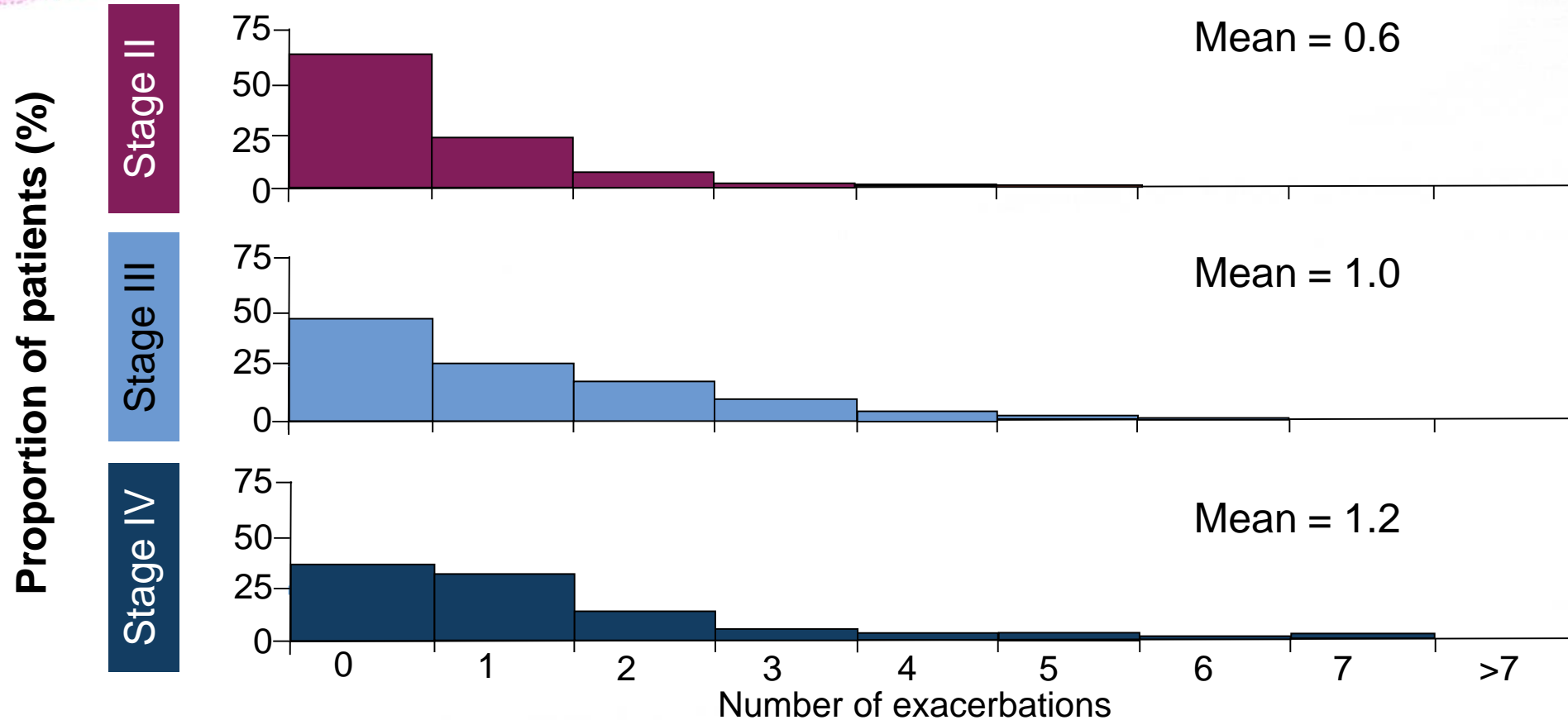


*Base: Patients: Long Survey (n = 231); Physician Patient Charts: General practitioners (n = 400), Respiriologists (n = 100)
Abbreviation: COPD = chronic obstructive pulmonary disease

References: 1. Ipsos Healthcare. 2014; 2. Pavord I, et al. *Int J Chron Obstruct Pulmon Dis* 2016;11:21-30; 3. Calverley PMA. *Proc Am Thorac Soc* 2004;1:121-124.



AECOPD Occurs in Patients With Moderate and Less Severe COPD





Anticipating COPD Exacerbations

- Predicting future exacerbation risk¹⁻⁵:
 - Exacerbation history is the best predictor of having ≥ 2 exacerbations per year (i.e., frequent exacerbations)
 - Other contributing risk factors include:

Smoking

Deteriorating
airflow limitation

Spirometric
severity

Higher blood
eosinophil counts in
patients with a history
of exacerbations

Prior or current
history of several
comorbidities

Depression

Hospitalization
within the past year

QUESTION 1:

What are the consequences of not identifying and treating patients with AECOPD?





Exacerbations and Mortality Rates

Exacerbations are a major cause of mortality, morbidity, reduced QoL and increased healthcare costs¹⁻³

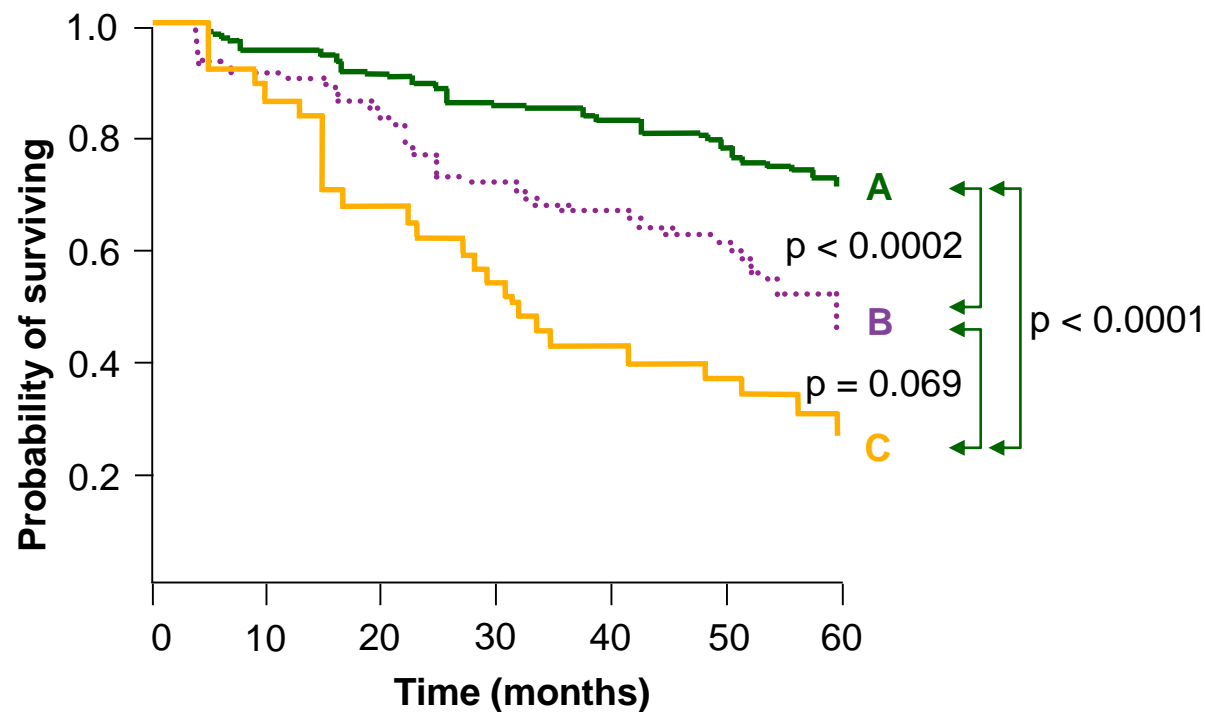
- One-third of patients with COPD are frequent exacerbators^{4,5*}
- As frequency of severe exacerbations increases, mortality increases⁶
- Each new severe exacerbation needing hospitalization^{6,7}:
 - Worsens the disease course
 - Increases risk of subsequent exacerbations
 - Increases risk of death

References: 1. Fabbri LM, et al. *Am J Respir Crit Care Med* 2006;173:1056-1065; 2. Flattet Y, et al. *Int J Chron Obstruct Pulmon Dis* 2017;12:467-475; 3. Larsson K, et al. *J Intern Med* 2013;273:584-594; 4. Kaplan AG. *Int J Chron Obstruct Pulmon Dis* 2015;10:2535-2548; 5. 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>. Accessed July 5, 2017; 6. Soler-Cataluna JJ, et al. *Thorax* 2005;60:925-931; 7. Suissa S, et al. *Thorax* 2012;67:957-963

*Defined as ≥ 2 exacerbations per year

Abbreviations: COPD = chronic obstructive pulmonary disease; QoL = quality of life

Higher mortality associated with more frequent severe acute AECOPD*



Group A

Patients with no acute exacerbations of COPD

Group B

Patients with 1–2 acute exacerbations of COPD requiring hospital management

Group C

Patients with ≥ 3 acute exacerbations of COPD requiring hospital management

Even 1–2 severe COPD exacerbations are associated with increased mortality (group B)

*Defined as any sustained increase in symptomatology compared with the baseline situation



Economic Burden of Exacerbations

- Unscheduled visits to doctors and hospitalizations for exacerbations:
 - >60% of COPD direct medical costs¹
- In 2007, the estimated cost of COPD exacerbations in Canada²:

Exacerbation	Average cost per exacerbation (\$)	Annual cost (\$ million)
Moderate*	641	163
Severe†	9,557	573

- Estimates for 2015²:
 - COPD-related hospitalizations would be twice that of 2007
 - Cost of severe exacerbations will rise to over \$1 billion per year

*Moderate: Visit to an outpatient facility, including ER, but not hospitalized, and medication change; †Severe: hospitalization
Abbreviations: COPD = chronic obstructive pulmonary disease; ER = emergency room

References: 1. Najafzadeh M, et al. *PLoS ONE* 2012;7:e46746;
2. Mittmann N, et al. *Respir Med* 2008;102:413-421.

QUESTION 2:

Are you actively identifying and assessing patients with exacerbations?





At Each Visit Ask Your Patients...

Y **N** — Have you experienced a chest cold or flare-up since we last met?

Y **N** — Were you given any medications for your chest cold or flare-up?

Y **N** — Have you taken any antibiotics for your chest since we last met?




Y **N** — Have you been to the emergency department or a walk-in clinic for any reason?




Y **N** — Are you able to do the same physical activities since your last visit?



Educate Patients to Recognize Exacerbations

- Educating patients to promptly recognize AECOPD is key^{1,2}

My actions	Stay Well 	Take Action 	Call For Help URGENT
I have sputum.	My usual sputum colour is: _____	Changes in my sputum, for at least 2 days. <input type="checkbox"/> Yes <input type="checkbox"/> No	My symptoms are not better after taking my flare-up medicine for 48 hours.
I feel short of breath.	When I do this: _____ _____	More short of breath than usual for at least 2 days. <input type="checkbox"/> Yes <input type="checkbox"/> No	I am very short of breath, nervous, confused and/or drowsy, and/or I have chest pain. 

My actions	Stay Well 	Take Action 	Call For Help
I use my daily puffers as directed.		If I checked 'Yes' to one or both of the above, I use my prescriptions for COPD flare-ups.	I will call my support contact and/or see my doctor and/or go to the nearest emergency department.
If I am on oxygen, I use _____L/min.		I use my daily puffers as usual. If I am more short of breath than usual, I will take ____ puffs of _____ up to a maximum of ____ times per day.	I will dial 911. 

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Produced in collaboration with the *COPD & Asthma Network of Alberta (CANA)*. The *Canadian Thoracic Society (CTS)* acknowledges the past contributions of *Living well with COPD* and the *Family Physician Airways Group of Canada*.



Abbreviations: AECOPD = acute exacerbations of COPD; COPD = chronic obstructive pulmonary disease; CTS = Canadian Thoracic Society; QoL = quality of life

I use my breathing and relaxation methods as taught to me. I pace myself to save energy.

If I am on oxygen, I will increase it from ____ L/min to ____ L/min.

Important information: I will tell my doctor, respiratory educator, or case manager **within 2 days** if I had to use any of my flare-up prescriptions. I will also make follow-up appointments to review my COPD Action Plan twice a year.

References: 1. Williams V, et al. *Prim Care Respir Med* 2014;24:14062; 2. O'Donnell DE, et al. *Can Respir J* 2008;15(SupplA):1A-8A; 3. Wilkinson TMA, et al. *AM J Respir Crit Care Med* 2004;169:1298-1303; 4. Canadian Thoracic Society. Available at: http://www.copdactionplan.com/1408_THOR_ActionPlan_v2.pdf. Accessed July 11, 2017; 5. British Columbia Ministry of Health. COPD Flare-Up Action Plan. Available at: http://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/copd_flare-up_action_plan.pdf. Accessed May 31, 2017; 6. Living Well With COPD. Available at: http://www.livingwellwithcopd.com/DATA/DOCUMENT/61_en-v-integrating-a-plan-of-action-into-your-life.pdf. Accessed June 12, 2017.

QUESTION 3:

Are your patients with COPD who are experiencing or at risk of AECOPD getting optimal therapy?





Are You Checking Your Patients' Inhaler Technique?

- Patient education about COPD should include effective inhaler technique¹
- Check inhaler technique at initiation and assess regularly²
 - Engage and work with Certified Respiratory Educators
- Prior to changing treatments, ensure current medications are being used optimally²

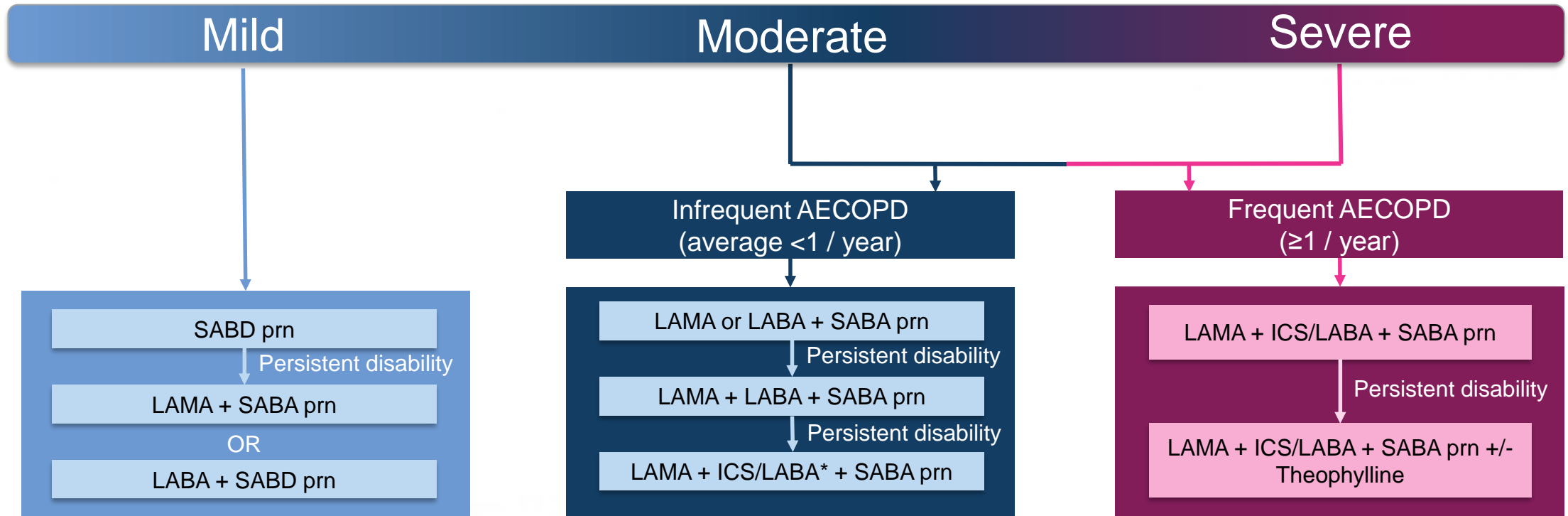
Ask patients to demonstrate
inhaler technique²

Ask patients
about adherence²



Intensifying Therapy

- For patients with moderate COPD on single or dual therapy with further exacerbations (≥ 1 per year), progress to LAMA + ICS/LABA



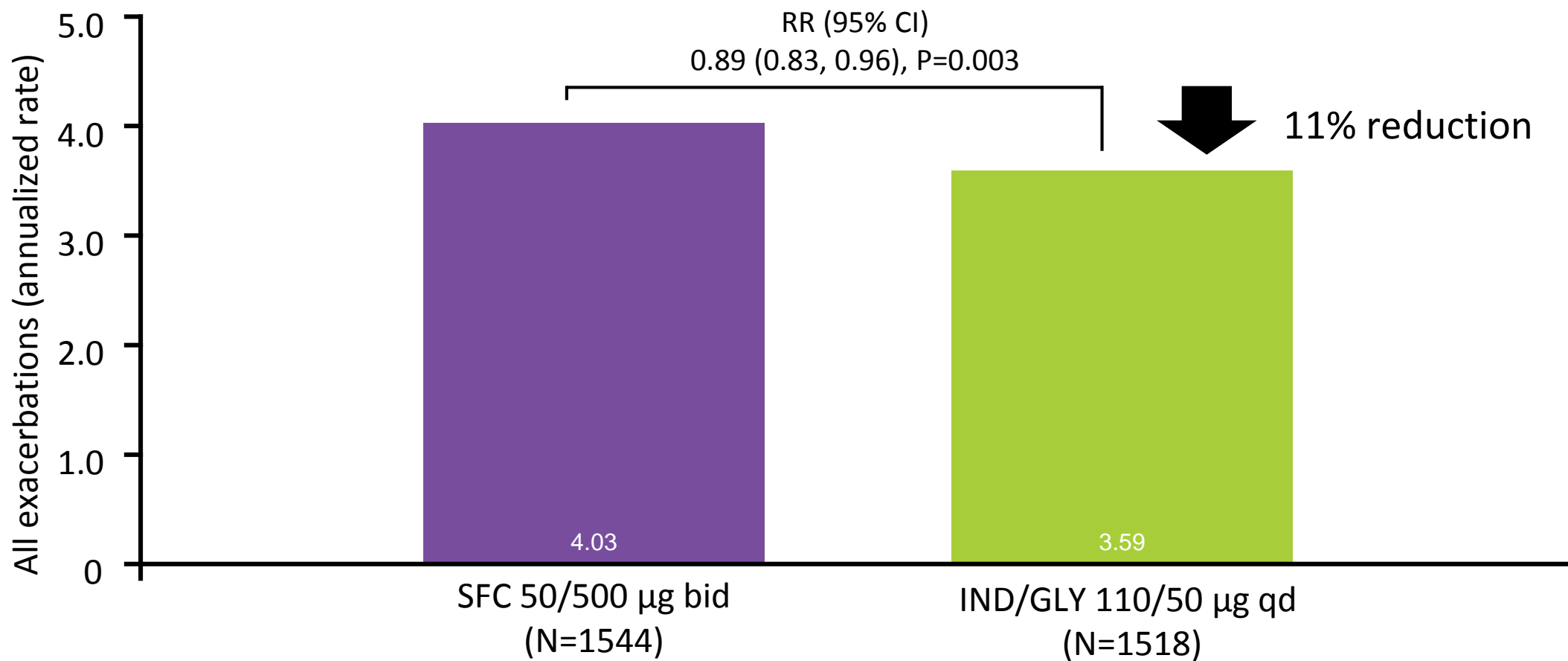
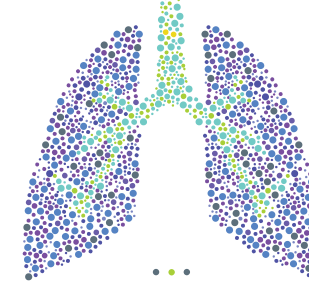
*Refers to the lower dose ICS/LABA

Note: Updated Canadian guidelines are expected in October 2017.

Abbreviations: AECOPD = acute exacerbation of chronic obstructive pulmonary disease; ICS = inhaled corticosteroid; LAAC = long-acting anticholinergic = LAMA; LABA = long-acting beta2-agonist; LAMA = long-acting muscarinic antagonist; prn = when necessary; SABA = short-acting beta2-agonist; SABD = short-acting bronchodilator.

Reference: 1. Adapted from O'Donnell DE, et al. *Can Respir J.* 2008;15:1A-8A under the terms of the Creative Commons Attribution License.

FLAME Study: LABA/LAMA showed superiority in reducing annual rate of all exacerbations vs. SFC



bid, twice daily; CI, confidence interval; GLY, glycopyrronium; IND, indacaterol; qd, once daily; RR, rate ratio; SFC, salmeterol/fluticasone propionate combination.
Wedzicha JA, et al. *N Engl J Med* 2016;374:2222-34.



Benefits of Triple Therapy vs. Single Therapy

- LAMA + ICS/LABA vs. LAMA alone:

RCT	T + ICS/LABA vs. T + placebo (n)	Reduction in exacerbation rate with T + ICS/LABA vs. T + placebo (%)	p value
CLIMB (Welte et al. ¹)	BUD/FOR 320/9 µg bid via a DPI (329 / 331)	62	< 0.001
NCT01397890 (Lee et al. ²)	BUD/FOR 320/9 µg bid via a DPI (287 / 290)	40.7	0.0032
TRINITY (Vestbo et al. ³)	BDP/FOR 200/12 bid via pMDI (538 / 1,075)	21	0.0095
OPTIMAL (Aaron et al. ⁴)	FP/SAL 500/50 µg bid via a DPI (145 / 156)	15	NS

- In a meta-analysis of 4 trials comparing T + FP/SAL to T alone, the proportion of patients who experienced ≥1 exacerbation was significantly lower in the T + FP/SAL group (OR = 0.73; p = 0.03)⁵

Abbreviations: bid = twice-daily; BDP = beclometasone dipropionate; BUD = budesonide; DPI = dry powder inhaler; FOR = formoterol; FP/SAL = fluticasone/salmeterol; ICS/LABA = inhaled corticosteroid/long-acting β₂-agonist; LAMA = long-acting muscarinic agent; NS = not significant vs control arm; pMDI = pressurized metered-dose inhaler; RCT = randomized controlled trial; T = tiotropium

References: 1. Welte T, et al. *Am J Respir Crit Care Med* 2009;180:741–750; 2. Lee S-D, et al. *Respirology* 2016;21:119-127; 3. Vestbo J, et al. *Lancet* 2017;389:1919-1929; 4. Aaron S, et al. *Ann Intern Med* 2007;146:545–555; 5. Liu Y, et al. *Eur J Intern Med* 2014;25:491-495.



Benefits of Triple Therapy Over Dual Therapy

- LAMA + ICS/LABA vs. ICS/LABA:
 - Decreased exacerbation risk^{1,2}; improved lung function and HRQoL^{1,2}

Study	Treatment	Exacerbation Results
TRILOGY ¹	BDP/FOR/GB (single inhaler) twice daily vs. BDP/FOR bid	23% reduction in exacerbations (RR = 0.77; $p = 0.005$)
FULFIL ²	FF/VI/UMEC (single inhaler) once daily vs. BUD/FOR bid	35% reduction in exacerbations ($p = 0.002$)

Abbreviations: BDP = beclometasone dipropionate; bid = twice daily; BUD = budesonide; FF = fluticasone furoate; FOR = formoterol fumarate; GB = glycopyrronium bromide; ICS: inhaled corticosteroid; LABA: long-acting beta2-agonist; LAMA = long-acting muscarinic antagonist; UMEC = umeclidinium; RR = rate ratio; VI = vilanterol

References: 1. Singh D, et al. *Lancet* 2016;388:963-973; 2. Lipson DA, et al. *Am J Respir Crit Care Med* 2017;Apr 4. doi: 10.1164/rccm.201703-0449OC.

QUESTION 4:

Is there a right time to take patients with COPD on triple therapy off the ICS?





WISDOM Trial¹

- First study to investigate the effect of stepwise withdrawal of ICS on exacerbation risk in patients with severe-to-very-severe COPD
- Results:
 - No change in risk of moderate or severe exacerbations
 - Greater decrease in FEV₁ at final step of ICS withdrawal and at week 52
 - Minor changes in health status
 - No change in dyspnea

Further studies required before the concept can be uniformly supported



Considerations for ICS Withdrawal

Consider Specialist Referral

GOLD 2017: New option to potentially withdraw ICS (i.e., LAMA + ICS/LABA to LAMA/LABA)¹

When should you refer to a specialist?

- Potential risks associated with withdrawal
- Concern about worsening lung function

Why discontinue ICS (i.e., Cost , Side effects)

How do you explain the benefits and risks to your patients?

How long should you wait before discontinuing ICS?

If you do discontinue an ICS, what would the appropriate follow-up regime be, and when do you re-instate the ICS?

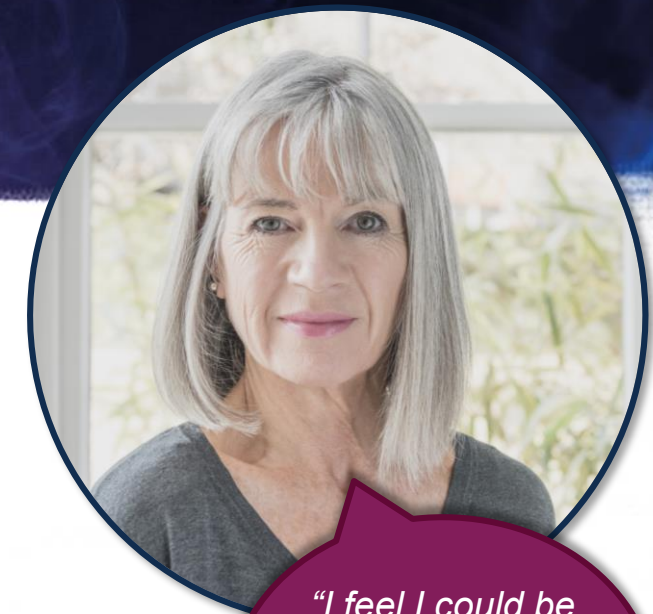
THE PATIENT'S COPD REALITY

MEET CLAIRE





Meet Claire



- 60-year-old female
- Diagnosed with COPD 3 years ago

FEV₁ 58% predicted;
MRC 3; CAT 12

Non-smoker
x 4 years

No other significant
comorbidities

Currently on a LAMA/LABA
with SABA prn (~2x/week)

- Good inhaler technique and adherent with prescribed medication
- No influenza vaccination last year; never received pneumococcal vaccination
- No history of hospitalizations for COPD
- Physical examination
 - No cyanosis or clubbing, normal vitals with SpO₂ 96%
 - Breath sounds are reduced with no focal signs; no findings of heart failure
- Two bad ‘chest colds’ this past year
 - Antibiotic therapy for both; prednisone for one

“I feel I could be much worse, and I am happy that I do not need to be on oxygen.”

Claire needs her therapy optimized to prevent future exacerbations

**WHAT IS YOUR CLINICAL
ASSESSMENT OF
CLAIRE'S COPD?**

**IS CLAIRE'S TREATMENT
OPTIMAL?**





Assessment

Moderate obstruction

Reported history of ongoing and frequent exacerbations despite LABA/LAMA inhaled therapy

Inadequate vaccination status

Lack of regular aerobic physical activity and/or enrollment in pulmonary rehabilitation

Current clinical presentation is not 'acceptable' and requires further optimization

While the patient is happy that she is not worse, we can genuinely help her be better

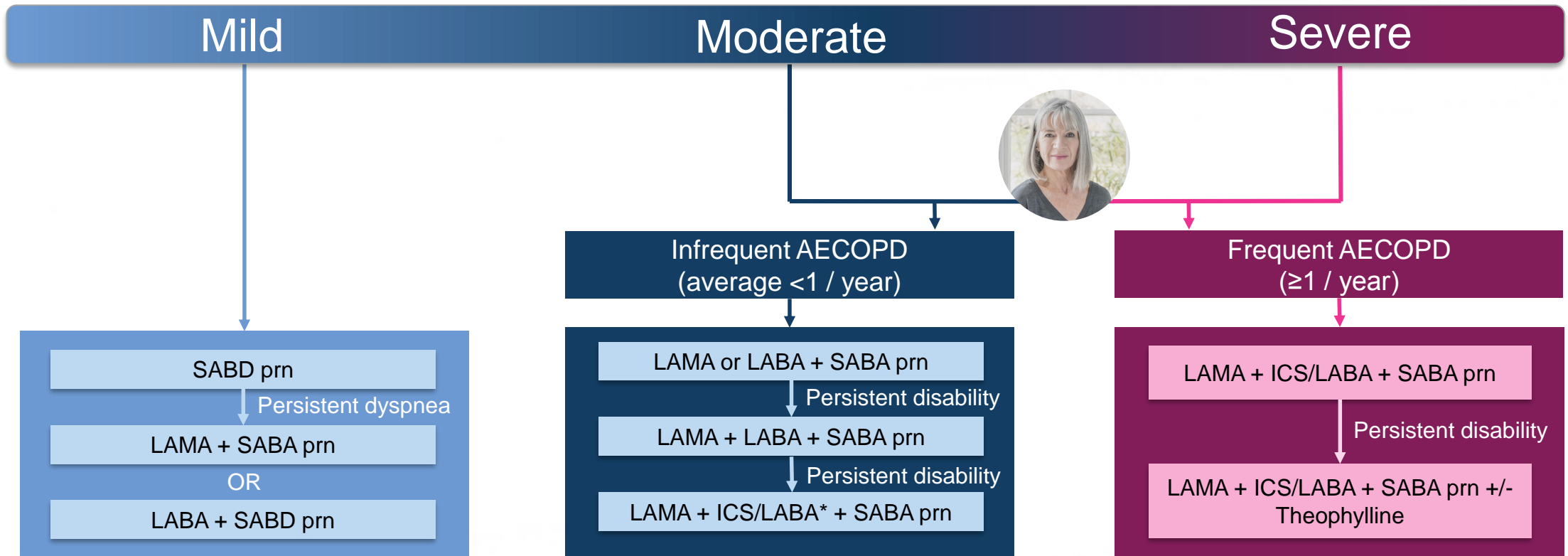
An important aspect of care is to raise patient's (and many clinician's) expectations and align them with current reality

We now have very effective therapies that are proven to reduce symptoms (shortness of breath and activity limitation) and prevent AECOPD¹



Assessment

- What are the important aspects of this patient's presentation?
- Despite current therapy, Claire is still experiencing AECOPD



*Refers to lower dose ICS/LABA

Abbreviations: AECOPD = acute exacerbation of chronic obstructive pulmonary disease; ICS = inhaled corticosteroid; LAAC = long-acting anticholinergic; LABA = long-acting beta2-agonist; LAMA = long-acting muscarinic antagonist; prn = when necessary; SABA = short-acting beta2-agonist; SABD = short-acting bronchodilator.

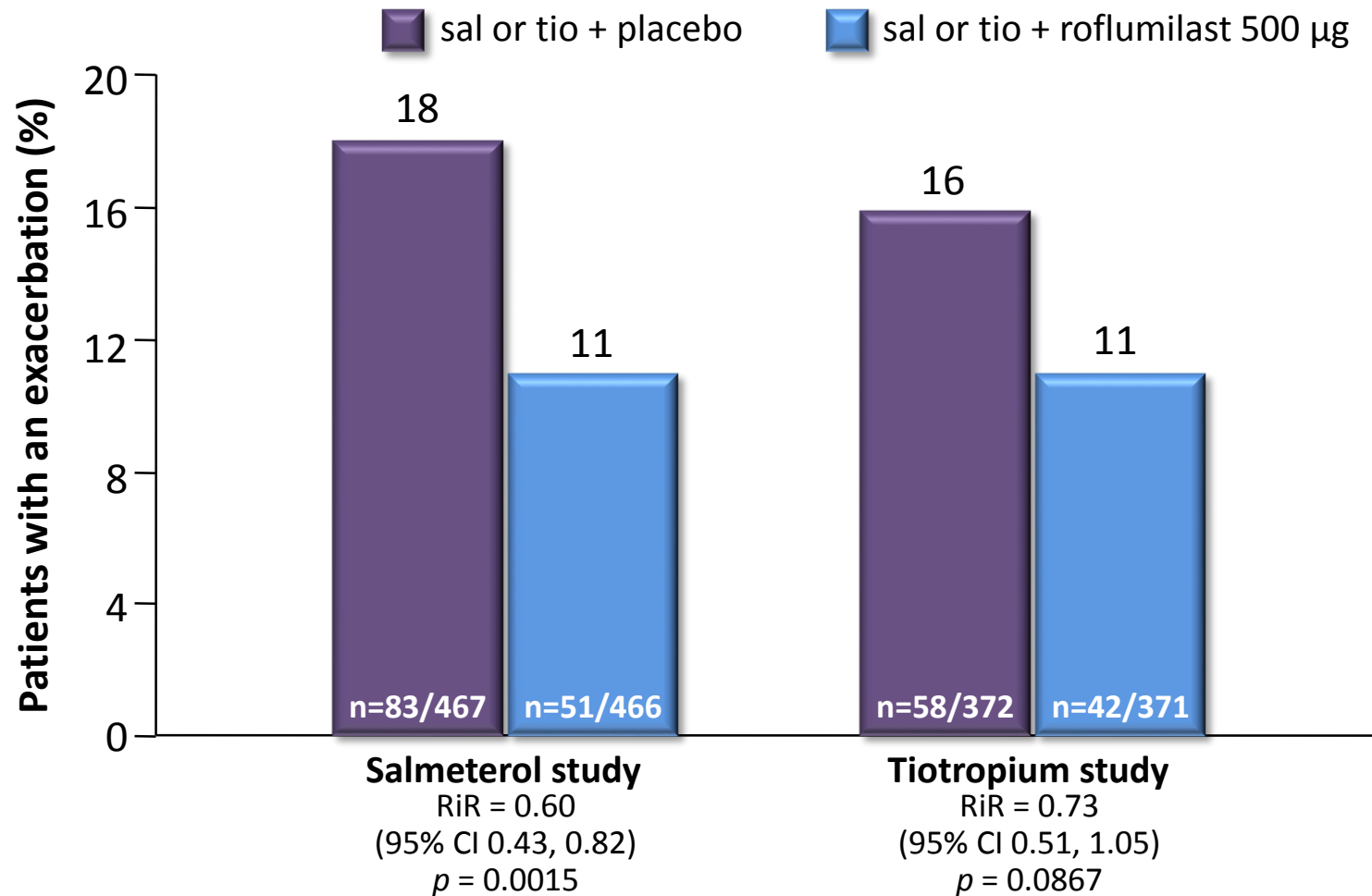
Reference: 1. Adapted from O'Donnell DE, et al. *Can Respir J*. 2008;15:1A-8A under the terms of the Creative Commons Attribution License.



Optimizing Pharmacotherapy

- Augment/optimize therapy to a LAMA + ICS/LABA
- Influenza and pneumococcal vaccinations
- Depending on the response, consider adding other oral pharmacologic therapies

Proportion of Patients with a Moderate or Severe Exacerbation



Exacerbation rates were based on a Poisson regression model.
Risk ratios (RiR) were based on a log binomial regression model.
Fabbri LM, et al. *Lancet*. 2009 Aug 29;374(9691):695-703.

Azithromycin for Prevention of Exacerbations of COPD

Richard K. Albert, M.D., John Connett, Ph.D.

The New England Journal of Medicine

august 25, 2011 vol. 365 no. 8

Warawut Suttison, GP

Results

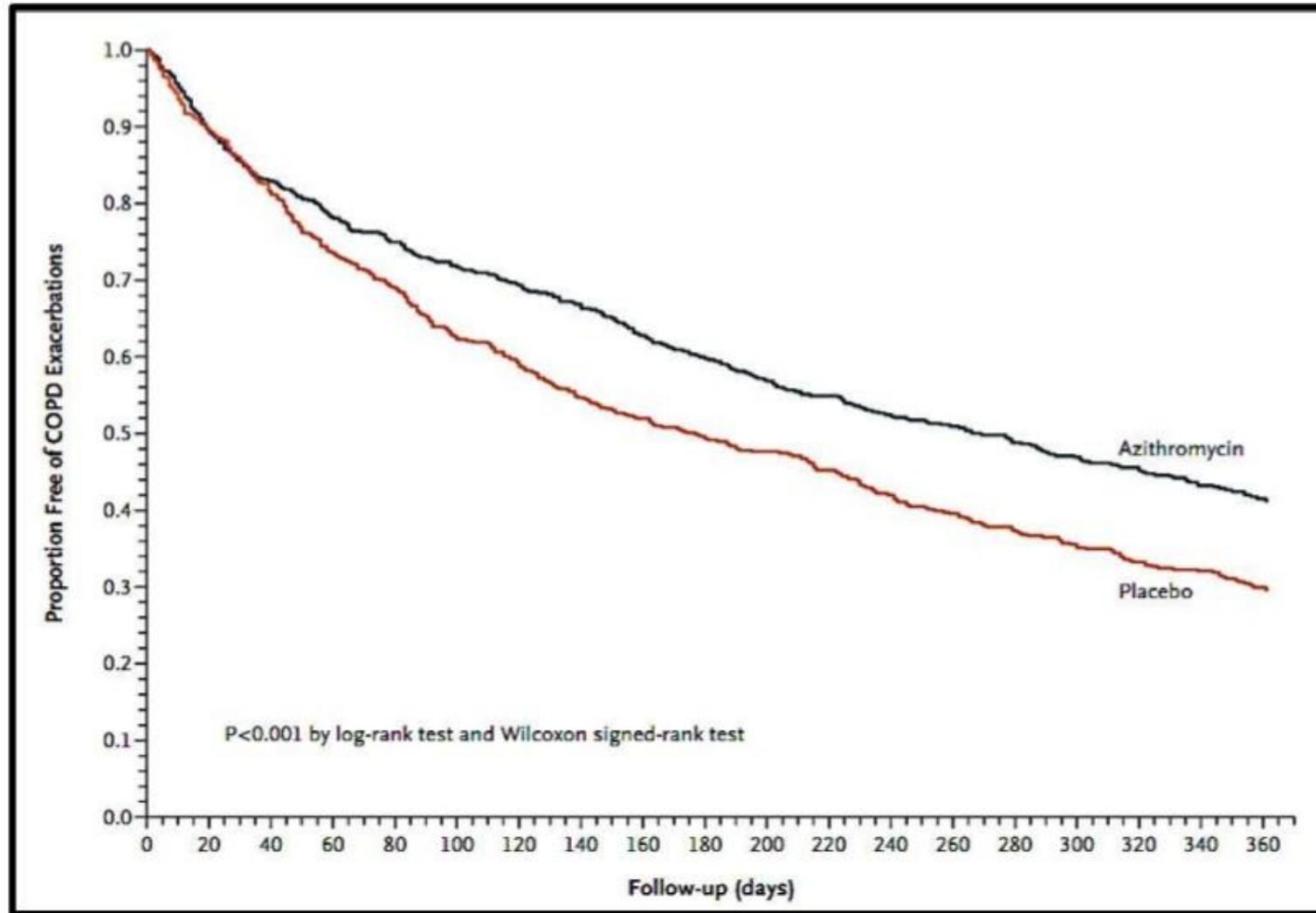


Figure 2. Proportion of Participants Free from Acute Exacerbations of (COPD) for 1 Year, According to Study Group.



Non Pharmacotherapy

- Don't forget **Pulmonary Rehabilitation**



Pulmonary Rehabilitation

- A review of 31 randomized controlled trials found statistically significant improvements for all outcomes
 - - Exercise capacity
 - -Functional capacity
 - -Quality of life
 - -Reduced exacerbations/Hospitalization

KEY TAKEAWAYS



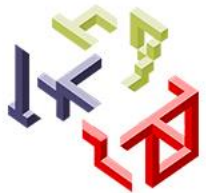


Key Takeaways

We *can* do better for our patients with AECOPD

- To optimize management and outcomes:
 - Ask patients a few important questions at each visit
 - Educate patients to recognize and report worsening symptoms consistent with an exacerbation
 - For patients experiencing exacerbations while on LAMA/LABA, intensify pharmacologic therapy to LAMA + ICS/LABA
 - Utilize vaccinations, active smoking cessation support, pulmonary rehabilitation, and work with a Certified Respiratory Educator
 - Refer to a respirologist, if appropriate
 - Raise patient (and clinician!) expectations





Useful Tools and Resources

BREATHWORKS™

Help for People with COPD

COPD Helpline 1-866-717-COPD (2673)

www.lung.ca

RESPTrec®
RESPIRATORY TRAINING & EDUCATOR COURSE

www.resptrec.org

Living Well with COPD™

Chronic Obstructive Pulmonary Disease

A plan of action for life

www.livingwellwithcopd.com