



PNEUMOLOGIA 2018
MILANO, 14 – 16 GIUGNO 2018
CENTRO CONGRESSI PALAZZO DELLE STELLINE



UNIVERSITY OF
GOTHENBURG



Nuovi farmaci in sviluppo per la BPCO

Leonardo M. Fabbri, MD, FERS

Professor of Respiratory and Internal Medicine, University of Modena and Reggio Emilia, (-2016)
Eminent Scholar of Respiratory and Internal Medicine, University of Ferrara
Visiting Professor of Respiratory and Internal Medicine, COPD Center, University of Gothenburg

NUOVI FARMACI IN SVILUPPO PER LA BPCO

Leonardo M. Fabbri, MD, FERS

The changes in the definition and assessement of severity of COPD

The recent studies of efficacy and safety of triple therapy in a single inhaler is likely to introduce major changes in the pharmacologic management of COPD

Anti IL-5 Moa, new experimental agents

TREAT THE PATIENT WITH COPD NOT JUST COPD

NUOVI FARMACI IN SVILUPPO PER LA BPCO

Leonardo M. Fabbri, MD, FERS

The changes in the definition and assessement of severity of COPD

The recent studies of efficacy and safety of triple therapy in a single inhaler is likely to introduce major changes in the pharmacologic management of COPD

Anti IL-5 Moa, new experimental agents

TREAT THE PATIENT WITH COPD NOT JUST COPD



COPD Definition

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



COPD

DEFINITION OF COPD 2011-2018



2011

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by progressive **airflow limitation that is associated with and abnormal and excessive chronic airway and lung inflammation** caused by usually caused by significant exposure to cigarette smoking and noxious particles or gases

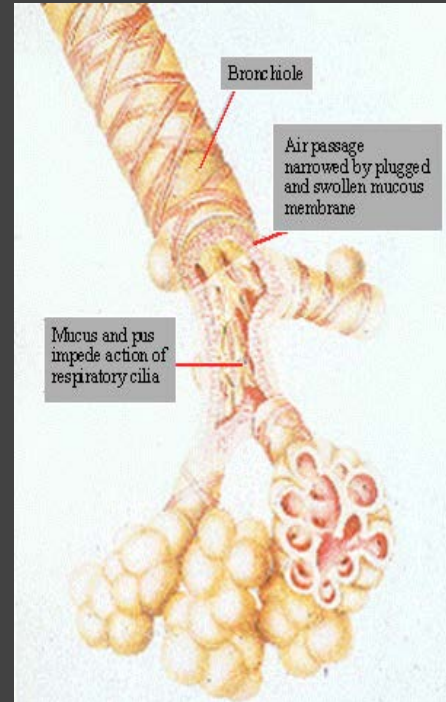
- The severity and prognosis of individual patients

2017

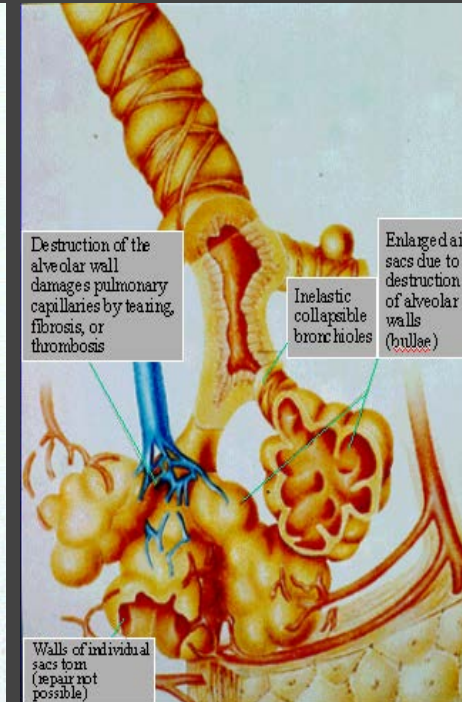
Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by **persistent respiratory symptoms and airflow limitation** that is due to **airway and/or alveolar abnormalities usually** caused by significant exposure to noxious particles or gases

COPD

- **GOLD Definition:** the presence of airflow limitation that is not fully reversible and a history of exposure to a noxious agent / risk factor (cigarette smoke)
- **Airflow limitation**
 - Small airways
 - Remodeling, fibrosis
 - Alveoli: emphysema
 - Destruction and enlargement of mature Airspace distal to terminal bronchioles



Small Airway
Obstruction



Emphysema



Diagnosis of COPD



SYMPTOMS

shortness of breath
chronic cough
sputum

EXPOSURE TO RISK FACTORS

tobacco
occupation
indoor/outdoor pollution

SPIROMETRY: Required to establish diagnosis



The NEW ENGLAND
JOURNAL of MEDICINE

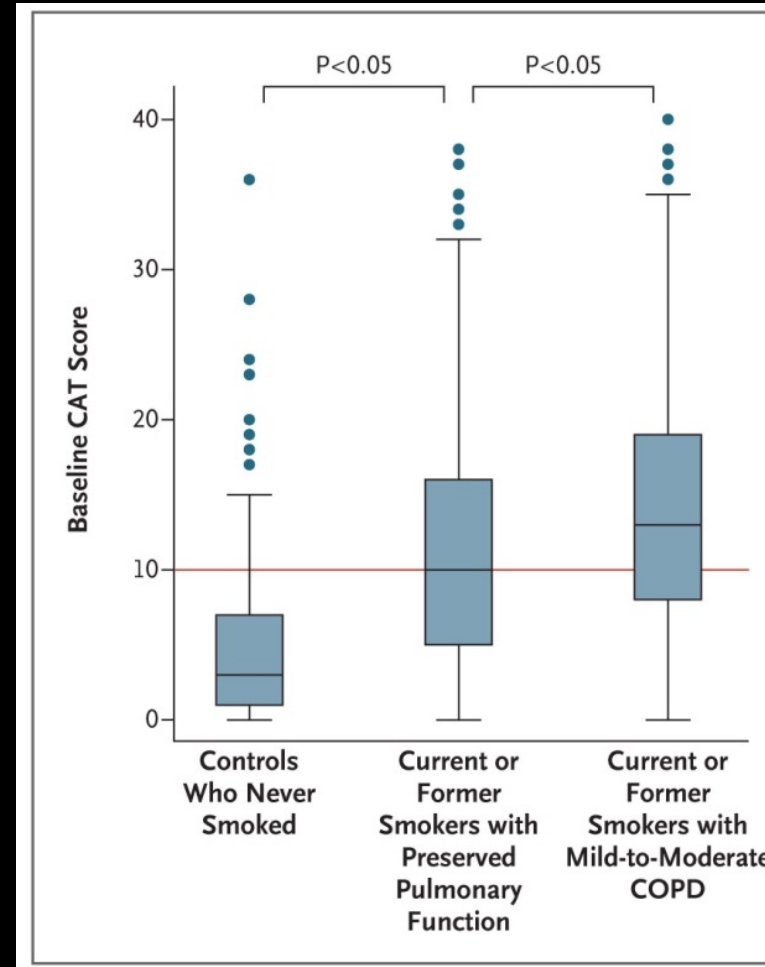
ORIGINAL ARTICLE

Clinical Significance of Symptoms in Smokers with Preserved Pulmonary Function

Prescott G. Woodruff, M.D., R. Graham Barr, M.D., Dr.P.H., Eugene Bleecker, M.D.,
Stephanie A. Christenson, M.D., David Couper, Ph.D., Jeffrey L. Curtis, M.D.,
Natalia A. Gouskova, Ph.D., Nadia N. Hansel, M.D., Eric A. Hoffman, Ph.D.,
Richard E. Kanner, M.D., Eric Kleerup, M.D., Stephen C. Lazarus, M.D.,
Fernando J. Martinez, M.D., Robert Paine, III, M.D., Stephen Rennard, M.D.,
Donald P. Tashkin, M.D., and MeiLan K. Han, M.D.,
for the SPIROMICS Research Group*

Woodruff PG et al. N Engl J Med 2016; 374:1811-21

SYMPTOMS (CAT \geq 10) ARE COMMON IN SMOKERS WITH PRESERVED PULMONARY FUNCTION



Woodruff PG et al. N Engl J Med 2016; 374:1811-21

INTERVENTIONAL THERAPY IN STABLE COPD

- ▶ **Lung volume reduction surgery (LVRS) is a surgical procedure in which parts of the lungs are resected to reduce hyperinflation,²⁶¹ making respiratory muscles more effective pressure generators by improving their mechanical efficiency.**
- ▶ **Due to the morbidity and mortality associated with LVRS, less invasive bronchoscopic approaches to lung reduction**

Table 3.11. Interventional therapy in stable COPD
Lung volume reduction surgery
<ul style="list-style-type: none"> • Lung volume reduction surgery improves survival in severe emphysema patients with an upper-lobe emphysema and low post-rehabilitation exercise capacity (Evidence A).
Bullectomy
<ul style="list-style-type: none"> • In selected patients bullectomy is associated with decreased dyspnea, improved lung function and exercise tolerance (Evidence C).
Transplantation
<ul style="list-style-type: none"> • In appropriately selected patients with very severe COPD, lung transplantation has been shown to improve quality of life and functional capacity (Evidence C).
Bronchoscopic interventions
<ul style="list-style-type: none"> • In select patients with advanced emphysema, bronchoscopic interventions reduces end-expiratory lung volume and improves exercise tolerance, health status and lung function at 6-12 months following treatment. Endobronchial valves (Evidence B); Lung coils (Evidence B).

NUOVI FARMACI IN SVILUPPO PER LA BPCO

Leonardo M. Fabbri, MD, FERS

The changes in the definition and assessement of severity of COPD

The recent studies of efficacy and safety of triple therapy in a single inhaler is likely to introduce major changes in the pharmacologic management of COPD

Anti IL-5 Moa, new experimental agents

TREAT THE PATIENT WITH COPD NOT JUST COPD



Manage stable COPD: Pharmacologic therapy FIRST CHOICE



GOLD 4	C	ICS + LABA or LAMA	D	ICS + LABA or/and LAMA	≥ 2
GOLD 3					
GOLD 2	A	SAMA <i>prn</i> or SABA <i>prn</i>	B	LABA or LAMA	1
GOLD 1					0
mMRC 0-1 CAT < 10		mMRC ≥ 2 CAT ≥ 10		Exacerbations per year	

ABCD Assessment Tool

Figure 2.4. The refined ABCD assessment tool

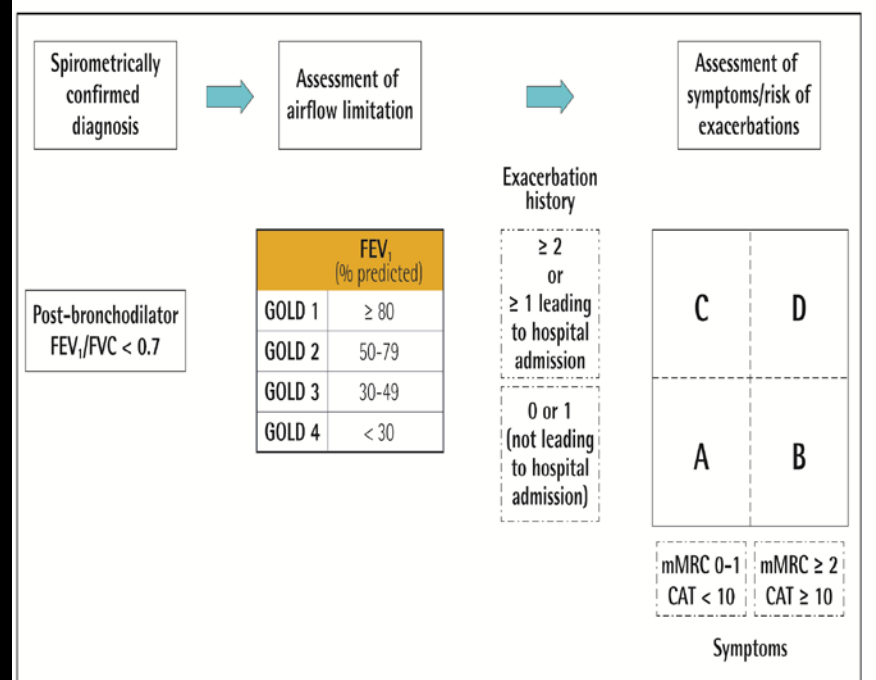
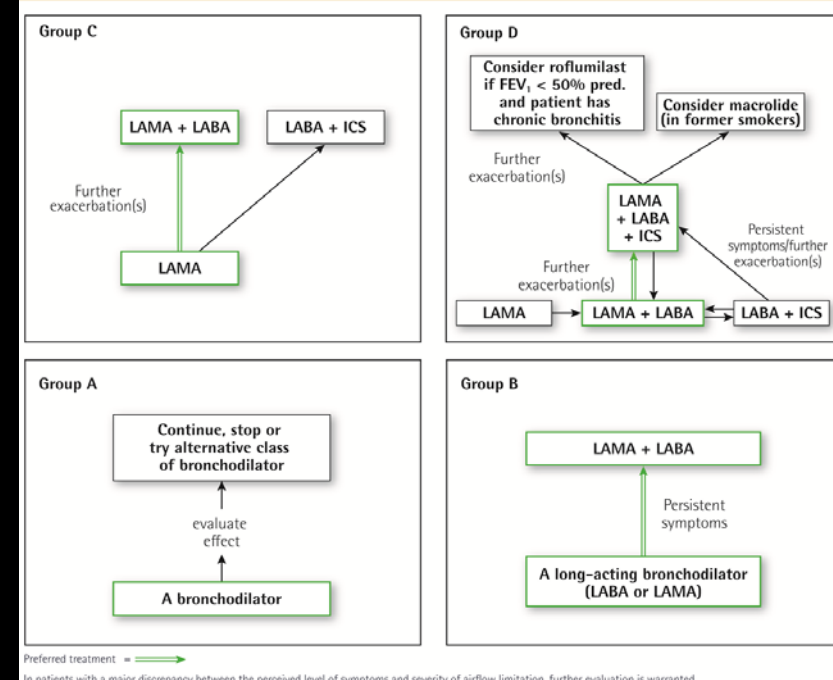
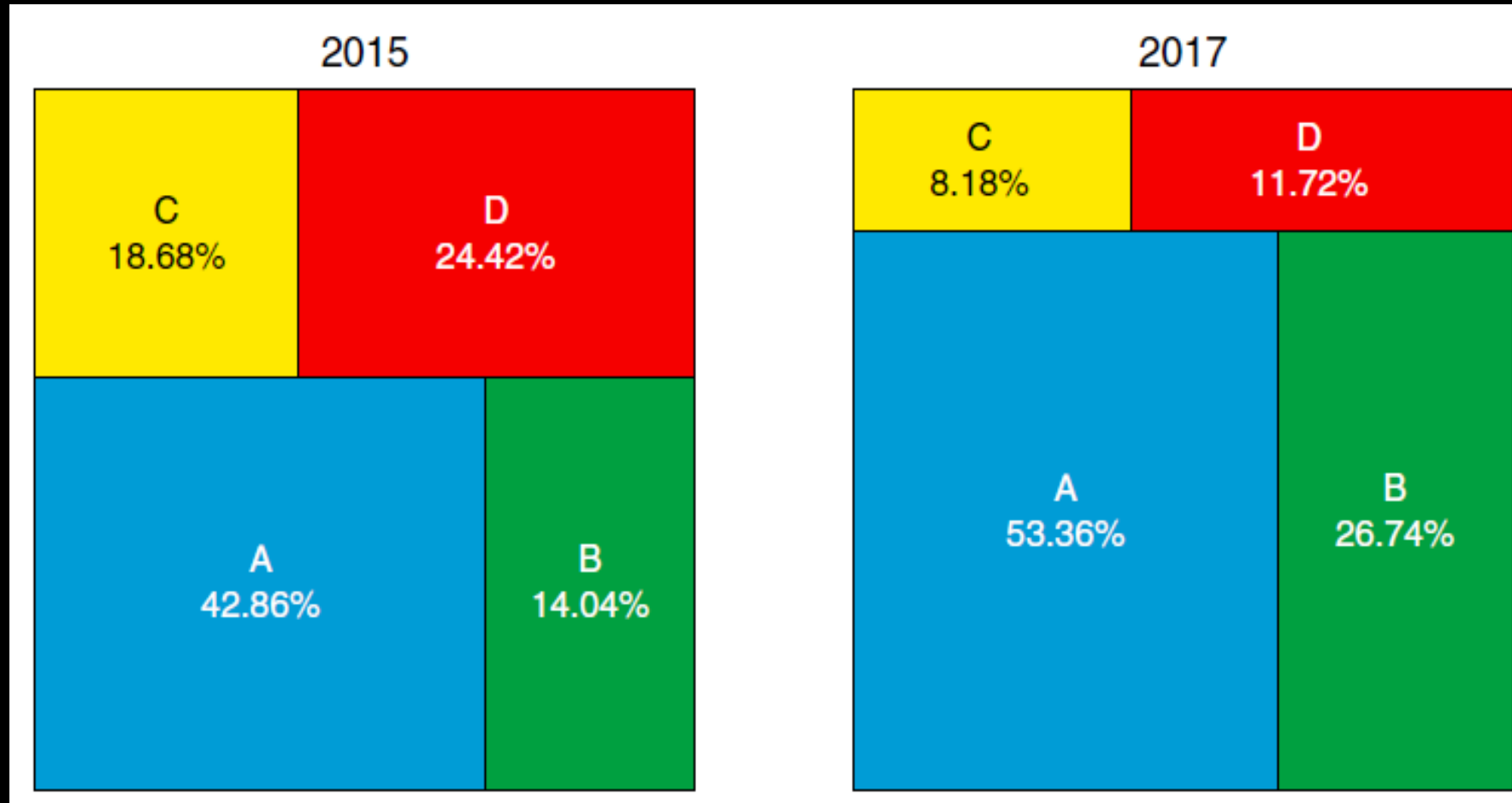


Figure 4.1. Pharmacologic treatment algorithms by GOLD Grade [highlighted boxes and arrows indicate preferred treatment pathways]

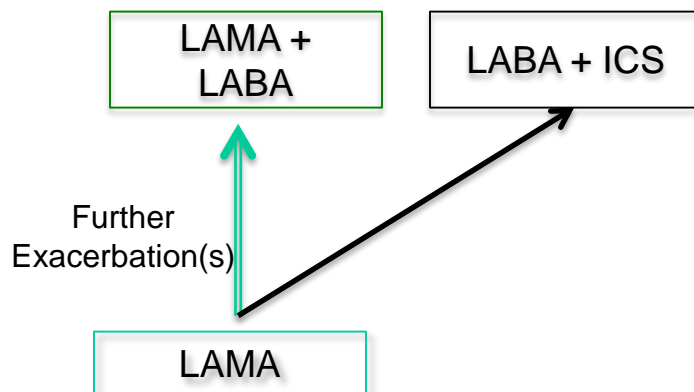


DISTRIBUTION OF THE SAME PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN THE DIFFERENT ABCD GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE GRADING GROUPS USING THE 2011

~~VERSION VERSUS THE NEW 2017 VERSION~~



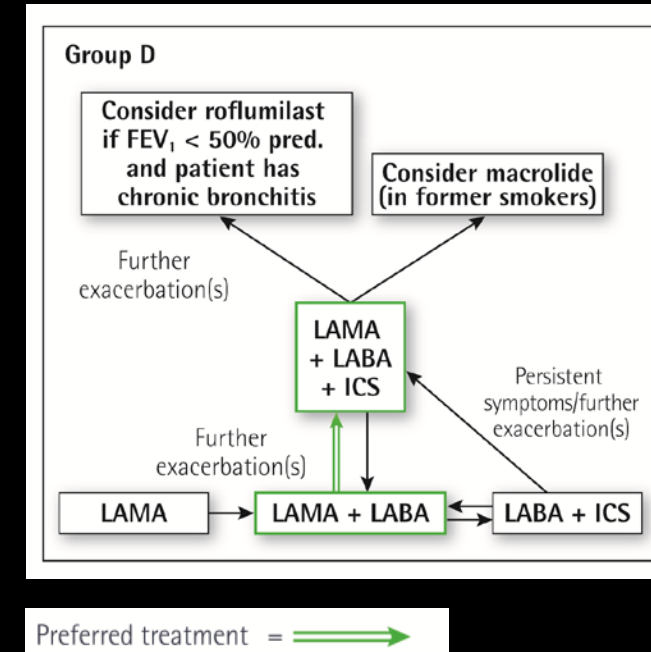
Group B



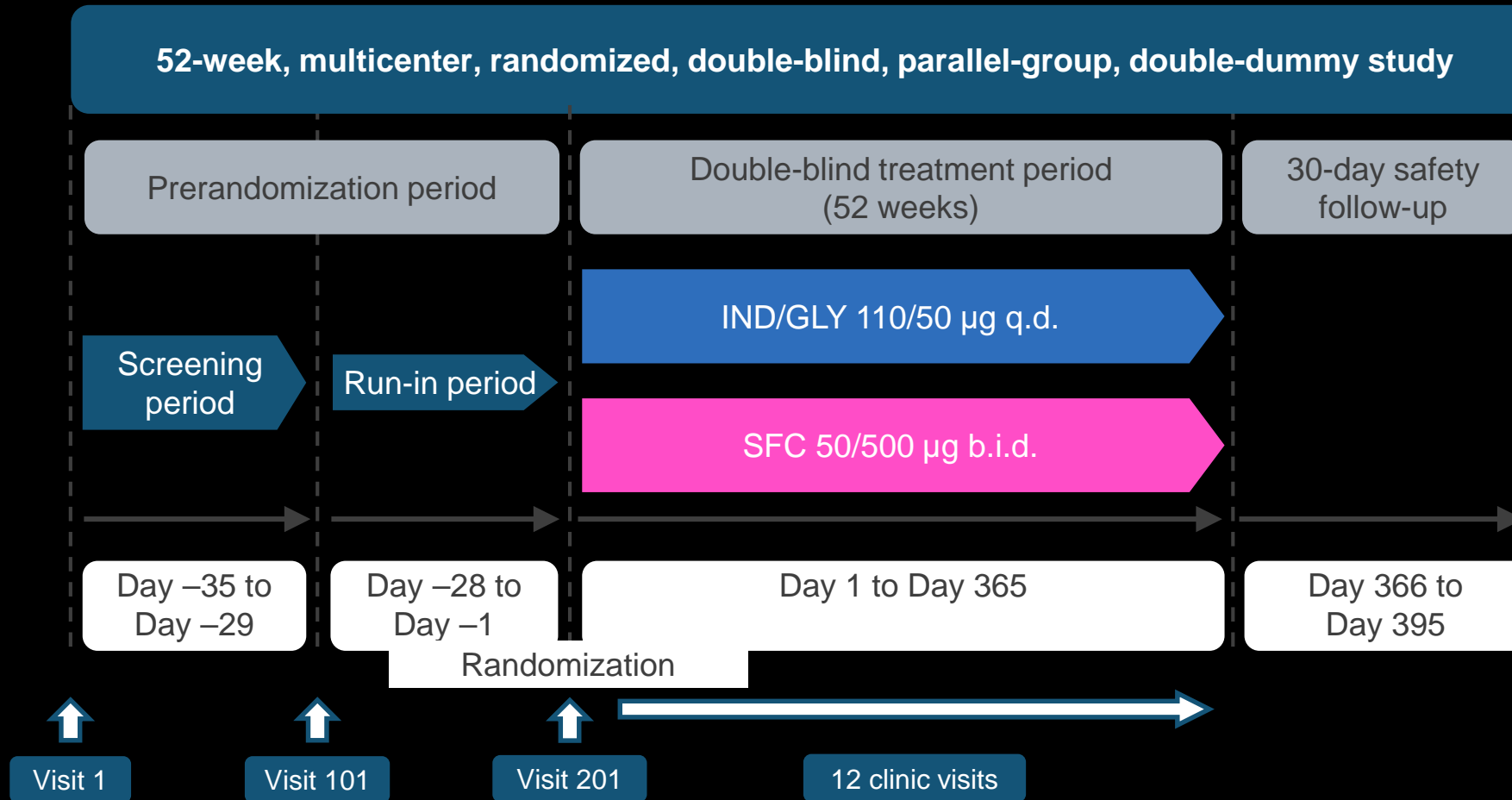
Pharmacologic treatment algorithms

Group D

- ▶ We recommend starting therapy with a LABA/LAMA combination because:
 - In studies with patient reported outcomes as the primary endpoint LABA/LAMA combinations showed superior results compared to the single substances. If a single bronchodilator is chosen as initial treatment, a LAMA is preferred for exacerbation prevention based on comparison to LABAs (for details see GOLD 2017 Chapter 3).
 - A LABA/LAMA combination was superior to a LABA/ICS combination in preventing exacerbations and other patient reported outcomes in Group D patients (for details see GOLD 2017 Chapter 3).
 - Group D patients are at higher risk of developing pneumonia when receiving treatment with ICS.

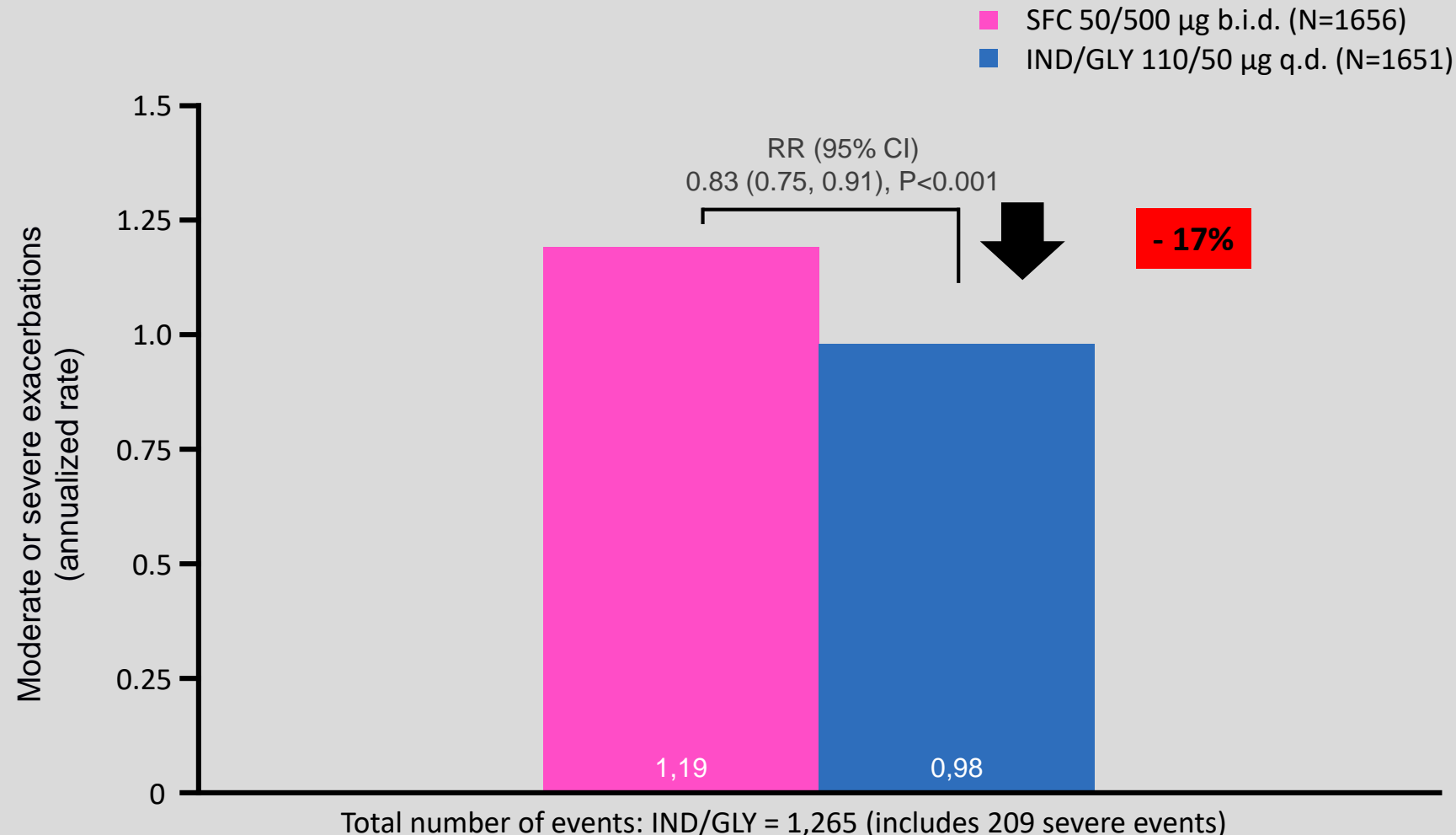


COMPARISON OF INDACATEROL/GLYCOPYRROMNIUM COMBINATION (110/50 µg) versus SALMETEROL/FLUTICASONE (50/500 µg) BID FOR THE ROW





IND/GLY showed superiority in reducing the annual rate of moderate or severe exacerbations (healthcare utilization) versus SFC

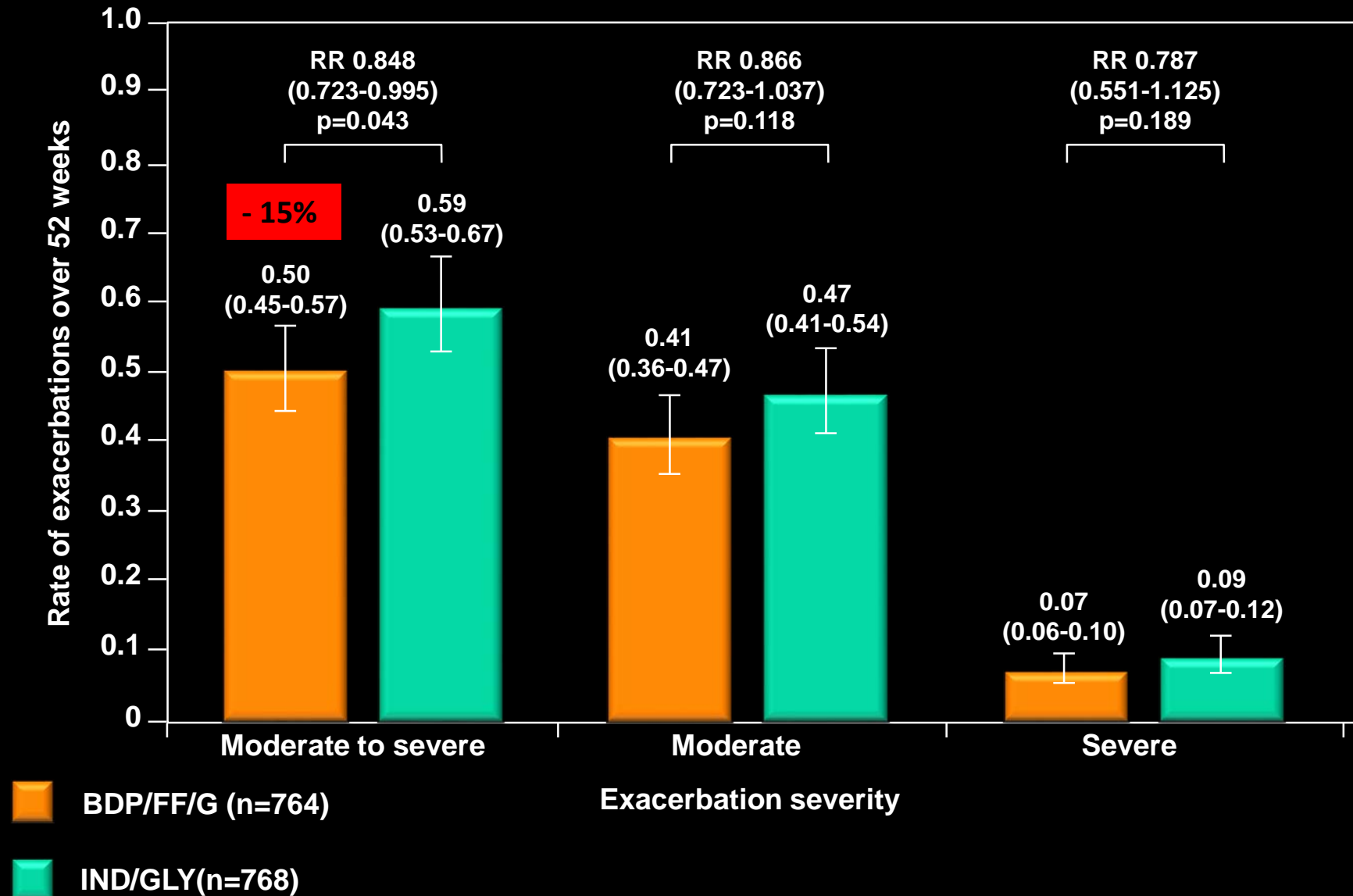


Analysis of the modified intention-to-treat set (mITT)

SFC = 1,452 (includes 241 severe events)

1. Wedzicha JA, et al. N Engl J Med. Online May 15, 2016
2. Wedzicha JA, et al. N Engl J Med. Online May 15, 2016 Supplementary appendix

TRIPLE IN A SINGLE INHALER IS SUPERIOR TO LABA/LAMA IN REDUCING EXACERBATIONS IN D AND B COPD



Papi A et al. Lancet 2018 ; 391(10125): 1076-1084

ONCE-DAILY SINGLE-INHALER TRIPLE THERAPY VERSUS DUAL THERAPY IN COPD

The NEW ENGLAND JOURNAL of MEDICINE

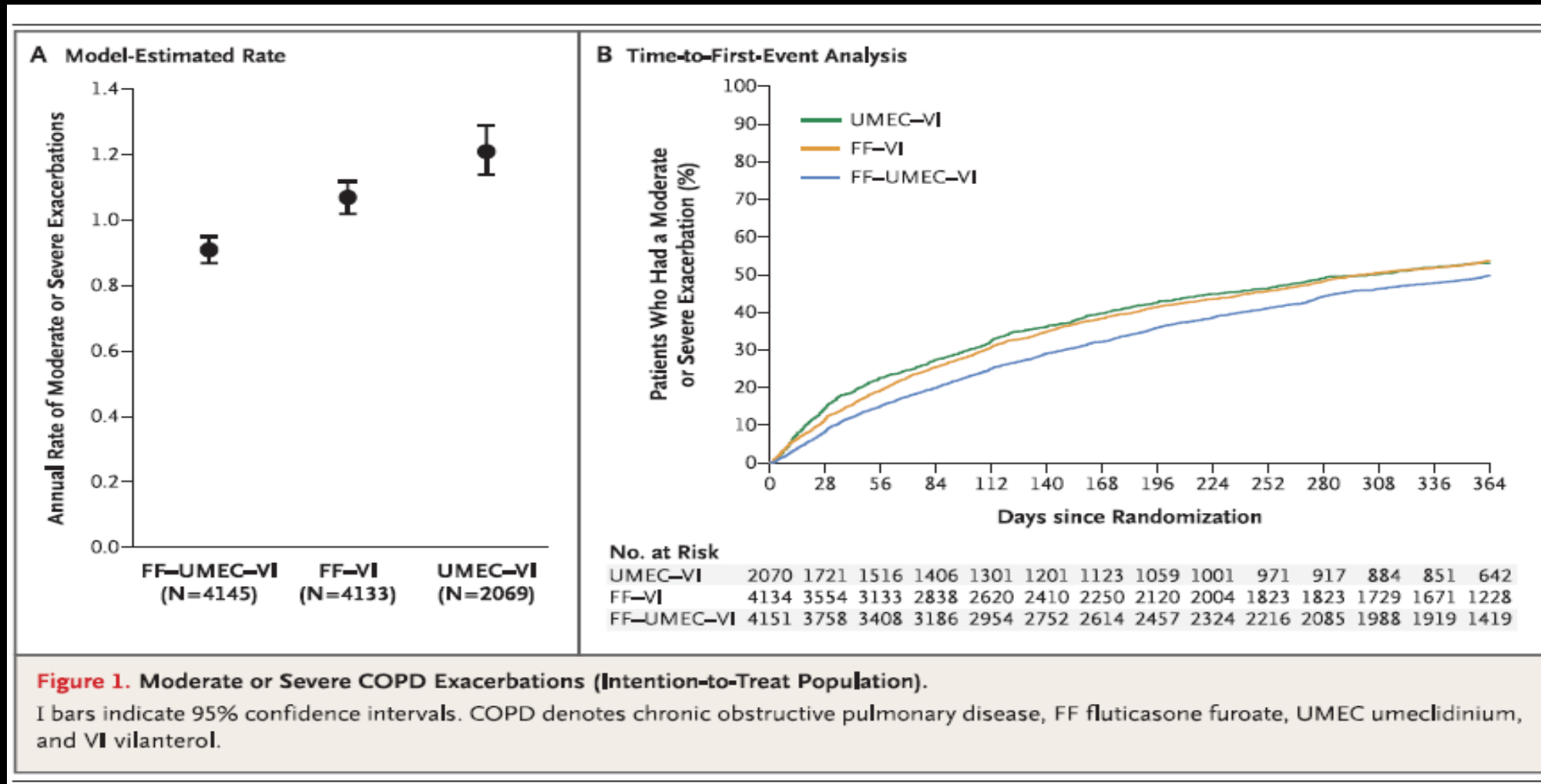
ORIGINAL ARTICLE

Once-Daily Single-Inhaler Triple versus Dual Therapy in Patients with COPD

David A. Lipson, M.D., Frank Barnhart, D.V.M., Noushin Brealey, M.D.,
Jean Brooks, M.Sc., Gerard J. Criner, M.D., Nicola C. Day, Ph.D.,
Mark T. Dransfield, M.D., David M.G. Halpin, M.D., MeiLan K. Han, M.D.,
C. Elaine Jones, Ph.D., Sally Kilbride, M.Sc., Peter Lange, M.D.,
David A. Lomas, M.D., Ph.D., Fernando J. Martinez, M.D., Dave Singh, M.D.,
Maggie Tabberer, M.Sc., Robert A. Wise, M.D., and Steven J. Pascoe, M.B., B.S.,
for the IMPACT Investigators

Lipson et al, New E J Med 18 April 2018

ONCE-DAILY SINGLE-INHALER TRIPLE THERAPY VERSUS DUAL THERAPY IN COPD



Lipson et al, New E J Med 18 April 2018

ONCE-DAILY SINGLE-INHALER TRIPLE THERAPY VERSUS DUAL THERAPY IN COPD

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Once-Daily Single-Inhaler Triple versus Dual Therapy in Patients with COPD

CONCLUSIONS

Triple therapy with fluticasone furoate, umeclidinium, and vilanterol resulted in a lower rate of moderate or severe COPD exacerbations than fluticasone furoate–vilanterol or umeclidinium–vilanterol in this population. Triple therapy also resulted in a lower rate of hospitalization due to COPD than umeclidinium–vilanterol. (Funded by GlaxoSmithKline; IMPACT ClinicalTrials.gov number, NCT02164513.)

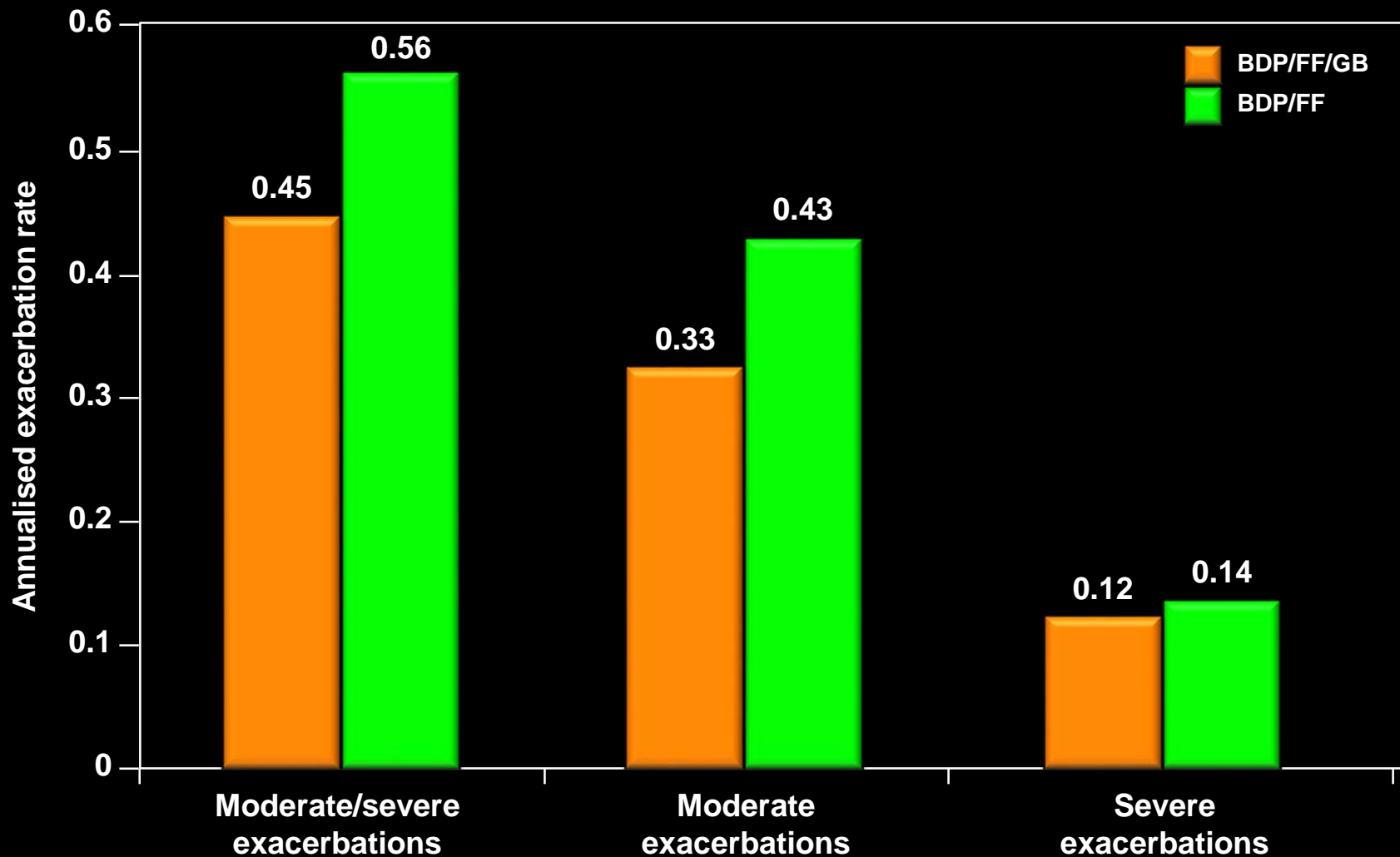
Lipson et al, New E J Med 18 April 2018

SINGLE-INHALER TRIPLE LABA/LAMA/ICS AND LABA/ICS REDUCE MORTALITY COMPARED TO LABA/LAMA DUAL THERAPY IN COPD B AND D PATIENTS

Death during treatment occurred in 50 patients (1%) in the triple-therapy group, 49 patients (1%) in the fluticasone furoate–vilanterol group, and 39 patients (2%) in the umeclidinium–vilanterol group. All-cause mortality was significantly lower with the regimens that included the inhaled glucocorticoid fluticasone furoate (triple therapy and fluticasone furoate–vilanterol) than with umeclidinium–vilanterol. The hazard ratio for triple therapy versus umeclidinium–vilanterol was 0.58 (95% CI, 0.38 to 0.88; 42% difference; unadjusted $P=0.01$), and the hazard ratio for fluticasone furoate–vilanterol versus umeclidinium–vilanterol was 0.61 (95% CI, 0.40 to 0.93; 39% difference; unadjusted $P=0.02$). The results of a

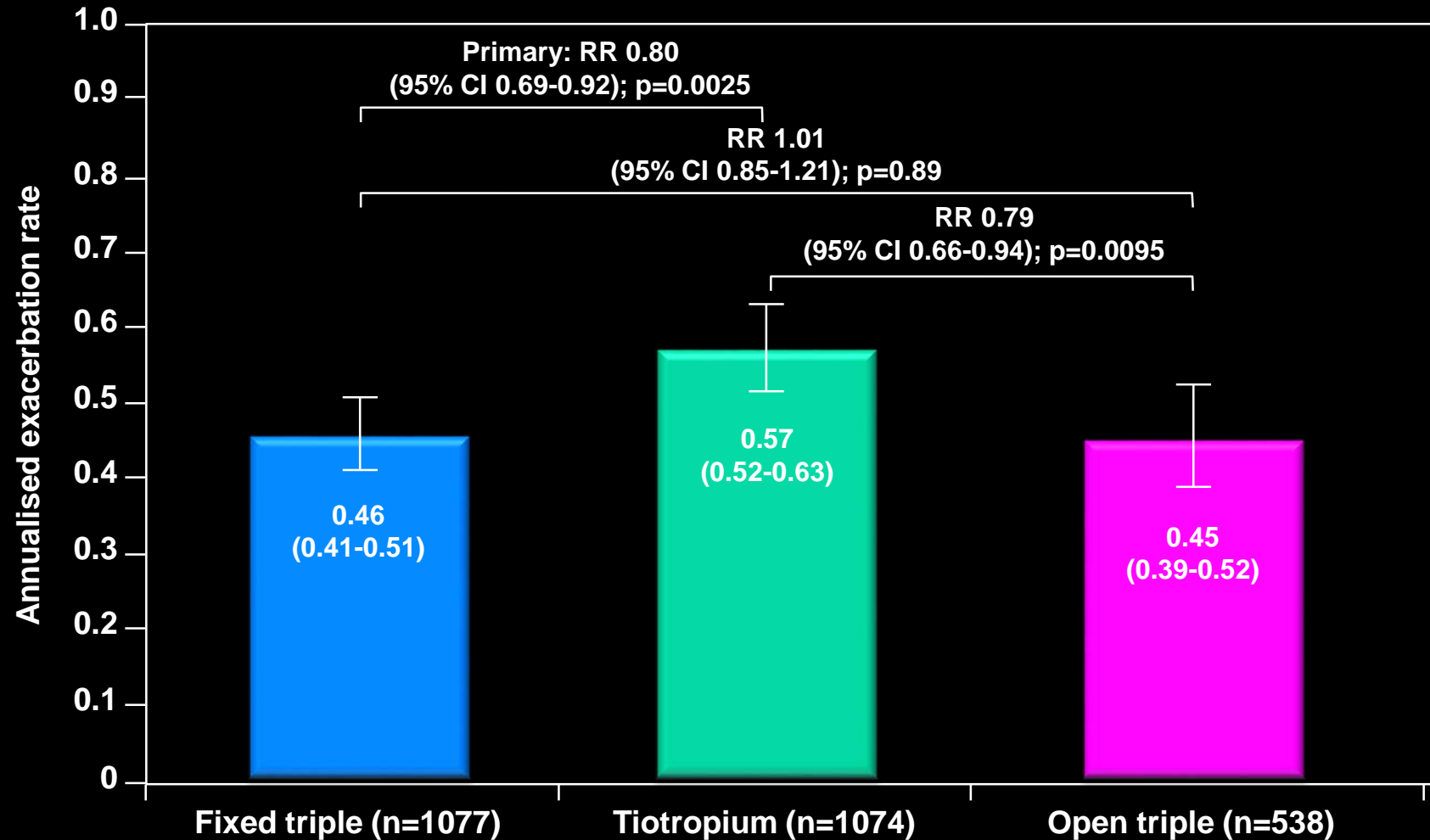
Lipson et al, New E J Med 18 April 2018

TRIPLE IN A SINGLE INHALER IS SUPERIOR TO LABA/ICS IN REDUCING EXACERBATIONS IN D AND B COPD



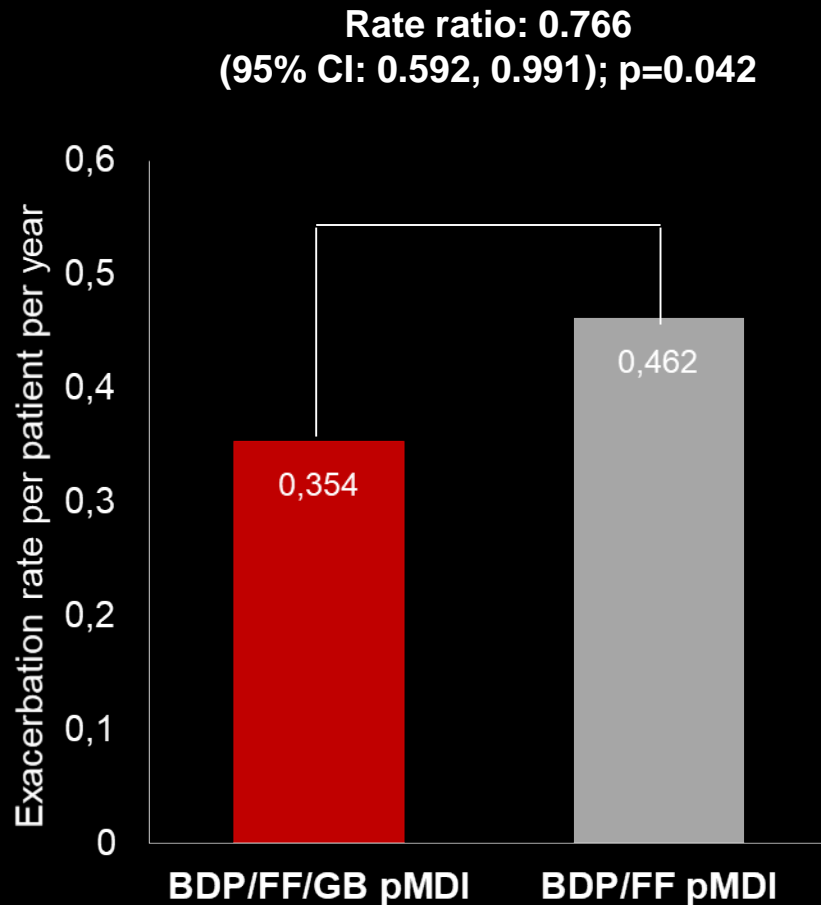
Singh D et al. Lancet 2016; 388: 963–73

TRIPLE IN A SINGLE INHALER IS SUPERIOR TO TIOTROPIUM IN REDUCING EXACERBATIONS IN D AND B COPD

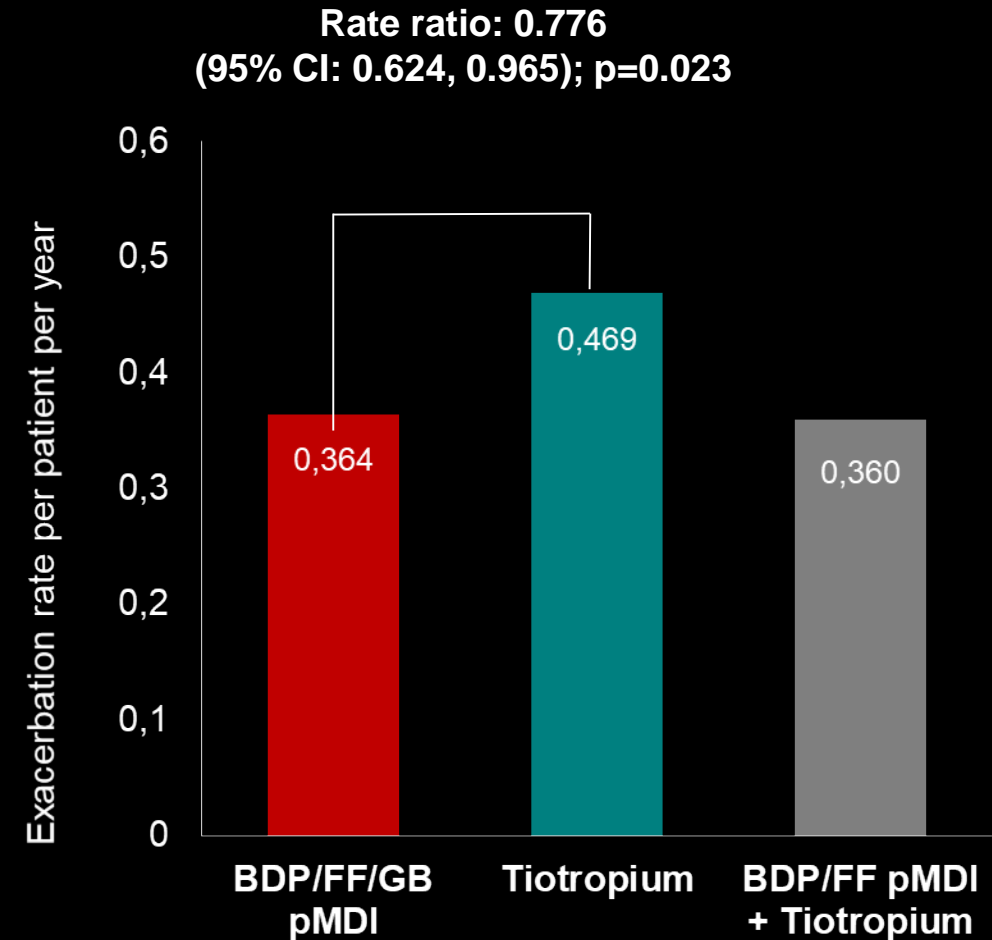


Vestbo J. et al., Lancet 2017; 389: 1919–29

MODERATE/SEVERE COPD EXACERBATIONS IN GOLD B PATIENTS



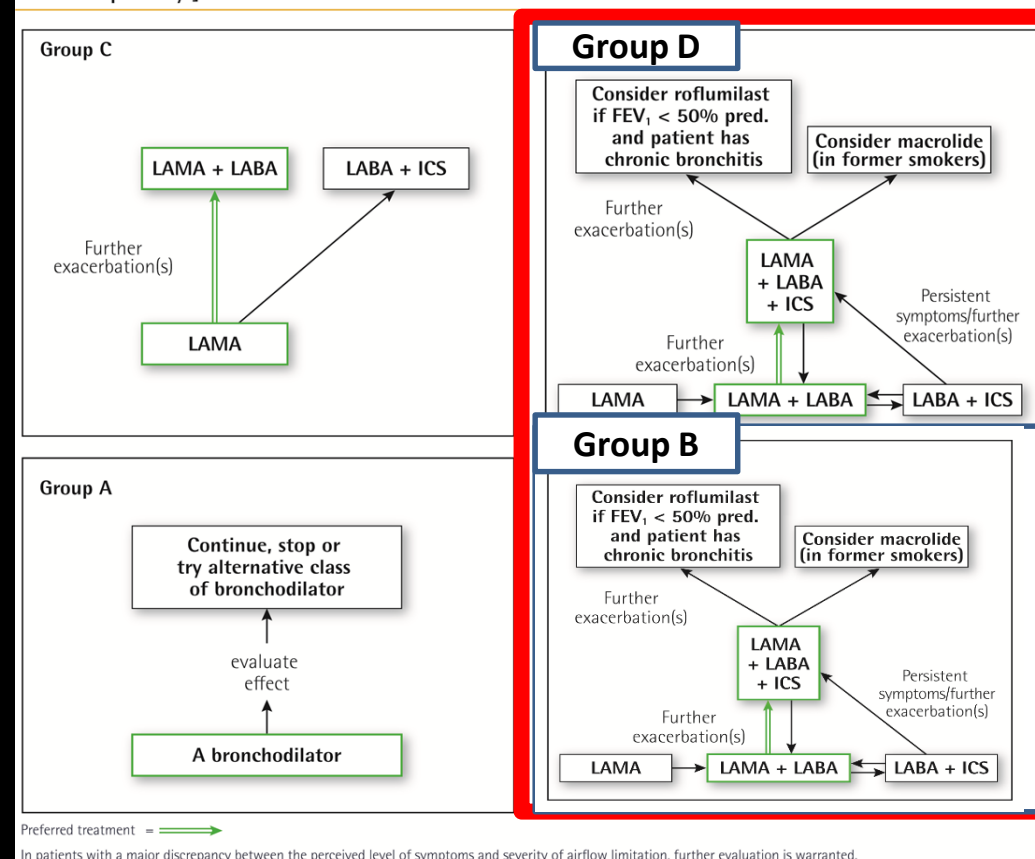
TRILOGY



TRINITY

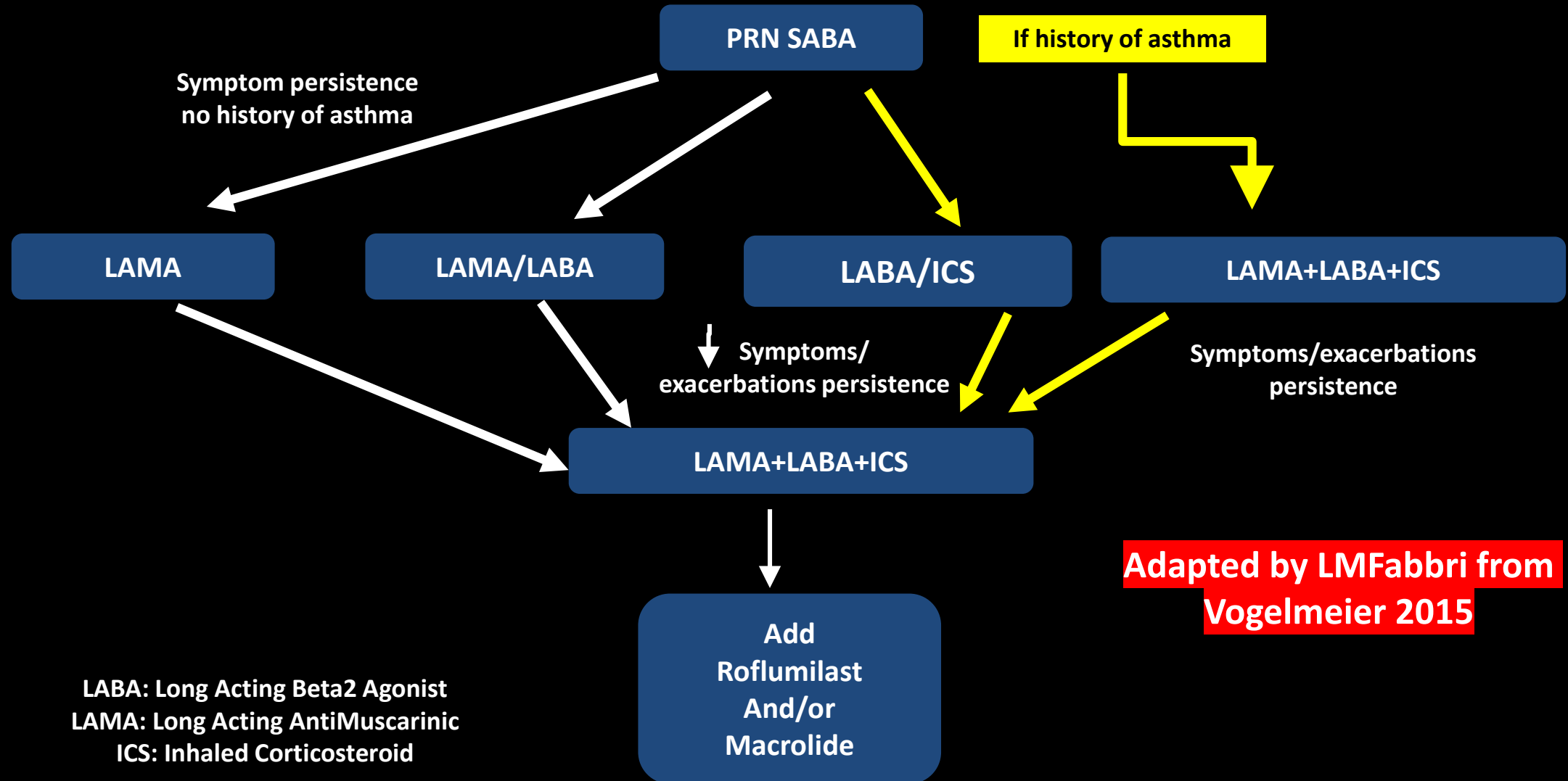
ABCD ASSESSMENT TOOL TREATMENT RECOMMENDATIONS

Figure 4.1. Pharmacologic treatment algorithms by GOLD Grade [highlighted boxes and arrows indicate preferred treatment pathways]



Suggestions to the Global Initiative for Chronic Obstructive Lung Disease

TREATMENT ALGORITHM FOR SYMPTOMATIC COPD PATIENTS WITH OR WITHOUT RISK OF EXACERBATIONS

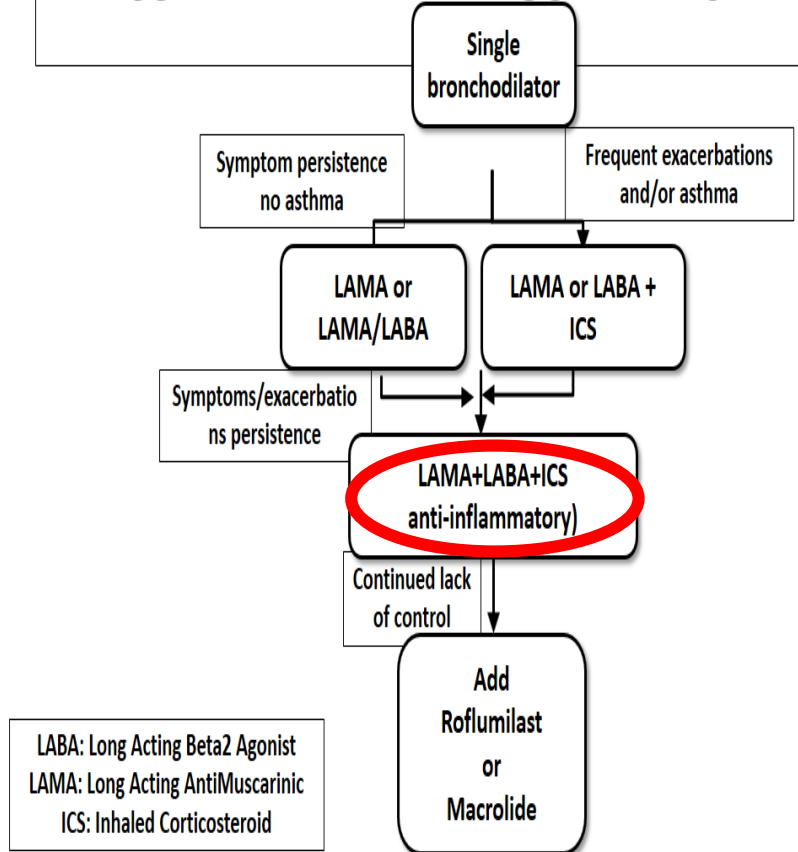


Adapted by LM Fabbri from
Vogelmeier 2015

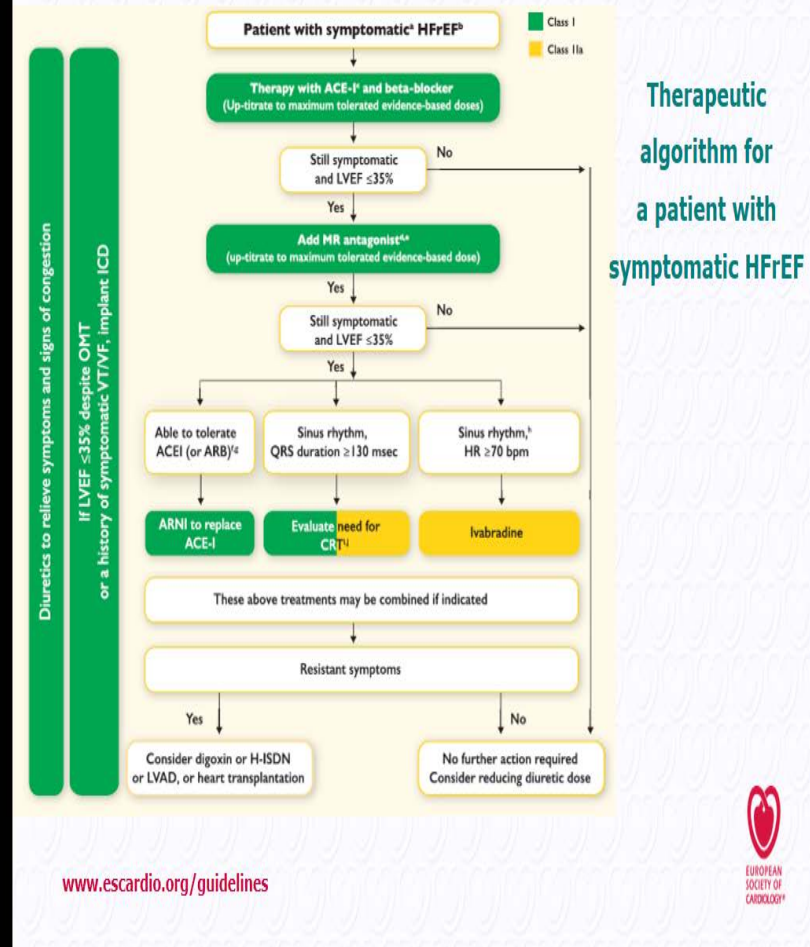
AT DOCTOR'S DISCRETION, DEPENDING ON CONDITIONS AT THE MOMENT OF THE FIRST TIME THE DOCTOR SEE THE PATIENT (eg after an acute exacerbation, uncontrolled under any type of regular treatment), PATIENTS CAN BE PUT DIRECTLY IN LAMA, LABA/ICS, TRIPLE OR EVEN ICS ONLY (if arrhythmia, chronic heart failure and ischemi heart disease)

COPD CHF TREATMENT ALGORYTHMS

COPD TREATMENT ALGORYTHMS



2017 GOLD Strategy Document



2016 ESC Guidelines on CHF

QUARTER-DOSE QUADRUPLE COMBINATION THERAPY FOR INITIAL TREATMENT OF HYPERTENSION

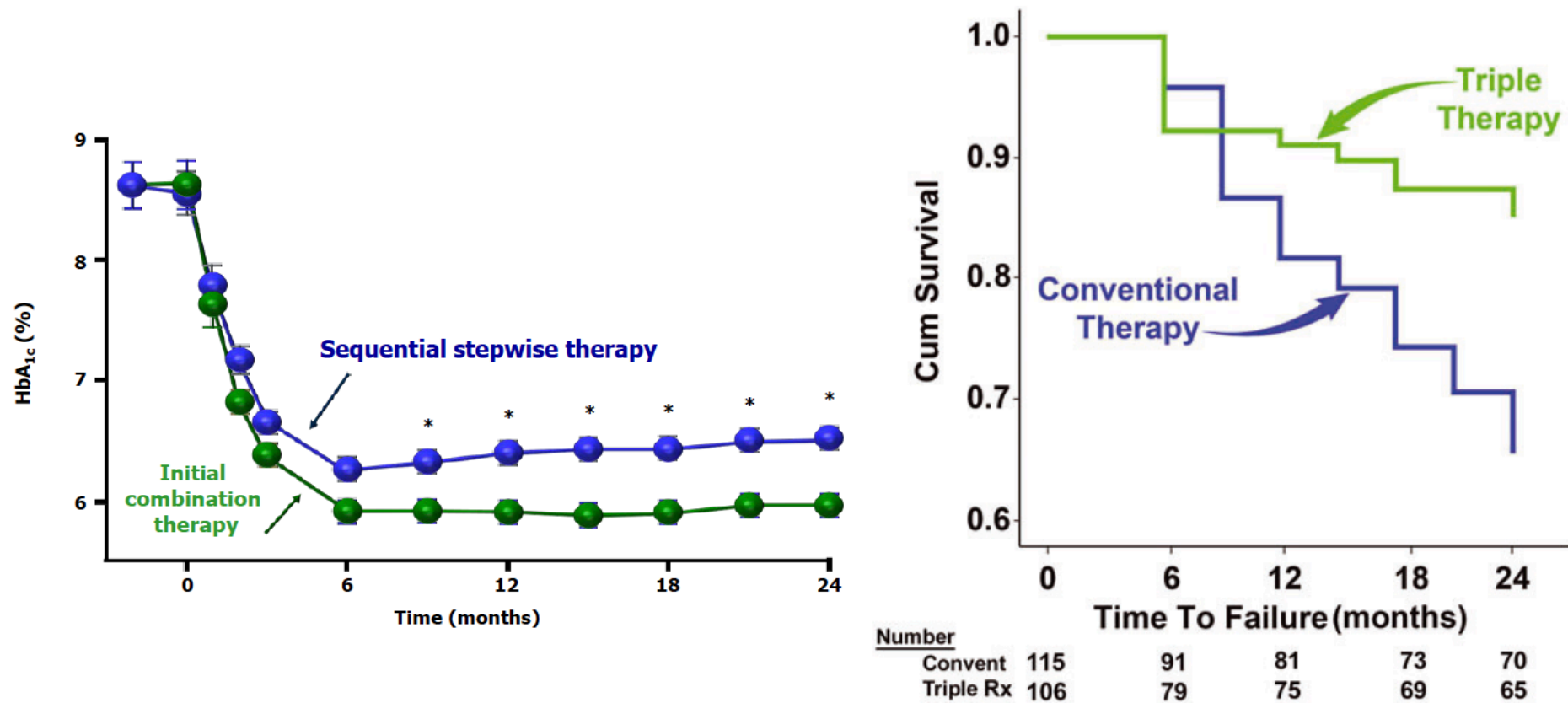
**Quarter-dose quadpill therapy could be
additive across classes and might confer a
clinically important reduction in blood
pressure**

**Further examination of the quadpill concept is
needed to investigate effectiveness against
usual treatment options and longer term
tolerability**

Chow CK et al, Lancet, 12 Feb 2017, on line

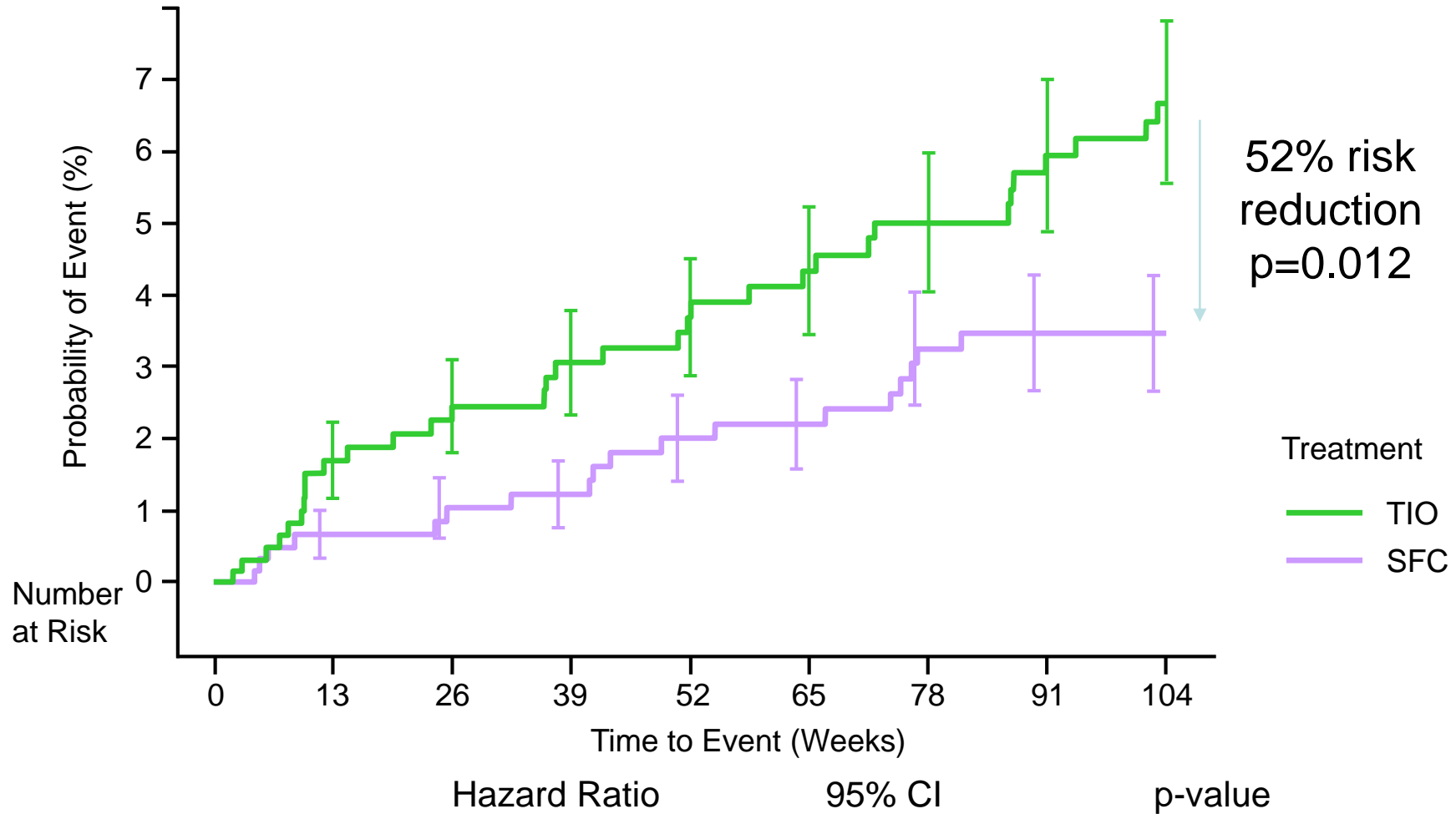
Initial combination therapy with metformin, pioglitazone and exenatide is more effective than sequential add-on therapy in subjects with new-onset diabetes

The intensive group was treated with MET/TZD/GLP-1 RA, and the conventional group was treated with metformin with sequential addition of an SU and then glargine insulin.



MORTALITY IN INSPIRE

*up to 2 weeks after treatment cessation; 7 patients excluded from analysis (3 SFC, 4 TIO)



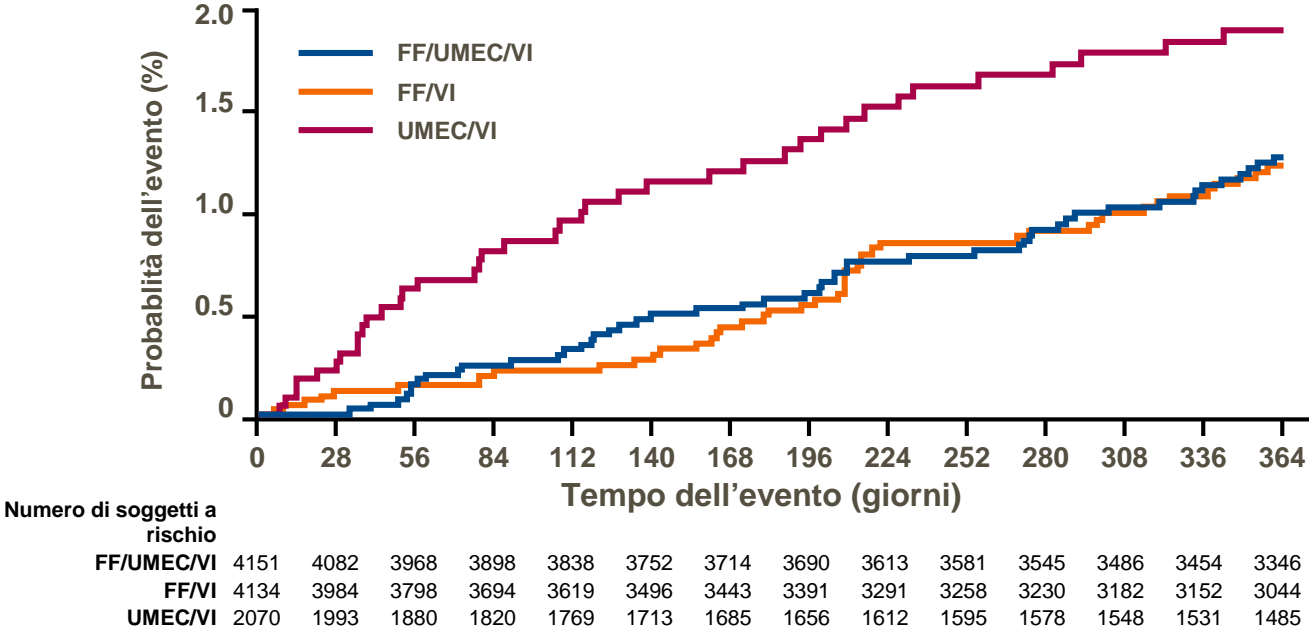
SFC vs TIO

0.48

(0.27, 0.85)

0.012

IMPACT MORTALITY (dati on-treatment)



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

FF: fluticasone furoate; UMEC: umeclidinio bromuro; VI: vilanterolo trifenatato; HR: hazard ratio

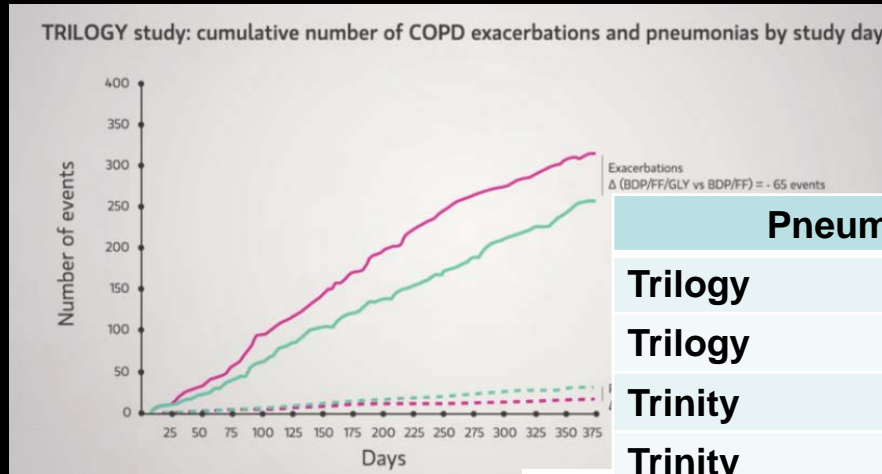
TREATMENT-EMERGENT ADVERSE EVENTS - TRIBUTE

Patients with	BDP/FF/G N = 764	IND/GLY N = 768
AEs	490 (64.1%)	516 (67.2%)
ADRs	43 (5.6%)	37 (4.8%)
SAEs	117 (15.3%)	130 (16.9%)
Serious ADRs	1 (0.1%)	1 (0.1%)
AEs leading to discontinuation	37 (4.8%)	47 (6.1%)
AEs leading to death	16 (2.1%)	21 (2.7%)
Any pneumonia	28 (3.7%)	27 (3.5%)

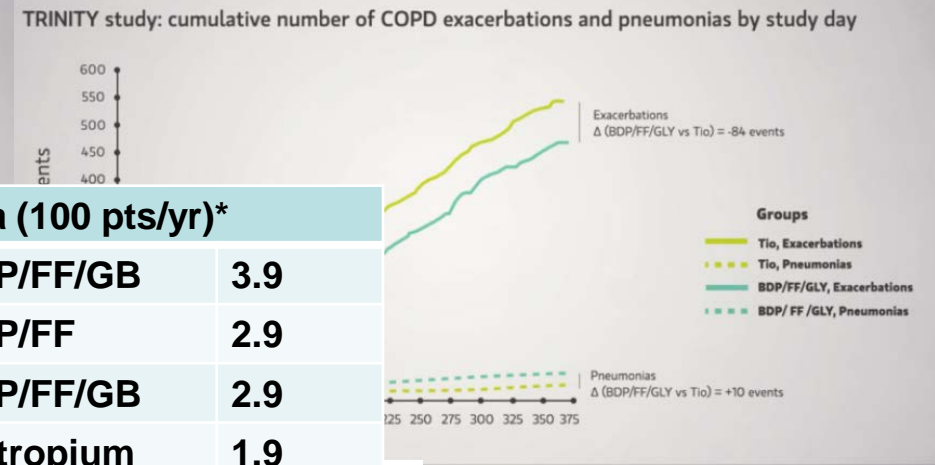
Papi A et al. Lancet 2018; 391(10125): 1076-84

RISK-BENEFIT RATIO (COPD EXACERBATIONS AND PNEUMONIAS) IN TRILOGY, TRINITY AND TRIBUTE STUDIES

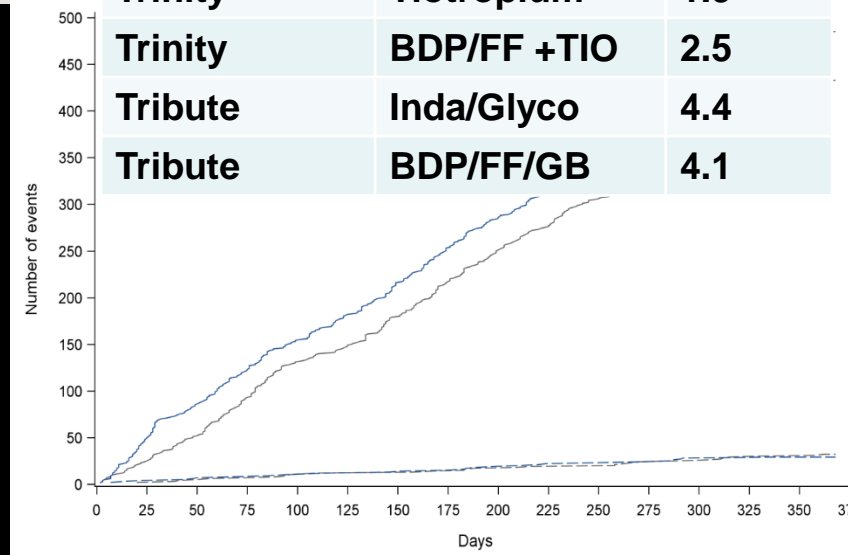
TRILOGY



TRINITY



Pneumonia (100 pts/yr)*		
Trilogy	BDP/FF/GB	3.9
Trilogy	BDP/FF	2.9
Trinity	BDP/FF/GB	2.9
Trinity	Tiotropium	1.9
Trinity	BDP/FF +TIO	2.5
Tribute	Inda/Glyco	4.4
Tribute	BDP/FF/GB	4.1



TRIBUTE

Singh D et al., Lancet 2016;

Vestbo J et al., Lancet 2017;

Papi A et al., Lancet 2018

RISK REDUCTION FOR HYPERTENSION, IHD, MI, ATRIAL FIBRILLATION IN TRIBUTE

Number (%) of patients	BDP/FF/G (N=764)	IND/GLY (N=768)
Adverse events	490 (64.1)	516 (67.2)
COPD worsening	273 (35.7)	288 (37.5)
Pneumonia	28 (3.7)	27 (3.5)
Hypertension	15 (2.0)	26 (3.4)
Cough	13 (1.7)	25 (3.3)
Ischemic heart disease	8 (1.0)	16 (2.1)
Serious adverse events	117 (15.3)	130 (16.9)
COPD worsening	61 (8.0)	69 (9.0)
Death	3 (0.4)	8 (1.0)
Ischemic heart disease	2 (0.3)	11 (1.4)
Myocardial infarction	1 (0.1)	8 (1.0)
Atrial fibrillation	0	7 (0.9)

Papi et al, The Lancet, Lancet 2018 Mar 17;391(10125):1076-1084

TREATMENT-EMERGENT ADVERSE EVENTS TRIBUTE

Number (%) of patients	BDP/FF/G (N=764)	IND/GLY (N=768)
Treatment-related adverse events	12 (1.6)	6 (0.8)
Oral candidiasis	12 (1.6)	6 (0.8)
Dry mouth	3 (0.4)	6 (0.8)
Cough	1 (0.1)	7 (0.9)
Treatment-related serious adverse events	1 (0.1)	1 (0.1)
Severe adverse events	86 (11.3)	87 (11.3)
Adverse events leading to death	16 (2.1)	21 (2.7)

Papi et al, The Lancet, Lancet 2018 Mar 17;391(10125):1076-1084

POOL DATA ON MORTALITY (ATS/ERS ABSTRACT)

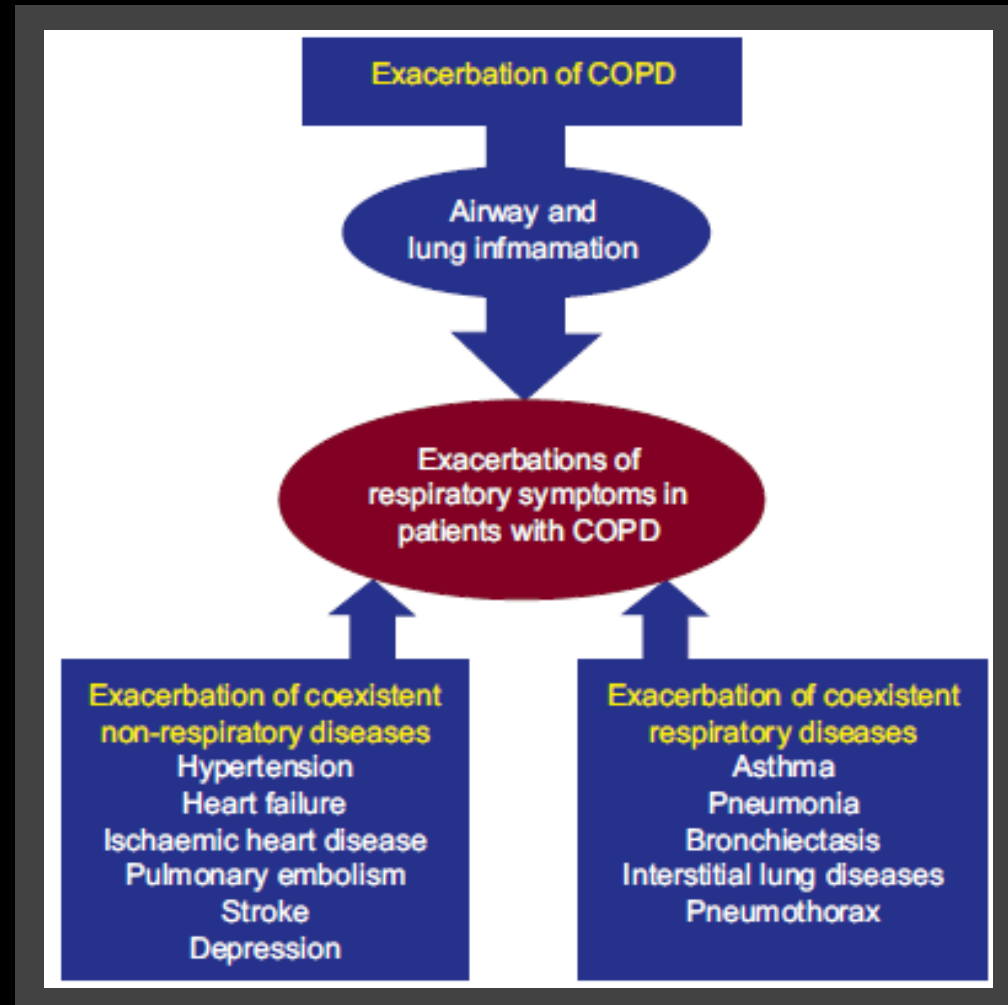
Table 1. Patients (%) with fatal AEs and Hazard Ratios for the treatment group comparisons in TRILOGY, TRINITY and TRIBUTE					
Study	Test	Comparator	Number of patients with event (%) - Test	Number of patients with event (%) - Comparator	Hazard Ratio (95% CI), p-value
Single					
TRILOGY	BDP/FF/G (N=687)	BDP/FF (N=680)	15 (2.2%)	16 (2.4%)	-
TRINITY	BDP/FF/G (N=1077)	TIO (N=1076)	20 (1.9%)	29 (2.7%)	-
	'	BDP/FF+TIO (537)	'	8 (1.5%)	-
TRIBUTE	BDP/FF/G (N=764)	IND/GLY (N=768)	16 (2.1%)	21 (2.7%)	
Pooled					
TRILOGY, TRINITY, TRIBUTE	BDP/FF/G, BDP/FF, BDP/FF+TIO (N=3745)	TIO, IND/GLY (N=1844)	75 (2.0%)	50 (2.7%)	0.72 (0.50; 1.02), p=0.066
	BDP/FF/G (N=2528)	TIO, IND/GLY (N=1844)	51 (2.0%)	50 (2.7%)	0.72 (0.49; 1.06), p=0.096

Scuri et al, Am J Respir Crit Care Med 2018;197:Abstract 7725

	BDP/FF/G, BDP/FF, BDP/FF+TIO (n=3745)	TIO, IND/GLY (N=1844)	
	N of patients with events (%)		HR (95%, CI), p-value
RESPIRATORY	19 (0.5%)	9 (0.5%)	1.01 (0.45; 2.22) p=0.990
NON-RESPIRATORY	56 (1.5%)	41 (2.2%)	0.65 (0.43; 0.97) p=0.037

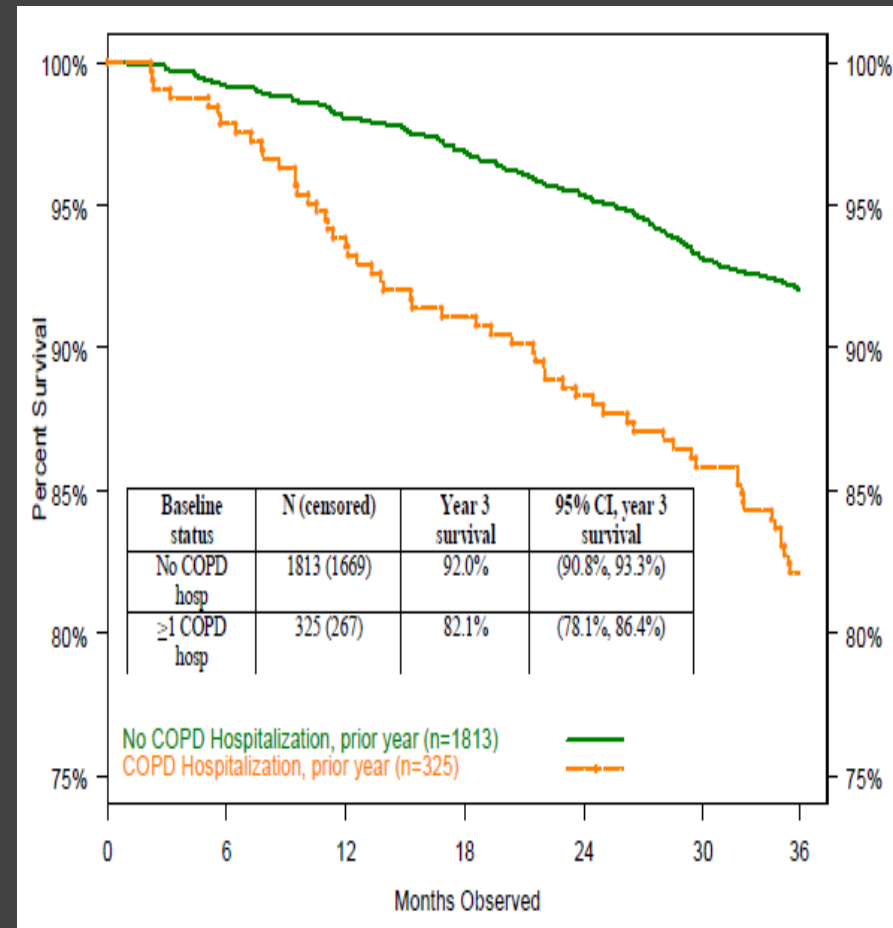
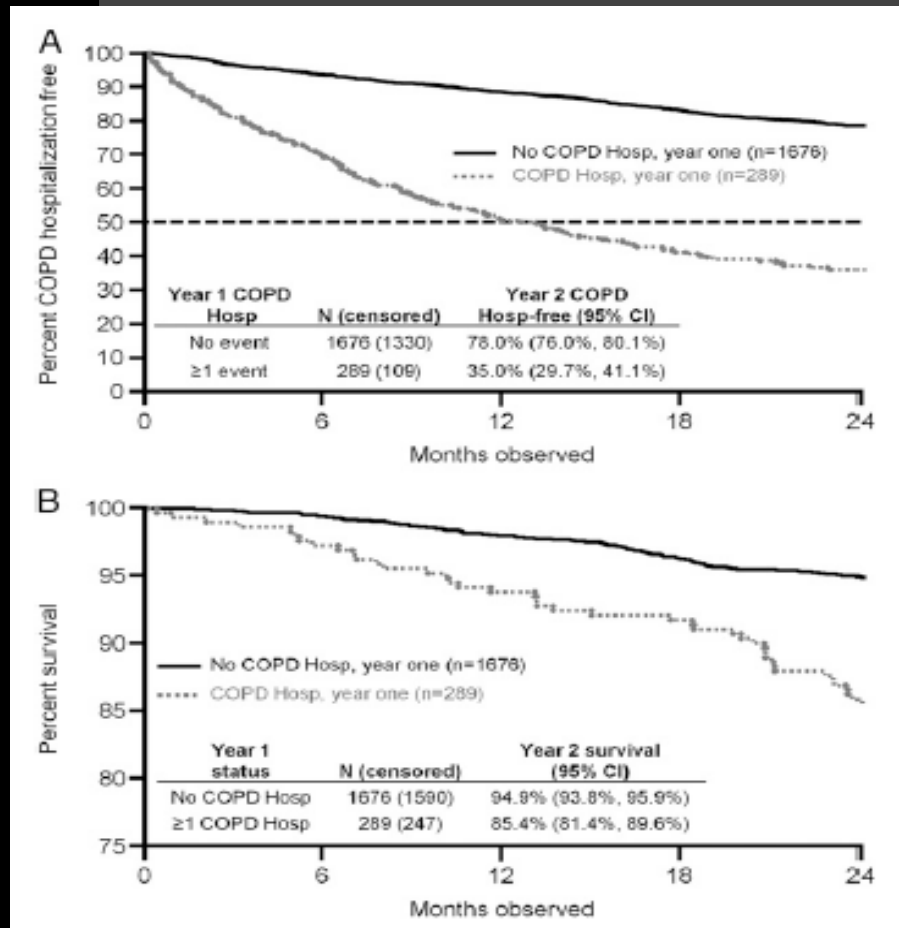
**ERS 2018
Submitted
Abstract**

EXACERBATIONS OF RESPIRATORY SYMPTOMS IN PATIENTS WITH COPD MAY NOT BE EXACERBATIONS OF COPD



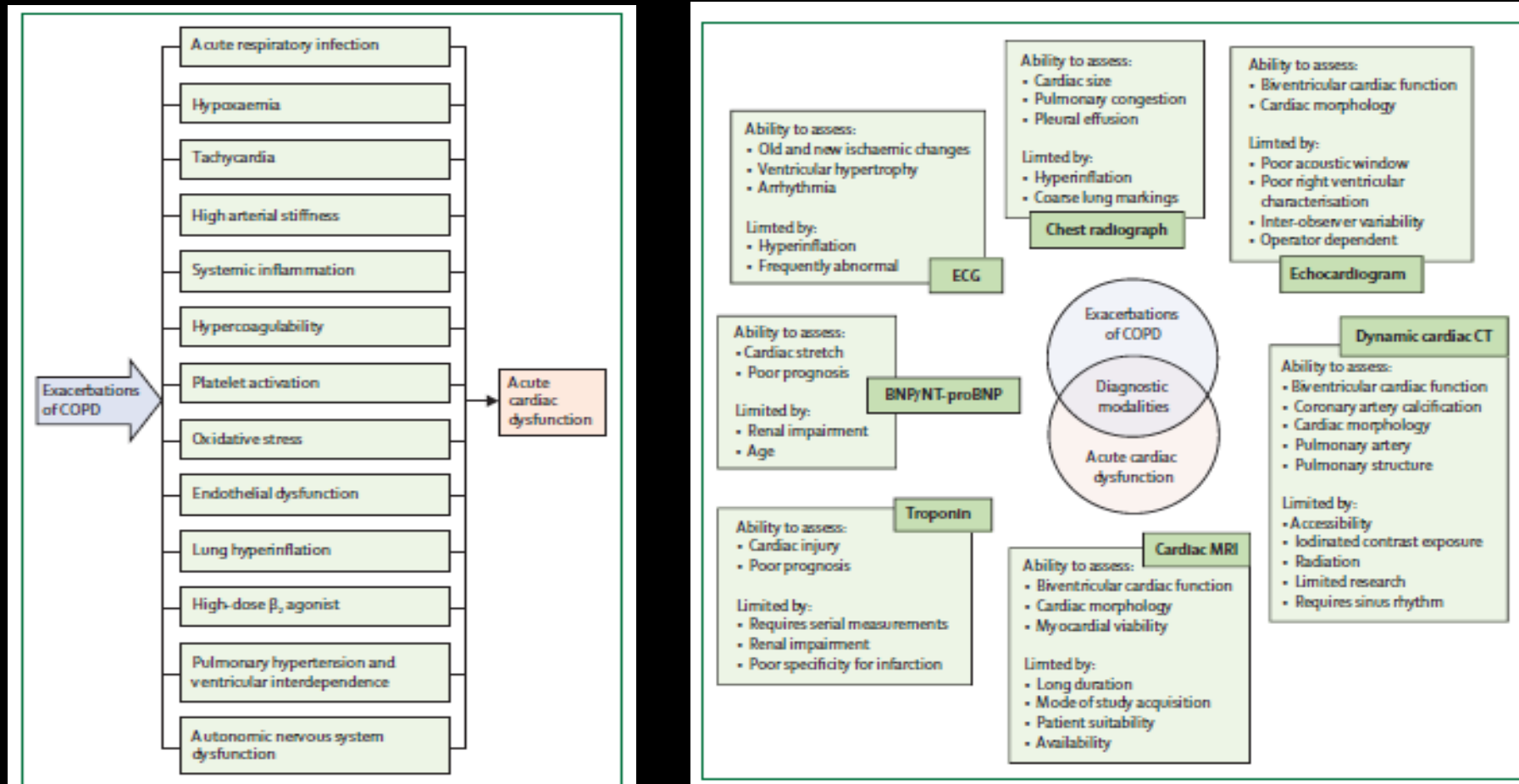
Beghé B, Verduri A, Roca M and Fabbri LM. Eur Respir J 2013; 41: 993-5
Roca M, Verduri A, Clini EM, Fabbri LM and Beghé B. Eur J Clin Invest, 2013;43:510

RISK OF MORTALITY IN PATIENTS WITH OR WITHOUT HISTORY OF HOSPITALIZATIONS DUE TO COPD EXACERBATIONS IN THE ECLIPSE STUDY

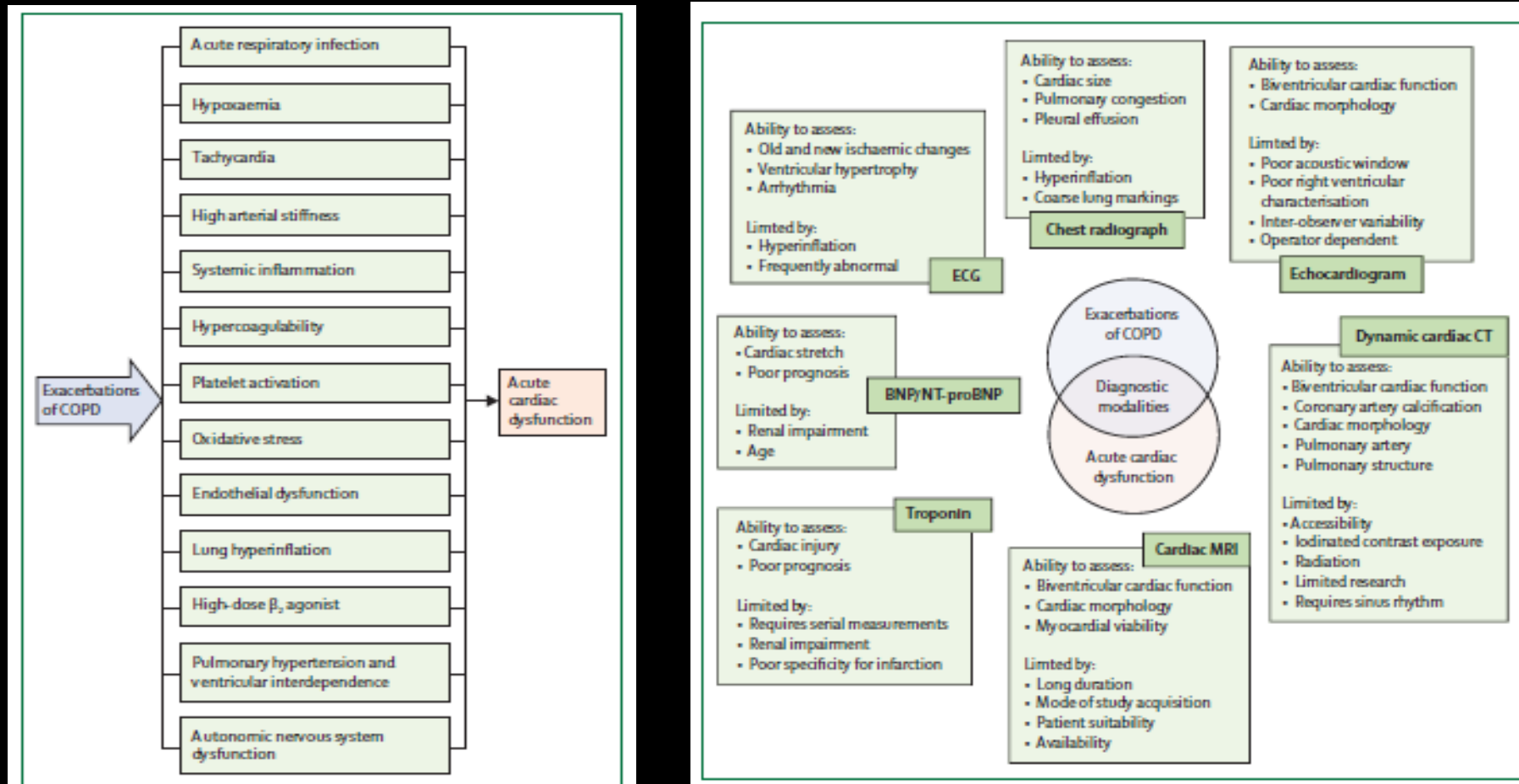


Mullerova et al, Chest 2015 Apr;147(4):999-1007

CARDIAC DYSFUNCTION DURING EXACERBATIONS OF COPD



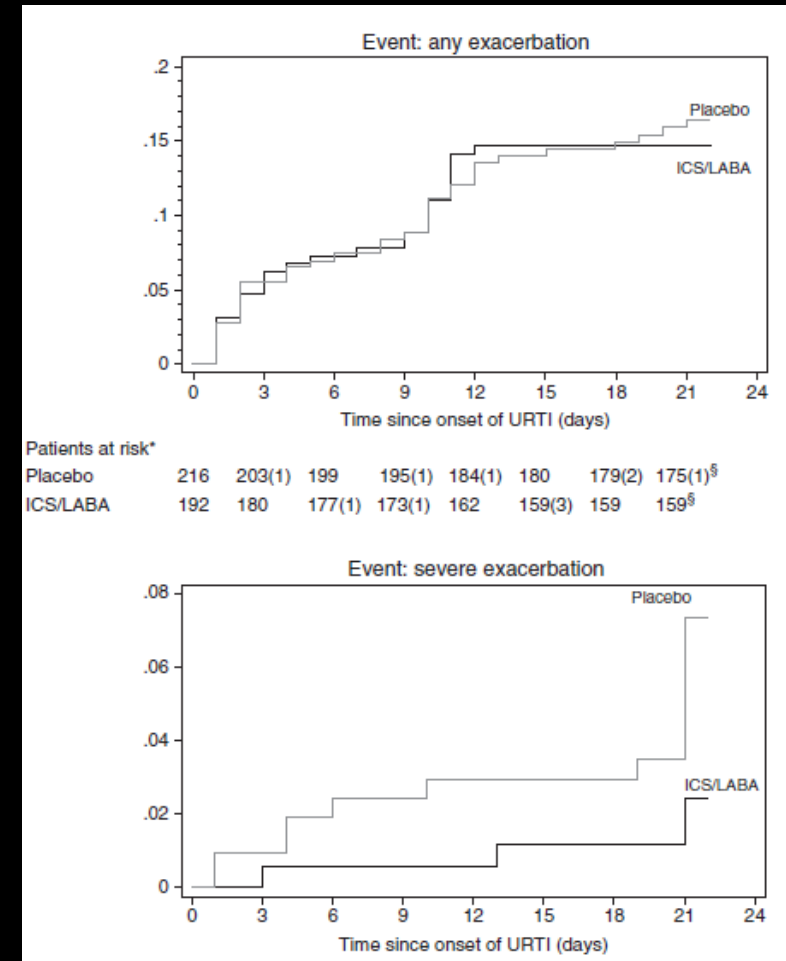
CARDIAC DYSFUNCTION DURING EXACERBATIONS OF COPD



INTENSIFIED THERAPY WITH INHALED CORTICOSTEROIDS AND LONG-ACTING B₂-AGONISTS AT THE ONSET OF UPPER RESPIRATORY TRACT INFECTION TO PREVENT CHRONIC OBSTRUCTIVE PULMONARY DISEASE EXACERBATIONS. A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

Intensified combination therapy with ICS/LABA for 10 days at URTI onset did not decrease the incidence of any COPD exacerbation but prevented severe exacerbation

Patients with more severe disease had a significant risk reduction for any exacerbation



Stolz et al, Am J Respir Cr Care Med 2018; 197(9):1136-1146

NUOVI FARMACI IN SVILUPPO PER LA BPCO

Leonardo M. Fabbri, MD, FERS

The changes in the definition and assessement of severity of COPD

The recent studies of efficacy and safety of triple therapy in a single inhaler is likely to introduce major changes in the pharmacologic management of COPD

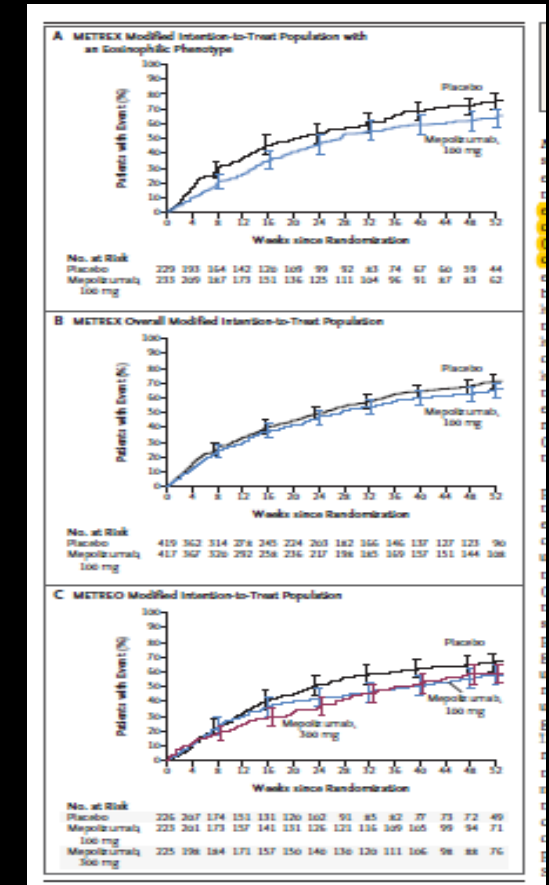
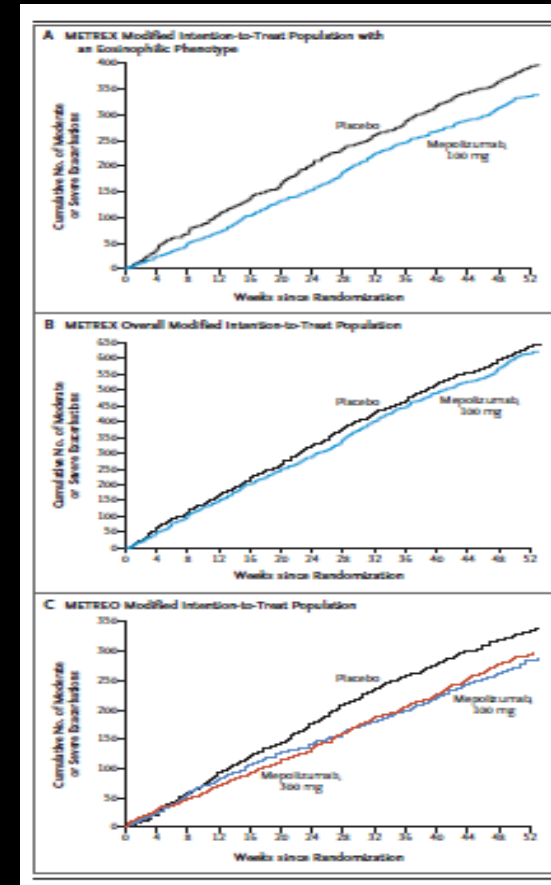
Anti IL-5 Moa, new experimental agents

TREAT THE PATIENT WITH COPD NOT JUST COPD

MEPOLIZUMAB FOR EOSINOPHILIC CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Mepolizumab at a dose of 100 mg was associated with a lower annual rate of moderate or severe exacerbations than placebo among patients with COPD and an eosinophilic Phenotype

This finding suggests that eosinophilic airway inflammation contributes to COPD exacerbations.



Pavord et al, N Engl J Med 2017; 377:1613-1629

ASTRAZENECA PRESS RELEASE

30 MAY 2018

TERRANOVA TRIAL DID NOT MEET THE PRIMARY ENDPOINT OF A STATISTICALLY-SIGNIFICANT REDUCTION OF EXACERBATIONS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

AstraZeneca and MedImmune, its global biologics research and development arm, today announced top-line results from TERRANOVA, the second of two pivotal Phase III trials for *Fasenra* (benralizumab) in patients with moderate to very severe chronic obstructive pulmonary disease (COPD)

The trial did not meet the primary endpoint of a statistically-significant reduction of exacerbations. This news follows the announcement earlier this month that the first pivotal Phase III trial, GALATHEA, did not meet its primary endpoint

EFFECTIVENESS OF ACUMAPIMOD ORAL P38 INHIBITOR IN THE TREATMENT OF ACUTE SEVERE EXACERBATIONS OF COPD: RESULTS OF THE AETHER PHASE II TRIAL

Mitogen-activated protein kinase p38, a key regulator in the inflammation pathway, is activated in COPD and by triggers of exacerbations

Acumapimod, an oral, p38 inhibitor is being investigated for the treatment of acute exacerbations

Acumapimod over 5 days of an acute exacerbation was well tolerated and demonstrated significant effects on need for re-hospitalisation for AECOPD

Acumapimod has demonstrated potential to deliver meaningful clinical benefits in the treatment of AECOPD through reduction in the patient and healthcare burden of treatment failures and recurrent exacerbations.

Wedzicha et al, Am J Respir Crit Care Med 2018;197:A7710

NUOVI FARMACI IN SVILUPPO PER LA BPCO

Leonardo M. Fabbri, MD, FERS

The changes in the definition and assessement of severity of COPD

The recent studies of efficacy and safety of triple therapy in a single inhaler is likely to introduce major changes in the pharmacologic management of COPD

Anti IL-5 Moa, new experimental agents

TREAT THE PATIENT WITH COPD NOT JUST COPD

The diagram illustrates the therapeutic approach to COPD, centered around a box titled "A MODIFICATION OF THERAPEUTIC RECOMMENDATIONS". This central box contains four treatment groups (A, B, C, D) with arrows indicating treatment escalation. The diagram shows the progression from "Cigarette smoke pollutants" to various clinical outcomes and organ systems.

Central Box: A MODIFICATION OF THERAPEUTIC RECOMMENDATIONS

- Group C:** LAMA + LABA → LAMA + LABA + ICS (Further exacerbations)
- Group D:** LAMA + LABA + ICS → LAMA + LABA + ICS (Further exacerbations)
- Group A:** Continue, stop or try alternative class of bronchodilator → A long-acting bronchodilator (LABA or LAMA)
- Group B:** LAMA + LABA → LAMA + LABA + ICS (Persistent symptoms)

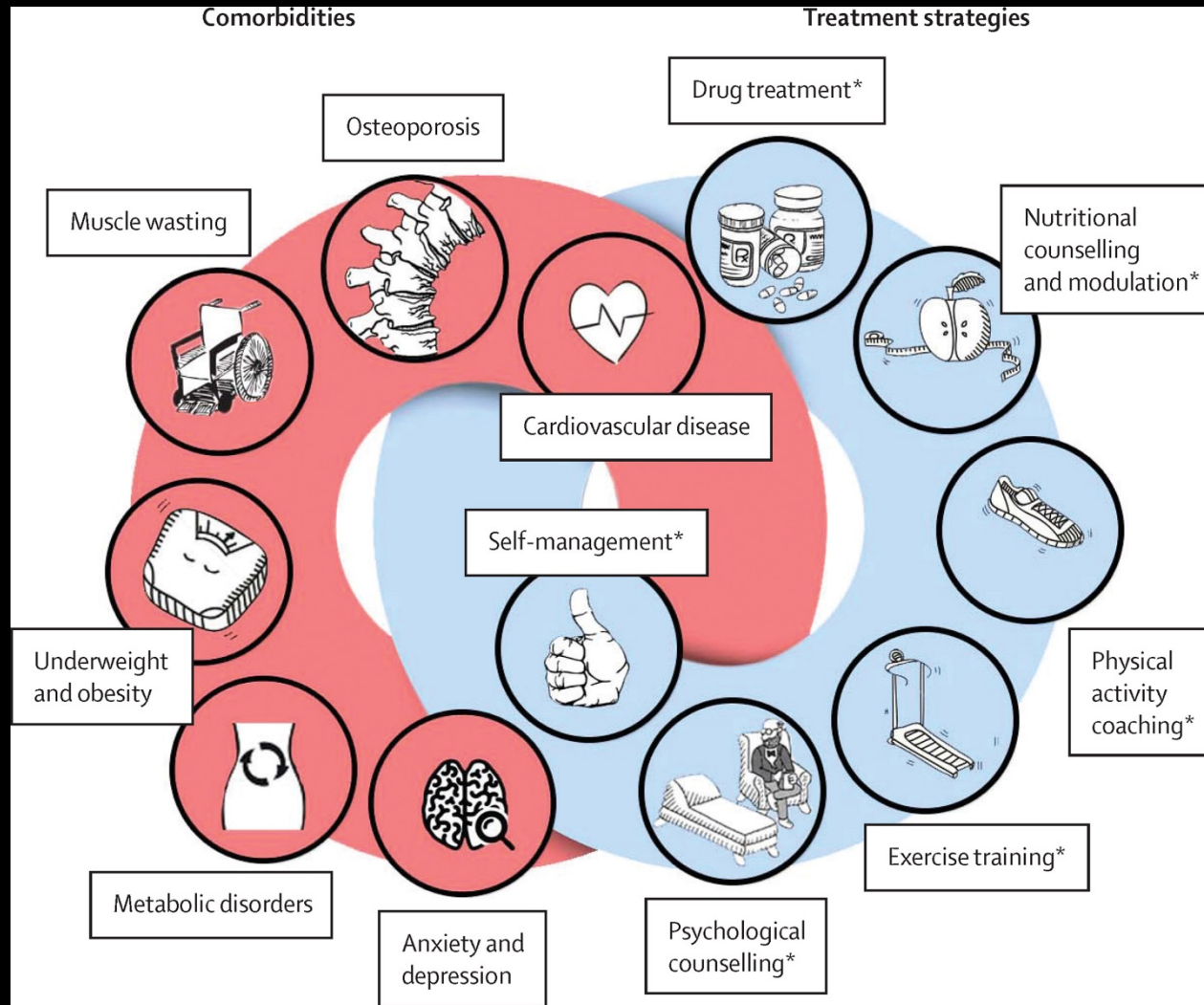
Organ Systems and Clinical Outcomes:

- Muscle:** Muscle weakness/wasting
- Pancreas:** Metabolic syndrome type 2 diabetes
- Bone:** Osteoporosis
- Liver:** +ve
- Heart:** Cardiovascular events
- Lung:** Central focus of the diagram

Biomarkers:

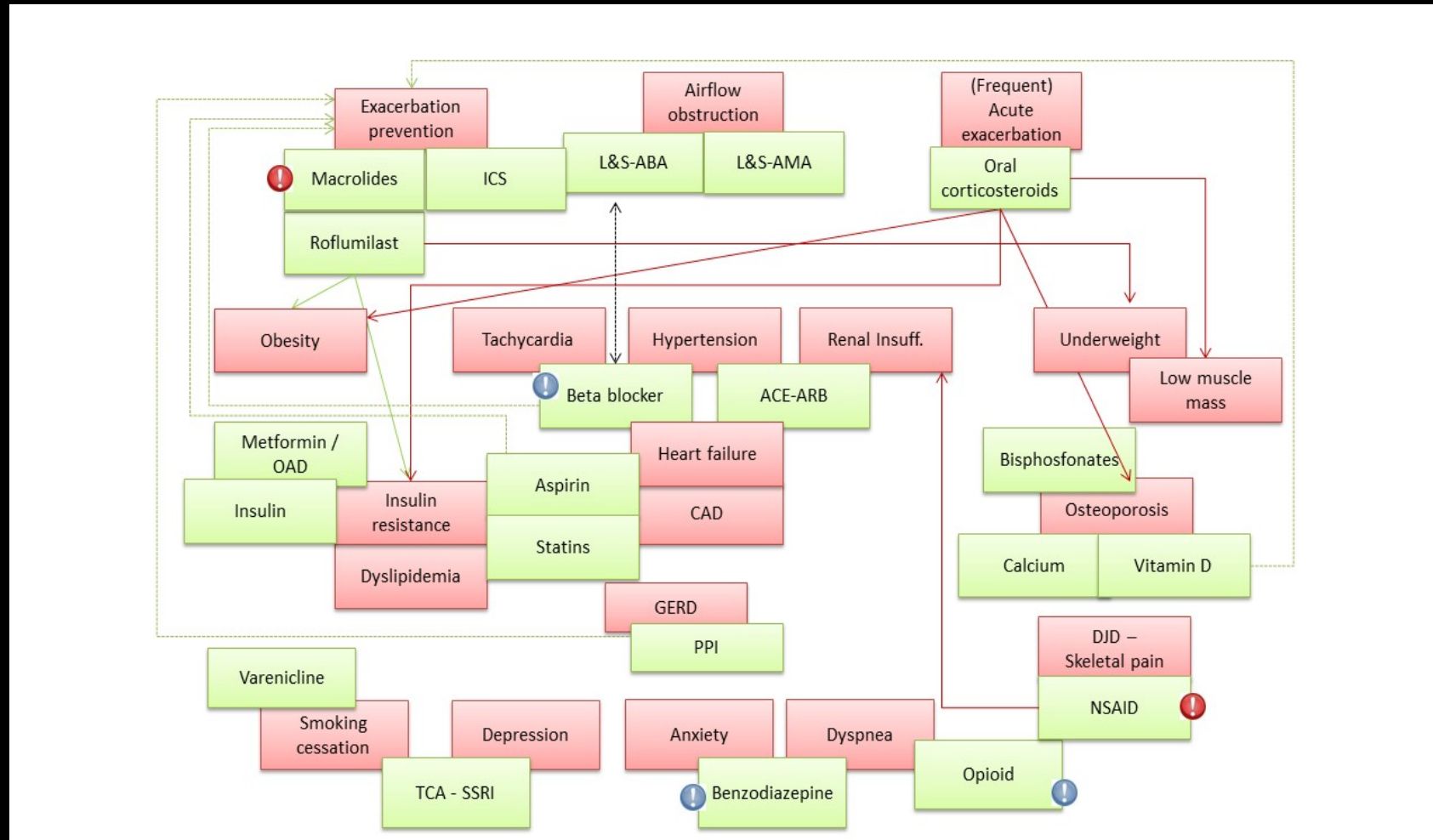
- CRP:** C-reactive protein, shown as a box that receives input from "Liver" and "Cardiovascular events", and has a dashed line connecting it to "CRP" (another box).

Figure 1



Vanfleteren et al. Lancet Respir Med 2016 Nov;4(11):911-924

THE PHARMACOLOGICAL PERSPECTIVE FOR AN INTEGRATED MANAGEMENT OF COPD AND ITS COMORBIDITIES

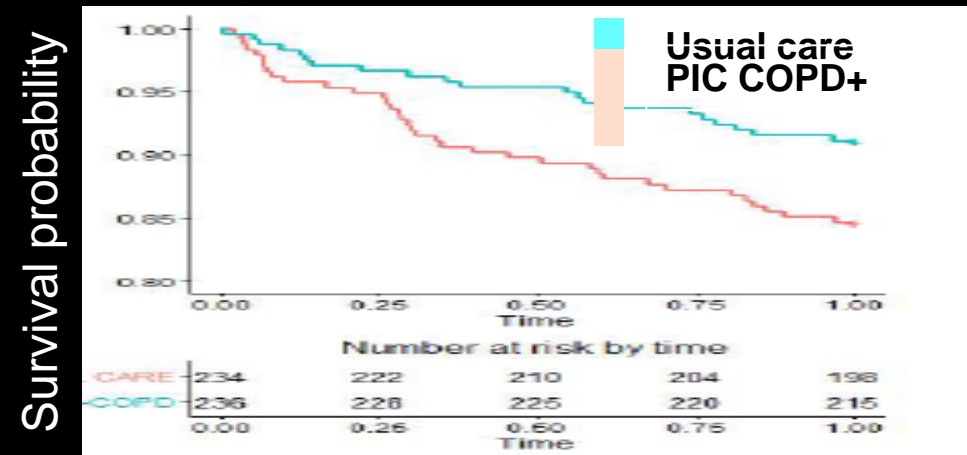
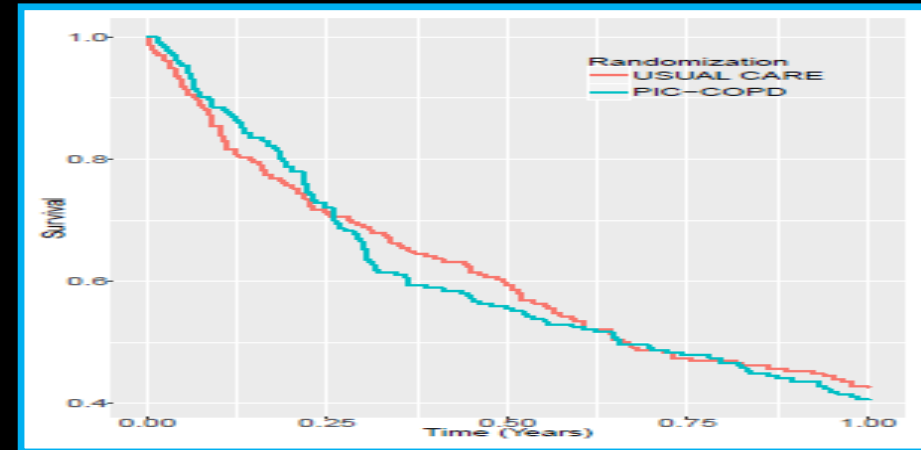


Vanfleteren et al. Lancet Respir Med 2016

PROGRAM OF INTEGRATED CARE FOR PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND MULTIPLE COMORBIDITIES (PIC COPD+): A RANDOMIZED CONTROLLED TRIAL

Our model resulted in

1. fewer ED presentations
2. hospital admissions
3. Estimated risk of death in the intervention group was nearly half that of the control



Istanboulia et al, Am J Respir Cr Care Med, April 2017, Abstract 6739

TIME FOR A LONGER AND BETTER LIFE FOR PATIENTS WITH COPD

In this issue of the journal are two important management studies consistently showing a considerable reduction of mortality in patients comprehensively treated with management plans that address not only the COPD component but also the complexity of multimorbidities

We believe it is time to conduct a properly designed and powered study with the goal of combining all these positive observations to achieve a better quality of life for patients with severe multimorbidities. Let's move this forward.

Vanfleteren, Ullman, Fabbri, Eur Respir J, January 2018

NUOVI FARMACI IN SVILUPPO PER LA BPCO

Leonardo M. Fabbri, MD, FERS

The changes in the definition and assessement of severity of COPD

The recent studies of efficacy and safety of triple therapy in a single inhaler is likely to introduce major changes in the pharmacologic management of COPD

Anti IL-5 Moa, new experimental agents

TREAT THE PATIENT WITH COPD NOT JUST COPD



PNEUMOLOGIA 2018
MILANO, 14 – 16 GIUGNO 2018
CENTRO CONGRESSI PALAZZO DELLE STELLINE



UNIVERSITY OF
GOTHENBURG



Nuovi farmaci in sviluppo per la BPCO

Leonardo M. Fabbri, MD, FERS

Professor of Respiratory and Internal Medicine, University of Modena and Reggio Emilia, (-2016)
Eminent Scholar of Respiratory and Internal Medicine, University of Ferrara
Visiting Professor of Respiratory and Internal Medicine, COPD Center, University of Gothenburg