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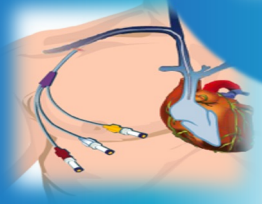
Dalla riduzione delle riacutizzazioni al dato di mortalità: la linearità della triplice terapia nella BPCO

3° Edizione

Area Critica in Medicina Interna

12 Aprile 2025

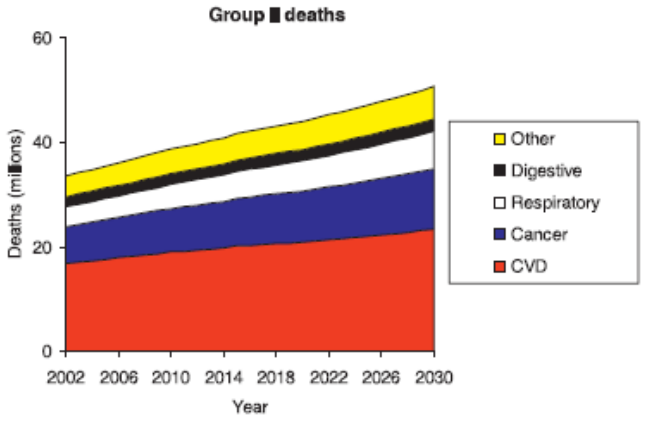


Savona
Nh Darsena Hotel

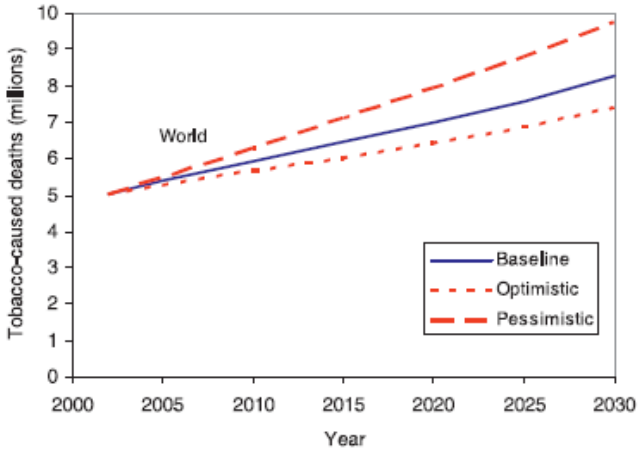
Projection of global mortality and burden of disease from 2002 from 2030

Table 1. Projected Average Annual Rates of Change in Age-Standardized Death Rates for Selected Causes: World, 2002–2020

Group	Cause	Average Annual Change (Percent) in Age-Standardized Death Rate	
		Males	Females
All Causes		−0.8	−1.1
Group I		−1.4	−1.9
	Tuberculosis	−5.4	−5.3
	HIV/AIDS	3.0	2.1
	Malaria	−1.3	−1.5
	Other infectious diseases	−3.4	−3.3
	Respiratory infections	−2.7	−3.4
	Perinatal conditions[a]	−1.7	−1.9
	Other Group I	−3.0	−3.6
Group II		0.0	−0.8
	Cancer	−0.2	−0.4
	Lung cancer	0.1	0.3
	Diabetes mellitus	1.1	1.3
	Cardiovascular diseases	−1.1	−1.2
	Respiratory diseases	0.3	−0.1
	Digestive diseases	−1.3	−1.7
	Other Group II	−0.7	−1.1
Group III		0.0	−0.2
	Unintentional injuries	−0.2	−0.2
	Road traffic accidents	1.1	1.1
	Intentional injuries	0.2	−0.2
	Self-inflicted injuries	−0.3	−0.4
	Violence	0.4	0.2



Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med. 2006 Nov;3(11):e442. doi: 10.1371/journal.pmed.0030442. PMID: 17132052; PMCID: PMC1664601.



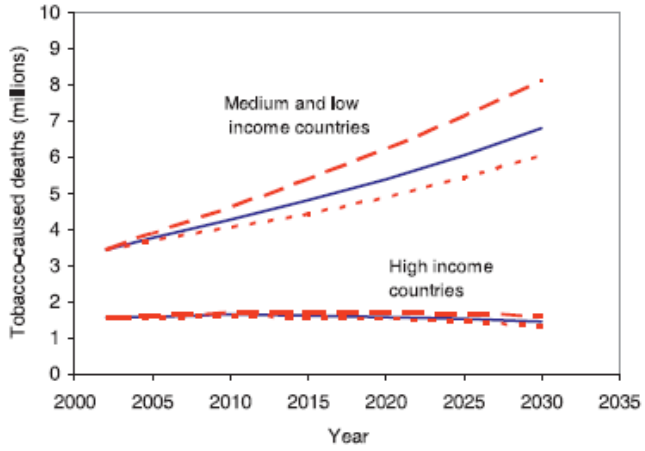


Figure 8. Projected Numbers of Tobacco-Caused Deaths for the World and for High-Income and Middle- plus Low-Income Countries, Three Scenarios, 2002–2030

doi: 10.1371/journal.pmed.0030442.g008

DEFINITION

An exacerbation of chronic obstructive pulmonary disease (ECOPD) is defined as an event characterized by increased dyspnea and/or cough and sputum that worsens in < 14 days which may be accompanied by tachypnea and/or tachycardia and is often associated with increased local and systemic inflammation caused by infection, pollution, or other insult to the airways.[304]

Riacutizzazione di BPCO

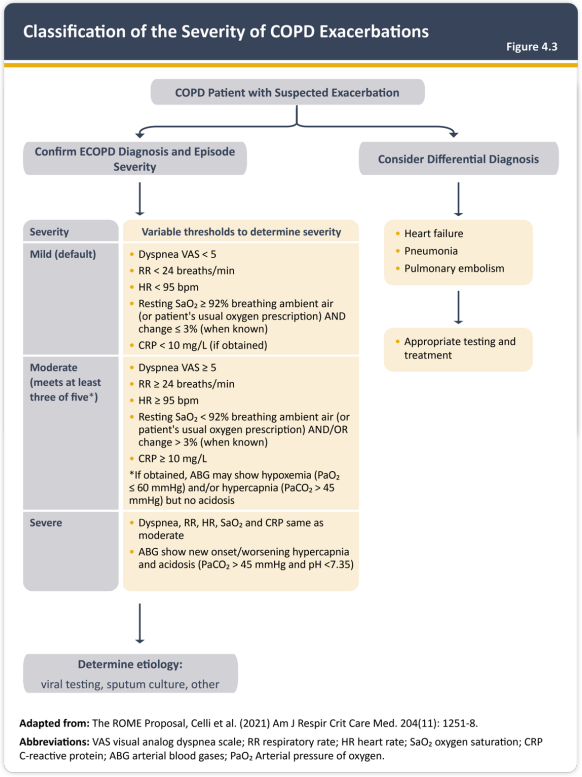
Exacerbations: Diagnosis and Assessment

Figure 4.2

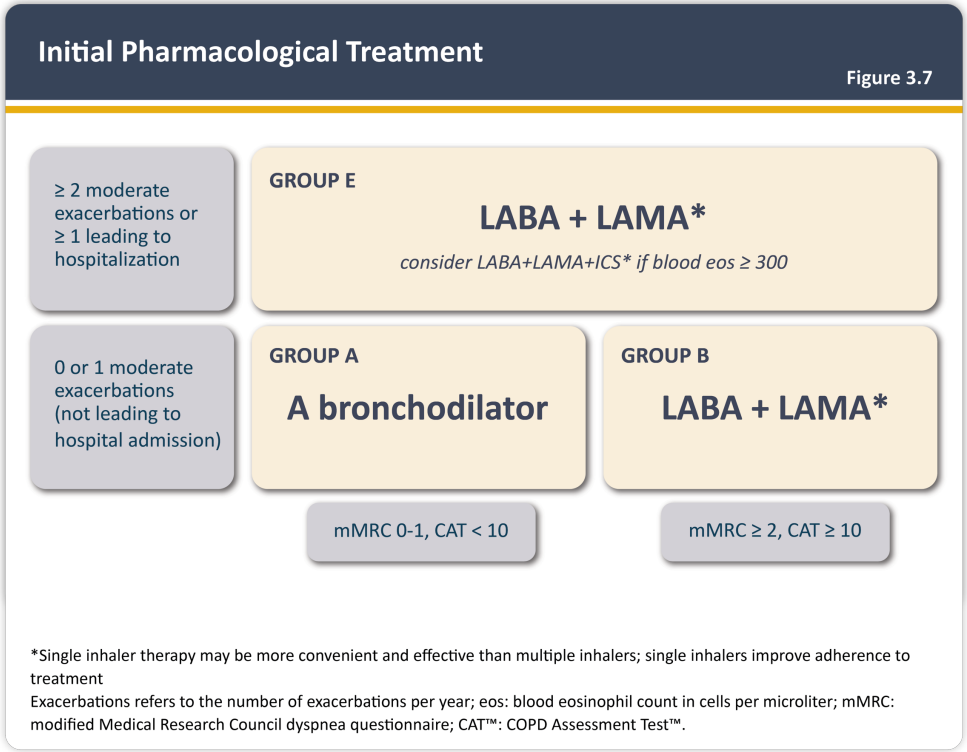
1.	Complete a thorough clinical assessment for evidence of COPD and potential respiratory and non-respiratory concomitant diseases, including consideration of alternative causes for the patient's symptoms and signs: primarily pneumonia, heart failure, and pulmonary embolism.
2.	**Assess:** a. Symptoms, severity of dyspnea that can be determined by using a VAS, and documentation of the presence of cough. b. Signs (tachypnea, tachycardia), sputum volume and color, and respiratory distress (accessory muscle use).
3.	Evaluate severity by using appropriate additional investigations such as pulse oximetry, laboratory assessment, CRP, arterial blood gases.
4.	Consider appropriate place of care.
5.	Establish the cause of the event (viral, bacterial, environmental, other).

Abbreviations: COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; VAS = visual analog scale.

Riacutizzazione di BPCO



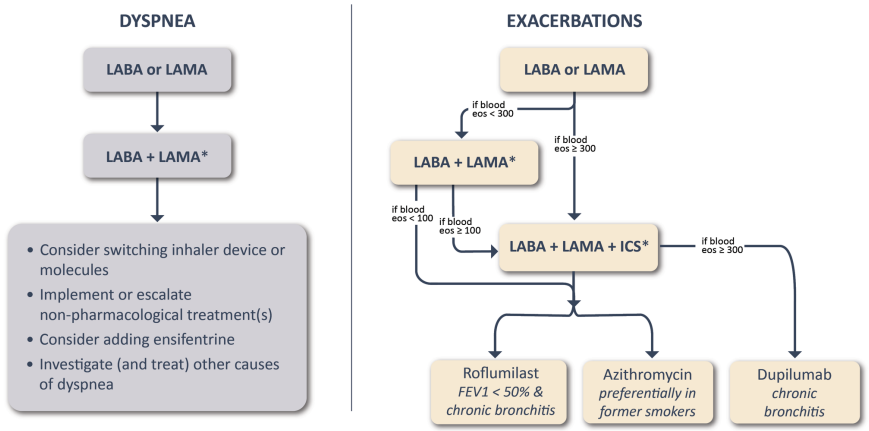
TERAPIA INIZIALE DELLA BPCO



FOLLOW-UP

Follow-up Pharmacological Treatment

Figure 3.9

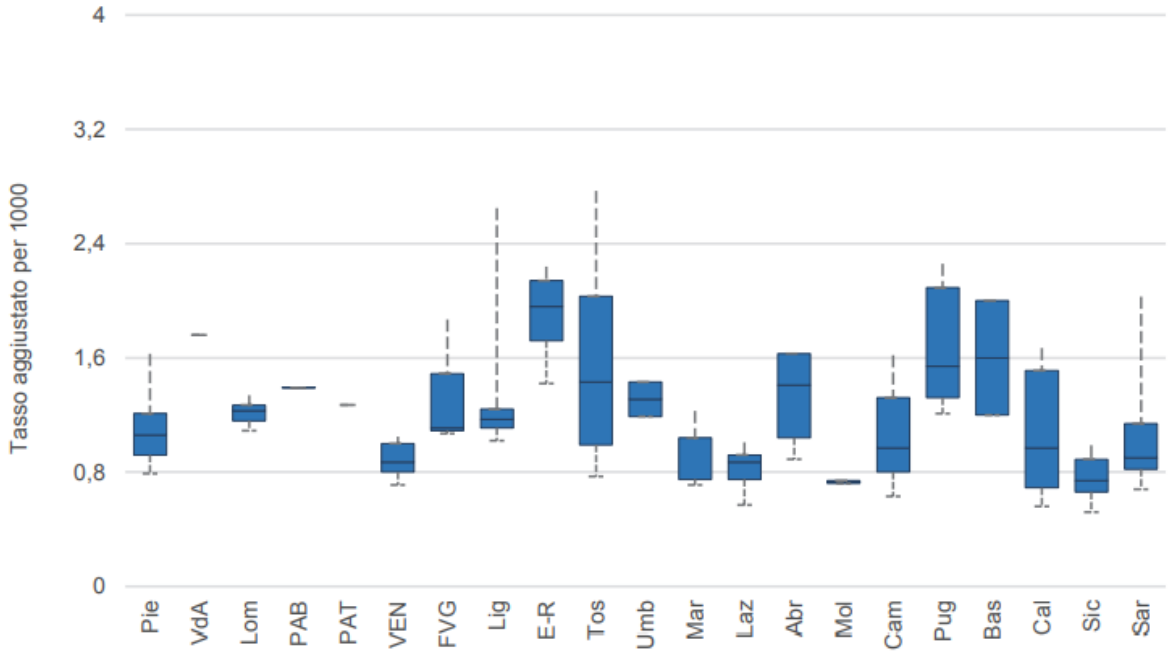


*Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment.

Consider de-escalation of ICS if pneumonia or other considerable side-effects. In case of blood eos ≥ 300 cells/µl de-escalation is more likely to be associated with the development of exacerbations.

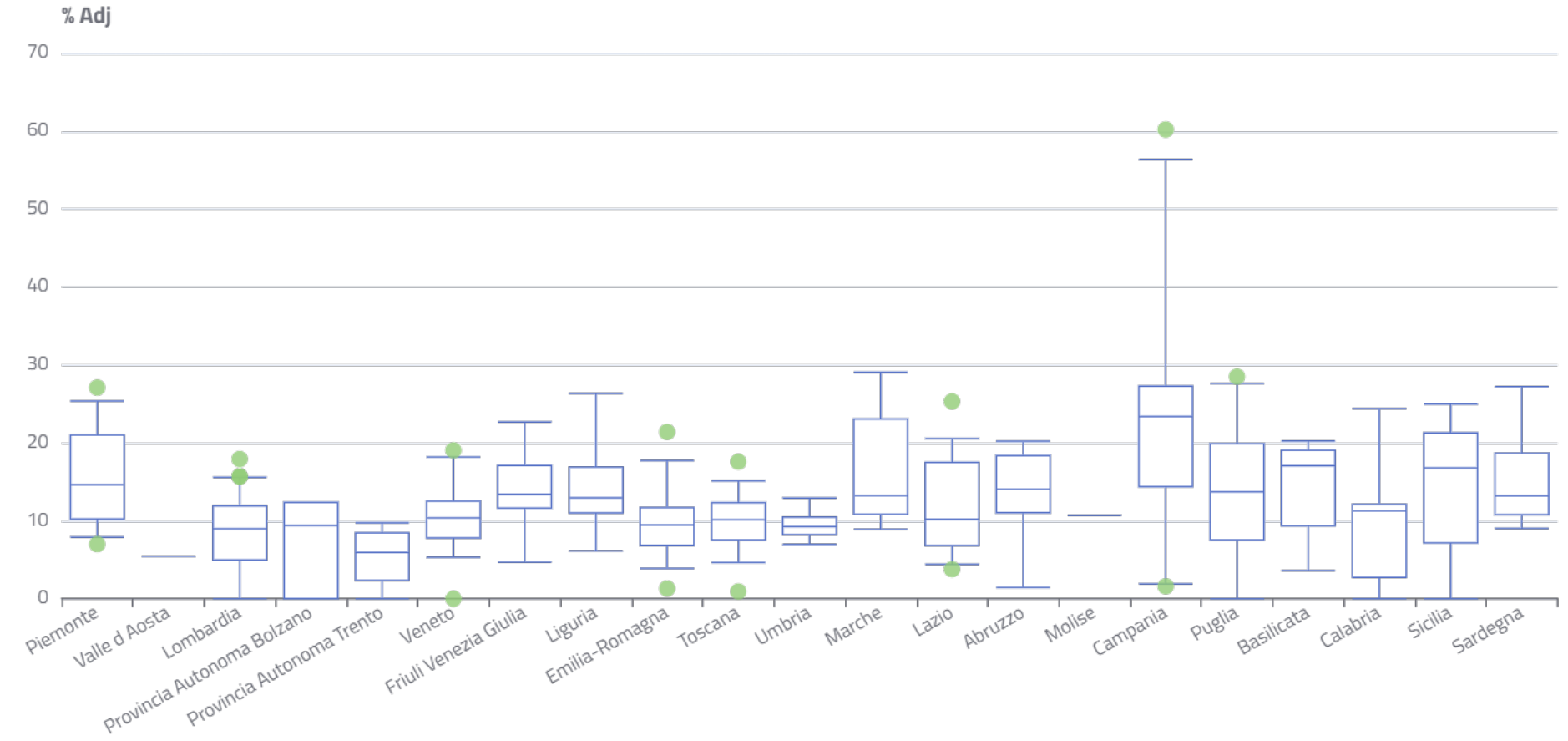
Exacerbations refers to the number of exacerbations per year.

Broncopneumopatia cronica ostruttiva: tassi di ospedalizzazione per area geografica. Italia, 2022



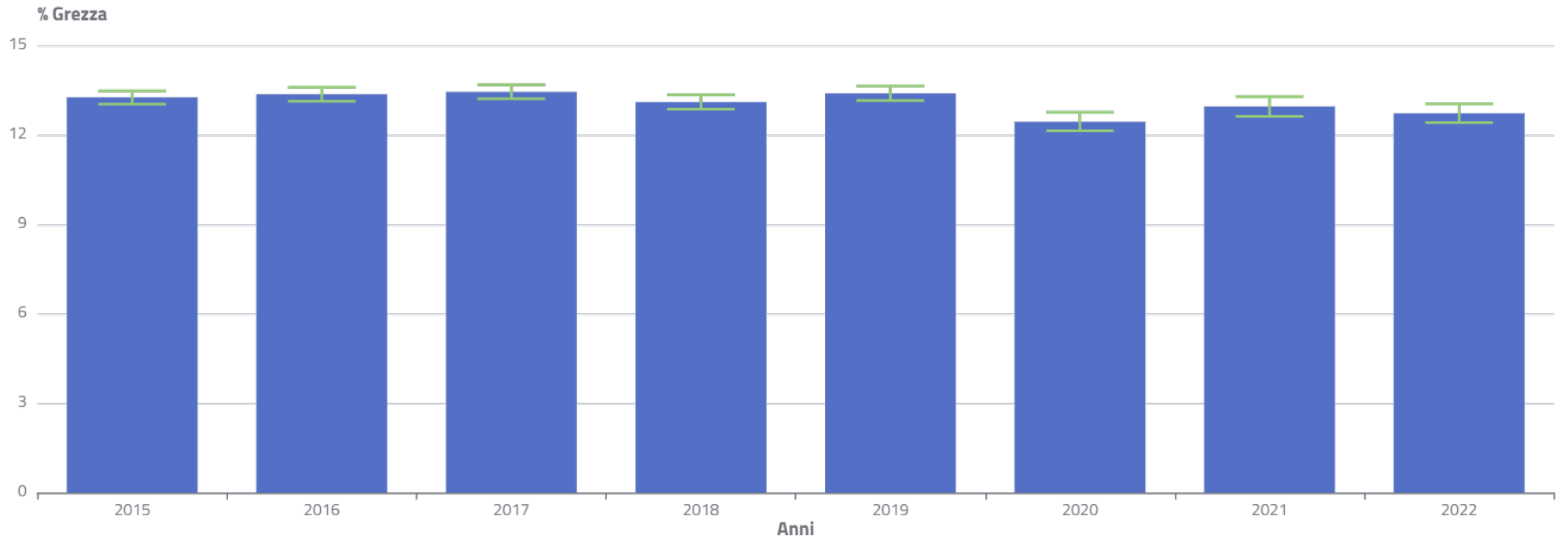
PNE 2022

BPCO riacutizzata: mortalità a 30 giorni (2022)

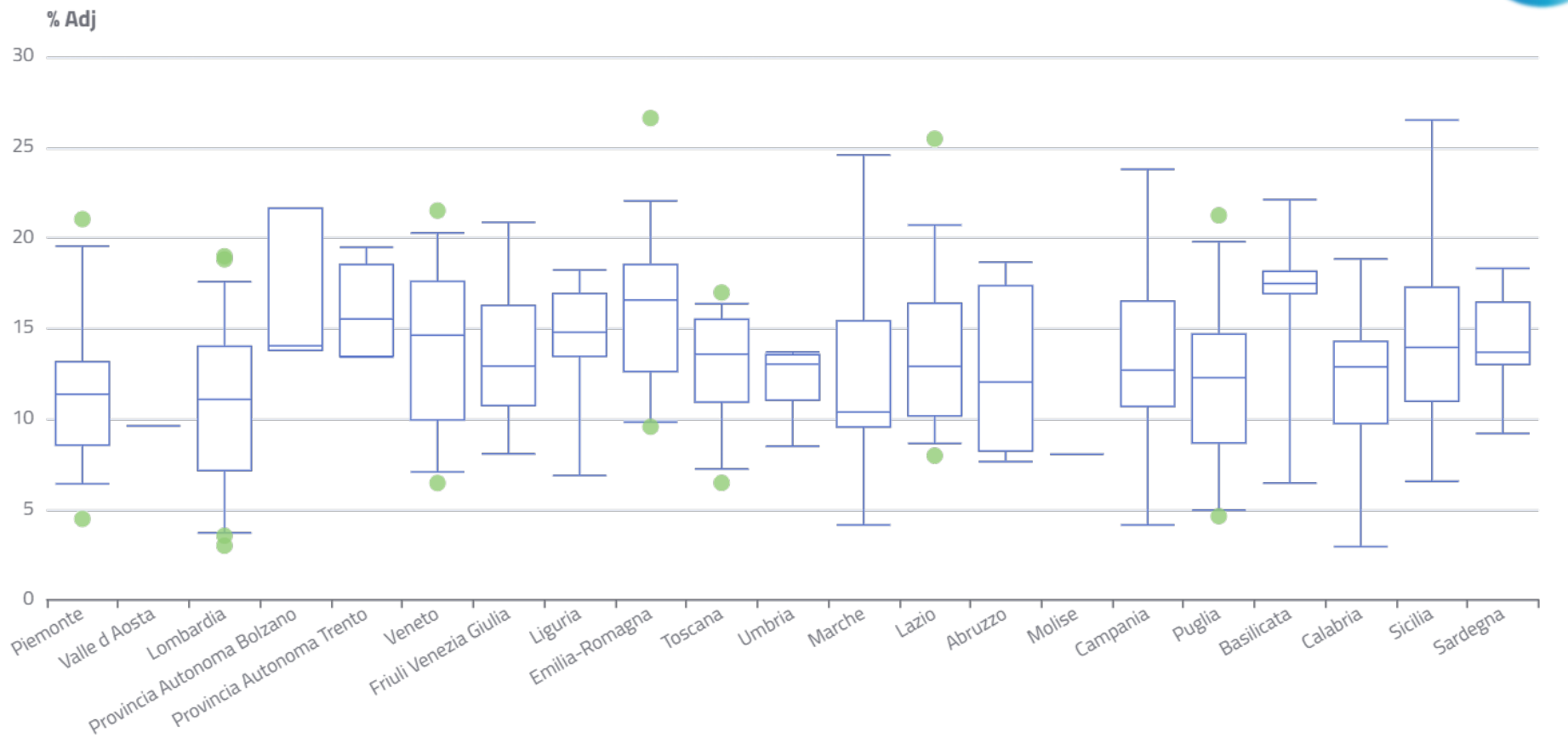


PNE 2022

BPCO riacutizzata: riammissioni ospedaliere a 30 giorni

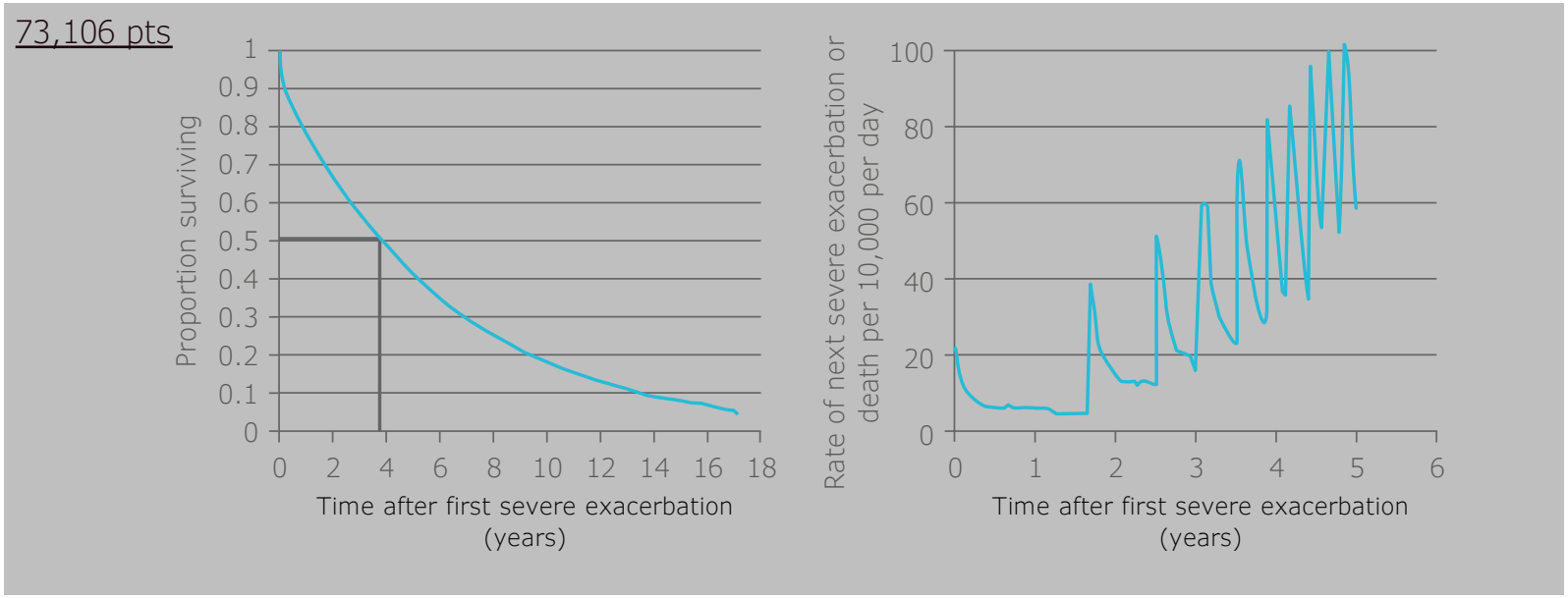


BPCO riacutizzata: riammissioni ospedaliere a 30 giorni (2022)



PNE 2022

IMPATTO DELLE RIACUTIZZAZIONI SULLA MORTALITA'



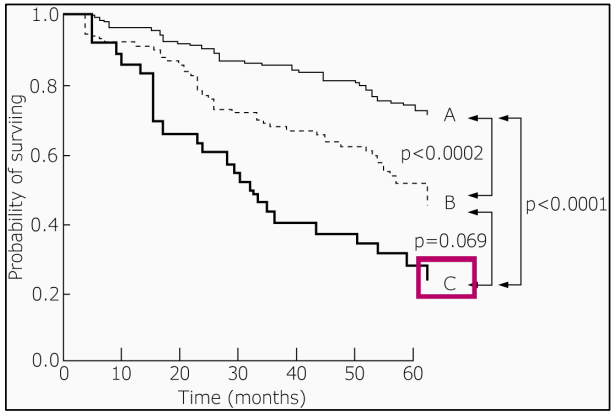
Un rapido decline dello stato di salute ed un aumentato rischio di morte dopo la seconda riacutizzazione severa è stato osservato nelle settimane successive seconda riacutizzazione

Adapted from Suissa S et al. Thorax 2012; 67: 957–63

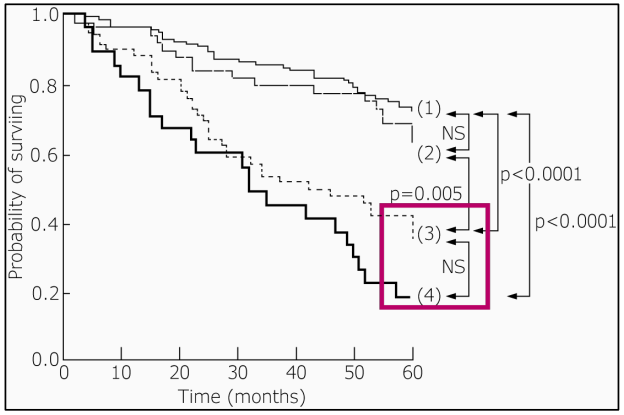
Exacerbation risk

Exacerbations of COPD (ECOPD) are episodes of acute respiratory symptom worsening often associated with increased local and systemic inflammation (see **Chapter 4**).[434-437] ECOPD are key events in the natural history of the disease because they impact significantly on the health status of the patient (often for a prolonged period of time), enhance the rate of lung function decline, worsen the prognosis of the patient and are associated with most of the healthcare costs of COPD.[438] ECOPD rates vary greatly between patients[439] and during follow-up.[440] The best predictor of having frequent exacerbations (defined as two or more exacerbations per year) is the previous history of exacerbations.[439] Worsening of airflow obstruction is associated with an increasing prevalence of exacerbations, hospitalization[377,441] and risk of death.[168,442]

Curve di sopravvivenza Kaplan-Meier per frequenza e gravità delle riacutizzazioni



Elaborato da Fig.1



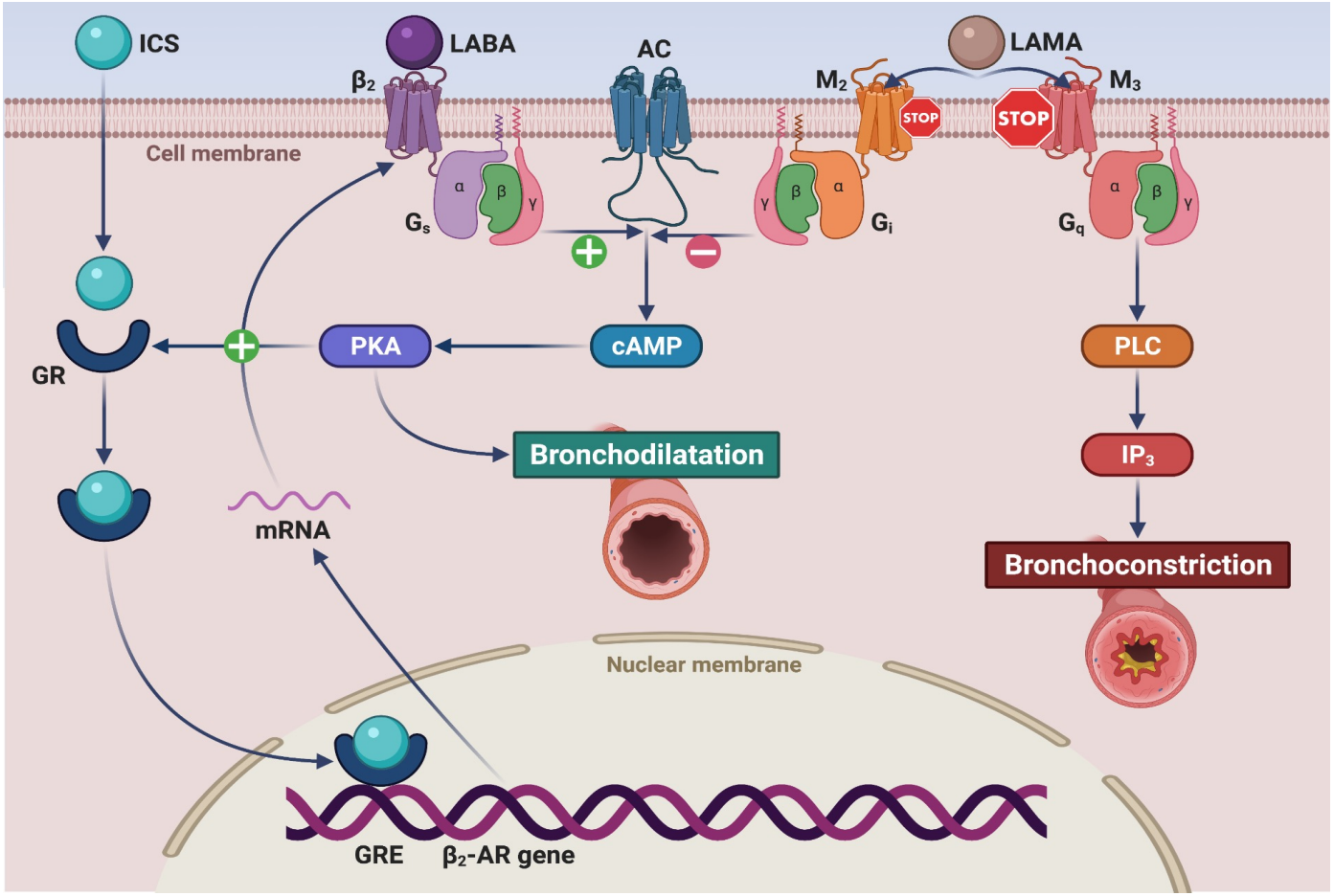
Curve di sopravvivenza di Kaplan-Meier **per frequenza di riacutizzazioni** in pazienti con BPCO: gruppo A, pazienti senza riacutizzazioni di BPCO; gruppo B, pazienti con 1-2 esacerbazioni acute di BPCO che richiedono una gestione ospedaliera; gruppo C, pazienti con >3 esacerbazioni acute di BPCO.

Curve di sopravvivenza di Kaplan-Meier **per gravità delle riacutizzazioni** nei pazienti con BPCO: (1) nessuna riacutizzazione della BPCO; (2) pazienti con esacerbazioni acute di BPCO che richiedono visite ai servizi di emergenza senza ricovero; (3) pazienti con esacerbazioni acute di BPCO che richiedono un ricovero ospedaliero; (4) pazienti con riammissioni.

Questo studio mostra per la prima volta che le riacutizzazioni gravi di BPCO hanno un impatto negativo indipendente sulla prognosi del paziente.
Infatti, la **mortalità aumenta con la frequenza e la gravità delle riacutizzazioni**

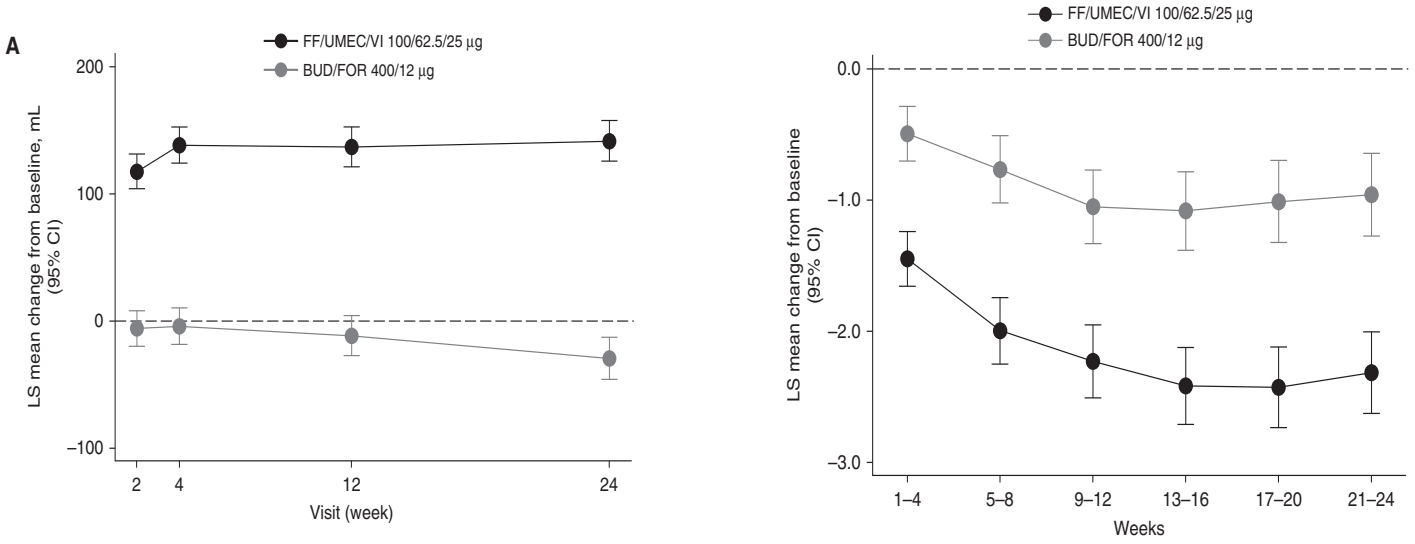
Soler-Cataluña J.J. et al. Thorax. 2005;60(11):925-31.

TRIPLICE TERAPIA



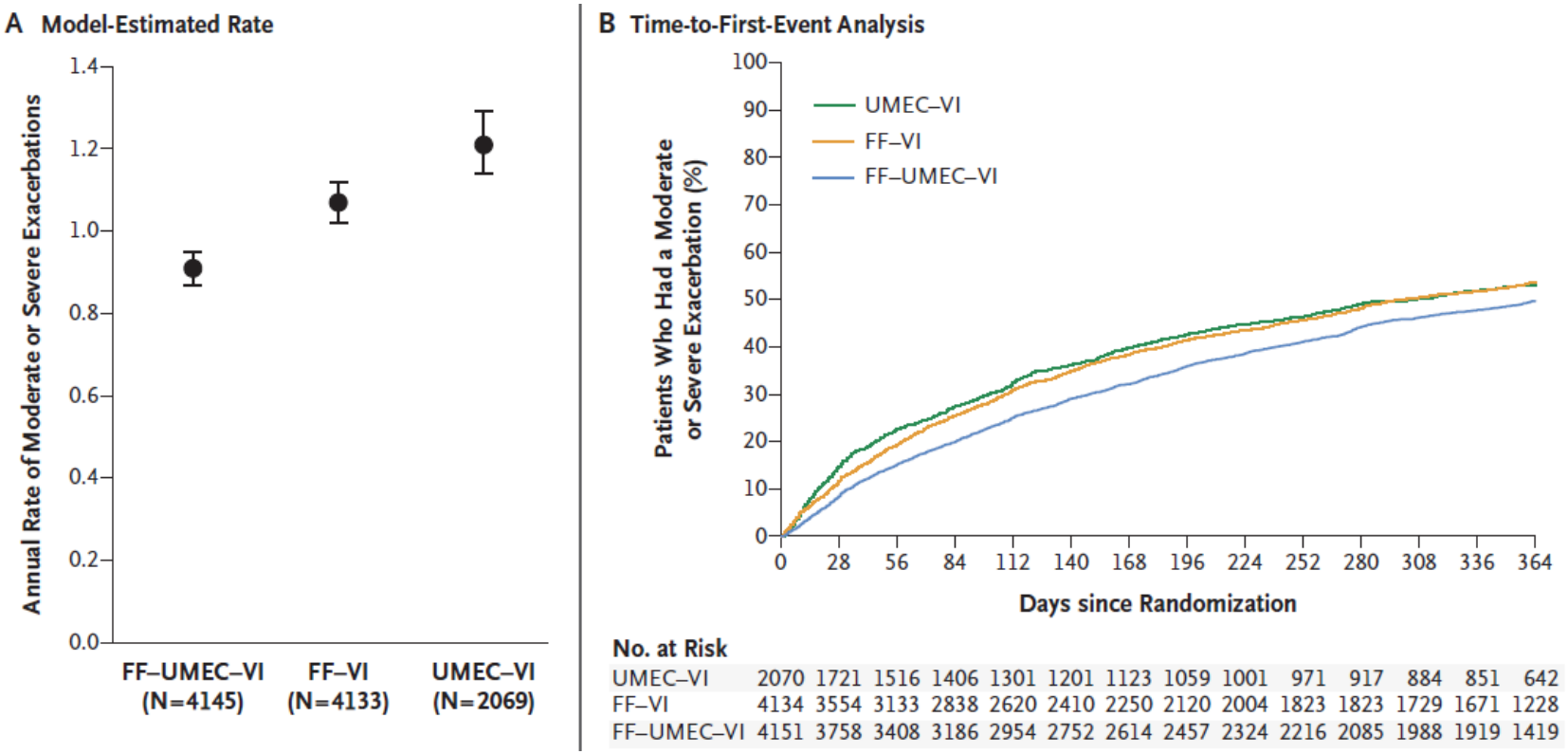
Pelaia C et al. *Expert Rev Respir Med* 16:183-195, 2022

FULFIL Trial: Once-Daily Triple Therapy in Patients with Chronic Obstructive Pulmonary Disease



Lipson DA et al. *Am J Respir Crit Care Med* 2017;196:438-446

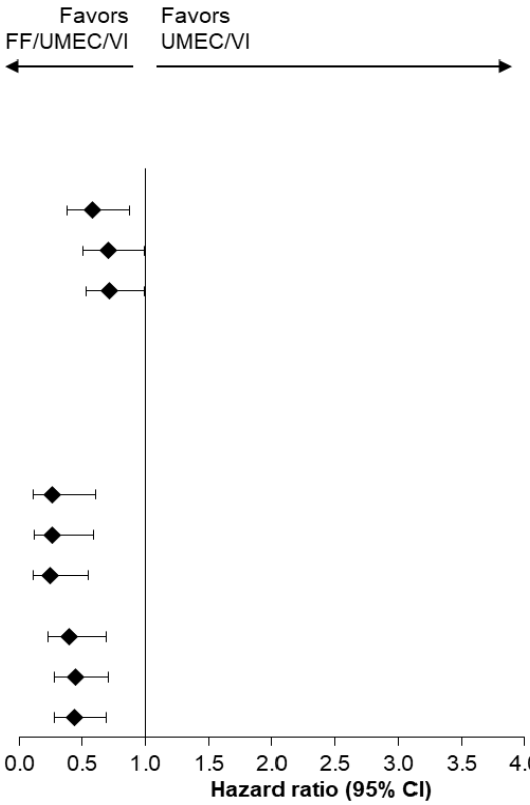
STUDIO IMPACT:ESACERBAZIONI



No. at Risk

UMEC–VI	2070	1721	1516	1406	1301	1201	1123	1059	1001	971	917	884	851	642
FF–VI	4134	3554	3133	2838	2620	2410	2250	2120	2004	1823	1823	1729	1671	1228
FF–UMEC–VI	4151	3758	3408	3186	2954	2752	2614	2457	2324	2216	2085	1988	1919	1419

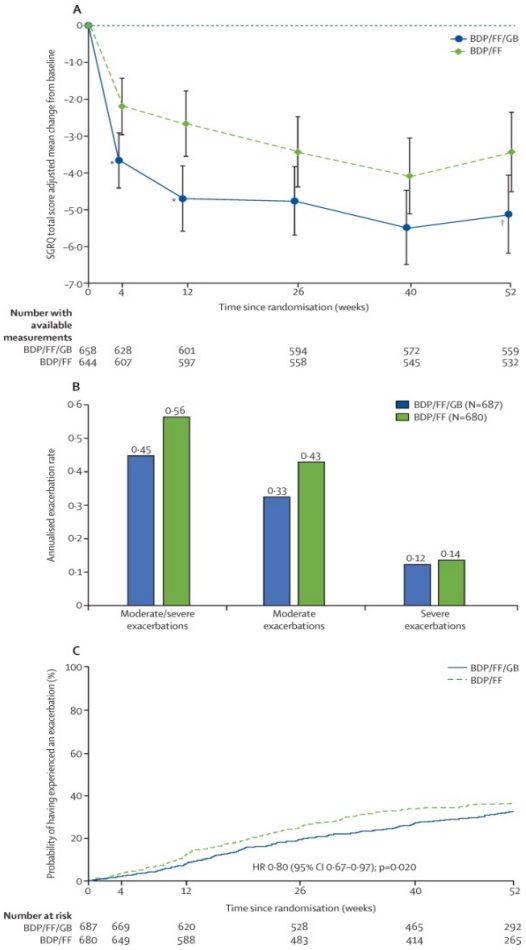
IMPACT (all-cause mortality)



	Patients with an event, n/N (%) FF/UMEC/VI	UMEC/VI	Hazard ratio (95% CI)	p-value
Overall				
On-treatment ACM	50/4151 (1.20)	39/2070 (1.88)	0.58 (0.38, 0.88)	0.011
ACM including off-treatment data	89/4151 (2.14)	60/2070 (2.90)	0.71 (0.51, 0.99)	0.043
ACM including off-treatment data (With additional vital status follow-up)	98/4151 (2.36)	66/2070 (3.19)	0.72 (0.53, 0.99)	0.042
Within 30 days				
On-treatment ACM	0/4151 (0)	7/2070 (0.34)	NA	
ACM including off-treatment data	0/4151 (0)	7/2070 (0.34)	NA	
ACM including off-treatment data (With additional vital status follow-up)	0/41551 (0)	7/2070 (0.34)	NA	
Within 60 days				
On-treatment ACM	8/4151 (0.19)	15/2070 (0.72)	0.26 (0.11, 0.61)	0.002
ACM including off-treatment data	9/4151 (0.22)	17/2070 (0.82)	0.26 (0.12, 0.59)	0.001
ACM including off-treatment data (With additional vital status follow-up)	9/4151 (0.22)	18/2070 (0.87)	0.25 (0.11, 0.55)	<0.001
Within 180 days				
On-treatment ACM	23/4151 (0.55)	27/2070 (1.30)	0.40 (0.23, 0.69)	0.001
ACM including off-treatment data	35/4151 (0.84)	38/2070 (1.84)	0.45 (0.28, 0.71)	<0.001
ACM including off-treatment data (With additional vital status follow-up)	36/4151 (0.87)	40/2070 (1.93)	0.44 (0.28, 0.69)	<0.001

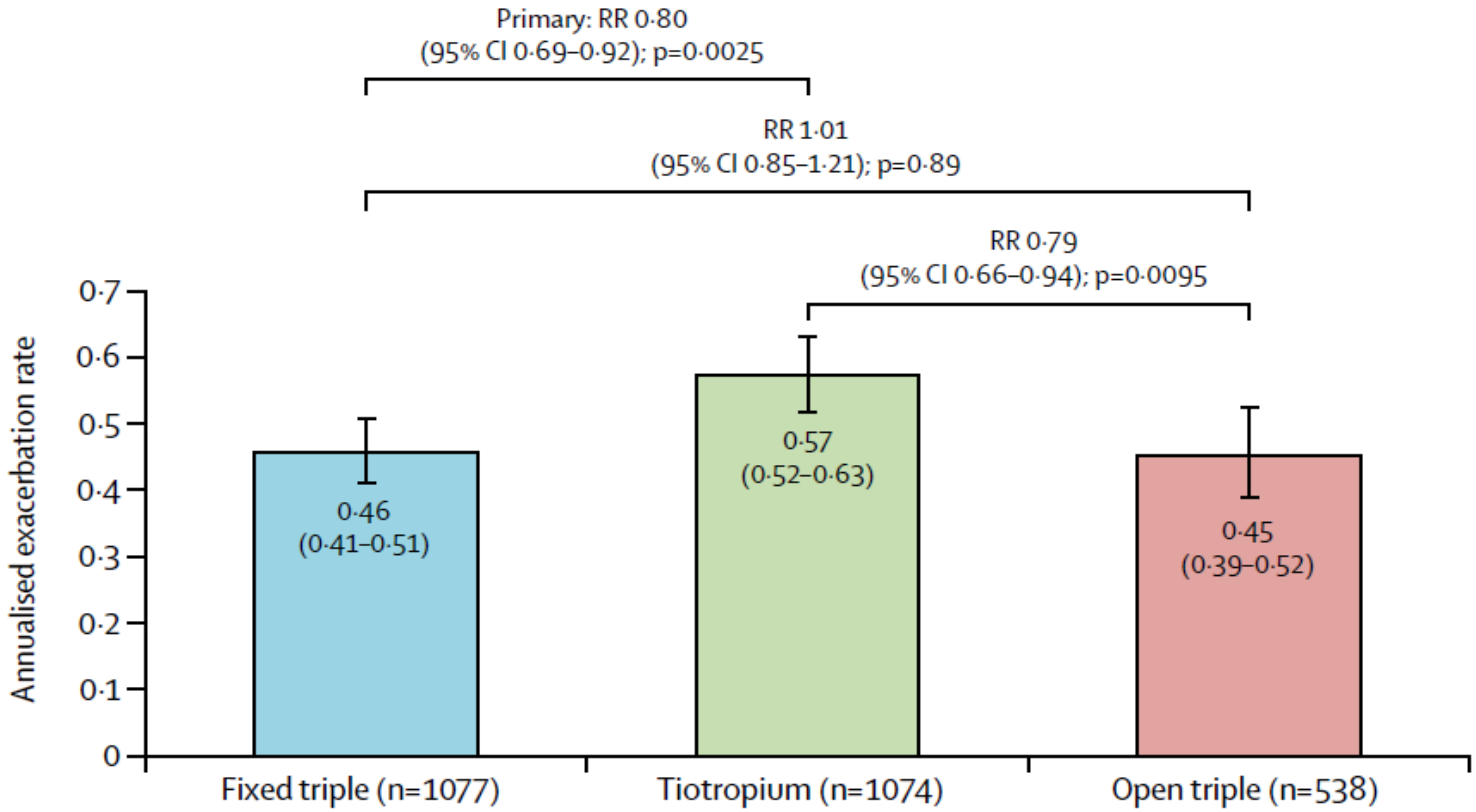
Lipson DA et al. *Am J Respir Crit Care Med* 201:1508-1516, 2020

STUDIO TRILOGY



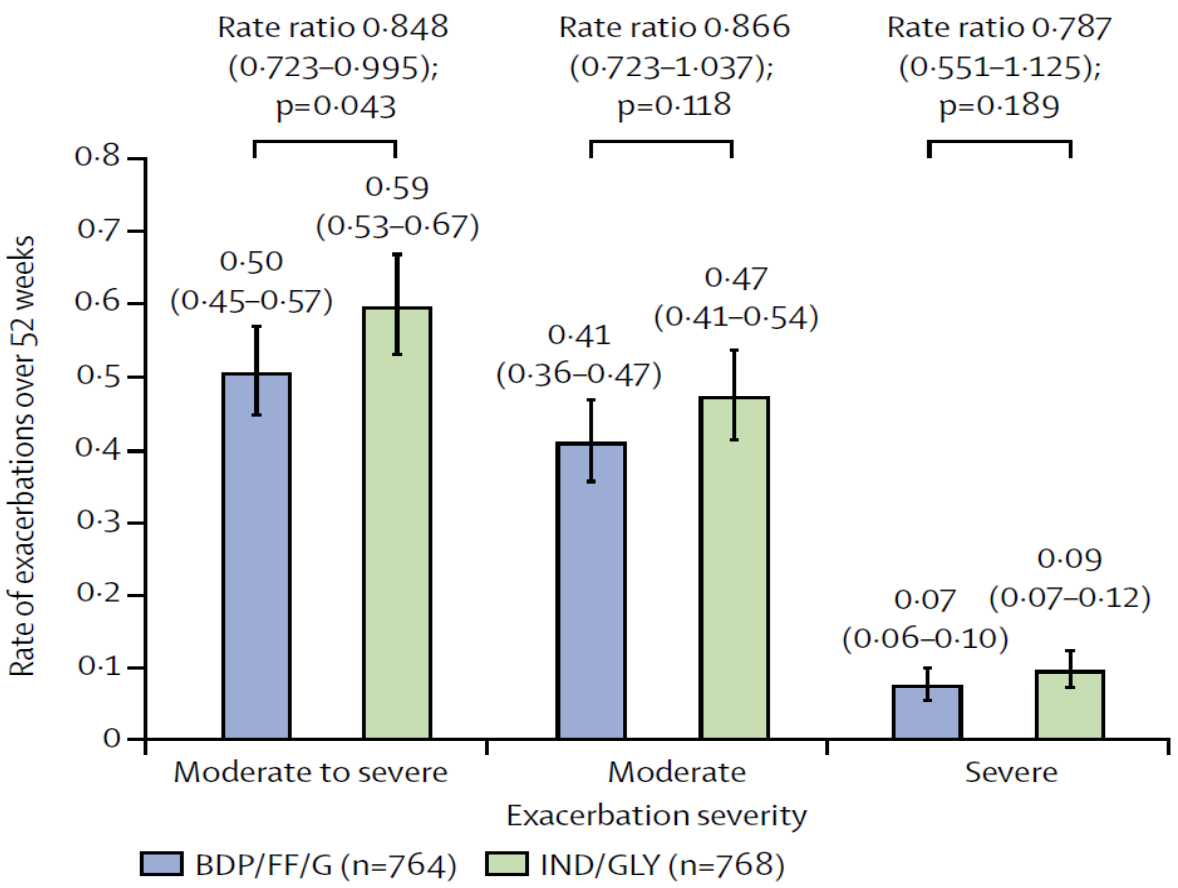
Singh D et al. Lancet 388:963-973, 2016

STUDIO TRINITY



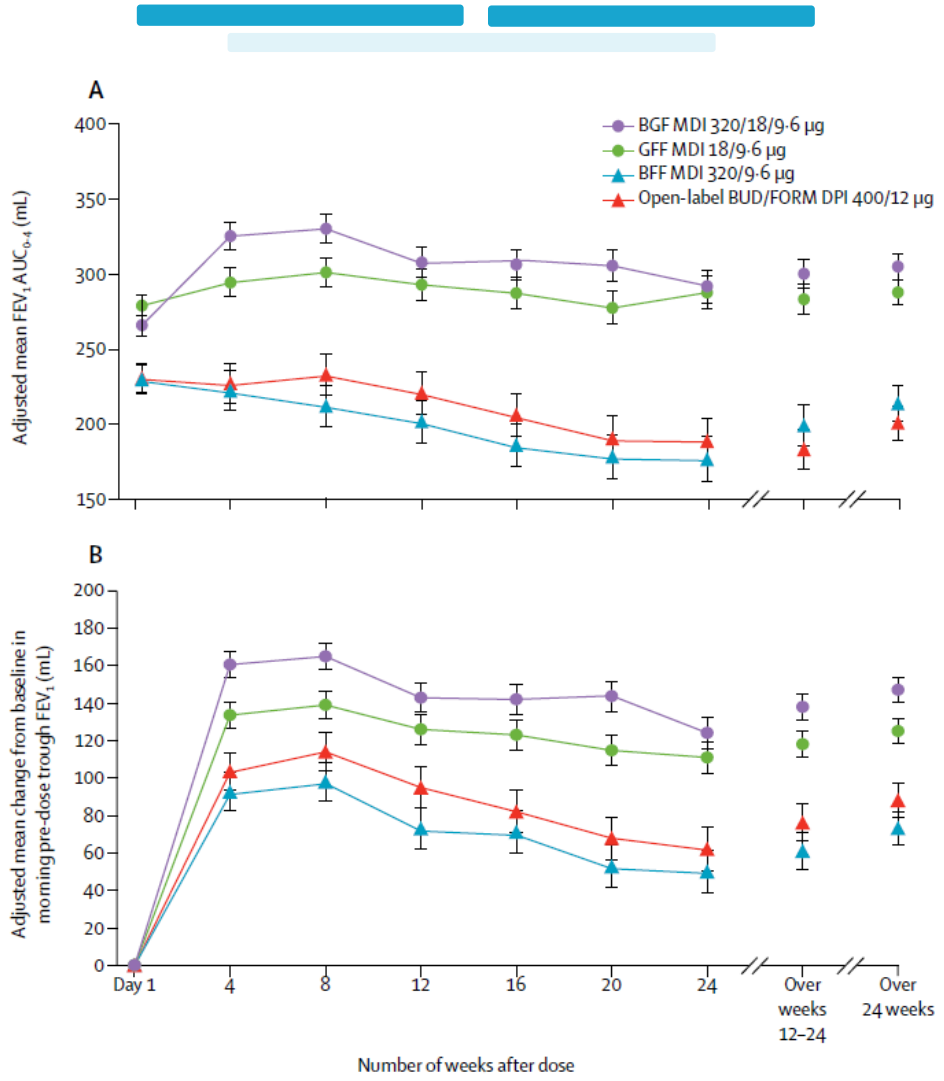
Vestbo J e Vestbo J et al. *Lancet* 389:1919-1929, 2017

STUDIO TRIBUTE



Papi A et al. *Lancet* 391:1076-1084

STUDIO KRONOS

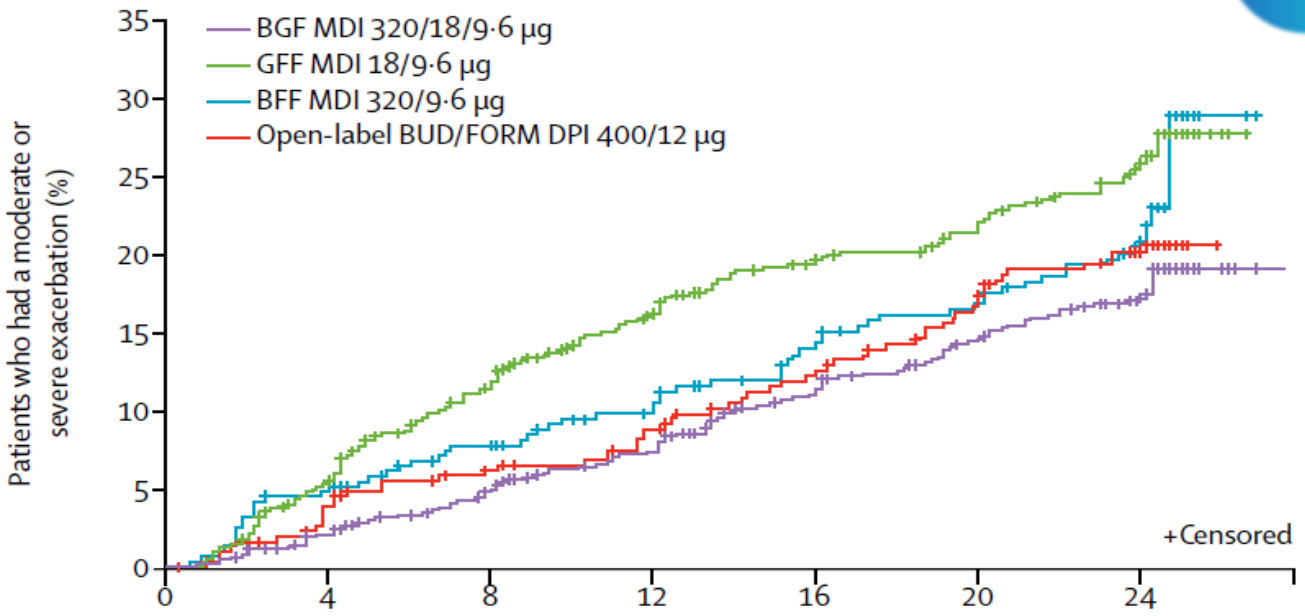


FEV1

Ferguson GT, et al. *Lancet Respir Med* 10:747-758, 2018

STUDIO KRONOS

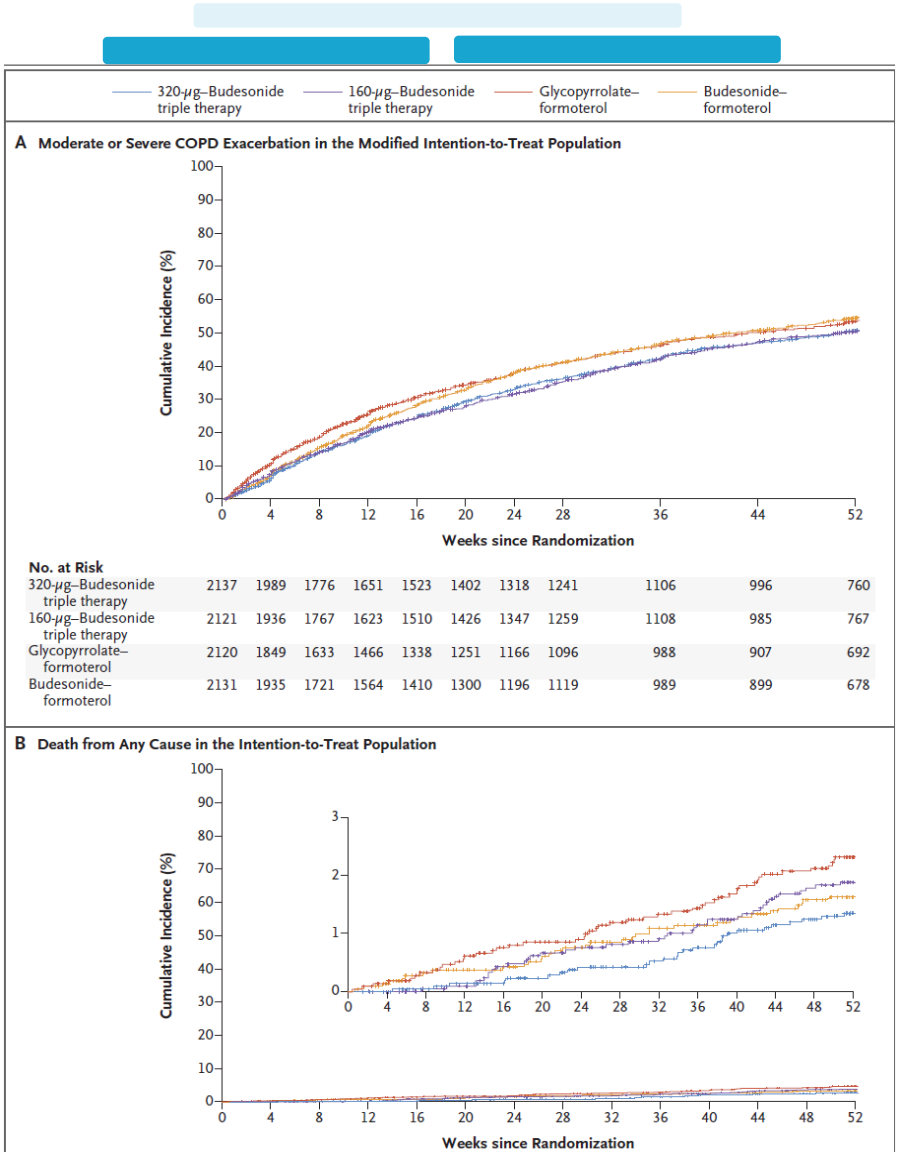
ESACERBAZIONI



Number at risk							
BGF MDI 320/18/9·6 µg	639	620	590	561	526	498	428
GFF MDI 18/9·6 µg	625	585	532	492	463	446	371
BFF MDI 320/9·6 µg	314	295	277	260	242	233	196
Open-label BUD/FORM DPI 400/12 µg	318	297	282	271	257	241	203

Ferguson GT, et al. *Lancet Respir Med* 10:747-758, 2018

STUDIO ETHOS



Rabe KF et al. *N Engl J Med* 383:35-48, 2020

International Journal of Chronic Obstructive Pulmonary Disease

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ORIGINAL RESEARCH

Exacerbation Burden in COPD and Occurrence of Mortality in a Cohort of Italian Patients: Results of the Gulp Study

Pierachille Santus[1], Fabiano Di Marco[2], Fulvio Braido[3], Marco Contoli[4], Angelo Guido Corsico[5], Claudio Micheletto[6], Girolamo Pelaia[7], Dejan Radovanovic[1], Paola Rogliani[8], Laura Saderi[9], Nicola Scichilone[10], Silvia Tanzi[11], Manlio Vella[11], Silvia Boarino[11], Giovanni Sotgiu[9], Paolo Solidoro[12]

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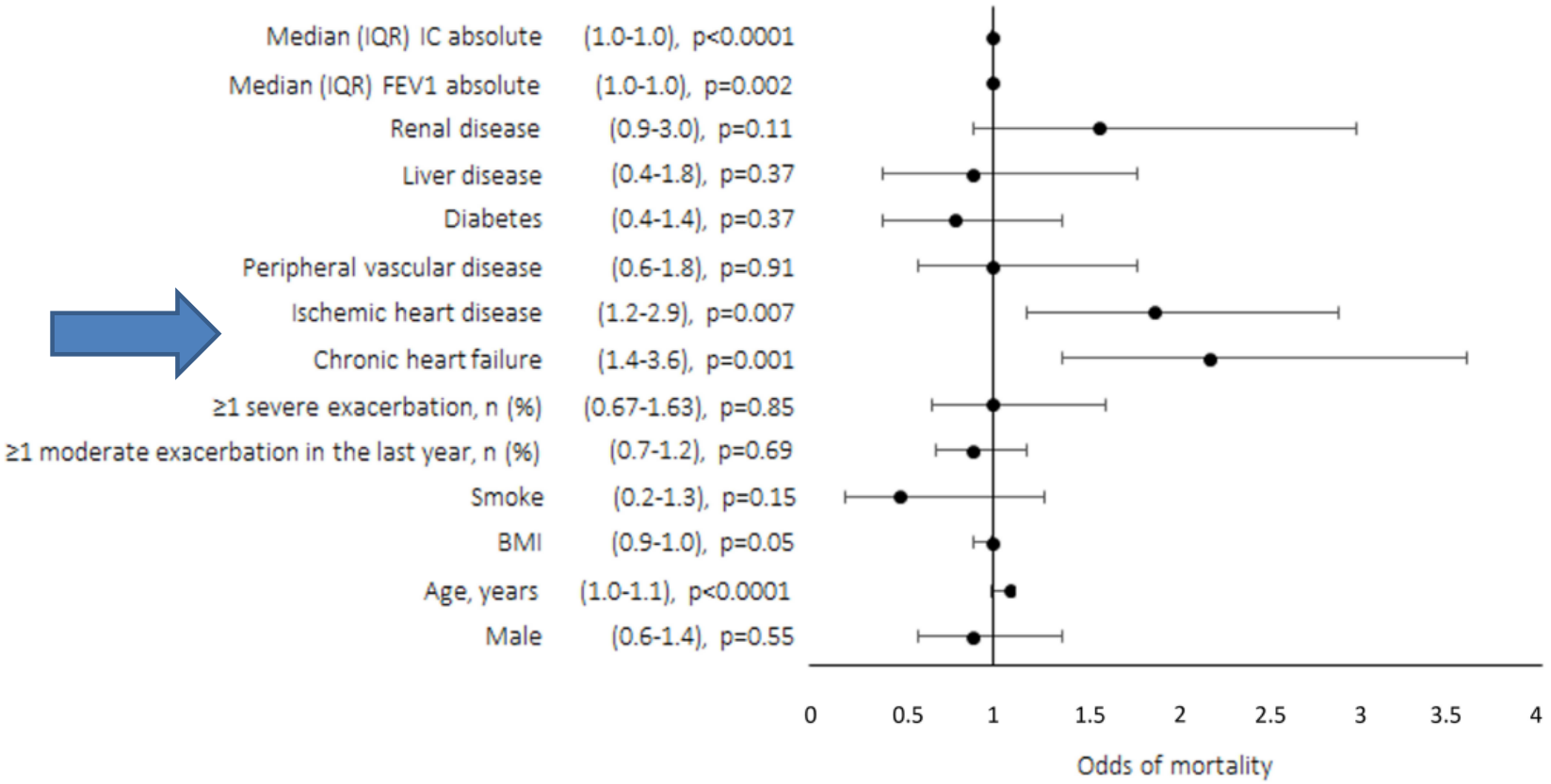
GULP STUDY



Santus P et al. *Int J Chron Obstruct Pulmon Dis* 19:607-618, 2024