COPD Stability:

Defining and Sustaining Disease Control

2025.6.14
양산부산대학교병원
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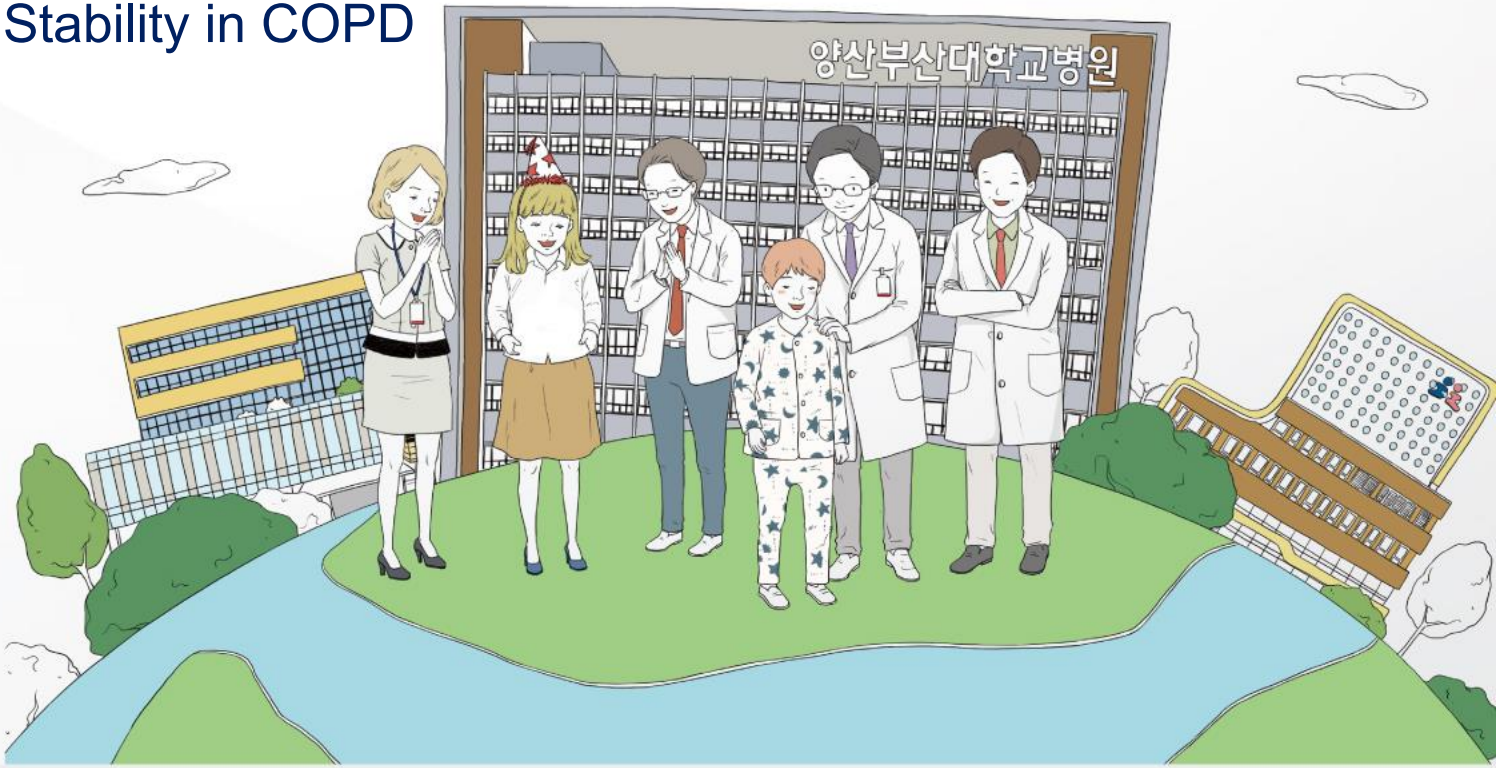

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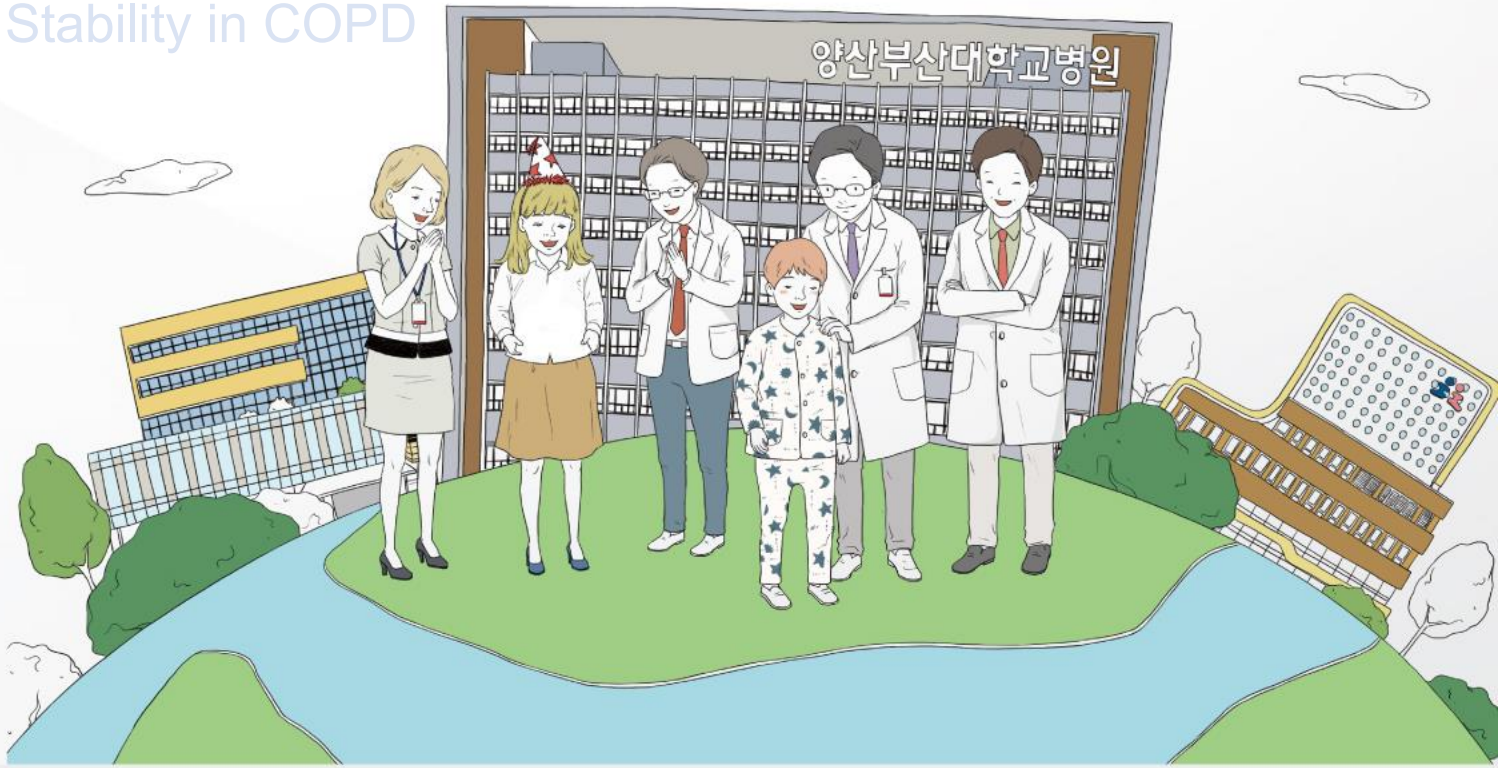


COPD Definition

- COPD is a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum production and/or exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction

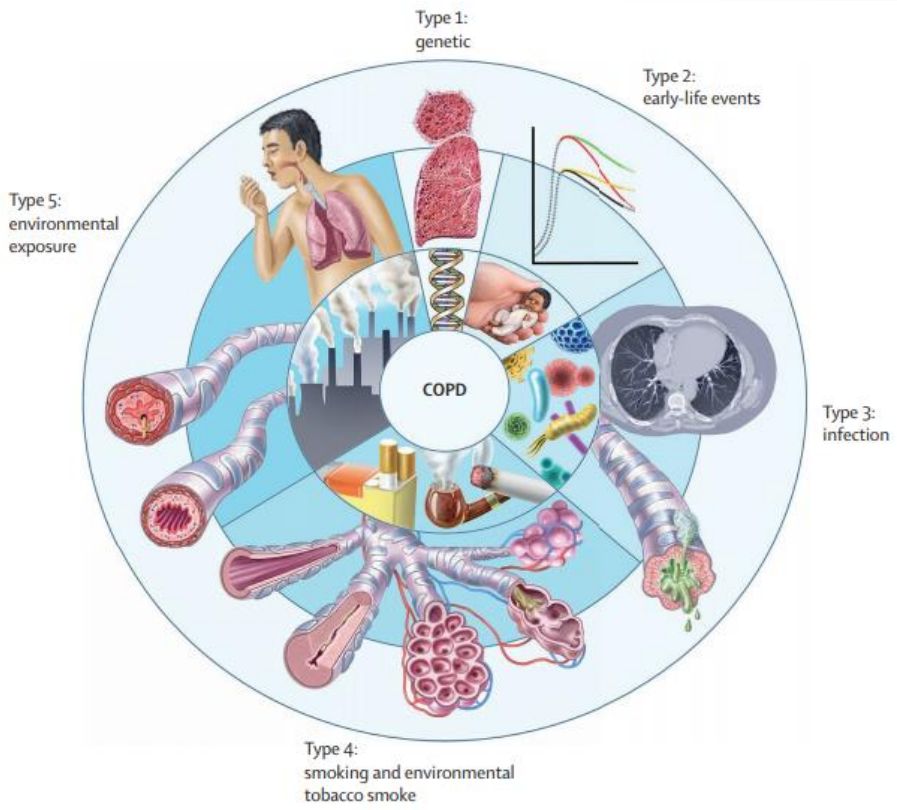
- COPD results from gene(G)-environment(E) interactions occurring over the lifetime(T) of the individual (GEtomics) that can damage the lungs and/or alter their normal development/aging processes.

Cause and Risk Factor

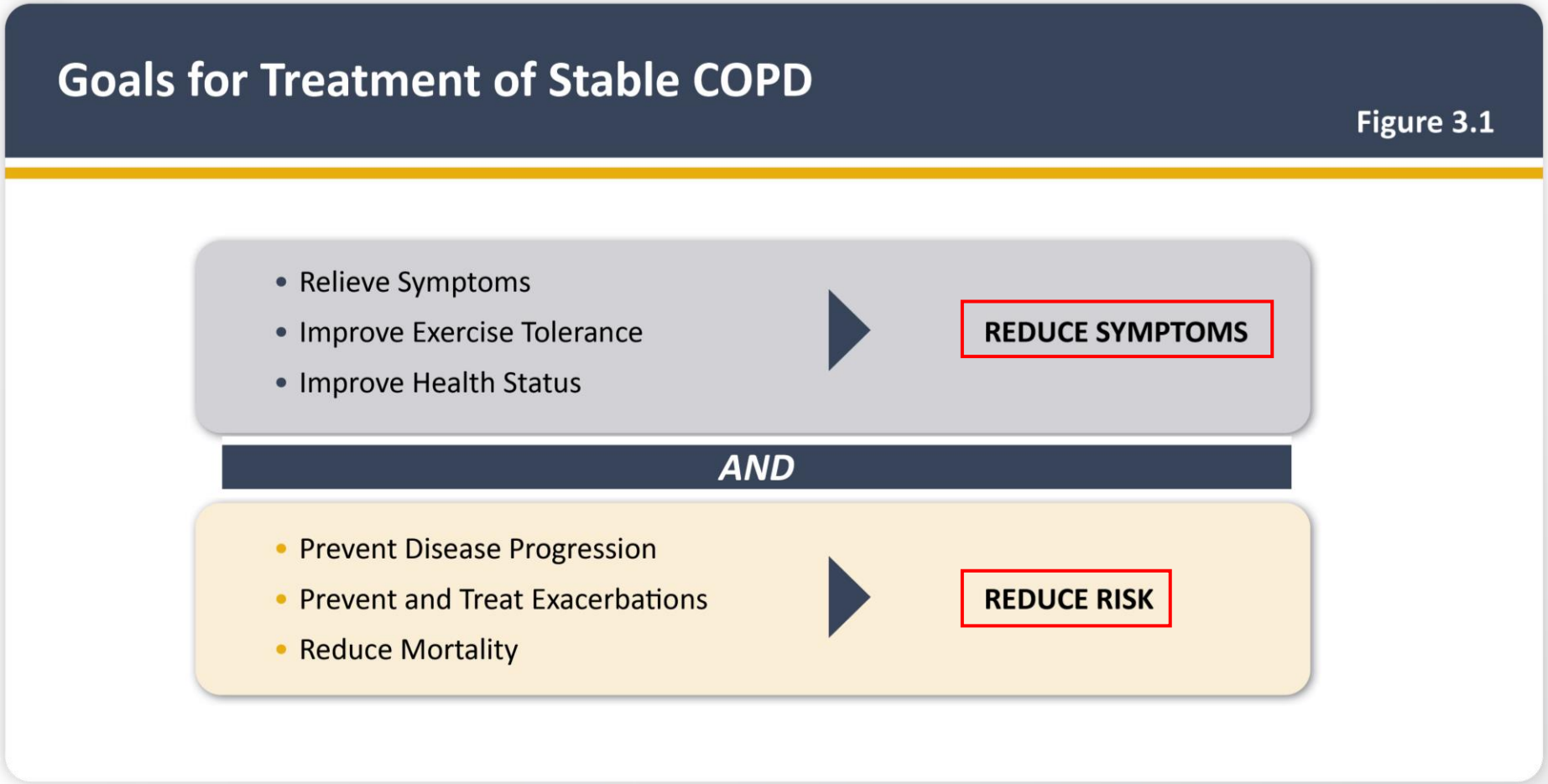
Proposed Taxonomy (Etiotypes) for COPD

Figure 1.2

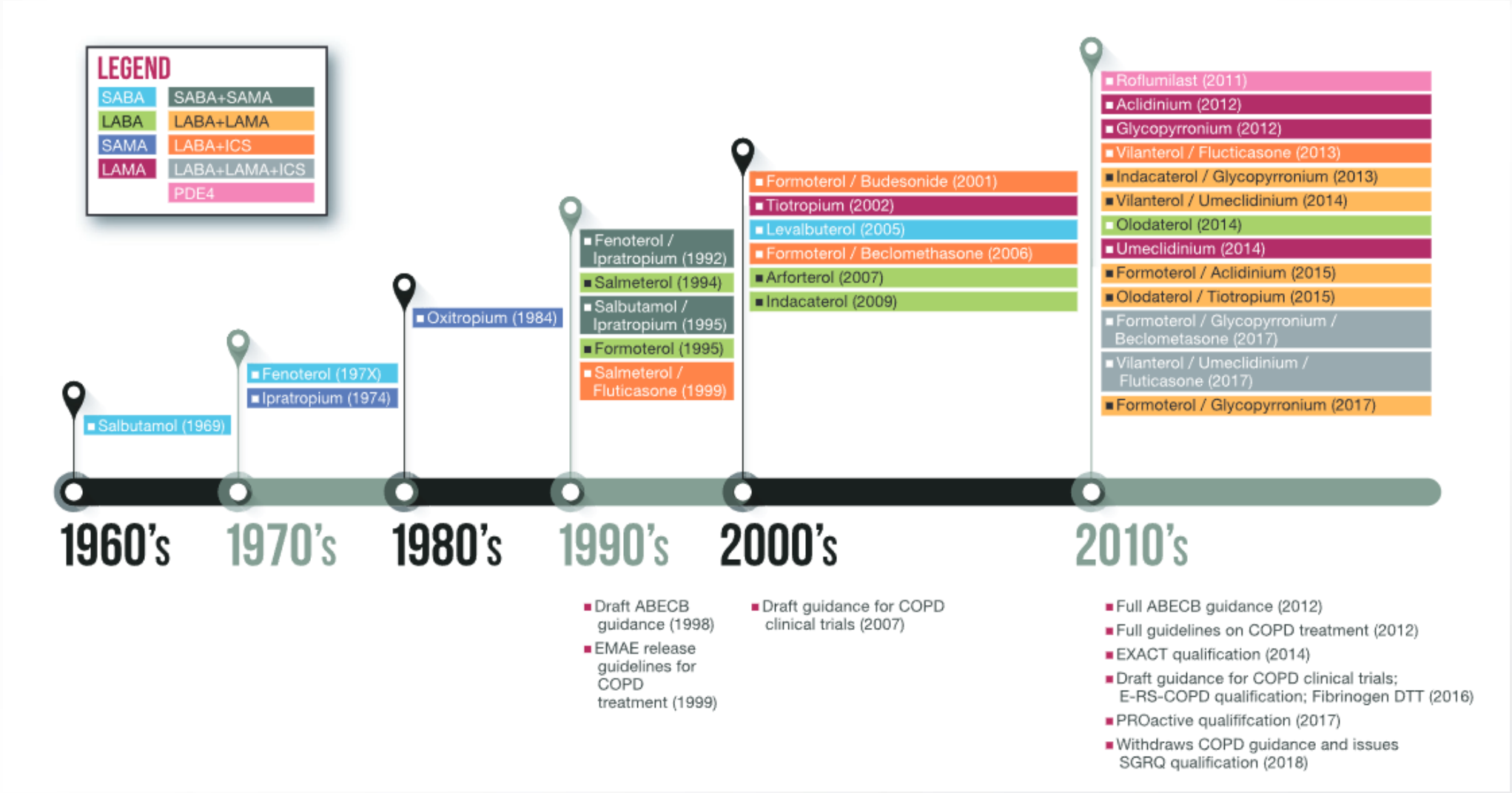
Classification	Description
Genetically determined COPD (COPD-G)	Alpha-1 antitrypsin deficiency (AATD) Other genetic variants with smaller effects acting in combination
COPD due to abnormal lung development (COPD-D)	Early life events, including premature birth and low birthweight, among others
Environmental COPD	
Cigarette smoking COPD (COPD-C)	• Exposure to tobacco smoke, including *in utero* or via passive smoking • Vaping or e-cigarette use • Cannabis
Biomass and pollution exposure COPD (COPD-P)	Exposure to household pollution, ambient air pollution, wildfire smoke, occupational hazards
COPD due to infections (COPD-I)	Childhood infections, tuberculosis-associated COPD, HIV-associated COPD
COPD & asthma (COPD-A)	Particularly childhood asthma
COPD of unknown cause (COPD-U)	



Goals for Treatment of COPD



Timeline of COPD drug approvals



Clin Pharmacol Ther . 2019 Dec;106(6):1222-1235.

The Unmet Needs in COPD treatment

TABLE 1 Trend of COPD related deaths, prevalence and DALYs from 1990 to 2021 by SDI quintiles.

	Global		High SDI		High-middle SDI		Middle SDI		Middle-Low SDI		Low SDI	
	1990	2021	1990	2021	1990	2021	1990	2021	1990	2021	1990	2021
No. (*10^6)												
Population	3074.03 (3013.3 to 3140.23)	5250.06 (5099.17 to 5412.24)	627.66(612.22 to 642.96)	858.55(834.81 to 882.73)	693.18(670.14 to 717.34)	999.56(957.89 to 1043.18)	958.21(925.71 to 988.96)	1698.31(1630.1 to 1765.58)	570.29(549.76 to 590.04)	1156.27(1092.99 to 1221.89)	221.7(215.58 to 227.89)	533.1(508.27 to 558.49)
DALYs	56.38(50.36 to 61.3)	78.63(71.36 to 85.76)	6.56(6.11 to 6.93)	9.92(9.02 to 10.63)	14.04(12.51 to 15.4)	13.19(11.57 to 14.9)	21.26(18.61 to 23.53)	26.35(23.2 to 29.79)	11.03(8.84 to 12.8)	22.52(19.97 to 25.14)	3.47(2.77 to 4.06)	6.6(5.75 to 7.53)
Deaths	2.48(2.19 to 2.7) <	3.62(3.21 to 4)	0.29(0.26 to 0.3)	0.44(0.39 to 0.47)	0.67(0.59 to 0.74)	0.66(0.57 to 0.76)	0.95(0.82 to 1.05)	1.26(1.08 to 1.45)	0.44(0.35 to 0.52)	0.99(0.87 to 1.11)	0.13(0.1 to 0.16)	0.26(0.23 to 0.3)
Prevalence	98.64(84.38 to 113.04) <	209.32(179.9 to 239.36)	28.11(24.15 to 32.17)	50.96(45.35 to 56.69)	24.24(20.63 to 28)	45(38.18 to 52.12)	25.27(21.41 to 29.12)	62.99(52.73 to 73.47)	15.84(13.54 to 18)	37.94(32.63 to 43.19)	5.09(4.33 to 5.81)	12.27(10.49 to 14.08)
Age-standardized rate (per 100,000)												
Deaths	71.92(64.47 to 77.53)	45.22(40.61 to 49.7)	25.53(23.71 to 26.5)	19.44(17.26 to 20.66)	79.53(70.61 to 86.61)	35.91(30.78 to 40.69)	92.07(74.17 to 107.46)	84.76(75.8 to 93.78)	123.89(109.19 to 134.8)	57.45(49.59 to 65.43)	77.67(61.91 to 91.44)	70.7(63.35 to 79.76)
DALYs	1492.64(1342.46 to 1609.3)	940.66(871.48 to 1014.59)	589.8(557.84 to 616.39)	471.22(437.45 to 498.84)	1511.32(1365.74 to 1635.67)	691.14(621.83 to 772.74)	1963.19(1602.24 to 2252.75)	1707.9(1558.88 to 1865.11)	2332.91(2063.49 to 2546.31)	1076.67(963.62 to 1201.24)	1673.81(1373.37 to 1936.99)	1457.94(1318.76 to 1617.05)
Prevalence	2550.02(2318.34 to 2806.32) >	2512.86(2293.93 to 2748.52)	2602.27(2359.28 to 2847.55)	2527.66(2364.4 to 2701.8)	2523.42(2287.88 to 2794.38)	2385.34(2149.82 to 2648.74)	2621.01(2378.69 to 2867.91)	2726.76(2478.22 to 2,979)	2459.97(2217.17 to 2717.88)	2463.19(2208.84 to 2735.96)	2190.49(1969.32 to 2409.53)	2337.52(2119.39 to 2567.85)
Percentage change, 1990–2021 (%)												
Deaths	−37.12(−43.37 to −27.68)		−23.85(−27.38 to −20.63)		−54.85(−61.65 to −46.85)		−7.93(−20.33 to 16.03)		−53.62(−60.31 to −44.06)		−8.96(−20.17 to 11.87)	
DALYs	−36.98(−42.37 to −28.54)		−20.1(−22.48 to −17.87)		−54.27(−60.12 to −47.24)		−13(−23.54 to 7.28)		−53.85(−59.73 to −45.6)		−12.9(−22.5 to 4.71)	
Prevalence	−1.46(−3.36 to 0.39)		−2.87(−5.71 to 0.64)		−5.47(−7.86 to −3.24)		4.03(2 to 5.89)		0.13(−2.9 to 2.84)		6.71(4.25 to 8.91)	
APC model estimate, Net drift (% per year)												
DALYs	−2.95(−3.02 to −2.89)		−0.63(−0.7 to −0.56)		−0.71(−0.79 to −0.63)		−2.71(−2.77 to −2.66)		−0.74(−0.84 to −0.65)		−1.66(−1.71 to −1.62)	
Deaths	−3.87(−4 to −3.74)		−0.82(−1 to −0.65)		−0.96(−1.12 to −0.8)		−2.71(−2.77 to −2.66)		−1.01(−1.2 to −0.82)		−2.18(−2.25 to −2.1)	
Prevalence	−0.35(−0.39 to −0.32)		−0.82(−1 to −0.65)		0(−0.01 to 0.01)		−0.18(−0.21 to −0.16)		0.09(0.07 to 0.11)		−0.17(−0.18 to −0.15)	

DALYs, disability-adjusted life years.

Global Burden of COPD Through 2050

Table. Global Projected COPD Prevalence, Cases, and Relative Change From 2020 to 2050 by Sex

Sex	2020	2030	2040	2050
Female				
Prevalence, %	7.8	8.1	8.34	8.33
Cases, No.	176 776 887	210 351 803	240 030 181	260 106 028
Relative change in prevalence, %	NA	3.8 (vs 2020)	2.5 (vs 2030)	−0.12 (vs 2040); 6.4 (vs 2020)
Relative change in cases, %	NA	19.0 (vs 2020)	14.1 (vs 2030)	8.4 (vs 2040); 47.1 (vs 2020)
Male				
Prevalence, %	13.4	12.5	11.6	10.6
Cases	303 080 615	322 532 353	333 145 741	331 449 760
Relative change in prevalence, %	-NA	−6.7 (vs 2020)	−7.2 (vs 2030)	−8.6 (vs 2040); −20.9 (vs 2020)
Relative change in cases, %	NA	6.4 (vs 2020)	3.3 (vs 2030)	−0.5 (vs 2040); 9.4 (vs 2020)
Global				
Prevalence, %	10.6	10.3	9.7	9.5
Cases, No.	479 857 502	532 884 156	573 175 922	591 555 788
Relative change in prevalence, %	NA	−2.8 (vs 2020)	−5.8 (vs 2030)	−2.1 (vs 2040); −10.4 (vs 2020)
Relative change in cases, %	NA	11.0 (vs 2020)	7.6 (vs 2030)	3.2 (vs 2040); 23.3 (vs 2020)

Abbreviation: NA, not applicable.

- Global COPD prevalence was projected to approach 600 million cases worldwide by 2050, which represents a relative growth of 23% in the number of individuals with COPD compared with 2020.
- **Future strategies** should **aim** to prevent COPD onset and establish concrete treatment goals for early and effective management to halt disease progression

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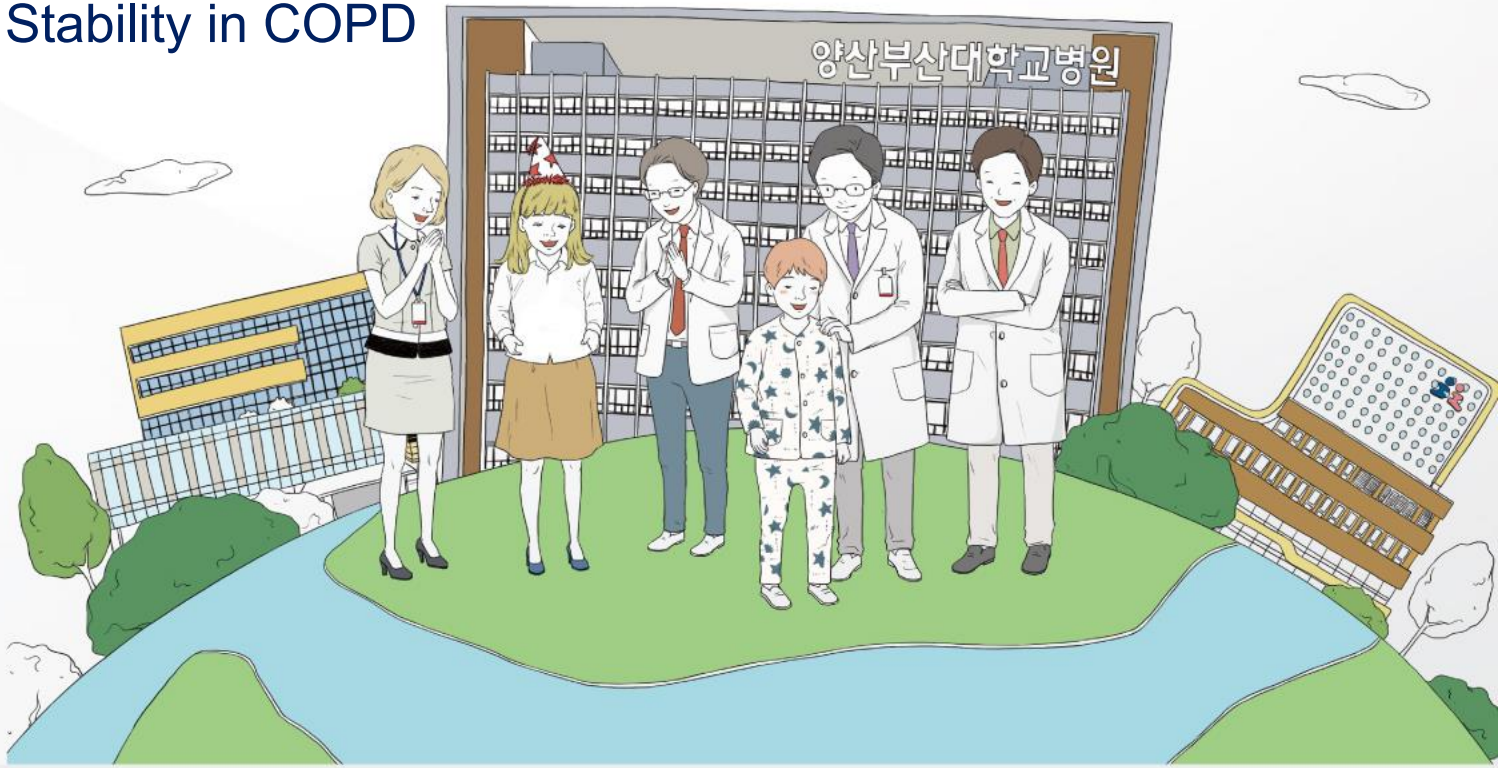
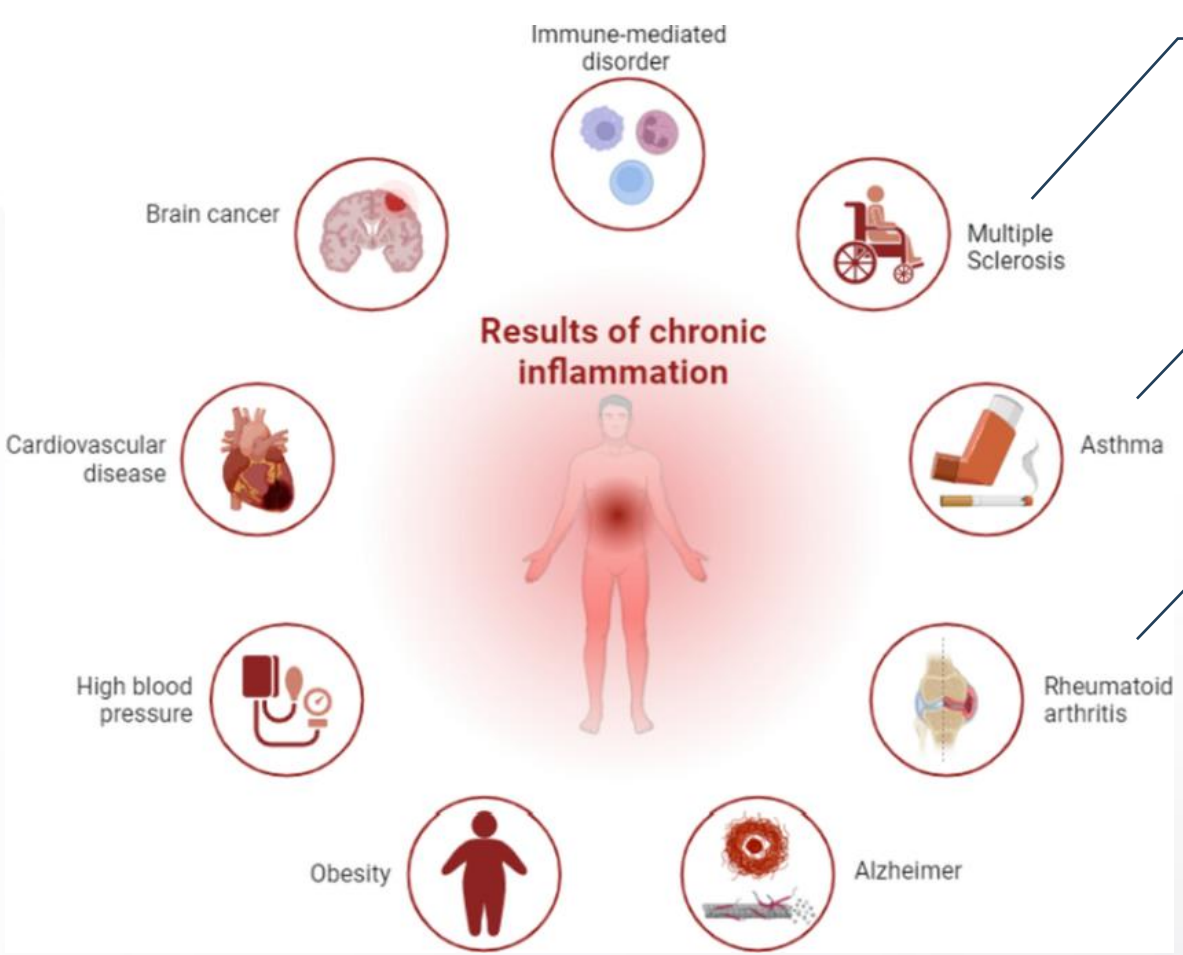


Managing Chronic Inflammation: Current Concepts



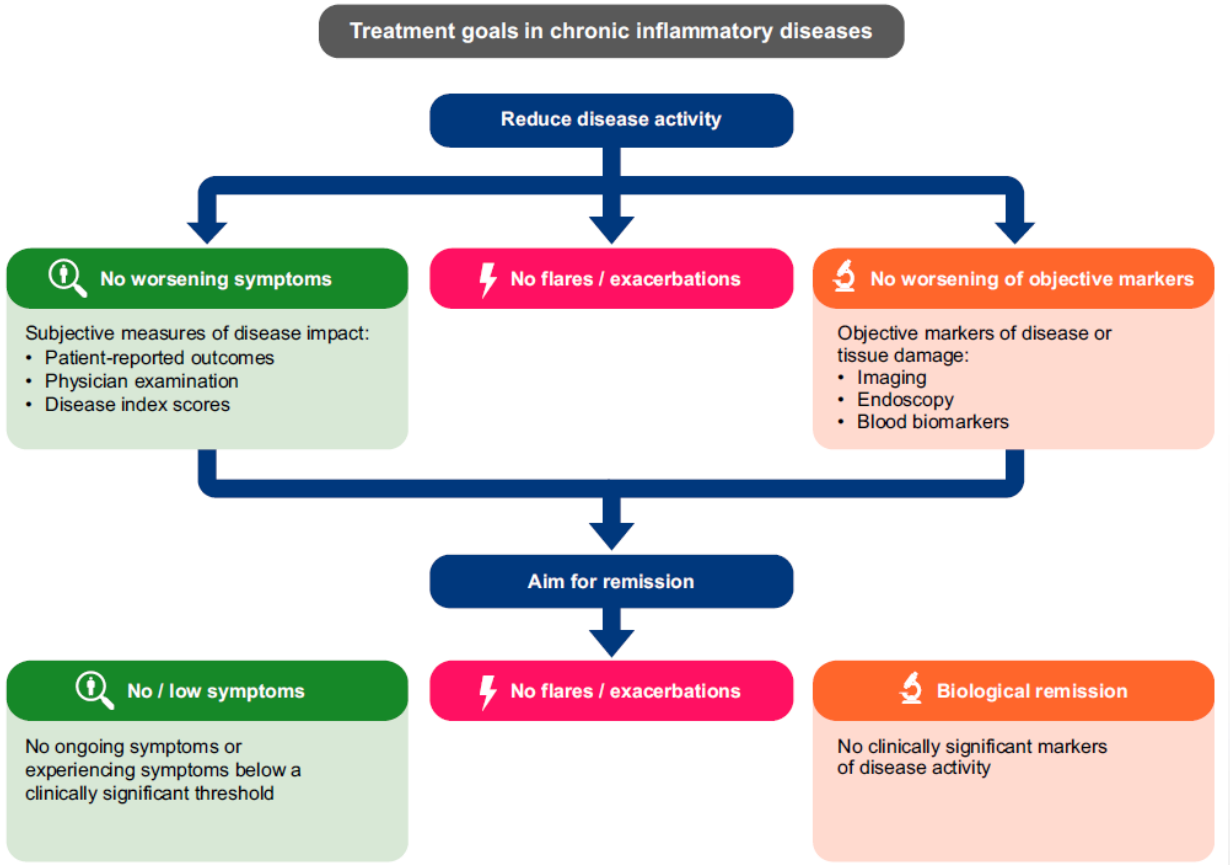
no evidence of disease activity (NEDA)

Remission

Remission

- Treatment goals of chronic inflammation disease should balance the need for **early diagnosis and manage the current burden** faced by patients, while also aiming toward a future where highly effective **disease-modifying therapies (DMTs)** might become available.

Development of related concepts to disease stability in other inflammatory diseases



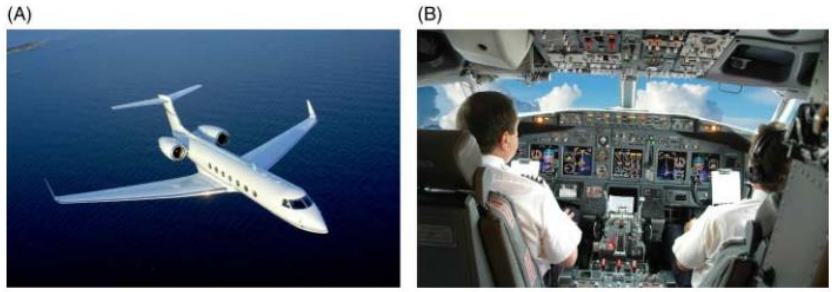
- Disease activity refers to reversible components of the disease, and other **chronic inflammatory diseases have developed management strategies designed to control disease activity.** Untreated disease activity may cause irreversible pathology, resulting in greater disease severity.

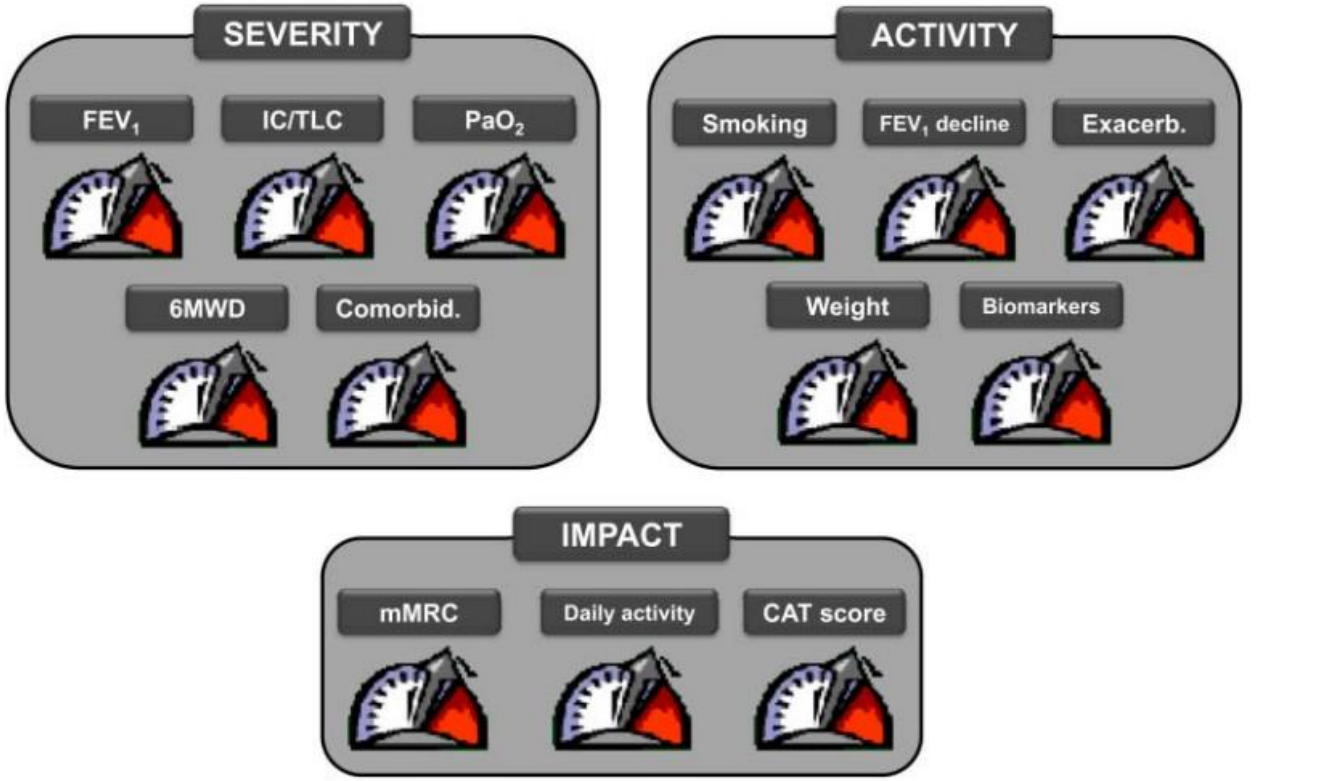
Am J Respir Crit Care Med . 2025 Mar;211(3):452-463.

OPINION

The COPD control panel: towards personalised medicine in COPD

Alvar Agusti,[1,2] William MacNee[3]

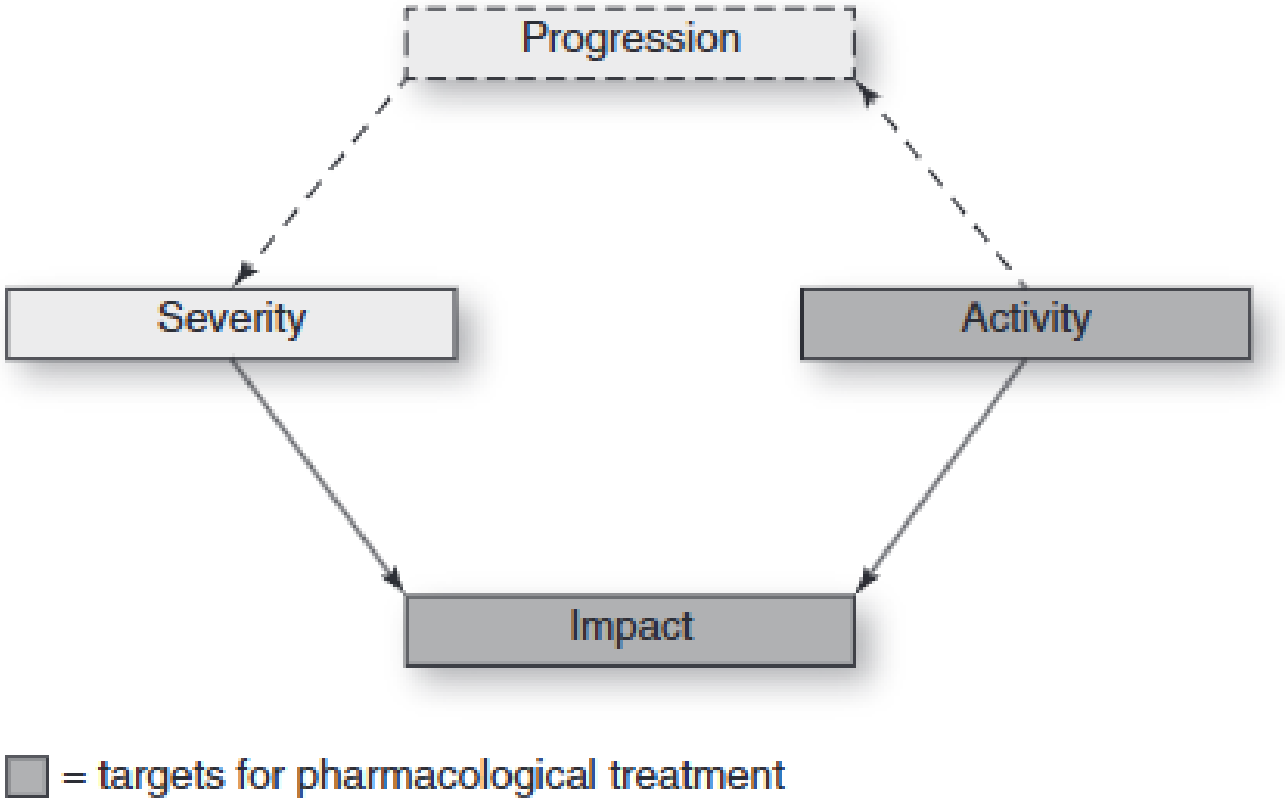




- **'COPD control panel'** should include at least three different domains of the disease: **severity**, **activity** and **impact**. Each of these domains presents information on different 'elements' of the disease with potential prognostic value and/or with specific therapeutic requirements.

Thorax . 2013 Jul;68(7):687-90.

The relationships between components of COPD



- These aspects of COPD are intrinsically linked, with **disease activity** driving disease progression, which in turn worsens disease severity and increases the impact on the patient

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PERSPECTIVES

The concept of control of COPD in clinical practice

Clinical control in COPD

- **Control = Low Impact (adjusted for severity) + Stability**

  Impact (Cross-sectional):
  - Measured by CAT or CCQ
  - Also assessed via dyspnea, rescue medication use, physical activity, and sputum color

  Stability (Longitudinal):
  - No exacerbations
  - No worsening in symptoms or CAT/CCQ scores

- Clinical control in COPD can support treatment adjustment decisions

[Translated article] Spanish COPD guidelines (GesEPOC) 2021: Updated pharmacological treatment of stable COPD☆,☆☆

Marc Miravitlles[a,b,*], Myriam Calle[c], Jesús Molina[d], Pere Almagro[e], José-Tomás Gómez[f], Juan Antonio Trigueros[g], Borja G. Cosío[b,h], Ciro Casanova[i], José Luis López-Campos[b,j], Juan Antonio Riesco[b,k], Pere Simonet[l], David Rigau[m], Joan B. Soriano[b,n], Julio Ancochea[b,n], Juan José Soler-Cataluña[b,o]

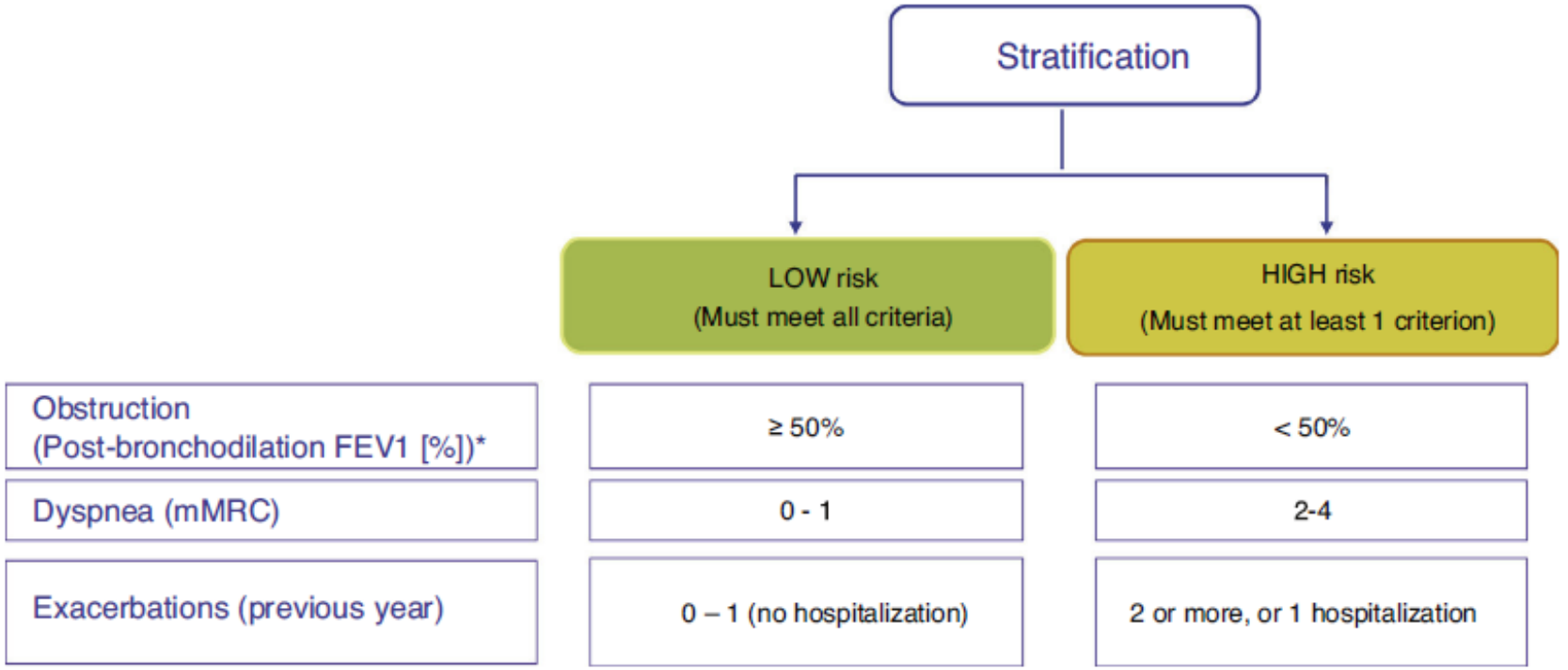


Fig. 1. Risk stratification in COPD patients.

Treatment of COPD in Spanish guideline

Table 1
Adaptation of the care level to risk levels.

	Therapeutic interventions	
Low risk	Smoking cessation	Counseling Specific treatment
	Therapeutic education	Structured therapeutic education program aimed at: • Promoting self-care • Therapeutic adherence Inhalation technique
	Physical activity	Regular exercise
	Vaccination	Anti-influenza Anti-pneumococcal (13-valent conjugate) Covid-19 Assess dTpa
	Alpha-1 antitrypsin deficiency	Augmentation treatment according to guidelines
	Pharmacological treatment	Bronchodilators
	Comorbidity	Treatment of the comorbidity
High risk	**Add to previous treatment:**	
	Pharmacological treatment	Guided by clinical phenotype Identify treatable traits
	Non-pharmacological treatment	Pulmonary rehabilitation Assess long-term home oxygen therapy Assess non-invasive ventilation Assess lung volume reduction in patients with extensive emphysema Assess lung transplant

Covid-19: coronavirus disease 2019; dTpa: Diphtheria, tetanus, acellular pertussis.

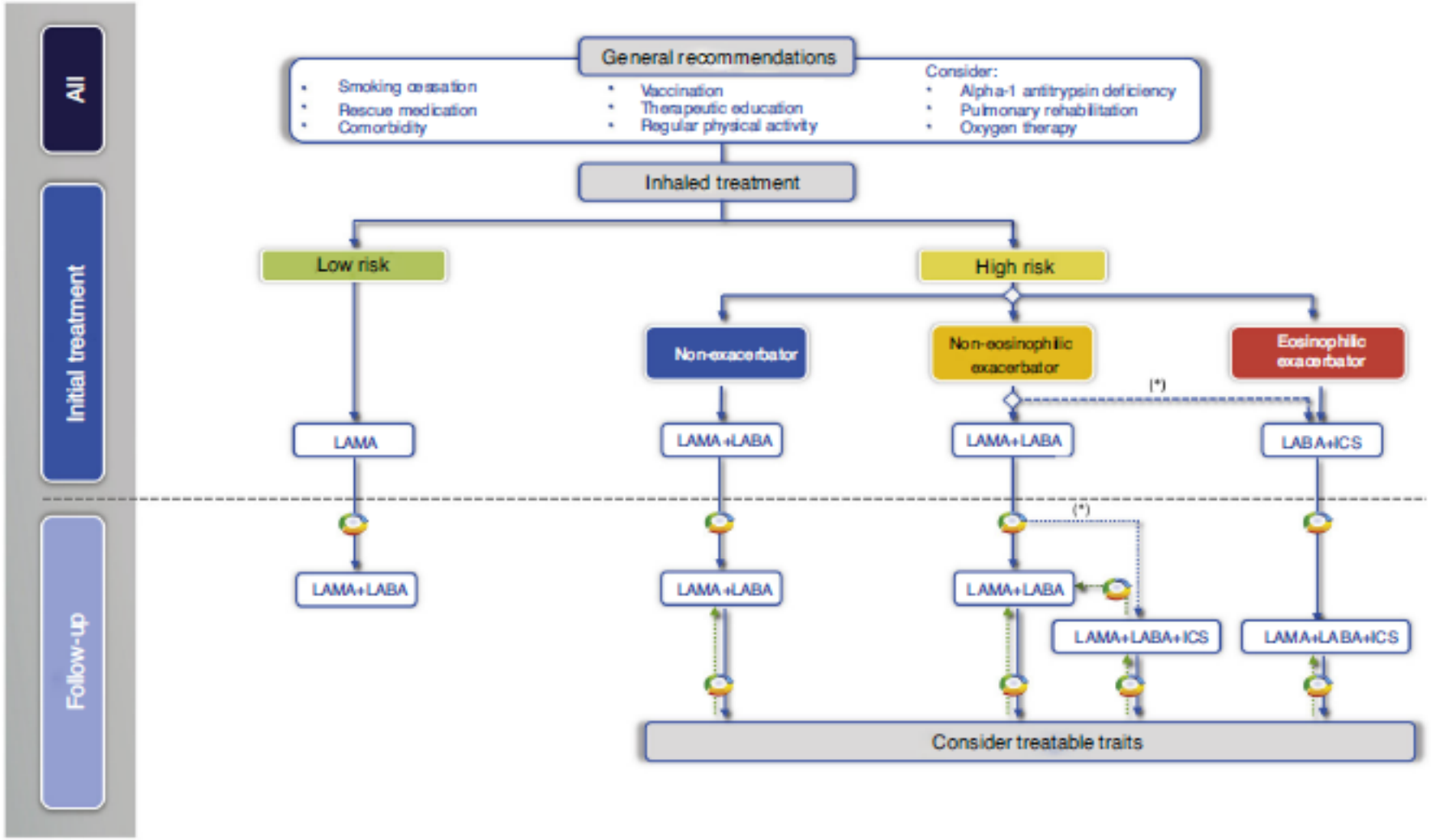


Fig. 2. Treatment of COPD guided by risk level and phenotype.
(*) Second-line in patients with blood eosinophils > 100 cells/mm^3, according to the frequency, severity and etiology of the exacerbations, assessing the risk of pneumonia.

COPD control in Spanish guideline

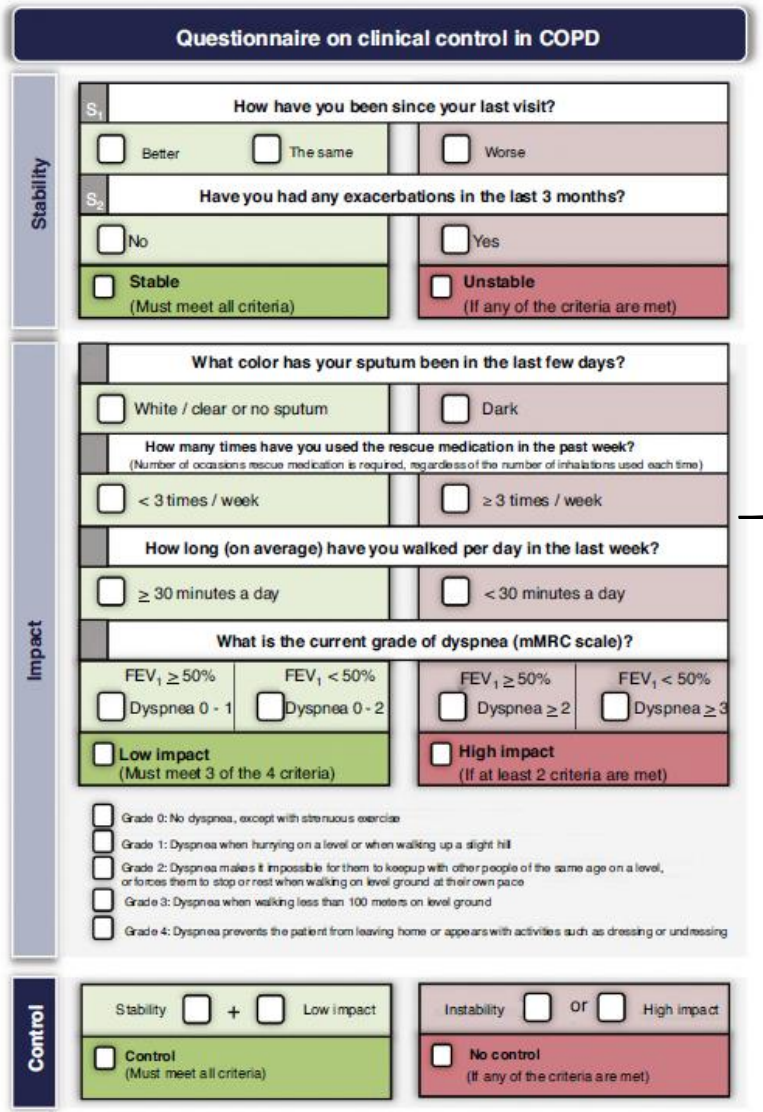
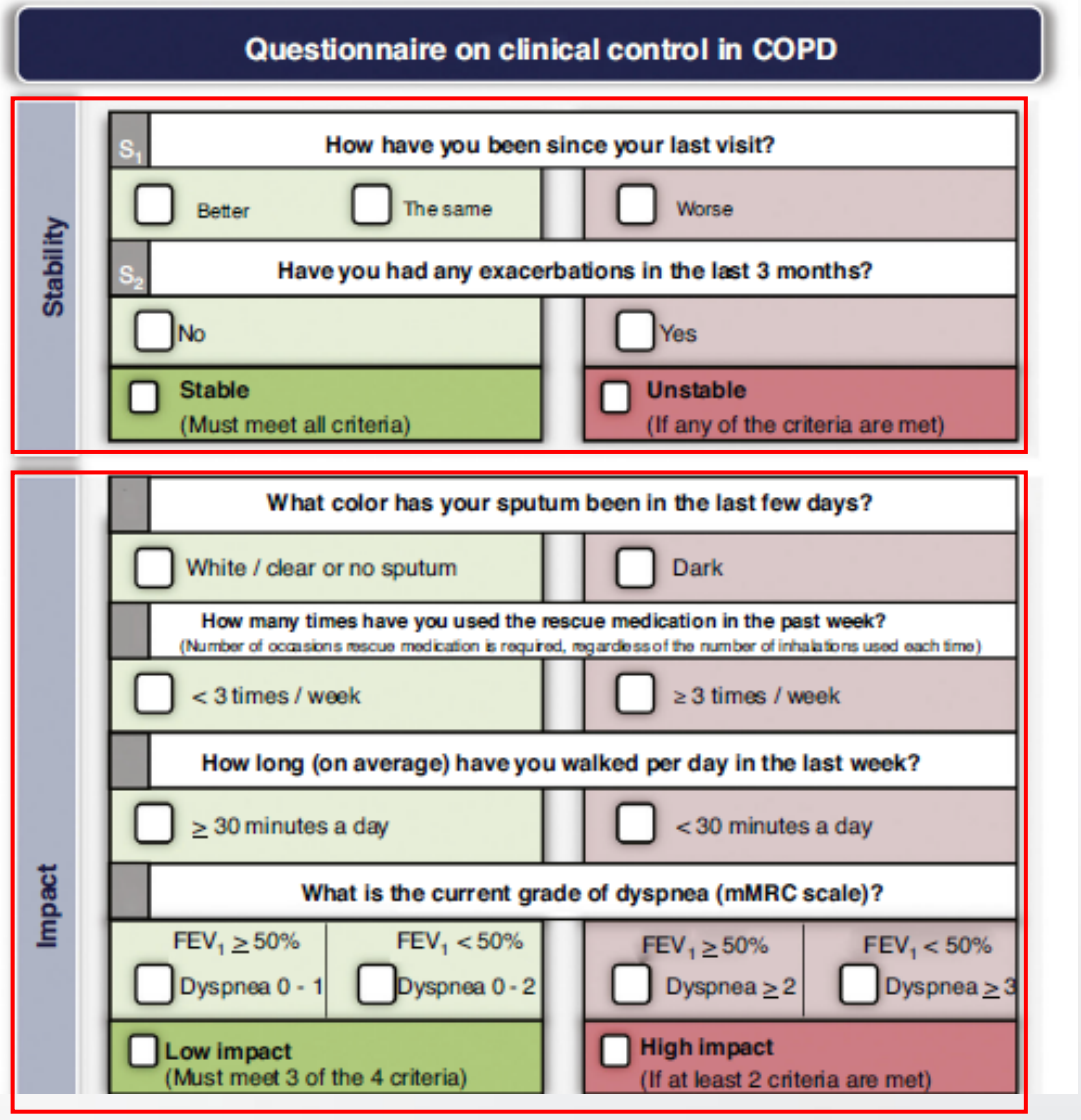


Fig. 3. COPD control criteria.



REVIEW Open Access

Measuring disease activity in COPD: is clinically important deterioration the answer?

Dave Singh[1*], Gerard J. Criner[2], Ian Naya[3,4], Paul W. Jones[3], Lee Tombs[5], David A. Lipson[6,7] and MeiLan K. Han[8]

- The composite clinically important deterioration (CID) endpoint concept was developed for a measure to assess the proportion of patients showing **disease stability** or **worsening** (which may be a marker of suboptimal treatment response or treatment failure) in response to pharmacological treatment.
- The CID endpoint was developed to assess disease worsening by **detecting early deteriorations in lung function (measured by FEV1)**, **health status(assessed by the SGRQ)**, and the **presence of exacerbations**.
- Post hoc and prospective analyses of clinical trial data have confirmed that the multidimensional **composite CID endpoint better predicts poorer medium-term outcomes compared with any single CID component alone**, and that it can demonstrate differences in treatment efficacy in short-term trials.

Table 1 Efficacy trials examining the effects of treatment escalation on overall CID incidence

Study description	CID definition	Treatments	Patient population
Dual bronchodilator combination therapy			
First retrospective CID analysis of two 24-week double-blind trials [5]	FEV_1, SGRQ, exacerbations	UMEC/VI vs placebo, TIO, UMEC or VI	High symptoms, mMRC score ≥ 2, low exacerbation risk
Retrospective pooled data from three 6-month double-blind trials [41]	FEV_1, SGRQ, exacerbations	UMEC/VI vs TIO	High symptoms, mMRC score ≥ 2, low exacerbation risk. Analyses of the ITT population and maintenance-naïve sub-group (31% of patients)
Retrospective pooled analysis of three 26-week, randomized, double-blind trials (SHINE, LANTERN & ILLUMINATE) [38]	Definition 1: FEV_1, SGRQ, exacerbations; Definition 2: TDI, SGRQ, exacerbations	IND/GLY vs SFC or TIO	High symptoms, low exacerbation risk (SHINE & LANTERN), exacerbation-free (ILLUMINATE)
Retrospective pooled analysis of two 24-week, randomized double-blind trials (AUGMENT & ACLIFORM) [44]	FEV_1, SGRQ, TDI, exacerbations	ACL/FORM vs ACL, FORM or placebo	Low to high symptoms, low exacerbation risk
Retrospective 52-week randomized double-blind trial (FLAME) [37]	FEV_1, SGRQ, exacerbations	IND/GLY vs SFC	High Symptoms, mMRC score ≥ 2, ≥ 1 exacerbation, stable on LAMA for 1 month
Retrospective 12-week, randomized, open-label, switching trial (CRYSTAL) [40]	Definition 1: FEV_1, TDI, exacerbations; Definition 2: FEV_1, CCQ, exacerbations; Definition 3: FEV_1, CCQ, TDI, exacerbations	Switch to IND/GLY from previous ICS/LABA or a single LABA or LAMA	Low to high symptoms, low exacerbation risk on open-label therapy, mMRC score ≥ 1
Prospective 24-week, randomized, double-blind trial (EMAX) [46]	Definition 1: FEV_1, SGRQ, exacerbations; Definition 2: FEV_1, CAT, exacerbations; Definition 3: SGRQ, CAT, TDI, exacerbations	UMEC/VI vs UMEC or SAL	High symptoms, ICS-free population, ≤ 1 moderate exacerbation in the past year
Multiple inhaler or single inhaler triple therapy			
Retrospective pooled analysis of four 12-week, randomized double-blind trials [43]	FEV_1, SGRQ, exacerbations	UMEC vs placebo added to existing open label ICS/LABA therapy	High symptoms, mMRC score ≥ 2, with or without exacerbations
Prospective, 52-week, randomized double-blind trial (FULFIL) assessed over 24 weeks (ITT population) and 52 weeks (extension population) [42]	Definition 1: FEV_1, SGRQ, exacerbations; Definition 2. FEV_1, CAT, exacerbations	FF/UMEC/VI vs BUD/FORM	High symptoms, FEV_1 < 50% and CAT ≥ 10 or FEV_1 ≥ 50 to < 80% and CAT ≥ 10, and ≥ 2 moderate or ≥ 1 severe exacerbation in the past year
Retrospective, three 52-week, randomized, double-blind trials (TRINITY, TRILOGY, TRIBUTE) [45]	Definition 1: FEV_1, SGRQ, exacerbations, death; Definition 2 (TRILOGY only): FEV_1, SGRQ, exacerbations, TDI, death[a]	TRINITY: BDP/FORM/GLY vs TIO (CID 1 & 2) TRILOGY: BDP/FORM/GLY vs BDP/FORM (CID 1) TRIBUTE: BDP/FORM/GLY vs IND/GLY (CID 1)	High symptoms, at-risk population, CAT ≥ 10, FEV_1 < 50% predicted plus ≥ 1 exacerbation in last year

CID Components

- **Lung Function**

  FEV_1 decline ≥ 100 mL (MCID)

- **Exacerbations**

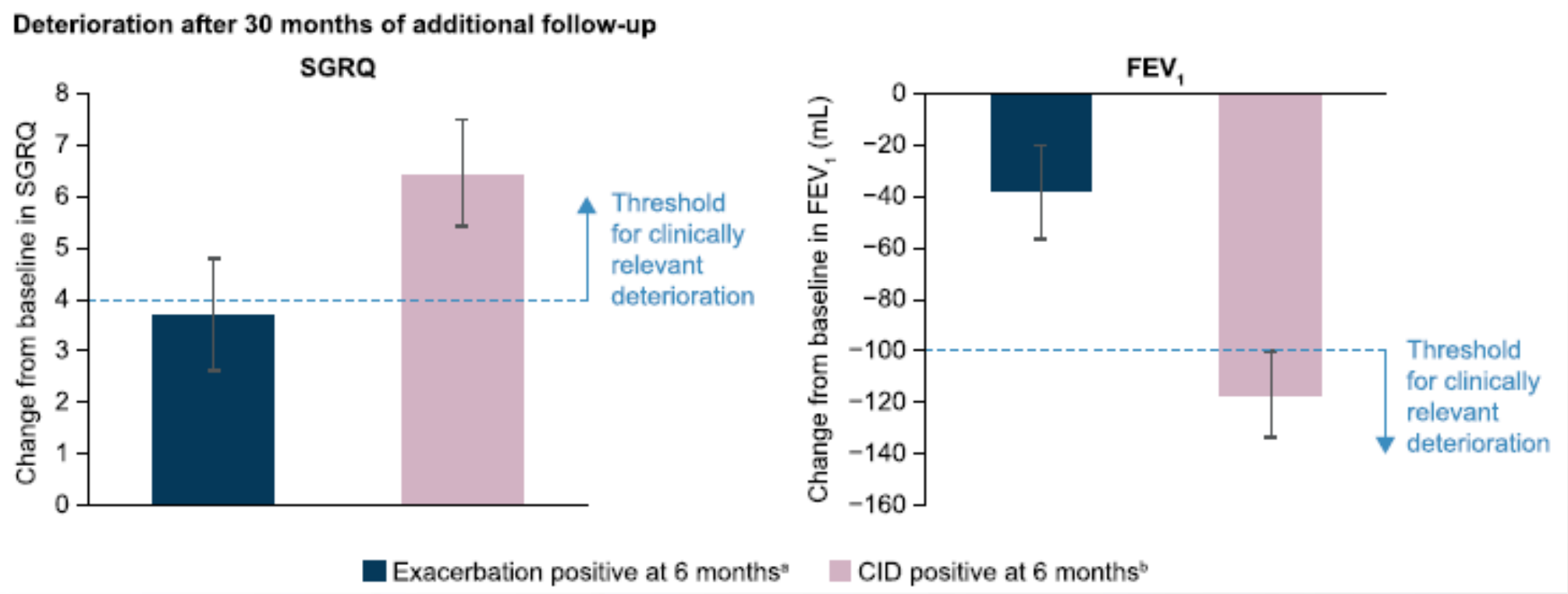
  Moderate: oral steroids and/or antibiotics

  Severe: hospitalization or ER visit

- **Health Status**

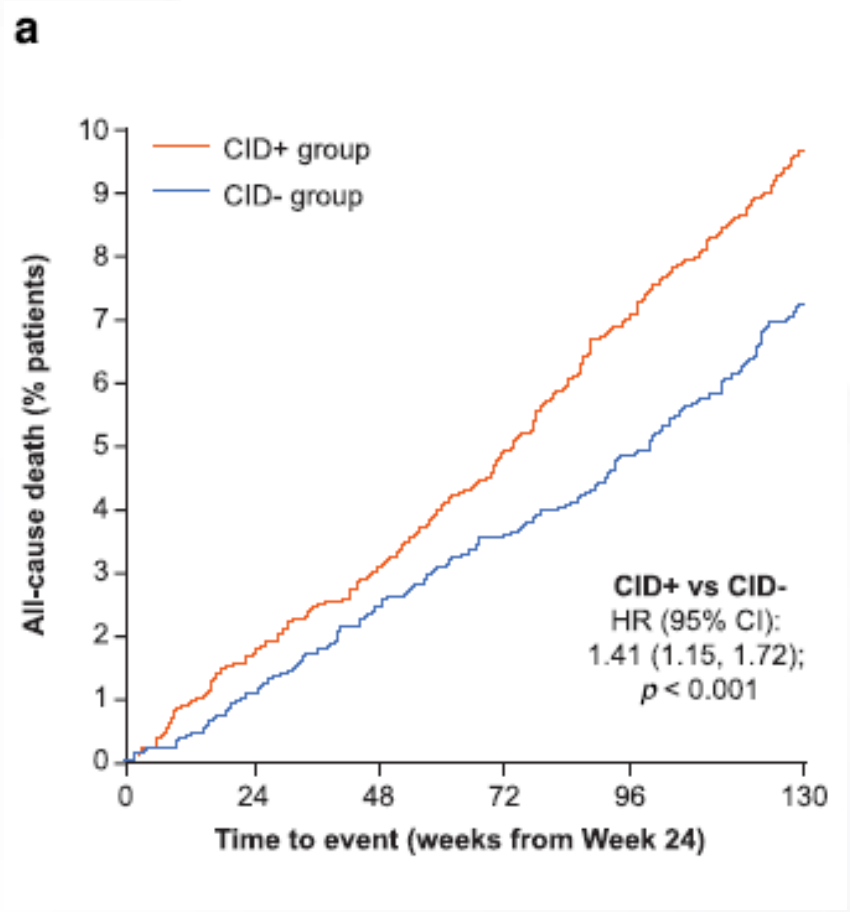
  SGRQ increase ≥ 4 units (MCID)

Exacerbations versus composite CID in measuring meaningful disease progression at 3 years in TORCH



Time to all-cause mortality based on CID status

TORCH



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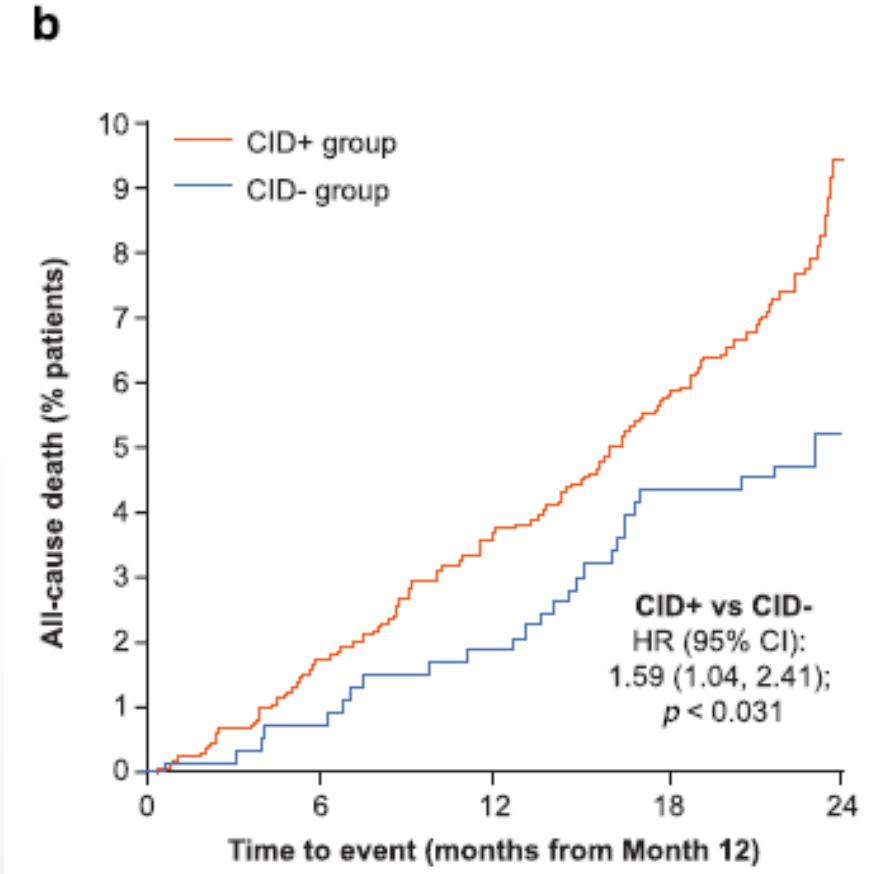


Risk of long-term adverse outcomes by CID status

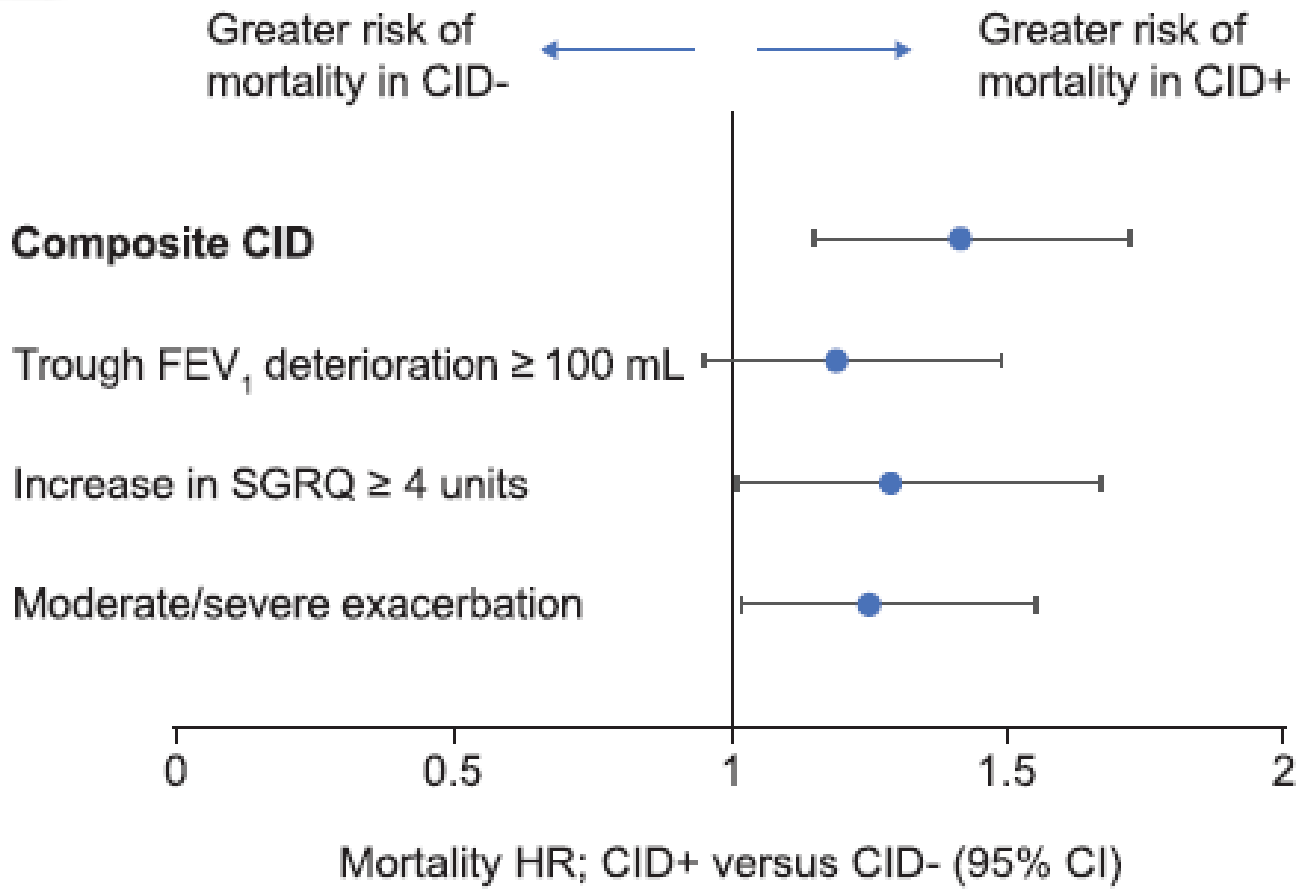
Table 2 Risk of long-term adverse outcomes by CID status in TORCH and ECLIPSE [48]

Outcome	TORCH (n = 5292)			ECLIPSE (n = 1953)		
	CID+ at 6 months [*N* = 2870], *n* (%)	CID- at 6 months [*N* = 2422], *n* (%)	% risk increase assessed at 7–36 months (95% CI)	CID+ at 12 months [*N* = 1442], *n* (%)	CID- at 12 months [*N* = 531], *n* (%)	% risk increase assessed at 13–36 months (95% CI)
Moderate/severe exacerbation	2082 (73)	1450 (60)	61 (50, 72)	1082 (75)	232 (44)	154 (120, 193)
Hospital admission for severe exacerbations	797 (28)	491 (20)	55 (38, 73)	454 (31)	66 (12)	181 (117, 263)
All-cause mortality	237 (8)	160 (7)	41 (15, 72)	121 (8)	27 (5)	59 (4, 141)

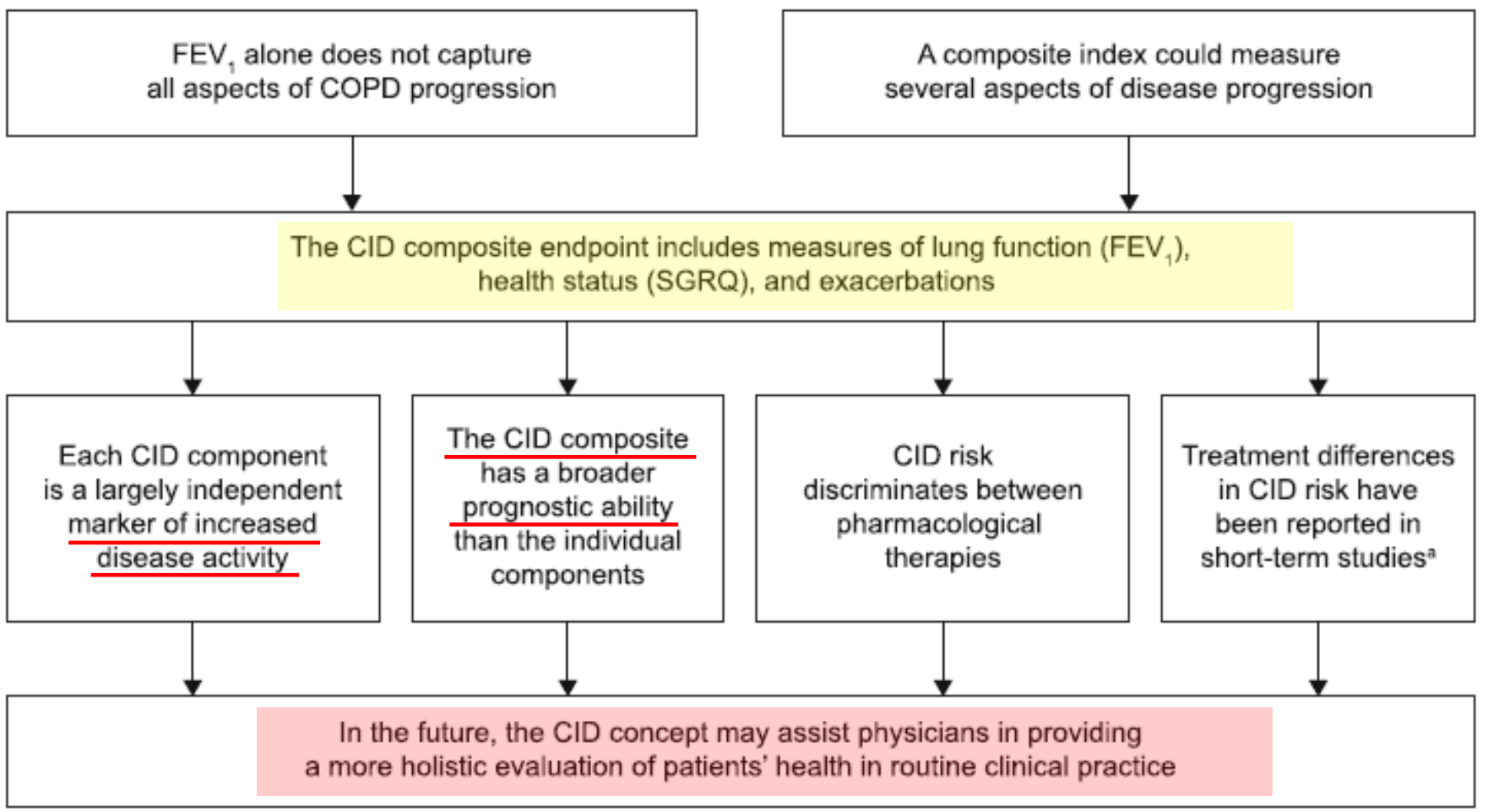
CID was defined as: FEV_1, deterioration ≥ 100 mL or SGRQ deterioration ≥ 4 units or a first moderate/severe exacerbation on any treatment in both trials. All comparisons are for CID+ versus CID- cohorts. $p < 0.05$ for all risk increases in both trials

CI confidence interval, *CID* clinically important deterioration; *CID+* cohort with a short-term deterioration (i.e. early unstable cohort); *CID-* cohort without a short-term deterioration (i.e. early stable cohort)

Prediction of all-cause mortality by CID status a over 30 months of follow-up in TORCH



Summary of the CID concept



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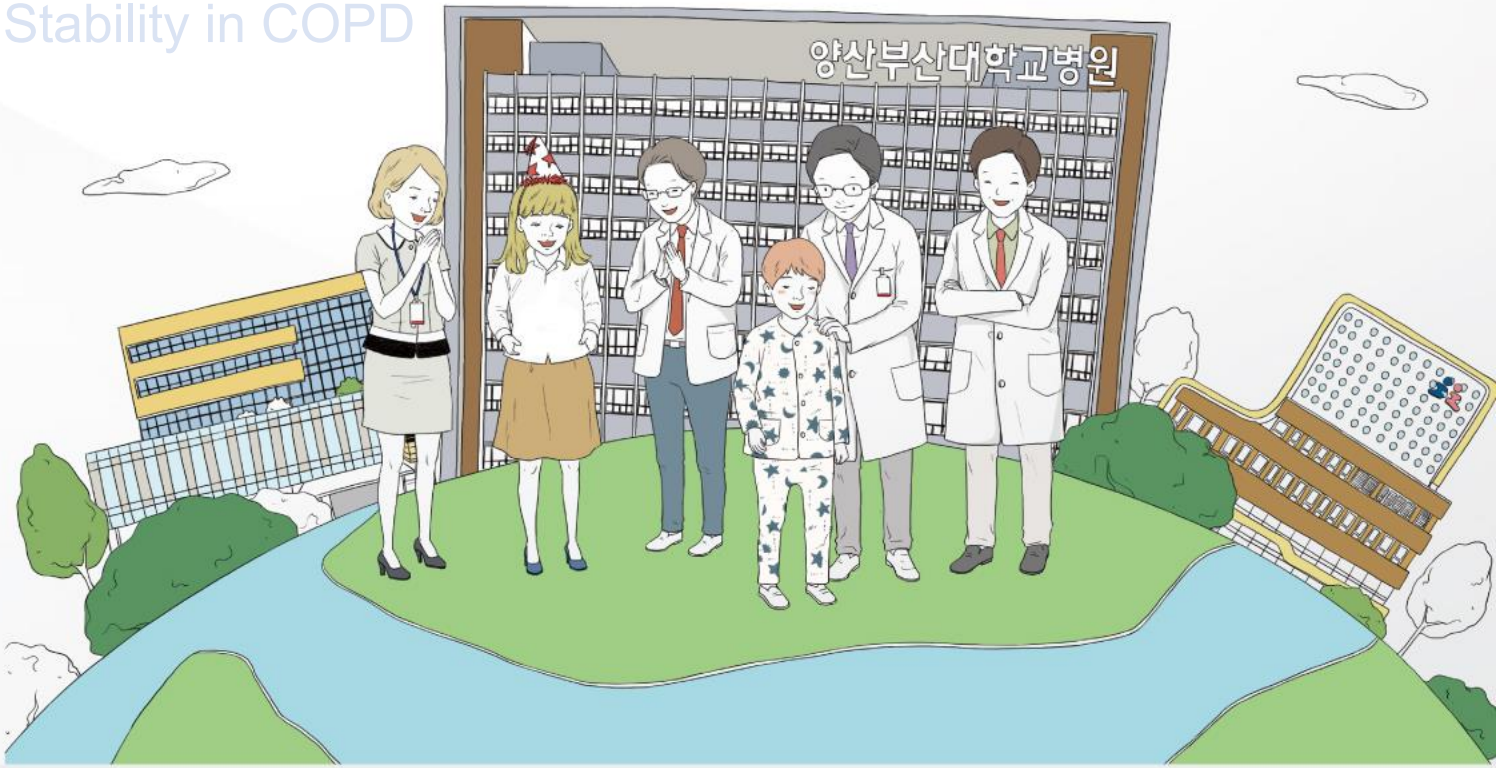
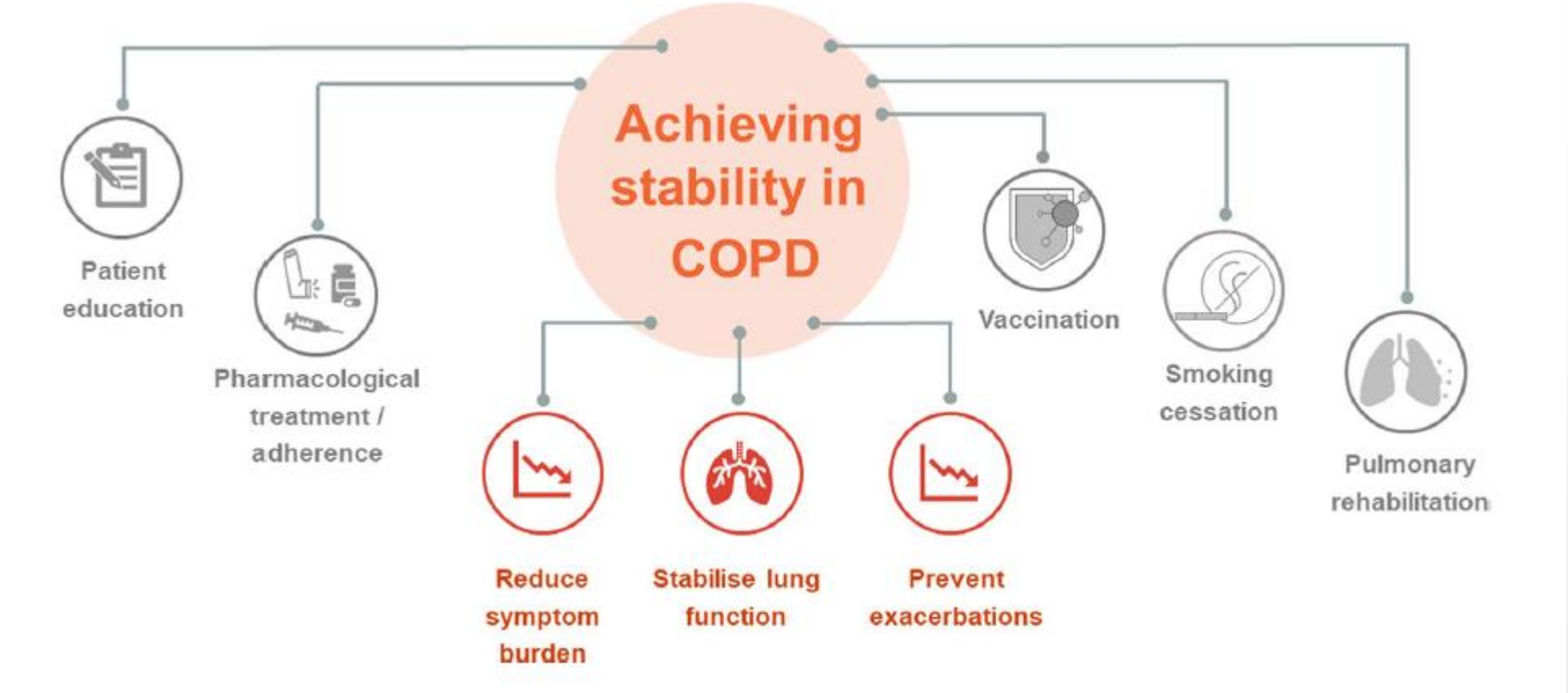
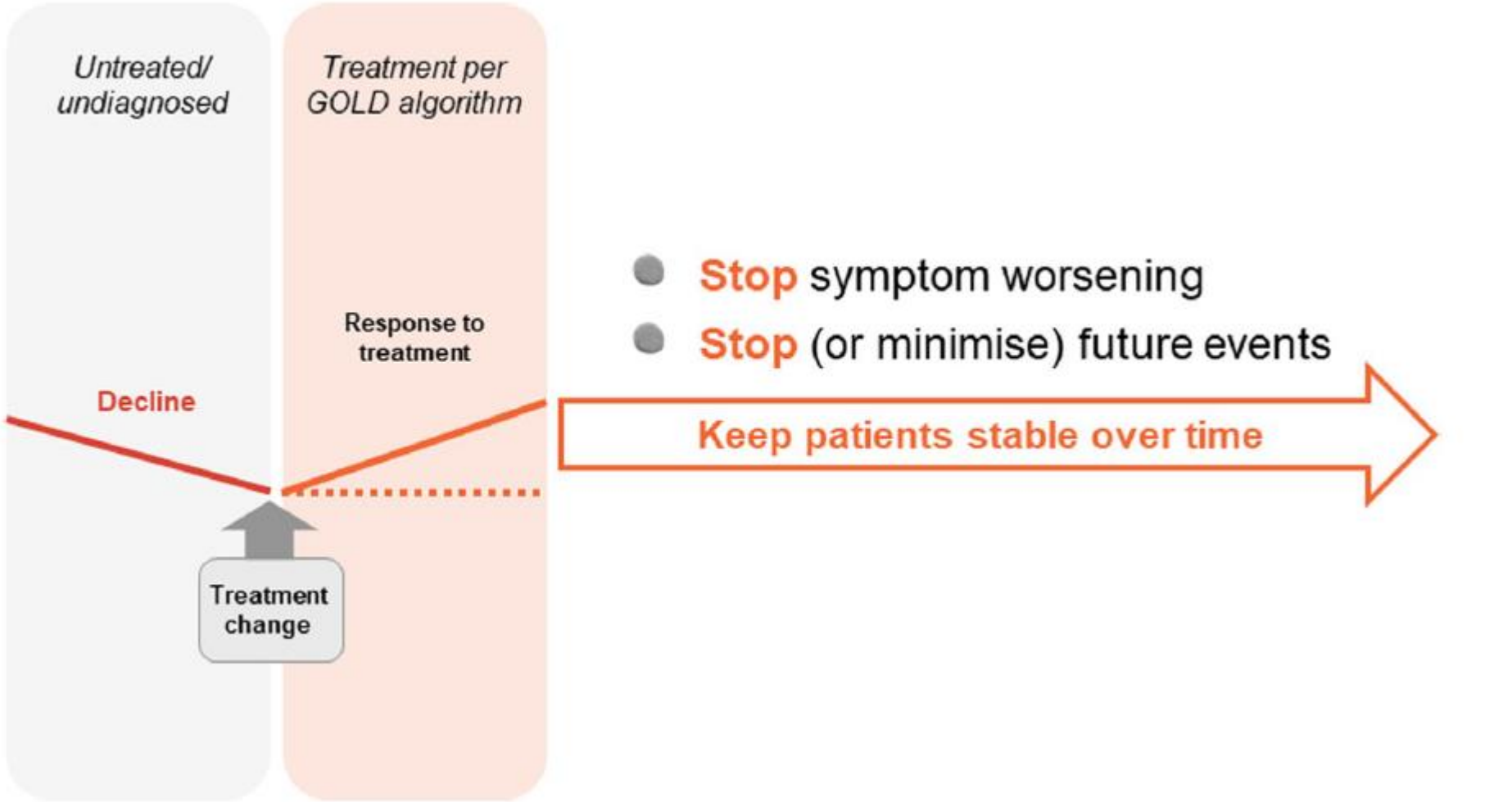


Key considerations for keeping patients with COPD stable over time



Schematic of disease stability, a framework that aligns to current treatment recommendations by GOLD



Is Disease Stability an Attainable Chronic Obstructive Pulmonary Disease Treatment Goal?

Dave Singh[1], MeiLan K. Han[2], Surya P. Bhatt[3], Marc Miravitlles[4], Chris Compton[5], Stefanie Kolterer[6], Tharishini Mohan[5], Suneal K. Sreedharan[5], Lee Tombs[7], and David M. G. Halpin[8]

[1]Centre for Respiratory Medicine and Allergy, Institute of Inflammation and Repair, Manchester Academic Health Science Centre, University of Manchester, Manchester University NHS Foundation Trust, Manchester, United Kingdom; [2]University of Michigan, Ann Arbor, Michigan; [3]Division of Pulmonary, Allergy, and Critical Care Medicine, University of Alabama at Birmingham, Birmingham, Alabama; [4]Pneumology Department, Hospital Universitari Vall d'Hebron, Vall d'Hebron Institut de Recerca (VHIR), Vall d'Hebron Barcelona Hospital Campus, CIBER de Enfermedades Respiratorias (CIBERS), Barcelona, Spain; [5]Global Medical Affairs, General Medicines, and [6]Specialty Medicines, GSK, London, United Kingdom; [7]Precise Approach Ltd., London, United Kingdom; and [8]University of Exeter Medical School, University of Exeter, Exeter, United Kingdom

ORCID IDs: 0000-0001-8918-7075 (D.S.); 0000-0002-9095-4419 (M.K.H.); 0000-0002-8418-4497 (S.P.B.); 0000-0002-9850-9520 (M.M.); 0009-0002-6798-4078 (T.M.); 0009-0004-0045-5838 (S.K.S.); 0000-0003-2009-4406 (D.M.G.H.).

- We propose **disease stability** as an **appropriate and attainable treatment goal**. Other disease areas have developed definitions of no disease activity or remission, which provide relevant information for defining and achieving stability for patients with COPD. Disease stability builds on related concepts already defined in COPD, such as clinical control and clinically important deterioration.

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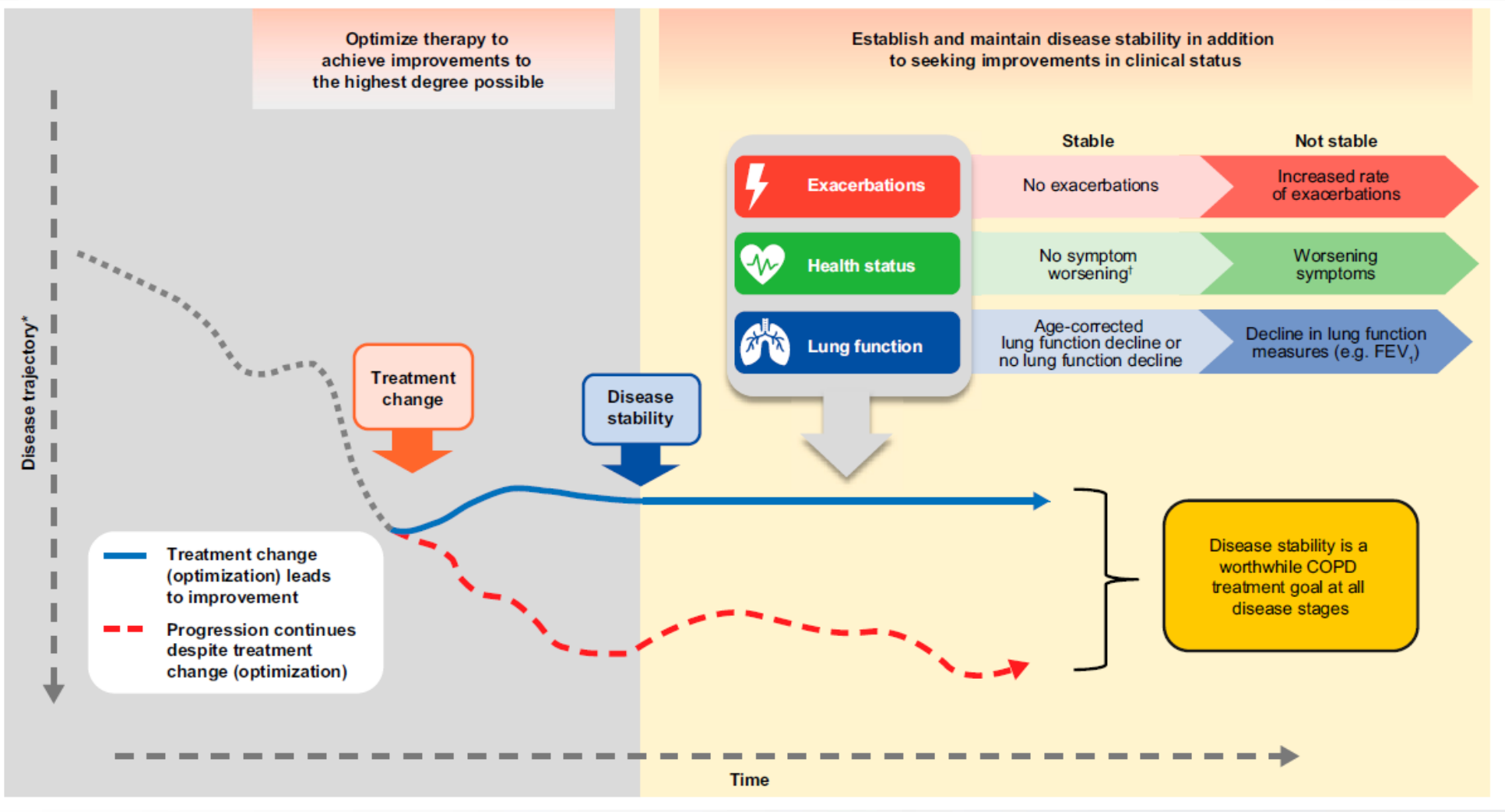
Disease stability across key clinical components



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Measuring Disease Stability in COPD

Table 1. Considerations for Potential Components of Disease Stability

Component	Attributes	Considerations
Exacerbations	• Lead to worse outcomes in the short and long term • Rates vary widely between patients • Yearly variation may not always reflect disease worsening • Subjective and often goes unreported	• Elimination of exacerbations? OR • Reducing current exacerbation rate or severity?
Health status	• Symptoms, physical activity, and quality of life • Impacted by daily symptom variability, comorbidities, and patient perception • Disease-specific measures may detect clinically meaningful changes	• Most relevant measures (i.e., research vs. in the clinic)? • Frequency/number of measurements needed to identify decline?
Lung function	• COPD involves persistent loss of lung function • Used to diagnose COPD • Spirometry is objective and inexpensive • Any decrease in lung function leads to poorer outcomes • High day-to-day and between-measurement variability	• Differing thresholds of decline based on severity (airflow limitation) • Accounting for age-related decline • Frequency/number of measurements needed to identify decline? • Most relevant spirometric measurements

Definition of abbreviation: COPD = chronic obstructive pulmonary disease.

Exacerbations

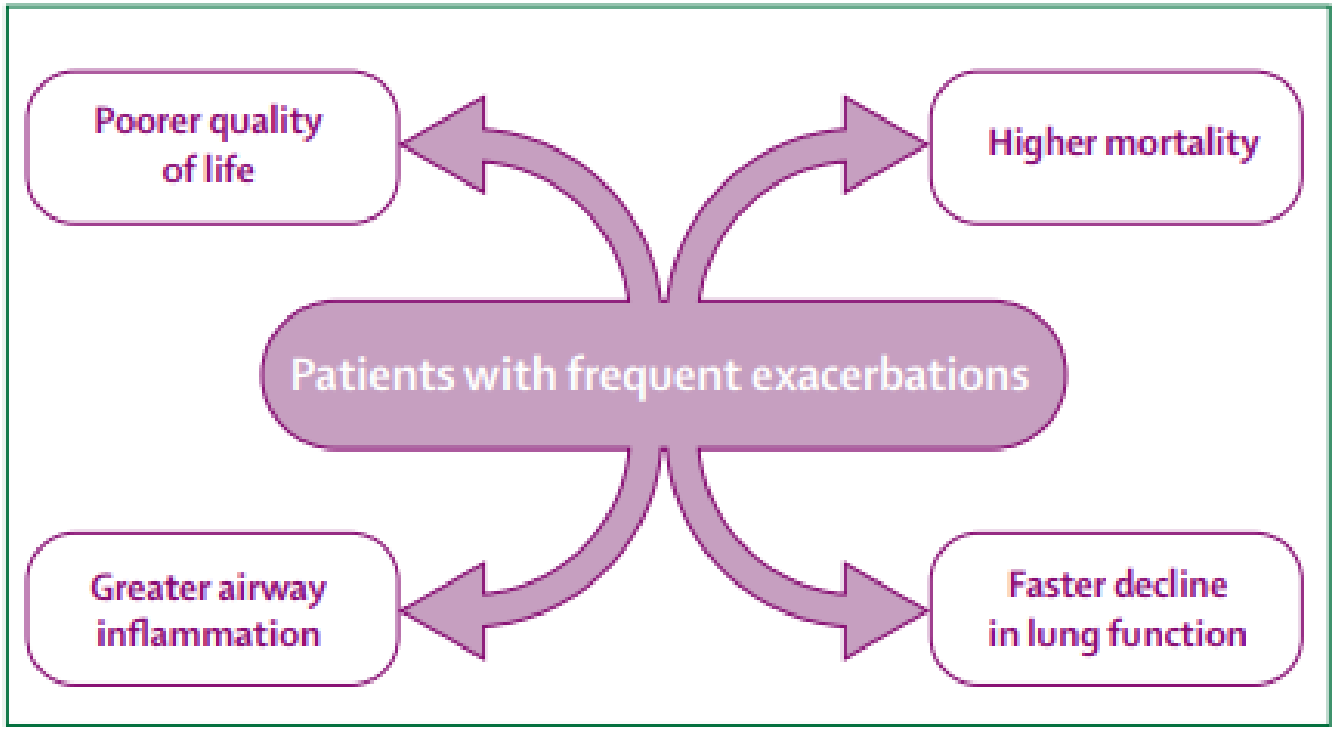

Figure 2: Effect of COPD exacerbations in the group with frequent exacerbations

- **Disease stability** might aim for patients to experience **no exacerbations in 1 year**, given the prognostic significance of having even one exacerbation.

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Effect of a single exacerbation on decline in lung function in COPD

David M.G. Halpin [a, *], Marc Decramer [b], Bartolome R. Celli [c], Achim Mueller [d], Norbert Metzdorf [e], Donald P. Tashkin [f]

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[e] Medicine TA Respiratory Diseases, Boehringer Ingelheim, Ingelheim am Rhein, 55216, Germany
[f] David Geffen School of Medicine, University of California Los Angeles, 10833 Le Conte Avenue, Los Angeles, CA 90095, USA

Study Design:

- Retrospective analysis using data from the UPLIFT® trial

Study Population:

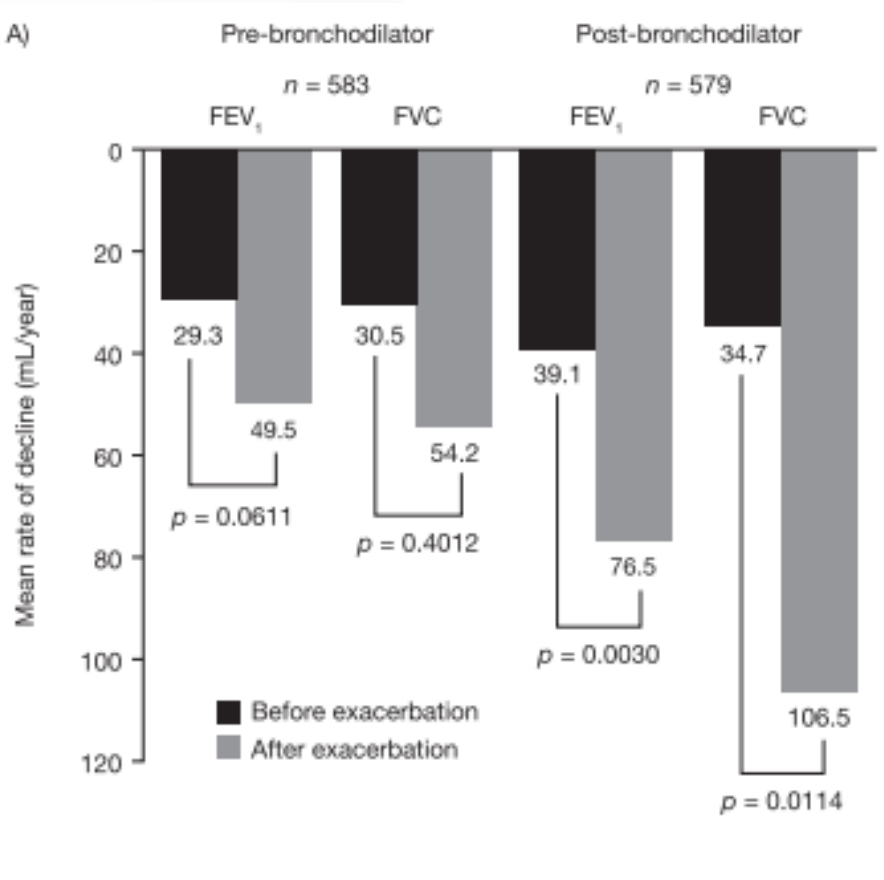
- Patients with a single moderate-to-severe exacerbation (exacerbator subgroup)
- Patients with no exacerbations during the study (non-exacerbator subgroup)

Comparison:

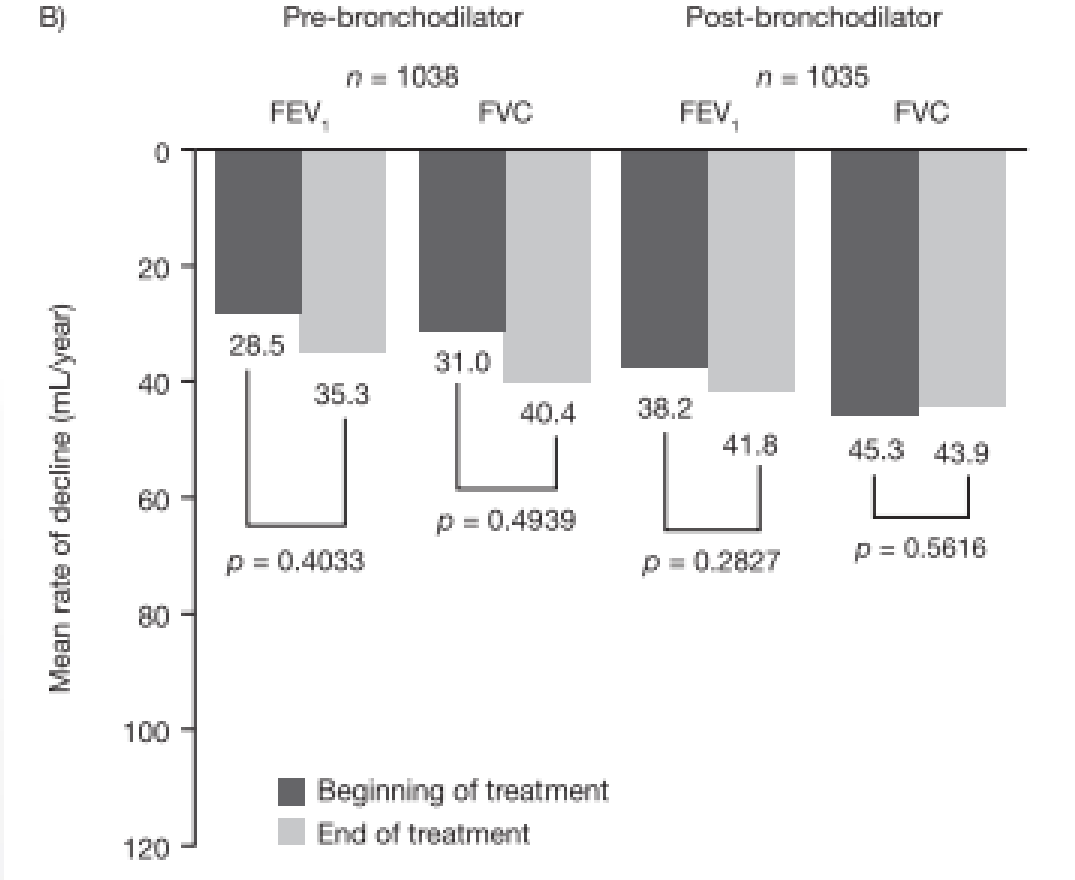
- Annual rates of decline in FEV_1 and FVC before and after the single exacerbation

Annual rates of lung function decline before and after the single exacerbation

Exacerbator subgroup



Non-exacerbator subgroup



Health Status

- **Health status assessment** includes domains such as cough, dyspnea, physical activity, and QoL, and is influenced by day-to-day symptom variability, comorbidities, and the patient's perception.
- Health status fluctuates over time, and **slowing its deterioration** can be an **important treatment goal**.
- **stability of health status** can be defined as the absence of clinically meaningful symptom worsening, or only minimal worsening that remains within the range of daily variation.

"Wellness in COPD" tool table/grid

KEY

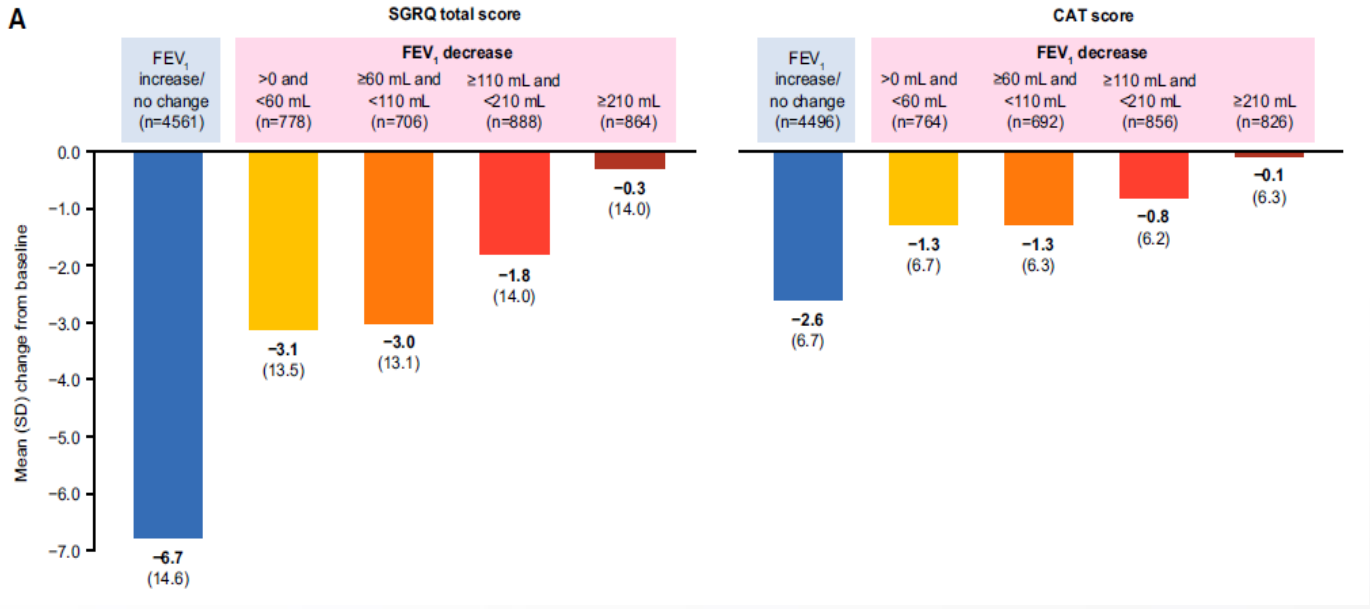
Very poor	Not good enough, if this criterion is important	Good enough	Recommended	Highly recommended

Tool/ Criteria	Validity/ Reliability	Responsive	Primary Care Population	Practical/ Easy to Administer	Tested in Practice	Other Languages
AQ20	☺	☺	☺	☺	😐	☹
BPQ-S	☺	😐	☺	😐	☹	☹
CARS	😐	☹	☹	😐	☹	☹
CAT	☺	☺	☺	☺	😐	☺
CCQ	☺	☺	☺	☺	☺	☺
CRQ	☺	☺	☺	☺	☺	😐
MRC-D	😐	😐	☺	☺	☺	😐
RIQ-MON10	☺	☺	😐	☺	☹	☹
SGRQ	☺	☺	😐	😐	😐	☺

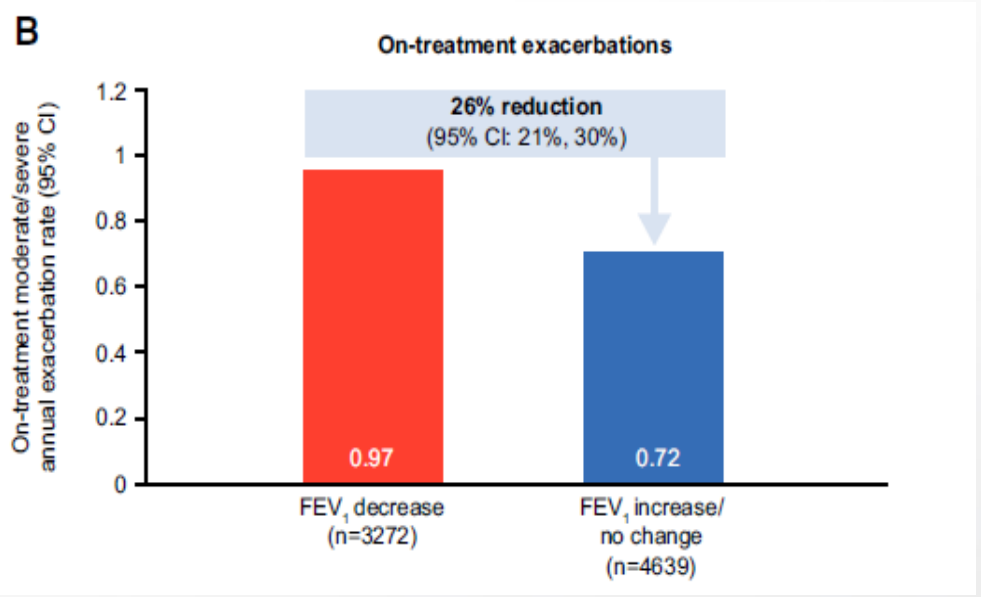
Lung Function

Effect of decline in FEV1 versus no change/improvement at Week 52.

Health status scores



Annual rate of exacerbation



- **Monitoring of both the current level of lung function and the trend over time** is crucial to assessing future risk, as evidence suggests that any **decrease in lung function is associated with poorer clinical outcomes.**

Definition of Disease Stability

Table 2. Preliminary Definition for Disease Stability

Components	Exacerbations: Frequency	Health Status: SGRQ or CAT	Lung Function: FEV_1
Thresholds*	No exacerbations	No worsening in SGRQ or CAT score; alternatively, no clinically significant worsening	No decrease; consideration of correction for age-related decline
Timeline	• 6–12 months, comprising one or multiple visits in that time • Benchmark current measurements against previous 6–12 months at each visit		
Individual vs. composite assessments	• Stability can be achieved in one or multiple components • Dependent on patient factors, availability of spirometry, and setting		
Context and setting	• Primary care or in-clinic and research settings • All disease severities, phenotypes/etiotypes, and interventions		
Other considerations	• "Clinically significant" worsening will require definition • Biomarkers may be implemented in future components once validated • An expert consensus on the definition of disease stability should be reached among key experts		

Definition of abbreviations: CAT = COPD Assessment Test; COPD = chronic obstructive pulmonary disease; SGRQ = St. George's Respiratory Questionnaire.
*Some patients may experience improvements with treatment optimization and other holistic interventions (e.g., smoking cessation, vaccination); this is also considered to be achieving disease stability.

- disease stability criteria may provide a clinical treatment goal and function as clinical trial endpoints. Future clinical trials and real-world studies should seek to validate and use disease stability as a treatment target to advance the standard of care for patients with COPD

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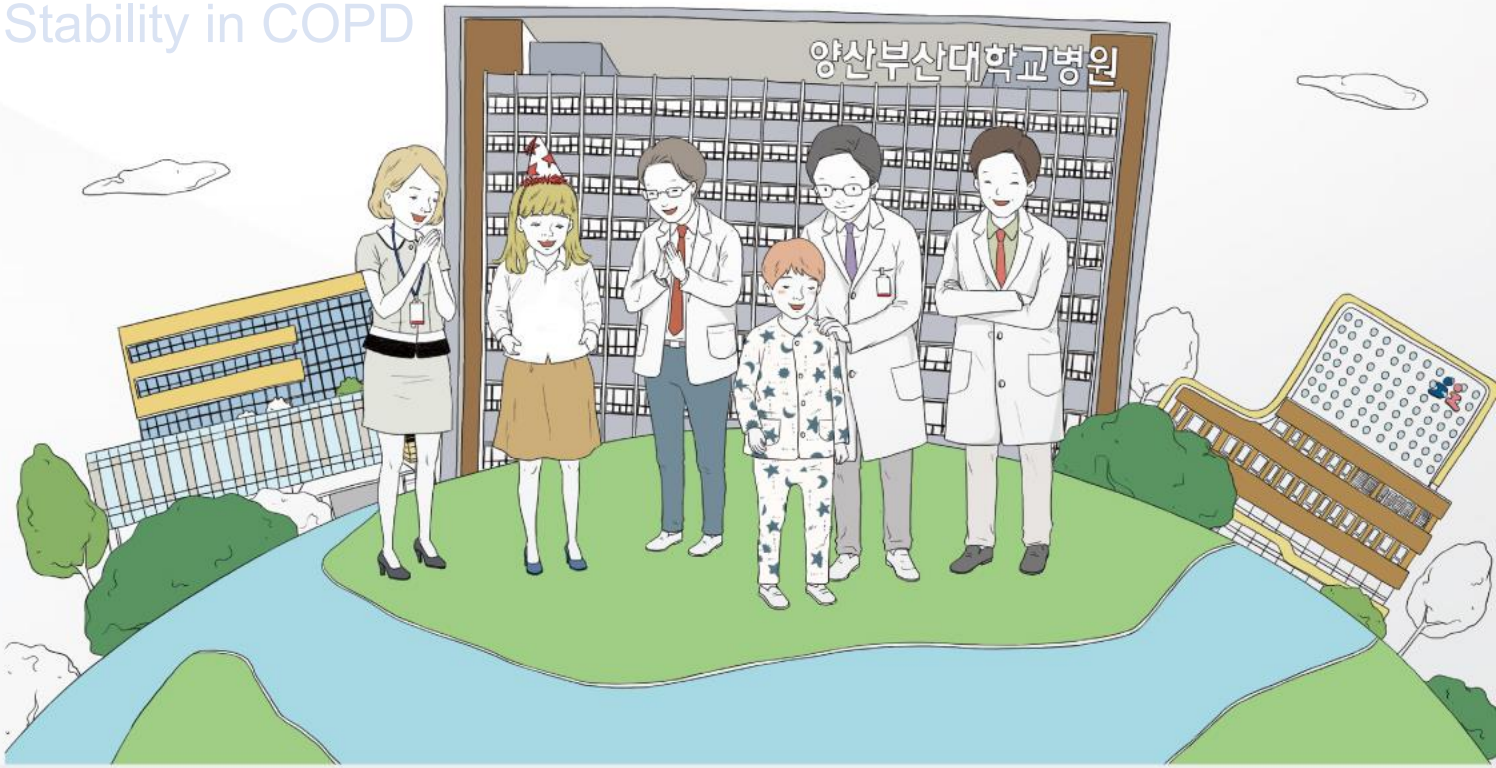


Clinical Outcomes in COPD with Disease Stability: Data from the KOCOSS Cohort

Study Design:

- Inclusion: Patients ≥ 40 years, post-bronchodilator $FEV_1/FVC < 0.7$
- Mortality Data: 10-year all-cause mortality linked with national death records
- **Definition of DS (+):**

  No moderate-to-severe exacerbation

  + No FEV_1 decline

  + No worsening in SGRQ for 1 year
- Analysis: Clinical outcomes compared between DS (+) and DS (–) groups

Table 1. Comparison of general characteristics according to presence of disease stability

	Disease stability (-)	Disease stability (+)	*P*-value
	N=1,492 (91.0%)	N=147 (9.0%)	
Age	68.6±7.7	68.5±7.8	0.829
Sex (male)	1373 (92.0%)	138 (93.9%)	0.524
Smoking status			0.252
- never smoker	131 (8.8%)	17 (11.6%)	
- ex-smoker	980 (65.7%)	87 (59.2%)	
- current smoker	380 (25.5%)	43 (29.3%)	
BMI	22.9±3.4	23.2±3.1	0.360
mMRC	1.4±0.9	1.3±0.8	0.364
SGRQc score	32.1±21.3	33.9±18.7	0.255
CAT score	14.8±8.0	14.0±7.2	0.231
Chronic bronchitis	167 (12.0%)	14 (10.0%)	0.579
History of asthma	429 (28.9%)	38 (26.0%)	0.526
GOLD severity stage			0.406
- I	119 (8.0%)	9 (6.1%)	
- II	737 (49.4%)	80 (54.4%)	
- III	507 (34.0%)	50 (34.0%)	
- IV	129 (8.6%)	8 (5.4%)	
Lung function test			
- FEV1 (%pred)	56.5±17.9	56.5±16.3	0.999
- FEV1 (L)	1.6±0.6	1.6±0.5	0.886
- FVC (%pred)	80.0±16.4	78.1±16.5	0.188
- FVC (L)	3.3±0.8	3.2±0.8	0.340
- FEV1/FVC	0.49±0.13	0.51±0.12	0.101
- DLco (%pred)	64.3±21.4	61.8±17.9	0.145
- RV/TLC	44.3±12.6	43.5±11.8	0.573
6MWD (m)	385.1±117.5	387.1±109.2	0.859
FeNO (ppb)	28.5±16.8	35.4±28.1	0.440
Radiologic findings (chest CT)			
- Emphysema	496 (57.1%)	45 (50.0%)	0.239
- Bronchiectasis	157 (18.1%)	15 (16.7%)	0.853

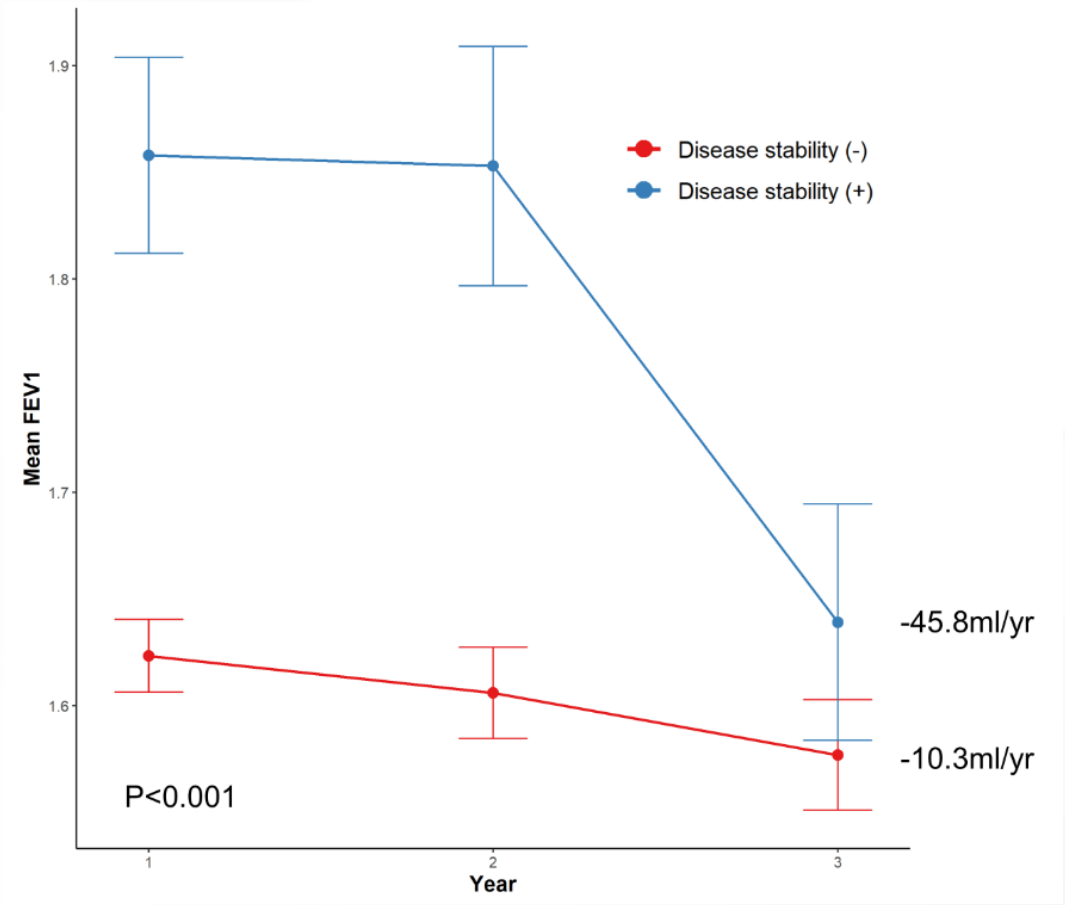
Exacerbations

Table 2. Comparison of exacerbation frequency according to presence of disease stability

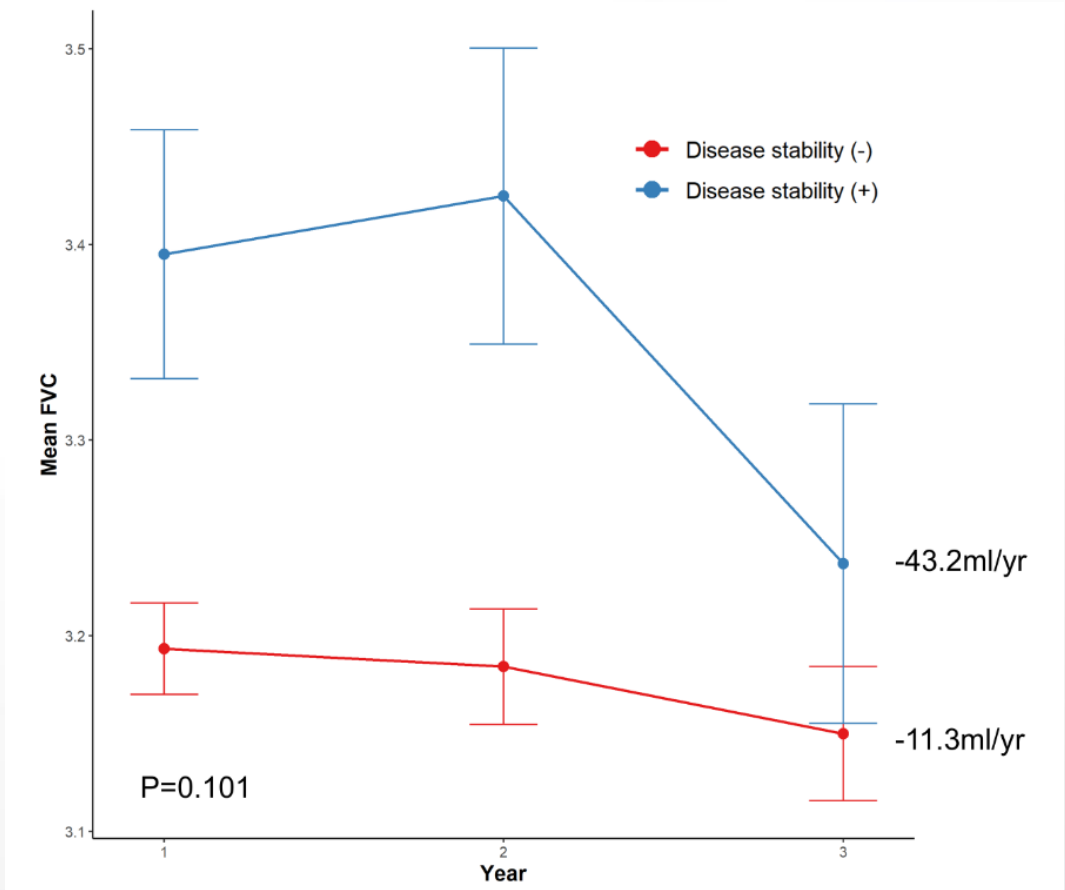
Exacerbations	IRR	95%CI	*P*-value
Moderate-to-severe	0.30	0.20-0.43	0.033
Severe	0.26	0.10-0.58	0.002

Lung Function Decline

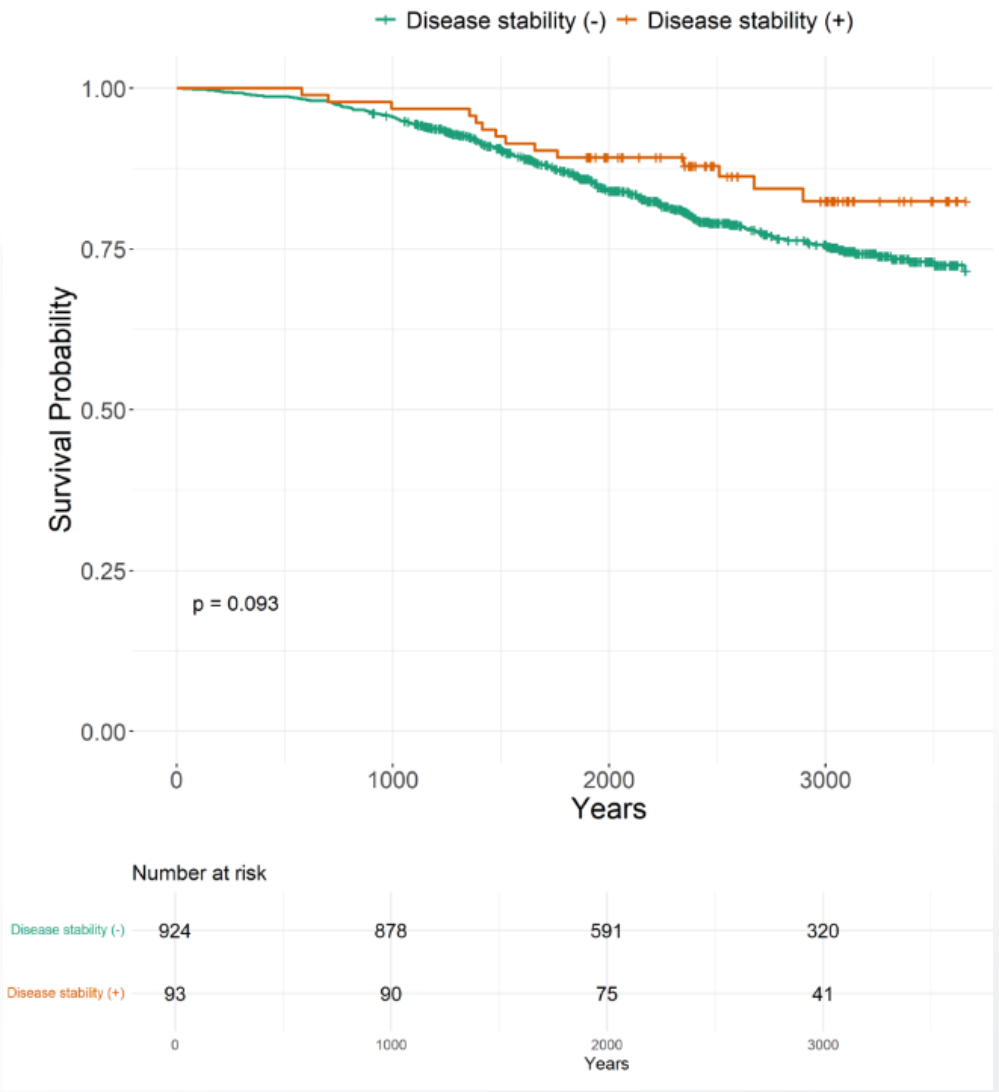
post-BD FEV1



post-BD FVC



All-Cause Mortality



All-Cause Mortality

Table 3. Cox proportional hazards regression of all-cause mortality according to disease stability

	Crude			Multivariate		
	HR	95%CI	*P* -value	HR	95%CI	*P* -value
Disease stability	0.63	0.37-1.09	0.096	0.58	0.34-0.99	0.047
Age	1.09	1.07-1.11	<0.001	1.07	1.05-1.09	<0.001
Female Sex	0.55	0.34-0.90	0.018	0.75	0.33-1.69	0.486
BMI	0.90	0.87-0.93	<0.001	0.88	0.84-0.92	<0.001
Smoking status						
- never smoker	(reference)			(reference)		
- past smoker	1.74	1.12-2.70	0.014	1.48	0.72-3.03	0.288
- current smoker	1.98	1.25-3.15	0.004	2.08	0.99-4.40	0.055

- The study found statistically significant reductions in acute exacerbations and mortality in COPD patients with DS. These findings imply that DS is a clinically valuable and achievable treatment goal in patients with COPD.

Summary

1. COPD는 악화와 점진적 진행을 동반하는 이질적 만성 질환이며, 기존 치료 목표(증상 완화, 악화 예방)는 장기적 질병 조절을 완전히 막기 어려워, 'Disease Stability' 가 새로운 치료 목표로 제안.

2. **disease stability** 정의:
   - FEV_1 감소 없음
   - 증상유지(SGRQ or CAT 악화 없음)
   - 중등도 이상 급성악화 없음

3. Disease stability에 대한 명확한 기준 정립과 객관적인 평가 방법 개발이 필요하며, 이를 위한 추가 연구가 필요함.

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환자 내몸

경청해 주셔서 감사합니다.

Thank you for your attention