GOLD UPDATE on COPD and the Importance of Accurate Dyspnea Evaluation

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MA-AZAP ML-4006-US-0212 Approved 11/16

What Is COPD?

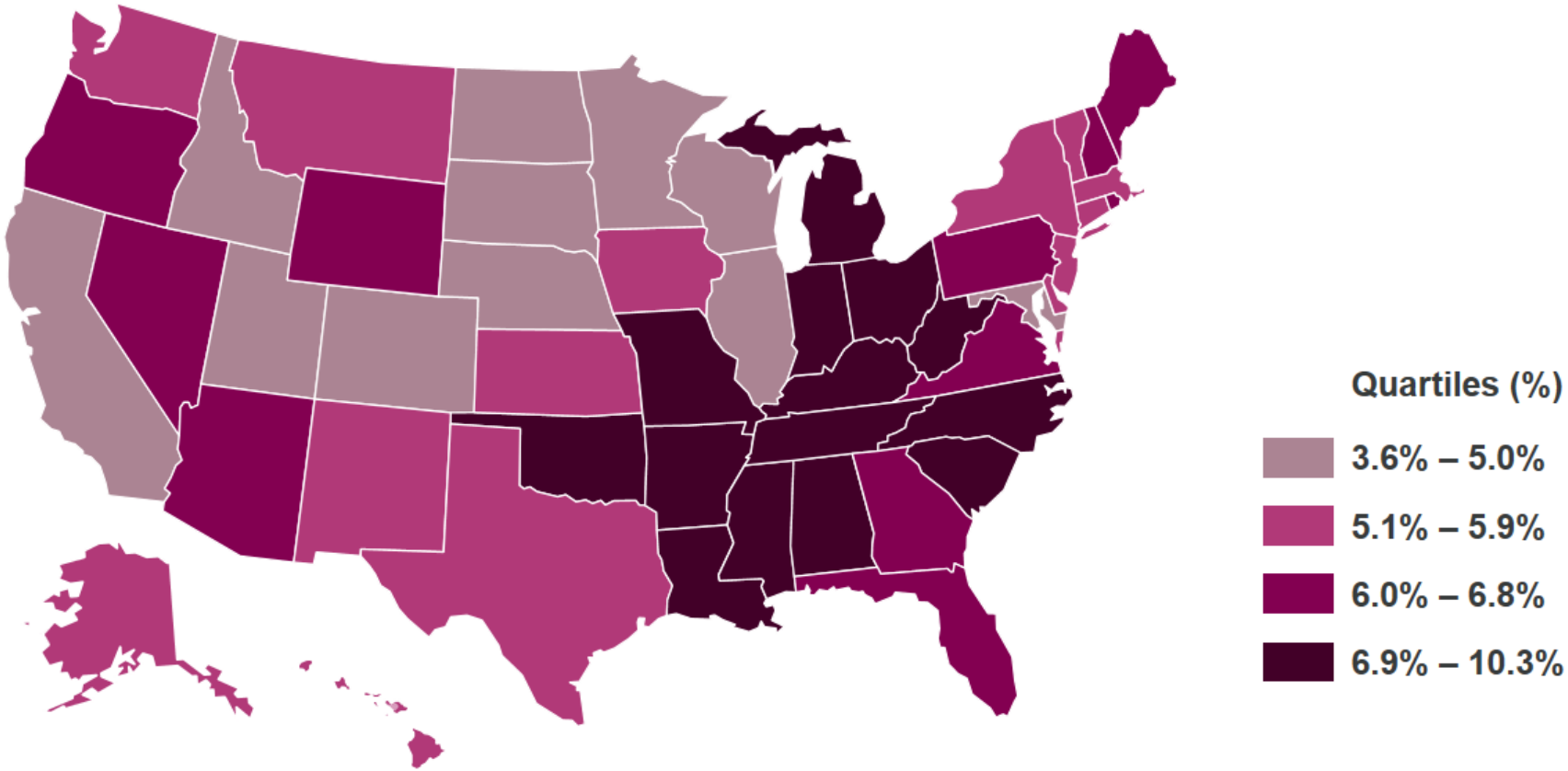
COPD is...

- **Preventable and treatable**
- Associated with significant **concomitant chronic diseases** which increase its **morbidity and mortality**
- 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**

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 January 6, 2017.

COPD Is a Nationwide Problem

In the United States, adults ≥18 years of age with COPD...



DC = District of Columbia

PR = Puerto Rico

GU = Guam

Centers for Disease Control (CDC), Behavioral Risk Factor Surveillance System, 2013. cdc.gov/features/copd-burden. Accessed November 18, 2015.

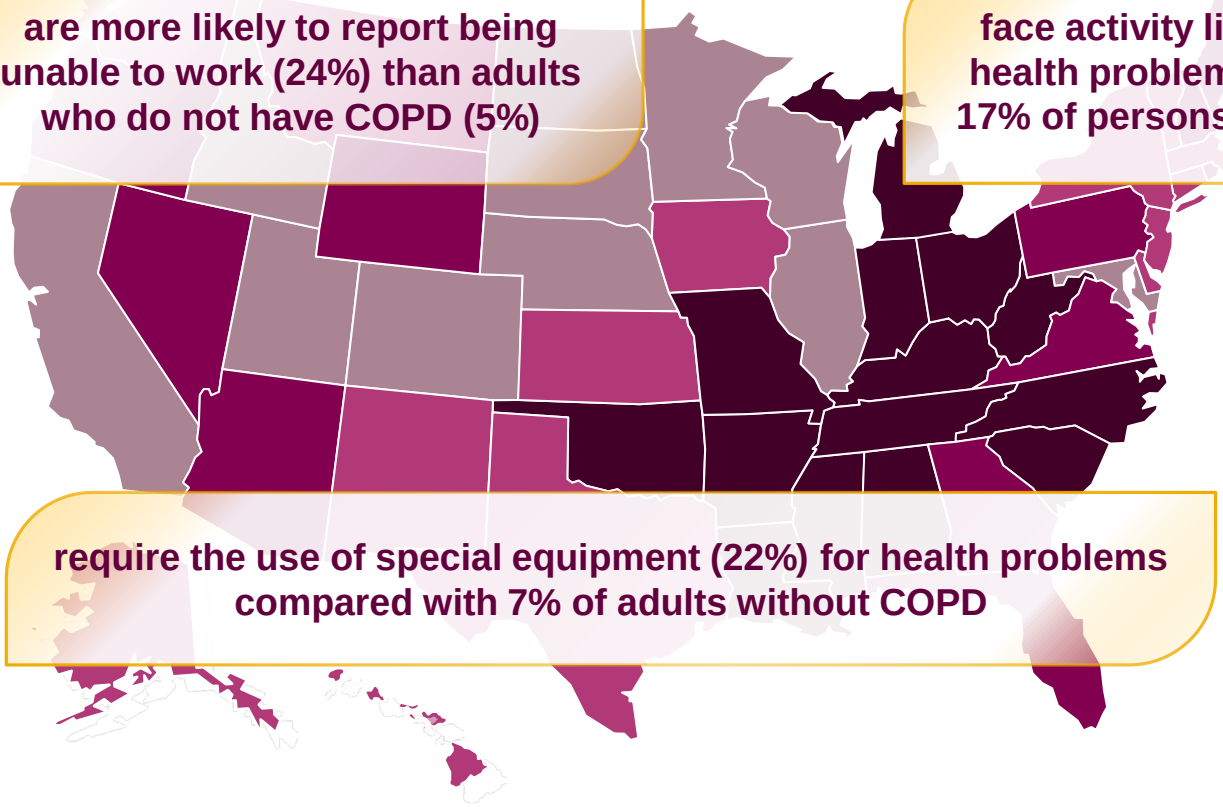
Wheaton AG, et al. *MMWR*. 2015;64(11):289-295.

COPD Is a Nationwide Problem

In the United States, adults ≥18 years of age with COPD...

are more likely to report being unable to work (24%) than adults who do not have COPD (5%)

face activity limitations as a result of health problems (50%) compared with 17% of persons who do not have COPD



require the use of special equipment (22%) for health problems compared with 7% of adults without COPD

Quartiles (%)

- 3.6% – 5.0%
- 5.1% – 5.9%
- 6.0% – 6.8%
- 6.9% – 10.3%

DC = District of Columbia PR = Puerto Rico GU = Guam

Centers for Disease Control (CDC), Behavioral Risk Factor Surveillance System, 2013. cdc.gov/features/copd-burden. Accessed November 18, 2015.

Wheaton AG, et al. *MMWR*. 2015;64(11):289-295.

COPD Arises From Damage and Inflammation in the Respiratory Tract

Respiratory Anatomy

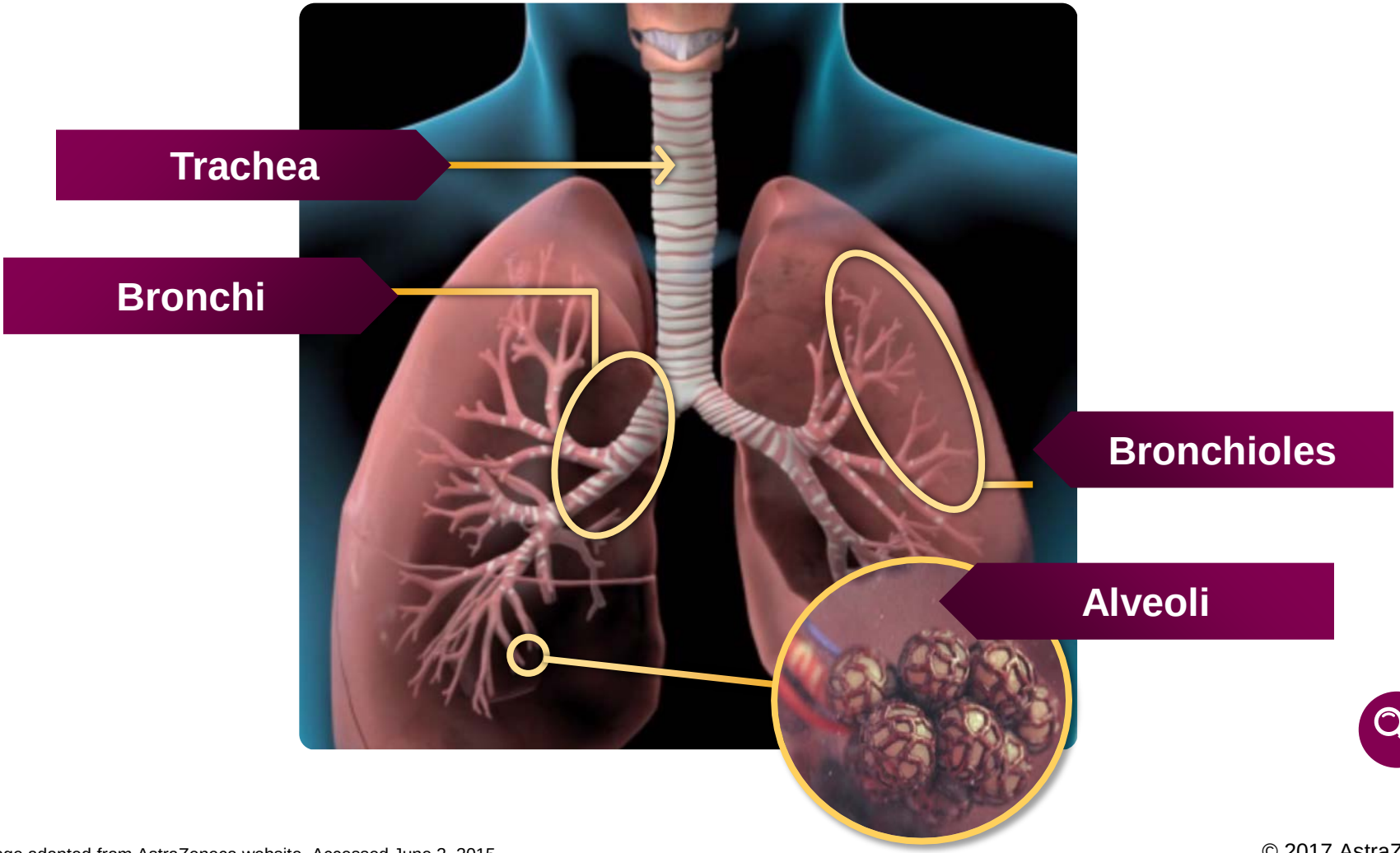


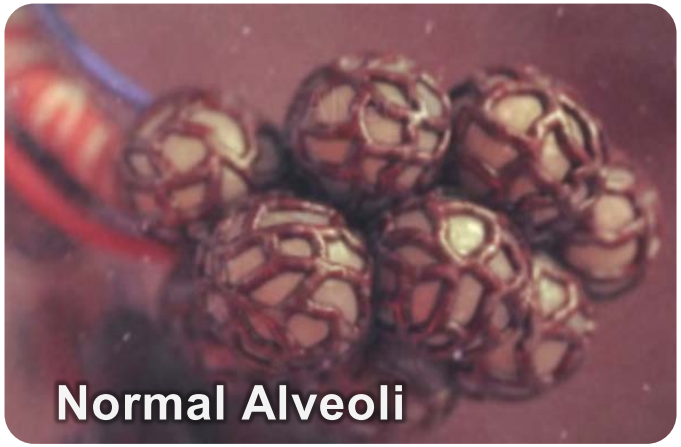
Image adapted from AstraZeneca website. Accessed June 2, 2015.

Chronic Bronchitis and Airway Inflammation

- In healthy lungs, the airways are elastic and flexible
- With chronic bronchitis, airways can become swollen or thicker than normal
- Chronic bronchitis may cause increased mucus production
- Airways may become partially obstructed, making it harder to get air out of the lung. The resulting hyperinflation also makes inspiration difficult

NIH. National Heart, Lung, and Blood Institute. COPD Learn More Breathe Better. NIH.gov website. http://www.nhlbi.nih.gov/files/docs/public/lung/copd-patient.pdf. Accessed December 17, 2015.
Images adapted from AstraZeneca website. Accessed December 17, 2015.

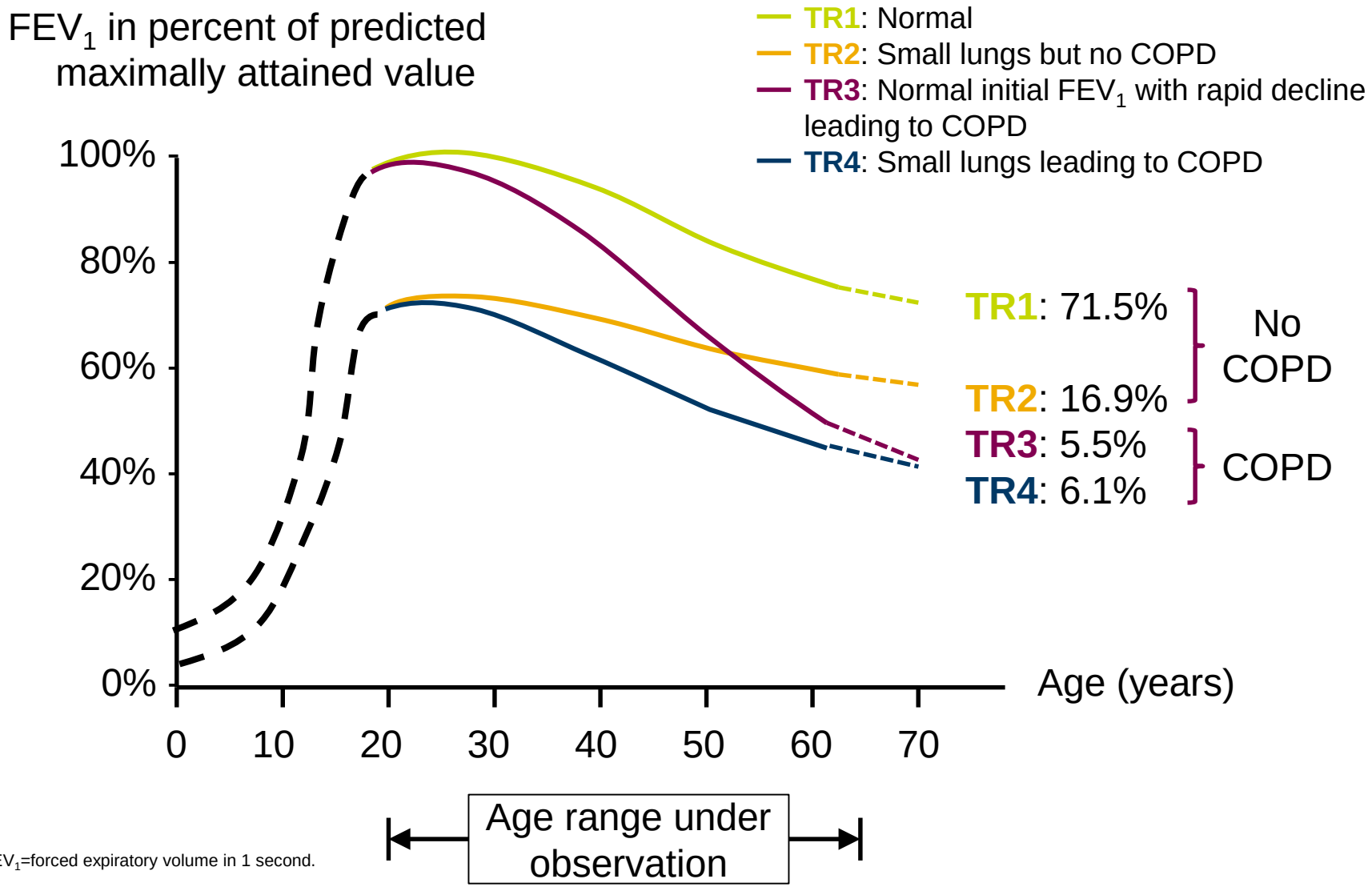
Emphysema Is Caused by Damage to the Alveoli Walls



- Healthy alveoli are elastic and capable of springing back to their original size after active inspiration
- Emphysema involves damage to the walls of the alveoli
- In emphysema, alveoli lose their elasticity, which impairs natural passive exhalation, resulting in trapping of air and hyperinflation

American Thoracic website. Accessed December 17, 2015.
Images adapted from AstraZeneca website. Accessed December 17, 2015.

FEV_1 Progression over Time



FEV_1=forced expiratory volume in 1 second.

Adapted from 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 January 6, 2017.

Global Strategy for the Diagnosis, Management, and Prevention of COPD

Key Indicators for a Diagnosis of COPD

Symptoms and Past Medical History

- **Dyspnea** – progressive, worse with exercise, persistent
- **Chronic cough** – may be intermittent and unproductive, recurrent wheeze
- **Chronic sputum production** – any pattern of chronic sputum production may indicate COPD
- Recurrent lower respiratory tract infections

History of Risk Factors

- Host factors (genetic, congenital/developmental)
- Tobacco smoke
- Smoke from home cooking/heating fuels
- Occupational dusts, vapors, fumes gases or chemicals

Family History of COPD and/or Childhood Factors

AND

Airflow Limitation

Post-bronchodilator FEV_1/FVC <0.70*

GOLD recommends active casefinding:

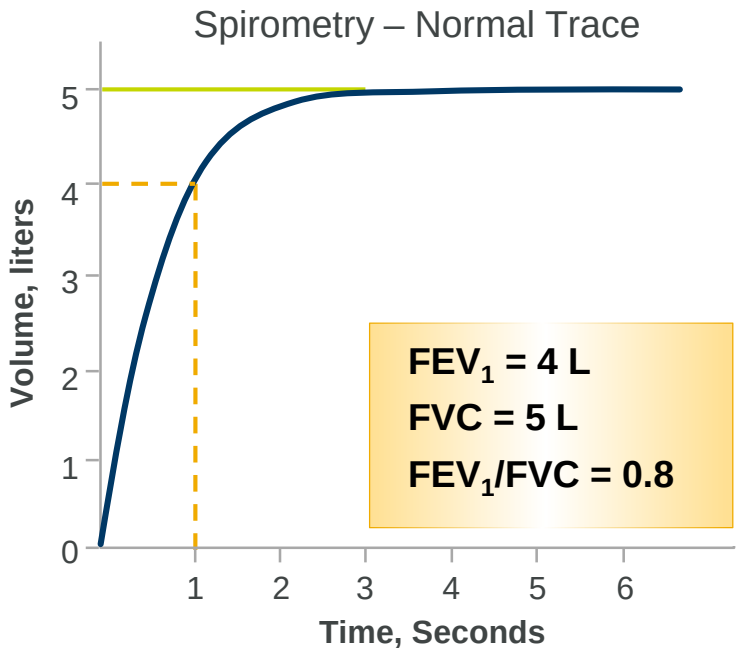
i.e. Performing spirometry in patients with symptoms and/or risk factors, but not screening spirometry

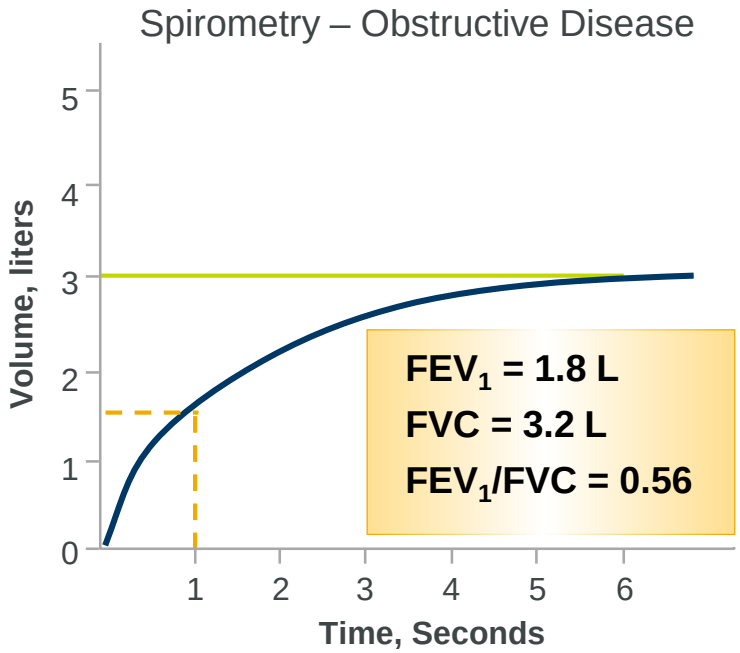
*Required for the diagnosis of COPD.
FEV_1=forced expiratory volume in 1 second; FVC=forced vital capacity.

Adapted from 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 January 6, 2017.

Use Spirometry to Confirm COPD Diagnosis[1]

Post-bronchodilator FEV_1/FVC <0.70 indicates COPD diagnosis





FEV_1: Amount of air exhaled in the first second during the FVC maneuver[2]

FVC: Total amount of air a person can forcibly exhale after maximum inhalation[2]

FEV_1 = forced expiratory volume in one second; FVC = forced vital capacity
Adapted from Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of COPD.

1. 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 January 6, 2017. **2.** Miller MR ,et al. *Eur Respir J*. 2005;26:319-338.

COPD Exacerbations: Risk Factors and Impact

Risk factors

- Frequent past exacerbations
- Severity of FEV_1 impairment
- Chronic bronchial mucus hypersecretion
- Daily cough and wheeze
- Increased age
- Persistent symptoms of chronic bronchitis
- Comorbid conditions, mainly cardiovascular disease

Impact

- More rapid decline of FEV_1
- Increased dyspnea
- Greater decline in health status
- Increased mortality

Anzueto, A. Impact of exacerbations on COPD. *Eur Respir Rev.* 2010;19:116,113–118.

The Refined ABCD Assessment tool (steps 1 and 2)

Spirometrically Confirmed Diagnosis

- Post-bronchodilator $FEV_1/FVC < 0.7$

Assessment of Airflow Limitation (FEV_1 % predicted)	
GOLD 1	≥ 80%
GOLD 2	50% - 79%
GOLD 3	30% - 49%
GOLD 4	< 30%

Adapted from 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 January 6, 2017.

The Refined ABCD Assessment tool (step 3)

Exacerbation history	Assessment of symptoms/risk of exacerbations	
≥ 2 or ≥ 1 leading to hospital admission	C	D
0 or 1 (not leading to hospital admission)	A	B
	mMRC 0-1 CAT < 10	mMRC ≥ 2 CAT ≥ 10

Symptoms

Adapted from 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 January 6, 2017.

Goals of COPD Management

Reduce Symptoms

- Relieve symptoms
- Improve exercise tolerance
- Improve health status

AND

Reduce Risk

- Prevent disease progression
- Prevent and treat exacerbations
- Reduce mortality

Adapted from 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 January 6, 2017.

Nonpharmacologic Management of COPD

Patient Group	Essential	Recommended	Depending on Local Guidelines
A	Smoking cessation (can include pharmacologic treatment)	Physical activity	Flu vaccination Pneumococcal vaccination
B-D	Smoking cessation (can include pharmacologic treatment) Pulmonary rehabilitation	Physical activity	Flu vaccination Pneumococcal vaccination

Adapted from 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 January 6, 2017.

Fletcher-Peto Curve: Impact of Smoking on Airflow

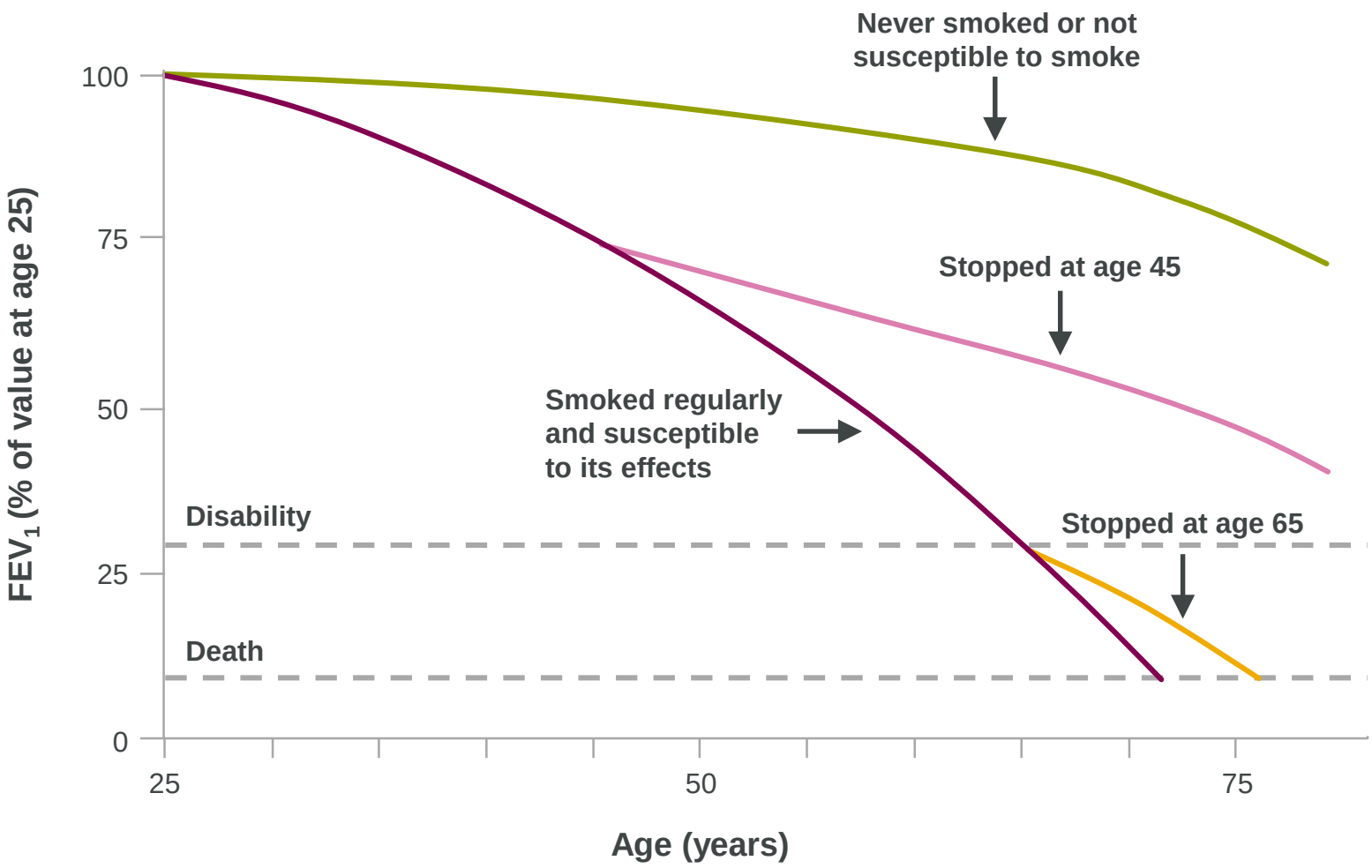
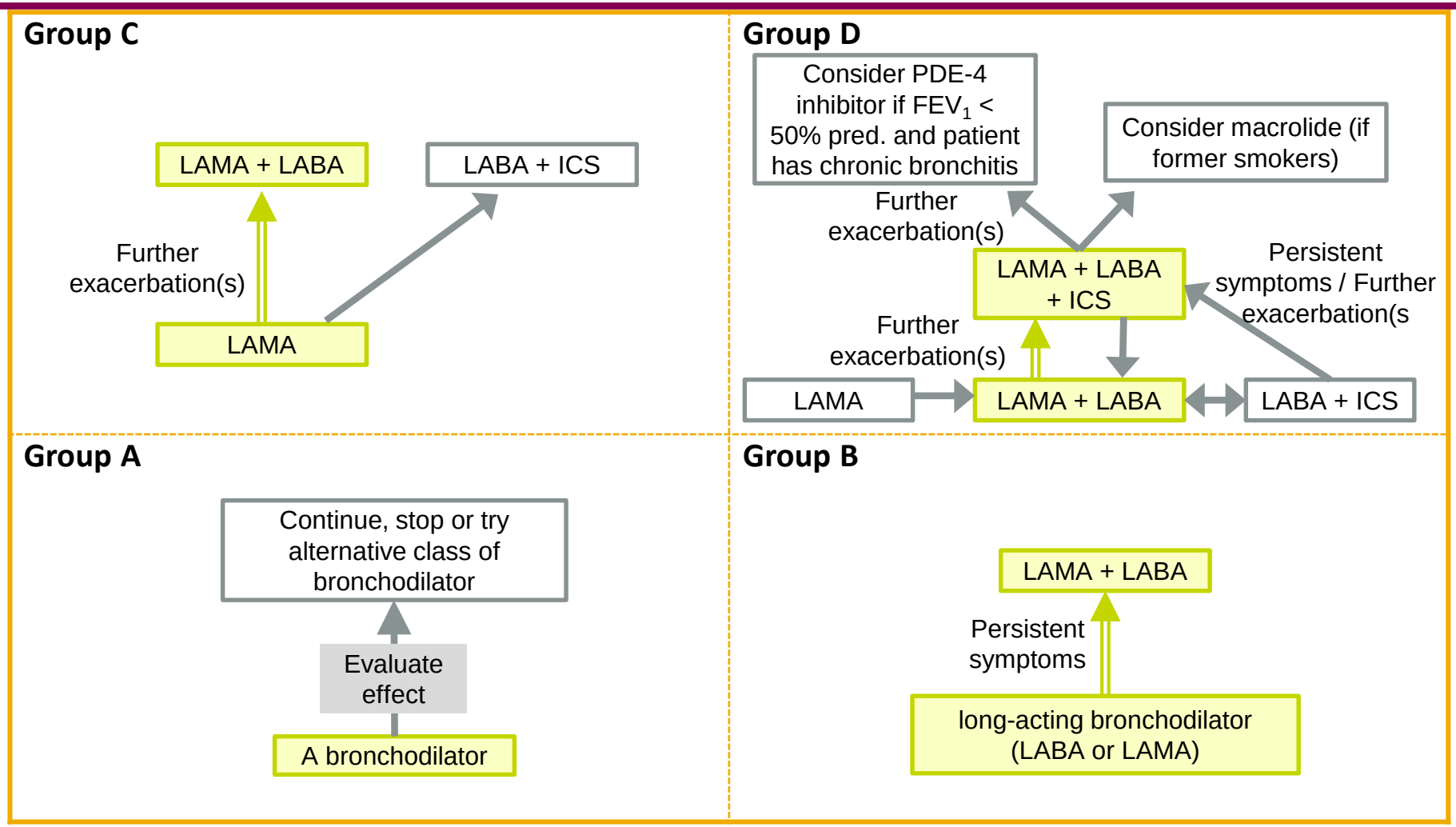


Figure adapted from Fletcher, C, Peto, R. *Br Med J.* 1977;1(6077):1645-1648.

Global Strategy for the Diagnosis, Management, and Prevention of COPD

Pharmacologic Treatment Algorithms



SABA = short-acting β_2-agonist; SAMA = short-acting muscarinic antagonist; LABA = long-acting β_2-agonist; LAMA = long-acting muscarinic antagonist; ICS = inhaled corticosteroid; PDE-4 = phosphodiesterase-4.
Adapted from 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 January 6, 2017.

Preferred treatment

Learning Objectives

Upon completion of this training, learners should be able to:

- ✓ Identify physical inactivity as an important problem in COPD and recognize its association with worsened disease
- ✓ Explain dyspnea as the driver of COPD inactivity
- ✓ Understand the importance of a full evaluation of COPD which includes a complete evaluation of dyspnea and its impact on activity levels

A COPD Patient's Perspective

*"My goals are probably similar to the goals of many patients as they age, but having COPD and its associated limitations, increases the importance of these goals. First, I want to remain **independent**. I have three grown daughters, one living close by, but I really prefer to manage my life without troubling my children. They have their own lives and their own needs."*

*"Second, I'd like to remain **mobile** for as long as possible. Mobility, to me as a COPD patient, means being able to get around my home and do household chores, such as bed-making and laundry. Outside the home, I want to continue to drive myself around, shop for groceries, make doctor visits, and do errands unassisted. Finally, I want to stay well and out of hospitals, except as a volunteer!"*

Cruse MA. *COPD*. 2007 Sep;4(3):279-81.

Are the Needs of COPD Patients Being Fully Met?

Studies report 30-70% of patients with COPD receive no treatment.[1]

Treatments when given are often sub-optimal.[1]

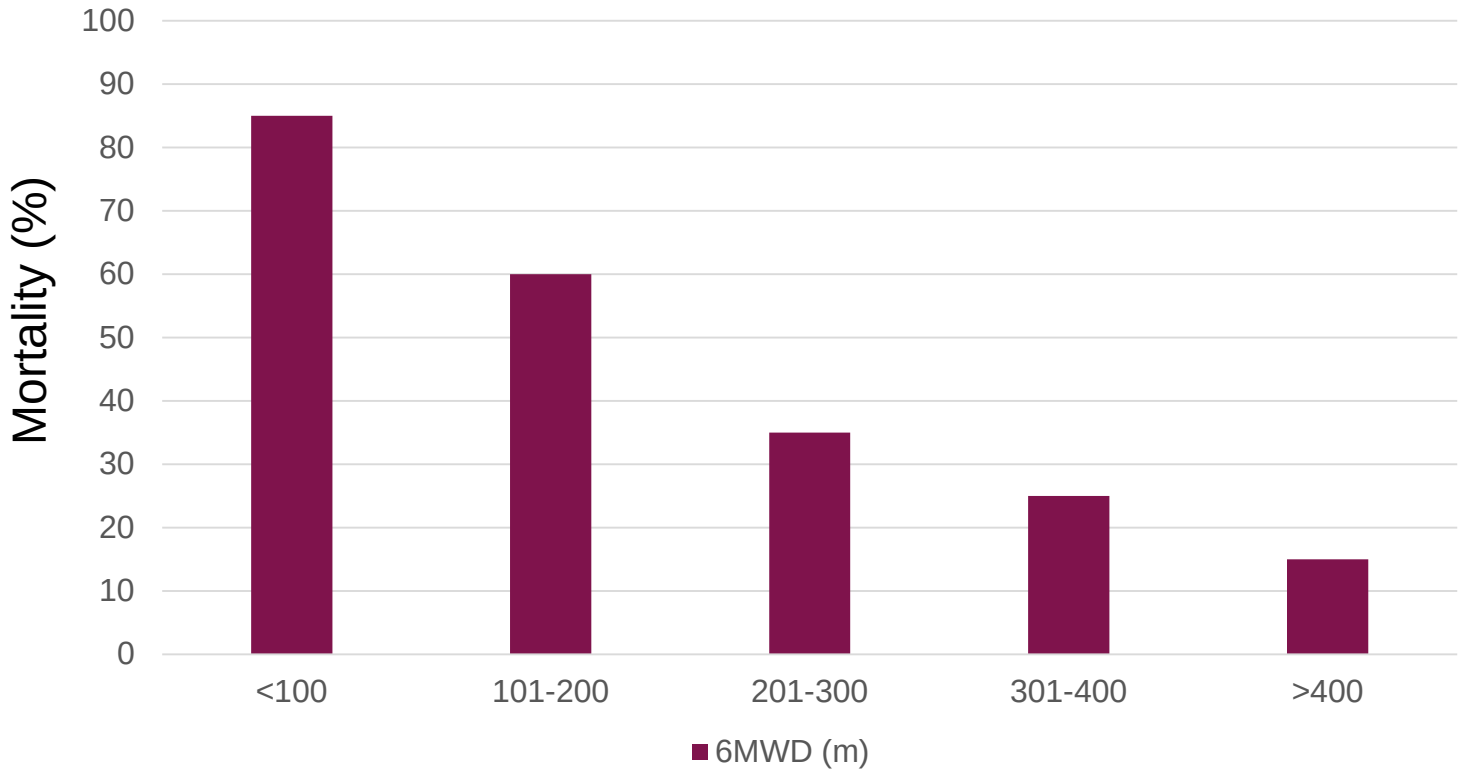
The **GOLD guidelines** recommend full symptom evaluation to select treatment in addition to evaluating comorbidities. However, this can be difficult for several reasons:[2]

- Patients can experience worsening dyspnea even in the setting of stable lung function.[3]
- Conventional tests used to identify activity limitation may not be able to assess impact of environmental and psychological changes on activity.[4]

1. Rennard S, et al. *COPD*. 2013 Jun;10(3):378-89; 2.Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017. Available from: http://www.goldcopd.org/; 3.Mahler DA, et al. *COPD*. 2012 Aug;9(5):522-7; 4. Bourbeau J. COPD. 2009 Jun;6(3):192-200.

Correlation Between Exercise Tolerance and COPD Outcomes

Mortality progressively decreases as the 6-min walking distance (6MWD) increases.

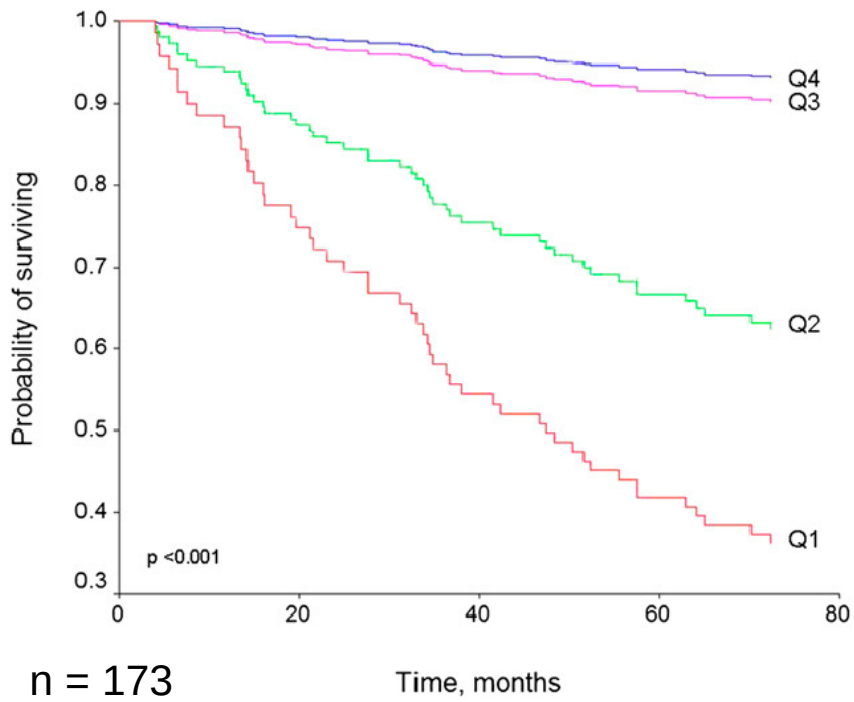


For distances <100 m, n=19; for 101-200 m, n=61; for 201-300 m, n=57; for 301-400 m, n=46; and for >400 m, n=15.

Pinto-Plata VM, et al. *Eur Respir J*. 2004 Jan;23(1):28-33.

Daily Activity and Outcomes

In patients with moderate to very severe COPD, daily physical activity was measured providing a mean of 1-min movement epochs as vector magnitude units (VMUs).

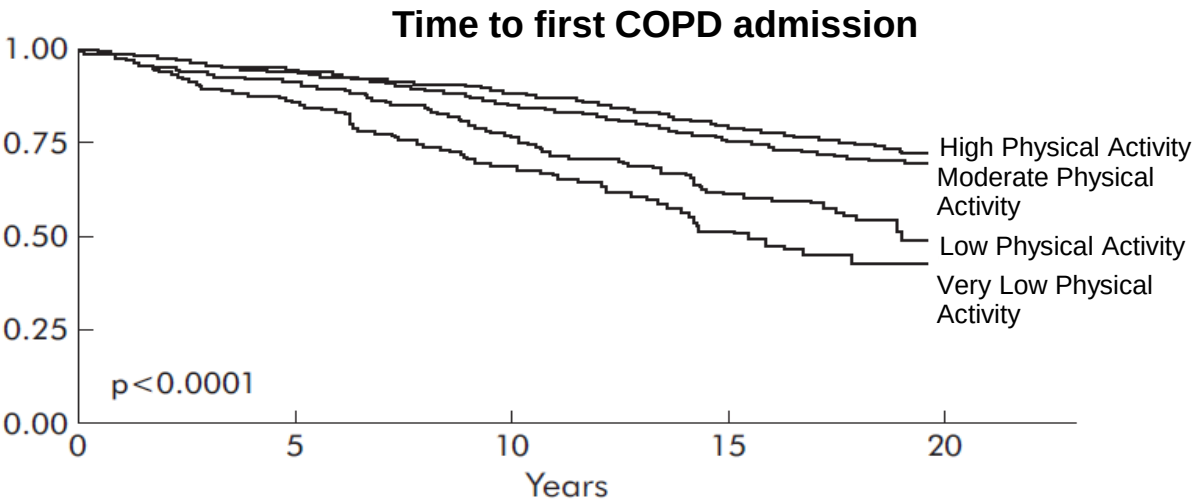


n = 173

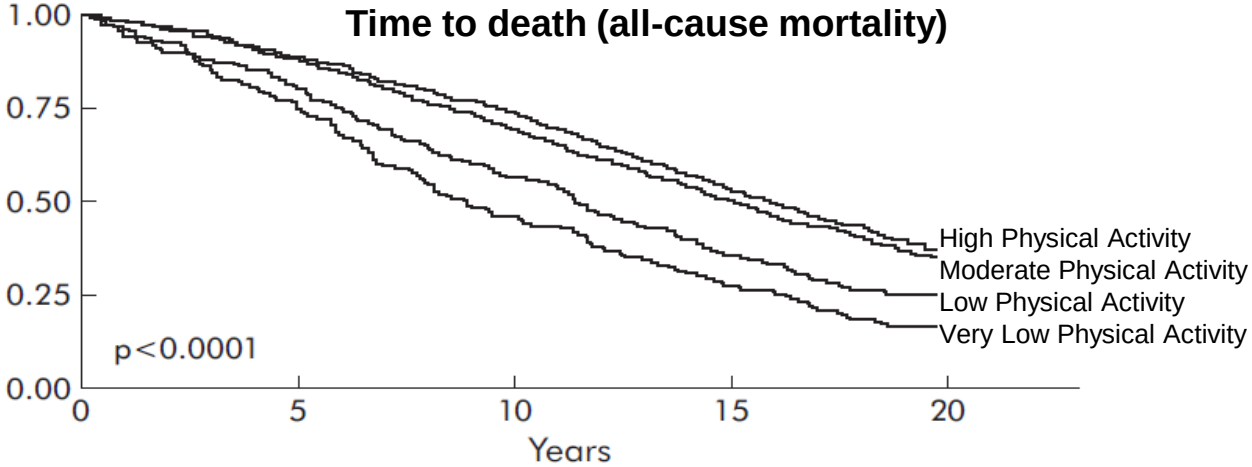
- **After adjusting for relevant confounders, increases in physical activity, showed decreases in mortality risk.**
- **In a multi-variate model, 3 independent predictors of mortality were comorbidity, endurance time, and daily physical activity.**
- **The time until first hospital admission due to COPD exacerbation was shorter for the patients with lower levels of physical activity.**

Garcia-Rio F, et al. *Chest*. 2012 Aug;142(2):338-46.

Physical Activity is Critically Important to Assess



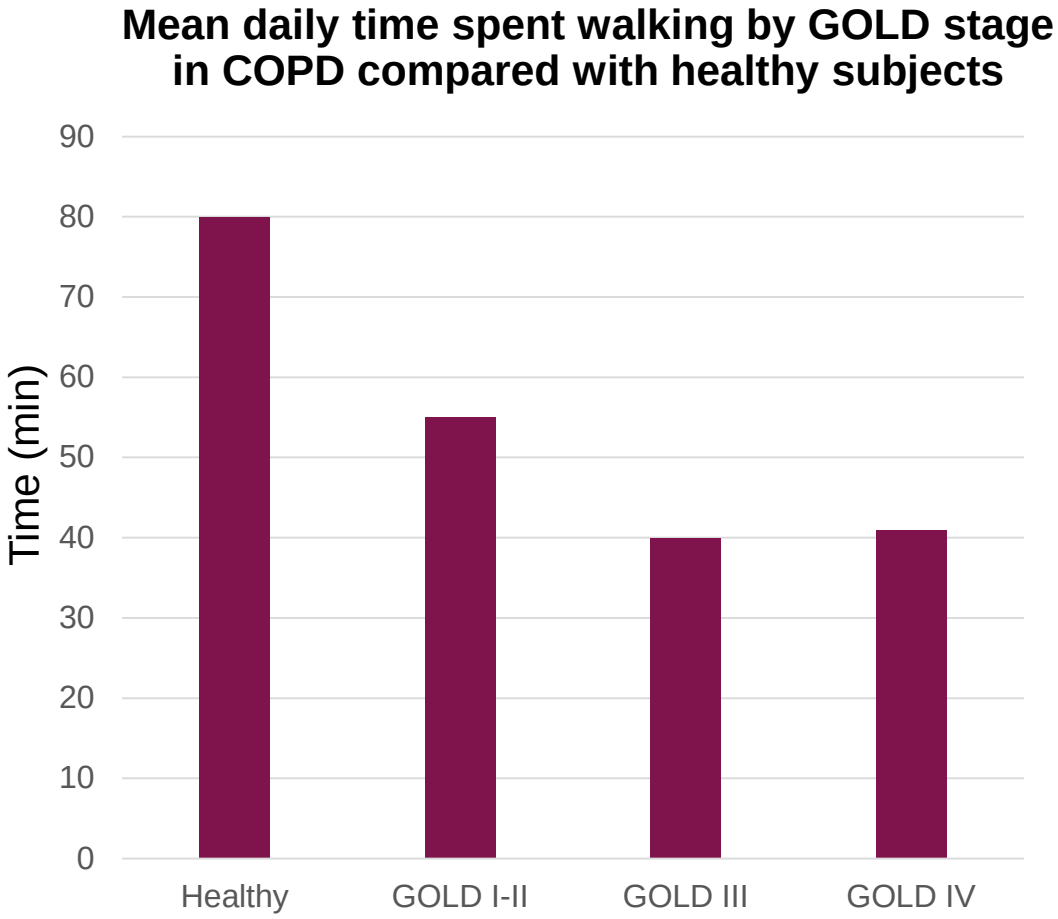
According to the Copenhagen City Heart Study, regular physical activity in COPD patients was associated with reduced chance of hospital admissions and all-cause death.



As an important determinant of COPD outcomes, limitations to physical activity should be evaluated and managed.

Troosters T, et al. *Respir Res*. 2013 Oct 30;14:115.

Dyspnea is a Key Reason for Physical Activity Reduction in COPD



- Activity limitation is a key manifestation of COPD and is in large part caused by dyspnea.
- COPD patients with moderate to mild lung function impairment can also experience a reduction in daily physical activity.
- Fatigue and leg discomfort can be factors in activity limitation.
- The ultimate goal of targeting dyspnea is to improve health status and survival by increasing physical activity.

GOLD=Global Initiative for Chronic Obstructive Lung Disease

Roche N. *Eur Respir Rev*. 2009 Jun;18(112):54-7.

What is “Control” in COPD?

After establishing the severity of COPD, the following points should be assessed during patient follow-up:

- ✓ Regular visits of COPD patients to the healthcare provider
- ✓ Smoking cessation
- ✓ Dietary recommendations aimed at achieving and maintaining an optimal bodyweight
- ✓ Regular physical activity
- ✓ Assessment of symptoms, including their degree of severity
- ✓ History of exacerbations
- ✓ Assessment of comorbidities that can interfere with COPD control
- ✓ Appropriate vaccination
- ✓ Periodical review of therapeutic regimens, patient compliance, and evaluation of side effects
- ✓ Measurement of patient’s QoL

Molina París J. *Expert Rev Respir Med*. 2013 Apr;7(2 Suppl):3-15.

Anticipatory Dyspnea

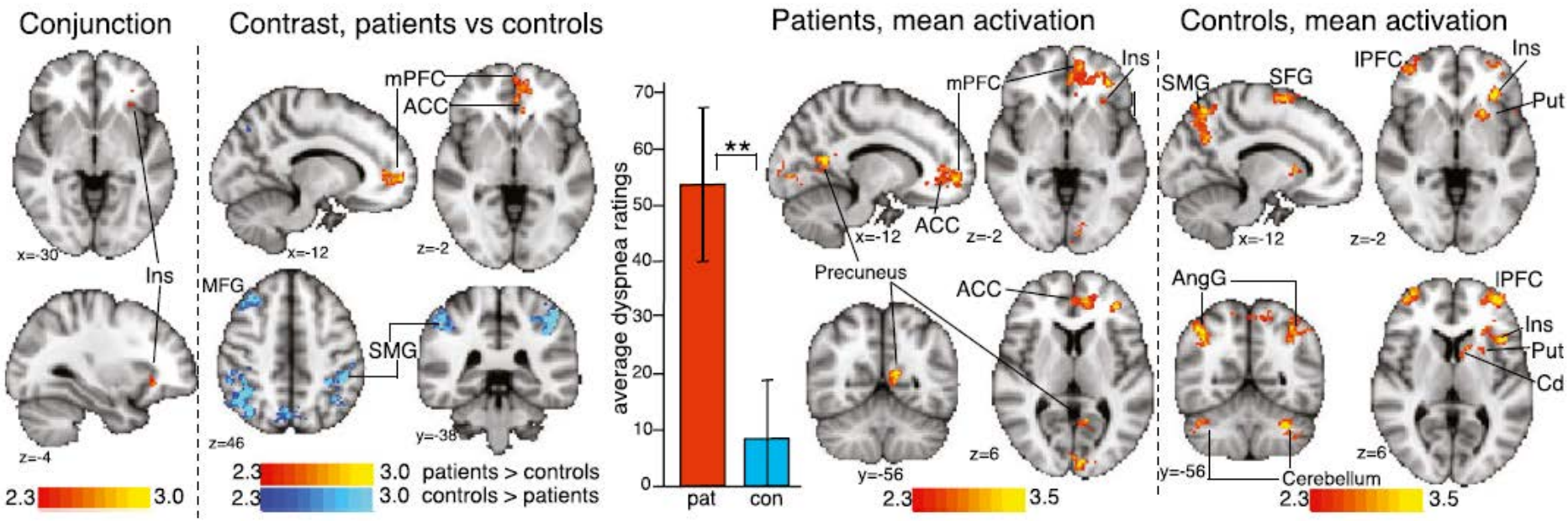
Patients may self-manage their disease by limiting their activities because of dyspnea or even to prevent becoming short of breath.[1]

Activity limitation may occur even in mild disease.[2]

The limitation in activity induced by dyspnea can be distressing and may lead to anxiety and depression, which are frequently observed in COPD.[3]

1. Apps LD, et al. *Int J Chron Obstruct Pulmon Dis*. 2014 Feb 26;9:257-63.
2. O'Donnell DE, et al. *Int J Chron Obstruct Pulmon Dis*. 2014 Jun 4;9:577-88.
3. Roche N. *Eur Respir Rev*. 2009 Jun;18(112):54-7.

Brain Processes Associated with Responses to Dyspnea-related Cues in COPD Patients



- **Investigators studied fMRI imaging to identify brain activity in 41 patients with COPD vs 40 control subjects after exposure to dyspnea-related word cues.**
  - **Participants viewed each word and rated it according to how breathless and how anxious it would make them feel on a visual analog scale (VAS) of 0 (not at all) to 10 (very much).**
- **In comparison to control subjects, patients with COPD showed stronger activation in the left -side mPFC and the ACC.**
- **Activity in these areas has previously been linked to pain and dyspnea.**
- **Depression, fatigue and vigilance may also be associated with activity observed in these areas.**

Herigstad M, et al. *Chest*. 2015 Oct;148(4):953-61.

Standardized Assessments Used to Assess Symptoms

Care can be improved with the use of scoring tools that are reliable, standardized, and sensitive to clinical changes. These tools should provide meaningful information and be acceptable for both patient and HCP use.[1]

Tool	Description	Pro	Con
SGRQ	50 item questionnaire assess QoL over multiple domains[2]	FDA acceptable endpoint, responsive to therapy[2]	Time-consuming[2]
CAT	8 item questionnaire with comprehensive symptom assessment[3]	Validated, relatively brief[1]	No definite MCID[1]
MMRC	5-item scale to assess the severity of breathlessness[3]	Relates well to other measures of health status, predicts future mortality risk[3]	Not sensitive to change with treatment and only measures dyspnea[1]
CCQ	Questionnaire with 10 items within 3 domains (symptoms, functional state, mental state)[1]	Validated, correlates with SGRQ and SF-36, has MCID (>0.4) and relatively short[1,2]	Has not been widely used in pharmaceutical trials[2]

1. Jones PW, et al. *Int J Chron Obstruct Pulmon Dis*. 2011;6:289-96.
2. Cazzola M, et al. *Int J Chron Obstruct Pulmon Dis*. 2015 Apr 7;10:725-38.
3. Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017. Available from: http://www.goldcopd.org/.

Clinical COPD Questionnaire

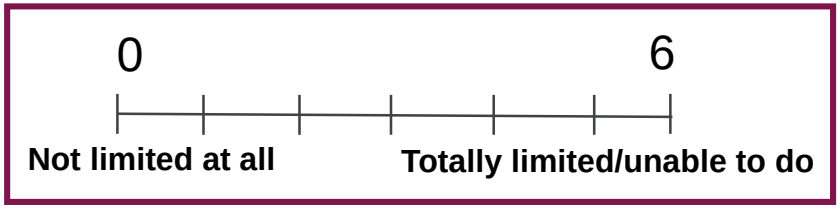
Patients are asked to answer the following questions. The time frame can be over 7 days.

How often did you feel…?

- SOB at rest
- SOB while doing physical activities
- Concerned about getting a cold or your breathing getting worse
- Depressed because of your breathing problems
- Did you cough
- Did you produce phlegm

Patients are asked to rate how limited they were during the following activities due to breathing problems.

- Strenuous activities (hurrying, climbing stairs, sports)
- Moderate activities (walking, housework, carrying things)
- Daily activities (dressing, washing themselves)
- Social activities (talking, being with children, visiting friends and family)



Clinical COPD Questionnaire. http://www.ccq.nl

Potential Ways to Assess Activity

Questionnaires[1]

Diaries[1,2]

Portable devices that monitor motion[1]

Patient/physician discussion

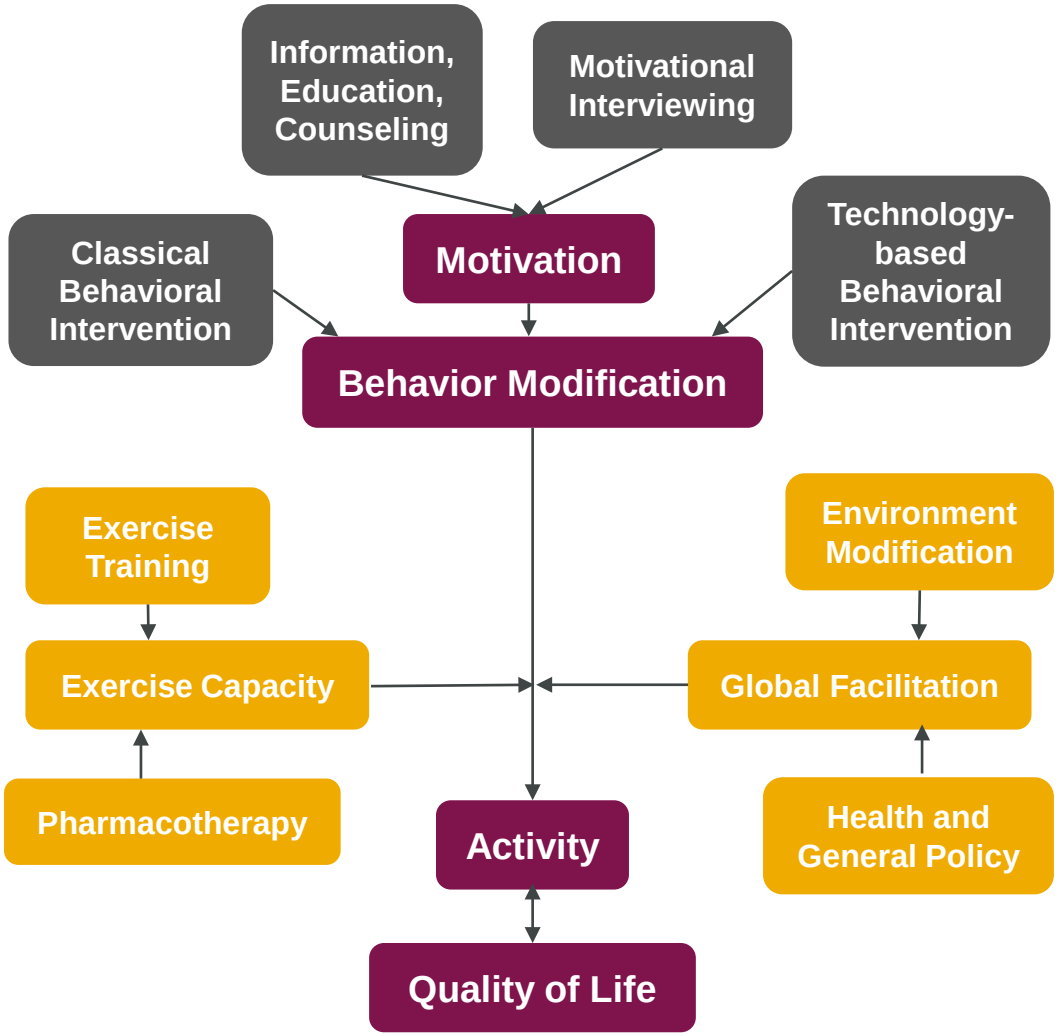
- Questions such as “Have you given up any activities as a result of shortness of breath or fatigue?” can be useful.[3]

1. Vorrink SN, et al. *Respir Res*. 2011 Mar 22;12:33.
2. Roche N. *Eur Respir Rev*. 2009 Jun;18(112):54-7.
3. Belfer MH, et al. *J Am Osteopath Assoc*. 2009 May;109(5):268-78; quiz 280-1.

A Multifactorial Approach to Increase Activity Levels in COPD

Interventions that can affect dyspnea, and/or exercise capacity include:[1]

- **Pharmacotherapy**
- **Pulmonary rehab**
- **Informal counseling**
- **Oxygen**
- **Surgical therapy for COPD**
- **Other interventions used in various combinations tailored to the patient**



Adapted from: Aguilaniu B, et al. *NPJ Prim Care Respir Med*. 2014 May 20;24:14014.

1. Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017. Available from: http://www.goldcopd.org/.
2. Aguilaniu B, et al. *NPJ Prim Care Respir Med*. 2014 May 20;24:14014.

Summary

Decreased activity is associated with poor COPD outcomes. Regular physical activity reduces hospital admissions and all-cause death.

The GOLD guidelines recommend full symptom evaluation to select treatment in addition to evaluating comorbidities. It is important to quantify the impact on the severity of breathlessness using a validated assessment.

Activity limitation is a key manifestation of COPD and is mainly caused by dyspnea. The ultimate goal of targeting dyspnea is to improve health status and survival by increasing physical activity.

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MMRC

The Modified Medical Research Council (MMRC) Dyspnoea Scale

Grade of dyspnoea	Description
0	Not troubled by breathlessness except on strenuous exercise
1	Shortness of breath when hurrying on the level *or* walking up a slight hill
2	Walks slower than people of the same age on the level because of breathlessness *or* has to stop for breath when walking at own pace on the level
3	Stops for breath after walking about 100 m *or* after a few minutes on the level
4	Too breathless to leave the house *or* breathless when dressing or undressing

CAT

COPD Assment Test

Example: I am very happy 0 1 2 3 4 5 I am sad

			SCORE
I never cough	0 1 2 3 4 5	I cough all the time	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is full of phlegm (mucus)	
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition	
I have lots of energy	0 1 2 3 4 5	I have no energy at all	

CLICK TO GET YOUR TOTAL SCORE!

CCQ

Date:_____

CLINICAL COPD QUESTIONNAIRE

Please **circle** the number of the response that best describes how you have been feeling during the **past week**.
(Only **one** response for each question).

On average, **during the past week**, how often did you feel:	never	hardly ever	a few times	several times	many times	a great many times	almost all the time
1. Short of breath **at rest**?	0	1	2	3	4	5	6
2. Short of breath **doing physical activities**?	0	1	2	3	4	5	6
3. **Concerned** about getting a cold or your breathing getting worse?	0	1	2	3	4	5	6
4. **Depressed (down)** because of your breathing problems?	0	1	2	3	4	5	6
In general, **during the past week**, how much of the time:							
5. Did you **cough**?	0	1	2	3	4	5	6
6. Did you **produce phlegm**?	0	1	2	3	4	5	6
On average, **during the past week**, how limited were you in these activities **because of your breathing problems**:	not limited at all	very slightly limited	slightly limited	moderately limited	very limited	extremely limited	totally limited /or unable to do
7. **Strenuous physical activities** (such as climbing stairs, hurrying, doing sports)?	0	1	2	3	4	5	6
8. **Moderate physical activities** (such as walking, housework, carrying things)?	0	1	2	3	4	5	6
9. **Daily activities at home** (such as dressing, washing yourself)?	0	1	2	3	4	5	6
10. **Social activities** (such as talking, being with children, visiting friends/ relatives)?	0	1	2	3	4	5	6

Back up

- MMRC
  https://www.verywell.com/guidelines-for-the-mmrc-dyspnea-scale-914740

- CAT
  http://www.catestonline.org/english/indexEN.htm

- Clinical COPD Questionnaire
  https://www.biomedcentral.com/content/supplementary/1465-9921-7-62-S1.PDF