

COPD Guidelines

Recommendations 2018

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COIs

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COPD 2018



- 15 million Americans diagnosed
- Estimates suggest 12 million more undiagnosed
- 70% of COPD sufferers are in workforce
- 43.2% saw physician re COPD in last year
- 17.7% had ER visit or hospitalization in last year
- COPD is now 3rd leading cause of disability in US
- COPD is now 4th leading cause of death in US trailing Heart Disease, Cancer, Unintentional Injuries
- Cost of care now over 50 billion dollars a year

What did the BRFSS tell us?

- Prevalence in 18 and up age group: 6.1%
- Prevalence in 45 and up age group 9.0%
- Women reported higher COPD rates: 6.5% vs 5.3%
- 24.9% of those with COPD never smoked
- Health disparities in COPD: 9.9% reported in individuals with income less than \$25,000
- Rural residents experienced higher age adjusted COPD prevalence, hospitalizations, and deaths than residents of urban areas: 8.2% vs 4.7%

2016 BRFSS/CDC Data



COPD CHALLENGES

- Identify more of the 12 million estimated to have COPD but as yet undiagnosed.
- Make sure those already diagnosed have been correctly diagnosed.
- Aim to have those appropriately diagnosed on appropriate therapy
- Move away from treating all COPD the same!



GUIDELINES

Definition

 Guidelines: A statement by which to determine a course of action. A guideline aims to streamline particular processes according to a set routine or sound practice. By definition, following a guideline is never mandatory. Guidelines are not binding and are not enforced.

• U.S. Dept. of Veterans Affairs

GRADE systematic approach to clinical guidelines

- Systematic collection of evidence
- The quality of evidence across studies for each important outcome
- Which outcomes are critical to a decision
- The overall quality of evidence across these critical outcomes
- The balance between benefits and harms
- The strength of recommendations.



PISEASETM

Rate of increase = 240 lines/year or 4 pages/year

GOLD 2017 Definition and Overview

- 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.
- The most common respiratory symptoms include dyspnea, cough and/or sputum production. These symptoms may be under-reported by patients.
- COPD may be punctuated by periods of acute worsening of respiratory symptoms, called exacerbations.
- In most patients, COPD is associated with significant concomitant chronic diseases, which increase morbidity and mortality.



COPD definition – some aspects regarding symptoms

- Chronic respiratory symptoms may precede the development of airflow limitation and may be associated with the development of acute respiratory events³
- Chronic respiratory symptoms also exist in individuals with normal spirometry^{3,4}
- A significant percentage have structural evidence of lung disease manifested by the varying presence of emphysema, airway wall thickening and gas trapping^{3,4}

4. EA Regan et al. JAMA Intern Med 2015; 175: 1539-49.

Combined Assessment of COPD



© 2015 Global Initiative for Chronic Obstructive Lung Disease

ABCD classification

- Pluses
 - ABCD" assessment tool of the 2011 GOLD update was a major advancement from the simple spirometric grading system of earlier GOLD versions
 - Incorporated patientreported symptoms
 - Highlighted the importance of exacerbation prevention in the management of COPD



≭ Minuses

- Performed no better than
 spirometric grades for mortality
 prediction or other important health
 outcomes
- Unable to assess the individual contributions of severity of airflow limitation from exacerbation frequency or severity
- Hindered initial ABCD assessment
 in subjects without spirometry (ER,
 hospitalized patient, initial
 outpatient assessment)

The GOLD refined ABCD assessment tool										
Di	agnosis _	Assess of air limita	Assessment of airflow limitation		+	Assessment of symptoms/risk of exacerbations				
					Exacerbation History					
		Grade	FEV ₁ (% pred.)		\geq 2 or \geq 1 leading to hospitalization	С	D			
FEV	/1/FVC<0.7	1	≥80		0 or 1 (not leading					
		2	50-79		to hospital admission)		В			
	San Multiple Co	3	3 30-49							
	AND INCOME IN THE REAL	4	<30			CAT < 10 CCQ < 1	CAT 10+ CCQ 1+			

A modification of therapeutic recommendations





Preferred treatment =

In patients with a major discrepancy between the perceived level of symptoms and severity of airflow limitation, further evaluation is warranted.



Americans with Obstructive Lung Disease Receive



RESULTS OF CAPPS: COPD-ASSESSMENT OF PRACTICE IN PRIMARY CARE



- Random sample of patients (50-150 per site) aged 40-89 with diagnosed COPD
- 1157 patients from 11 US primary care sites
- Main outcome measures were adherence to GOLD guidelines, assessed via 3 components:

Spirometry dx documented-27%

Are comorbidities if present treated appropriately-25%

- Are adequate risk reduction measures being taken-32%
- Only 3% of patients met all components
- Belletti et al Current Medical Research and Opinion 2013;29:8



AND PHYSICIAN ASSISTANTS' KNOWMLEDGE AND

BELIEFS REGARDING COPD:2007-1014

- 426 PCPs, 148 NPs/PAs
- In 2014 about half of responders reported awareness and use of COPD guidelines (49% of PCPs, 46% of NPs/PAs)
- 31% of PCPs and 27% of NPs/PAs reported lack of awareness or use of any COPD guidelines
- Most striking difference between 2007-2014 marked increase in beliefs of all clinicians in ability of COPD treatments to reduce symptoms (75%) and exacerbations (85%)

Yawn et al JCOPDF 2016 http://dx.doi.org/10.153.26/jcopdf.3.3.2015.0168

POCKET CONSULTANT







MOBILE APP

FREE- APP STORE: SEARCH- COPDFOUNDATION









SEVEN SEVERITY DOMAINS

- 1. Spirometry Grades
- 2. Regular Symptoms
- 3. Exacerbations
- 4. Oxygenation
- 5. Emphysema
- 6. Chronic bronchitis
- 7. Comorbidities



SEVERITY DOMAIN: SPIROMETRY GRADES

Spirometry Grades:

- SG 0 Normal spirometry does not rule out emphysema, chronic bronchitis, asthma, or risk of developing either exacerbations or COPD.
- SG 1 Mild: Post bronchodilator FEV₁/FVC ratio<0.7, FEV₁≥60% predicted.
- SG 2 Moderate: Post bronchodilator FEV₁/FVC ratio<0.7, 30%≤FEV₁<60% predicted.
- SG 3 Severe: Post bronchodilator FEV₁/FVC ratio<0.7, FEV₁<30% predicted.
- SG U Undefined: FEV₁/FVC ratio>0.7, FEV₁<80% predicted. This is consistent with restriction, muscle weakness, and other pathologies.





SEVERITY DOMAIN: REGULAR SYMPTOMS

- Dyspnea at rest or exertion
- Chronic cough/ sputum
- Use COPD Assessment Test (CAT) or mMRC Breathless Scale to follow course of disease
- Presence of regular symptoms has therapeutic implications

COPD ASSESSMENT TEST (CAT)

A CAT score over 10 suggests
 significant symptoms

- A change in CAT score of 2 or more suggests a possible change in health status
- A worsening of CAT score could be explained by an exacerbation, poor medication adherence, poor inhaler technique, or progression of COPD or comorbid condition.
 An adjustment in therapy may be needed.





MMRC BREATHLESSNESS SCALE

Grade	Description of Breathlessness
0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on level ground or walking up a slight hill
2	On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace
3	I stop for breath after walking about 100 yards or after a few minutes on level ground
4	I am too breathless to leave the house or I am breathless when dressing

Chris Stenton. The MRC breathlessness scale. Occup Med (Lond)(2008)58(3): 226-227 doi:10.1093/occmed/kqm162, Table 1. By permission of Oxford University Press on behalf of the Society of Occupational Medicine.



PULMONARY REHABILITATION IMPROVES CRQ DYSPNEA

Mean Difference (95% CI)



Lacasse et al, Cochrane Database of Systematic Reviews 2006; Issue 4; Art. No.: CD003793

TREADMILL ENDURANCE TIME IMPROVES WITH COMBINATION TIOTROPIUM AND PULMONARY REHABILITATION RANDOMIZED TO TIOTROPIUM OR PLACEBO



Casaburi et al. Chest. 2005;127:809-817 (A).





From: A Systematic Review With Meta-Analysis of Dual Bronchodilation With LAMA/LABA for the Treatment of Stable COPD

Chest. 2016;149(5):1181-1196. doi:10.1016/j.chest.2016.02.646



Figure Legend:

Overall forest plot meta-analysis of the impact of long-acting muscarinic antagonist/long-acting β2-agonist combinations on trough FEV1 and subgroup analysis performed on lower and higher doses of aclidinium (A), formoterol (F), glycopyrronium (G), indacaterol (I), olodaterol (O), tiotropium (T), umeclidinium (U), and vilanterol (V). Because of the scarce number of studies, the subgroup analysis of the glycopyrronium/formoterol combination was performed vs glycopyrronium and formoterol administered as monocomponents. The doses of medications are expressed as micrograms and results as the mean difference (mL) vs monocomponents.

SEVERITY DOMAIN: EXACERBATIONS



- High Risk:
 - Two or more exacerbations in past year
 - Especially if FEV1<50% predicted
- High risk for exacerbations has therapeutic implications



IMPACT OF EXACERBATIONS IN COPD





MANAGEMENT OF ACUTE EXACERBATIONS IN COPD

- Oxygen as needed
- Maximize bronchodilator therapy
- Add systemic steroids if baseline FEV1<50% predicted
- Add antibiotics in patients with 2 or more symptoms: worsening dyspnea, increased sputum volume, increased sputum purulence
- Consider noninvasive ventilation (NIPPV) in severe exacerbations to minimize need for intubation and ventilator support



COPD EXACERBATIONS PREVENTIVE MEASURES

- Smoking cessation
- Immunizations-influenza vaccine
- Long acting bronchodilators
- Inhaled corticosteroids
- Phosphodiesterase inhibitors
- Mucolytics/Antioxidants
- Macrolides
- Pulmonary Rehabilitation
- Lung Volume Reduction Surgery
- Augmentation therapy in Alpha 1 deficiency
- Beta blockers? Statins XXX
- Case Management



- 1368 centers, 16,485 patients
- Moderate COPD with heightened cardiovascular risk
- Compared with placebo Fluticasone Furoate (FF) and Vilanterol VI) reduced the rare of moderate and/or severe exacerbations by 29% and the rate of hospitalized exacerbations by 27%
- These relative effects were similar whether subjects had a history of exacerbations the year before the study or an FEV1<60% predicted.
- FF/VI also reduced rate of exacerbations treated with corticosteroids alone or with corticosteroids plus antibiotics but not rates of those treated with antibiotics alone.
- Martinez FJ, et al.; Am J Respir Crit Care Med. First published online 21 Oct 2016 as DOI: 10.1164/rccm.201607-1421OC

TRILOGY STUDY



- 1367 patients with symptomatic severe or very severe COPD at risk for exacerbations
- BDP/FF/GB vs BDP/FF -26 weeks
- Triple therapy: Greater improvement in lung function, health related quality of life and prevention of moderate to severe exacerbations but no better improvement in dyspnea
- First study showing clinical benefits of stepping up COPD patients from LABAICS to Triple therapy

Singh et al Lancet 2016;388:963-73

FLAME TRIAL



NEJM 5/25/16 DOI:1056/NEJMOA1516385

- Indacaterol-Glycopyrronium (IG) 1680 pts vs Salmetrol-Fluticasone SF) 1682 pts
- IG reduced exacerbations 11% better than SF
- IG longer time to first exacerbation 71 days vs 51 days
- Annual rate of moderate or severe exacerbations
 lower in IG group 0.98 vs 1.19
- Incidence of pneumonia 3.2% in IG group vs 4.8% in SF group

IMPACT STUDY



LIPSON ET AL NEJM 4/18/18 DOI:10.1056/NEJMOA1713901

• GSK study 10,355 patients –fluticasone/umeclidinium/vilanterol:

15% reduction in moderate/severe exacerbations vs fluticasone/vilanerol

25% reduction vs umeclidinium/vilanterol

Annual rate of exacerbations lower with triple regardless of eos level altho greater reduction In those with eos>150 cells/microliter

Annual rate of severe exacerbations resulting in hospitalization triple 0.13 vs 0.19 for LAMA/LABA

Higher incidence of pneumonia in steroid groups

All cause mortality lower with triple regimen



BLOOD EOSINOPHIL COUNT TO PREDICT TREATMENT RESPONSE

Retrospective analysis have shown:

Greater exacerbation reduction with ICS/LABA vs LABA or LAMA in patients with blood eos 2% or higher.

Increased rate of exacerbations on ICS withdrawal from triple therapy in patients with blood eos 2% or higher.

Blood eosinophil count <2% is associated with higher risk of pneumonia, independent of treatment.

Impact of eosinophil count on exacerbation risk less clear in ECLIPSE and SPIROMICS data sets



MACRO STUDY

- Once daily azithromycin in addition to usual care
- Decreased frequency of AECOPD
- 1.48 vs 1.83 /patient-year p=0.01, HR for acute exacerbation per patient year -0.73.
- Median time to first exacerbation 266 days vs 174 days p<0.001
- Improved quality of life of exacerbation prone COPD patient
- Hearing loss more common-25%vs20%
- Cardiac concerns-QTc interval



SEVERITY DOMAIN: CHRONIC BRONCHITIS

- Cough, sputum most days for at least 3 months in at least 2 years
- Presence of chronic bronchitis has therapeutic implications

REACT STUDY



MARTINEZ ET AL THELANCET 2015 HTTP://DX.DOI.ORG/10.1016/S01406736(14)62410-7

- 1935 pts with severe COPD -98% on ICS/LABA
- 1346 of these (70%) also on LAMA
- Despite these inhaled therapies frequent exacerbations and impaired health status
- Adding Roflumilast vs placebo -24.3% reduction in severe exacerbations, 23.9% reduction in exacerbations requiring hospitalizations.
- No difference in mortality between Roflumilast and placebo groups
- Adverse events more common in Roflumilast (11%) vs placebo (5%)



SEVERITY DOMAIN: OXYGENATION

- Oxygenation should be checked in symptomatic patients with moderate or severe COPD
- Severe hypoxemia: resting O2 sat <88% or arterial pO2<55 mmHg
- Episodic hypoxemia: exercise or nocturnal desaturation
- Severe hypoxemia has therapeutic implications
- Episodic hypoxemia may have therapeutic implications in some cases



THE LONG TERM OXYGEN TREATMENT TRIAL NEJM 375:17; 2016

To test whether supplemental Oxygen would result in longer term survival and delay to first hospitalization in stable COPD with moderate resting desaturation (O2 sats 89-93%) or in stable COPD with moderate exercise induced desaturation (O2 sats 80-89%)

738 patients at 42 centers followed for 1-6 years

In patients with stable COPD and resting or exercise-induced moderate desaturation, the prescription of long-term supplemental oxygen did not result in a longer time to death or first hospitalization than no long-term supplemental oxygen, nor did it provide sustained benefit with regard to any of the other measured outcomes.



SEVERITY DOMAIN: EMPHYSEMA

- Presence of emphysema should be evaluated in patients with severe COPD
- Reduced density on CT scan
- Can be diffuse or localized
- Abnormal high lung volumes
- Abnormal low diffusion capacity
- Localized emphysema particularly localized to upper lung zones could have therapeutic implications



LUNG VOLUME REDUCTION SURGERY IS APPROPRIATE IN SUBGROUPS OF COPD



. NEJM 2003;348:2059-73



SEVERITY DOMAIN: COMORBIDITIES



- Comorbidities are extremely common in COPD and impact morbidity, hospitalization and re-hospitalization rates and mortality.
- Evidence suggests that COPD may be an independent risk factor for the development of cardiovascular disease, lung cancer, depression, osteoporosis.
- Defining and treating comorbid conditions, particularly cardiovascular, are critical components of COPD care.

IMPACT OF COMORBIDITIES ON COPD MORTALITY



(MANNINO ET AL THORAX 2003)



Comorbidities and Risk of Mortality in Patients with Chronic Obstructive Pulmonary Disease

Miguel Divo¹, Claudia Cote^{2†}, Juan P. de Torres³, Ciro Casanova⁴, Jose M. Marin⁵, Victor Pinto-Plata¹, Javier Zulueta³, Carlos Cabrera⁶, Jorge Zagaceta³, Gary Hunninghake¹, and Bartolome Celli¹; for the BODE Collaborative Group



Am J Respir Crit Care Med. 2012; 186:155-61



	CO	Gı PD	uid Tre	le ea	to tn	ner	nt				
Smoking cess	All patients should receive: Smoking cessation; vaccination for influenza, pneumococcus, pertussis, alpha-1 testing										
	short acting bronchodilator (as needed)	LAMA or LABA or LAMA plus LABA	ICS/LABA	roflumilast	oxygen	exercise/ pulmonary rehabilitation	lung volume reduction surgery	azithromycin			
Spirometry Grade SG1 Mild	N	0									
SG 2/3 Moderate/ Severe	N	N	0	0.							
Regular symptoms	R	N	0			X **					
Exacerbation risk high		2 .	R .	0.				0.			
Oxygenation severe hypoxemia					N						
episodic hypoxemia					0						
Emphysema							0				
Chronic bronchitis				0.							
Comorbidities Realuate and treat identified comorbid conditions											

COPD FOUNDATION GUIDE 2016





FEV₁=Forced expiratory volume 1 second; FVC=Forced vital capacity; CAT=COPD Assessment Test; MMRC=Dyspnea assessment test; SABD=Short acting bronchodilator – includes SABA=Short acting beta-2 agonist; SAMA=Short acting muscarinic agent, and combined SAMA/SABA; LAMA=Long acting muscarinic agent; LABA=Long acting beta-2 agonist; ICS = Inhaled corticosteroid



The presence of eosinophilia may help select those exacerbators who could benefit from addition of ICS.

For those with recurrent exacerbations despite inhaled regimen consider:

a. Adding PDE4 Inhibitor Roflumilast (if chronic bronchitic) and/or b. Adding Macrolide (if not active smoker) as immune modulator.

COPD patients with FEV,<60% should have O2 saturation assessed.

a. Resting O2 sats < 88% merit assessment for Oxygen therapy.

b. COPD patients with O2 sats
88% should have arterial blood gas tested and if significant hypercapnea consider for sleep study and potential noninvasive ventilation.

COPD patients with FEV1≤ 45% should undergo Chest CT scanning and evaluation for Lung Volume Reduction Surgery or if FDA approves, bronchoscopic Lung Volume Reduction.

Annual low-dose CT scan for lung cancer screening - ages 55-79 years with 30 packyears and cigarette smoking in the last 15 years.



COPD 2018

- Almost always preventable, Almost always treatable
- LAMA/LABA may well be mainstay of Rx for most with significant COPD
- Pulmonary Rehabilitation works
- Those with more severe COPD and frequent exacerbations more likely to benefit from triple Rx
- ICS role may be defined by eosinophilia
- To treat COPD need to address comorbid conditions
- Improve communication
- All COPD is not the same and future therapies need to address this issue!