Global Initiative for the Diagnosis, Management and Prevention of Chronic Obstructive Lung Disease (GOLD) 2017 Report

Supplementary Appendix – Tables & Figures

Table S1. Description of levels of evidence

Evidence category	Sources of evidence	Definition
A	Randomized controlled trials (RCTs) Rich body of high quality evidence without any significant limitation or bias	Evidence is from endpoints of well-designed RCTs that provide consistent findings in the population for which the recommendation is made without any important limitations. Requires high quality evidence from ≥ 2 clinical trials involving a substantial number of subjects, or a single high quality RCT involving substantial numbers of patients without any bias.
B	Randomized controlled trials (RCTs) with important limitations Limited Body of Evidence	Evidence is from RCTs that include only a limited number of patients, post hoc or subgroup analyses of RCTs or meta analyses of RCTs. Also pertains when few RCTs exist, or important limitations are evident (methodologic flaws, small numbers, short duration, undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent).
C	Non-randomized trials Observational studies	Evidence is from outcomes of uncontrolled or non-randomized trials or from observational studies.
D	Panel consensus judgment	Provision of guidance is deemed valuable but clinical literature addressing the subject is insufficient. Panel consensus is based on clinical experience or knowledge that does not meet the above stated criteria.

Table S2. Vaccination for stable COPD

- Influenza vaccination reduces serious illness and death in COPD patients **(Evidence B).**
- The 23-valent pneumococcal polysaccharide vaccine (PPSV23) reduces the incidence of community-acquired pneumonia in COPD patients aged < 65 years with an FEV_1 < 40% predicted and in those with comorbidities **(Evidence B).**
- In the general population of adults ≥ 65 years the 13-valent conjugated pneumococcal vaccine (PCV13) reduces bacteremia and serious invasive pneumococcal disease **(Evidence B).**

Table S3. Commonly used maintenance medications in COPD

Drug	Inhaler (mcg)	Solution for nebulizer (mg/ml)	Oral	Vials for injection (mg)	Duration of action (hours)
Beta$_2$-agonists					
Short-acting					
Fenoterol	100-200 (MDI)	1	2.5 mg (pill), 0.05% (syrup)		4-6
Levalbuterol	45-90 (MDI)	0.1, 0.21, 0.25, 0.42			6-8
Salbutamol (albuterol)	90, 100, 200 (MDI & DPI)†	1, 2, 2.5, 5 mg/ml	2, 4, 5 mg (pill), 8 mg (extended release tablet) 0.024%/0.4 mg (syrup)	0.1, 0.5 mg	4-6, 12 (extended release)
Terbutaline	500 (DPI)		2.5, 5 mg (pill)	0.2, 0.25, 1 mg	4-6
Long-acting					
Arformoterol		0.0075†			12
Formoterol	4.5-9 (DPI)	0.01^			12
Indacaterol	75-300 (DPI)				24
Olodaterol	2.5, 5 (SMI)				24
Salmeterol	25-50 (MDI & DPI)				12
Anticholinergics					
Short-acting					
Ipratropium bromide	20, 40 (MDI)	0.2			6-8
Oxitropium bromide	100 (MDI)				7-9
Long-acting					
Aclidinium bromide	400 (DPI), 400 (MDI)				12
Glycopyrronium bromide	15.6 & 50 (DPI)†		1 mg (solution)	0.2 mg	12-24
Tiotropium	18 (DPI), 2.5 & 5 (SMI)				24
Umeclidinium	62.5 (DPI)				24
Combination of short-acting beta$_2$-agonist plus anticholinergic in one device					
Fenoterol/ipratropium	50/20 (SMI)	1.25, 0.5 mg in 4ml			6-8
Salbutamol/ipratropium	100/20 (SMI), 75/15 (MDI)	0.5, 2.5 mg in 3ml			6-8
Combination of long-acting beta$_2$-agonist plus anticholinergic in one device					
Formoterol/aclidinium	12/400 (DPI)				12
Formoterol/glycopyrronium	9.6/14.4 (MDI)				12
Indacaterol/glycopyrronium	27.5/15.6 & 110/50 (DPI)†				12-24
Vilanterol/umeclidinium	25/62.5 (DPI)				24
Olodaterol/tiotropium	5/5 (SMI)				24
Methylxanthines					
Aminophylline			105 mg/ml (solution)	250, 500 mg	Variable, up to 24
Theophylline (SR)			100-600 mg (pill)	250, 400, 500 mg	Variable, up to 24
Combination of long-acting beta$_2$-agonist plus corticosteroids in one device					
Formoterol/ beclomethasone	6/100 (MDI & DPI)				
Formoterol/budesonide	4.5/160 (MDI), 4.5/80 (MDI), 9/320 (DPI), 9/160 (DPI)				
Formoterol/mometasone	10/200, 10/400 (MDI)				
Salmeterol/fluticasone	5/100, 50/250, 5/500 (DPI), 21/45, 21/115, 21/230 (MDI)				
Vilanterol/fluticasone furoate	25/100 (DPI)				
Phosphodiesterase-4 inhibitors					
Roflumilast			500 mcg (pill)		

MDI = metered dose inhaler; DPI = dry powder inhaler; SMI = soft mist inhaler

* Not all formulations are available in all countries; in some countries other formulations and dosages may be available

† Dose availability varies by country

^ Formoterol nebulized solution is based on the unit dose vial containing 20 mcg in a volume of 2.0 ml

† Dose varies by country

Table S4. Other pharmacologic treatments

Alpha-1 antitrypsin augmentation therapy
• Intravenous augmentation therapy may slow the progression of emphysema (**Evidence B**).
Antitussives
• There is no evidence of benefit of antitussives in patients with COPD (**Evidence C**).
Vasodilators
• Vasodilators do not improve outcomes and may worsen oxygenation (**Evidence B**).

Table S5. Pulmonary rehabilitation, self-management and integrative care in COPD

Pulmonary rehabilitation
• Pulmonary rehabilitation improves dyspnea, health status and exercise tolerance in stable patients (**Evidence A**). • Pulmonary rehabilitation reduces hospitalizations in patients with recent exacerbation (≤ 4 weeks from prior hospitalization) (**Evidence B**).
Education and self-management
• Education alone is not effective (**Evidence C**). • Self-management intervention with communication with a health care professional improves health status and decreases hospitalizations and emergency department visits (**Evidence B**).
Integrated care programs
• Integrated care and telehealth have no benefit at this time (**Evidence B**).

Table S6. Palliative care, end of life and hospice care in COPD

- Opiates, neuromuscular electrical stimulation (NMES), oxygen and fans blowing air onto the face can relieve breathlessness **(Evidence C).**
- In malnourished patients, nutritional supplementation may improve respiratory muscle strength and overall health status **(Evidence B).**
- Fatigue can be improved by self-management education, pulmonary rehabilitation, nutritional support and mind-body interventions **(Evidence B).**

Table S7. Oxygen therapy and ventilatory support in stable COPD

Oxygen therapy
• The long-term administration of oxygen increases survival in patients with severe chronic resting arterial hypoxemia (**Evidence A**). • In patients with stable COPD and moderate resting or exercise-induced arterial desaturation, prescription of long-term oxygen does not lengthen time to death or first hospitalization or provide sustained benefit in health status, lung function and 6-minute walk distance (**Evidence A**). • Resting oxygenation at sea level does not exclude the development of severe hypoxemia when traveling by air (**Evidence C**).
Ventilatory support
• NPPV may improve hospitalization-free survival in selected patients after recent hospitalization, particularly in those with pronounced daytime persistent hypercapnia ($PaCO_2$ ≥ 52 mmHg) (**Evidence B**).

Table S8. Interventional therapy in stable COPD

Lung volume reduction surgery
• Lung volume reduction surgery improves survival in severe emphysema patients with upper–lobe emphysema and low post–rehabilitation exercise capacity (**Evidence A**).
Bullectomy
• In selected patients bullectomy is associated with decreased dyspnea, improved lung function and exercise tolerance (**Evidence C**).
Transplantation
• In appropriately selected patients with very severe COPD, lung transplantation improves quality of life and functional capacity (**Evidence C**).
Bronchoscopic interventions
• In select patients with advanced emphysema, bronchoscopic interventions reduce end-expiratory lung volume and improve exercise tolerance, health status and lung function at 6-12 months following treatment. Endobronchial valves (**Evidence B**); Lung coils (**Evidence B**).

Figure S1. Goals for treatment of stable COPD

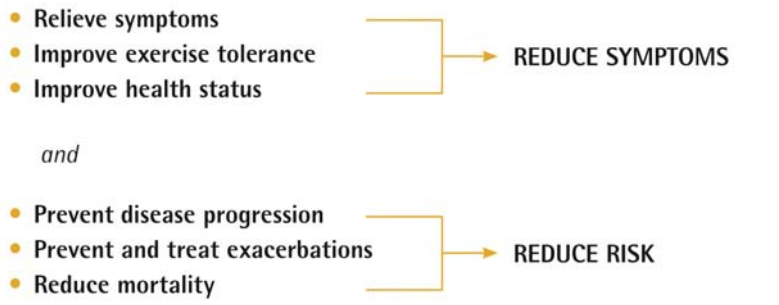

Table S9. Key points for the use of non-pharmacologic treatments

Education, self-management and pulmonary rehabilitation
• Education improves patient's knowledge but there is no evidence that education alone changes patient behavior. • Education in self-management with the support of a case manager with or without a written action plan is recommended for prevention of exacerbation complications such as hospitalization (**Evidence B**). • Rehabilitation is indicated in all patients with relevant symptoms and/or a high risk for exacerbation and is the most effective intervention to improve exercise capacity and health status (**Evidence A**). • Physical activity is a strong predictor of mortality (**Evidence A**). Patients should be encouraged to increase the level of physical activity.
Vaccination
• Influenza vaccination is recommended for all patients with COPD (**Evidence A**). • Pneumococcal vaccination: the PCV13 and PPSV23 are recommended for all patients > 65 years of age, and in younger patients with significant comorbidities including chronic heart or lung disease (**Evidence B**).
Nutrition
• Consider nutritional supplementation in malnourished patients with COPD (**Evidence B**).
End of life and palliative care
• All clinicians managing patients with COPD should be aware of the effectiveness of palliative approaches to control symptoms (**Evidence D**). • End of life care should include discussions with patients and their families about their views on resuscitation and advance directive preferences (**Evidence D**).
Treatment of hypoxemia
• In patients with severe resting hypoxemia long-term oxygen therapy is indicated as it has been shown to reduce mortality (**Evidence A**). • In patients with stable COPD and resting or exercise—induced moderate desaturation, prescription of long-term oxygen does not lengthen time to death or first hospitalization or provide sustained benefit in quality of life, lung function and 6-minute walk distance (**Evidence A**). • Resting oxygenation at sea level does not exclude the development of severe hypoxemia when travelling by air (**Evidence C**).
Treatment of hypercapnia

- NIV should be the first mode of ventilation used in COPD patients with acute respiratory failure because it improves gas exchange, reduces the need for intubation, decreases hospitalization duration and improves survival (**Evidence A**).
- In patients with severe chronic hypercapnia and a history of hospitalization for acute respiratory failure, long term non-invasive ventilation may be considered (**Evidence B**).

Intervention bronchoscopy and surgery

- Lung volume reduction surgery improves lung function, exercise capacity and quality of life in selected patients with upper-lobe emphysema and survival in a subset with upper lobe emphysema and low post rehabilitation exercise performance (**Evidence A**).
- In select patients with advanced emphysema, bronchoscopic interventions reduces end-expiratory lung volume and improves exercise tolerance, quality of life and lung function at 6-12 months following treatment endobronchial valves (**Evidence B**) or lung coils (**Evidence B**).
- In selected patients with a large bulla surgical bullectomy may be considered **(Evidence C).**
- In patients with very severe COPD (progressive disease, BODE score of 7 to 10, and not candidate for lung volume reduction) lung transplantation may be considered for referral with at least one of the following: (1) history of hospitalization for exacerbation associated with acute hypercapnia (Pco_2 > 50 mm Hg); (2) pulmonary hypertension and/or cor pulmonale, despite oxygen therapy; or (3) FEV_1 < 20% and either DLCO < 20% or homogenous distribution of emphysema **(Evidence C).**

Table S10. Potential indications for hospitalization assessment*

- Severe symptoms such as sudden worsening of resting dyspnea, high respiratory rate, decreased oxygen saturation, confusion, drowsiness.
- Acute respiratory failure.
- Onset of new physical signs (e.g., cyanosis, peripheral edema).
- Failure of an exacerbation to respond to initial medical management.
- Presence of serious comorbidities (e.g., heart failure, newly occurring arrhythmias, etc.).
- Insufficient home support.

*Local resources need to be considered.

Table S11. Discharge criteria and recommendations for follow-up

- Full review of all clinical and laboratory data.
- Check maintenance therapy and understanding.
- Reassess inhaler technique.
- Ensure understanding of withdrawal of acute medications (steroids and/or antibiotics).
- Assess need for continuing any oxygen therapy.
- Provide management plan for comorbidities and follow-up.
- Ensure follow-up arrangements: early follow-up < 4 weeks, and late follow-up < 12 weeks as indicated.
- All clinical or investigational abnormalities have been identified.

1–4 weeks follow-up ↓

- Evaluate ability to cope in his/her usual environment.
- Review and understanding treatment regimen.
- Reassessment of inhaler techniques.
- Reassess need for long-term oxygen.
- Document the capacity to do physical activity and activities of daily living.
- Document symptoms: CAT or mMRC.
- Determine status of comorbidities.

12–16 weeks follow-up ↓

- Evaluate ability to cope in his/her usual environment.
- Review understanding treatment regimen.
- Reassessment of inhaler techniques.
- Reassess need for long-term oxygen.
- Document the capacity to do physical activity and activities of daily living.
- Measure spirometry: FEV_1.
- Document symptoms: CAT or mMRC.
- Determine status of comorbidities.

Table S12. Interventions that reduce the frequency of COPD exacerbations

Intervention class	Intervention
Bronchodilators	LABAs LAMAs LABA + LAMA
Corticosteroid-containing regimens	LABA + ICS LABA + LAMA + ICS
Anti-inflammatory (non-steroid)	Roflumilast
Anti-infectives	Vaccines Long term macrolides
Mucoregulators	N-acetylcysteine Carbocysteine
Various others	Smoking cessation Rehabilitation Lung volume reduction