**OPTIMIZING MANAGEMENT OF COPD IN THE PRACTICE SETTING**

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**DISCLOSURES**

I have no financial or other disclosures

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**Global Initiative for Chronic Obstructive Lung Disease**

GLOBAL STRATEGY FOR THE DIAGNOSIS, MANAGEMENT, AND PREVENTION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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**GOLD Website Address**

**www.goldcopd.org**

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**Chronic Obstructive Pulmonary Disease (COPD)**

- COPD is currently the fourth leading cause of death in the world.¹
- COPD is projected to be the 3rd leading cause of death by 2020.²
- More than 3 million people died of COPD in 2012 accounting for 6% of all deaths globally.
- Globally, the COPD burden is projected to increase in coming decades because of continued exposure to COPD risk factors and aging of the population.

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Prevalence

Prevalence of COPD
► Systematic review and meta-analysis (Halbert et al, 2006)
► Included studies carried out in 28 countries between 1990 and 2004
► Prevalence of COPD was higher in smokers and ex-smokers compared to non-smokers
► Higher ≥40 year group compared to those < 40
► Higher in men than women.

Prevalence

Prevalence of COPD
► Estimated 384 million COPD cases in 2010.
► Estimated global prevalence of 11.7% (95% CI 8.4%–15.0%).
► Three million deaths annually.
► With increasing prevalence of smoking in developing countries, and aging populations in high-income countries, the prevalence of COPD is expected to rise over the next 30 years.
► By 2030 predicted 4.5 million COPD related deaths annually.

Economic and Social Burden

Economic burden of COPD
► COPD is associated with significant economic burden.
► COPD exacerbations account for the greatest proportion of the total COPD burden.
► European Union:
  ➢ Direct costs of respiratory disease ~6% of the total healthcare budget
  ➢ COPD accounting for 56% (38.6 billion Euros) of the cost of respiratory disease.
► USA:
  ➢ Direct costs of COPD are $32 billion
  ➢ Indirect costs $20.4 billion.

GOLD Objectives

► To provide a non-biased review of the current evidence for the assessment, diagnosis and treatment of patients with COPD.
► To highlight short-term and long-term treatment objectives organized into two groups:
  ➢ Relieving and reducing the impact of symptoms, and
  ➢ Reducing the risk of adverse health events that may affect the patient in the future.
► To guide symptoms assessment and health status measurement.

GOLD 2017 Report: Chapters

1. Definition and Overview
2. Diagnosis and Initial Assessment
3. Evidence Supporting Prevention & Maintenance Therapy
4. Management of Stable COPD
5. Management of Exacerbations
6. COPD and Comorbidities

COPD Definition

► 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.
Factors that influence disease progression

- Genetic factors
- Age and gender
- Lung growth and development
- Exposure to particles
- Socioeconomic status
- Asthma & airway hyper-reactivity
- Chronic bronchitis
- Infections

Pathology, pathogenesis & pathophysiology

- Pathology
  - Chronic inflammation
  - Structural changes

- Pathogenesis
  - Oxidative stress
  - Protease-antiprotease imbalance
  - Inflammatory cells
  - Inflammatory mediators
  - Peribronchiolar and interstitial fibrosis

- Pathophysiology
  - Airflow limitation and gas trapping
  - Gas exchange abnormalities
  - Mucus hypersecretion
  - Pulmonary hypertension
OVERALL KEY POINTS (1 of 2):

► 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.

► The main risk factor for COPD is tobacco smoking but other environmental exposures such as biomass fuel exposure and air pollution may contribute.

OVERALL KEY POINTS (2 of 2):

► Besides exposures, host factors predispose individuals to develop COPD. These include genetic abnormalities, abnormal lung development and accelerated aging.

► 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 its morbidity and mortality.

OVERALL KEY POINTS (1 of 2):

► COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease.

► Spirometry is required to make the diagnosis; the presence of a post-bronchodilator FEV1/FVC < 0.70 confirms the presence of persistent airflow limitation.

► The goals of COPD assessment are to determine the level of airflow limitation, the impact of disease on the patient's health status, and the risk of future events (such as exacerbations, hospital admissions, or death), in order to guide therapy.

OVERALL KEY POINTS (2 of 2):

► Concomitant chronic diseases occur frequently in COPD patients, including cardiovascular disease, skeletal muscle dysfunction, metabolic syndrome, osteoporosis, depression, anxiety, and lung cancer. These comorbidities should be actively sought and treated appropriately when present as they can influence mortality and hospitalizations independently.

Spirometry

<table>
<thead>
<tr>
<th></th>
<th>FVC</th>
<th>FEV₁</th>
<th>FEV₁/FVC</th>
<th>Order PFTs for RV &amp; TLC</th>
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<tr>
<td>Obstruction</td>
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<td>&lt; 70%</td>
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<td>Restriction</td>
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<td>&gt; 70%</td>
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</table>

Severity of Obstruction

• FEV₁ determines severity
• Use % predicted values

• GOLD staging for COPD
  – FEV₁/FVC < 70%
  – FEV₁:
    • Gold 1 (Mild) = > 80%
    • Gold 2 (Moderate) = 50–79%
    • Gold 3 (Severe) = 30–49%
    • Gold 4 (Very severe) = < 30%
Assessment of Symptoms

**COPD Assessment Test (CAT):** An 8-item measure of health status impairment in COPD (http://catestonline.org).

**Breathlessness Measurement using the Modified British Medical Research Council (mMRC) Questionnaire:** relates well to other measures of health status and predicts future mortality risk.

Choice of thresholds

- COPD Assessment Test (CAT™)
- Chronic Respiratory Questionnaire (CCQ®)
- St George’s Respiratory Questionnaire (SGRQ)
- Chronic Respiratory Questionnaire (CRQ)
- Modified Medical Research Council (mMRC) questionnaire

Assessment of Exacerbation Risk

- COPD exacerbations are defined as an acute worsening of respiratory symptoms that result in additional therapy.

  - Classified as:
    - **Mild** (treated with SABDs only)
    - **Moderate** (treated with SABDs plus antibiotics and/or oral corticosteroids) or
    - **Severe** (patient requires hospitalization or visits the emergency room). Severe exacerbations may also be associated with acute respiratory failure.

  - Blood eosinophil count may also predict exacerbation rates (in patients treated with LABA without ICS).

2011 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 patient-reported 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)
OVERALL KEY POINTS:

► The management strategy for stable COPD should be predominantly based on the individualized assessment of symptoms and future risk of exacerbations.

► All individuals who smoke should be strongly encouraged and supported to quit.

► The main treatment goals are reduction of symptoms and future risk of exacerbations.

► Management strategies are not limited to pharmacologic treatments, and should be complemented by appropriate non-pharmacologic interventions.

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Pharmacologic treatment algorithms

**Group A**
► All Group A patients should be offered bronchodilator treatment based on its effect on breathlessness. This can be either a short- or a long-acting bronchodilator.
► This should be continued if symptomatic benefit is documented.

**Group B**
► Initial therapy should consist of a long-acting bronchodilator. Long-acting inhaled bronchodilators are superior to short-acting bronchodilators taken as needed (prn) and are therefore recommended.
► There is no evidence to recommend one class of long-acting bronchodilators over another for initial relief of symptoms in this group of patients. In the individual patient, the choice should depend on the patient’s perception of symptom relief.
► For patients with persistent breathlessness on monotherapy the use of two bronchodilators is recommended.

**Group C**
► Initial therapy should consist of a single long-acting bronchodilator. In two head-to-head comparisons the tested LAMA was superior to the LABA regarding exacerbation prevention, therefore we recommend starting therapy with a LAMA in this group.
► Patients with persistent exacerbations may benefit from adding a second long-acting bronchodilator (LABA/LAMA) or using a combination of a long-acting beta₂-agonist and an inhaled corticosteroid (LABA/ICS). All ICS increases the risk for developing pneumonia in some patients, our primary choice is LABA/LAMA.
Pharmacologic treatment algorithms

**Group D**

- We recommend starting therapy with a LABA/LAMA combination because:
  - In studies with patient reported outcomes as the primary endpoint LABA/LAMA combinations showed superior results compared to the single substances. If a single bronchodilator is chosen as initial treatment, a LAMA is preferred for exacerbation prevention based on comparison to LABAs (for details see GOLD 2017 Chapter 3).
  - A LABA/LAMA combination was superior to a LABA/ICS combination in preventing exacerbations and other patient reported outcomes in Group D patients (for details see GOLD 2017 Chapter 3).
  - Group D patients are at higher risk of developing pneumonia when receiving treatment with ICS.

**Group D (continued)**

- In some patients initial therapy with LABA/ICS may be the first choice. These patients may have a history and/or findings suggestive of asthma-COPD overlap. High blood eosinophil counts may also be considered as a parameter to support the use of ICS, although this is still under debate (for details see Chapter 2 and Appendix).

- In patients who develop further exacerbations on LABA/LAMA therapy we suggest two alternative pathways:
  - Escalation to LABA/LAMA/ICS. Studies are underway comparing the effects of LABA/LAMA vs. LABA/LAMA/ICS for exacerbation prevention. Switch to LABA/ICS. However, there is no evidence that switching from LABA/LAMA to LABA/ICS results in better exacerbation prevention. LABA/ICS therapy does not positively impact exacerbations/symptoms; a LAMA can be added.

If patients treated with LABA/LAMA/ICS still have exacerbations the following options may be considered:

- Add roflumilast. This may be considered in patients with an FEV1 < 50% predicted and chronic bronchitis, particularly if they have experienced at least one hospitalization for an exacerbation in the previous year.

- Add a macrolide. The best available evidence exists for the use of azithromycin. Consideration to the development of resistant organisms should be factored into decision making.

- Stopping ICS. A reported lack of efficacy, an elevated risk of adverse effects (including pneumonia) and evidence showing no significant harm from withdrawal supports this recommendation (see Chapter 3 for further details).

Non-Pharmacologic Treatment

- Education and self-management
- Physical activity
- Pulmonary rehabilitation programs
- Exercise training
- Self-management education
- End of life and palliative care
- Nutritional support
- Vaccination
- Oxygen therapy

Evidence Supporting Prevention & Maintenance Therapy

**OVERALL KEY POINTS (1 of 3):**

- Smoking cessation is key. Pharmacotherapy and nicotine replacement reliably increase long-term smoking abstinence rates.
- The effectiveness and safety of e-cigarettes as a smoking cessation aid is uncertain at present.
- Pharmacologic therapy can reduce COPD symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance.
- Each pharmacologic treatment regimen should be individualized and guided by the severity of symptoms, risk of exacerbations, side-effects, comorbidities, drug availability and cost, and the patient’s response, preference and ability to use various drug delivery devices.

- Inhaler technique needs to be assessed regularly.
Evidence Supporting Prevention & Maintenance Therapy

OVERALL KEY POINTS (2 of 3):

► Influenza vaccination decreases the incidence of lower respiratory tract infections.
► Pneumococcal vaccination decreases lower respiratory tract infections.
► Pulmonary rehabilitation improves symptoms, quality of life, and physical and emotional participation in everyday activities.
► In patients with severe resting chronic hypoxemia, long-term oxygen therapy improves survival.
► In patients with stable COPD and resting or exercise-induced moderate desaturation, long-term oxygen treatment should not be prescribed routinely. However, individual patient factors must be considered when evaluating the patient’s need for supplemental oxygen.

Evidence Supporting Prevention & Maintenance Therapy

OVERALL KEY POINTS (3 of 3):

► In patients with severe chronic hypercapnia and a history of hospitalization for acute respiratory failure, long-term non-invasive ventilation may decrease mortality and prevent re-hospitalization.
► In select patients with advanced emphysema refractory to optimized medical care, surgical or bronchoscopic interventional treatments may be beneficial.
► Palliative approaches are effective in controlling symptoms in advanced COPD.

GOLD Levels of Evidence

► Smoking cessation has the greatest capacity to influence the natural history of COPD.
► If effective resources and time are dedicated to smoking cessation, long-term quit success rates of up to 25% can be achieved.

Smoking Cessation

Vaccination

► Influenza vaccination can reduce serious illness (such as lower respiratory tract infections requiring hospitalization) and death in COPD patients.
► Pneumococcal vaccinations, PCV13 and PPSV23, are recommended for all patients ≥ 65 years of age.

Rehabilitation, Education & Self-Management

► Pulmonary rehabilitation improves dyspnea, health status, and exercise tolerance in stable patients (Evidence A).
► Pulmonary rehabilitation reduces hospitalizations among patients who have had a recent exacerbation (3.4 events per year for rehabilitation vs. 5.0 events for usual care) (Evidence B).

Table 3.6: Pulmonary rehabilitation, self-management, and integrative care in COPD

- Pulmonary rehabilitation improves dyspnea, health status, and exercise tolerance in stable patients (Evidence A).
- Pulmonary rehabilitation reduces hospitalizations among patients who have had a recent exacerbation (3.4 events per year for rehabilitation vs. 5.0 events for usual care) (Evidence B).
- Self-management intervention with communication with a health care professional improves health status and decreases hospitalizations and emergency department visits (Evidence B).
- Integrative care programs (e.g., exercise and nutrition) have not demonstrated benefit at this time (Evidence B).
Non-Pharmacologic Treatment

Oxygen therapy

Long-term oxygen therapy is indicated for stable patients who have:

► PaO₂ at or below 7.3 kPa (55 mmHg) or SaO₂ at or below 88%, with or without hypercapnia confirmed twice over a three week period; or

► PaO₂ between 7.3 kPa (55 mmHg) and 8.0 kPa (60 mmHg), or SaO₂ of 88%, if there is evidence of pulmonary hypertension, peripheral edema suggesting congestive cardiac failure, or polycythemia (hematocrit > 55%).

Oxygen Therapy & Ventilatory Support in Stable COPD

► During exacerbations of COPD, Noninvasive ventilation (NIV) in the form of noninvasive positive pressure ventilation (NPPV) is the standard of care for decreasing morbidity and mortality in patients hospitalized with an exacerbation of COPD and acute respiratory failure.

Table 3: Oxygen therapy and ventilatory support in stable COPD

<table>
<thead>
<tr>
<th>Oxygen therapy</th>
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<tr>
<td><em>In patients with stable COPD and moderate to severe exercise-induced external dyspnea, 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).</em></td>
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<td><em>Oxygen therapy at sea level does not exclude the development of severe hypercapnia when tending to altitude.</em> (Evidence B)</td>
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<tr>
<td><em>NIV improves hospitalization-free survival in selected patients after recent hospitalization, particularly in those with admitted exercise-prompted hypercapnia (Evidence C).</em></td>
</tr>
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Non-Pharmacologic Treatment

Palliative, End of Life & Hospice Care

► In many patients, the disease trajectory in COPD is marked by a gradual decline in health status and increasing symptoms, punctuated by acute exacerbations that are associated with an increased risk of dying.

► Although mortality rates following hospitalization for an acute exacerbation of COPD are declining, reported rates still vary from 23% to 80%.

Interventional Therapy in Stable COPD

► Lung volume reduction surgery (LVRS). LVRS is a surgical procedure in which parts of the lungs are resected to reduce hyperinflation,261 making respiratory muscles more effective pressure generators by improving their mechanical efficiency.

<table>
<thead>
<tr>
<th>Table 3.1: Interventional procedures in stable COPD</th>
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<td>LVRS is a surgical procedure in which parts of the lungs are resected to reduce hyperinflation, making respiratory muscles more effective pressure generators.261</td>
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<table>
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<th>Table 3.2: Palliative care, end of life and hospice care in COPD</th>
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Interventional Therapy in Stable COPD

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<tbody>
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<td>In selected patients with heterogeneous or homogenous emphysema and significant hyperinflation refractory to optimized medical care, surgical or bronchoscopic modes of lung volume reduction (e.g., endobronchial one-way valves or lung coils) may be considered.</td>
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<tr>
<td>In selected patients with a large bulla, surgical bullectomy may be considered.</td>
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<tr>
<td>In selected patients with very severe COPD and without relevant contraindications, lung transplantation may be considered.</td>
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Interventional Therapy in Stable COPD

<table>
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<td>Due to the morbidity and mortality associated with LVRS, less invasive bronchoscopic approaches to lung reduction have been examined.</td>
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Monitoring and Follow-up

Monitoring disease progression and development of complications and/or comorbidities

- **Measurements.** Decline in FEV₁ can be tracked by spirometry performed at least once a year.
- **Symptoms.** At each visit, information on symptoms since the last visit should be collected, including cough and sputum, breathlessness, fatigue, activity limitation, and sleep disturbances.
- **Exacerbations.** The frequency, severity, type and likely causes of all exacerbations should be monitored.
- **Imaging.** If there is a clear worsening of symptoms, imaging may be indicated.
- **Smoking status.** At each visit, the current smoking status and smoke exposure should be determined followed by appropriate action.

Monitoring and Follow-up

Pharmacotherapy and other medical treatment

In order to adjust therapy appropriately as the disease progresses, each follow-up visit should include a discussion of the current therapeutic regimen.

Monitoring should focus on:

- Dosages of prescribed medications.
- Adherence to the regimen.
- Inhaler technique.
- Effectiveness of the current regime.
- Side effects.

Treatment modifications should be recommended.

COPD and Comorbidities

Some common comorbidities occurring in patients with COPD with stable disease include:

- Cardiovascular disease (CVD)
- Heart failure
- Ischaemic heart disease (IHD)
- Arrhythmias
- Peripheral vascular disease
- Hypertension
- Osteoporosis
- Anxiety and depression
- COPD and lung cancer
- Metabolic syndrome and diabetes
- Gastrooesophageal reflux (GERD)
- Bronchiectasis
- Obstructive sleep apnea

COPD and Comorbidities

COPD as part of multimorbidity

- An increasing number of people in any aging population will suffer from multimorbidity, defined as the presence of two or more chronic conditions, and COPD is present in the majority of multi-morbid patients.
- Multi-morbid patients have symptoms from multiple diseases and thus symptoms and signs are complex and most often attributable to several causes in the chronic state as well as during acute events.
- There is no evidence that COPD should be treated differently when part of multi-morbidity; however, it should be kept in mind that most evidence comes from trials in patients with COPD as the only significant disease.
- Treatments should be kept simple in the light of the unbearable polypharmacy that these patients are often exposed to.

Summary

- COPD is a major cause of morbidity, mortality, and economic burden worldwide.
- GOLD has attempted to:
  - Provide a non-biased review of the current evidence for the assessment, diagnosis and treatment of patients with COPD.
  - To highlight short-term and long-term treatment objectives organized into two groups:
    - Relieving and reducing the impact of symptoms, and
    - Reducing the risk of adverse health events that may affect the patient in the future.
  - To guide symptoms assessment and health status measurement.

Summary

- Spirometry is used to establish airflow obstruction and diagnosis.
- Further goals of assessment are to establish the impact of symptoms on the patient's health status, and to assess the risk for future events, both of which help to guide therapy.
- There is evidence supporting non-pharmacologic treatment as well.
- Concomitant chronic diseases occur frequently in COPD patients, including cardiovascular disease, skeletal muscle dysfunction, metabolic syndrome, osteoporosis, depression, anxiety, and lung cancer. These comorbidities should be actively sought and treated appropriately when present as they can influence mortality and hospitalizations independently.
Summary

► The diagnosis and treatments for COPD are changing
  ► New data suggests patients develop COPD along different paths
  ► Additional tools such as HRCT may allow us to diagnose patients at an earlier stage
  ► New biological characterization schemes have promise to personalize treatment with novel therapies
  ► GOLD continues to use new data to enhance our understanding of the management of patients with COPD, and to continually refine treatment paradigms

Questions?