Global Strategy for Diagnosis, Management and Prevention of COPD, 2014: Chapters

Definition and Overview
Diagnosis and Assessment
Therapeutic Options
Manage Stable COPD
Manage Exacerbations
Manage Comorbidities
Asthma COPD Overlap Syndrome (ACOS)

Therapeutic Options: Key Points

- Smoking cessation has the greatest capacity to influence the natural history of COPD. Health care providers should encourage all patients who smoke to quit.
- Pharmacotherapy and nicotine replacement reliably increase long-term smoking abstinence rates.
- All COPD patients benefit from regular physical activity and should repeatedly be encouraged to remain active.

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Appropriate pharmacologic therapy can reduce COPD symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance.

None of the existing medications for COPD has been shown conclusively to modify the long-term decline in lung function.

Influenza and pneumococcal vaccination should be offered depending on local guidelines.

Counseling delivered by physicians and other health professionals significantly increases quit rates over self-initiated strategies. Even a brief (3-minute) period of counseling to urge a smoker to quit results in smoking quit rates of 5-10%.

Nicotine replacement therapy (nicotine gum, inhaler, nasal spray, transdermal patch, sublingual tablet, or lozenge) as well as pharmacotherapy with varenicline, bupropion, and nortriptyline reliably increases long-term smoking abstinence rates and are significantly more effective than placebo.
Brief Strategies to Help the Patient Willing to Quit Smoking

- **ASK** Systematically identify all tobacco users at every visit
- **ADVISE** Strongly urge all tobacco users to quit
- **ASSESS** Determine willingness to make a quit attempt
- **ASSIST** Aid the patient in quitting
- **ARRANGE** Schedule follow-up contact.

Therapeutic Options: Risk Reduction

- Encourage comprehensive tobacco-control policies with clear, consistent, and repeated nonsmoking messages.
- Emphasize primary prevention, best achieved by elimination or reduction of exposures in the workplace. Secondary prevention, achieved through surveillance and early detection, is also important.
- Reduce or avoid indoor air pollution from biomass fuel, burned for cooking and heating in poorly ventilated dwellings.
- Advise patients to monitor public announcements of air quality and, depending on the severity of their disease, avoid vigorous exercise outdoors or stay indoors during pollution episodes.
Global Strategy for Diagnosis, Management and Prevention of COPD

Therapeutic Options: COPD Medications

- **Beta₂-agonists**
  - Short-acting beta₂-agonists
  - Long-acting beta₂-agonists
- **Anticholinergics**
  - Short-acting anticholinergics
  - Long-acting anticholinergics
- **Combination short-acting beta₂-agonists + anticholinergic in one inhaler**
- **Combination long-acting beta₂-agonists + anticholinergic in one inhaler**
- **Methylxanthines**
- **Inhaled corticosteroids**
  - Combination long-acting beta₂-agonists + corticosteroids in one inhaler
  - Systemic corticosteroids
- **Phosphodiesterase-4 inhibitors**

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- Bronchodilator medications are central to the symptomatic management of COPD.
- Bronchodilators are prescribed on an as-needed or on a regular basis to prevent or reduce symptoms.
- The principal bronchodilator treatments are beta₂-agonists, anticholinergics, theophylline or combination therapy.
- The choice of treatment depends on the availability of medications and each patient’s individual response in terms of symptom relief and side effects.
Long-acting inhaled bronchodilators are convenient and more effective for symptom relief than short-acting bronchodilators.

Long-acting inhaled bronchodilators reduce exacerbations and related hospitalizations and improve symptoms and health status.

Combining bronchodilators of different pharmacological classes may improve efficacy and decrease the risk of side effects compared to increasing the dose of a single bronchodilator.

Regular treatment with inhaled corticosteroids improves symptoms, lung function and quality of life and reduces frequency of exacerbations for COPD patients with an FEV₁ < 60% predicted.

Inhaled corticosteroid therapy is associated with an increased risk of pneumonia.

Withdrawal from treatment with inhaled corticosteroids may lead to exacerbations in some patients.
An inhaled corticosteroid combined with a long-acting beta₂-agonist is more effective than the individual components in improving lung function and health status and reducing exacerbations in moderate to very severe COPD.

Combination therapy is associated with an increased risk of pneumonia.

Addition of a long-acting beta₂-agonist/inhaled glucocorticosteroid combination to an anticholinergic (tiotropium) appears to provide additional benefits.

Chronic treatment with systemic corticosteroids should be avoided because of an unfavorable benefit-to-risk ratio.
In patients with severe and very severe COPD (GOLD 3 and 4) and a history of exacerbations and chronic bronchitis, the phosphodiesterase-4 inhibitor, roflumilast, reduces exacerbations treated with oral glucocorticosteroids.

Theophylline is less effective and less well tolerated than inhaled long-acting bronchodilators and is not recommended if those drugs are available and affordable.

There is evidence for a modest bronchodilator effect and some symptomatic benefit compared with placebo in stable COPD. Addition of theophylline to salmeterol produces a greater increase in FEV₁ and breathlessness than salmeterol alone.

Low dose theophylline reduces exacerbations but does not improve post-bronchodilator lung function.
Influenza vaccines can reduce serious illness. Pneumococcal polysaccharide vaccine is recommended for COPD patients 65 years and older and for COPD patients younger than age 65 with an FEV$_1$ < 40% predicted.

The use of antibiotics, other than for treating infectious exacerbations of COPD and other bacterial infections, is currently not indicated.

**Alpha-1 antitrypsin augmentation therapy:** not recommended for patients with COPD that is unrelated to the genetic deficiency.

**Mucolytics:** Patients with viscous sputum may benefit from mucolytics; overall benefits are very small.

**Antitussives:** Not recommended.

**Vasodilators:** Nitric oxide is contraindicated in stable COPD. The use of endothelium-modulating agents for the treatment of pulmonary hypertension associated with COPD is not recommended.
All COPD patients benefit from *exercise training programs* with improvements in exercise tolerance and symptoms of dyspnea and fatigue.

Although an effective pulmonary rehabilitation program is 6 weeks, the longer the program continues, the more effective the results.

If exercise training is maintained at home, the patient's health status remains above pre-rehabilitation levels.

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**Oxygen Therapy:** The long-term administration of oxygen (> 15 hours per day) to patients with chronic respiratory failure has been shown to increase survival in patients with severe, resting hypoxemia.

**Ventilatory Support:** Combination of noninvasive ventilation (NIV) with long-term oxygen therapy may be of some use in a selected subset of patients, particularly in those with pronounced daytime hypercapnia.
**Therapeutic Options: Surgical Treatments**

*Lung volume reduction surgery (LVRS)* is more efficacious than medical therapy among patients with upper-lobe predominant emphysema and low exercise capacity.

*LVRS* is costly relative to health-care programs not including surgery.

In appropriately selected patients with very severe COPD, *lung transplantation* has been shown to improve quality of life and functional capacity.

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**Therapeutic Options: Other Treatments**

**Palliative Care, End-of-life Care, Hospice Care:**

- Communication with advanced COPD patients about end-of-life care and advance care planning gives patients and their families the opportunity to make informed decisions.
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Asthma COPD Overlap Syndrome (ACOS)

Identification and reduction of exposure to risk factors are important steps in prevention and treatment.

Individualized assessment of symptoms, airflow limitation, and future risk of exacerbations should be incorporated into the management strategy.

All COPD patients benefit from rehabilitation and maintenance of physical activity.

Pharmacologic therapy is used to reduce symptoms, reduce frequency and severity of exacerbations, and improve health status and exercise tolerance.
Manage Stable COPD: Key Points

- Long-acting formulations of β₂-agonists and anticholinergics are preferred over short-acting formulations. Based on efficacy and side effects, inhaled bronchodilators are preferred over oral bronchodilators.

- Long-term treatment with inhaled corticosteroids added to long-acting bronchodilators is recommended for patients with high risk of exacerbations.

- Long-term monotherapy with oral or inhaled corticosteroids is not recommended in COPD.

- The phosphodiesterase-4 inhibitor roflumilast may be useful to reduce exacerbations for patients with FEV₁ < 50% of predicted, chronic bronchitis, and frequent exacerbations.
Manage Stable COPD: Goals of Therapy

- Relieve symptoms
- Improve exercise tolerance
- Improve health status

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

Reduce symptoms
Reduce risk

Manage Stable COPD: All COPD Patients

Avoidance of risk factors
- smoking cessation
- reduction of indoor pollution
- reduction of occupational exposure

Influenza vaccination
### Manage Stable COPD: Non-pharmacologic

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Essential</th>
<th>Recommended</th>
<th>Depending on local guidelines</th>
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<tbody>
<tr>
<td>A</td>
<td>Smoking cessation (can include pharmacologic treatment)</td>
<td>Physical activity</td>
<td>Flu vaccination Pneumococcal vaccination</td>
</tr>
<tr>
<td>B, C, D</td>
<td>Smoking cessation (can include pharmacologic treatment) Pulmonary rehabilitation</td>
<td>Physical activity</td>
<td>Flu vaccination Pneumococcal vaccination</td>
</tr>
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</table>

### Manage Stable COPD: Pharmacologic Therapy

*Medications in each box are mentioned in alphabetical order, and therefore not necessarily in order of preference.*

<table>
<thead>
<tr>
<th>Patient</th>
<th>Recommended First choice</th>
<th>Alternative choice</th>
<th>Other Possible Treatments</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>SAMA prn or SABA prn</td>
<td>LAMA or LABA or SABA and SAMA</td>
<td>Theophylline</td>
</tr>
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<td>B</td>
<td>LAMA or LABA</td>
<td>LAMA and LABA</td>
<td>SABA and/or SAMA Theophylline</td>
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<td>C</td>
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<td>LAMA and LABA or LAMA and PDE4-inh. or LABA and PDE4-inh.</td>
<td>SABA and/or SAMA Theophylline</td>
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<tr>
<td>D</td>
<td>ICS + LABA and/or LAMA</td>
<td>ICS + LABA and LAMA or ICS+LABA and PDE4-inh. or LABA and LABA or LAMA and PDE4-inh.</td>
<td>Carbocysteine SABA and/or SAMA Theophylline</td>
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Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Stable COPD: Pharmacologic Therapy

RECOMMENDED FIRST CHOICE

<table>
<thead>
<tr>
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<th>GOLD 1</th>
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<tr>
<td><strong>C</strong></td>
<td><strong>D</strong></td>
<td></td>
<td></td>
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<tr>
<td>ICS + LABA or LAMA</td>
<td>ICS + LABA and/or LAMA</td>
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</tr>
</tbody>
</table>

Exacerbations per year

- 0 (not leading to hospital admission)
- 1 (not leading to hospital admission)
- 2 or more or ≥ 1 leading to hospital admission
- 1 (not leading to hospital admission)

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Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Stable COPD: Pharmacologic Therapy

ALTERNATIVE CHOICE

<table>
<thead>
<tr>
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<td><strong>A</strong></td>
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Exacerbations per year

- 0 (not leading to hospital admission)
- 1 (not leading to hospital admission)
- 2 or more or ≥ 1 leading to hospital admission
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Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Stable COPD: Pharmacologic Therapy

OTHER POSSIBLE TREATMENTS

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<td>mMRC 0-1</td>
<td>CAT ≥ 10</td>
<td>mMRC ≥ 2</td>
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- **A**
  - Theophylline
  - SABA and/or SAMA

- **B**
  - Theophylline
  - SABA and/or SAMA

- **C**
  - Carbocysteine
  - SABA and/or SAMA
  - Theophylline

- **D**
  - 2 or more leading to hospital admission
  - 1 (not leading to hospital admission)
  - Exacerbations per year

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An exacerbation of COPD is:

“an acute event characterized by a worsening of the patient’s respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication.”

The most common causes of COPD exacerbations are viral upper respiratory tract infections and infection of the tracheobronchial tree.

Diagnosis relies exclusively on the clinical presentation of the patient complaining of an acute change of symptoms that is beyond normal day-to-day variation.

The goal of treatment is to minimize the impact of the current exacerbation and to prevent the development of subsequent exacerbations.
Short-acting inhaled beta₂-agonists with or without short-acting anticholinergics are usually the preferred bronchodilators for treatment of an exacerbation.

Systemic corticosteroids and antibiotics can shorten recovery time, improve lung function (FEV₁) and arterial hypoxemia (PaO₂), and reduce the risk of early relapse, treatment failure, and length of hospital stay.

COPD exacerbations can often be prevented.
Arterial blood gas measurements (in hospital): PaO₂ < 8.0 kPa with or without PaCO₂ > 6.7 kPa when breathing room air indicates respiratory failure.

Chest radiographs: useful to exclude alternative diagnoses.

ECG: may aid in the diagnosis of coexisting cardiac problems.

Whole blood count: identify polycythemia, anemia or bleeding.

Purulent sputum during an exacerbation: indication to begin empirical antibiotic treatment.

Biochemical tests: detect electrolyte disturbances, diabetes, and poor nutrition.

Spirometric tests: not recommended during an exacerbation.

Oxygen: titrate to improve the patient’s hypoxemia with a target saturation of 88-92%.

Bronchodilators: Short-acting inhaled beta₂-agonists with or without short-acting anticholinergics are preferred.

Systemic Corticosteroids: Shorten recovery time, improve lung function (FEV₁) and arterial hypoxemia (PaO₂), and reduce the risk of early relapse, treatment failure, and length of hospital stay. A dose of 40 mg prednisone per day for 5 days is recommended.
Manage Exacerbations: Treatment Options

Oxygen: titrate to improve the patient’s hypoxemia with a target saturation of 88-92%.

Bronchodilators: Short-acting inhaled beta₂-agonists with or without short-acting anticholinergics are preferred.

Systemic Corticosteroids: Shorten recovery time, improve lung function (FEV₁) and arterial hypoxemia (PaO₂), and reduce the risk of early relapse, treatment failure, and length of hospital stay. **A dose of 40 mg prednisone per day for 5 days is recommended.** Nebulized magnesium as an adjuvent to salbutamol treatment in the setting of acute exacerbations of COPD has no effect on FEV₁.

Antibiotics should be given to patients with:

- Three cardinal symptoms:
  - increased dyspnea
  - increased sputum volume
  - and increased sputum purulence.
- Who require mechanical ventilation.
Noninvasive ventilation (NIV) for patients hospitalized for acute exacerbations of COPD:

- Improves respiratory acidosis, decreases respiratory rate, severity of dyspnea, complications and length of hospital stay.
- Decreases mortality and needs for intubation.

Marked increase in intensity of symptoms
- Severe underlying COPD
- Onset of new physical signs
- Failure of an exacerbation to respond to initial medical management
- Presence of serious comorbidities
- Frequent exacerbations
- Older age
- Insufficient home support
COPD often coexists with other diseases (comorbidities) that may have a significant impact on prognosis. In general, presence of comorbidities should not alter COPD treatment and comorbidities should be treated as if the patient did not have COPD.
Cardiovascular disease (including ischemic heart disease, heart failure, atrial fibrillation, and hypertension) is a major comorbidity in COPD and probably both the most frequent and most important disease coexisting with COPD. Benefits of cardioselective beta-blocker treatment in heart failure outweigh potential risk even in patients with severe COPD.

Osteoporosis and anxiety/depression: often under-diagnosed and associated with poor health status and prognosis.

Lung cancer: frequent in patients with COPD; the most frequent cause of death in patients with mild COPD.

Serious infections: respiratory infections are especially frequent.

Metabolic syndrome and manifest diabetes: more frequent in COPD and the latter is likely to impact on prognosis.
A chapter on Asthma and COPD Overlap Syndrome (ACOS) is in preparation by the Science Committees of the Global Initiative for Asthma (GINA) and the Global Initiative for Chronic Obstructive Lung Disease (GOLD).

It is expected to be available with the release of the GINA 2014 document *Global Strategy for Asthma Management and Prevention* in the Spring 2014 and will be posted on the GOLD website when it is available.
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Global Strategy for Diagnosis, Management and Prevention of COPD, 2013: Summary

- Prevention of COPD is to a large extent possible and should have high priority
- Spirometry is required to make the diagnosis of COPD; the presence of a post-bronchodilator FEV₁/FVC < 0.70 confirms the presence of persistent airflow limitation and thus of COPD
- The beneficial effects of pulmonary rehabilitation and physical activity cannot be overstated
Assessment of COPD requires assessment of symptoms, degree of airflow limitation, risk of exacerbations, and comorbidities.

Combined assessment of symptoms and risk of exacerbations is the basis for non-pharmacologic and pharmacologic management of COPD.

Treat COPD exacerbations to minimize their impact and to prevent the development of subsequent exacerbations.

Look for comorbidities - and if present treat to the same extent as if the patient did not have COPD.
WORLD COPD DAY  
November 19, 2014  

Raising COPD Awareness Worldwide  
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GOLD Website Address

http://www.goldcopd.org

ADDITIONAL SLIDES PREPARED BY PROFESSOR PETER J. BARNES, MD
NATIONAL HEART AND LUNG INSTITUTE
LONDON, ENGLAND
### ASTHMA vs COPD

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<tr>
<th>INFLAMMATION</th>
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<tr>
<td><strong>Cells</strong></td>
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<td>Neutrophils</td>
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<tr>
<td></td>
<td>Eosinophils</td>
<td>CD8⁺ T cells</td>
</tr>
<tr>
<td></td>
<td>CD4⁺ T cells</td>
<td>Macrophages +++</td>
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<tr>
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<td>Macrophages +++</td>
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<td>LTB₄</td>
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<tr>
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<td>IL-4, IL-5</td>
<td>IL-8, TNF-α</td>
</tr>
<tr>
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<td>ROS +</td>
<td>ROS +++</td>
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<td><strong>Response to steroids</strong></td>
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**Professor Peter J. Barnes, MD**  
National Heart and Lung Institute, London UK

### AIR TRAPPING IN COPD

**Normal**  
- **Inspiration**  
  - small airway  
  - alveolar attachments  

**COPD**  
- **Inflammation**  
  - thickened airway  
- **Loss of alveolar attachments**  
- **Loss of elasticity (emphysema)**

**Expiration**  
- **Airway closure**

**Professor Peter J. Barnes, MD**  
National Heart and Lung Institute, London UK
EVOLUTION OF INFLAMMATION IN COPD

At risk  GOLD1  GOLD2  GOLD3  GOLD4

Macrophages  Neutrophils

INNATE IMMUNITY

Dendritic cells

ACQUIRED IMMUNITY

T cells  B cells

Th17 CELLS

IL-6  IL-23  TGFB

Th17

RORyt  STAT3

TNF-α  IL-17A

IL-21

IL-22

IL-6

Neutrophils

CXCL1  CXCL8  Epithelial cells

↑ IL-10

↑ acute phase proteins

B cell  CD8+ cell
**Nrf2 AND ANTIOXIDANT GENE REGULATION**

BZip transcription factor

Nrf2(-/-): ↑ emphysema in smoking mice

Nrf2 activity in lung
↑ in normal smokers
↓ in COPD patients
Malhotra et al: AJRCCM 2008

No ↑ with ox stress in COPD
Due to Nrf2 acetylation
(linked to ↓ HDAC2 and SIRT1)

---

**COPD EXACERBATIONS**

Bacteria  Viruses  Non-infective

Macrophages  Epithelial cells

TNF-α  CXCL8  CXCL5  IL-6

Neutrophils

Oxidative stress