

SUMMARY HANDOUT

Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease Revised 2011



This summary was prepared for distribution to participants at the GOLD Symposium in Shanghai, China sponsored by the Asian Pacific Society of Respiriology. The GOLD 2011 report is scheduled to be posted on the GOLD website – www.goldcopd.org - in late 2011 and is still in final editing. Thus, some of the materials presented in this summary may be modified in the final GOLD 2011 report prior to its release.

NOVEMBER 2011

GLOBAL STRATEGY FOR THE DIAGNOSIS, MANAGEMENT, AND PREVENTION OF COPD (Revised 2011)

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TABLE OF CONTENTS

Global Strategy for Diagnosis, Management and Prevention of COPD 2011

Introduction

Chapter 1. Definition and Overview

- Key Points
- Definition
- Burden Of COPD
 - Prevalence
 - Morbidity
 - Mortality
 - Economic Burden
 - Social Burden
- Factors That Influence Disease Development And Progression
 - Genes
 - Age and Gender
 - Lung Growth and Development
 - Exposure to Particles
 - Socioeconomic Status
 - Asthma/Bronchial Hyperreactivity
 - Chronic Bronchitis
 - Infections
- Pathology, Pathogenesis And Pathophysiology
 - Pathology
 - Pathogenesis
 - Pathophysiology
 - Airflow Limitation and Air Trapping*

Chapter 2. Diagnosis and Assessment

- Key Points
- Diagnosis
 - Symptoms
 - Medical History
 - Physical Examination
 - Spirometry
- Assessment Of Disease
 - Assessment of Symptoms
 - Spirometric Assessment
 - Assessment of Exacerbation Risk
 - Assessment of Comorbidities
 - Relationship Between Symptoms, Airflow Limitation, and Exacerbations
 - Combined COPD Assessment
 - Additional Investigations
- Differential Diagnosis

Chapter 3. Therapeutic Options

- Key Points
- Smoking Cessation
 - Pharmacotherapy for Smoking Cessation
- Pharmacologic Therapy for Stable COPD
 - Overview of Medications

- Bronchodilators
- Corticosteroids
- Phosphodiesterase-4 Inhibitors
- Other Pharmacologic Treatments
 - Vaccines
 - Alpha-1 Antitrypsin Augmentation Therapy
 - Antibiotics
 - Mucolytic and Antioxidant Agents
 - Immunoregulators
 - Antitussives
 - Vasodilators
 - Narcotics (morphine)
 - Others
- Non-Pharmacologic Therapies
 - Rehabilitation
- Other Treatments
 - Oxygen Therapy
 - Ventilatory Support
 - Surgical Treatments

Chapter 4. Management of Stable COPD

- Key Points
- Introduction
- Identify And Reduce Exposures
 - Tobacco Smoke
 - Occupational Exposures
 - Indoor And Outdoor Pollution
- Treatment of Stable COPD
 - Moving from Clinical Trials to Recommendations for Routine Practice
 - Treatment Strategy
- Non-Pharmacologic Treatment
 - Physical Activity
 - Rehabilitation
- Pharmacologic Treatment
 - Bronchodilators - Recommendations
 - Corticosteroids and Phosphodiesterase-4 Inhibitors - Recommendations
- Monitoring And Follow-Up
 - Monitor Disease Progression and Development of Complications
 - Monitor Pharmacotherapy and Other Medical Treatment
 - Monitor Exacerbation History
 - Monitor Comorbidities
 - Surgery in the COPD Patient

Chapter 5. Management of Exacerbations

Key Points

Definition

Diagnosis

Assessment

Treatment Options

 Pharmacologic Treatment

 Respiratory Support

Hospital Discharge And Follow-Up

Home Management Of Exacerbations

Prevention of COPD Exacerbations

Chapter 6. COPD and Comorbidities

Key Points

Introduction

Cardiovascular Disease

Osteoporosis

Anxiety and Depression

Lung Cancer

Infections

Metabolic Syndrome and Diabetes

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GLOBAL STRATEGY FOR THE DIAGNOSIS, MANAGEMENT, AND PREVENTION OF COPD (Revised 2011)

INTRODUCTION

Much has changed in the 10 years since the first GOLD report, *Global Strategy for the Diagnosis, Management, and Prevention of COPD*, was published. This major revision builds on the strengths from the original recommendations and incorporates new knowledge.

One of the strengths was the treatment objectives. These have stood the test of time, but are now organized into two groups: objectives that are directed towards immediately relieving and reducing the impact of symptoms, and objectives that reduce the risk of adverse health events that may affect the patient at some point in the future. (Exacerbations are an example of such events.) This emphasizes the need for clinicians to maintain a focus on both the short-term and long-term impact of COPD on their patients.

A second strength of the original strategy was the simple, intuitive system for classifying COPD severity. This was based upon the FEV₁ and was called a staging system because it was believed, at the time, that the majority of patients followed a path of disease progression in which the severity of the disease tracked the severity of the airflow limitation. Much is now known about the characteristics of patients in the different GOLD stages – for example, their level of risk of exacerbations, hospitalization, and death. However at an individual patient level, the FEV₁ is an unreliable marker of the severity of breathlessness, exercise limitation, and health status impairment. This report retains the GOLD classification system because it is a predictor of future adverse events, but the term “Stage” is now replaced by “Grade.”

At the time of the original report, improvement in both symptoms and health status was a GOLD treatment objective, but symptoms assessment did not have a direct relation to the choice of management, and health status measurement was a complex process largely confined to clinical studies. Now, there are simple and reliable questionnaires designed for use in routine daily clinical practice. These are available in many languages.

These developments have enabled a new assessment system to be developed that draws together a measure of the impact of the patient’s symptoms and an assessment of the patient’s risk of having a serious adverse health event in the future. In turn, this new assessment system has led to the construction of a new approach to management– one that matches assessment to treatment objectives. The new management approach can be used in any clinical setting anywhere in the world and moves COPD treatment towards personalised medicine – matching the patient’s therapy more closely to his or her needs.

BACKGROUND

Chronic Obstructive Pulmonary Disease (COPD), the fourth leading cause of death in the world, represents an important public health challenge that is both preventable and treatable. COPD is a major cause of chronic morbidity and mortality throughout the world; many people suffer from this disease for years, and die prematurely from it or its complications. Globally, the COPD burden is projected to increase in coming decades because of continued exposure to COPD risk factors and aging of the population.

In 1998, with the cooperation of the National Heart, Lung, and Blood Institute, NIH and the World Health Organization, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) was implemented. Its goals were to increase awareness of the burden of COPD and to improve prevention and management of COPD through a concerted worldwide effort of people involved in all facets of health care and health care policy. An important and related goal was to encourage greater research interest in this highly prevalent disease.

In 2001, GOLD released its first report, *Global Strategy for the Diagnosis, Management, and Prevention of COPD*. This report was not intended to be a comprehensive textbook on COPD, but rather to summarize the current state of the field. It was developed by individuals with expertise in COPD research and patient care and was based on the best-validated concepts of COPD pathogenesis at that time, along with available evidence on the most appropriate management and prevention strategies. It provided state-of-the-art information about COPD for pulmonary specialists and other interested physicians and served as a source document for the production of various communications for other audiences, including an Executive Summary, a Pocket Guide for Health Care Professionals, and a Patient Guide.

Immediately following the release of the first GOLD report in 2001, the GOLD Board of Directors appointed a Science Committee, charged with keeping the GOLD documents up-to-date by reviewing published research, evaluating the impact of this research on the management recommendations in the GOLD documents, and posting yearly updates of these documents on the GOLD Website. The first update to the GOLD report was posted in July 2003, based on publications from January 2001 through December 2002. A second update appeared in July 2004, and a third in July 2005, each including the impact of publications from January through December of the previous year. In January 2005, the GOLD Science Committee initiated its work to prepare a comprehensively updated version of the GOLD report; it was released in 2006. The methodology used to create the annual updated documents, and the 2006 revision, appears at the front of each volume.

During the period from 2006 to 2010, again annual updated documents were prepared and released on the GOLD Website, along with the methodology used to prepare the documents and

the list of published literature reviewed to examine the impact on recommendations made in the annual updates. In 2009, the GOLD Science Committee recognized that considerable new information was available particularly related to diagnosis and approaches to management of COPD that warranted preparation of a significantly revised report. The work on this new revision was implemented in mid-2009 while at the same time the Committee prepared the 2010 update.

METHODOLOGY

In September 2009 and in May and September 2010 while preparing the annual updated reports (<http://www.goldcopd.org>), Science Committee members began to identify the literature that impacted on major recommendations, especially for COPD diagnosis and management. Committee members were assigned chapters to review for proposed modifications and soon reached consensus that the report required significant change to reach the target audiences – the general practitioner and the individuals in clinics around the world who first see patients who present with respiratory symptoms that could lead to a diagnosis of COPD. In the summer of 2010 a writing committee was established to produce an outline of proposed chapters, which was first presented in a symposium for the European Respiratory Society in Barcelona, 2010. The writing committee considered recommendations from this session in throughout fall 2010 and spring 2011. During this period the GOLD Board of Directors and GOLD National Leaders were provided summaries of the major new directions recommended. During the summer of 2011 the document was circulated for review to GOLD National Leaders, and other COPD opinion leaders in a variety of countries. The names of the individuals who submitted reviews appear in the front of this report. In September 2011 the GOLD Science Committee reviewed the comments and made final recommendations. The report was launched during a symposium hosted by the Asian Pacific Society of Respirology in November 2011.

NEW ISSUES PRESENTED IN THIS REPORT

1. This document has been considerably shortened in length by limiting to Chapter 1 the background information on COPD. Readers who wish to access more comprehensive information about the pathophysiology of COPD are referred to a variety of excellent textbooks that have appeared in the last decade.
2. Chapter 2 includes information on diagnosis and assessment of COPD. The definition of COPD has not been significantly modified but has been reworded for clarity.
3. Assessment of COPD is based on the patient's level of symptoms, future risk of exacerbations, the severity of the spirometric abnormality, and the identification of

comorbidities. Whereas spirometry was previously used to support a diagnosis of COPD, spirometry is now required to make a confident diagnosis of COPD.

4. The spirometric classification of airflow limitation is divided into four Grades (GOLD 1, Mild; GOLD 2, Moderate; GOLD 3, Severe; and GOLD 4, Very Severe) using the fixed ratio, postbronchodilator $FEV_1/FVC < 0.7$, to define airflow limitation. It is recognized that use of the fixed ratio (FEV_1/FVC) may lead to more frequent diagnoses of COPD in older adults with mild COPD as the normal process of aging affects lung volumes and flows, and may lead to under-diagnosis and in adults younger than 45 years. The concept of staging has been abandoned as a staging system based on FEV_1 alone was inadequate and the evidence for an alternative staging system does not exist. The most severe spirometric Grade, GOLD 4, does not include reference to respiratory failure as this seemed to be an arbitrary inclusion.

5. A new chapter (Chapter 3) on therapeutic approaches has been added. This includes descriptive information on both pharmacologic and non-pharmacologic therapies, identifying adverse effects, if any.

6. Management of COPD is presented in three chapters: Management of Stable COPD (Chapter 4); Management of COPD Exacerbations (Chapter 5); and COPD and Comorbidities (Chapter 6), covering both management of comorbidities in patients with COPD and of COPD in patients with comorbidities.

7. In Chapter 4, Management of Stable COPD, recommended approaches to both pharmacologic and non-pharmacologic treatment of COPD are presented. The chapter begins with the importance of identification and reduction of risk factors. Cigarette smoke continues to be identified as the most commonly encountered risk factor for COPD and elimination of this risk factor is an important step toward prevention and control of COPD. However, more data are emerging to recognize the importance of other risk factors for COPD that should be taken into account where possible. These include occupational dusts and chemicals, and indoor air pollution from biomass cooking and heating in poorly ventilated dwellings - the latter especially among women in developing countries.

8. In previous GOLD documents, recommendations for management of COPD were based solely on spirometric category. However, there is considerable evidence that the level of FEV_1 is a poor descriptor of disease status and for this reason the management of stable COPD based on a strategy considering both disease impact (determined mainly by symptom burden and activity limitation) and future risk of disease progression (especially of exacerbations) is recommended.

9. Chapter 5, Management of Exacerbations, presents a revised definition of a COPD exacerbation.

10. Chapter 6, Comorbidities and COPD, focuses on cardiovascular diseases, osteoporosis, anxiety and depression, lung cancer, infections, and metabolic syndrome and diabetes.

LEVELS OF EVIDENCE

Levels of evidence are assigned to management recommendations where appropriate. Evidence levels are indicated in boldface type enclosed in parentheses after the relevant statement e.g., (**Evidence A**). The methodological issues concerning the use of evidence from meta-analyses were carefully considered. This evidence level scheme (**Table A**) has been used in previous GOLD reports, and was in use throughout the preparation of this document.

Table A. Description of Levels of Evidence		
Evidence Category	Sources of Evidence	Definition
A	Randomized controlled trials (RCTs). Rich body of data.	Evidence is from endpoints of well-designed RCTs that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.
B	Randomized controlled trials (RCTs). Limited body of data.	Evidence is from endpoints of intervention studies that include only a limited number of patients, posthoc or subgroup analysis of RCTs, or meta-analysis of RCTs. In general, Category B pertains when few randomized trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.
C	Nonrandomized trials. Observational studies.	Evidence is from outcomes of uncontrolled or nonrandomized trials or from observational studies.
D	Panel Consensus Judgment.	This category is used only in cases where the provision of some guidance was deemed valuable but the clinical literature addressing the subject was deemed insufficient to justify placement in one of the other categories. The Panel Consensus is based on clinical experience or knowledge that does not meet the above-listed criteria

KEY POINTS OF THE CHAPTERS

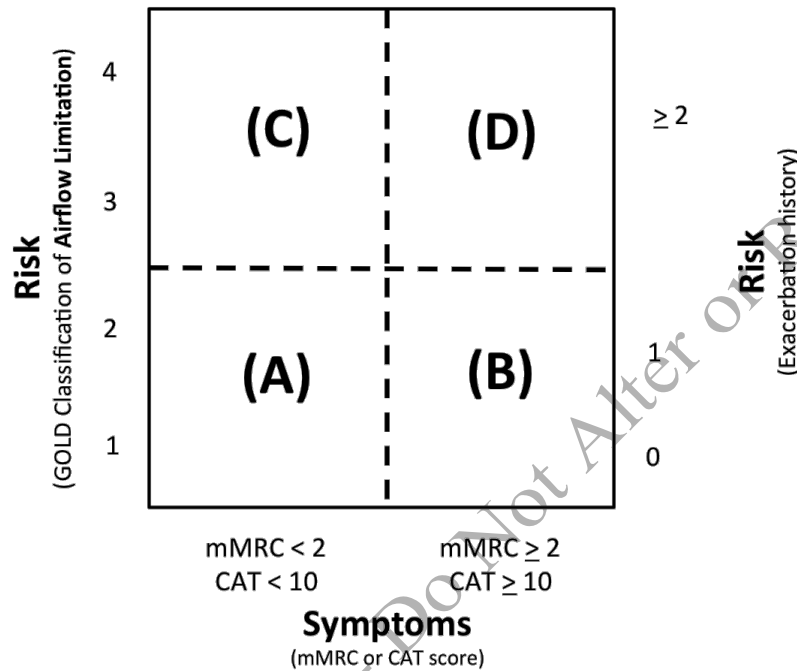
CHAPTER 1: DEFINITION AND OVERVIEW

- *Chronic Obstructive Pulmonary Disease (COPD), a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients.*
- COPD is a leading cause of morbidity and mortality worldwide and results in an economic and social burden that is both substantial and increasing.
- Inhaled cigarette smoke and other noxious particles such as smoke from biomass fuels cause lung inflammation, a normal response that appears to be modified in patients who develop COPD. This chronic inflammatory response may induce parenchymal tissue destruction (resulting in emphysema), and disrupt normal repair and defense mechanisms (resulting in small airway fibrosis). These pathological changes lead to air trapping and progressive airflow limitation, and in turn to breathlessness and other characteristic symptoms of COPD.

CHAPTER 2. DIAGNOSIS AND ASSESSMENT

- A clinical diagnosis of 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 in this clinical context; the presence of a postbronchodilator $FEV_1/FVC < 0.70$ confirms the presence of persistent airflow limitation and thus of COPD.
- The goals of COPD assessment are to determine the severity of the disease, including the severity of airflow limitation, the impact on the patient's health status, and the risk of future events (such as exacerbations, hospital admissions, or death), in order to guide therapy.
- Comorbidities occur frequently in COPD patients, including cardiovascular disease, skeletal muscle dysfunction, metabolic syndrome, osteoporosis, depression, and lung cancer. Given that they can occur in patients with mild, moderate and severe airflow limitation and influence mortality and hospitalizations independently, comorbidities should be actively looked for, and treated appropriately if present.

Association Between Symptoms, Spirometric Classification, and Future Risk of Exacerbations



Patient Group A - Low Risk, Less Symptoms

Typically GOLD 1 or GOLD 2 (Mild or Moderate airflow limitation) and/or ≤ 1 exacerbation per year *and* mMRC Grade < 2 or CAT score < 10

Patient Group B - Low Risk, More Symptoms

Typically GOLD 1 or GOLD 2 (Mild or Moderate airflow limitation) and/or ≤ 1 exacerbation per year *and* mMRC ≥ 2 or CAT score ≥ 10

Patient Group C - High Risk, Less Symptoms

Typically GOLD 3 or GOLD 4 (Severe or Very Severe airflow limitation) and/or ≥ 2 exacerbations per year *and* mMRC Grade < 2 or CAT score < 10

Patient Group D - High Risk, More Symptoms

Typically GOLD 3 or GOLD 4 (Severe or Very Severe airflow limitation) and/or ≥ 2 exacerbations per year *and* mMRC Grade ≥ 2 or CAT score ≥ 10

CHAPTER 3. THERAPEUTIC OPTIONS

- In patients who continue to smoke, smoking cessation is very important. Pharmacotherapy and nicotine replacement reliably increase long-term smoking abstinence rates.
- Appropriate pharmacologic therapy can reduce COPD symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance.
- To date, none of the existing medications for COPD has been shown conclusively to modify the long-term decline in lung function.
- Each pharmacological treatment regimen needs to be patient-specific, guided by severity, drug availability, and the patient's response.
- Influenza and pneumococcal vaccination should be offered to every COPD patient; they appear to be more effective in older patients and those with more severe disease or cardiac comorbidity.
- All patients who get short of breath when walking on their own pace on level ground should be offered rehabilitation; it can improve symptoms, quality of life, and physical and emotional participation in everyday activities.

Formulations and Typical Doses of COPD Medications*					
Drug	Inhaler (mcg)	Solution for Nebulizer (mg/ml)	Oral	Vials for Injection (mg)	Duration of Action (hours)
Beta₂-agonists					
Short-acting					
Fenoterol	100-200 (MDI)	1	0.05% (Syrup)		4-6
Levalbuterol	45-90 (MDI)	0.21, 0.42			6-8
Salbutamol (albuterol)	100, 200 (MDI & DPI)	5	5 mg (Pill), 0.024%(Syrup)	0.1, 0.5	4-6
Terbutaline	400, 500 (DPI)		2.5, 5 mg (Pill)		4-6
Long-acting					
Formoterol	4.5-12 (MDI & DPI)	0.01 [¶]			12
Arformoterol		0.0075			12
Indacaterol	75-300 (DPI)				24
Salmeterol	25-50 (MDI & DPI)				12
Tulobuterol			2 mg (transdermal)		24
Anticholinergics					
Short-acting					
Ipratropium bromide	20, 40 (MDI)	0.25-0.5			6-8
Oxipropium bromide	100 (MDI)	1.5			7-9
Long-acting					
Tiotropium	18 (DPI), 5 (SMI)				24
Combination short-acting beta₂-agonists plus anticholinergic in one inhaler					
Fenoterol/Ipratropium	200/80 (MDI)	1.25/0.5			6-8
Salbutamol/Ipratropium	75/15 (MDI)	0.75/0.5			6-8
Methylxanthines					
Aminophylline			200-600 mg (Pill)	240 mg	Variable, up to 24
Theophylline (SR)			100-600 mg (Pill)		Variable, up to 24
Inhaled corticosteroids					
Beclomethasone	50-400 (MDI & DPI)	0.2-0.4			
Budesonide	100, 200, 400 (DPI)	0.20, 0.25, 0.5			
Fluticasone	50-500 (MDI & DPI)				
Combination long-acting beta₂-agonists plus corticosteroids in one inhaler					
Formoterol/Budesonide	4.5/160, 9/320 (DPI)				
Salmeterol/Fluticasone	50/100, 250, 500 (DPI) 25/50, 125, 250 (MDI)				
Systemic corticosteroids					
Prednisone			5-60 mg (Pill)		
Methyl-prednisolone			4, 8, 16 mg (Pill)		
Phosphodiesterase-4 inhibitors					
Roflumilast			500 mcg (Pill)		24

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


*Not all formulations are available in all countries; in some countries, other formulations may be available.

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

CHAPTER 4: MANAGEMENT OF STABLE COPD

- Identification and reduction of exposure to risk factors are important steps in the prevention and treatment of COPD. All individuals who smoke should be encouraged to quit.
- The level of FEV₁ is an inadequate descriptor of the impact of the disease on patients and for this reason individualized assessment of symptoms and future risk of exacerbation should also be incorporated into the management strategy for stable COPD.
- Pharmacologic therapy is used to reduce symptoms, reduce frequency and severity of exacerbations, and improve health status and exercise tolerance. Existing medications for COPD have not been conclusively shown to modify the long-term decline in lung function that is the hallmark of this disease.
- For both beta₂-agonists and anticholinergics, long-acting formulations 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 inhibitor roflumilast may be useful to reduce exacerbations for patients with FEV₁ <50% of predicted, chronic bronchitis, and frequent exacerbations.
- Influenza vaccines can reduce the risk of serious illness (such as hospitalization due to lower respiratory tract infections) and death in COPD patients.
- Currently, the use of antibiotics is not indicated in COPD, other than for treating infectious exacerbations of COPD and other bacterial infections.
- All COPD patients with breathlessness when walking at their own pace on level ground appear to benefit from rehabilitation and maintenance of physical activity, improving their exercise tolerance and quality of life, and reducing symptoms of dyspnea and fatigue.

Goals for Treatment of Stable COPD

<ul style="list-style-type: none"> • Relieve symptoms • Improve exercise tolerance • Improve health status <p style="text-align: center;"><i>and</i></p> <ul style="list-style-type: none"> • Prevent disease progression • Prevent and treat exacerbations • Reduce mortality 	 <p style="margin-top: 10px;">REDUCE SYMPTOMS</p> <p style="margin-top: 10px;">REDUCE RISK</p>
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Pharmacologic Management of COPD

Group	FIRST CHOICE*	SECOND CHOICE*	ALTERNATIVE CHOICE†
A	Short-acting anticholinergic prn <i>or</i> Short-acting beta ₂ -agonist prn	Long-acting anticholinergic <i>or</i> Long-acting beta ₂ -agonist <i>or</i> Short-acting beta ₂ -agonist + Short-acting anticholinergic	Theophylline
B	Long-acting anticholinergic <i>or</i> Long-acting beta ₂ -agonist	Long-acting anticholinergic + Long-acting beta ₂ -agonist	Theophylline Short-acting beta ₂ -agonist +/or Short-acting anticholinergic
C	Inhaled corticosteroid + Long-acting beta ₂ -agonist <i>or</i> Long-acting anticholinergic	Long-acting anticholinergic + Long-acting beta ₂ -agonist	Theophylline Short-acting beta ₂ -agonist +/or Short-acting anticholinergic <i>Consider</i> Phosphodiesterase4- inhibitor
D	Inhaled corticosteroid + Long-acting beta ₂ -agonist <i>or</i> Long-acting anticholinergic	Inhaled corticosteroid + Long-acting anticholinergic + Long-acting beta ₂ -agonist <i>or</i> Inhaled corticosteroid + Long-acting beta ₂ -agonist + Phosphodiesterase4-inhibitor <i>or</i> Long-acting anticholinergic + Phosphodiesterase4-inhibitor <i>or</i> Inhaled corticosteroid + Long-acting anticholinergic <i>or</i> Long-acting anticholinergic + Long-acting beta ₂ -agonist	Theophylline Short-acting beta ₂ -agonist +/or Short-acting anticholinergic Carbocysteine

*Medications in each box are mentioned in alphabetical order

†Medications in this column can be used alone or in combination with other options in the First and Second Choice columns.

CHAPTER 5: MANAGEMENT OF EXACERBATIONS

- 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.*
- Exacerbations of COPD can be precipitated by several factors. The most common causes appear to be viral upper respiratory tract infections and infection of the tracheobronchial tree.
- The diagnosis of an exacerbation relies exclusively on the clinical presentation of the patient complaining of an acute change of symptoms (baseline dyspnea, cough, and/or sputum production) that is beyond normal day-to-day variation.
- The goal of treatment in COPD exacerbations 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. Smoking cessation, influenza and pneumococcal vaccination, knowledge of current therapy including inhaler technique, and treatment with long-acting inhaled bronchodilators, with or without inhaled corticosteroids, reduces the number of exacerbations and hospitalizations.

CHAPTER 6: COPD AND COMORBIDITIES

- COPD often coexists with other diseases (comorbidities) that may have a significant impact on prognosis.
- In general, the presence of comorbidities should not alter COPD treatment and comorbidities should be treated as if the patient did not have COPD.
- Cardiovascular disease is a major comorbidity in COPD and probably both the most frequent and most important disease coexisting with COPD.
- Osteoporosis and depression are also major comorbidities in COPD, are often underdiagnosed, and are associated with poor health status and prognosis.
- Lung cancer is frequently seen in patients with COPD and has been found to be the most frequent cause of death in patients with mild COPD.

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) has received unrestricted educational donations from Almirall, AstraZeneca, Boehringer-Ingelheim, Chiesi Group, Dey Pharmaceuticals, Forest Laboratories, GlaxoSmithKline, Grupo Ferrer, Merck, Nonin, Novartis, Nycomed, Pearl Therapeutics and Pfizer.

The members of the GOLD Committees are solely responsible for the statements in the *Global Strategy for Diagnosis, Management and Prevention of COPD*, revised 2011.