Differential Diagnosis of Chronic Obstructive Pulmonary Disease

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Faculty Disclosure

Company	Nature of Affiliation	Unlabeled Product Usage
• Pfizer • Boehringer Ingelheim	• Speakers Bureau • Speakers Bureau	• None • None

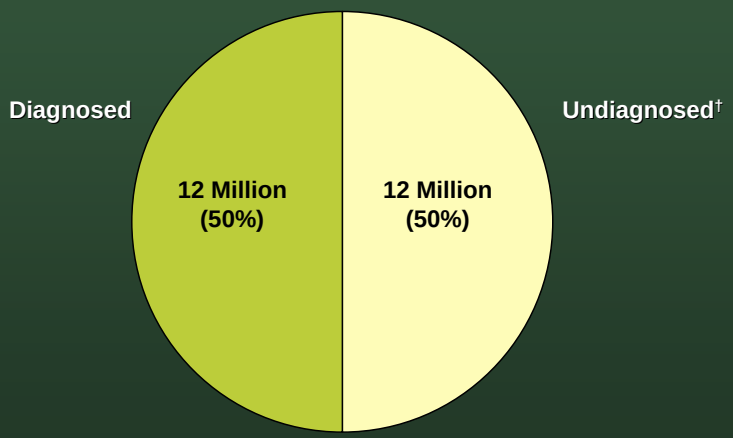
Current Definition of COPD

- A **preventable and treatable** disease
- Associated with significant **extrapulmonary effects** and important **comorbid conditions**
- Characterized by airflow limitation that is
  - **Partially reversible**
  - **Usually progressive**
  - Associated with an **abnormal inflammatory response** to noxious particles or gases

Global Initiative for Chronic Obstructive Disease. Global strategy for the diagnosis, management, and prevention of COPD. Updated 2008. http://www.goldcopd.com/Guidelineitem.asp?l1=2&l2=1&intId=989. Accessed November 21, 2008.

COPD Remains Underdiagnosed

24 Million COPD Cases Estimated in the US*



*Data for diagnosed and total number of cases of COPD are derived from two different CDC surveys, from 2006 and 1988-1994 respectively.
†Assumption based on available data from CDC.

American Lung Association. http://www.lungusa.org/atf/cf/%7B7a8d42c2-fcca-4604-8ade-7f5d5e762256%7D/COPD_DEC07.PDF. Accessed February 16, 2009.

Where Can We Improve COPD Management?

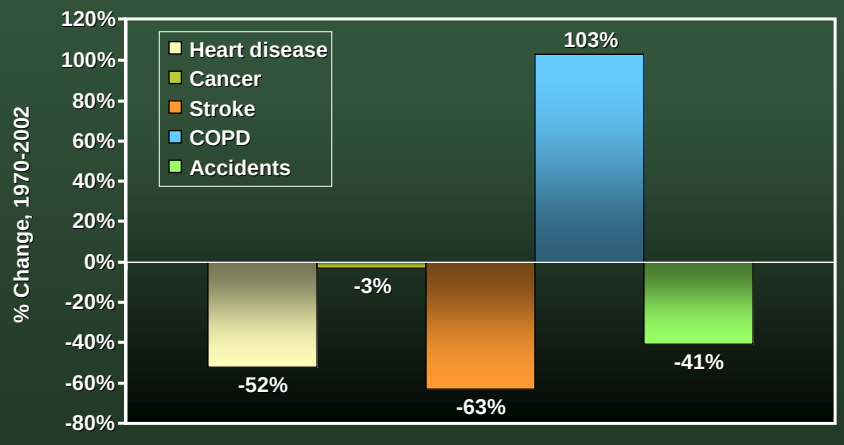
COPD remains underdiagnosed[1]
- Awareness of COPD guidelines suboptimal[2]
- Spirometry used inconsistently[2]
- Mortality increasing among women[3]
- Present in the fifth decade of life,[4] though early symptoms may be missed[2]

Early diagnosis and treatment may lead to better outcomes[5]

Diagnosis and treatment may prevent or delay progression of lung function decline and symptoms[5]
- Spirometry is key to the diagnosis of COPD[5]
- Education represents an opportunity to improve outcomes for COPD patients[2,5]

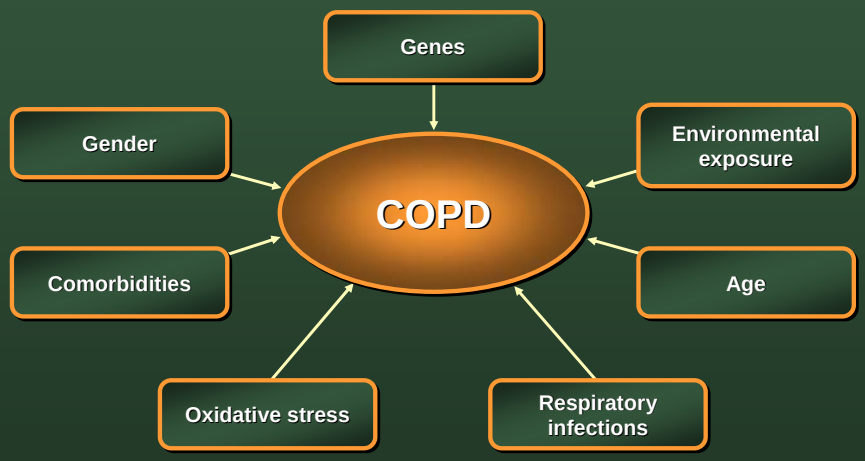
1. Mannino DM et al. *MMWR Surveillance Summary*. 2002;51:1-16.
2. Yawn BP, Wollan PC. *Int J COPD*. 2008;3:311-317.
3. Deaths from chronic obstructive pulmonary disease—United States, 2000-2005. *MMWR Morb Mortal Wkly Rep*. 2008;57:1229-1232.
4. American Association for Respiratory Care. http://www.aarc.org/resources/confronting_copd/exesum.pdf. Accessed February 11, 2009.
5. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2008. http://www.goldcopd.com/Guidelineitem.asp?l1=2&l2=1&intId=989. Accessed November 21, 2008.

Top 5 Causes of Death: COPD on the Rise



Jemal A et al. *JAMA*. 2005;294:1255-1259.

Factors That May Influence COPD



Adapted from Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2008. http://www.goldcopd.com/Guidelineitem.asp?l1=2&l2=1&intId=989. Accessed November 21, 2008.

Spirometry Is Essential for Diagnosing COPD

If . . .

Chronic symptoms = cough, sputum, and/or shortness of breath

And . . .

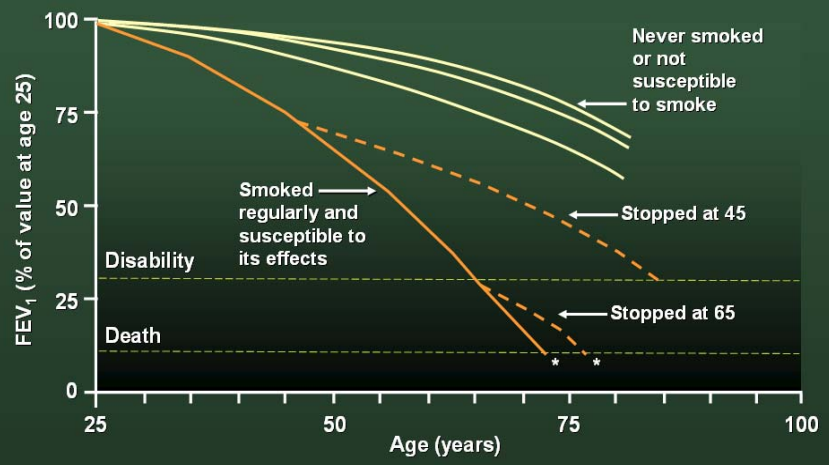
Exposure to risk factors = tobacco, occupational irritants, and/or indoor/outdoor pollution

Then . . .

Spirometry* to confirm COPD diagnosis
• $FEV_1/FVC < 0.70$ • FEV_1 determines staging

*Additional testing: chest x-ray, echocardiogram, arterial blood gas, sputum analysis, computed tomography (CT) scan.
Global Initiative for Chronic Obstructive Lung Disease. Global strategy for diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2008. http://www.goldcopd.com/Guidelineitem.asp?l1=2&l2=1&intId=989. Accessed November 21, 2008.

Smoking Cessation and Reduced Decline in FEV_1



*Death, the underlying cause of which is irreversible chronic obstructive lung disease, whether the immediate cause of death is respiratory failure, pneumonia, cor pulmonale, or aggravation of other heart disease by respiratory insufficiency. Although this shows rate of loss of FEV_1 for one particular susceptible smoker, other susceptible smokers will have different rates of loss, thus reaching "disability" at different ages.

Adapted with permission from Fletcher C et al. *Br Med J*. 1977;1:1645-1648.

Spirometry Is a Useful Tool to Assess COPD Severity and Progression

Stage	Severity	Post-bronchodilator FEV_1/FVC	FEV_1 % Predicted	Typical Symptoms
I	Mild	<0.70	≥80	Chronic cough and sputum production
II	Moderate	<0.70	50 to <80	Dyspnea + above
III	Severe	<0.70	30 to <50	Progressive dyspnea
IV	Very Severe	<0.70	<30	Respiratory failure, right heart failure, weight loss, arterial hypoxemia + above

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What Is Asthma? What Is COPD?

Asthma[1]	COPD[2]
• A **chronic inflammatory disorder** of the airways in which many cells and factors play a role • Inflammation results in – **Recurrent symptoms** – Variable **airflow obstruction** that is mostly **reversible** – Increase in existing **bronchial hyperresponsiveness**	• A **preventable and treatable** disease • Associated with significant **extrapulmonary effects** and important **comorbid conditions** • Characterized by airflow limitation that is – **Not fully reversible** – **Usually progressive** – Associated with an **abnormal inflammatory response** to noxious particles or gases

1. National Heart, Lung and Blood Institute. National Asthma Education and Prevention Program. http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf. Accessed August 29, 2007.
2. Global Initiative for Chronic Obstructive Lung Disease. http://www.goldcopd.org/Guidelineitem.asp?l1=2&l2=1&intId=989. Accessed November 21, 2008.

Differentiating COPD and Asthma

	Asthma	COPD
Onset[1]	Early in life (often childhood)	Mid-life
Triggers[1]	Allergens	Cigarette smoke, occupational pollutants
Symptoms[1]	Variable	Slowly progressive
Airflow limitation[1]	Largely reversible	Partially reversible
Clinical features[2,3]	Episodic wheeze, chest tightness, cough, dyspnea	Chronic dyspnea, cough, sputum, wheeze
Inflammatory cells[1]	Primarily eosinophils	Primarily neutrophils

1. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2008. http://www.goldcopd.com/Guidelineitem.asp?l1=2&l2=1&intId=989. Accessed November 21, 2008.
2. Currie GP, Legge JS. Chapter 3: Diagnosis. Blackwell BMJ Books. December 2006.
3. Dewar M, Curry RW. *Am Fam Physician*. 2006;73:669-676.

Comparing and Contrasting Asthma and COPD

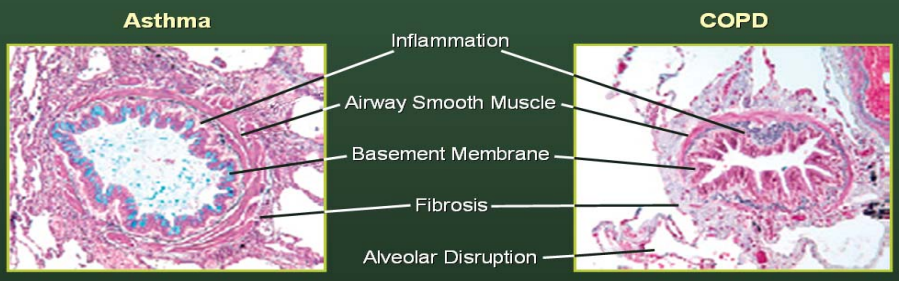
	Asthma[1]	COPD[2]
Airflow obstruction	Intermittent	Chronic
First-line monotherapy	ICS*	Long-acting bronchodilators†
Inflammatory cells	Eosinophils, mast cells, $CD4^+$ T lymphocytes	Neutrophils, macrophages, $CD8^+$ T lymphocytes
Lung pathophysiology	Epithelial cell injury, inflammation	Parenchymal tissue destruction (emphysema), small airway fibrosis

*In patients with persistent asthma.
†In patients with COPD of at least moderate severity.

1. National Heart, Lung and Blood Institute. National Asthma Education and Prevention Program. http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf. Accessed August 29, 2007.
2. Global Initiative for Chronic Obstructive Lung Disease. http://www.goldcopd.org/Guidelineitem.asp?l1=2&l2=1&intId=989. Accessed November 21, 2008.

Pathophysiological Changes in Asthma and COPD

Contrasting Histopathology of Asthma and COPD



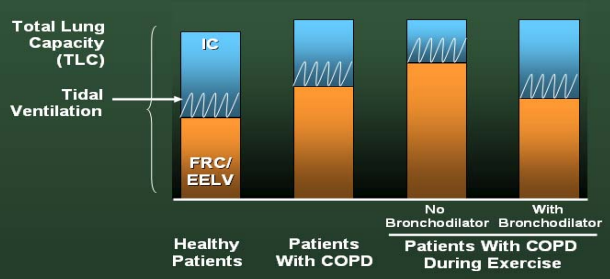
Adapted with permission from Barnes PJ. *Nature Rev Immunol*. 2008;8:183-192.

Physiologic Differences Between Asthma and COPD

	Asthma	COPD
Elastic recoil	Normal	Decreased
Diffusion capacity (DL_{CO})	Normal or Increased	Decreased
Lung volume	Normal	Hyperinflation
Bronchodilator response	Flow-dominant	Volume-dominant

Sciurba FC. *Chest*. 2004;126:117S-124S.

Hyperinflation Is a Hallmark of COPD[1-3]



- Increases FRC (EELV)
- Decreases IC
- Increases volume at which tidal breathing occurs
- Worsens with exercise and reduces exercise tolerance (dynamic hyperinflation)

IC = inspiratory capacity; FRC = functional residual capacity; EELV = end expiratory lung volume.
1. Adapted with permission from Sutherland ER et al. *N Engl J Med*. 2004;350:2689-2697.
2. ODonnell DE et al. *Am J Resp Crit Care Med*. 2001;164:770-777.
3. Stubbing DG et al. *J Appl Physiol*. 1980;49:511-515.

Spirometry Is Essential in Both Asthma and COPD

Asthma	COPD
• Necessary to establish a diagnosis[1]	• Essential for diagnosis[3]
• Low FEV_1 is strongly predictive of risk for exacerbations[1,2]	• Used to determine severity, which is linked to – Treatment decisions – Prognosis
• Important in assessing control[1]	

1. National Heart, Lung and Blood Institute. National Asthma Education and Prevention Program. http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf. Accessed August 29, 2007.
2. Fuhlbrigge AL et al. *J Allergy Clin Immunol.* 2001;107:61-67.
3. Global Initiative for Chronic Obstructive Lung Disease. http://www.goldcopd.org/Guidelineitem.asp?l1=2&l2=1&intId=989. Accessed November 21, 2008.

Goals of COPD Management

Short Term and Long Term	• Relieve symptoms • Minimize side effects • Improve exercise tolerance • Prevent and treat exacerbations and complications • Improve health status • Prevent disease progression • Reduce mortality

COPD management includes both pharmacologic and nonpharmacologic treatment.
Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2008. http://www.goldcopd.com/Guidelineitem.asp?l1=2&l2=1&intId=989. Accessed November 21, 2008.

Overview of COPD Pathophysiology

Cigarette Smoke | Susceptibility Genes | Gender | Proteinases/ Cell Mediators | Oxidative Stress | Environmental Irritants | Respiratory Infections

Exacerbations | Chronic Bronchitis | Emphysema | Systemic/ Extrapulmonary Effects | Mucociliary Dysfunction | Structural Changes

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Other Diagnoses That Can Have Similar Presentations

Diagnosis	Signs/Symptoms	Recommended testing
Congestive Heart Failure[1,2]	• Fine basilar crackles on auscultation	• Chest x-ray • Lung function testing • Echocardiogram
Bronchiectasis[1,3]	• Large volumes of purulent sputum • Commonly associated with bacterial infection • Coarse crackles/clubbing on auscultation	• CT scan • Lung function testing
Cystic fibrosis[2,4]	• Onset at any age	• Chest x-ray • Sweat test • Genetic testing
Obliterative Bronchiolitis[1,2]	• Onset in younger age, nonsmokers • May have history of rheumatoid arthritis or fume exposure	• CT scan
Diffuse Panbronchiolitis[1]	• Most patients are male and nonsmokers • Almost all have chronic sinusitis	• Chest X-ray • High resolution CT scan

CT = computed tomography.

1. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2008. http://www.goldcopd.com/Guidelineitem.asp?l1=2&l2=1&intId=989. Accessed November 21, 2008.
2. Dewar M, Curry RW. *Am Fam Physician*. 2006;73:669-676.
3. National Heart, Lung and Blood Institute. *Bronchiectasis*. http://www.nhlbi.nih.gov/health/dci/Diseases/brn/brn-diagnosis.html. Accessed January 27, 2009.
4. National Heart, Lung and Blood Institute. *Cystic fibrosis*. http://www.nhlbi.nih.gov/health/dci/Diseases/cf/cf-diagnosis.html. Accessed January 29, 2009.

Diagnostic Testing Considerations

- Spirometry
- Chest x-ray
- Echocardiogram
- CT scan

When to refer to a specialist?

Nonpharmacologic Therapy to Manage COPD

Smoking Cessation

Patient Education

Vaccination

Pulmonary Rehabilitation

Oxygen Therapy

Surgical and Non-surgical Alternatives

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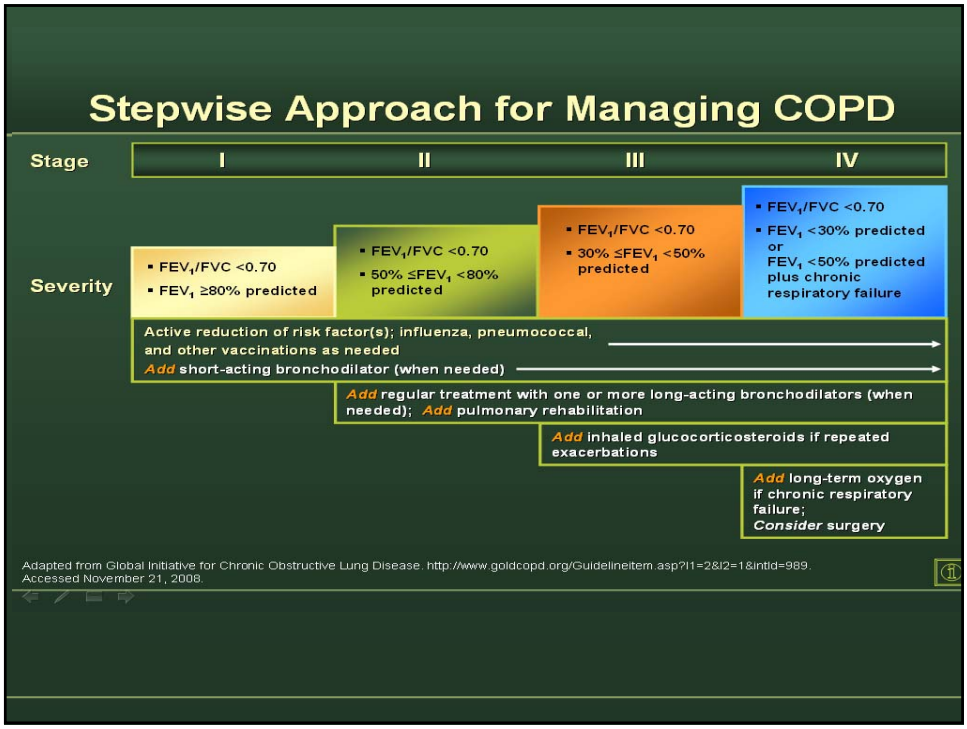

Assessing Asthma Control and Adjusting Therapy in Youths ≥12 Years of Age and Adults

Components of Control		Well Controlled	Not Well Controlled	Very Poorly Controlled
Impairment	Symptoms	≤2 days/week	>2 days/week	Throughout the day
	Nighttime awakenings	≤2x/month	1-3x/week	≥4x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	SABA use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week	Several times per day
	FEV_1 or peak flow	>80% predicted/ personal best	60%-80% predicted/ personal best	<60% predicted/ personal best
	Validated questionnaires ATAQ ACQ ACT	 0 ≤0.75 ≥20	 1-2 ≥1.5 16-19	 3-4 N/A ≤15
Risk	**Exacerbations requiring oral systemic corticosteroids**	**0-1/year**	**≥2/year**	
		Consider severity and interval since last exacerbation		
	Progressive loss of lung function	Evaluation requires long-term follow-up		
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk		
Recommended Action for Treatment		• Maintain current step • Regular follow-ups every 1-6 months to maintain control • Consider step down if well controlled for at least 3 months	• Step up 1 step and • Reevaluate in 2 to 6 weeks • For side effects, consider alternative treatment options	• Consider short course of oral systemic corticosteroids • Step up 1-2 steps, and • Reevaluate in 2 weeks • For side effects, consider alternative treatment options

Adapted from National Heart, Lung and Blood Institute. National Asthma Education and Prevention Program. http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf. Accessed August 29, 2007.

Classifying Asthma Severity and Initiating Treatment in Youths ≥12 Years of Age and Adults

Components of Severity		Intermittent	Persistent		
			Mild	Moderate	Severe
Impairment Normal FEV_1/FVC: 8-19 yr 85% 20-39 yr 80% 40-59 yr 75% 60-80 yr 70%	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3-4x/month	>1x/week but not nightly	Often 7x/week
	SABA use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily and not more than 1x on any day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung Function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 >60% but <80% predicted • FEV_1/FVC reduced 5%	• FEV_1 <60% predicted • FEV_1/FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0-1/year	≥2/year		
		Consider severity and interval since last exacerbation Frequency and severity may fluctuate over time for patients in any severity category			
		Relative annual risk of exacerbations may be related to FEV_1			
Recommended Step for Initiating Treatment		Step 1	Step 2	Step 3	Step 4 or 5
				and consider short course of oral systemic corticosteroids	
		In 2 to 6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly			

EIB = exercise-induced bronchospasm; FEV_1 = forced expiratory volume in one second; FVC = forced vital capacity.
Adapted from National Heart, Lung and Blood Institute. National Asthma Education and Prevention Program. http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf. Accessed August 29, 2007.

Stepwise Approach for Managing Asthma in Patients Aged ≥12 Years

Intermittent Asthma

Persistent Asthma: Daily Medication
Consult with asthma specialist if Step 4 care or higher is required.
Consider consultation at Step 3.

Step 1	Step 2	Step 3	Step 4	Step 5	Step 6
Preferred: SABA PRN	***Preferred:*** Low-dose ICS (A) ***Alternative:*** Cromolyn (A), LTRA (A), Nedocromil (A), or Theophylline (B)	***Preferred:*** Low-dose ICS + LABA (A) OR Medium-dose ICS (A) ***Alternative:*** Low-dose ICS + either LTRA (A), Theophylline (B), or Zileuton (D)	***Preferred:*** Medium-dose ICS + LABA (B) ***Alternative:*** Medium-dose ICS + **either** LTRA (B), Theophylline (B), or Zileuton (D)	***Preferred:*** High-dose ICS + LABA (B) AND Consider Omalizumab for Patients Who Have Allergies (B)	***Preferred:*** High-dose ICS + LABA + Oral Corticosteroid AND Consider Omalizumab for Patients Who Have Allergies

Step Up If Needed
(first, check adherence, environmental control, and comorbid conditions)

Assess Control

Step Down If Possible
(and asthma is well controlled at least 3 months)

Each Step: Patient education, environmental control, and management of comorbidities
Steps 2-4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma

Quick-Relief Medication for All Patients
- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of systemic oral corticosteroids may be needed
- Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment

ICS = inhaled corticosteroids; LABA = long-acting β_2-agonist; LTRA = leukotriene receptor antagonist.
Adapted from National Heart, Lung and Blood Institute. National Asthma Education and Prevention Program. http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf. Accessed August 29, 2007.

Key Principles of Pharmacological Therapy for Asthma and COPD

Asthma[1]	COPD[2]
Step therapy up/down based on assessment of asthma control	Treatment is cumulative, with medications added as the disease progresses
Inhaled corticosteroids are recommended therapy in the long-term control of asthma due to their anti-inflammatory effects	Bronchodilators are central to symptom management in COPD
LABAs are contraindicated as monotherapy	ICS monotherapy not recommended
LABAs are used in combination with ICS for long-term control and symptom prevention	ICS used in combination with LABAs can improve lung function and health status

ational Heart, Lung and Blood Institute. National Asthma Education and Prevention Program. http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf. ccessed August 29, 2007.
lobal Initiative for Chronic Obstructive Lung Disease. http://www.goldcopd.org/Guidelineitem.asp?l1=2&l2=1&intId=989. Accessed November 21, 2008.