Chronic Obstructive Pulmonary Disease: Improving Control of Symptoms and Optimizing Patient Outcomes

A application-based CPE activity presented during the
2013 ICHP Annual Meeting (50th Anniversary)

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Chronic Obstructive Pulmonary Disease:
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ACTIVITY FACULTY

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Dr. Williams earned his Bachelor of Science in pharmacy and Doctor of Pharmacy degrees at the University of Kentucky in Lexington. He is a board-certified pharmacotherapy specialist, as well as a certified asthma educator. He has received fellow recognition from the American Society of Health-System Pharmacists, American College of Clinical Pharmacy, and American Pharmacists Association.

Dr. Williams focuses his practice, teaching, and research on the management of patients with pulmonary and infectious diseases. He is a member of the National Asthma Education and Prevention Program Coordinating Committee of the National Heart, Lung, and Blood Institute and several other boards. He currently serves as Treasurer of the North Carolina Pharmacists Association.

Dr. Williams has published research papers and book chapters in the area of pulmonary diseases and infectious diseases, and he regularly speaks on these topics at national and international professional programs. He has trained hundreds of pharmacists and students about pulmonary and immunization sciences, as well as practice considerations related to these topics.

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Chronic Obstructive Pulmonary Disease: Improving Control of Symptoms and Optimizing Patient Outcomes

ACTIVITY OVERVIEW

This activity will provide an overview of the incidence, clinical course, morbidity, and mortality associated with chronic obstructive pulmonary disease (COPD). Because there is no cure for COPD, strategies that control symptoms and prevent disease progression are important. In addition, minimizing exacerbations is a major goal of treatment. The role of pharmacists in managing patients with COPD will be described, including the use of emerging treatment options.

Patient scenarios will be included throughout the presentation, and there will be time for questions and answers at the end.

LEARNING OBJECTIVES

At the conclusion of this application-based CPE activity, attendees should be able to

- Outline the incidence, mortality, and morbidity of chronic obstructive pulmonary disease (COPD) in the United States.
- Apply current evidence-based guidelines for managing patients with COPD in order to meet management goals.
- Examine emerging treatment options for the management of COPD.
- Incorporate at least one strategy for improving outcomes for patients with COPD into practice.

CONTINUING EDUCATION ACCREDITATION

The American Society of Health-System Pharmacists is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This activity provides 1 hour (0.1 CEU) of continuing pharmacy education credit (ACPE activity # 0204-0000-13-448-L01-P).

Attendees must complete a Continuing Pharmacy Education Request online and may print their official ASHP statements of continuing pharmacy education credit at the ASHP eLearning site (elearning.ashp.org) immediately following this activity.

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Instructions for Processing CE Credit with Enrollment Code

Pharmacists and Technicians: All ACPE accredited activities which are processed on the eLearning site will be reported directly to CPE Monitor. To claim pharmacy credit, you must have your NABP e-Profile ID, birth month, and birth day. If you do not have an NABP e-Profile ID, go to www.MyCPEMonitor.net for information and application. Please follow the instructions below to process your CPE credit for this activity.

1. The **ASHP eLearning** site allows participants to obtain statements of continuing education credit conveniently and immediately using any computer with an internet connection. Type the following link into your web browser to access the e-Learning site: **http://elearning.ashp.org/my-activities**
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   Note: The Enrollment Code was announced at the end of the live activity.
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Date of Activity	Activity Title	Enrollment Code	Credit Hours
September 20, 2013	Chronic Obstructive Pulmonary Disease: Improving Control of Symptoms and Optimizing Patient Outcomes	_ _ _ _ _	1.0

NEED HELP? Contact **eLearning@ashp.org.**

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  - Susan R. Dombrowski, M.S., B.S.Pharm. (reviewer)

Objectives

- Describe the incidence, mortality, and morbidity of chronic obstructive pulmonary disease (COPD) in the United States
- Apply current evidence-based guidelines for managing patients with COPD
- Examine emerging treatment options for the management of COPD
- Outline a plan for involving pharmacists in the management of patients with COPD

Ray—The Case Study

- Ray is a 63 year-old male known to have COPD who visits his clinician because he feels that his albuterol inhaler is not working well
- The patient was diagnosed with COPD five years ago attributed to a 48 pack year smoking history (Continues to smoke about ¾ PPD)
- Patient is s/p MI three years ago and treated with metoprolol, lisinopril, and furosemide

Ray—The Case Study

- Over the past few months, Ray has noticed decreased exercise tolerance
- He gets SOB easily and feels that his albuterol is not working as well as it has in the past. He uses it PRN and has often required it two or three times daily
- He has not been hospitalized or in the ED because of his COPD
- His physical exam is relatively unremarkable and his chest x-ray shows some scarring consistent with his tobacco history
- Pulse oximetry is 91% and spirometry reveals:
  - FEV_1 is 2.4 L (75% predicted); FVC is 3.49 L (85% predicted) with a ratio of 69%

What is the most important thing that Ray can do now to minimize disease progression?

a. Start an inhaled steroid
b. Start a long-acting anticholinergic agent
c. Initiate chronic supplemental oxygen therapy
d. Stop smoking
e. Each of the above

Chronic Obstructive Pulmonary Disease

"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."

2013 GOLD Guidelines. www.goldcopd.org

Chronic Obstructive Pulmonary Diseases

- Chronic respiratory diseases (primarily COPD) are the 3rd leading cause of death in the U.S.
- Affects 15 million Americans (6.3% of population), with women (6.7%) reporting higher prevalence than men (5.2%)
- Prevalence in smokers is higher (13.3%) compared with former smokers (6.8%) or never smokers (2.8%)
- Approximately 20% of diagnosed patients have not undergone spirometry and 63% with poor lung function by spirometry are not diagnosed with COPD

CDC. *MMWR Morb Mortal Wkly Rep.* 2012; 61(46):938-43.

Among the top 5 leading causes of death, only COPD reflects an increasing rate.

Jemal A et al. *JAMA.* 2005; 294:1255-9.

Risk Factors for COPD

- **Tobacco Smoke**
- **Everything else (other occupational and environmental gases)**

Inflammation in COPD

Protease-Antiprotease Imbalance in COPD

Consequences of Chronic Inflammation in COPD

Decramer M. *Eur Respir Rev.* 2006; 15:51-7.

Global Initiative for Chronic Obstructive Pulmonary Disease

- Available at www.goldcopd.com

- First version published in 2001
- Most recent update: February 2013

COPD: Key Indicators

- Patient symptoms (DOE, chronic cough, chronic sputum production)
- History of exposure to risk factors (tobacco smoke, smoke from home cooking or heating, occupational dusts or chemicals)
- Scores on self-assessment scales (MMRC, CAT™)
- Spirometry grade (1, 2, 3, 4)
- Physical exam (lung exam, CV exam)
- Chest X-ray (low, flat diaphragms)
- Arterial blood gas (respiratory failure)

Spirometry is essential for diagnosis and grading of COPD and monitoring progression

Post-bronchodilator FEV_1 is recommended for the diagnosis and assessment of COPD

American Thoracic Society, European Respiratory Society. Standards for the diagnosis and management of patients with COPD. 2004 (URL in reference list).
Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of COPD. Updated 2013 (URL in reference list.

Combined Assessment of COPD

- Three components determine severity
  - Spirometry to assess degree of airflow limitation
  - Symptoms assessment (various tools)
  - Risk for exacerbations

COPD Classification
(2013 GOLD Guidelines)

MMRC = Modified Medical Research Council Dyspnea Scale
CAT™ = COPD Assessment Test™

MMRC Questionnaire: Breathlessness Self-Assessment

Severity	Score	Level of Breathlessness
None	0	Only breathlessness with strenuous exercise
Mild	1	Short of breath hurrying or walking up a slight hill
Moderate	2	Walks slower than age group or has to stop for breath when walking on the level at own pace
Severe	3	Stops for breath after walking 100 meters or a few minutes on the level
Very Severe	4	Breathless when dressing/undressing or too breathless to leave the house

MMRC patient questionnaire available at http://copd.about.com

COPD Assessment Test™ (CAT)*

- Eight questions; 5-point scale
- (0 = least severe; 5 = most severe)
  - Cough
  - Phlegm (mucus)
  - Chest tightness
  - Breathless walking up a hill or one flight of stairs
  - Activity limitations
  - Confident to leave home
  - Sleep
  - Energy
- Assessment
  - Minimum score: 0
  - Maximum score: 40

* This assessment tool is a trademark of the GlaxoSmithKline group of companies.

COPD Classification
(2013 GOLD Guidelines)

Treatment Goals: Stable COPD

Reduce Symptoms

- Relieve symptoms
- Improve exercise tolerance
- Improve overall health status

Reduce Risks

- Prevent disease progression
- Prevent and treat exacerbations
- Reduce mortality
- Prevent and treat complications
- Minimize side effects

2013 GOLD Guidelines. www.goldcopd.org

COPD Management: Areas Where Strong Evidence of Benefit Exists

- Smoking cessation advice, including the use of pharmacotherapies to assist cessation attempts
- Immunization against influenza and pneumococcus according to the ACIP recommendations
- Pulmonary rehabilitation for patients with moderate to severe disease
- Supplemental oxygen therapy for patients with oxygen saturation < 88%

Enlarged version of slide on page 15.

Pharmacotherapy Recommendations for COPD

Patient Group (Classification)	Recommended 1st Choices	Alternative Choices	Other Options
A	• Short-acting anticholinergic PRN • Short-acting β_2 agonist PRN	• Long-acting anticholinergic • Long-acting β_2 agonist • Short-acting β_2 agonist and short-acting anticholinergic in combo	• Theophylline
B	• Long-acting anticholinergic • Long-acting β_2 agonist	• Long-acting anticholinergic plus Long-acting β_2 agonist	• Short-acting anticholinergic PRN • Short-acting β_2 agonist PRN • Combo of two above • Theophylline
C	• Inhaled corticosteroid plus long-acting β_2 agonist • Long-acting anticholinergic	• Long-acting anticholinergic plus Long-acting β_2 agonist • Either of the above agents with phosphodiesterase-4 inhibitor	• Short-acting anticholinergic PRN • Short-acting β_2 agonist PRN • Combo of two above • Theophylline
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New Options for COPD

- Aclidinium bromide (Tudorza Pressair)
  - Long-acting anticholinergic* (inhaled) twice daily
- Albuterol and ipratropium (Combivent)
  - Respimat delivery device (inhaled) four times daily)
- Fluticasone furoate/vilanterol (Breo Ellipta)
  - ICS/LABA combo (inhaled) once daily
- Indacaterol maleate (Arcapta Neohaler)
  - LABA (inhaled) once daily
- Roflumilast (Daliresp)
  - PDE-4 inhibitor (oral) once daily

ICS = inhaled corticosteroid
LABA = long-acting β_2 agonist
PDE = phosphodiesterase

*Also called long-acting antimuscarinic agent (LAMA)

Remember Ray? In addition to smoking cessation, what would you recommend next for his therapy?

a. He should be started on tiotropium.
b. Ipratropium should be added through the use of combo inhaler (albuterol/ipratropium) that can be scheduled.
c. He should be started on salmeterol.
d. He should be started on an inhaled corticosteroid.

How does symptom relief occur in a condition that is largely fixed or only partly reversible?

- Changes in chest 'dynamics'
- Reduction in dyspnea, "the most troublesome symptom"
- Defines central role of bronchodilators

Static and Dynamic Lung Volumes in COPD

O'Donnell DE. *Chest*. 2000; 117:42S-7S.

First-line Pharmacotherapy

- Current pharmacotherapy does not affect the natural course of COPD
- Although other options may be appropriate, Ray's symptoms can be managed with
  - Combination inhaler (albuterol + ipratropium) scheduled plus PRN

What other factors should be considered before making changes to Ray's pharmacotherapy regimen?

- Adherence
- Inhaler technique
- Avoidance of triggers for his symptoms
- Impact of comorbidities

- Also, administer influenza vaccine annually and pneumococcal vaccine once now

Common Comorbidities that Perturb COPD Control

- Cardiovascular disease, including CHF
- Diabetes mellitus
- Arthritis disorders
- Declining cognitive function

Ray—The Case Study 9 months later

- Ray has been using a combination inhaler with albuterol and ipratropium. He reports using it 3 times a day regularly now, and often two additional times for SOB.
- It lasts for a short while, but he feels he is getting worse.
- He continues to smoke, but has reduced to ½ PPD.
- He has not experienced an exacerbation.
- Spirometry reveals an FEV_1 of 70%.

In addition to smoking cessation, what would you recommend for Ray now?

a. Continue current therapy; it seems to be working
b. Add a long-acting bronchodilator
c. Initiate an inhaled corticosteroid
d. Consider roflumilast

Long-acting Bronchodilators: β_2 Agonists and Anticholinergics

- For patients with chronic symptoms and/or frequent use of short-acting bronchodilators, these agents
  - Are more effective at relieving symptoms and improving lung function
  - Are more convenient to use
  - Reduce exacerbation frequency

Pharmacotherapy Recommendations for COPD

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Choosing a Long-acting Bronchodilator

- Expert guidelines do not favor one class over the other
- Long-acting β_2 agonists
  - Salmeterol, formoterol, arformoterol, indacaterol
- Long-acting anticholinergic agents
  - Tiotropium, aclidinium

What side effects and risks are associated with long-acting bronchodilator use?

- Both classes are generally well tolerated, but possible safety concerns
- Long-acting β_2 agonists
  - Cardiac arrhythmias (including death), tachycardia, tremor, hypokalemia, hyperglycemia, sleep disturbances
- Long-acting anticholinergics
  - Dry mouth, taste disturbances, constipation, gastroesophageal reflux, urinary retention, blurred vision, stroke risk(?)

Cardiovascular Safety of Long-acting Bronchodilators in COPD

- Compared risk of newly prescribed long-acting anticholinergics and long-acting β_2 agonists
- Nested case-control analysis of retrospective cohort (using Canadian health care database)
- 191,005 eligible patients, aged 66 and older
- 28% experienced hospitalization or ED visit for CV event

Gershon A et al. *JAMA Intern Med*. 2013 May 20:1-9. [Epub ahead of print]

Risk of Hospitalization or ED Visit Based on Therapy

Gershon A et al. *JAMA Intern Med*. 2013 May 20:1-9. [Epub ahead of print]

Long-acting Bronchodilators in COPD

- No mortality benefit established
- No effect on natural decline in spirometry
- Good benefit in reducing symptoms
- Greatest benefit is reduction in exacerbations
- One class not clearly superior to the other

Significant Issues in COPD Pharmacotherapy

- Which long-acting bronchodilator should be used first?
- Are combinations of long-acting bronchodilators beneficial and cost effective?
- When should inhaled corticosteroids be introduced into the regimen?

Ray—The Case Study Two Years Later

- Ray is now receiving tiotropium and salmeterol inhalers that he uses on a regular schedule plus PRN albuterol that he uses 1 to 2 times daily.
- Over the past 15 months, he has experienced 3 exacerbations each treated with prednisone and antibiotics.
- For one, he was hospitalized for 4 days.
- He stopped smoking 2 months ago and is doing well with this quit attempt.

What would you recommend for Ray now?

a. Continue current regimen; it seems to be working
b. Add an inhaled corticosteroid
c. Start roflumilast
d. Start azithromycin

COPD Classification (2013 GOLD Guidelines)

Pharmacotherapy Recommendations for COPD

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ICS (Combo) Options for COPD

- Budesonide/formoterol (Symbicort)
  - Twice daily
- Fluticasone furoate/vilanterol (Breo Ellipta)
  - Once daily
- Fluticasone propionate/salmeterol (Advair)
  - Twice daily
- Mometasone/formoterol (Dulera)
  - Twice daily

What about reducing exacerbations?

- How important is that?
- Which therapies have an impact?
- What is the extent of reduction?
- Is there a benefit from combinations?
- Are there other therapies that may be useful here?

Acute Exacerbation of COPD

- "An acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variation and leads to a change in medication."
- May be treated as outpatient or in hospital depending on severity

2013 GOLD Guidelines. www.goldcopd.org

Treating COPD Exacerbations

- Standard therapies include (~ 1 to 2 weeks of)
  - Intensification of short-acting bronchodilator therapy
  - Systemic corticosteroids
  - Antibiotics
  - Short-term use of supplemental oxygen
- The recent 'REDUCE' trial demonstrated that 5 days of oral corticosteroids was non-inferior to 14 days and reduced overall exposure to steroids

Leuppi JD et al. *JAMA*. 2013 May 21:1-9. [Epub ahead of print]

COPD

- Reducing exacerbation frequency and severity is a major goal of chronic treatment

Mortality Following COPD Exacerbations

Anzueto A. *Eur Respir Rev.* 2010; 19:113-8.

Exacerbations

- Long-acting β_2 agonists and long-acting anticholinergics reduce exacerbation frequency
- ICSs reduce exacerbation frequency
- Emerging therapies (PDE-4 inhibitors) reduce exacerbation frequency
- Azithromycin reduces exacerbation frequency
- Benefit of combinations in reducing exacerbation frequency is unclear

Efficacy of Various Chronic COPD Therapies in Reducing the Risk for Exacerbations

Treatments	OR vs. Placebo	OR vs. Long-acting β_2 agonists	OR vs. Long-acting Anticholinergics	OR vs. Inhaled Corticosteroids
Long-acting β_2 agonists	0.77 (0.71-0.84)			
Long-acting anticholinergics	0.71 (0.64-0.78)	0.91 (0.81-1.03)		
Inhaled corticosteroids	0.78 (0.70-0.86)	1.00 (0.90-1.13)	1.10 (0.97-1.23)	
Long-acting β_2 agonists + inhaled corticosteroids	0.72 (0.65-0.80)	0.93 (0.84-1.04)	1.02 (0.90-1.16)	0.93 (0.82-1.05)

Puhan MA et al. *BMC Med.* 2009; 7:2.

Reducing Exacerbations

- Exacerbations hasten disease progression
- Reducing exacerbation frequency is an appropriate goal of therapy
- Long-acting bronchodilators and inhaled corticosteroids reduce frequency by ~ 20-25%
- Roflumilast and azithromycin have also been used to reduce exacerbations
- Selection of therapy is patient specific and based on clinician experience

Pharmacotherapy Recommendations for COPD

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Summary for COPD Management

- Renewed interest and greater optimism exists for managing COPD
- Pharmacotherapy can control symptoms and reduce exacerbations
- Numerous options available; optimal combinations are not clear
- Opportunities exist at all stages of COPD to assist and advise patients

Potential Roles for Pharmacists in Assisting Patients with COPD

- Advising and assisting about tobacco cessation
- Recommending and administering vaccine
- Monitoring and educating to improve adherence
- Ensuring optimal pharmacotherapy to meet goals
- Providing medication therapy management services
- Performing spirometry testing

American Pharmacists Association Foundation. *J Am Pharm Assoc*. 2011; 51:203-11.
Cawley MJ et al. *J Am Pharm Assoc*. 2013; 53:307-15.

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B	• Long-acting anticholinergic • Long-acting β_2 agonist	• Long-acting anticholinergic plus Long-acting β_2 agonist	• Short-acting anticholinergic PRN • Short-acting β_2 agonist PRN • Combo of two above • Theophylline
C	• Inhaled corticosteroid plus long-acting β_2 agonist • Long-acting anticholinergic	• Long-acting anticholinergic plus Long-acting β_2 agonist • Either of the above agents with phosphodiesterase-4 inhibitor	• Short-acting anticholinergic PRN • Short-acting β_2 agonist PRN • Combo of two above • Theophylline
D	• Inhaled corticosteroid plus long-acting β_2 agonist • Long-acting anticholinergic • Combo of both above	• Inhaled corticosteroid plus long-acting β_2 agonist and long-acting anticholinergic • Inhaled corticosteroid plus long-acting β_2 agonist and phosphodiesterase-4 inhibitor • Long-acting anticholinergic and long-acting β_2 agonist • Long-acting anticholinergic plus phosphodiesterase-4 inhibitor	• Short-acting β_2 agonist • Short-acting anticholinergic • Combo of two above • Carbocysteine • Theophylline

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SELF–ASSESSMENT QUESTIONS

1. The prevalence of chronic respiratory diseases in the United States is

   a. Higher in women than in men.
   b. Lower in women than in men.
   c. About the same for men and women.

2. A 56-year-old woman who recently relocated visits the internal medicine clinic to get established as a new patient. She is a smoker and has used an albuterol inhaler as needed for two years but has not been diagnosed with chronic obstructive pulmonary disease (COPD). Her use of the inhaler has increased recently, sometimes up to three times a day. The clinician suspects COPD. According to the GOLD guidelines, how should the clinician use spirometry to diagnose and manage this patient's pulmonary disease?

   a. Conduct spirometry testing at this visit to determine the patient's grade of COPD, which is based on the post-bronchodilator forced expiratory volume in one second (FEV_1).
   b. Conduct spirometry testing to determine the patient's stage of COPD, which is based on the pre-bronchodilator FEV_1.
   c. Conduct spirometry testing to determine the patient's grade of COPD, which is based on the post-bronchodilator forced vital capacity (FVC).
   d. Skip spirometry testing since the patient is not in acute distress.

3. Which of the following would be the primary strategy for helping this patient minimize disease progression?

   a. Prescribe an inhaled steroid.
   b. Prescribe a long-acting anticholinergic agent.
   c. Provide smoking cessation assistance.
   d. Demonstrate proper inhaler technique.

4. A 67-year-old man with long-standing COPD is treated with a combination inhaler (inhaled corticosteroid plus long-acting β_2 agonist) and a long-acting inhaled anticholinergic. Despite this therapy, he has been treated for COPD exacerbations in the emergency department twice in the past 8 months. Which of the following therapies is most appropriate to consider for his chronic regimen?

   a. Initiate daily prednisone therapy.
   b. Double the dose of the long-acting β_2 agonist in his current regimen.
   c. Add roflumilast to his current regimen.
   d. Add montelukast to his current regimen.

Answers

1. a
2. a
3. c
4. c