Care of the Hospitalized Patient with Acute Exacerbation of COPD

COPD Guideline Team

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Patient population: Adult, non-critically-ill hospitalized patients with acute exacerbation of COPD (AECOPD).

Objectives: To provide an evidence-based blueprint for the acute care of patients with AECOPD, in order to standardize and improve the quality of care for these patients.

Key points

Definitions. AECOPD can be defined as an acute event characterized by a worsening of the patient's respiratory symptoms (e.g., worsening dyspnea, worsening cough, and/or changes in the character or amount of sputum) that is beyond normal day-to-day variations, and leads to a change in medication.

Diagnosis (Figure 1)

- The diagnosis of AECOPD is usually made by a clinical assessment that combines historical features, identification of triggers of worsening disease, physical exam findings and ruling out other conditions with similar clinical presentations.
- Testing should include a CBC, a CXR, influenza nasal swab (seasonal), and an ECG in most patients. Additional testing is indicated when an alternate condition is suspected *[I, D]*.

Assessment of Severity and Intensity of Care. The early evaluation for patients with COPD should identify patients that will require hospitalization, ventilatory support, or ICU admission (**Figure 1**) *[I, D]*.

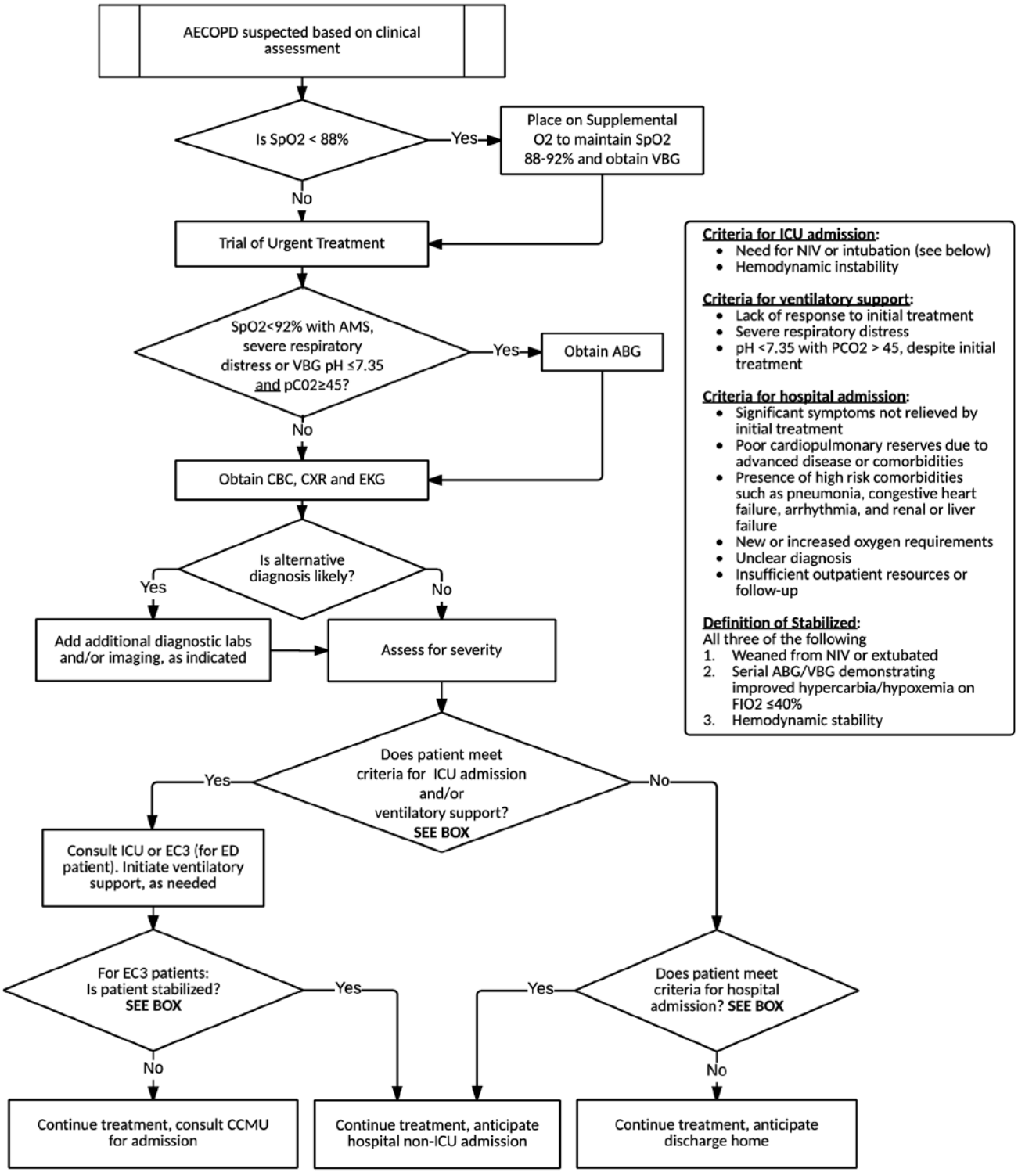
Treatment

- Inhaled bronchodilators
  - Patients hospitalized with AECOPD should be treated with inhaled albuterol and/or ipratropium, with dose and frequency titrated to effect (**Table 3**) *[I, C]*.
  - Metered-dose inhalers (MDI's), with spacer devices, are the preferred delivery method for short-acting bronchodilators, unless the patient's condition or preference warrants the use of a nebulizer.
- Corticosteroids
  - Most patients who are hospitalized with an exacerbation of COPD should be treated with systemic corticosteroids, unless side-effects are limiting *[I, A]*.
  - A dose of prednisone, 40 mg orally daily, for a 5-day course, is appropriate for most patients, and a dose taper is unnecessary (**Table 3**) *[I, A]*.
- Antibiotics
  - Most patients who are hospitalized with AECOPD should be treated with antibiotics (**Tables 3 and 4, and Figure 2**) *[II, A]*.
- A 5-day duration of antibiotics is likely adequate for inpatients that demonstrate rapid improvement *[II, D]*. Longer courses (7-10 days) may be considered for patients with severe illness or those who are slow to respond to treatment.
- Supportive care
  - Acute oxygen therapy. Oxygen should be provided to treat hypoxemia to a pulse-ox target of 88-92% *[II, D]*.
  - Non-invasive positive pressure ventilatory support (NIPPV).
    - NIPPV in the form of BiPAP (or CPAP) should be initiated in patients with AECOPD who have persistent or worsening respiratory distress, hypoxemia, or respiratory acidosis despite medical therapy (**Figure 1**) *[I, A]*.
    - NIPPV should be initiated early in AECOPD *[I, A]*.
    - Predictors for success and contraindications should be highlighted when considering the use of NIPPV (**Table 5**) *[I, D]*.
    - Patients who are started on NIPPV should be monitored closely, and the decision whether or not to intubate should be made within 2 hours of starting NIPPV *[I, D]*.
- Preventative care in the hospital should include smoking cessation interventions *[I, A]*, appropriate vaccinations *[II, A]*, and venous thromboembolism prevention *[I, A]*.
- A comprehensive approach to discharge is recommended (I, D)
  - Key elements of the hospital discharge are summarized in **Table 6**.

*** Strength of recommendation:**
I = generally should be performed; II = may be reasonable to perform; III = generally should not be performed.

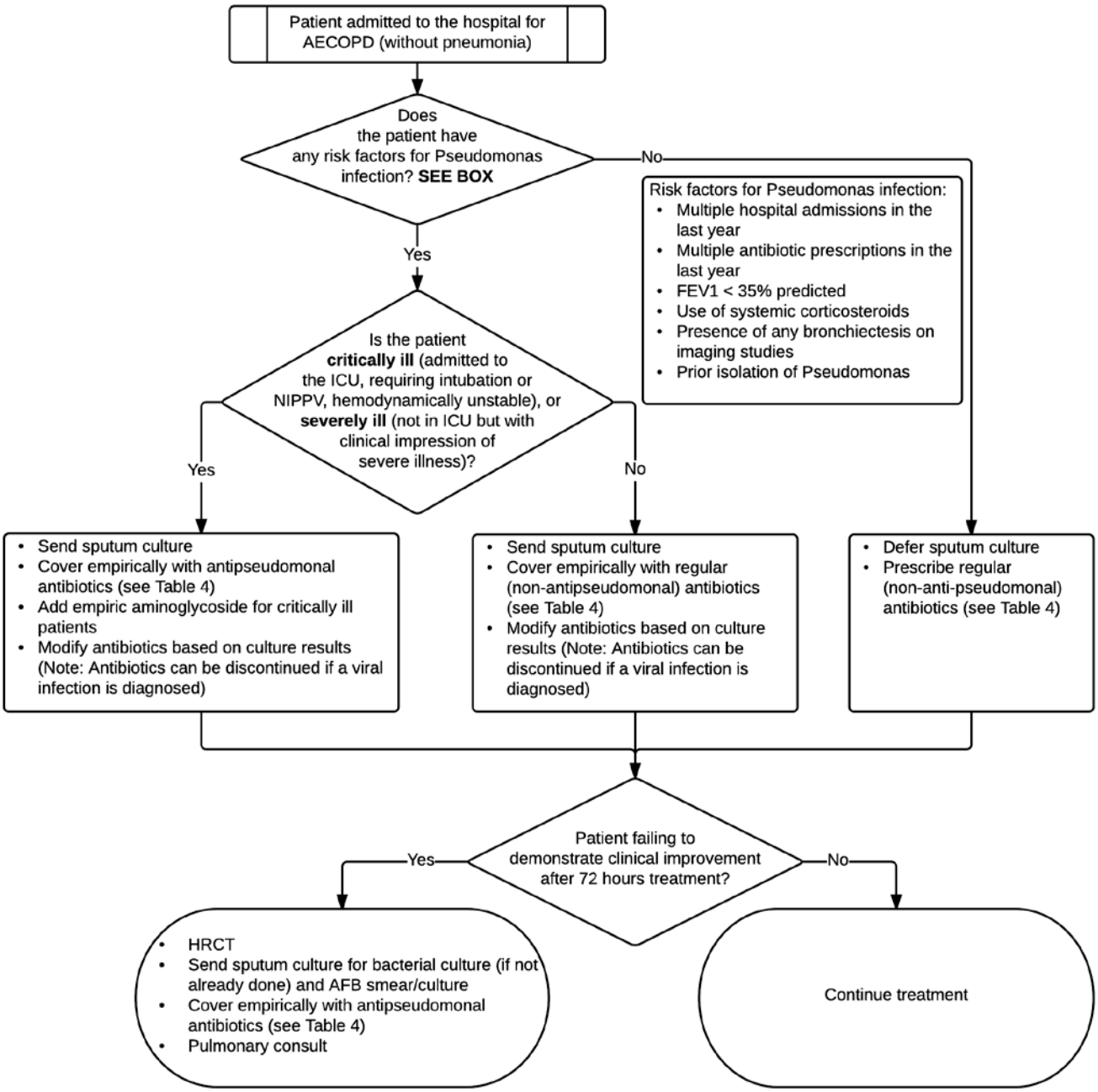
Level of evidence supporting a diagnostic method or an intervention:
A= systematic reviews of randomized controlled trials, B= randomized controlled trials, C=systematic review of non-randomized controlled trials or observational studies, non-randomized controlled trials, group observation studies (e.g., cohort, cross-sectional, case control), D= individual observation studies (case or case series), E =opinion of expert panel.

Figure 1. Diagnostic Algorithm and Assessment of Severity[3,14]



AMS= altered mental status, ABG = arterial blood gas, EC3 = Emergency Critical Care Center, CCMU = Critical Care Medical Unit, NIV = Non-invasive ventilation, VBG = venous blood gas

Figure 2. An Approach to Antibiotic Choice and Use of Sputum Culture for Hospitalized Patients with AECOPD*



*This algorithm represents a logical approach, but there is no strong evidence to guide decisions about when to use sputum cultures or empiric antipseudomonal antibiotics.

AFB= acid-fast bacilli, FEV1= forced expiratory volume measure, HRCT = high resolution computed tomography, NIPPV= non-invasive positive pressure ventilation.

Table 1. Factors Determining COPD Disease Severity

Diagnosis of COPD – Chronic Airflow Obstruction (spirometry)

Airflow obstruction post-bronchodilator (not fully reversible) of FEV1/FVC <0.70

Extent of Airflow Limitation (spirometry)[2]

Limitation	FEV1 % predicted	Symptoms
Mild	≥80%	Individual may or may not be aware lung function is abnormal.
Moderate	50-79%	Patients typically seek medical attention at this stage due to respiratory symptoms or an exacerbation.
Severe	30-49%	Dyspnea, reduced exercise capacity, and repeated exacerbations impact quality of life.
Very severe	<30%	Quality of life significantly impaired; exacerbations may be life-threatening.

Symptom Severity

Either dyspnea symptoms (mMRC) or symptom impact (CAT) can be used

mMRC (Modified Medical Research Council) Dyspnea Scale[3]

Score equivalent to point value for highest level question to which respondent answers "Yes."

Dyspnea Query	Score
Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?	0
Do you have to walk slower than people of your age on level ground because of shortness of breath?	1
Do you ever have to stop for breath when walking at your own pace on level ground?	2
Do you ever have to stop for breath when walking about 100 yards (or after a few minutes) on level ground?	3
Are you too short of breath to leave the house or short of breath on dressing or undressing?	4

CAT™ (COPD Assessment Test)[4]

For each item below, place a mark (X) in the box that best describes you currently. Be sure to select only one response for each question.

								Score
Example: I am very happy	⓪	ⓧ	②	③	④	⑤	I am very sad	
I never cough	⓪	①	②	③	④	⑤	I cough all the time	
I have no phlegm (mucus) in my chest at all	⓪	①	②	③	④	⑤	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	⓪	①	②	③	④	⑤	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	⓪	①	②	③	④	⑤	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	⓪	①	②	③	④	⑤	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	⓪	①	②	③	④	⑤	I am not al all confident leaving my home because of my lung condition	
I sleep soundly	⓪	①	②	③	④	⑤	I don't sleep soundly because of my lung condition	
I have lots of energy	⓪	①	②	③	④	⑤	I have no energy at all	
							Total Score	

Exacerbation Risk

During the past year, how many exacerbations occurred? How many of the exacerbations required hospitalization?

Low risk	0 – 1 exacerbations and 0 hospitalized exacerbations
Increased risk	≥ 2 exacerbations or ≥ 1 hospitalized exacerbation

Other Aspects of Severity

Oxygen, need for continuous

Comorbid conditions, e.g., asthma ("asthma overlap"), cardiovascular, heart failure, diabetes, psychiatric disorders) –

FEV1 = Forced expiratory volume measure.

Modified from UMHS Ambulatory COPD Clinical Care Guideline: http://www.med.umich.edu/1info/FHP/practiceguides/copd/copd.pdf

Table 2. ABG and VBG Correlation

Meta-analysis	pH (pooled MD)	pCO_2 (pooled MD)
Kelly[8]	0.035	5.7 mmHg
Lim and Kelly[1]	0.028	5.92 mmHg
Bloom, Grundlingh et al.[5]	0.033	4.41 mmHg
Clinical Utility	In non-shock states and when mixed respiratory and metabolic acid base conditions are not present, pH correlates very closely between ABG and VBG and can be reliably substituted	$pvCO_2 < 45$ mmHg reliably excludes arterial hypercarbia (defined as $paCO_2 \geq 50$ mmHg). However, $pvCO_2$ and $paCO_2$ do not correlate closely enough to substitute VBG for ABG to measure absolute degree of hypercarbia.

MD = mean difference between ABG and VBG values.

Table 3. Treatment Modalities for COPD

Table 3A. Treatment Modalities for Acute Exacerbations of COPD

Modality	Specific medication or intervention	When to use	Dose / route / duration	Notes
Short-acting bronchodilators	Albuterol	As the primary bronchodilator in AECOPD	MDI: 2-4 puffs INH q 4 h, and q 2 h PRN Nebulizer: 2.5-5 mg INH q 4 h, and q 2 h PRN	Can cause tachycardia, especially in high doses. It is reasonable to hold long-acting beta-agonists and anticholinergics when receiving scheduled doses of short-acting agents.
	Ipratropium	Can be used as a substitute for, or added to albuterol in AECOPD	MDI: 2 puffs INH q 4 h Nebulizer: 0.5 mg INH q 4 h	Combination products containing both albuterol and ipratropium (i.e., Combivent and Duoneb) are available. It is reasonable to hold long-acting beta-agonists and anticholinergics when receiving scheduled doses of short-acting agents.
	Levalbuterol	Not recommended for routine use		May result in less beta-adrenergic side effects than albuterol, but there is a paucity of clinical data supporting its use, and it is expensive.
Corticosteroids	Prednisone	Most hospitalized patients with AECOPD	40 mg PO daily for 5 days, for most patients	5-day duration is adequate for most patients. Longer courses may be considered for patients who are slow to respond to treatment.
	Methyl-prednisolone (IV)	If patient is unable to take oral formulation	40 mg IV daily	There is no evidence that higher doses are more effective.
Antibiotics (treatment)	See Table 4	Most hospitalized patients with COPD. Note: Patients diagnosed with pneumonia* should be treated with antibiotics appropriate for that diagnosis (**CAP and HCAP)	See Table 4. Duration of 5-10 days recommended.	5-day duration is probably adequate for most patients. Longer courses may be considered for patients with severe illness or those who are slow to respond to treatment.
O_2	Usually delivered via nasal cannula, other delivery strategies are also available (e.g., face mask)	Administer for hypoxemia (e.g., O_2 saturation < 88%)	0.5-6 liters/min via nasal cannula is usually sufficient	Target O_2 saturation = 88-92% during acute exacerbation. Avoid overcorrection of O_2 saturation, which may lead to acute CO_2 retention.
Ventilatory support	Invasive or non-invasive	Criteria for initiating ventilator support are shown in Figure 1		See also Table 5 for info on NIPPV

*The discussion of pneumonia treatment is outside the scope of this document.
**These links are available for UMHS staff only.

See 3B (next page) for Treatment Modalities for Chronic COPD

Table 3B. Treatment Modalities for Chronic COPD*

Modality	Specific Med	When to use	Dose / route / duration	Notes
Short-acting bronchodilators	Albuterol	Rescue	2-4 puffs INH q 4-6 hours prn	
Long-acting bronchodilators	Tiotropium Formoterol, Salmeterol	Prescribe to all patients admitted for AECOPD at discharge	Tiotropium: - Handihaler: 1 capsule INH daily - Respimat: 2 puffs daily Formoterol: 1 capsule INH BID Salmeterol: 1 puff INH BID	
Inhaled corticosteroids		Patients with FEV1 < 50 and at least 1 AECOPD yearly		There are many combination products containing both corticosteroids and long-acting bronchodilators (e.g., Advair, Symbicort)
Antibiotics (prophylaxis)	Azithromycin	Criteria for use: FEV1 < 50% , recurrent exacerbations (at least 2 in the prior year), and not currently smoking	250 mg PO daily, or 500 mg PO TIW, duration uncertain (literature reports up to 12 months)	Exclusion criteria: allergy to macrolides, prolonged QT interval (QTc > 450 milliseconds), or taking concomitant medications that cause prolongation of the QT interval
Phosphodiesterase -4 inhibitor	Roflumilast	Patients with COPD associated with chronic bronchitis and a history of frequent or severe exacerbations	500 mcg PO daily	Avoid use in patients with a history of depression with suicidal behavior/ideations; instruct patients/caregivers to report psychiatric symptoms and consider discontinuation of therapy in such patients
O_2	Usually delivered via nasal cannula	Criteria for use of continuous home O_2: Room air O_2 saturation < 89% (or paO_2 <56), OR Room air O_2 saturation of 89% (or paO_2 of 56-59) + one of the following three features: LE edema suggestive of CHF, pulmonary HTN/cor pulmonale, or erythrocytosis (hematocrit > 56%)		Target O_2 saturation $\geq$ 90% long-term. Note: Patients can also qualify for ambulatory home O_2 if they meet the criteria for home oxygen while ambulating, even if they do not meet those criteria at rest

*See the ambulatory COPD guideline for additional information about chronic medications.

BID= twice daily, CHF= chronic heart failure, FEV1= Forced expiratory volume measure, HTN= hypertension, INH= inhalation, LE= lower extremity, PO= orally, TIW= three times per week.

Table 4. Antibiotics for AECOPD

Antibiotic	Usual Dose	Important Adverse Effects	Notes
Non-anti-pseudomonal agents			
Azithromycin	500mg PO day 1 then 250mg x 4 days	QT prolongation	Not recommended for patients who are currently receiving azithromycin as prophylaxis.
Cefuroxime	500mg PO BID*, or 1.5 g IV q8hr*		Preferred agent when unable to take oral medications.
Amoxicillin/ Clavulanate	875mg PO BID*	Diarrhea	
Doxycycline	200mg x1, then 100mg PO BID	Photosensitivity	Preferred agent in patients allergic to (or intolerant of) beta-lactams and azithromycin. Separate administration from divalent/trivalent cations (2 hours prior to dose or 4-6 hours after dose).
Anti-pseudomonal agents			
Piperacillin/ Tazobactam	4.5g IV q6hr*	Diarrhea, leukopenia, neutropenia	Preferred anti-pseudomonal inpatient agent (due to risk of resistance with floroquinolones).
Cefepime	2 g IV q8hr*		
Levofloxacin	750 mg PO daily*	QT prolongation	For patients with severe penicillin and cephalosporin allergy (anaphylaxis, angioedema, hives). Usage associated with increased risk of C. difficile infection. Higher rate of Pseudomonas resistance than beta-lactam therapy. Separate administration from divalent/trivalent cations such as calcium, magnesium, or iron dietary supplements (2 hours prior to dose or 4-6 hours after dose).

*Require dose adjustment in the setting of renal insufficiency (internal link for UMHS staff: Antimicrobial Dosing Recommendations for Adult Patients)

BID= twice daily, PO= orally, q8hr= every 8 hours, TIW= three times per week.

Table 5. Non-invasive Positive Pressure Ventilation

Predictors of success in using non-invasive positive pressure ventilation	Contraindications for non-invasive positive pressure ventilation
Younger age Lower acuity of illness (APACHE score) Able to cooperate, better neurologic score (i.e. GCS ≥10) Less air leaking, intact dentition Moderate to severe hypercarbia ($PaCo_2$ >45 mmHg, <92 mmHg) Moderate to severe acidemia (pH <7.35, >7.10) Improvements in gas exchange and heart and respiratory rates within first two hours	Cardiac or respiratory arrest Nonrespiratory organ failure Severe encephalopathy (i.e. GCS <10) Severe upper gastrointestinal bleeding Hemodynamic instability or unstable cardiac arrhythmia Facial or neurological surgery, trauma, or deformity Upper airway obstruction Inability to cooperate/protect airway Inability to clear secretions High risk for aspiration (e.g. edentulous patient or presence of nasogastric tube)

Table based on recommendations in "International Consensus Conferences in Intensive Care Medicine: Noninvasive Positive Pressure Ventilation in Acute Respiratory Failure". *Am J Respir Crit Care Med*. 2001;163(1):283-291. Organized jointly by the American Thoracic Society, the European Respiratory Society, the European Society of Intensive Care Medicine, and the Societe de Reanimation de Langue Francaise, and approved by ATS Board of Directors, December 2000.

Table 6. The Key Elements of Hospital Discharge for Patients with AECOPD

Key element	Notes
Ensure the patient's discharge readiness	• The patient's dyspnea should be improved to the point that the patient can eat, sleep, walk, and correctly use inhaler medications (assuming that the patient was able to do these things at baseline). • The patient should be clinically stable for 12-24 hours, with short-acting bronchodilators required no more frequently than every 4 hours.
Ensure an appropriate COPD medication regimen at discharge	• Complete antibiotic and corticosteroid courses, if initiated in the hospital. • Inhaler regimen should include, at minimum, a long-acting bronchodilator and a rescue inhaler (see the ambulatory COPD guideline for additional information on chronic inhaler management). • Consider inhaled corticosteroids and prophylactic antibiotics on a case-by-case basis (Table 3B).
Ensure patient education about critical elements of care, including correct inhaler technique	• All patients should be educated on the importance of adherence to the inhaler regimen, correct inhaler technique, and counseled on smoking cessation if appropriate. (At UM, education about respiratory medications is provided by the respiratory therapist.)
Assess the patient's need for home O_2	• Home O_2 should be provided if the patient meets the following criteria: - Room air O_2 saturation < 89% (or pO_2 <56), or - Room air O_2 saturation of 89% (or pO_2 of 56-59) + one of the following three features: LE edema suggestive of CHF, pulmonary HTN/cor pulmonale, or erythrocytosis (hematocrit > 56%).
Refer eligible patients for pulmonary rehabilitation	• CMS requires PFT's demonstrating at least moderate disease (FEV1/FVC < 0.70 and FEV1 <80% predicted) to qualify for pulmonary rehabilitation.
Ensure that the patient has appropriate, timely follow-up	• At the time of discharge, consider the use of an assessment tool to estimate readmission risk (at UH, the LACE score is automatically calculated for all patients, see Table 7). - At UH, we recommend that patients at high risk for readmission be seen 7-10 days after discharge, and patients at moderate or low risk be seen within one month of discharge. • Followup in a clinical setting familiar with transitional care can be beneficial. (At UM, schedule patients through the COPD Transitional Care Management Clinic, see Appendix A). • Schedule full PFT's (including bronchodilators) 4-6 weeks after AECOPD, if not previously performed.

CHF=congestive heart failure, CMS= Centers for Medicare and Medicaid Services, HTN=hypertension, LE= lower extremity, PFT= pulmonary function testing, UM= University of Michigan.

Table 7. LACE Index for the Quantification of Risk of Death or Unplanned Readmission Within 30 Days After Discharge

Attribute	Value	Points*
Length of stay, d ("L")	<1	0
	1	1
	2	2
	3	3
	4-6	4
	7-13	5
	≥ 14	7
Acute (emergent) admission ("A")	Yes	3
Comorbidity (Charlson comorbidity index score †) ("C")	0	0
	1	1
	2	2
	3	3
	≥ 4	5
Emergency department visit during previous 6 mo ("E")	0	0
	1	1
	2	2
	3	3
	≥ 4	4

*A patient's final LACE score is calculated by summing the points of the attributes that apply to the patient.
†The Charlson comorbidity index score was calculated using 1 point for history of myocardial infarction, peripheral vascular disease, cerebrovascular disease or diabetes without complications; 2 points for congestive heart failure, chronic obstructive pulmonary disease, mild liver disease or cancer; 3 points for dementia or connective tissue disease; 4 points for moderate to severe liver disease or HIV infection; and 6 points for metastatic cancer.[2]

Background and Definitions

Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory disease of the lungs which leads to a progressive decline in lung function. The disease is tightly linked with cigarette smoking, and results in chronic symptoms (dyspnea, cough, and sputum production), often punctuated with periodic acute exacerbations of the disease. COPD is the third leading cause of death in the United States. The management of COPD can be divided into two main sections – the chronic management of the disease, and the management of acute exacerbations of the disease. The evaluation and management of the chronic aspects of the disease are covered in the ambulatory COPD guideline. In contrast, the present guideline will address the evaluation and management of the hospitalized patient with an acute exacerbation of COPD (AECOPD). The care of critically-ill patients with AECOPD is outside of the scope of this guideline.

AECOPD can be defined as an acute event characterized by a worsening of the patient's respiratory symptoms (e.g., worsening dyspnea, worsening cough, and/or changes in the character or amount of sputum) that is beyond normal day-to-day variations, and leads to a change in medication.[3] In most cases, patients hospitalized for AECOPD will have an established diagnosis of COPD. When admitting a COPD patient to the hospital, a clinician should understand the severity of the patient's underlying disease, which is determined by several factors, including clinical factors (which can be assessed by symptom severity scores), the patients forced expiratory volume in 1 second (FEV1), frequency of exacerbations, and the need for home oxygen, as shown in Table 1. These factors are helpful in determining the appropriate chronic therapies that should be recommended for the patient, as discussed further in the ambulatory COPD guideline. Some patients may present with AECOPD without having received a prior diagnosis of COPD. For these patients, the underlying diagnosis of COPD may be assumed, based on chronic symptoms and risk factors, but formal diagnostics with pulmonary function testing (PFT's) should be performed in follow-up, after recovery from the acute exacerbation.

Patients with underlying COPD are more likely to experience exacerbations if they have certain risk factors. These include a history of exacerbations requiring treatment, prior hospitalizations, and more severe airflow limitations, as demonstrated by PFT's.

Diagnosis

Clinical Assessment. Diagnosis of AECOPD is usually made by a clinical assessment that combines exploration of historical features, identification of triggers of worsening disease, physical exam findings, and elimination (ruling out) of other conditions in the differential diagnosis that mimic AECOPD. Patients with AECOPD typically report an acute change in baseline dyspnea, cough and/or sputum production. Dyspnea may be described as persistent, progressive, increasing with exertion, associated with chest heaviness, or the sensation of air hunger. Cough may be chronic in nature but progressive from intermittent to constant or associated with a change in sputum consistency, color, or volume.[4]

In addition to determining change in symptoms, specific triggers for AECOPD should be identified. The most common trigger is a concomitant viral or bacterial respiratory infection that leads to an acute worsening of baseline disease. Exposure to increasing airborne irritants such as ongoing smoking, second-hand smoke, occupational fumes/chemicals or air pollution may also trigger AECOPD. Additionally, interruption or non-compliance with maintenance medications (e.g., bronchodilators or inhaled steroids) or long-term home oxygen use may contribute. One-third of AECOPD will have no identifiable trigger.[3]

The physical exam is generally unhelpful in identifying AECOPD. However it may assist with ruling in or out other conditions in the differential diagnosis. A complete set of vital signs should be obtained including temperature and pulse oximetry. Mental status should be assessed. Patients with worsening hypercarbia due to AECOPD may appear altered or somnolent. Pulmonary findings in advanced disease may include tachypnea, wheezing, rhonchi, decreased air movement or accessory respiratory muscle use. Inspection of the thorax may reveal signs of hyperinflation or a "barrel" chest. The cardiac exam should include assessment for distant heart sounds, displaced point of maximal impulse (PMI), murmurs, rubs or gallops. Signs of volume overload including jugular venous distention and peripheral edema should be noted. Systemically, patients may have evidence of new or worsening central cyanosis and may appear cachectic in advanced disease.

Differential Diagnosis. The differential diagnosis of AECOPD is broad. There are several conditions which act as mimics or augment the severity of AECOPD. The differential diagnosis should be narrowed based on historical and physical exam features. Primary pulmonary conditions include pulmonary embolus, pneumonia, pneumothorax, pleural effusion, asthma, interstitial lung disease, and chronic aspiration. Primary cardiovascular conditions may include CHF exacerbation, ischemic heart disease, arrhythmia and hypertensive urgency/emergency. Concurrent illness is always possible and AECOPD can be triggered by an additional exacerbating illness.

Smoking is an established risk factor for the development of COPD but may also place the patient at a higher risk for other comorbid conditions on the differential including ischemic heart disease, hypertension and malignancy.

Pulmonary embolism (PE) should always be considered in patients being evaluated for AECOPD. A meta-analysis of 550 patients demonstrated a 20-25% prevalence of PE in patients hospitalized for AECOPD. Therefore, this condition should be considered when the diagnosis is unclear, or if the

patient has other PE risk factors such as decreased mobility, history of thromboembolic disease or malignancy.[5]

Diagnostic Approach. The evaluation of all patients with suspected AECOPD should include a minimum of a complete blood count (CBC), a chest x-ray (CXR) and an electrocardiogram (ECG). A CBC can help identify an anemia or polycythemia, both potential causes of dyspnea. Additionally, the presence of a leukocytosis can reinforce suspicion for underlying infection and is independently associated with greater frequency of hospitalization in AECOPD. A CXR may show hyperinflation in COPD but overall is not useful in establishing the diagnosis of an AECOPD.[3] However, CXR can be useful in ruling out other conditions in the differential diagnosis (e.g., pneumonia, pneumothorax, pleural effusion, malignancy, interstitial lung disease) and, in one study, the CXR prompted a change in short-term management of about 20% of patients based on abnormalities discovered.[4] ECG should be obtained to rule out myocardial ischemia, arrhythmia or evidence of right heart strain if PE is suspected. Additional testing should be driven by the clinical suspicion for the presence of other conditions in the differential diagnosis.

If AECOPD is suspected and patient's SpO_2 is < 88%, an initial venous blood gas (VBG) should be obtained. (An initial ABG may be obtained instead, however VBG is associated with reduced pain and time to collection).[6] A VBG can provide screening for respiratory acidosis and hypercarbia, without the pain and risks associated with arterial puncture. Correlation between VBG and ABG is excellent for both pH and HCO3 measurement for patients that are not in shock or affected by mixed respiratory and metabolic acid-base disorders.[4] In several studies, a venous $pCO_2 \geq 45$ mmHg has demonstrated 100% sensitivity in detecting arterial hypercarbia. Stated conversely, a $pvCO_2 \leq 45$ mmHg had a 100% negative predictive value for the presence of a $paCO_2 \geq 50$ mmHg.[7-10] Assuming the pH is abnormal (ruling out chronic compensated hypercarbia), a VBG is generally sufficient to use as a screening test for acute respiratory acidosis, and can help inform decisions regarding initiation of medical management and the need for non-invasive ventilation.[11] However, the correlation between $paCO_2$ and $pvCO_2$ is limited, and an ABG must be obtained when assessing the degree of hypercarbia (see Table 2).

Additionally, an ABG should be obtained when SpO_2 is less than 92%[12] with evidence of altered mental status and/or respiratory distress, and prior to initiation of non-invasive or mechanical ventilation,[4] when time allows, in order to guide the effect of therapy. However, if an arterial line is not present, the provider may elect to obtain a VBG and ABG at the same time. If the VBG is found to correlate closely with the ABG pH value, and the provider is satisfied knowing the pH trend (but not the absolute value of hypercarbia), a VBG may be use subsequently to follow the patient's response to treatment. This might avoid the need for serial arterial punctures in some situations.

If congestive heart failure (CHF) is in the differential diagnosis, a brain natriuretic peptide (BNP) level should be ordered. An elevated BNP in the presence of other clinical factors suggesting CHF exacerbation (e.g., pleural effusion, pulmonary edema, distended neck veins, lower extremity edema) should prompt the clinician to consider CHF as a principal diagnosis. However, in one study, the median BNP level was moderately elevated in AECOPD requiring hospitalization (72.7 pg/mL) as compared to pre-AECOPD levels (19.4 pg/mL). These patients had no evidence of systolic dysfunction on corresponding echocardiogram. BNP returned to baseline (14.6 pg/mL) after resolution of AECOPD, suggesting moderate elevation of BNP level with AECOPD regardless of presence of heart failure.[13] As such, the BNP value should be used as a clinical adjunct and should be interpreted in the context of the remainder of the clinical presentation.

If ischemic heart disease is considered, a troponin level should also be added. Ischemic heart disease is more likely with a history of exertional chest pain and/or dyspnea with the presence of cardiac risk factors (e.g., diabetes, smoking, hypertension [HTN], hyperlipidemia, significant family history) and concerning findings of ischemia or infarction on the ECG.

Pulmonary embolus should always be considered in patients presenting with suspicion for AECOPD because of the high rate of this diagnosis. D-dimer testing should only be considered in patients with low risk for PE (based on Well's criteria, or other clinical assessment of pre-test probability). Of note, the d-dimer may be elevated, despite lack of PE, due to the inflammatory process associated with AECOPD. Overall, pulmonary embolus protocol CT scans (PECT) are not routinely recommended in the diagnostic work-up of AECOPD, but should be utilized when pulmonary embolism remains a significant concern.[3]

Finally, ruling out concomitant viral or bacterial respiratory infection is paramount, as this is the most common trigger for AECOPD (refer to section on History). An influenza swab should be considered in the appropriate seasons. Procalcitonin may have utility in confirming the presence or absence of a concomitant infection, but there is lack of confirmatory evidence to support its routine use in the acute presentation (see the discussion on procalcitonin in the Antibiotics section, below). Likewise, sputum cultures are not routinely recommended for AECOPD, however circumstances exist where they can be of benefit in guiding therapy (see the sections on Antibiotics and Refractory AECOPD, below).

Assessment of Severity and Intensity of Care (Figure 1). All patients presenting with AECOPD require an assessment of the severity of illness, which will determine the intensity of the treatment required (i.e., the need for hospitalization, ventilator support, or intensive care). This assessment is based principally on the clinical assessment described above. In addition, the patient's response to initial treatment (e.g., supplemental oxygen, inhaled beta-agonists) should be considered. Patients that do not respond quickly to these measures may require more intensive interventions.

Use of Non-Invasive Positive Pressure Ventilation (NIPPV) (Figure 1). Patients should be started on non-invasive positive pressure ventilation (NIPPV) support if there is clinical evidence of worsening respiratory distress despite supplemental oxygen use (e.g., fatiguing respiratory muscles, retractions, use of accessory muscles) or if there is evidence of acute respiratory acidosis on VBG or ABG (pH < 7.35 and pCO_2 > 45 mmHg) as shown in Figure 1. Early use of NIPPV in AECOPD with respiratory failure is associated with lower mortality, more rapid improvement in ABG values, lower endotracheal intubation rate, less treatment failures and shorter hospital lengths of stay[14] (see also the section on NIPPV, below).

Determining Need for Hospital Admission (Figure 1). The criteria for hospital admission for AECOPD are listed in Figure 1.

Patients more likely to be admitted to the hospital include those who have the following characteristics:

- Required hospital admission for AECOPD in preceding 12 months
- Have more severe airflow limitations (severe or very severe disease by spirometry, see Table 1)
- Worsening cough, wheeze or dyspnea
- Overall poor health status
- Older age
- Radiologic evidence of emphysema
- Increased evidence of systemic inflammation (elevated WBC, CRP, fibrinogen)

Overall, the need for hospitalization for AECOPD is associated with poorer prognosis and increased mortality.[15]

Determining Need for Intensive Care Unit Admission. Evaluation by and subsequent admission to critical care units (at UMHS, the Emergency Critical Care Center [EC3, for ED patients] or the Critical Care Medicine Unit [CCMU]) should be considered when there is a noted lack of improvement in response to a trial of urgent/emergent therapies (e.g., oxygen, bronchodilators, steroids, antibiotics, NIPPV). This may be ascertained by the patient's subjective symptoms, clinical appearance, or worsening hypoxemia or respiratory acidosis despite use of oxygen and/or NIPPV. Additionally, the need for endotracheal intubation and invasive ventilation and/or hemodynamic instability should prompt evaluation by EC3 or the ICU.

In general, ED patients transferred to EC3 will undergo an extended period of evaluation and treatment. If the patient is able to be extubated/weaned off of NIPPV, has serial ABGs or VBG demonstrating improvement in hypercarbia and/or hypoxemia on $FIO_2 \leq 40\%$ and demonstrates hemodynamic stability, admission to a non-ICU setting may be considered. If these clinical endpoints are unable to be met within six hours of EC3 transfer, admission to the CCMU should be considered and the CCMU fellow consulted.

Treatment

The acute treatment of AECOPD is multimodal, and often includes the use of inhaled bronchodilators; the administration of corticosteroids and antibiotics; and the use of supportive respiratory therapies, including supplemental oxygen and ventilatory support (see Table 3). Of note, there is very little evidence to support the use of mucolytics or cough suppressants in the treatment of these patients.

Inhaled bronchodilators. Patients hospitalized with AECOPD should be treated with inhaled albuterol, with dose and frequency titrated to effect (Table 3A).[3,16]

A short-acting anticholinergic, such as ipratropium, can be used in combination with the albuterol, although it is uncertain if the combination results in greater efficacy than monotherapy.[16] Ipratropium can also be used alone, especially for patients who do not tolerate albuterol (see Table 3).

Levalbuterol (a formulation containing only the R-isomer of albuterol) is not recommended for routine use in patients with AECOPD. Although there is some evidence that levalbuterol may provide bronchodilation with less beta-adrenergic side effects than albuterol,[17] there is only limited clinical data supporting its use, and no data directly supporting its use in AECOPD.

Metered-dose inhalers (MDI's) are the preferred delivery method for short-acting bronchodilators.[3,18] Exceptions should be considered when the patient condition (e.g., severe dyspnea, anxiety) or preference warrants the use of a nebulizer. There does not appear to be a difference in FEV1 response when comparing MDI's and small volume nebulizer as the route of medication delivery. Per UMHS policy, respiratory therapists are empowered to determine the appropriate mode of medication delivery, and update the electronic medical record orders, when appropriate (UMHS staff can view the policy at http://www.med.umich.edu/i/respcare/uhcvc/pdfs/4 1 3 Aerosolized Bronchodilator Protocol.pdf).

In most cases, the patient's long-acting bronchodilators can be withheld in the acute phase of the illness when they are being treated with frequent, short-acting bronchodilators. Similarly, inhaled corticosteroids are often held while the patient is treated with systemic corticosteroids. However, when symptoms improve and inhaled bronchodilator therapy is not required more frequently than every four hours, patients should be transitioned to their expected outpatient inhaled medication regimen. If a nebulizer has been used, the patient should be transitioned to an MDI, if applicable. Prior to patient discharge, a long-acting bronchodilator (a long-acting anticholinergic or a long-acting beta-2-agonists) should be resumed, or added if the patient was not already taking one at the time of admission. Additional recommendations for the chronic medical management of patients with COPD can be found in the ambulatory COPD guideline.

Selection of the appropriate medication/delivery device should be based upon several factors (e.g., patient preference, ease of use, cost, and insurance coverage). Education on proper technique for using the device(s) should be done while the patient is in the hospital, with the patient preparing and administering their own medication to demonstrate comprehension. If the patient is not able to take the prescribed medications effectively, a different medication/delivery device should be prescribed. At the UMHS, this educational step is performed and documented by the respiratory therapist, and happens automatically for all patients prescribed inhaled therapies (there is no need to write a specific order). An example of a patient educational tool is shown in Appendix B.

Corticosteroids. Most patients who are hospitalized with an exacerbation of COPD should be treated with *systemic* corticosteroids (The evidence supporting the use of *inhaled* corticosteroids for AECOPD is very limited). A Cochrane meta-analysis demonstrated that there are several benefits to the use of corticosteroids in this population.[19] Corticosteroid use typically results in a reduction of symptoms and improvement in spirometric measurements when given for AECOPD. In addition, the risk of treatment failure is reduced (NNT = 9 patients treated with corticosteroids to prevent 1 treatment failure). Most of the treatment failures in the placebo groups were patients who went on to require increased intensity of treatment, including the addition of corticosteroids. In non-ICU inpatients, the length-of-stay was decreased by an average of 1.2 days in patients treated with systemic corticosteroids. However, no mortality benefit has been demonstrated for the use of corticosteroids in this population.

Although most hospitalized patients will benefit from corticosteroid treatment for AECOPD, it should be noted that some patients will suffer side-effects from these agents, and may not tolerate them. The adverse effects of systemic corticosteroids include hyperglycemia, insomnia, psychiatric disturbances (including psychosis), muscle wasting, osteoporosis, and increased appetite/weight gain.[20] Of these, hyperglycemia is the most common.[19] Hyperglycemia can usually, but not always, be actively managed to allow the continued use of the corticosteroids. Insulin may be required to control blood glucose levels when using corticosteroids in the hospital setting. Problems such as severe hyperglycemia, severe insomnia, or psychiatric disturbances may require discontinuation of the corticosteroids.

A dose of prednisone, 40 mg orally daily, for a 5-day course, is appropriate for most patients hospitalized with AECOPD, and a dose taper is unnecessary. Since most of the adverse effects of corticosteroids are directly related to the extent of exposure to the medication, there is good reason to use the lowest dose and shortest duration that is effective. However, there are limited data on which to base decisions about dose, route, and duration of corticosteroid treatment in AECOPD. No randomized trials have directly compared doses for patients with AECOPD. A large cohort study[21] and a meta-analysis[22] have both demonstrated that initial daily doses of < 80 mg prednisone equivalents are as effective as initial doses > 80 mg daily, and the GOLD guidelines suggest an initial dose of 40 mg of prednisone daily.[3] There is no theoretical reasoning or evidence to suggest that intravenous corticosteroids are more effective than orally administered ones.[19,21] Oral glucocorticoids are highly bioavailable, and the intravenous administration of these medications should be reserved for patients that are unable to take the medications by mouth or absorb the medications via an enteral route. An older study of corticosteroids in AECOPD concluded that a two-week duration of prednisone was as effective as an eight-week course,[23] and a more recent study demonstrated that a five-day course of prednisone was as effective as a 14-day course.[24] The later study was a randomized controlled study of 311 hospitalized patients with AECOPD, and there was no benefit to the longer course of therapy, even when considering re-exacerbations over 6 months.

Although a 5-day duration of corticosteroids should become the standard treatment, there may be times when a longer course of corticosteroids might be considered. Patients who are slow to respond to treatment might rationally receive an extended course. In most cases, short courses of treatment with corticosteroids (<3 weeks) should not have a clinically important suppressive effect on the pituitary-adrenal axis, and a dose taper is not required. However, patients treated with longer courses of corticosteroids may benefit from more gradual cessation of these medications.

Antibiotics (Figure 2, Tables 3 and 4). Most patients who are hospitalized with AECOPD should be treated with antibiotics. Studies suggest that antibiotics do improve outcomes in these patients, even though the majority of the underlying infections are probably viral in nature. It is likely that antibiotics are only of benefit in a subset of patients with a bacterial infection of the airways. However, antibiotics are used broadly in patients with severe AECOPD since, as discussed below, it is difficult to identify the subset of patients that suffer from a bacterial infection.

Patients diagnosed with pneumonia in this setting should be appropriately treated for pneumonia. The details of pneumonia treatment will not be presented here, but are available elsewhere (e.g. CAP and HCAP [These links are available to UMHS staff only]).

Most hospitalized patients with AECOPD, without findings of pneumonia, should also be treated with antibiotics (although the recommended antibiotic regimen may differ from that recommended for pneumonia). In this population, antibiotics have been demonstrated to reduce the rate of treatment failure in a Cochrane meta-analysis.[25] Of note, only three of the trials in the meta-analysis included non-critically-ill inpatients. In these studies, antibiotic-treated patients experienced fewer treatment failures, but they did not see any benefit in mortality or hospital length of stay. However, a large, retrospective database study examining over 84,000 patients has demonstrated an association between the use of antibiotics and a reduction in both mortality and readmission rates.[26]

Despite the above recommendation, and the supporting evidence, it is still widely believed that a sizable portion of patients with AECOPD will derive no benefit from antibiotics. This belief is based on several observations, including the fact that most of the related infections are probably viral, and the fact that the magnitude of benefit of antibiotics is relatively small, overall. In fact, in the meta-analysis described above, no benefit of antibiotics treatment was demonstrated for outpatients. This suggests that patients with more severe illness (including inpatients) may be more likely to benefit from the use of antibiotics.

The 2014 GOLD guidelines recommend prescribing antibiotics for all patients with 3 of the cardinal symptoms (dyspnea, change in sputum volume, and change in sputum purulence), or increased sputum purulence and one other cardinal symptom.[3] One systematic review demonstrated that patients with all three of the cardinal symptoms were more likely to benefit from antibiotics than those with fewer symptoms.[27]

The role of serum procalcitonin testing in the evaluation and management of AECOPD remains uncertain. Although several studies suggest that the use of such testing may reduce antibiotic use in this population,[28-30] the existing data do not allow for firm conclusions about how the test should influence the clinical approach to these patients. At this time, we do not recommend procalcitonin testing as a standard part of the evaluation for patients presenting with AECOPD.

When used, antibiotics should be selected based on their coverage of the most common bacteria implicated in causing AECOPD. *H. influenza*, *M. catarrhalis*, and *S. pneumoniae* are the most common bacteria isolated from the sputum of patients with AECOPD. Chlamydia and mycoplasma are less commonly identified, and their pathogenic role is less certain. Pseudomonas and Enterobacteriaceae are also implicated in some cases. Ideally, local resistance patterns should also be considered in choosing antibiotics.

The optimal antibiotics for AECOPD in hospitalized patients are not well defined, but the most commonly used agents are summarized in Table 4. Amoxicillin/clavulonate, second- or third-generation cephalosporins, respiratory floroquinolones, advanced macrolides, and doxycycline have all been studied.[31-32] Some agents that were frequently used for this indication in the past are no longer considered first line treatments. These include amoxicillin without clavulonate (given the frequent beta-lactamase production in non-typable *H. influenza* and Morexella), and trimethoprim/sulfamethoxazole (waning efficacy against *S. pneumonia*). A meta-analysis of 19 studies comparing quinolones, macrolides, and amoxicillin/clavulonate demonstrated no difference in treatment success, while amoxicillin/clavulonate caused more diarrhea than quinolones, and quinolones seemed to have fewer recurrences at 26 weeks than macrolides.[31] Doxycycline, when added to steroid treatment in hospitalized AECOPD patients, results in better treatment success, fewer symptoms, and less off-study antibiotic use at 10 days, but there was no difference at 30 days, compared to placebo.[32]

Figure 2 and Table 4 provide guidance about antibiotic choice in patients with AECOPD. Pseudomonas has been traditionally reported in 5-15% of sputum isolates from patients with COPD.[33] However, pseudomonas is thought to be more common in patients with more severe disease. In a recent study from Spain of patients with severe COPD (average FEV1 36% predicted) and AECOPD, 28.7% of sputum isolates were Pseudomonas, and it was the single most common organism recovered.[34] Pseudomonas infection is more likely in patients with risk factors such as severe COPD (e.g. FEV1< 35% predicted or high BODE score), prior hospital admissions within the last year, multiple antibiotic courses for recent exacerbations, use of systemic corticosteroids, prior isolation of Pseudomonas, bronchiectasis, or mechanical ventilation.[33,35] Empiric anti-pseudomonal coverage, such as levofloxacin or piperacillin-tazobactam, may be indicated for more severely ill patients with these risk factors.

Sputum culture is not helpful in most patients with AECOPD (without pneumonia), but may be useful in patients who are at high-risk for Pseudomonas infection, or those who are not responding to therapy (e.g. after 72 hours), as shown in Figure 2. In these cases, the results of the sputum culture are more likely to provide information that will alter the management, by demonstrating a specific organism that might not respond to typical AECOPD antibiotic regimens.

Typically, antibiotics should be continued for 5-10 days. Meta-analysis of primarily outpatient studies has demonstrated that a 5-day course is as efficacious as a 7-10 day course of antibiotics.[36,37] However, it is not clear if those studies apply to inpatients, who may be more severely ill. A 5-day course of antibiotics may be appropriate for patients demonstrating a good clinical response, while slower responders might require a longer treatment course. The duration of antibiotic treatment for patients with Pseudomonas infections and those with significant bronchiectasis have not been well-studied, and abbreviated treatment may not be appropriate for these patients. In patients with Respiratory Syncytial Virus or Influenza infection confirmed by PCR, consideration should be given to discontinuation of empiric antibiotics.

Antibiotic prophylaxis Antibiotic prophylaxis with azithromycin has been demonstrated to decrease the frequency of AECOPD and hospitalizations in moderate-severe COPD,[38,39] and this therapy can be recommended for patients who meet all of the following criteria: FEV1 <50%, recurrent exacerbations (at least 2 in the prior year), and not currently smoking.[40] Exclusion criteria include the following: allergy to macrolides, prolonged QT interval (QTc > 450 milliseconds), or taking concomitant medications that cause prolongation of the QT interval.[41] The decision to start prophylactic azithromycin should ideally be made in conjunction with the patient's PCP and/or outpatient pulmonologist, as patients will need close follow-up due to the potential adverse events that are associated with azithromycin therapy (e.g. QT prolongation, hearing loss).

For additional information about prophylactic azithromycin, see Table 3B.

Refractory AECOPD. In cases where a patient fails to improve after 72 hours of standard therapy, additional actions should be taken to identify the possible causes of treatment failure. A non-contrast high-resolution computed tomogram (HRCT) of the chest may be helpful in determining an alternative diagnosis such as a previously undetected infiltrative disease. A sputum culture, if not sent initially, should be sent for gram stain and culture, and also for acid-fast bacilli (AFB) staining, which would detect Mycobacterium avium complex (MAC). A Pulmonary consult is also appropriate to assist with patients that are refractory to standard treatment.

Supportive Care

Patients hospitalized with AECOPD require additional supportive care, often including supplemental oxygen and sometimes ventilatory support.

Supplemental oxygen. Oxygen should be provided to treat hypoxemia. The usual pulse-ox target is 88-92%, to prevent hypercapnea that can be seen with high-doses of oxygen.[3,4] AECOPD itself is not usually associated with severe hypoxemia, and oxygen provided via nasal cannula is usually sufficient. When initiating oxygen therapy, clinicians should be vigilant for signs of worsening hypercapnea, such as alterations in mental status. If seen, these may require sampling of the arterial blood gases for evaluation, and possibly additional respiratory support.

Ventilatory support. Ventilatory support should be initiated in patients with AECOPD who have persistent or worsening hypoxemia or respiratory acidosis despite medical therapy. The GOLD guidelines recommend initiating ventilator support for respiratory acidosis (arterial pH $\leq$7.35 and/or $PaCO_2$ $\geq$45 mm Hg) or severe dyspnea with signs of respiratory muscle fatigue or increased work of breathing.[3] The benefits of using NIPPV in AECOPD are well established. A recent Cochrane review evaluated 14 RCT's comparing NIPPV plus usual care vs. usual care alone.[14] The relative risk of intubation when using NIPPV was 0.41 with a number needed to treat (NNT) of 4. The relative risk of mortality was 0.52 with a NNT of 10. The benefits of NIPPV in hypoxemic respiratory failure are less clear.[42]

Noninvasive positive pressure ventilation (NIPPV) with either bilevel positive airway pressure (BiPAP) or continuous positive airway pressure (CPAP) should be first line therapy when initiating ventilator support. BiPAP may be better tolerated than CPAP. When considering NIPPV, it is helpful to recognize both the predictors of success and the contraindications to this treatment, as established in an international consensus conference in 2001 (see Table 5).[42]

NIPPV should be started immediately, when necessary, as the intervention seems to be most effective when initiated early in the course of treatment. At the UMHS, sustained treatment with NIPPV is provided only in the ED or intensive care units (not on general medical/surgical floors). If a patient on a general floor requires NIPPV, the Rapid Response Team (RRT) should be paged. That team can facilitate the initiation of NIPPV, but the critical care consultant should also be called to assist in transfer of the patient to the appropriate level of care.

Patients should be monitored closely after initiating NIPPV. A repeat ABG should be obtained within 2 hours of initiation. Improvement of pH and PCO_2 within 2 hours has been linked to success of NIPPV.[43,44] If a patient fails to improve after 2 hours, or worsens within 2 hours of starting NIPPV, intubation and initiation of mechanical ventilation should be considered. The intensive care of an AECOPD patient, including intubation and ventilator management, is outside of the scope of this guideline.

Chronic nocturnal-NIPPV. At this time, the evidence does not support the widespread use of nocturnal-non-invasive positive pressure ventilation (nocturnal-NIPPV) therapy. NIPPV has been proven to be effective in treating acute exacerbations of COPD. Consequently, nocturnal-NIPPV has been proposed as an intervention for stable hypercapnic patients with COPD. A Cochrane review published in 2013 indicated that nocturnal-NIPPV at home for at least three months in hypercapnic patients with stable COPD had no consistent clinically or statistically significant effect on gas exchange, exercise tolerance, health-related quality of life (HRQoL), lung function, respiratory muscle strength or sleep efficiency.[45] However, one recent trial did demonstrate a benefit with this therapy.[46]

Airway clearance techniques. We do not recommend airway clearance techniques as a standard part of AECOPD treatment, although they may be appropriate in select cases. Although airway clearance techniques (percussion and postural drainage, positive expiratory pressure devices, etc.) are sometimes used in the treatment of AECOPD, there are only limited data to support this practice.[47]

Nutritional support. Malnourished COPD patients should be offered a nutritional support program employing oral nutritional supplements and consultation with a dietician. Malnutrition is a common comorbidity in COPD. Although the role of nutritional support in the management of AECOPD is uncertain, there is limited evidence demonstrating that nutritional support can result in increased body weight, measurable improvements in respiratory and non-respiratory muscle strength, modest increases in timed walk-distance tests, and improvements in some quality of life measurements in malnourished COPD patients.[48,49]

Palliative care. Clinicians are strongly encouraged to engage patients in shared decision making regarding goals of therapy, including advanced care planning and advance directives. Severe COPD increases risk of respiratory failure and is a leading cause of death. A palliative focus for care should be discussed with patients desiring less aggressive therapy, avoidance of endotracheal intubation, or comfort care measures (symptomatic care) at the end of life.

Therapies with proven effectiveness for management of dyspnea at the end of life include opioids and oxygen. A detailed discussion of palliative and end-of-life care is beyond the scope of this guideline.

Preventative Care in the Hospital

When a patient is hospitalized for AECOPD, there are several preventative care considerations. These include efforts directed at smoking cessation, efforts directed at prevention of hospital acquired venous thromboembolism (VTE), and administration of appropriate vaccinations.

Smoking cessation. When a patient is admitted with AECOPD, the patient's smoking status should be assessed. Current smokers should be encouraged to quit smoking, the smoking cessation service should be consulted, and pharmacologic smoking cessation aids should be used, when appropriate.

Smoking is the primary risk factor for the development of COPD in the United States, and smoking contributes to the progression of lung disease. The effectiveness of brief counseling interventions to encourage smoking cessation in hospitalized patients remains uncertain, and there is some evidence that success is greatest if the interventions continue beyond the time of hospital discharge.[50] However, there is evidence that the combined use of counseling and pharmacologic interventions can successfully increase quit rates in a variety of settings.[51] Information about smoking cessation is available via the UMHS Tobacco Treatment Guideline.

Vaccinations. Patients admitted with AECOPD should be given vaccinations for Influenza and Pneumococcus, if they have not already received these vaccinations within the appropriate time frame. [52,53] The Influenza vaccine has been shown to decrease AECOPD in patients with COPD.[54] Although the Pneumococcal vaccine has not been shown to reduce AECOPD, it does appear to decrease the risk of invasive Pneumococcal disease in a general population.[55] Of note, the most recent guidelines for Pneumococcal vaccination recommend the combined use of the 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among adults aged ≥65 years, so practice in this area may change in the coming years.[56] The UMHS Hospital utilizes a nurse-driven, standing order policy for these vaccines to assure that they are offered to all at-risk, hospitalized patients.

VTE prophylaxis. Inpatients with AECOPD should be prescribed appropriate prophylaxis for venous thromboembolism, as COPD is widely regarded as a risk factor for venous thromboembolism. Therapy typically is guided by a formal risk assessment for each patient.

Hospital Discharge

Hospital readmission rates after AECOPD are very high. Therefore, it is important to take the appropriate steps to assure a safe discharge for these patients, by considering all of the elements in Table 6.

Determining when an AECOPD patient is ready for discharge can be difficult. These patients are, often, chronically ill and have multiple comorbidities. Sometimes they are also severely functionally limited because of their underlying lung disease, or physical deconditioning. Table 6 describes the GOLD Guidelines recommendations for the assessment of discharge readiness.[3]

At the time of discharge, it is important for the provider to ensure that the patient will be discharged on the optimal medication regimen for ongoing treatment of the AECOPD, and for chronic COPD maintenance therapy (the ambulatory COPD guideline contains additional information about chronic, maintenance therapy in these patients). Corticosteroids and antibiotics should be continued, as described above. The inhaler regimen should include, at minimum, a long-acting bronchodilator (beta-agonist or anti-cholinergic), and a short-acting albuterol inhaler for rescue. Inhaled corticosteroids are not typically used in the treatment of AECOPD, but they may be added for patients with severe obstruction (FEV1<50% predicted) who suffer from frequent exacerbations (e.g., at least 1/year). In some cases, the use of long-term prophylactic antibiotics could also be considered (see Table 3B).

In all cases, prior to home discharge, a respiratory therapist should reinforce the importance of and the appropriate technique for the use of all inhaler medications. Many patients are noncompliant with their inhaler medications, or self-administer them with poor technique. Patient education can improve adherence and technique, and decrease hospitalizations for AECOPD.[57] An example of a patient education tool is shown in Appendix B.

Patients should be prescribed home O_2 if they meet the criteria listed in Table 6. At the time of discharge from the hospital, some patients may still require supplemental oxygen to maintain appropriate oxygenation (e.g., O_2 saturation > 89%). Studies in the 1980's demonstrated a survival benefit for patients with resting hypoxemia when they were treated with continuous home oxygen therapy. Since then, criteria for oxygen therapy in guidelines[3] and CMS requirements have aligned.

Oxygen prescribed in this way is intended to be used continuously, and patients are often provided with portable oxygen devices for use with ambulation.

For patients with marginal resting O_2 saturations, consider testing the O_2 saturation with ambulation. CMS also allows the above criteria to be met while the patient is ambulating, as long as the oxygen saturation or PO_2 is documented to improve with the addition of supplemental oxygen. This has led to widespread prescription of portable oxygen for use with exertion in patients who do not meet these criteria at rest. However, the benefits of oxygen used in this way are

much less clear. A meta-analysis of four studies has concluded that the use of oxygen with exertion, for patients who do not need oxygen at rest, does improve symptoms (dyspnea and fatigue), but there is no data to suggest a mortality benefit.[55]

It is generally recommended that patients who are started on oxygen during an AECOPD should be reassessed at the post-discharge follow-up visit. After recovery from the acute exacerbation, some patients will no longer need the supplemental oxygen to maintain an adequate oxygen saturation, and the oxygen therapy can be discontinued in these patients. Of note, patients with established, chronic hypoxemia (that precedes the acute exacerbation) are typically continued on that level of oxygen, at minimum, during the hospitalization and after discharge, even if they do not meet the above criteria at the time of discharge. Long-term use of oxygen may have a reparative effect, and lead to improvements in oxygenation over time, and these may reverse if the oxygen therapy is removed.

Most patients who are hospitalized with AECOPD should be referred to a pulmonary rehabilitation program after discharge (see Table 6 for specific criteria). Enrollment in pulmonary rehabilitation after AECOPD has been linked to decreased mortality and hospitalization rates, and improvements in quality-of-life.[58] Initiating a rehabilitation program while the patient is hospitalized does not appear to improve these results.[59]

Lastly, all patients should be given close post-hospital follow-up. Although the optimal timing of this appointment is not certain, the GOLD Guidelines suggest that it be scheduled 4-6 weeks after hospital discharge.[3] We recommend that patients with high risk for readmission follow up within 7-10 days, and those with low or moderate readmission risk follow up within 30 days. Several models that predict readmission risk scores are available such as LACE, ED 30, Discharge 30, and GRACE.[60] For example, at the UMHS Hospital, the LACE score (Table 7) is used to estimate the risk for readmission for all patients. Follow up in a clinic familiar with transitional care management can be beneficial. For example, at UH, follow-up can be provided within the suggested time frame through the COPD Transitional Care Management Clinic (see Appendix A).

If the patient has never had full pulmonary function testing, it is reasonable to perform this testing 4-6 weeks after recovery from the exacerbation. In addition, spirometry might be repeated in follow-up if the patient's symptoms have not improved to baseline, or if the patient has not had spirometry performed in the last year.

Related National Guidelines

The UMHS Clinical Guideline on Chronic Obstructive Pulmonary Disease is consistent with:

Global Initiative for Chronic Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease (updated 2014).

Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society.

Management of COPD Working Group. (2007). VA/DoD clinical practice guideline for the management of outpatient chronic obstructive pulmonary disease. Washington (DC): Department of Veterans Affairs, Department of Defense.

Related National Performance Measures

At this time the UMHS tracks three clinical performance measures defined by HEDIS specifically for the diagnosis and treatment of AECOPD.

Use of Spirometry Testing in the Assessment and Diagnosis of COPD (SPR): The percentage of members 40 years of age and older with a new diagnosis of COPD or newly active COPD, who received appropriate spirometry testing to confirm the diagnosis.

Pharmacotherapy Management of COPD Exacerbation – Bronchodilator: 1. The percentage of COPD exacerbations for members 40 years of age and older who had an acute inpatient discharge or ED visit on or between January 1–November 30 of the measurement year and who were dispensed appropriate medications. 2. Dispensed a bronchodilator (or there was evidence of an active prescription) within 30 days of the event.

Pharmacotherapy Management of COPD Exacerbation - Systemic Corticosteroid: The percentage of COPD exacerbations for members 40 years of age and older who had an acute inpatient discharge or ED visit on or between January 1–November 30 of the measurement year and who were dispensed appropriate medications. 2. Dispensed a systemic corticosteroid (or there was evidence of an active prescription) within 14 days of the event.

Guideline Development Methodology

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Guideline Development Team and Disclosures

The multidisciplinary guideline development team consisted of:

- Primary care physicians: Rommel L. Sagana, MD, David H. Wesorick, MD.

- Specialists: Benjamin S. Bassin, MD, Todd E. Georgia, RRT, Linda J. Stuckey, PharmD.
- A guideline development methodologist: F. Jacob Seagull, PhD, Learning Health Sciences.
- Literature search services were provided by informationists at the Taubman Health Sciences Library, University of Michigan Medical School.

The UMHS endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is made to provide readers with information that might be of potential importance to their evaluation of the information.

No relevant personal financial relationships with commercial entities: Benjamin S. Bassin, MD, Todd E. Georgia, RRT, Rommel L. Sagana, MD, F. Jacob Seagull, PhD, Linda J. Stuckey, PharmD, David H. Wesorick, MD.

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Strategy for Literature Search

Within the Medline (Ovid) database, the following search strategy was used.
1. exp *Pulmonary Disease, Chronic Obstructive/ or (COPD or chronic obstructive pulmonary).ti.
2. Inpatients/ or exp Hospitalization/ or exp Hospital Units/ or (acute or exacerbat* or hospitali* or inpatient*).ti,ab.
3. patient care/ or critical care/ or life support care/ or nursing care/ or perioperative care/ or preoperative care/ or terminal care/ or exp medical staff/ or nursing staff, hospital/ or exp personnel, hospital/ or physicians/ or hospitalists/
4. 2 or 3
5. 1 and 4

Results were limited to English language and 2013 to November, 2014 directly, and literature reviewed through the GOLD guideline (updated 2015), which included literature beginning in 2001.[3] The Main search retrieved 860 references. When the search hedges for Guidelines, Clinical Trials, and Cohort Studies were added, the base results are as follow:

COPD -Guidelines, total results were 13
COPD -Clinical Trials, total results were 215
COPD -Cohort Studies, total results were 167

The MEDLINE In-Process database was also searched using the strategy in the search strategies document. The search retrieved 386 documents. The results with the hedges applied are:

Guidelines, total results were 7
Clinical Trials, total results were 85
Cohort Studies, total results were 114

Within the Cochrane Database of Systematic Reviews, 22 reviews were found using the strategy in the search strategies document.

The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was supplemented with very recent clinical trials known to expert members of the panel. Negative trials were specifically sought. The search was a single cycle.

Level of evidence supporting a diagnostic method or an intervention:

A= systematic reviews of randomized controlled trials
B= randomized controlled trials
C=systematic review of non-randomized controlled trials or observational studies, non-randomized controlled trials, group observation studies (e.g., cohort, cross-sectional, case control)
D= individual observation studies (case or case series)
E =opinion of expert panel.

Search details and evidence tables available at http://www.uofmhealth.org/provider/clinical-care-guidelines.

Recommendations

Guideline recommendations were based on prospective randomized controlled trials if available, to the exclusion of other data; if RCTs were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size. The "strength of recommendation" for key aspects of care was determined by expert opinion.

The strength of recommendations regarding care were categorized as:

I = Generally should be performed
II = May be reasonable to perform
III = Generally should not be performed

Review and Endorsement

Drafts of this guideline were reviewed in clinical conferences and by distribution for comment within departments and divisions of the University of Michigan Medical School to which the content is most relevant: Family Medicine, Internal Medicine, Emergency Medicine, Respiratory Therapy and Pharmacy. The Executive Committee for Clinical Affairs of the University of Michigan Hospitals and Health Centers endorsed the final version.

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Appendix A. COPD Transitional Care Management Clinic

PROGRAM DETAILS

What to expect during your visit?

Our entire team will be available to assist you with the following issues:

Severity of COPD and appropriate treatment:
- We will review with you use of your inhalers and other COPD medications.

Other medical conditions:
- Our tobacco cessation specialist can assist.

Review your need for oxygen or respiratory assist devices:
- If you are using oxygen or a CPAP or BIPAP machine, we will review your needs and assist with any equipment issues that you may have.

Review your ability to exercise:
- We will review your needs and options for physical activity, including need for pulmonary rehabilitation.

Review your emotional and social needs:
- We want to provide the best support possible for you to achieve your overall wellness goals.

HEALTH SYSTEM
UNIVERSITY OF MICHIGAN

COPD Transitional Care Management Clinic

3rd Floor Taubman Center, Reception C
1500 E. Medical Center Dr.
Ann Arbor, MI 48109-5360

Phone: 1-888-284-5864 8am – 5pm
Fax: 734-936-3494

Clinic Appointments: Friday: 7:30 am – Noon

COPD Transitional Care Management Clinic

A Program to Keep You Healthy and Safe at Home

HEALTH SYSTEM
UNIVERSITY OF MICHIGAN

DESIGNED WITH YOU IN MIND

You are being referred to this clinic because you have chronic obstructive pulmonary disease (COPD) and you have recently been discharged from the hospital.

At the University of Michigan we are working to help you control your COPD.

Our goals are to:

- Reduce and control your symptoms
- Increase your physical activity and exercise tolerance
- Educate you about COPD
- Prevent future complications
- Help you breathe easier and be more active

For More Information About the COPD Transitional Care Management Clinic at the University of Michigan
Call 888-284-5864

WE WANT TO HELP

READMISSIONS AFTER DISCHARGE WITH COPD ARE FREQUENT

One of five hospitalized patients with COPD is readmitted within 30 days of their hospital discharge.

Transitioning in and out of the hospital can be a stressful experience. COPD patients face additional challenges:

- COPD patients often use several inhaled medications that may have unique devices for proper medication use.
- COPD patients frequently have other medical problems including including cardiac and renal disease.
- COPD patients often have special nutritional, psychological and physical activity needs.
- When appointments are required with multiple specialists, care coordination can be challenging.

GETTING STARTED

We have designed a new resource, only for COPD patients:

The COPD Transitional Care Management Clinic

In this new Clinic you will be seen by an experienced healthcare team, with participation of Pulmonary Physicians, Nurses, Dietitians, Social Workers, Tobacco Cessations Specialists, and Respiratory Therapists.

After you leave the hospital some things could change. Your treatment may include new drugs, new equipment or even new doctors. We want to help you to navigate that complex environment.

WHAT TO BRING TO OUR CLINIC?

Please bring to our clinic:

- Medications including inhalers
- Friends or family that are part of your support team
- Most importantly, bring us your questions and we will do our best to answer them.

A PROGRAM TO KEEP YOU HEALTHY AND SAFE AT HOME

Appendix B. Example of an Inhaled Medication Patient Education Tool

Protocol for Inpatient Teach to Goal Implementation for Inhaler Education

1. Baseline evaluation
    a. What device/dose do you take at home? How often?
    b. Can you walk me through your technique (verbalize)?
    c. Can you demonstrate (without activation of medication, i.e. pantomime)?
        i. Assess baseline technique via verbalization and pantomime.
        ii. Record baseline score.
2. Correct the issues identified and demonstrate technique to patient (pantomime).
3. Teach-back evaluation
    a. Have patient prepare and administer medication through device.
    b. Assess teach-back technique and record score.
        i. If successful use of device, allow patient to administer 2nd dose (if applicable).
        ii. If unsuccessful attempt, assist patient in dose(s).

- If patient demonstrates correct technique on their device (achieves 100%), continue to assess technique with subsequent treatments and correct issues, if needed.
- If not 100% correct, perform additional teach-back session(s) during subsequent scheduled treatment time(s) until 100% correct or max of 3 sessions completed. Record score when 100% achieved or score at end of 3 sessions. Continue to assess technique with subsequent treatments.
- If successful technique felt unlikely – e.g. dementia – recommend different device or delivery mode (e.g. nebulizer) to team for outpatient regimen.

Metered Dose Inhaler (MDI) Checklist:

Steps taken by patient	**Baseline** Correct – 1 Incorrect – 0	**Teach-back** Correct – 1 Incorrect – 0
Knows correct outpatient medication and dosing schedule		
Verbalizes appropriate technique		
Removes cap of inhaler and spacer (if using spacer)		
Shakes inhaler up and down. Attaches inhaler to back of spacer (if using spacer)		
Breathes OUT fully, away from spacer/inhaler		
Puts spacer mouthpiece (if using spacer) or inhaler mouthpiece into mouth and closes lips		
Activates inhaler by pressing down on canister 1 time		
Breathes IN SLOWLY, filling lungs with medicine		
Holds breath for at least 5 seconds (with or without spacer in mouth)		
Removes spacer/inhaler from mouth before breathing normally		
Breathes normally for at least 30-60 seconds		
Repeats sequence for second puff		
Rinses mouth (if applicable)		

(Modified from: Press et al.: Misuse of Respiratory Inhalers; JGIM 2011)