Vol. 13 No. 2 April-June' 17

Asthma Focus

Management of COPD exacerbations: Recommendation from European Respiratory Society/American Thoracic Society guideline

Key Points

1. WHO estimates show that 235 million people currently suffer from asthma.
2. Asthma deaths will increase in the next 10 years if urgent action is not taken. Asthma cannot be cured, but proper diagnosis, treatment and patient education can result in good asthma control and management.
3. Asthma occurs in all countries regardless of level of development. Over 80% of asthma deaths occur in low and lower-middle income countries. For effective control, it is essential to make medications affordable and available, especially for low-income families.
4. Asthma is a chronic disease characterized by recurrent attacks of breathlessness and wheezing, which vary in severity and frequency from person to person.
5. Symptoms may occur several times in a day or week in affected individuals. For some people the symptoms become worse during physical activity or at night. Failure to recognize and avoid triggers that lead to a tightened airway can be life threatening and may result in an asthma attack, respiratory distress and even death.
6. Through appropriate treatment such as using inhaled corticosteroids to ease bronchial inflammation, the number of asthma-related deaths can be reduced.

Ref: www.who.int/features/factfiles/asthma/asthma_facts/en

The chronic and progressive course of chronic obstructive pulmonary disease (COPD) is often punctuated by “exacerbations”, defined clinically as episodes of increasing respiratory symptoms, particularly dyspnoea, cough and sputum production, and increased sputum purulence. COPD exacerbations have a negative impact on the quality of life of patients with COPD, accelerate disease progression, and can result in hospital admissions and death. Evidence-based clinical practice guidelines have been developed by other organisations that recommend inhaled bronchodilator therapy for patients having a COPD exacerbation, as well as supplemental oxygen for hypoxaemic patients. They also make recommendations related to systemic steroids, antibiotic therapy, noninvasive mechanical ventilation (NIV) and home-based management. The purpose of our guidelines is to update the latter recommendations and to address specific questions regarding the treatment of COPD exacerbations that are not answered by existing guidelines. For the following six questions, we employed a systematic review of the literature followed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to develop treatment recommendations.

1) Should oral corticosteroids be used to treat ambulatory patients who are having a COPD exacerbation?
2) Should antibiotics be used to treat ambulatory patients who are having a COPD exacerbation?
3) Should intravenous or oral corticosteroids be used to treat patients who are hospitalised with a COPD exacerbation?
4) Should NIV be used in patients who are hospitalised with a COPD exacerbation associated with acute or acute-on-chronic respiratory failure?
5) Should a home-based management programme (hospital-at-home) be implemented in patients with COPD exacerbations?
6) Should pulmonary rehabilitation be implemented in patients hospitalised with a COPD exacerbation?

While the focus of this guideline is the treatment of COPD exacerbations; the following questions have also been answered through a narrative supplement.

A. What is the optimal approach to diagnose a COPD exacerbation?
B. What are the conditions to include in the differential diagnosis?
C. What tests are required to assess the severity of a COPD exacerbation?
D. How should a patient be followed during recovery from a COPD exacerbation?

The target audience of this guideline is specialists in respiratory medicine who manage adults with COPD. General internists, primary care physicians, emergency medicine clinicians, other healthcare professionals and policy makers may also benefit from these guidelines. These guidelines provide the basis for rational decisions in the treatment of COPD exacerbations and not to be used as dictates.

SQUARE
PHARMACEUTICALS LTD.
BANGLADESH

Asthma Focus

DIAGNOSIS AND EVALUATION

Optimal approach to diagnose a COPD exacerbation

Diagnosis of an exacerbation is generally based upon an acute worsening of the patient's usual pattern of respiratory symptoms: increased dyspnea, cough, sputum, and/or sputum purulence. There is no validated biomarker of a COPD exacerbation. Respiratory tract infection with bacteria or viruses seems to be the most common cause. Some exacerbations are mild and self-limiting and may not be reported to healthcare professionals, instead being managed by patients at home on their own. Other exacerbations are moderate and severe and require ambulatory treatment and hospitalisation, respectively. The diagnostic evaluation should include an assessment of the severity of the exacerbation. A number of factors should be considered when evaluating the severity of an exacerbation, including the severity of symptoms (particularly dyspnea), the presence of certain clinical signs (cyanosis, increased respiratory effort, and altered mentation), reductions in physical activity tolerance, and the severity of airway obstruction. Not all will be present, but the co-occurrence of several of these symptoms and signs should alert the clinician of a severe exacerbation. The decision about whether or not to refer the patient to a hospital requires that the severity of the exacerbation be considered in the context of the patient's age and preferences regarding intensive therapy, social support and co-morbidities. In some circumstances, other investigations may also help in the decision-making regarding hospitalization or in ensuring that appropriate therapy is provided, such as an assessment of hypoxemia, hypercapnia, electrocardiogram, and spirometry with flow-volume loops. Further research is needed to define the optimal approach to diagnose a COPD exacerbation, including the development and validation of biomarkers.

Conditions to consider in the differential diagnosis

Several conditions may result in symptoms and signs similar to those of a COPD exacerbation or co-occur along with a COPD exacerbation and therefore, should be investigated in patients suspected of having a COPD exacerbation (Table S1).

Table S1: Differential Diagnosis of a COPD exacerbation

Types	Conditions
Infectious	Pneumonia Tuberculosis
Cardiac	Congestive heart failure Ischemic heart disease Cardiac dysrhythmia (e.g., atrial fibrillation with rapid ventricular response, supraventricular tachyarrythmia, bradycardia)
Pleural	Pneumothorax Pleural effusion
Other	Upper airway obstruction Pulmonary embolism Lung cancer Aspiration

These conditions include the following: pneumonia, pulmonary embolism, pneumothorax, pleural effusion, congestive heart failure (i.e., left ventricular failure/pulmonary edema), ischemic heart disease, cardiac dysrhythmia, lung cancer, tuberculosis, upper airway obstruction, and aspiration.

Tests required to assess the severity of an exacerbation

Clinical signs, including limited respiratory effort, cyanosis, and diminished level of consciousness indicate a severe exacerbation. Diagnostic testing may be helpful in patients having a COPD exacerbation (Table S2).

Table S2: Diagnostic tests used to evaluate patients with a possible COPD exacerbation

Diagnostic test	Rationale
Pulse oximetry	Assists in the decision of whether or not to perform arterial blood gases and is useful for adjusting and monitoring supplemental oxygen therapy.
Arterial blood gases	Identifies need for ventilatory support or changes in the level of support using noninvasive or invasive mechanical ventilation; arterial blood gases are also preferred to assess oxygenation over pulse oximetry in cases of suspected methemoglobinemia or carboxyhemoglobinemia.
Chest radiograph	Used to exclude other medical conditions or identify co-existing conditions (e.g., heart failure).
Sputum culture	Useful to identify antibiotic-resistant pathogens in patients whose exacerbation is due to a bacterial infection and has not improved with initial antibiotic therapy.
Blood tests	A whole blood count may identify leukocytosis, polycythemia, or anemia. Biochemical tests may reveal abnormalities associated with COPD or co-morbidities.
Blood tests	May identify coexisting cardiac disease (dysrhythmias, ischemia)
Blood tests	Useful to confirm obstructive lung disease in patients who have never had spirometry or to evaluate possibility of upper airway obstruction in patients with an atypical presentation.

Pulse oximetry may assist in the decision about whether or not to perform arterial blood gas measurements (generally performed if the resting SpO2 is 5% during mild exertion) and is also useful for adjusting and monitoring supplemental oxygen therapy. Arterial or venous blood gases measurement is needed to identify hypercapnia (generally defined as PaCO2 greater than 45 mmHg), which may occur in patients with acute or acuteon-chronic respiratory failure. This can help determine the adequacy of ventilation in spontaneously breathing patients, as well in patients treated with mechanical ventilation. Arterial blood gases measurement has the added advantage of assessing oxygenation.

Asthma Focus

Spirometry is not a routine part of the evaluation or management of a COPD exacerbation because it can be difficult to perform due to patient's symptoms, although one study found that adequate quality spirometry can be obtained in the majority of hospitalized, non-intensive care patients. However, if a patient has never had spirometry confirming airflow obstruction and is not responding to treatment recommendations in this guideline, spirometry with flow volume loops in the acute setting can be useful in excluding alternative diagnoses, including upper airway obstruction. In exacerbations treated in hospital, a chest X-ray can help to exclude other medical conditions. Exacerbations associated with airway bacterial infection usually present with increased sputum purulence. If a bacterial exacerbation does not respond to the initial antibiotic therapy, then a sputum culture with antibiotic sensitivity testing may help guide further therapy. Endotracheal aspiration may also be helpful in hospitalized patients who require invasive mechanical ventilation. Routine culture of sputum for all patients is considered to be of limited benefit, although it is occasionally performed for surveillance of antimicrobial resistance.

Blood tests are routine in hospitalized patients or patients with severe disease. Whole blood count may reveal increased total white blood cells count, polycythemia, or anemia. Biochemical tests (electrolytes, glucose, creatinine, urea, D-dimer) may reveal abnormalities associated with COPD exacerbation and/or co-morbidities that could contribute to a more severe COPD exacerbation. An electrocardiogram (ECG) or biomarkers of myocardial injury (e.g., serum troponin levels, creatine kinaseMB), chest computerized tomography with intravenous contrast for pulmonary embolism, echocardiography, and/or thoracic ultrasound may identify conditions that could contribute to a more severe COPD exacerbation or mimic a COPD exacerbation. Further research is needed to define the optimal approach for assessing the severity of COPD exacerbations, as well as tests needed to identify co-occurring conditions in patients with COPD exacerbations.

Follow-up during recovery from a COPD exacerbation

It is important to monitor the response of a COPD exacerbation to treatment, but the optimal approach for individual patients is not well understood. Regular assessment of clinical symptoms and signs, as well as observation of the patient's functional capacity can help identify the need for treatment intensification for COPD, complications of therapy (e.g., diarrhea), or the presence of additional cooccurring conditions. Pulse oximetry should be used to monitor the recovery of patients with hypoxemic respiratory failure, whereas arterial blood gas measurements should be used to monitor the recovery of patients with respiratory failure who are hypercapnic and/or acidotic until they are stable. In their clinical practices, most of the guideline panel members follow the oxygenation of patients who are hypoxemic during an exacerbation for the initial three months following discharge to determine whether or not there are indications for initiating, continuing, or discontinuing long-term oxygen therapy at home. Daily monitoring of pulmonary function tests should not be performed during recovery from a COPD exacerbation. Recent data suggest that patients hospitalized for COPD exacerbation are at less risk for rehospitalisation if an outpatient evaluation occurs early in the post hospitalization period (8). Patients with exacerbations treated in the community are likely to require similar follow up to ensure improvement. Further research is needed to define the optimal approach for follow-up in patients recovering from a COPD exacerbation.

Managing Exacerbations

Should oral corticosteroids be used to treat patients whose COPD exacerbation is mild enough to be treated as an outpatient?

The Task Force identified four outcomes a priori as critical to guiding treatment recommendations: treatment failure (composite of unscheduled visit to the physician, return to the emergency department because of worsening respiratory symptoms, hospitalisation or unmasking of study medication due to worsening respiratory symptoms), hospital admissions, mortality and time to next COPD exacerbation. Change in quality of life and serious adverse events were considered “important” outcomes to guide treatment recommendations.

Data from three trials identified in systematic review were pooled via meta-analysis where oral corticosteroids caused a trend toward fewer hospital admissions (7.9% versus 17%; relative risk (RR) 0.49, 95% CI 0.23-1.06). There was no significant difference in treatment failure (26.5% versus 42.4%; RR 0.69, 95% CI 0.22-2.19) or mortality (1.1% versus 1.1%; RR 0.99, 95% CI 0.06-15.48). The effect on treatment failure would be clinically important if real, but there were too few events to confirm or exclude the effect and the analysis was limited by severe heterogeneity of uncertain cause, as sensitivity analyses failed eliminate the heterogeneity. Data regarding length of hospital stay or time to next exacerbation were not reported in the three studies. Patients who received oral corticosteroids had better lung function, measured as the FEV1 (mean difference 0.16 L higher, 95% CI 0.04-0.28 L higher) but no significant difference in quality of life measured by the Chronic Respiratory Questionnaire score (mean difference 0.38 higher, 95% CI 0.09 lower to 0.85 higher) or serious adverse effects (2.2% versus 1.1%; RR 1.97, 95% CI 0.18-21.29).

Benefits: Oral corticosteroids improved lung function in ambulatory patients having a COPD exacerbation. There was also a trend toward fewer hospitalisations.

Harms: Various adverse effects were reported in the studies, including seizures, insomnia, weight gain, anxiety, depressive symptoms and hyperglycaemia. However, it is unclear whether the methods used to assess harms were similar across the studies and there were too few serious adverse events reported

Asthma Focus

to adequately evaluate the difference in the risk of harms with oral corticosteroids versus placebo in patients with COPD exacerbations treated in the ambulatory setting.

Other considerations: There was no information in any of the trials regarding the time to next exacerbation and inadequate information to have confidence regarding the effects of systemic corticosteroids on several outcomes considered critical or important to decision making (hospitalisation, mortality and serious adverse events).

Conclusions: A course of oral corticosteroids for 9-14 days in outpatients with COPD exacerbations improves lung function and causes a trend toward fewer hospitalisations. No effect on treatment failure, mortality or adverse effects has been demonstrated, although there were too few events in the trials to definitively confirm or exclude an effect on any of these outcomes. The Task Force judged that the benefits of oral corticosteroids probably outweigh the adverse effects, burdens and costs, but was uncertain due to its very low confidence in the accuracy of the estimated effects.

Recommendation from other Guidelines: The 2010 NICE guidelines concluded that, in the absence of significant contraindications, oral corticosteroids should be used in conjunction with other therapies in all patients admitted to hospital with an exacerbation of COPD and considered in patients in the community who have an exacerbation with a significant increase in breathlessness that interferes with daily activities. The 2014 Global Initiative for Chronic Obstructive Lung Disease (GOLD) strategy document concluded that "systemic corticosteroids are beneficial in the management of COPD. They shorten recovery time, improve lung function and hypoxemia, and may reduce the risk of early relapse, treatment failure, and length of hospital stay. A dose of 30-40 mg prednisone per day for 5 days is recommended". For ambulatory patients with an exacerbation of COPD, ERS/ATS recommendation suggests a short course (_14 days) of oral corticosteroids (conditional recommendation, very low quality of evidence).

Recommendation from the Task Force: A short course of oral corticosteroids as14 days.

Should antibiotics be administered to ambulatory patients who are having a COPD exacerbation?

The Task Force identified a priori six outcomes as critical to guiding treatment recommendations: treatment failure (composite of death, no resolution or deterioration), adverse events, time to next COPD exacerbation, hospitalisation, length of hospital stay and death. Among the trials that were pooled, one randomly assigned 310 ambulatory patients who were having a COPD exacerbation to receive placebo or amoxicillin/ clavulanate for 8 days, while the other randomly assigned 116 similar patients to receive placebo or any one of the following for 7-10 days: trimethoprim/ sulfamethoxazole, amoxicillin or doxycycline. Antibiotic therapy decreased treatment failure (27.9% versus 42.2%; RR 0.67, 95% CI 0.51-0.87); this effect was driven entirely by lack of resolution and deterioration, since no deaths were reported. It also prolonged the time to the next exacerbation (difference of medians 73 days, p=0.015). There was a trend toward more adverse events among patients who received antibiotic therapy (14.6% versus 7.9%; RR 1.84, 95% CI 0.95-3.57), although most of the adverse events were described as mild. Data regarding hospitalisation, length of hospital stay and death were not reported.

Benefits: Antibiotic therapy reduced the risk of treatment failure and increased the time between COPD exacerbations.

Harms: Patients who received antibiotic therapy had a trend toward more adverse events, most of which were mild gastrointestinal side effects (e.g. diarrhoea).

Other considerations: In this evaluation of ambulatory exacerbations, there was no information in either trial about several outcomes of interest to the Task Force; specifically, the hospital admission rate, length of hospital stay and mortality.

Conclusions: The use of antibiotics in ambulatory patients with exacerbations of COPD reduces the treatment failure rate and increases the time to the next exacerbation. However, the majority of patients avoided treatment failure even in the placebo group (58%), suggesting that not all exacerbations require treatment with antibiotics. Effectiveness studies should be conducted in real-life situations to confirm the findings of efficacy trials. Identifying biomarkers of bacterial infection may allow the patient population that definitively requires antibiotic treatment to be more precisely selected. Additional research is needed to identify patients in whom antibiotic therapy is needed.

Other considerations: There was no information in either trial **Should NIV be used in patients who are hospitalised with a COPD exacerbation associated with acute or acute-on-chronic respiratory failure?**

The Task Force identified a priori five outcomes as critical to guiding treatment recommendations: death, intubation, length of hospital stay, length of ICU stay and nosocomial pneumonia. Complications of treatment (e.g. aspiration or barotrauma) and pH 1 h after intervention were considered important outcomes. All of the trials enrolled hospitalised patients with respiratory failure due to a COPD exacerbation. In the overwhelming majority of the studies, the patients had confirmed acute or acute-on-chronic hypercapnic respiratory failure; a few of the studies did not specify that the respiratory failure was hypercapnic. Most the trials compared usual care plus NIV to usual care alone, although a few assigned patients to usual care plus NIV or usual care plus sham NIV. Due to the nature of the intervention, most of the trials were not blinded to the patients, caregivers or assessors. When the trials were pooled via meta-analysis (evidence profile 4 in the supplementary material), patients who received NIV had a lower mortality rate (7.1% versus 13.9%; RR 0.54, 95% CI 0.38-0.76), were less

likely to require intubation (12% versus 30.6%; RR 0.43, 95% CI 0.35-0.53), had a shorter length of hospital stay (mean difference 2.88 days fewer, 95% CI 1.17-4.59 days fewer) and ICU stay (mean difference 4.99 days fewer, 95% CI 0-9.99 days fewer) and had fewer complications of treatment (15.7% versus 42%; RR 0.39, 95% CI 0.26-0.59). There was no difference in the pH after 1 h (mean difference 0.02, 95% CI 0.01-0.06). When we repeated the analyses using only the studies that had confirmed acute or acute-on-chronic hypercapnic respiratory failure, the results were essentially the same.

Benefits: NIV reduced the need for intubation, mortality, complications of therapy, and length of both hospital stay and ICU stay in patients with acute or acute-on-chronic respiratory failure due to a COPD exacerbation.

Harms: There were no reports of adverse consequences; to the contrary, complications of therapy were reduced in patients who received NIV.

Other considerations: Most of the trials had a serious risk of bias due to uncertain allocation concealment and lack of blinding. For some outcomes, the estimated effects were inconsistent across studies or the number of events and patients were small, diminishing confidence in the estimated effects. Similarly, one of the outcomes of interest, the rate of nosocomial pneumonia, could not be assessed because the data were either not reported or incompletely reported. These considerations contributed to grading the quality of evidence as low.

Conclusions and research needs: Use of NIV in patients with acute or acute-on-chronic respiratory failure due to a COPD exacerbation reduces the need for intubation, mortality, complications of therapy, length of hospital stay and length of ICU stay. Future research will determine strategies for optimising the delivery of NIV, including the optimal technique and interface type selection. We need studies to address how to titrate and wean patients from NIV ventilation and how to better determine which physiological effects should be expected during the application of NIV that predict treatment success or failure.

The efficacy of home NIV in patients following a COPD-related hospitalisation when NIV was utilised to treat acute-on-chronic respiratory failure is also an area that requires additional study. Recent data have reported conflicting outcomes regarding home NIV in the severe COPD outpatient population. Effectiveness studies should be conducted in real-life situations to confirm the findings of efficacy trials. Other research opportunities are related to decision-making about whether or when to intubate or not, as well as the use of NIV by healthcare providers, patients and family members.

Recommendation from other guidelines: The 2010 NICE guidelines did not discuss the use of NIV in COPD exacerbations. In the 2004 NICE guidelines, however, it was stated that NIV should be used as the treatment of choice for persistent hypercapnic ventilatory failure during exacerbations despite optimal medical therapy. The 2014 GOLD strategy document states that, in patients with acute respiratory failure due to a COPD exacerbation, NIV improves respiratory acidosis and decreases the intubation rate, mortality, respiratory rate, severity of breathlessness, complications (e.g. ventilator-associated pneumonia) and length of hospital stay.

They recommend the use of NIV in patients with 1) respiratory acidosis or 2) severe dyspnoea with clinical signs suggestive of respiratory muscle fatigue, increased work of breathing, or both, such as use of respiratory accessory muscles, paradoxical motion of the abdomen or retraction of the intercostal spaces. For hospitalised patients with acute or acute-on-chronic hypercapnic respiratory failure due to a COPD exacerbation, ERS/ATS recommend the use of NIV (strong recommendation, low quality of evidence).

Taskforce recommendation: The strong recommendation despite the panel's low confidence in the estimated effects reflects the panel's consensus opinion that the overwhelming majority of patients would want NIV given the possibility of one or more important clinical benefits with minimal risk of harm. Many of the trials excluded patients with any of the following: inability to cooperate, protect the airway or clear secretions; severely impaired consciousness; facial deformity; high aspiration risk; or recent oesophageal stenosis.

Should a home-based management programme (hospital-at-home) be implemented in patients with COPD exacerbations?

A home-based management programme involving nurses and potentially other healthcare professionals (e.g. physicians, social workers and physical therapists), also known as “hospital-at-home”, offers the option of an early assisted hospital discharge or an alternative to hospitalisation in patients presenting to the emergency department with a COPD exacerbation. Clinical trials have compared home-based management to usual care in patients with COPD exacerbations who meet other additional eligibility criteria (e.g. no impairment of consciousness, decompensated heart failure or other acute condition or need for mechanical ventilation).

The Task Force identified a priori three outcomes as critical to guiding treatment recommendations: death, hospital readmission and time to first readmission. Hospital-acquired infections and quality of life were considered important outcomes. When the trials were pooled via meta-analysis (evidence profile 5 in the supplementary material), home-based management reduced hospital readmissions (26.8% versus 34.2%; RR 0.78, 95% CI 0.62-0.99) and was associated with a trend towards lower mortality (5.6% versus 8.5%; RR 0.66, 95% CI 0.41-1.05). There was no difference in the time to first readmission (mean difference of 8 days longer among patients in the home-based management group, 95% CI 19.7 days longer to 3.7 days shorter). No data were reported on hospital-acquired infections or quality of life.

Asthma Focus

Benefits: Utilisation of a home-based management model reduced the number of hospital readmissions and, possibly, mortality in patients with COPD exacerbations.

Harms: Adverse events were not an outcome reported in any of the included trials; therefore, there exists no data regarding the potential harms of the home-based management model.

Other considerations: For most of the outcomes, the number of events and patients in the trials were small, diminishing confidence in the estimated effects. There was no information reported for one outcome of interest to the Task Force, the rate of hospital-acquired infections.

In addition, there was insufficient information to draw conclusions regarding another outcome of interest, quality of life (i.e. among the three trials that reported quality of life, one did not provide standard deviations, another only provided St George's Respiratory Questionnaire scores for a subgroup of participants and a third measured generic health-related quality of life using the EuroQoL-5D scale). Moreover, the eligibility criteria varied across studies and the capacity of health systems to deliver home-based care for this population may vary. There is also a large geographical variability in their availability. Studies are also needed to identify the components of home-based COPD care required for benefit and how such requirements may vary based on the variable contexts in which patients live.

Conclusions and research needs: The home-based management programme model in patients with a COPD exacerbation reduces hospital admissions, making it a safe and effective way of discharging patients with additional home-based support in appropriately selected patients. This may increase the availability of hospital beds and reduce pressure on clinicians to discharge patients whose readiness is uncertain. The home-based model might also reduce mortality; however, there were too few deaths in the trials to definitively confirm or exclude an effect.

One of the major research needs for home-based management is the development of algorithms to screen patients to determine which are or are not appropriate for home-based care. Some studies suggest that home treatment of COPD exacerbations should be considered in all patients unless there are mental status changes, confusion, hypercarbia, refractory hypoxaemia, serious comorbid conditions or inadequate social support. However, these criteria need to be evaluated prospectively to define the most appropriate selection criteria.

The feasibility of home-based administration of medications for COPD exacerbations (i.e. systemic corticosteroids, antibiotics, nebulised bronchodilators and supplemental oxygen) may vary by patient characteristics (e.g. ability to carry out activities of daily living and level of social support) or by the capacity of the health system or home health agency. Studies are needed to define the patient selection criteria and key elements of the home-based programme (e.g. nurse or inter-professional teams that include a physician, respiratory therapist or social worker; treatment plan at home; criteria for treatment failure at home; and need for hospitalisation). Finally, studies are needed to prospectively evaluate the potential for heterogeneity of treatment effects according to whether the home-based management programme is intended to avoid a hospitalisation or to facilitate early discharge from the hospital to home. Many of these studies may be best conducted as effectiveness studies in real-life situations; at a minimum, effectiveness studies should be conducted to confirm the findings of efficacy trials.

Should pulmonary rehabilitation be implemented in patients hospitalised with a COPD exacerbation?

The Task Force identified a priori three outcomes as critical to guiding the formulation of treatment recommendations: death, hospital readmission and quality of life. Exercise capacity was considered an important outcome. Pooling the trials via meta-analysis (evidence table 6) suggested that pulmonary rehabilitation following admission for an exacerbation may have reduced hospital readmissions (45.0% versus 50.8%; RR 0.65, 95% CI 0.42-1.00), improved quality of life as measured by a change in the St George's Respiratory Questionnaire score (mean difference -11.75, 95% CI -19.76 to -3.75) and improved exercise capacity as measured by the 6-min walking test (mean difference +88.89 m, 95% CI +26.67 m to +151.11 m).

However, these estimates were uncertain due to inconsistent results for across trials (I2 =69% for hospital readmissions, I2 =70% for quality of life and I2 =97% for exercise capacity). With respect to mortality, we excluded one trial from the mortality analysis because the panel decided that its measurement of deaths in the ICU was potentially misleading; when the remaining trials were pooled, there was no significant difference among those who did or did not receive pulmonary rehabilitation (19.6% versus 14.1%; RR 1.44, 95% CI 0.97-2.13; I2 =0% for mortality).

Four of the trials evaluated adverse outcomes, three of which detected none. The remaining trial reported that six (19%) out of 32 patients had at least one adverse event (two events occurred in two patients in the control group, whereas 11 events occurred in four patients in the exercise groups). Only one of these adverse events was considered to be serious; a patient in one of the experimental groups had an episode of atrial fibrillation with accompanying chest pain.

Benefits: Pulmonary rehabilitation initiated during hospitalisation increased exercise capacity. Pulmonary rehabilitation initiated within 3 weeks following discharge reduced hospital readmissions and improved quality of life. Pulmonary rehabilitation initiated within 8 weeks following discharge increased exercise capacity.

Harms: Pulmonary rehabilitation initiated during hospitalisation increased mortality. Other serious adverse events occurring during pulmonary rehabilitation were rare.

Asthma Focus

Other considerations: The reliability of the estimated effects for all outcomes other than mortality is limited by inconsistency across trials in both the primary analysis and the stratified analysis. In addition to inconsistency, confidence in the estimated effects for all other outcomes was reduced because all of the trials had a risk of bias due to uncertain allocation concealment, lack of adherence to the intention-to-treat principle and/ or lack of blinding.

Conclusions and research needs: Pulmonary rehabilitation implemented during hospitalisation increases mortality. Pulmonary rehabilitation implemented within 3 weeks after discharge following a COPD exacerbation reduces hospital admissions and improves quality of life, while pulmonary rehabilitation implemented within 8 weeks after discharge increases exercise capacity. Research is needed to identify the interventions that provide the greatest benefits; some studies suggest that a combination of regular exercise with breathing technique training may be best, but additional investigations are needed. Studies employing methodologies of implementation science (also known as knowledge translation) are needed to test strategies that systematically target barriers and facilitators of integrating pulmonary rehabilitation into the care of patients with COPD exacerbations after hospital discharge.

Recommendation from other guidelines: The 2010 NICE guidelines concluded that "pulmonary rehabilitation should be made available to all appropriate people with COPD including those who have had a recent hospitalization for an acute exacerbation". ERS/ATS recommendations for patients who are hospitalised with a COPD exacerbation is the initiation of pulmonary rehabilitation within 3 weeks after hospital discharge (conditional recommendation, very low quality of evidence). For patients who are hospitalised with a COPD exacerbation, ERS/ATS suggest not initiating pulmonary rehabilitation during hospitalisation (conditional recommendation, very low quality of evidence).

Remarks from task force: Early pulmonary rehabilitation refers to a programme that consists of physical exercise and education, which begins within 3 weeks of the start of treatment of the exacerbation.

Summary: The Task Force utilised comprehensive evidence syntheses to inform its judgments regarding the balance of benefits versus burdens, adverse effects and costs; the quality of evidence; the feasibility; and the acceptability of various interventions for COPD exacerbations. A strong recommendation was made for NIV in patients with acute hypercapnic respiratory failure. Conditional recommendations were made for oral corticosteroids in outpatients, oral rather than intravenous corticosteroids in hospitalised patients, antibiotic therapy, home-based management of appropriately selected patients, and initiation of pulmonary rehabilitation within 3 weeks of hospital discharge (table 1). A conditional recommendation was made against the initiation of pulmonary rehabilitation during hospitalisation. The systematic review and GRADE methodology we employed for this ERS/ATS guideline indicated, in several instances, a sparse evidence base. In such cases, we recommend more definitive studies. These recommendations should be reconsidered as new evidence becomes available.

TABLE 1 Recommendations for the treatment of chronic obstructive pulmonary disease (COPD) exacerbations

	Recommendation	Strength	Quality of evidence
1	For ambulatory patients with an exacerbation of COPD, we suggest a short course (<14 days) of oral corticosteroids	Conditional	Very low
2	For ambulatory patients with an exacerbation of COPD, we suggest the administration of antibiotics	Conditional	Moderate
3	For patients who are hospitalised with a COPD exacerbation, we suggest the administration of oral corticosteroids rather than intravenous corticosteroids if gastrointestinal access and function are intact	Conditional	Low
4	For patients who are hospitalised with a COPD exacerbation associated with acute or acute-on-chronic respiratory failure, we recommend the use of noninvasive mechanical ventilation Strong Low	Conditional	Low
5	For patients with a COPD exacerbation who present to the emergency department or hospital, we suggest a home-based management programme (hospital-at-home) Conditional Moderate	Conditional	Moderate
6	For patients who are hospitalised with a COPD exacerbation, we suggest the initiation of pulmonary rehabilitation within 3 weeks after hospital discharge Conditional Very low	Conditional	Very low
7	For patients who are hospitalised with a COPD exacerbation, we suggest not initiating pulmonary rehabilitation during hospitalisation	Conditional	Very low

Reference : *European Respiratory Journal 49.3 (2017): 1600791*

Vol. 13 No. 2 April-June' 17

Asthma Focus

Congratulations!!!

The Winners of Asthma Focus Quiz Competition

Vol. 13 No. 1

1. **Dr. Bashir Ahmed**
   MBBS, DTCD, MD
   Professor, NIDCH
   Mohakhali Dhaka
2. **Dr. R. C. Bormon**
   MBBS, DTCD
   Samorita Private Hospital
   Faridpur
3. **Dr. Md Annaz Mus Sakib**
   MBBS, D-Card
   Assistant Professor
   National Medical College, Dhaka
4. **Dr. Anisur Rahman Rasel**
   MBBS, FCPS (Part-2)
   Medical Officer, Department of Pediatrics
   Comilla Medical College
5. **Dr. Wasim Hossain**
   MBBS, DTCD
   Sapla Diagnostic Centre
   Laxmipur, Rajshahi

Editorial Note

Dear Doctor,

We are happy to present you the 2nd issue of "Asthma Focus" Newsletter, 2017. In this issue we have concentrated 'Management of COPD exacerbations: Recommendation from European Respiratory Society/ American Thoracic Society guideline'. We hope you will enjoy reading the publication!

We appreciate your comments and queries.

Please participate in Quiz competition & win prizes.

For further information: **Product Management Department,** Square Centre, 48 Mohakhali C/A, Dhaka-1212, ***web :*** www.squarepharma.com.bd
Production by: RainsCom, Cell: 01715380902, e-mail: rains.com2013@gmail.com