Review

Non-Pharmacological Management of Chronic Obstructive Pulmonary Disease

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INTRODUCTION:

Chronic Obstructive Pulmonary Disease (COPD) is the most common lung disease in the world¹. It accounts for the highest rate of hospital admissions among major chronic illnesses in Canada and is currently the fourth leading cause of death in the world2. By 2020, it is expected to be the third leading cause of death in the world³. Given its overwhelming prevalence in society, it carries with it a significant economic, social and personal burden. The key to decreasing the burden of COPD is modification of environmental exposures, including domestic, industrial, vehicular and personal tobacco exposure. Risk factor modification, including smoking cessation may be more powerful than aggressive testing strategies. Currently, the focus of treatment is appropriate bronchodilator therapy; however, non-pharmacological management must not be forgotten. Much like bronchodilator therapy, non-pharmacological therapy provides symptomatic improvement and better quality of life. In fact, some of the non-pharmacologic strategies, such as smoking cessation and long term oxygen, can prolong life expectancy, a feat that pharmacological therapies have yet to achieve.

COPD is characterized by incompletely reversible airflow limitation⁴ and is often associated with a smoking history and increasing age. Because of its insidious onset and the non-specific nature of its symptoms (cough, slow and progressive dyspnea), the effects of COPD are not often noticed until years after the disease has begun. This often leads to the diagnosis of COPD in the advanced stages, limiting interventions and treatment options⁵.

It has been shown by Tantucci et al that the most rapid decline in lung function occurs early in the disease course, particularly GOLD Stages II and III⁶. Thus, early diagnosis and intervention is essential to try and prevent rapid decline in FEV1. Aggressive testing strategies, smoking cessation efforts, and initiation of treatments may be beneficial during these early stages⁷⁻¹⁰. Because patients do not often perceive symptoms of early or worsening disease, or they attribute them to deconditioning and increasing age, primary care providers need to screen those at risk for COPD and be sure to ask patients about their symptoms at routine visits¹¹.

Smoking is the leading risk factor for the development of

COPD⁵ and is a key component on history that should trigger further questioning to elucidate symptoms suggestive of this disease. The GOLD Strategy suggests that COPD should be suspected in anyone over the age of forty, who has dyspnea, chronic cough or sputum production with appropriate risk factors. Risk factors include a family history of COPD, tobacco exposure, exposure to cooking or home heating fuels or occupational dusts/chemicals² (Table 1).

Table 1:

Key indicators that increase the pre-test probability of COPD

Indicators:	Description:	
Dyspnea	Progressive	
	Worse with exercise	
	Persistent	
Chronic Cough	May be intermittent and may be non-productive	
Chronic Sputum	Any pattern of sputum production	
Exposures	Tobacco smoke	
	Exposure to home cooking or home heating fuels	
	Occupational dusts/chemicals	

Once a patient has been identified as having symptoms and risk factors suggestive of COPD, formal diagnosis is of the utmost importance. The gold standard for the diagnosis of COPD is based on spirometry. Given that COPD is characterized by airflow limitation that is not fully reversible, spirometry will demonstrate a post-bronchodilator FEV1/FVC of <0.7. The severity of COPD is largely based on FEV1 and differs according to different guidelines (GOLD vs ATS) (Table 2) However, given the heterogeneity of symptoms for

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a given FEV1, GOLD has developed groups A, B, C, D which help categorize severity based on multiple factors, including FEV1, number of exacerbations and level of symptoms based on MRC dyspnea scale or CAT score².

Table 2: Spirometric Classification of COPD

	GOLD	ATS
Mild	FEV1 ≥ 80%	FEV1 ≥ 70%
Moderate	FEV1 50% - 79%	FEV1 60-69%
Moderately Severe	-	FEV1 50-59%
Severe	FEV1 30-49%	FEV1 35-49%
Very Severe	FEV1 <30%	FEV1 <35%

Once COPD has been diagnosed, the focus must switch to decreasing the rate of decline in lung function including modification of risk factors and management of symptoms. These goals are achieved by both pharmacological and non-pharmacological therapy. The mainstay of pharmacological therapy is bronchodilators, while non-pharmacological methods include smoking cessation, pulmonary rehabilitation, immunizations and long term oxygen among others. While physicians are good at initiation of bronchodilator therapy, non-pharmacologic management is often forgotten despite these modalities providing symptomatic improvement and mortality benefits. This article will focus on non-pharmacological interventions and their beneficial impact on those with COPD.

SMOKING CESSATION

Smoking is known to be the largest risk factor to contribute to the development of COPD in susceptible hosts. Therefore, smoking cessation is of the utmost importance in halting the progression of lung function decline and should be implemented as soon as a diagnosis is made, particularly when COPD is diagnosed in the early stages. This is one of the few interventions that have been shown to have a mortality benefit. The Lung Health Study demonstrated that participants with mild to moderate COPD who stopped smoking experienced an improvement in FEV1 in the year after quitting and had a subsequent rate of decline in FEV1 that was half the rate of decline among continued smokers. This was comparable to never smokers¹². In addition, smoking cessation, regardless of severity of lung disease, has been shown to have a mortality benefit¹³, secondary to the reduction in cardiovascular and lung cancer mortality¹⁴.

While complete cessation and abstinence have shown a decreased rate of decline in FEV1, reduction in the amount of cigarettes smoked per day or intermittent quitting did not achieve the same rate of decline in FEV1 achieved in those with complete and sustained cessation, unless the percent reduction was very marked (>85%)¹⁴. This re-emphasizes the need for complete and sustained cessation.

The benefits of smoking cessation are clear, however, the rates of success among current smokers in maintaining a smokefree lifestyle are still low. A large proportion of moderate to severe COPD patients continue to smoke, ranging from 30.4% to 43.0%¹⁵⁻¹⁷ despite having to live with the symptoms and limitations of COPD. The difficulty in smoking cessation is attributed to nicotine, which is the addictive drug in tobacco. Nicotine leads to the release of dopamine which is a key mediator of pleasure and reward and the foundation for the addiction¹⁸. In addition to nicotine itself, smoking is situational and occurs socially. Therefore, both the nicotine dependence and conditioned behaviours must be overcome to successfully quit smoking.

When dealing with smoking cessation, it is best to think of it in itself as a chronic disease. The goal is abstinence and the reality is that there will be relapses along the way and patients will often have several attempts before successfully quitting. Seventy-five percent of Americans wish to quit, yet only 3% achieve prolonged abstinence in a given year 18 . In order to improve the success rate, pharmacological therapy is often required. There are many different modalities to facilitate and maintain smoking cessation. We briefly review each modality here:

Communication: At each visit, a physician should ask the patient about their smoking habits, their willingness or desire to quit and advise smokers to stop. Information on both the pharmacological and non-pharmacological options for smoking cessation should be provided to patients¹⁹. It has been demonstrated that patients advised to quit by a physician had more attempts and were more successful at smoking cessation¹⁹. Patients with spirometric evidence of COPD who had these results communicated to them, they have a higher rate of smoking cessation when compared to smokers who do not have COPD^{20,21}. Therefore, at each visit, the physician should communicate the risks of smoking, benefits of cessation and modalities available to facilitate quitting.

Nicotine Replacement Therapy (NRT): NRT has a 2 fold increase in smoking cessation rates when compared to placebo¹⁸. The goal of NRT is to provide the patient with the addictive nicotine without using the harmful tobacco, facilitating avoidance from cigarettes. There are many formulations, including gum, lozenge, transdermal patch, inhaler and a nasal spray. The transdermal patch is the preferred method, as it has the most reliable and steady delivery of nicotine. The oral forms have variable absorption depending on how quickly or long one chews, if saliva is swallowed quickly and if acidic beverages are consumed in close proximity to the use of the oral NRTs²³. Side effects of all forms include insomnia and disturbing dreams. For the transdermal patch, this can be overcome by wearing the patch during the day and removing it at bedtime, however, this may lead to a stronger craving for a cigarette in the morning as the blood nicotine levels will be low. The nicotine inhaler, despite providing less systemic absorption of nicotine, is beneficial for those with conditioned behaviours leading

	Benefits vs Placebo	Optimal Dose	Side Effects	Combination vs Single Agent Therpay
Nicotine Replacement Therapy (NRT)	2 fold increase in smoking cessation compared to placebo	Depends on amount of cigarettes smoked/ day at quit date	Insomnia, disturbing dreams, nasal irritation(for nicotine nasal sprays)	Combination long and short acting NRT more successful than single agent
Bupropion	2 fold increase in smoking cessation compared to placebo	150mg po bid x 7-12weeks	Insomnia, lowers seizure threshold, suicidal thoughts/ actions	Bupropion + NRT more successful than either agent alone
Varenicline	2-4 fold increase in smoking cessation compared to placebo	1mg po bid x 12 weeks	Insomnia, depression, suicidal thoughts/ actions, disturbing dreams, GI side effects	Conflicting data on superiority of varenicline + NRT vs varenicline alone
E-cigarettes	Unclear at present time, further studies required	N/A	Unregulated	N/A

Table 3: Smoking Cessation Therapies

to smoking. Nicotine nasal sprays have the most rapid absorption however have side effects of nasal irritation. Combination of short and long acting nicotine replacement is the preferred method, allowing for a steady baseline level of nicotine with the transdermal patch and rapid peaks with the short acting formulations. Combination NRT is associated with higher abstinence rates than single NRT formulations, with a smoking cessation rate of 31.5% for combination NRT compared to 17.6% for single agent NRT [24].

- a) Bupropion: Bupropion is an antidepressant that has been shown to nearly double quit rates when compared to placebo (19.1% vs 10.6%)²⁴ and results are similar when specifically looked at in the COPD population (16% bupropion vs 9% placebo)²². The dose of choice is 150mg po bid and bupropion exerts its effects by potentiating dopaminergic and noradrenergic signaling. This helps to reduce craving and attenuate withdrawal symptoms²⁵. Insomnia is the greatest side effect. Bupropion also lowers the seizure threshold and is therefore contraindicated in patients with seizure history or increased risk for seizure activity. The combination of bupropion plus NRT is more effective than either agent alone.
- b) Varenicline: Varenicline is one of the more effective smoking cessation agents, with an abstinence rate of 27.6% vs 10.6% for placebo, 19.1% for bupropion and 17.6% for single agent NRT²⁴. This drug reduces withdrawal symptoms as it is a partial agonist of the nicotinic receptor. It also reduces the rewarding and reinforcement effects of nicotine. Side effects associated with its use include gastrointestinal intolerance, insomnia, visual disturbances and this drug carries a black box warning given its possibility to cause neuropsychiatric symptoms including depressed mood, suicidal thoughts or actions¹⁸.
- c) Electronic Nicotine Delivery Systems "E-cigarettes": Electronic cigarettes (e-cigarettes) are battery-powered devices that deliver nicotine in an aerosolized form²⁶. They come in a variety of brands and flavours. Companies claim that e-cigarettes are less harmful than conventional cigarettes, can be used where one cannot smoke and that they are an effective quitting aid²⁷. These claims and the ease of acquisition through online internet sites, has led to increased popularity of e-cigarettes among cigarette smokers that are attempting to quit. E-cigarettes, however, are largely unregulated and are of unknown safety²⁸. Their role in smoking cessation has not yet been determined. There are only a few studies looking at the e-cigarette in smoking cessation. These studies have suggested there may be a role for their use in smoking cessation, however, they are small studies and have methodological issues. In a few randomized controlled trials, no statistical difference was found in smoking cessation rates between e-cigarettes, nicotine patch and placebo e-cigarette group²⁹. In the cross sectional analysis by Brown et al, e-cigarette users were more likely to report abstinence than those who used NRT bought over the counter or no aid at all³⁰. The controversy on the use of e-cigarettes is evident even between various respiratory societies. While the Forum on International Respiratory Societies (FIRS) has recently published a position statement stating that e-cigarettes should be restricted or banned until more information about their safety is available³¹, Public Health England (PHE), while acknowledging potential harms and the need for further data, state that the opportunity to utilize this technology into current smoking cessation paradigms should not be missed³². Therefore, while there may be role for e-cigarettes in smoking cessation, larger randomized controlled trials are needed to confirm these results. At

the present time, it is recommended to use FDA approved pharmacotherapy as first-line treatment.

IMMUNIZATION

It is known that in patients with COPD, exacerbations lead to a more rapid decline in lung function, increased morbidity and mortality. In addition, because of the limited number of therapies available to treat exacerbations, prevention is important. Vaccinations are one way to reduce exacerbations. It has been demonstrated that inactivated influenza vaccines in COPD patients resulted in a significant reduction in the total number of exacerbations per vaccinated subject compared with those who received placebo³³. Wongsurakiat et al described an absolute 21.3% reduction in the incidence of acute respiratory illness following influenza vaccination³⁴.

Pneumococcal vaccination is currently recommended in the NICE guidelines to be given in addition to annual influenza vaccination in people with COPD³⁵. However, the evidence supporting the use of the pneumococcal vaccine is not as robust as for influenza. The studies completed were retrospective and included elderly persons with any form of chronic lung disease, not just COPD. In this population, Nichol et al found a reduction in the number of hospitalizations for pneumonia, fewer deaths and lower health care costs in those who had received the pneumococcal vaccine³⁶. Those who had received both pneumococcal and influenza vaccines had further reduction in hospitalization rates and death rates compared to those who had only received one of the two vaccinations³⁶.

PULMONARY REHABILITATION:

Maintaining physical activity and muscle strength is important for every patient suffering from COPD. Physical activity can be achieved through enrollment in an organized program, such as pulmonary rehabilitation (PR). Pulmonary Rehabilitation is described as 'an evidence-based, multidisciplinary and comprehensive intervention for patients with COPD that is designed to reduce symptoms, optimize functional status, increase patient participation and reduce healthcare costs through stabilizing or reversing systemic manifestations of the disease'³⁷. It is a proven effective modality in the treatment of COPD and is part of COPD management guidelines.

Ideal candidates for PR are both males and females with moderate, severe or very severe COPD³⁸. It should be offered to those patients with COPD who remain symptomatic despite bronchodilator therapy and should be implemented within one month following an acute exacerbation³⁸. Exacerbations are associated with a decline in quality of life, premature death and an increased readmission rate³⁹. Post an exacerbation; patients are less active leading to further decline in endurance and muscle mass. When compared to usual care post an exacerbation, PR demonstrated a significant reduction in hospital readmission rates and death in addition to increased exercise tolerance and symptomatic improvement ³⁹.

In addition to its proven benefit post an exacerbation, PR has

beneficial outcomes in many other important patient domains, such as dyspnea, exercise performance, disability and quality of life. Despite these positive outcomes, the effect on FEV1 has been mixed. Recently, however, the FIRST study by Incorvaia et al demonstrated that in patients with COPD on standard pharmacotherapy, pulmonary rehabilitation led to an improvement in FEV1 over a three year period whereas controls had a decline⁴⁰.

These benefits are achieved through a program focused on both aerobic and resistance training. This combination of therapy is more effective than either therapy alone³⁸ and targets the peripheral muscle dysfunction that is prevalent in patients with COPD. Weakness is attributed to a vicious cycle of dyspnea and fatigue leading to a more sedentarry lifestyle.

Despite the clear benefits of PR in many patient related domains, PR is often an under-utilized resource. There are many obstacles preventing its implementation to the large number of COPD patients who are candidates for it. Some of these include under-recognition of its value, lack of knowledge on who would be an ideal candidate, lack of availability and patient factors such as mobility. For those with COPD where hospital based PR is not possible for lack of availability, transportation or time commitment issues, a structured program is not always required to notice the benefits of exercise. Home exercise programs, or programs through the local gym can provide the aerobic and muscle strengthening benefits where PR is not available or feasible. The NICE guidelines concluded that PR is effective in all settings including hospital inpatient, hospital outpatient, the community and home⁴¹. As such, a home or community based program overseen by a multidisciplinary and multiprofessional team is an option for those where hospital programs are not available or not possible.

Therefore, as supported by the NICE guidelines, PR is effective in management of patients with COPD in both the acute setting (post exacerbation) and in patients with symptomatic stable disease. Both hospital based and home or community programs are effective and should be utilized based on their availability and patient convenience.

NON-INVASIVE VENTILATION (NIV):

a) Acute NIV:

Non-Invasive positive pressure ventilation (NIPPV) is a proven modality to decrease morbidity, improve survival and decrease the need for mechanical ventilation in COPD patients who develop acute respiratory failure. Its benefit has been proven in various settings, including the ICU, ward and emergency department in patients with moderate to severe respiratory acidosis⁴¹. Length of hospital stay is reduced and fewer complications, such ventilator acquired pneumona, prolonged weaning and other nosocomial infections are encountered when NIV is used in the appropriate population during an exacerbation⁴².

NIV is also effective in facilitating extubation in patients mechanically ventilated for an acute exacerbation. Patients extubated to NIV had fewer re-intubations, fewer tracheostomies, shorter ICU stays, improved ICU survival and fewer complications including nosocomial pneumonia⁴³. Because of these positive results, NIV should be considered in patients that require mechanical ventilation for respiratory failure particularly in those who have failed traditional weaning.

b) Chronic NIV:

The use of chronic NIV in patients with COPD is more controversial. The results are varied with respect to patient related outcomes. Struik et al have recently completed a randomized control trial examining the use of NIV in COPD patients with prolonged hypercapnea post NIV use for acute respiratory failure. The results of this study demonstrated no improvement in survival, number of respiratory readmissions, exacerbations, lung function, health related quality of life, mood state or daily activity levels of dyspnea in the NIV group versus standard therapy. This was despite having improvements in daytime PaCO2 and nocturnal transcutaneous PCO2 measurements in the NIV group⁴⁴. Despite this lack of convincing evidence for its use, there are some clear situations where chronic NIV proves beneficial. One of these situations is in the patient with combination of COPD and obstructive sleep apnea (OSA). Patients with combined COPD and OSA who are not treated with appropriate NIV, like continuous positive airway pressure (CPAP) for example, experience higher rates of hospitalizations and mortality when admitted with a COPD exacerbation⁴⁵. The use of CPAP for combined OSA and COPD also reduces pulmonary hypertension rates and nocturnal hypoxemia⁴⁶.

LONG TERM OXYGEN THERAPY (LTOT):

According to the British Thoracic Society (BTS), long term oxygen therapy is recommended for patients with a PaO2 ≤7.3kPa or a PaO2 between 7.3kPa and 8kPa with signs of peripheral edema, polycythemia (hematocrit >55%) or pulmonary hypertension. In this population, long term oxygen therapy is one of the few interventions that prolong life expectancy⁴⁷. It also reduces pulmonary hypertension and hematocrit⁴⁷. Continuous oxygen therapy, worn for 24h/d is

superior to nocturnal oxygen in those with severe hypoxemia (PaO2 \leq 7.3kPa or a PaO2 of \leq 8kPa cor-pulmonale)⁴⁸. Situational oxygen is also recommended for those who desaturate with exertion or have hypoxemia at night.

AMBULATORY OXYGEN THERAPY

For patients on LTOT who are motivated to use oxygen outside the home, ambulatory oxygen should be prescribed. Ambulatory oxygen is also indicated for those patients not on LTOT but who have exercise arterial desaturation⁴⁹. In this population, arterial oxygen desaturation is defined as a fall in SaO2 of 4% to a value <90%. In addition to desaturation, these patients must also demonstrate improvement in exercise capacity and/or dyspnea with oxygen. The goal is to maintain oxygen saturation >90% during exercise.

SHORT-BURST OXYGEN THERAPY

Short burst oxygen therapy refers to the intermittent use of supplemental oxygen at home for intervals in the range of 10-20min to relieve symptoms of dyspnea. According the the NICE guidelines, short-burst oxygen therapy should only be considered for episodes of severe breathlessness in patients with COPD not relieved by other treatments⁴⁹. This mode of oxygen delivery should only continue to be prescribed if there is improvement in breathlessness with its use.

EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO):

ECMO in the form of an extracorporeal CO2 remover (ECCO2R) is a new modality being used to treat COPD exacerbations to prevent the need for mechanical ventilation and the associated morbidity associated with intubation. As demonstrated above, non-invasive ventilation is superior to mechanical ventilation in terms of mortality, complications and hospital length of stay. However, 15-26% of patients with an acute exacerbation of COPD fails non-invasive ventilation and requires transition to mechanical ventilation. These patients have a higher mortality than those initially treated with mechanical ventilation⁵⁰. There are no current guidelines on the use of ECMO for COPD exacerbations as its use in this indication is new. Studies have shown that the Novalung could prevent intubation in 90% of patients with a trend to decreasing hospital length of stay⁵⁰. Another device, the Hemolung, had similar findings. These studies were small and not randomized; however, there is a trend to decrease mechanical ventilation and mortality. It is likely that in the

Table 4: Physiological indications for long-term oxygen therapy (LTOT) BTS Guidelines

P a, O_2 k P a	$Sa,O_2\%$	LTOT indication	Qualifying condition
≤7.3	≤88	Absolute	None
7.3-8	89	Relative with qualifier	"P" pulmonale, polycythemia >55% History of oedema
≥8	≥90	None except with qualifier	$\label{eq:continuous} Exercise \ desaturation \\ Sleep \ desaturation \ not \ corrected \ by \ CPAP \\ Lung \ disease \ with \ severe \ dyspnoea \ responding \ to \ O_2$

future we will see this modality being used more in centers that have access to it.

LUNG VOLUME REDUCTION SURGERY (LVRS) AND ENDOBRONCHIAL PROCEDURES:

LVRS is an effective treatment option in patients with heterogeneous upper zone emphysema and reduced exercise tolerance⁵¹. According to the National Emphysema Treatment Trial (NETT) trial, LVRS has shown to be superior to medical treatment. LVRS has improved maximal ventilation rate and tidal volume and has lower BORG dyspnea scores⁵². However, surgery carries a high risk of morbidity, particularly in patients with severe COPD, who often have additional co-morbidities. Thus, newer, non-surgical, less invasive strategies have been developed to potentially offer benefit to those patients who would not be candidates for LVRS. These non-surgical procedures are referred to as bronchoscopic lung volume reduction.

The most common bronchoscopic lung volume reduction devices include: endobronchial valves, foam sealant, metallic coils, airway bypass stents and vapor thermal ablation. Lung volume reduction coils (LVRC) are being used in patients with severe emphysema and hyperinflation. In a small randomized study, patients allocated to the LVRC versus usual care had higher SGRQ scores than those allocated to usual care⁵³. Endobronchial valves, another bronchoscopic lung volume reduction procedure, functions by allowing air out of the treated area, but not to re-enter it, eliminating the affected emphysematous regions from ventilation and eventually leading to lobar atelectasis⁵⁴. The Endobronchial Valve for Emphysema Palliation Trial (VENT) demonstrated modest improvement in FEV1, distance walked in 6 minutes, dyspnea and quality of life; however, there were increased complications such as pneumonia and pneumothoax when compared to usual medical care⁵⁵.

There appears to be some promise in the bronchoscopic lung volume reduction devices for patients who are not candidates for surgery. NICE guidelines recognize that there may be a subgroup of patients that may benefit from this procedure; however, at this time these procedures are experimental and only available in highly specialized centres. Further research is in progress to determine which patients would be ideal candidates and further data is required before the procedures are accepted as general practice.

LUNG TRANSPLANT:

Lung transplant is offered to people with untreatable, endstage lung disease with a limited life expectancy. COPD is one such lung disease and is currently the most common indication for a double lung transplant⁵⁵. According to the International Society for Heart and Lung Transplantation, the disease specific criteria for referral of patients with COPD include an FEV1 \leq 30% while having maximized both pharmacological and non-pharmacological therapy, including bronchodilators, home oxygen, smoking cessation and pulmonary rehabilitation. In addition, they should have a BODE index exceeding 5⁵⁶. Other criteria for transplantation include patients with a BODE index of 7-10 plus a history of hospitalization for exacerbation associated with acute hypercapnia, pulmonary hypertension or cor pulmonale or an FEV1 of less than 20% with either a DLCO of less than 20% or a homogeneous distribution of emphysema⁵⁶.

The survival benefit for patients with COPD receiving a transplant is not as robust as for transplant in other respiratory conditions, such as idiopathic pulmonary fibrosis, cystic fibrosis and primary pulmonary hypertension⁵⁷. The benefits from lung transplant in this population are improved respiratory function, endurance and quality of life as opposed to prolonging of life⁵⁷.

There are many factors that must be taken into consideration when referring a patient for lung transplant. Each transplant centre has different criteria for when to refer and different contraindications. (Table 5) If a patient seems like an appropriate candidate and is willing, a referral to a transplant centre should be made.

END OF LIFE (EOL)CARE:

COPD accounts for 48% of all deaths in England between 2007 and 2009 and is the main cause of chronic lung disease deaths³⁵. Patients with COPD typically experience the last few months to years of their life marked by progressive dyspnea, functional decline and social isolation⁵⁸. Their quality of life has been compared to those with lung cancer⁵⁹. As with any non-curable chronic illness, goals of care and end of life discussions must occur. The discussion should focus on education of the disease course and management of end of life issues, such as symptom control and advanced health care directives. The prognosis of COPD is often difficult to predict as the disease is marked by progressive decline in lung function with increasing symptoms. There are episodes of acute illness and associated co-morbid conditions. Because prognosis is difficult to predict, it is often unclear as to when to begin end of life care discussions and palliative symptom management. These discussions should definitely occur when the FEV1 is <30%, abnormal blood gases are present or when cor-pulmonale with pulmonary hypertension develops⁶⁰ as these patients are found to have the poorest prognosis. The End of Life Strategy detailed in the NICE guidelines suggests an integrated multidisciplinary approach involving spiritual care, social care, supports and information to patients, carers and families. These services should occur as end of life approaches35.

The major symptoms experienced by end-stage COPD patients include dyspnea, pain, fatigue and insomnia⁶⁰. Opiods, both regular dosed and breakthrough is the mainstay of treatment for dyspnea. Benzodiazepenes can be used as adjuncts to opioids to control severe dyspnea. Insomnia is often improved simply through dysnpea control⁶⁰. Initial discussions and management should be undertaken by the primary physician managing the patients COPD, however, a referral to a palliative care physician is warranted as

Table 5:

Contraindication to Lung Transplant from 2006 ISHLT Guidelines

Absolute and relative contraindications for lung transplantation

Absolute contraindications:

Malignancy in the last 2 years, with the exception of cutaneous squamous and basal cell tumors

Untreatable advanced dysfunction of another major organ system

Noncurable chronic extrapulmonary infection, including chronic active HBV, HCV and HIV

Significant chest wall or spinal deformity

Documented nonadherence or inability to follow through with medical therapy or office follow-up, or both

Untreatable psychiatric or psychologic condition associated with the inability to cooperate or comply with medical therapy

Absence of a consistent or reliable social support system

Substance addiction that is either active or within the last 6 months

Relative contraindications:

Age older than 65 years

Critical or unstable clinical condition (e.g., shock, mechanical ventilation or ECMO)

Severely limited functional status with poor rehabilitation potential

Colonization with highly resistant or highly virulent bacteria, fungi or mycobacteria

Severe obesity defined as a BMI exceeding 30 kg/m²

Chronic mechanical ventilation

Unstable extrapulmonary medical conditions that have not resulted in end-stage organ damage

symptoms progress or if not effectively managed by conventional modalities.

PRIMARY VS SECONDARY CARE:

The management of COPD requires a multidisciplinary approach and a good working relationship between primary care and respirology subspecialists when involved. As outlined above, the non-pharmacological management of a COPD patient is multifaceted. Most therapies can be initiated or supported by both primary care and subspecialist physicians such as immunizations and smoking cessation. Table 6 outlines when primary care physicians should consider referral to a respirologist to aid in the diagnosis and management of the patient with COPD³⁵.

Table 6:

NICE Guidelines: When Respirology Consultation is Appropriate

- Diagnostic Uncertainty
- Suspected severe COPD
- Patient wants a second opinion
- Onset of cor pulmonale
- Assessment for oxygen therapy
- Bullous lung disease
- A rapid decline in FEV1
- Assessment for pulmonary rehabilitation
- Assessment for lung volume reduction surgery
- Assessment for lung transplantation
- Onset of symptoms under 40years of age or a family history of alpha-1 antitrypsin deficiency
- Frequent infections
- Hemoptysis

CONCLUSION:

COPD is the most prevalent lung disease in the world and has major personal, social and economic implications. By 2020, it is anticipated to become the third leading cause of death in the world. This paper describes the non-pharmacological modalities available for patients with this disease. Several of these are very low-cost yet effective interventions while others are very sophisticated and, as yet, not clearly evidence-based. However, both clinicians and commissioners will derive useful information from this paper for the provision of comprehensive, cross-sectional, multidisciplinary and multiprofessional care for this large and diverse group of patients.

CONFLICTS OF INTEREST:

Katherine A. Safka: None Declared

R. Andrew McIvor: has been an investigator and has received honoraria for attending advisory boards and providing educational events for pharmaceutical companies including Almiral, AstraZeneca, Boehringer-Ingelheim, Merck, Novartis and Pfizer

REFERENCES:

- Mittmann, N. Et al. The cost of moderate and severe COPD exacerbations to the Canadian healthcare system. Respir Med. 2008;102(3):413-21.
- Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: Executive summary 2013.
 Bethesda: Global Initiative for Chronic Obstructive Lung Disease (GOLD); 2014. Available online from: http://www.goldcopd.org/ guidelines-global-strategy-for-diagnosis-management.html [Last accessed December 2014).
- Sood A, Petersen H, Blanchette CM, Picchi MA, Belinsky SA, Tesfaigzi Y. Wood smoke exposure and gene promoter methylation are associated with increased risk for COPD in smokers. Am J Respir Crit Care Med. 2010;182(9): 1098-104.

- Burgel PR, Paillasseur JL, Roche, N. Identification of clinical phenotypes using cluster analyses in COPD patients with multiple comorbidities. *BioMed Res Int*.2014;2014:420134.
- Csikesz NG, Gartman, EJ. New developments in the assessment of COPD: early diagnosis is key. Int J Chron Obstruct Pulmon Dis. 2014;9:277-86.
- Tantucci C, Modina D. Lung function decline in COPD. Int J Chron Obstruct Pulmon Dis. 2012;7:95-9.
- Anthonisen NR, Connett JE, Kiley JP, Altose MD, Bailey WC, Buist AS, et al. Effects of smoking intervention and the use of inhaled anticholinergic bronchodilator on the rate of decline of FEV1. The Lung Health Study. JAMA. 1994;272(19):1497-505.
- Decramer M, Cooper CB. Treatment of COPD: the sooner the better? Thorax. 2010;65(9):837-41.
- Decramer M, Miravitlles M, Price D, Roman-Rodriguez M, Lior C, Welte T, et al. New horizons in the early stage COPD – improving knowledge, detection and treatment. Respir Med. 2011;105(11):1576-87.
- Fletcher C, Peto R. The natural history of chronic airflow obstruction. Br Med J. 1977;1(6077):1645-8.
- Mosenifar Z. Differentiating COPD from asthma in clinical practice. Postgrad Med. 2009;121(3): 105-12.
- Scanlon PD, Connett JE, Waller LA, Altose MD, Bailey WC, Buist AS, et al. Smoking cessation and lung function in mild-to-moderate chronic obstructive pulmonary disease. The Lung Health Study. Am J Respir Crit Care Med. 2000;161(2 pt 2):381-92.
- Pelkonen M, Tukiainen H, Tervahauta M, Notkoala IL, Kivela SL, Salorinne Y, et al. Pulmonary function, smoking cessation and 30 year mortality in middle aged Finnish men. Thorax. 2000;55(9):746-50.
- Tashkin DP, Murray RP. Smoking cessation in chronic obstructive pulmonary disease. Respir Med. 2009;103(7):963-74.
- Calverley PM, Anderson JA, Celli B, et al. Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease. N Engl J Med. 2007;356(8):775-89.
- Tashkin DP, Celli B, Decramer M, et al. Regional patterns in the characteristics of patients recruited into a long-term global clinical trial in COPD (UPLIFT). Am J Respir Crit Care Med. 2005;2:A412.
- Wedzicha JA, Calverley PM, Seemungal TA, Hagan G, Ansari Z, Stockley RA, INSPIRE investigators. The prevention of chronic obstructive pulmonary disease exacerbations by salmeterol/fluticasone propionate or tiotropium bromide. Am J Respir Crit Care Med. 2008;177(1):19-26.
- 18. Rennard SI, Daughton DM. Smoking cessation. Clin Chest Med. 2014;35(1):165-76.
- Fiore MC, Jaen CR, Baker TB, et al. Treating to bacco use and dependence: 2008 update. Clinical practice guidelines. Rockville, MD US Department of Health and Human Services, Public Health Service; 2008.
- Bednarek M, Gorecka D, Wielgomas J, Czajkowska-Malinowska M, Regula J, Mieszko-Filipczyk G, et al. Smokers with airway obstruction are more likely to quit smoking. *Thorax*. 2006;61(10):869-73.
- Stratelis G, Molstad S, Jakobsson P, Zetterstrom O. The impact of repeated spirometry and smoking cessation advice on smokers with mild COPD. Scand J Prim Health Care. 2006;24(3):133-9.
- Wagena EJ, van der Meer RM, Ostelo RJWG, Jacobs JE, van Schayck CP. The efficacy of smoking cessation strategies in people with chronic obstructive pulmonary disease: results from a systematic review. Resp Med. 2004;98(9):805-15.
- Jiloha RC. Pharmacotherapy of smoking cessation. *Indian J Psychiatry*. 2014;56(1):87-95.
- Cahill K, Stevens S, Lancaster T. Pharmacological treatments for smoking cessation. *JAMA*. 2014;311(2):193-4.

- Lerman C, Shields PG, Wileyto EP, Audrain J, Hawk LH, Pinto A, et al. Effects of dopamine transporter and receptor polymorphisms on smoking cessation in a bupropion clinical trial. Health Psychol. 2003;22(5):541-8.
- Pepper JK, Emery SL, Ribisl KM, Southwell BG, Brewer NT. Effects of advertisements on smokers' interest in trying e-cigarettes: the roles of product comparison and visual cues. *Tob Control*. 2014;23(Suppl 3):iii31-iii36.
- 27. Zhu SH, Sun JY, Bonnevie E, Cummins SE, Gamst A, Yin L, Lee M. Four hundred and sixty brands of e-cigarettes and counting: implications for product regulation. *Tob Control*. 2014;23(Suppl 3):iii2-iii9.
- Harrell PT, Simmons VN, Correa JB, Padhya TA, et al. Electronic nicotine delivery systems ("e-cigarettes"): review of safety and smoking cessation efficacy. *Otolaryngol Head Neck Surg.* 2014;151(3):381-93
- Nowak D, Jorres RA, Ruther T. E-Cigarettes prevention, pulmonary heatlh, and addiction. *Dtsch Arztebf Int*. 2014;111(20):349-55.
- Brown J, Beard E, Kotz D, Michie S, West R. Real-world effectiveness of e-cigarettes when used to aid smoking cessation: a cross-sectional population study. *Addiction*. 2014;109(9):1531-40.
- Schraufnagel DE, Blasi F, Drummond MB, Lam DC, Latif E, Rosen MJ, et al. Electronic cigarettes: a position statement of the forum of international respiratory societies. Am J Respir Crit Care Med. 2014;90(6):611-8.
- Britton J and Bogdanovica I. Electronic cigarettes: A report commissioned by Public Health England. London: Public Health England; 2014. Available online from: https://www.gov.uk/government/uploads/ system/uploads/attachment_data/file/311887/Ecigarettes_report.pdf [Last accessed December 2014].
- Poole P, Chacko EE, Wood-Baker R, Cates CJ. Influenza vaccine for patients with chronic obstructive pulmonary disease (Review). Cochrane Database Syst Rev. 2006; Issue 1: CD002733.
- 34. Wongsurakiat P, Maranetra KN, Wasi C, Kositanont U, Dejsomritrutai W, Charoenratanakul S. Acute respiratory illness in patients with COPD and the effectiveness of influenza vaccination: a randomized controlled study. *Chest.* 2004;**125(6)**:2011-20.
- NICE guidelines. Chronic obstructive pulmonary disease: Management
 of chronic obstructive pulmonary disease in adults in primary and
 secondary care (partial update). London: NICE National Institute for
 Health and Care Excellence; 2010.
- Nichol KL, Baken L, Wuorenma J, Nelson A. The heath and economic benefits associated with pneumococcal vaccination of elderly persons with chronic lung disease. *Arch Intern Med.* 1999;159(20):2437-42.
- 37. Nici L, ZuWallak R, Wouters E, Donner CF. On pulmonary rehabilitation and the flight of the bumblebee: the ATS/ERS Statement on pulmonary rehabilitation. *Eur Respir J.* 2006;28(3):461-2.
- 38. Marciniuk DD, Brooks D, Butcher S, Debigare R, Dechman G, Ford G, *et al.* Optimizing pulmonary rehabilitation in chronic obstructive pulmonary disease practical issues: a Canadian Thoracic Society Clinical Practice Guideline. *Can Respir J.* 2010;**17**(4):159-68.
- Puhan M, Scharplatz M, Troosters T, Walters EH, Steurer J. Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2009; 21(1): CD005305.
- Incorvaia C, Russo A, Foresi A, Berra D, Elia R, Passalacqua G, et al. Effects of pulmonary rehabilitation on lung function in chronic obstructive pulmonary disease: the FIRST study. Eur J Phys Rehabil Med. 2014;50(4):419-26.
- NICE guidelines. Chronic obstructive pulmonary disease: Management
 of chronic obstructive pulmonary disease in adults in primary and
 secondary care (partial update) London: National Institute for Health
 and Care Excellence; 2010.
- 42. Ambrosino N, Vagheggini G. Non-invasive ventilation in exacerbations of COPD. *Int J Chron Obstruct Pulmon Dis.* 2007;**2**(4):471-6.

- Conti G, Antonelli M, Navalesi P, Rocco M, Bufi M, Spadetta G, Meduri GU. Noninvasive vs. conventional mechanical ventilation in patients with chronic obstructive pulmonary disease after failure of medical treatment in the ward: a randomized trial. *Intensive Care Med*. 2002;28(12):1701-7.
- Girault C, Daudenthun I, Chevron V, Tamion F, Leroy J, Bonmarchand G. Noninvasive ventilation as a systematic extubation and weaning technique in acute-on-chronic respiratory failure: a prospective, randomized controlled study. Am J Respir Crit Care Med. 1999;160(1):86-92.
- Struik FM, Sprooten RT, Kerstiens HA, Bladder G, Zinjen M, Asin J, et al. Nocturnal non-invasive ventilation in COPD patients with prolonged hypercapnia after ventilatory support for acute respiratory failure: a randomised, controlled, parallel-group study. *Thorax*. 2014;69(9):826-34.
- Marin JM, Soriano JB, Carrizo SJ, Boldova A, Celli BR. Outcomes in patients with chronic obstructive pulmonary disease and obstructive sleep apnea: the overlap syndrome. *Am J Respir Crit Care Med*. 2010;182(3):325-31.
- 47. McNicholas WT, Verbraecken J, Marin JM. Sleep disorders in COPD: the forgotten dimension. *Eur Respir Rev.* 2013;**22**(**129**):365-75.
- Stoller JK, Panos RJ, Krachman S, Doherty DE, Make B and the Long-term Oxygen Treatment Trial Research Group. Oxygen therapy for patients with COPD: current evidence and the long-term oxygen treatment trial. *Chest*. 2010;138(1):179-87.
- Nocturnal Oxygen Therapy Trial Group. Continuous or nocturnal oxygen therapy in hypoxemic chronic obstructive lung disease: a clinical trial. *Ann Intern Med.* 1980;93(3):391-8.
- British Thoracic Society (BTS) Working Group on Home Oxygen Services. Clinical component for the home oxygen service in England and Wales. Jan 2006. Available online from: https://www.brit-thoracic.org.uk/document-library/clinical-information/oxygen/home-oxygen-guideline-(adults)/bts-home-oxygen-in-adults-clinical-component/ [Last accessed December 2014].
- Lund LW, Federspiel WJ. Removing extra CO2 in COPD patients. Curr Respir Care Rep. 2013;2:131-138.
- Murphy PB, Zoumot Z, Polkey MI. Noninvasive ventilation and lung volume reduction. Clin Chest Med. 2014;35(1):251-69.
- Criner GJ, Belt P, Sternberg AL, Mosenifar Z, Make BJ, Utz JP, Sciurba F; National Empysema Treatment Trial Research Group. Effects of lung volume reduction surgery on gas exchange and breathing pattern during maximum exercise. Chest. 2009;135(5):1268-79.

- Shah PL, Zoumot Z, Singh S, Bicknell SR, Ross ET, Quiring J, Hopkinson NS, Kemp SV, RESET trial Study Group. Endobronchial coils for the treatment of severe emphysema with hyperinflation (RESET): a randomised controlled trial. *Lancet Respir Med*. 2013;1(3):233-40.
- Cohen E. Bronchoscopic treatment of end-stage chronic obstructive pulmonary disease. Curr Opin Anaesthesiol. 2014;27(1):36-43.
- Herth FJ, Noppen M, Valipour A, Leroy S, Vergnon JM, Ficker JH, Egan JJ, Gasparini S, Agusti C, Holmes-Higgin D, Ernst A; International VENT Study Group. Efficacy predictors of lung volume reduction with Zephyr valves in a European cohort. Eur Respir J. 2012;39(6):1334-42.
- Orens JB, Estenne M, Arcasoy S, Conte JV, Corris P, Egan JJ, et al. International Guidelines for the selection of lung transplant candidates: 2006 update – a consensus report from the Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation. (Consensus Document). J Heart Lung Transplant. 2006;25(7):745-55.
- Aziz F, Penupolu S, Xu X, He J. Lung transplant in end-staged chronic obstructive pulmonary disease (COPD) patients: a concise review. J Thorac Dis. 2010;2(2):111-6.
- NICE guidelines. Chronic obstructive pulmonary disease: Management
 of chronic obstructive pulmonary disease in adults in primary and
 secondary care (partial update) London: National Institute for Health
 and Care Excellence; 2010.
- 60. Spathis A, Booth S. End of life care in chronic obstructive pulmonary disease: in search of a good death. *Int J Chron Obstruct Pulmon Dis*. 2008;**3(1)**:11-29.
- 61. Gore JM, Brophy CJ, Greenstone MA. How well do we care for patients with end stage chronic obstructive pulmonary disease (COPD)? A comparison of palliative care and quality of life in COPD and lung cancer. *Thorax*. 2000;55(12):1000-6.
- Dean MM. End-of-life care for COPD patients. Prim Care Respir J. 2008:17(1):46-50.
- NICE guidelines. Chronic obstructive pulmonary disease: Management
 of chronic obstructive pulmonary disease in adults in primary and
 secondary care (partial update) London: National Institute for Health
 and Care Excellence; 2010.
- NICE guidelines. Chronic obstructive pulmonary disease: Management
 of chronic obstructive pulmonary disease in adults in primary and
 secondary care (partial update) London: National Institute for Health
 and Care Excellence; 2010.