

A SELECTION OF TEN CURRENT READINGS ON TOPICS RELATED TO
CHRONIC RESPIRATORY DISEASE UPDATE AVAILABLE AS FREE FULL-TEXT

Selection of readings made by A/Prof Goh Lee Gan

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Reading 1 - Inhaled corticosteroids

Gartlehner G, Hansen RA, Carson SS, Lohr KN. Efficacy and safety of inhaled corticosteroids in patients with COPD: a systematic review and meta-analysis of health outcomes. *Ann Fam Med*. 2006 May-Jun;4(3):253-62.

URL: <http://www.annfammed.org/cgi/content/full/4/3/253>

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ABSTRACT

PURPOSE: We wanted to review systematically the efficacy, effectiveness, and safety of inhaled corticosteroids with respect to health outcomes in patients with chronic obstructive pulmonary disease (COPD).

METHODS: We searched MEDLINE, EMBASE, The Cochrane Library, and the International Pharmaceutical Abstracts to identify relevant articles. We limited evidence to double-blinded randomised controlled trials (RCTs) for efficacy, but we also reviewed observational evidence for safety. Outcomes of interest were overall mortality, exacerbations, quality of life, functional capacity, and respiratory tract symptoms. When possible, we pooled data to estimate summary effects for each outcome.

RESULTS: Thirteen double-blinded RCTs determined the efficacy of an inhaled corticosteroid compared with placebo; 11 additional studies assessed the safety of inhaled corticosteroid treatment in patients with asthma or COPD. Overall, COPD patients treated with inhaled corticosteroids experienced significantly fewer exacerbations than patients taking placebo (relative risk [RR] = 0.67; 95% CI, 0.59-0.77). No significant difference could be detected for overall mortality (RR = 0.81; 95% CI, 0.60-1.08). Evidence on quality of life, functional capacity, and respiratory tract symptoms is mixed. Adverse events were generally tolerable; pooled discontinuation rates did not differ significantly between inhaled corticosteroid and placebo treatment groups (RR = 0.92; 95% CI, 0.74-1.14). Observational evidence, however, indicates a dose-related risk of cataract and open-angle glaucoma. Severe adverse events, such as osteoporotic fractures, are rare; the clinical importance of the additional risk is questionable.

CONCLUSIONS: Overall, the risk-benefit ratio appears to favor inhaled corticosteroid treatment in patients with moderate to severe COPD. Existing evidence does not indicate a treatment benefit for patients with mild COPD.

Reading 2 - Guidelines

Abramson MJ, Crockett AJ, Frith PA, McDonald CF. COPDX: an update of guidelines for the management of chronic obstructive pulmonary disease with a review of recent evidence. *Med J Aust.* 2006 Apr 3;184(7):342-5.

URL: http://www.mja.com.au/public/issues/184_07_030406/abr10742_fm.html

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ABSTRACT

Long-acting beta(2) agonists are an effective and convenient treatment for chronic obstructive pulmonary disease (COPD), but do not significantly improve lung function. The long-acting anticholinergic tiotropium, which can be taken once daily, decreases exertional dyspnoea and increases endurance by reducing hyperinflation. The role in COPD of the combination of a long-acting beta(2) agonist and a glucocorticoid in a single inhaler remains unclear. The minimum duration of an effective pulmonary rehabilitation program that includes exercise training is 6 weeks. Long-term treatment with inhaled glucocorticoids may reduce the rate of decline in lung function, but the effect is small. Aminophylline should no longer be routinely used in acute exacerbations of COPD. Non-invasive positive pressure ventilation (NPPV) reduces mortality and hospital stay in patients with acute hypercapnic ventilatory failure; it is also an effective weaning strategy for patients who require intubation. Further studies are required to clarify the role of NPPV in the long-term management of stable COPD.

Reading 3 - Dyspnoea

Rabe KF. Improving dyspnea in chronic obstructive pulmonary disease: optimal treatment strategies. *Proc Am Thorac Soc.* 2006 May;3(3):270-5.

URL: <http://pats.atsjournals.org/cgi/reprint/3/3/270>

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) is a common disease with a global impact in terms of morbidity and mortality. Patients usually consult their doctor because of symptoms, and among those, dyspnoea at rest or under exercise is one of the most common. The sensation of dyspnoea is experienced differently among individuals with COPD and may be based on diverse factors, such as muscle fatigue, patient perception, or trapped volumes. Treatment algorithms for COPD emphasise a stepwise approach to therapy depending on the severity of the disease, which, for reasons of convenience, is primarily based on spirometric impairment. Drugs that alter bronchial smooth muscle tone and increase inspiratory capacity have clinical efficacy for the dyspnoeic patient, most likely based on their effect on lung function, whereas the effects of anti-inflammatory therapy with inhaled corticosteroids is more difficult to explain. The following short review aims to give an overview of the available clinical information of clinical trials performed over the last couple of years.

Reading 4 - Exacerbation prevention

Burge PS. Prevention of exacerbations: how are we doing and can we do better? Proc Am Thorac Soc. 2006 May;3(3):257-61.

URL: <http://pats.atsjournals.org/cgi/reprint/3/3/257>

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ABSTRACT

Prevention of exacerbations of chronic obstructive pulmonary disease (COPD) can involve removing the cause or reducing the patient's vulnerability to the cause. This article addresses the following issues: What is the problem during an exacerbation, what are the causes of an exacerbation, what can prevent exacerbations, and who are we? The difference between a patient with COPD during an exacerbation and after recovery is small. It is unlikely that patients with early COPD experience less exposure to exacerbation causes than those with severe disease; it is just that the consequences are more severe for those with severe disease. Interventions that produce small absolute benefits can therefore have a disproportionately large effect on exacerbation reduction. Recognised causes include season, cold weather, pollution events, bacterial infection, viral infection, and treatment withdrawal. Countries with warmer climates have much larger mortality in cold weather than those with colder climates. Reducing exacerbations in more temperate climates may be altered as much by changes in clothing and bedroom heating as by changes in treatment. Taking more exercise in cold weather may be the underlying reason for the reduction of exacerbations after pulmonary rehabilitation. Influenza vaccination reduces influenza severity and reduces transmission from health care workers to patients. There are a number of pharmacologic interventions shown to reduce (the effect of) exacerbations, including inhaled corticosteroids, long-acting beta-agonists, long-acting anticholinergics, mucolytics, and perhaps antibiotics that reduce *Haemophilus* carriage. The effect of the bronchodilators is additive to inhaled corticosteroids; how far the other interventions are complementary is unclear. So far, we have had a very medical response to COPD exacerbations. Altering social and behavioral aspects is likely to be complementary.

Reading 5 - Exacerbation assessment, staging and epidemiology

Vestbo J. Clinical assessment, staging, and epidemiology of chronic obstructive pulmonary disease exacerbations. Proc Am Thorac Soc. 2006 May;3(3):252-6.

URL: <http://pats.atsjournals.org/cgi/reprint/3/3/252>

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ABSTRACT

Patients presenting with an exacerbation of chronic obstructive pulmonary disease (COPD) are initially assessed to ensure that a proper diagnosis has been made and that relevant differential diagnoses are excluded. Although guidelines provide indicators for use, very little systematic research has been done in initial assessment of COPD exacerbations. Next, the assessment should aim at stratifying patients for risk of poor outcome. For this, predictors of poor prognosis as well as knowledge of favorable treatments can be used. However, no formal and validated staging system exists today. Given the frequency and impact of COPD exacerbations, there seems to be a need for systematic research in this area.

Reading 6 - Health economics

Halpin DM. Health economics of chronic obstructive pulmonary disease. *Proc Am Thorac Soc.* 2006 May;3(3):227-33.

URL: <http://pats.atsjournals.org/cgi/reprint/3/3/227>

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ABSTRACT

Studies describing the economic impact of chronic obstructive pulmonary disease (COPD) are used for several purposes. There can, however, be limitations as costs based on results of a clinical trial are likely to be significantly different from real world practice. Sometimes, it may be more useful to capture the costs of the important components accurately rather than the often unachievable aim of capturing every cost however small. Burden of illness studies can help identify clinical targets or patterns of care – for example, hospitalisation – that are major health care cost drivers. In the United Kingdom, burden of COPD studies suggest an annual cost of £781 - £1,154 per patient. Cost analyses can be divided into four types: cost minimisation, cost-effectiveness, cost benefit, and cost utility. Utilities such as quality-adjusted life year (QALY) measure the effectiveness of different therapies, and can be obtained in various ways and in different populations, potentially leading to significant differences in the results. Payers often apply cost per QALY thresholds when assessing whether a new therapy should be used or not. In the United Kingdom, it is accepted that there is a sigmoid relationship between the cost per QALY and the likelihood of a therapy being recommended, with a lower inflection between £5,000 and £15,000, below which rejection is unlikely and an upper inflection between £25,000 and £35,000, above which acceptance is unlikely, but not impossible. On this basis, pulmonary rehabilitation and inhaled steroids are unlikely to be rejected but lung volume reduction surgery may be.

Reading 7 - Pulmonary rehabilitation

Hill NS. Pulmonary rehabilitation. *Proc Am Thorac Soc.* 2006;3(1):66-74.

URL: <http://pats.atsjournals.org/cgi/reprint/3/1/66>

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ABSTRACT

Pulmonary rehabilitation programs use multidisciplinary teams to optimise physical and social functioning of patients with chronic respiratory impairment. These programs provide rehabilitation in inpatient, outpatient, or home settings, using at least three sessions weekly (one may be unsupervised) for at least 6 week. The programs usually consist of exercise training, education, and psychosocial/behavioral components. Upper extremity exercises and instruction on breathing technique are included in most rehabilitation programs and reduce dyspnoea, but the contribution of these to improved functional capacity remains unproven. Decreases in the sensation of dyspnoea, increased functional exercise capacity, and enhanced quality of life of patients with chronic obstructive pulmonary disease (COPD) are established benefits of pulmonary rehabilitation. Evidence is lacking for the efficacy of rehabilitation for patients with non-COPD causes of pulmonary impairment, but many of these patients probably benefit. Despite the availability of strong evidence to support the efficacy of pulmonary rehabilitation programs in patients with severe COPD, third-party reimbursement policies have been inconsistent. Nonetheless, enrollment in a pulmonary rehabilitation program is encouraged for all appropriate candidates with chronic respiratory impairment, particularly for those with severe COPD.

Reading 8 - Evidence-based optimism

Celli BR. Chronic obstructive pulmonary disease: from unjustified nihilism to evidence-based optimism. *Proc Am Thorac Soc.* 2006;3(1):58-65

URL: <http://pats.atsjournals.org/cgi/reprint/3/1/58>

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) has been associated with a nihilistic attitude. On the basis of current evidence, this nihilistic attitude is totally unjustified. The disease must be viewed through the lens of a new paradigm: one that accepts COPD as not only a pulmonary disease, but also as one with important measurable systemic consequences. COPD is not only preventable, but also treatable. Smoking cessation, oxygen for hypoxemic patients, lung reduction surgery for selected patients with emphysema, and noninvasive ventilation during severe exacerbations have all been shown to impact on mortality. In addition, pulmonary rehabilitation, pharmacologic therapy, and lung transplantation improve patient-centered outcomes such as health-related quality of life, dyspnoea, exercise capacity, and even exacerbations and hospitalisations. Caregivers should familiarise themselves with the multiple complementary forms of treatment and individualise therapy to the particular situation of each patient. The future for patients with this disease is bright as its pathogenesis and clinical and phenotypic manifestations are unraveled. The advent of newer and more effective therapies will lead to a decline in the contribution of this disease to poor world health.

Reading 9 - Aerosol therapy

Rau JL. Practical problems with aerosol therapy in COPD. *Respir Care.* 2006 Feb;51(2):158-72.

URL: <http://www.rcjournal.com/contents/02.06/02.06.0158.pdf>

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ABSTRACT

Inhaled aerosol drugs commonly used by patients with chronic obstructive pulmonary disease include short-acting and long-acting bronchodilators, as well as corticosteroids. These agents are available in a variety of inhaler devices, which include metered-dose inhalers (MDI), breath-actuated MDIs, nebulizers, and, currently, 5 different models of dry powder inhaler (DPI). There is evidence to suggest that multiple inhaler types cause confusion among patients and increase errors in patient use. Problems with MDIs include failure to coordinate inhalation with actuation of the MDI, inadequate breath-hold, and inappropriately fast inspiratory flow. Lack of a dose counter makes determining the number of remaining doses in an MDI problematic. Patient misuse of MDIs is compounded by lack of knowledge of correct use among health-care professionals. Several factors often seen with elderly patients have been identified as predictive of incorrect use of MDIs. These include mental-state scores, hand strength, and ideomotor dyspraxia. Holding chambers and spacers are partially intended to reduce the need for inhalation-actuation coordination with MDI use. However, such add-on devices can be subject to incorrect assembly. Possible delays between MDI actuation and inhalation, rapid inspiration, chamber electrostatic charge, and firing multiple puffs into the chamber can all reduce the availability of inhaled drug. Because they are breath-actuated, DPIs remove the need for inhalation-actuation synchrony, but there is evidence that patient errors in use of DPIs may be similar to those with MDIs. One of the biggest problems is loading and priming the DPI for use, and this may be due to the fact that every DPI model in current use is different. Medical personnel's knowledge of correct DPI use has also been shown to be lacking. The