COPD-X Summary of Changes V2.51 September 2017

The latest update of The COPD-X Plan: Australian and New Zealand Guidelines for the Management of COPD has been provided by Lung Foundation Australia in conjunction with the Thoracic Society of Australia and New Zealand following the September 2017 meeting of the COPD-X Guidelines Committee.

Implications for Clinical Practice

All changes made to the document are outlined below and those in the shaded boxes are differentiated as the most significant and likely to have an impact on clinical practice.

Executive Summary

Heading changed to Key Recommendations of the COPD-X Guidelines which now incorporates the NHMRC level of evidence and GRADE strength of recommendation for each.

C. Confirm diagnosis and assess severity

Additional bullet point "Symptoms of exertional breathlessness, cough and sputum" when considering a COPD diagnosis.

C4.1 Confirm or exclude asthma

Reference to the presence of coexisting COPD and asthma in some patients and the recommendations for treatment. COPD patients with features of asthma should receive inhaled corticosteroid therapy (to treat the asthma component), as well as long-acting bronchodilators (LABA). LABA monotherapy should be avoided in patients who have a component of asthma (Global Initiative for Asthma 2017).

C5.4 Chest x-rays

Inclusion of a reference to support the statement that the chest x-ray is not accurate for the diagnosis of COPD [1].

O. Optimise Function

O1.2.3 Long-acting bronchodilator combinations (LAMA/LABA)

Review and revision of whole section to include an introductory paragraph listing the LAMA/LABA fixed dose combinations in a single inhaler. These combinations (aclidinium/formoterol; glycopyrronium/indacaterol; tiotropium/olodaterol; umeclidinium/vilanterol; and glycopyrrolate/formoterol) have been clearly labelled within their sections and the detailed discussion refined.

In the paragraph comparing the glycopyrronium/indacaterol combination with fluticasone/salmeterol, it was noted in the previous version of COPD-X that patients receiving glycopyrronium/indacaterol had a lower annual rate of exacerbations. In this version, it is stated

that the reduction of exacerbations was independent of baseline eosinophil count and use of inhaled corticosteroids at time of recruitment [2].

In addition, a paragraph has been added based on a Cochrane review which analysed 11 RCTs (9,839 patients) studying LAMA/LABA vs. ICS/LABA therapy [3]. Compared to ICS/LABA, LAMA/LABA resulted in a small reduction in the rate of exacerbations, no significant change in mean SGRQ score (although there was a higher proportion achieving the MCID) and a small improvement in FEV_1. Pneumonia rates were lower, and there was no change in mortality. Even with some limitations (heterogeneity of studies, relatively short duration and low to moderate quality evidence), this systematic review supports the use of LAMA/LAMA fixed dose combinations over ICS/LABA inhalers, when initiating long-acting inhaled medicines. Further RCTs of ICS/LABA/LAMA in a single inhaler are awaited, to clarify their efficacy compared to LAMA/LABA.

O4.1 Inhaled corticosteroids and long-acting beta2-agonists in combination (ICS/LABA)

Addition of a paragraph discussing an open label randomised trial in 75 UK general practices where 2,799 patients were randomised to a combination of fluticasone furoate/vilanterol or usual care [4]. The trial design was unique in that patients in the control group were permitted to continue their current inhalers rather than all take the same treatment, the trial was performed in general practice and the majority of patients only had contact with study staff at baseline and at 12 months. The rate of moderate or severe exacerbations was 8.4% lower with fluticasone furoate/vilanterol compared with usual care. There was no increase in pneumonia rates.

O7.2.2 Safety of beta-blockers

Addition of a sentence stating that despite a paucity of evidence to suggest harm, beta-blockers are still under-utilised in COPD for guideline-based indications such as systolic heart failure [5].

O7.3 Osteoporosis

Inclusion of evidence stating that patients with vertebral compression fractures, visualised on a lateral chest x-ray, had more frequent admissions, longer length of hospital stay, and increased mortality in the two years after admission [6].

O8.1 Treatment of hypoxaemia and pulmonary hypertension

The sections on ventilatory support have been removed and instead included in new standalone section **P11 Long-term home non-invasive ventilation**.

O9.2 Lung volume reduction surgery and bronchoscopic interventions

Change to section heading to specify “bronchoscopic interventions”.

At the end of the paragraph discussing six RCTs examining endobronchial valves, addition of a sentence to state that by 12 months, 22% of patients in the Klooster 2015 RCT required permanent valve removal [7].

O10. Palliative and supportive care

The section heading now includes reference to "supportive care". The whole section has been reviewed and updated by a respiratory physician with specialisation in palliative and supportive care. The World Health Organisation 2002 definition is quoted. The section includes discussion of general and specialist palliative care and the importance of such services in COPD patients as early access can improve survival. Barriers to accessing palliative care are outlined. Specific sub-headings have been included: Supportive care - symptom control (discussing breathlessness); Non-pharmacological management of breathlessness; and Pharmacological management of breathlessness – opioids and benzodiazepines. A **Breathlessness management strategies** box complements this wording. The key points of this section are summarised as:

1. Palliative care should be considered early and should include symptom control and addressing psychosocial and spiritual issues.
2. Active treatment of persisting symptoms or challenging issues may require a multidisciplinary team (which includes primary care, respiratory medicine, and palliative care).
3. The introduction of palliative and supportive care principles and discussion of goals of care should be routine in patients with persisting symptoms despite optimal disease-directed treatment.

P: Prevent deterioration

P11 Long-term home non-invasive ventilation

The wording for this new section has been moved from **O8.1 Treatment of hypoxaemia and pulmonary hypertension**. A new paragraph has been included based on a trial of long-term non-invasive ventilation (NIV) in highly selected patients who remained hypercapnic and hypoxic two to four weeks after resolution of respiratory acidosis due to an exacerbation of COPD [8]. 116 patients were randomised to continuous home oxygen or continuous home oxygen plus home NIV and high NIV pressures were used. Median NIV adherence at 12 months was high at 7.6 hours. The 12-month risk of readmission or death was 63.4% in the home oxygen plus home NIV group vs. 80.4% in the home oxygen alone group. There was no mortality difference at 12 months. The section concludes with the statement, "Referral for specialist opinion at an institution with expertise in this area should be sought."

P12 Alpha1-antitrypsin deficiency

Further amendments have been made to the section, after consultation with the Thoracic Society of Australia and New Zealand (TSANZ) and discussion at the TSANZ COPD Short Course where this topic was presented.

New wording has now been added stating that the evidence to date demonstrates that AAT augmentation modifies the development of emphysema, and that it is unclear if AAT therapy improves clinical outcomes. A statement has been included to indicate that studies of cost-effectiveness have not yet been conducted.

D: Develop a plan of care

Inclusion of a paragraph discussing an intensive, comprehensive health coaching intervention that included a motivational interviewing-based intervention delivered via telephone, a written action plan for exacerbations including the use of antibiotics and oral steroids, and an exercise prescription. This intervention decreased COPD-related hospitalisations at one, three and six months after hospital discharge, but not at one year after discharge. Disease-specific quality of life improved significantly in the health coaching group compared with the control group at 6 and 12 months, based on the Chronic Respiratory Disease Questionnaire emotional score and physical score. There were no differences between groups in measured physical activity at any time point [9]. It should be noted that several of these individual components have been shown to be effective in isolation.

D1. Support team

This section and its individual sub-sections have been reviewed and extensively revised, including the addition of supporting references for individual professions where available.

D4. Telehealth

Inclusion of wording discussing a 12 month program of home-based telerehabilitation which included both an exercise program at home (three times weekly) following a two month hospital-based pulmonary rehabilitation program, as well as self management education; regular review by a team of health professionals via phone or Skype weekly; self monitoring of lung function; and access to a helpline. This program was compared with a hospital-based pulmonary rehabilitation program twice weekly and to usual care. The control group had no initial pulmonary rehabilitation and both groups received sustained intensive pulmonary rehabilitation. Both home-based telerehabilitation and centre-based pulmonary rehabilitation reduced exacerbations and hospitalisations compared with usual care. The home-based telerehabilitation group also had a lower rate of ED attendances in the 12 months of follow-up than the hospital-based group and usual care group. The home-based program was intensive and the results impressive, however a cost analysis was not included in the study [10].

D5. Treat anxiety and depression

Addition of wording referring to the importance of screening for clinically significant anxiety and depression, during admissions for exacerbations [11].

D7 End-of-life issues

This section has been removed to avoid duplication of the information in the newly revised section **O10. Palliative and supportive care**.

D7.1 Palliative care services

This section has been removed to avoid duplication of the information in the newly revised section **O10. Palliative and supportive care**.

X: Manage eXacerbations

Inclusion of a sentence stating that retrospective analysis of data from the UPLIFT (tiotropium study) demonstrated an accelerated loss of lung function after a single COPD exacerbation [12].

X2.2.3 Antibiotics for treatment of exacerbations

Inclusion of an additional sentence discussing the measurement of procalcitonin levels to determine the use of antibiotics. In most clinical trials, use of antibiotics was discouraged if procalcitonin was 0.1ng/ml or lower and encouraged if procalcitonin was above 0.25ng/ml.

A meta-analysis of eight randomised or quasi-randomised trials, evaluating 1,062 patients, compared procalcitonin-based protocols to initiate or discontinue antibiotics, versus standard care in COPD exacerbation [13]. Procalcitonin-based protocols decreased antibiotic prescription without affecting clinical outcomes such as rate of treatment failure, length of hospitalisation, exacerbation recurrence rate or mortality. Since the publication of this meta-analysis, a further trial has also reported that procalcitonin-based protocols reduce antibiotic use without increasing complications [14].

X3.2 Non-invasive ventilation

Review and revision of section based on publication of level I evidence that non-invasive ventilation reduces mortality and intubation rates in acute hypercapnic ventilatory failure [15]. Non-invasive ventilation (NIV) should be strongly considered in patients with an exacerbation of COPD who present with hypercapnic respiratory failure as defined on an arterial blood gas with a $PaCO_2$ above 45mmHg and a pH less than 7.35 [15]. NIV is an effective and safe means of treatment of ventilatory failure. Its use allows preservation of cough, physiological air warming and humidification, and normal swallowing, feeding and speech. Applying NIV in addition to conventional therapy reduces the risk of mortality by 46% and decreases the risk of needing endotracheal intubation by 65% [15]. This benefit is similar for patients with mild acidosis (pH 7.30 to 7.35) vs. a more severe nature (pH < 7.30), and when NIV is applied in a ward or intensive care unit [15]. The use of NIV reduces hospital length of stay [15].

X3.6 Pulmonary rehabilitation

This section has been reviewed and expanded to include level I evidence of the benefits of pulmonary rehabilitation. A systematic review of 17 studies [16] reported the effects of pulmonary rehabilitation in 1,477 participants who were in the recovery phase of a recent hospitalisation for an exacerbation of COPD. The rehabilitation was commenced between two days and two weeks after the exacerbation, and was provided in inpatient, outpatient, and home settings, with a program duration between four days and six months. Pulmonary rehabilitation significantly improved health-related quality of life and exercise capacity in the short-term (median of five months for health-related quality of life and a median of three months for exercise capacity). Pulmonary rehabilitation also reduced hospital readmissions. The follow-up period for collection of hospitalisation data ranged from three to 18 months, with a median duration of nine months. There was no significant

effect on mortality.

In the Australian and New Zealand health care context, inpatient pulmonary rehabilitation is not easily accessible, whereas access to outpatient pulmonary rehabilitation is more feasible. Accordingly, the authors of the Australian and New Zealand Pulmonary Rehabilitation Guidelines [17] performed a meta-analysis of five outpatient pulmonary rehabilitation studies (program duration 6-12 weeks), commenced within two weeks of hospital discharge. Consistent with the Puhan review, large benefits for health-related quality of life and exercise capacity were found. In contrast, no statistically significant reduction in hospital readmissions was found, most likely due to the small sample. Importantly, no adverse events were reported. Overall, the Australian and New Zealand Pulmonary Rehabilitation Guidelines recommend that outpatient pulmonary rehabilitation is provided after an exacerbation of COPD, commencing within two weeks of hospital discharge [16].

A definition of a COPD exacerbation has been included in this section as follows: Exacerbations of COPD are characterised by worsening dyspnoea and fatigue, decreased exercise tolerance and a reduction in health-related quality of life [18, 19]. Individuals are typically less active following hospitalisation for an exacerbation of COPD and this low level of activity may persist for several weeks [20]. Quadriceps muscle strength is often reduced during an exacerbation and may be a contributor to inactivity [21].

X4 Uptake and impact of guidelines for exacerbations

Inclusion of a paragraph based on a European study which found that hospitalised COPD patients with an exacerbation received on average only 41% of key diagnostic, pharmacological and non-pharmacological recommendations from clinical guidelines, including low uptake of provision of smoking cessation advice, inhaler technique education and referral to pulmonary rehabilitation [22]

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