

COPD-X Summary of Changes V2.50 June 2017

Implications for Clinical Practice

The following changes have been identified as being the most significant and likely to have an impact on clinical practice.

O. Optimise Function

O5.1 Inhaler technique

Inclusion of new wording on the importance of correct inhaler technique based on two 2017 studies and addition of an introductory sentence stating that incorrect inhaler technique is common and is associated with worse outcomes.

Correct inhaler technique is associated with fewer severe exacerbations. An observational study involving 2,935 patients with COPD, reported that in individuals who were treated for at least three months, the occurrence of prior (past three months) severe exacerbation was significantly associated with at least one observed critical error using prescribed inhalers (Molimard 2017).

A systematic review and meta-analysis of 72 studies involving asthma and COPD patients, reported that 50-100% of patients performed at least one handling error. The pooled summary results for pMDI estimated an overall error rate of 86.6% and for DPIs it was 60.9% (Chrystyn 2017) [evidence level I].

O6.8 Chest physiotherapy (Airway clearance techniques)

Review and update of the section, including mention of the different devices available in Australia and discussion of the factors involved in choosing an appropriate device (the level of expertise of the therapist and availability and cost). The wording emphasised that patients with evidence of chronic sputum production should be referred to a physiotherapist for assessment and education regarding the most appropriate airway clearance techniques (ACTs) based on their clinical features. It was noted that conventional chest physiotherapy (defined as any combination of gravity-assisted drainage, percussion, vibrations and directed coughing /huffing) was now used less commonly.

O9.2 Lung volume reduction surgery and other techniques

Inclusion of data from a 2017 meta-analysis of endobronchial lung volume reduction surgery (van Agteren 2017). Results from 14 trials comprising almost 2,000 participants were analysed. The authors concluded that evidence for short-term (up to one year) improvements in disease status were most evident for studies testing endobronchial valves (five studies) and coils (three studies), including improvements in lung function and quality of life. The authors noted a significant increase in adverse events. The odds ratio for an adverse event reported for trials examining endobronchial valves was 5.85 and the overall odds ratio for an adverse event amongst all endobronchial lung volume reduction techniques was 3.00. Pneumothorax rates of over 20% were reported in several endobronchial valve trials. It is important to note the authors' concerns regarding the lack of sham bronchoscopy and/or unclear status of blinding in some studies that may cause a risk of bias.

P: Prevent deterioration

P2.2 Pneumonia

Addition of an introductory sentence stating that pneumococcal immunisation is recommended for all patients with COPD. Inclusion of level I evidence from a 2017 Cochrane Review (Walters 2017) which stated that people with COPD vaccinated with injectable polyvalent pneumococcal vaccines were less likely to experience an episode of community-acquired pneumonia; vaccination also reduced the likelihood of an exacerbation of COPD. Evidence was insufficient in this meta-analysis for comparison of different pneumococcal vaccine types and expert opinion was divided about whether to continue to advise use of the 23-valent polysaccharide vaccine or to replace its use with the far more effective conjugate vaccine.

D: Develop a plan of care

D3. Self-management

Discussion of the benefits of COPD Action Plans on reduced emergency department (ED) visits and hospital admissions. A review by Howcroft reported that use of action plans with a single short educational component, along with ongoing support directed at use of the action plan reduced ED visits and hospital admissions with no change to mortality or quality of life (Howcroft 2016). The number needed to treat to reduce one hospital admission was 19. Studies that included an exercise program and longer education sessions were not included in this review. A subsequent RCT not included in this review confirmed a reduction in ED visits (Zwerink 2016).

All Changes

Change from eformoterol to formoterol throughout in line with changes brought about by TGA in June 2017.

C. Confirm diagnosis and assess severity

Addition of a new paragraph based on a study which followed up of a cohort of children aged 10 to 16 initially recruited in 1964. This demonstrated that childhood participants who had wheezy bronchitis and asthma had an increased risk of COPD by mean age of 61, compared to cohort control (Tagiyeva 2016).

O. Optimise Function

O1.2.1 Long-acting muscarinic antagonists (LAMA)

Addition of a sentence stating that compared to placebo, aclidinium reduced the rate of moderate-severe exacerbations (Wedzicha 2016).

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

Addition of a new paragraph discussing the adverse events of tiotropium and olodaterol fixed dose combinations (FDC). These were mainly COPD exacerbations and infections and were comparable between the FDCs and the monocomponents. Changes in breathlessness at 24 weeks assessed by transition dyspnoea index (TDI) did not show clinically significant differences between FDC and monocomponents (Ferguson 2017).

Citation of another systematic review of the efficacy and safety of umeclidinium/vilanterol (Wang 2016) showing similar results to the evidence previously cited in COPD-X.

Addition of wording discussing two phase III randomized, double blind, and placebo controlled trials which investigated the efficacy and safety of a novel glycopyrrolate/formoterol (GFF) metered dose inhaler (MDI) in patients with moderate-to-very severe COPD over 24 weeks. Compared to placebo, the GFF MDI showed greater change from baseline in morning predose trough FEV₁ in both trials. In one study, GFF MDI showed significant differences in SGRQ total score vs. placebo and glycopyrrolate MDIs. In both studies, GFF MDI showed a significant reduction in rescue albuterol use vs. placebo MDI. In one study, a significant reduction in albuterol use vs. glycopyrrolate MDI was seen, with nominal significance vs. formoterol MDI. GFF MDI had a safety and tolerability profile similar to that of placebo MDI, monocomponent MDIs, and open-label tiotropium (Martinez 2017).

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

Addition of new wording regarding fluticasone furoate/vilanterol which reduced the rate of exacerbations treated with corticosteroids alone, or with corticosteroids and antibiotics, but not those treated with antibiotics alone (Martinez 2016).

O5.1 Inhaler technique

Inclusion of new wording on the importance of correct inhaler technique based on two 2017 studies and addition of an introductory sentence stating that incorrect inhaler technique is common and is associated with worse outcomes.

Correct inhaler technique is associated with fewer severe exacerbations. An observational study involving 2,935 patients with COPD, reported that in individuals who were treated for at least three months, the occurrence of prior (past three months) severe exacerbation was significantly associated with at least one observed critical error using prescribed inhalers (Molimard 2017).

A systematic review and meta-analysis of 72 studies involving asthma and COPD patients, reported that 50-100% of patients performed at least one handling error. The pooled summary results for pMDI estimated an overall error rate of 86.6% and for DPIs it was 60.9% (Chrystyn 2017) [evidence level I].

O6.1 Pulmonary rehabilitation

Inclusion of an additional study, a randomised controlled equivalence trial by Holland et al (Holland 2017) which adds to the stated benefit of rehabilitation provided to patients in the home setting. This program was comparable to the traditional pulmonary rehabilitation model. The proviso was that programs involved regular contact to facilitate exercise participation and exercise progression.

O6.5 Physical activity and sedentary behaviour

Inclusion of a sentence stating that sedentary behaviour defined as more >8.5 hrs/ day spent in sedentary behaviour in a cohort of 101 Brazilian COPD patients was an independent risk factor for mortality (Furlanetto 2017) [evidence level III].

O6.8 Chest physiotherapy (Airway clearance techniques)

Review and update of the section, including mention of the different devices available in Australia and discussion of the factors involved in choosing an appropriate device (the level of expertise of the therapist and availability and cost). The wording emphasised that patients with evidence of chronic sputum production should be referred to a physiotherapist for assessment and education regarding the most appropriate airway clearance techniques (ACTs) based on their clinical features. It was noted that conventional chest physiotherapy (defined as any combination of gravity-assisted drainage, percussion, vibrations and directed coughing /huffing) was now used less commonly.

O6.10 Nutrition

Following review of the section in the previous COPD-X update, new wording was added in the obesity section based on a meta-analysis of 17 studies which evaluated the dose-response relationship between BMI and mortality. Compared to healthy weight COPD individuals, the risk of death in the underweight group was increased, whereas the risk was reduced in those who were overweight and obese. There was a nonlinear relationship between mortality and BMI categories. Those with a BMI <21.75 kg/m² had the greatest risk of dying. Once BMI exceeded 32 kg/m² the

protective effect of high BMI was no longer evident (Guo 2016).

07. Comorbidities

Addition of a sentence stating that both comorbid chronic respiratory conditions and comorbid psychiatric disorders were found to be associated with a higher risk of frequent (≥ 2 per year) exacerbations (Westerik 2017).

07.10 Alcohol and sedatives

Addition of a new paragraph discussing the risks of administering opioids in older adults with COPD. In a population-based cohort of 130,979 community-dwelling older adults with COPD, new opioid users were associated with significantly increased risk of emergency room visits for COPD or pneumonia. This study did not specifically look at patients that were prescribed opioids for relief of dyspnoea. Opioid use was also associated with significantly increased risk for COPD or pneumonia-related mortality and all-cause mortality, but significantly decreased outpatient exacerbations. New opioid use and, in particular, use of the generally more potent opioid-only agents, was associated with increased adverse respiratory outcomes and mortality. It was noted that a careful, individualised approach needed to be taken when administering opioids to older adults with COPD, given the potential for adverse respiratory outcomes (Vozoris 2016).

09.2 Lung volume reduction surgery and other techniques

Addition of new wording throughout the section including:

Discussion of the effects on mortality of Lung Volume Reduction Surgery (LVRS) based on a 2016 Cochrane review (van Agteren 2016). The authors noted that this review was very heavily influenced by data from the National Emphysema Treatment Trial (NETT) - 96% of the patients contributing to the long term mortality data were enrolled in the NETT study. The authors concluded that short-term mortality was higher for LVRS than for control, but long-term mortality favoured LVRS. The authors made note of high post-operative complications, especially persistent air leak and pneumonia.

Addition of a 2016 randomised controlled trial examining endobronchial valves (Valipour 2016) which specifically recruited patients with intact pleural fissures and homogeneous rather than upper lobe predominant emphysema. Significant clinical improvements at 6 months were noted, but a 26% pneumothorax rate was reported.

Inclusion of data from a 2017 meta-analysis of endobronchial lung volume reduction surgery (van Agteren 2017). Results from 14 trials comprising almost 2,000 participants were analysed. The authors concluded that evidence for short-term (up to one year) improvements in disease status were most evident for studies testing endobronchial valves (five studies) and coils (three studies), including improvements in lung function and quality of life. The authors noted a significant increase in adverse events. The odds ratio for an adverse event reported for trials examining endobronchial valves was 5.85 and the overall odds ratio for an adverse event amongst all endobronchial lung volume reduction techniques was 3.00. . Pneumothorax rates of over 20% were reported in several endobronchial valve trials. It is important to note the authors' concerns regarding the lack of sham

bronchoscopy and/or unclear status of blinding in some studies that may cause a risk of bias.

Addition of wording from an open label, multi centre, randomised control trial of staged, single lobe segmental steam thermal ablation on 70 patients with severe COPD and hyperinflation (Herth 2016b). All patients had undergone pulmonary rehabilitation and had a six minute walk distance over 140m. Patients with incomplete fissures and collateral ventilation were not excluded. At six months, there was a significant improvement in lung function and quality of life but not six minute walk distance. 24% of patients undergoing steam thermal ablation experienced a COPD exacerbation compared with 4% of controls. It was noted that the procedure was not available in Australasia and its precise role was not yet clear, but as further long term data emerged, the treatment might be an option for patients with severe COPD and hyperinflation with collateral ventilation.

Inclusion of a final paragraph discussing the use of valves and coils, which noted that in highly selected patients with severe COPD and hyperinflation, endobronchial valves might be appropriate if collateral ventilation could be excluded and endobronchial coils (although not currently available in Australia) might be an option if collateral ventilation was present. It was recommended that these therapies should only be considered in specialised centres (Shah 2014) and all patients being considered for lung volume reduction should be referred for pulmonary rehabilitation and discussed by an expert panel that included a radiologist, respiratory physician, interventional pulmonologist and thoracic surgeon (Herth 2016a).

P: Prevent deterioration

P2.2 Pneumonia

Addition of an introductory sentence stating that pneumococcal immunisation is recommended for all patients with COPD. Inclusion of level I evidence from a 2017 Cochrane Review (Walters 2017) which stated that people with COPD vaccinated with injectable polyvalent pneumococcal vaccines were less likely to experience an episode of community-acquired pneumonia; vaccination also reduced the likelihood of an exacerbation of COPD. Evidence was insufficient in this meta-analysis for comparison of different pneumococcal vaccine types and expert opinion was divided about whether to continue to advise use of the 23-valent polysaccharide vaccine or to replace its use with the far more effective conjugate vaccine.

P7 Mucolytic therapy

Change to evidence level (II to I) for opening statement “Mucolytics can reduce the frequency and duration of exacerbations” and inclusion of updated Cochrane Review by Poole et al and additional reference by Cazzola et al (Poole 2015, Cazzola 2015).

P8. Humidification therapy

Inclusion of new final sentence “In the acute setting, high flow nasal oxygen has a role in hypoxic respiratory failure where hypercapnia has been excluded (Stephan 2015, Frat 2015).”

D: Develop a plan of care

D3. Self-management

Inclusion of concluding sentence at end of second paragraph stating that COPD multidisciplinary care, incorporating elements such as exercise, self-management education and exacerbation management could improve exercise capacity and health-related quality of life, and reduce hospitalisation.

Discussion of the benefits of COPD Action Plans on reduced emergency department (ED) visits and hospital admissions. A review by Howcroft reported that use of action plans with a single short educational component, along with ongoing support directed at use of the action plan reduced ED visits and hospital admissions with no change to mortality or quality of life (Howcroft 2016). The number needed to treat to reduce one hospital admission was 19. Studies that included an exercise program and longer education sessions were not included in this review. A subsequent RCT not included in this review confirmed a reduction in ED visits (Zwerink 2016).

D4. Telehealth

Inclusion of a paragraph discussing an RCT that evaluated a simple nurse initiated telephone follow-up of COPD patients following admission to hospital with an acute exacerbation of COPD or pneumonia. There was no reduction in readmission or mortality at 30 or 84 days post discharge. The intervention group received a nurse initiated phone call at two days post discharge and further calls if deemed necessary. At 30 and 84 days the proportion of those readmitted in the intervention and control groups was 33% and 34%, and 32% and 27%, respectively. The intervention group did report more confidence in disease management (Lavesen 2016).

X: Manage eXacerbations

X3.4 Clearance of secretions

Inclusion of a new final paragraph highlighting the importance of assessing whether airway clearance techniques (ACT) were appropriate and if so, choosing the most suitable technique, given the negative impact of exacerbations on symptoms such as dyspnoea and fatigue. It was also noted that the choice of ACT needed to be guided by a physiotherapist experienced in this type of clinical presentation.

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