Summary of Changes V2.44, December 2015

C. Confirm diagnosis and assess severity

C2.5 COPD case finding

Change to section heading from "COPD screening devices for targeted case finding" and minor change to introductory sentence.

O. Optimise Function

O1.1.2 Short-acting muscarinic antagonists (SAMA)

Addition of new last sentence in last paragraph based on updated Cheyne 2015 Cochrane Review – there was no substantial difference in mortality with tiotropium delivered by the Respimat device compared to the HandiHaler.

O1.2.1 Long-acting muscarinic antagonists (LAMA)

Change to wording on aclidinium in penultimate paragraph based on Cochrane systematic review (Ni 2014) - aclidinium resulted in marginal improvements in quality of life and FEV_1 compared with placebo and reduced the number of patients with exacerbations requiring hospitalisation compared to placebo.

Addition of new last paragraph discussing a network meta-analysis of clinical trials of at least 12 weeks duration comparing the efficacy of LAMAs in preventing moderate-to-severe and severe COPD exacerbations. The evidence suggested that there were no statistically significant differences among LAMAs. Tiotropium dry powder inhaler was the only LAMA formulation which reduced severe exacerbations.

O1.2.2 Long-acting $beta_2$-agonists (LABA)

Citation of reference by Geake 2015 comparing indacaterol with placebo and removal of older references. Addition of sentence on efficacy of indacaterol compared to twice daily $beta_2$-agonists based on Geake 2015 – no clinically significant difference in FEV_1, dyspnoea or quality of life.

New paragraph on based on Decramer 2013 paper stating once-daily treatment with indacaterol via Breezhaler or tiotropium bromide via HandiHaler in patients with severe COPD and a history of exacerbations gave equally effective and clinically relevant improvements in lung function, health status, and breathlessness. Patients receiving indacaterol had a 29% higher annual rate of exacerbations versus patients receiving tiotropium.

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

Addition of wording on the efficacy and safety of umeclidinium/vilanterol in patients with moderate to severe COPD based on a systematic review by Rodrigo 2015. The systematic review found benefits in mean trough FEV_1 compared with the monocomponents, tiotropium (via HandiHaler) or fluticasone

propionate/salmeterol (via Accuhaler). Umeclidinium/vilanterol also reduced the likelihood of exacerbations compared with the monocomponents. There were no differences in dyspnoea, QoL, or exacerbation risk between umeclidinium/vilanterol and tiotropium. Donohue 2015 reported that umeclidinium/vilanterol improved lung function compared with fluticasone proprionate/salmeterol, although there were no differences in dyspnoea or quality of life.

O4.1 Inhaled corticosteroids and long-acting beta$_2$-agonists in combination (ICS/LABA)

New wording at end of section based on Crim 2015 paper regarding pneumonia risk which was significantly higher in all fluticasone furoate/vilanterol treatment groups compared with the vilanterol group when administered once daily.

O6.1 Physical activity

New reference by McNamara 2014 added to emphasise inactivity and sedentary behaviour are heightened in COPD patients with comorbidities.

O9.2 Lung volume reduction surgery and other techniques

Rewording of paragraph discussing Zephyr endobronchial valves based on new evidence by Davey 2015 adding to two previously cited trials (Herth 2012 and Sciurba 2010). The trials which recruited highly selected patients, reported very small improvements in FEV_1; some improvement in quality of life (Sciurba and Herth); and improvement in exercise outcomes (Herth and Davey). Data on adverse events were conflicting. Davey recognised the high complication rates and called for future trials to compare valve placement with surgical lung volume reduction.
New sentence added on endobronchial coils based on Zoumot 2015 paper showing improvement in quality of life, six minute walk distance (and to a lesser degree lung function) at day 180 and 360.
New paragraph added based on Come 2015 paper discussing an RCT using Emphysematous Lung Sealant (ELS). The trial was terminated early due to loss of funding prior to the 12 month pre-specified endpoints and limited data at 6 months showed significant improvements in spirometry, 6MWD, QoL and dyspnoea. However the complication rate was unacceptably high - increased hospitalisations and serious adverse events with two deaths in the intervention arm and no deaths in the control arm.

O10.1 Opioids

New wording added suggesting regular low dose oral morphine may be considered for treating breathlessness in patients with severe COPD that persists despite optimal medical management (Ekstrom 2015). Compared with placebo, the 2015 systematic review and meta-analysis found small short-term benefits in dyspnoea with minimal adverse effects, but no effects on exercise capacity and unclear effects on quality of life.

D: Develop a plan of care

D3. Self-management

Inclusion of new wording based on a systematic review (Majothi 2015) which failed to demonstrate any positive effect of COPD self management following admission to hospital as a distinct intervention on all cause mortality or health care utilisation (hospitalisation). The studies did have methodological weaknesses and there was heterogeneity in the interventions and outcome measures.

D5. Treat anxiety and depression

Addition of a new sentence stating that case management to support adherence to antidepressant medication in conjunction with attending pulmonary rehabilitation has been associated with improvements in both depression and dyspnoea-related disability(Alexopoulos 2014).

X: Manage eXacerbations

Inclusion of reference by Mullerova 2015, which reported risk factors and outcomes of hospitalised exacerbations of COPD in the ECLIPSE cohort. Data showed that a history of prior hospitalisation for COPD was the strongest predictor of subsequent hospitalisation. This data also confirmed 12 month mortality rates were significantly higher in patients hospitalised for COPD compared to those without hospitalisation.

X2.2 Optimise treatment

Addition of wording from a study by Tang 2014 which discussed the level of adherence to GOLD for managing patients hospitalised with a COPD exacerbation. Evidence showed that although the adherence to pharmacological, rehabilitation and vaccination management reduced health care costs, uptake of GOLD recommendations has had little evaluation. A study in a Victorian hospital demonstrated significant overuse of antibiotics and oxygen, as well as a greater evidence practice gap in general medical units than respiratory medical units.

X2.2.2 Systemic corticosteroids for treatment of exacerbations

Inclusion of wording from a study by Bafadhel 2014 who re-analysed data from three additional RCTs that examined the use of oral corticosteroids in COPD exacerbations. Blood eosinophils >2% were a useful biomarker to determine which patients benefit from systemic corticosteroids.

X3.5 Develop post-discharge plan and follow-up

Addition of a paragraph based on a study by Jennings 2015 who "bundled" non-pharmacological interventions which individually have shown some promise in reducing COPD admissions. The bundle included smoking cessation counselling, screening for gastroesophageal reflux disease and depression or anxiety, standardised inhaler education, and a 48-h post-discharge telephone call. The intervention did not reduce 30 or 90 day COPD readmission rates. Where bundles have omitted proven components such as pulmonary rehabilitation, there has been no benefit for readmissions.

Appendix 2. Explanation of inhaler devices

- Inclusion of "propionate" after fluticasone in Accuhaler section of "Dry powder inhalers".

- Inclusion of Respimat under "Soft mist inhalers".

- Inclusion of Seebri (glycopyrronium) and Ultibro (indacaterol/glycopyrronium) in Breezhaler section of "Dry powder inhalers".

- Inclusion of Brimica (aclidinium/eformoterol) in Genuair section of "Dry powder inhalers".

- Inclusion of Breo (fluticasone furoate/vilanterol trifenatate) in Ellipta section of "Dry powder inhalers".