Summary of Changes V2.45, March 2016

C. Confirm diagnosis and assess severity

C2.3 Spirometry

Further evidence added to illustrate the importance of spirometry in diagnosing COPD. The study by Jain 2015 reviewed 333 patients with physician-diagnosed COPD and/or asthma and found that a third had neither asthma nor COPD, and a quarter may not have any form of airflow limitation. Spirometry had been performed in less than a third of the patients studied.

O. Optimise Function

O1.2.1 Long-acting muscarinic antagonists (LAMA)

A network meta-analysis (Ismaila 2015) showed that LAMAs have similar efficacy in terms of change in FEV_1, SGRQ, dyspnoea index and rescue medications. However, there are no direct head to head comparisons of LAMAs.

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

A Cochrane systematic review of ten studies (Farne 2015) found that the combination of tiotropium and a LABA provided small improvements in health-related quality of life over 3 to 12 months and bronchodilation compared to tiotropium alone. Similar results were found for a LABA plus tiotropium compared to a LABA alone. The clinical importance of these small benefits was uncertain. No statistically significant differences in mortality or hospital admissions were found. The majority of participants in these studies had severe COPD.

A network meta-analysis of LAMA/LABA combinations compared with monotherapies (Oba 2016) found that the fixed dose combinations provided small benefits in lung function and quality of life compared with their monocomponents, with no increase in adverse outcomes. Combination therapy reduced moderate to severe exacerbations compared with LABA alone but not compared with LAMA alone. Effects on severe exacerbations were similar with both combination and monotherapies.

O3.2 Inhaled corticosteroids (ICS)

Addition of wording from a nested case-control analysis of over 100,000 patients treated with ICS in Canada (Suissa 2015) relating to the decrease in pneumonia rates following cessation of treatment with ICS. The study found that cessation of ICS was associated with a 36% decrease in the rate of severe pneumonia events defined as hospitalisation or death from pneumonia during the study period. The decreasing rate of serious pneumonia occurred rapidly, going from 20% reduction in the first month to 50% reduction by the fourth month after discontinuation. The risk reduction was more marked with cessation of fluticasone than cessation with budesonide.

Addition of wording based on level II evidence by Rossi 2014 stating that milder COPD patients (FEV_1 50 to 80% predicted and no exacerbations in the past 12

months) were able to be switched from ICS to indacaterol with no significant differences in FEV_1, dyspnoea score, SGRQ score or frequency of exacerbations over six months, providing reassurance that switching from salmeterol/fluticasone to indacaterol appeared to be safe in this group of milder patients.

O7.2 Cardiac disease

Further evidence added from a systematic review and meta-analysis (Chen 2015) that COPD patients possess an increased burden of cardiovascular disease (ischaemic heart disease, dysrhythmia, heart failure, pulmonary circulatory disorders and arterial diseases) when compared to the normal population. This result was mainly driven by angina.

O9.2 Lung volume reduction surgery and other techniques

Inclusion of new evidence on the use of endobronchial valves (Klooster 2015 and Wood 2014) to add to the previously cited studies by Sciurba 2010, Herth 2010 and Davey 2015. All the trials recruited highly selected COPD patients with severe obstruction and gas trapping and excluded patients with significant hypercapnia and poor mobility. Improvements in FEV_1 were reported in all but the Wood trial and data on improvement in exercise outcomes was variable - with positive results in the trials by Herth, Davey and Klooster. Data on adverse events was significant. The Sciurba and Wood trials reported high hospital admissions for COPD exacerbations, Klooster reported an 18% pneumothorax rate and Davey reported small numbers of severe complications. The Klooster trial had the most impressive results, possibly as it was the most thorough in excluding patients with collateral ventilation. Based on the new evidence, there was no change to the conclusion that endobronchial valves may provide a benefit to highly selected patients but should only be considered in specialised centres and cannot yet be recommended as routine therapy.

Inclusion of new wording on lung volume reduction coil treatment from Deslee 2014 who reported on the largest non-blinded randomised control trial to date. 100 highly selected patients were randomised to usual care or bilateral coil placement. All patients had under gone pulmonary rehabilitation. The pre-specified primary end point of percentage of patients achieving a 54m improvement in 6 minute walk distance at 6 months was met (36% vs. 18%). However at 12 month follow up there was no significant difference in mean improvement in 6 minute walk distance. There were sustained improvements in spirometry and quality of life at 12 months. Pneumonia rates were higher in the coil group (18% vs. 4%) but pneumothorax rates were similar between the two groups. Cost effectiveness analysis found the treatment to be prohibitively expensive.

O9.3 Lung Transplantation

Review of lung transplantation section with inclusion of additional wording discussing the type of patients who should be referred to a transplant centre and those in whom lung transplantation is contraindicated. The new wording also includes expected one, five and 10 year survival rates post-transplant.

P: Prevent deterioration

P10. Oxygen therapy

Review and revision of oxygen therapy section with change from the recommendation that long-term oxygen therapy should be at least 15 hours per day to an average usage of 18 hours per day.

Addition of McDonald 2016 reference (Clinical Practice Guideline on Adult Domiciliary Oxygen Therapy: Executive summary from the Thoracic Society of Australia and New Zealand).

There has been substantial review of the "Intermittent Oxygen Therapy" sub-section which states that ambulatory oxygen therapy should not be offered routinely to patients who do not qualify for long term oxygen therapy. This conclusion is based on a Cochrane Review (Ameer 2014). However, it is stated that the use of short-term intermittent oxygen therapy may be considered for people who experience oxygen desaturation on exertion; patients living in isolated areas or prone to sudden life- threatening episodes while they are awaiting medical attention or evacuation by ambulance; and patients travelling by air.

A sub-section called "Ambulatory oxygen therapy during pulmonary rehabilitation" has been added.

P11 Alpha1-antitrypsin deficiency

Inclusion of wording on the use of intravenous alpha-1 antitrypsin augmentation therapy in 177 COPD patients with severe alpha1-antitrypsin (AAT) deficiency (Chapman 2015). Whilst the study showed some improvements in radiologically-defined outcomes, the optimal dosing regimen has not yet been determined, and cost-effectiveness is not known. Results from additional RCTs underway are awaited.

X: Manage eXacerbations

Inclusion of a sentence based on a small study (Shapira-Rootman 2015) which found that approximately 1 in 5 patients hospitalised with a COPD exacerbation were found to have pulmonary embolism.

Appendix 3. Long term oxygen therapy

Addition of McDonald 2016 reference (Clinical Practice Guideline on Adult Domiciliary Oxygen Therapy: Executive summary from the Thoracic Society of Australia and New Zealand). This replaces the 2005 TSANZ Position Paper on adult domiciliary oxygen therapy (McDonald 2005).

Amendments made to the “Choosing the right method” of domiciliary oxygen therapy sub-section with “Oxygen concentrators” split into “Stationary oxygen concentrators” and “Portable oxygen concentrators” and some amendments made to “Cylinders”.