COPD-X Summary of Changes V2 64

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Snapshot of the evidence review cycle for V2 64 - June 2021

The latest update of The COPD-X Plan has been provided by Lung Foundation Australia following the June 2021 meeting of the COPD-X Guidelines Committee. 19 changes are outlined in this summary.

Changes within sections with new citations = 19

6 out of 19

Changes are significant and likely to have an impact on clinical practice.

Implications for Clinical Practice

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

Change	Section	Type of change	Relevant key recommendation	Page number
1	Revised foreword including multiple new citations to population level data from the Australian Institute for Health and Welfare.	2011 foreword revised by current Co-Chairs on behalf of Committee.	N/A	P11-12

C: Case finding and diagnosis

Change	Section	Type of change	Relevant key recommendation	Page number
C1 Aetiology and natural history				
2	Updated Box 2 highlighting risk factors.	Updated list from GOLD Report 2018 to risk factors listed in GOLD Report 2021.	N/A	P24
3	In the Tasmanian Longitudinal Health Study, there were five different asthma /allergy trajectory patterns demonstrated in the prospective cohort of participants. This cohort included n=7380 initial participants at seven years of age, to n=2689 of the original participants at 53 years of age. Those with early onset-onset persistent asthma and allergies were most likely to develop COPD (OR 5.3, 95% CI 3.2-8.6.), followed by late-onset asthma and allergies (OR 3.8, 95% CI 2.4-4.6) (Bui 2021). This highlights the need for a personal approach including the management of treatable traits to potentially prevent progression to COPD.	New paragraph at the end of C1, including new citation, decribing prospective cohort study.	N/A	P24-25
C2.5 COPD case finding				
4	Patients that are added to a COPD register as a result of a systematic screening programme (Haroon 2020) received significantly higher levels of appropriate clinical care. However only one in five case-found patients were actually registered in the database to potentially go on to receive such care. Case finding is only likely to improve clinical care if patients with newly identified disease are promptly added to an active primary care COPD register.	New paragraph at end of section, including new citation.	N/A	P30

O. Optimise function

Change	Section	Type of change	Relevant key recommendation/s	Page number
O3.2 Inhaled corticosteroids (ICS)				
5	In a large, real-world, retrospective, Swedish cohort study, patients with COPD (n = 9651) were more susceptible to bone fractures and osteoporosis than those of the same age and sex without COPD (Janson 2021). The treatment of COPD patients, especially with high-dose ICS (⩾640 µg day), was associated with a higher risk of bone fractures and osteoporosis-related events (risk ratio 1.52 (95% CI 1.24–1.62). Screening of patients with COPD for osteoporosis and identifying those at high risk of fracture (those with comorbidities such as asthma, cardiovascular disease and depression), may be beneficial. In some patients, reducing the dose or discontinuation of ICS might be warranted [evidence level III-2].	New citation and wording added to existing section describing retrospective cohort study.	**Assessment is the first step to optimising function.** [evidence level III-2, strong recommendation] **Optimise function using a stepwise approach.** [evidence level I, strong recommendation]	P46
O4.2 Inhaled corticosteroids and long-acting beta2-agonists and long-acting antimuscarinics in combination (ICS/LABA/LAMA) ➢ *Budesonide/formoterol/glycopyrronium*				
6	A network meta-analysis of ETHOS, KRONOS, IMPACT, and TRILOGY studies (n = 21,909) comparing triple ICS/LABA/LAMA FDC with dual LABA/LAMA and ICS/LBA FDCs administered via the same inhaler device in COPD patients (Calzetta 2020) found that regardless of the level of blood eosinophil count at baseline, the triple ICS/LABA/LAMA FDC was the most effective treatment in reducing the risk of exacerbation, compared to LABA/LAMA FDC (RR 0.45, 95% CrI 0.32–0.61, P < 0.05) and ICS/LABA FDC (RR 0.73, 95%CrI 0.54–0.99, P < 0.05) [evidence level I]. In patients with low level of blood eosinophil count at baseline, LABA/LAMA and ICS/LABA FDCs were equally effective in preventing exacerbations (RR 1.12, 95%CrI 0.83–1.35, P > 0.05). FDCs including an ICS were affected by an increased risk of pneumonia. No increased cardiovascular risk was detected in the FDCs that included two bronchodilators. A network meta-analysis of 19 studies (n=37,741 patients with COPD) found that budesonide/formoterol/glycopyrronium had comparable efficacy and safety to other fixed dose and open triple therapy combinations (Bourdin 2021) [evidence level I].	New citations and wording added to existing section describing network meta-analysis studies.	**Assessment is the first step to optimising function.** [evidence level III-2, strong recommendation] **Optimise function using a stepwise approach.** [evidence level I, strong recommendation]	P53
7	The combinations of both *beclometasone/formoterol/glycopyrronium* and *budesonide/formoterol/glycopyrronium* are now available in Australia and have been approved for listing as PBS subsidised medications.	Availability of triple therapies in Australia changed.		P53

	O4.2 Inhaled corticosteroids and long-acting beta2-agonists and long-acting antimuscarinics in combination (ICS/LABA/LAMA) ➢ *O4.2.1 Eosinophil count and inhaled corticosteroids*			
8	In an Australian study by MacDonald et al (2019), low blood eosinophil counts (<50/uL) during admission for acute exacerbation of COPD were associated with bacterial infection, increased length of stay and a higher 12 month mortality, while just over half of exacerbations associated with higher eosinophil counts (>150/uL) also demonstrated evidence of infection, likely requiring antibiotic therapy (MacDonald 2019).	New citation included with brief additional wording.	**Assessment is the first step to optimising function.** [evidence level III-2, strong recommendation] **Optimise function using a stepwise approach.** [evidence level I, strong recommendation]	P55
9	A meta-analysis by You et al (2020) compared outcomes of acute exacerbations of COPD (AECOPD) with and without eosinophilia (defined as an eosinophil count ≥2% or an absolute eosinophil count ≥0.34x109). Outcomes were better overall for eosinophilic AECOPD, with decreased hospital mortality (OR0.59, 95% CI 0.31-0.95, p=0.03), decreased length of stay (OR=0.72,95% CI-1.44 to -0.00, p=0.05), higher FEV1 (mean difference =0.14, 95% CI 0.08-0.2, p<0.00001) and a lower risk of arrhythmias 9 (OR=1.5, 95% CI 1.01-2.21, p=0.04). It was noted that there were more males among the non-eosinophilic group (OR=1.34, 95% CI 1.15-1.56, p=0.0002), but that steroid use did not differ between the groups (You & Shi 2020). The majority of studies in this meta-analysis were single centre and retrospective in design.	New citation and wording added to end of existing section discussing meta-analsis.		P56
	O4.3 Biologic therapies			
10	A Cochrane systematic review of randomised controlled trials comparing anti-IL-5 therapy with placebo in adults (≥40 years old) with a diagnosis of COPD (as defined by GOLD 2020) and with frequent exacerbations included three studies each of mepolizumab (1530 participants) and benralizumab (4012 participants), both comparing anti-IL-5 therapy versus placebo. No head-to-head comparison trials were identified. Mepolizumab 100 mg reduces the rate of moderate or severe exacerbations by 19% in those with an eosinophil count of at least 150/microlitre (rate ratio (RR) 0.81, 95% confidence interval (CI) 0.71 to 0.93; participants = 911; studies = 2, high-certainty evidence). In participants with lower eosinophils, mepolizumab 100 mg may reduce exacerbations (RR 0.92, 95% CI 0.82 to 1.03; participants = 1285; studies = 2, moderate-certainty evidence). Benralizumab 100 mg reduces the rate of severe exacerbations requiring hospitalisation in those with an eosinophil count of at least 220/ microlitre (RR 0.63, 95% CI 0.49 to 0.81; participants = 1512; studies = 2, high-	New wording and citation added discussing systematic review.	**Assessment is the first step to optimising function.** [evidence level III-2, strong recommendation] **Optimise function using a stepwise approach.** [evidence level I, strong recommendation]	P57-58

	certainty evidence). Anti-IL-5 therapies appear to be safe in individuals with COPD and are likely to reduce the rate of moderate and severe exacerbations in the highly selected group of people who have both COPD and higher levels of blood eosinophils. Lung function and health-related quality of life were not improved (Donovan 2020) [evidence level I]. Further research is needed to elucidate the role of monoclonal antibodies in the management of COPD. It is not clear whether there is a threshold blood eosinophil level above which these drugs may be effective. Cost effectiveness data are also critical to inform clinical decision making, given the high cost of these therapies.			
	O5.1 Inhaler technique			
11	Inclusion of new diagram regarding important considerations for the prescriptions of inhaler devices, especially for older people.	New Figure added.	**Adherence and inhaler technique need to be checked on a regular basis** [evidence level I, strong recommendation].	P59
	O6.2 Exercise training			
12	A systematic review and meta-analysis (de Lima 2020) including 3 studies and 145 participants suggests elastic resistance training may be an alternative to convention resistance training using weight machines for improving knee extensor muscle strength due to similar effects [evidence level I].	New wording and citation added discussing systematic review and meta-analysis.	**Non-pharmacological strategies (such as pulmonary rehabilitation and regular exercise) should be provided to all patients with COPD** [evidence level I, strong recommendation].	P664
	O6.5 Physical activity and sedentary behaviour			
13	Pedometer-based physical activity promotion as a stand-alone intervention, or alongside pulmonary rehabilitation, improved steps per day (approximate improvement of 1000 steps per day) compared with usual care in a systematic review and meta-analysis (Armstrong 2019). Further studies are needed, but physical activity counselling in the context of a pulmonary rehabilitation program shows promise in terms of increasing physical activity in daily life.	New wording and citation added discussing systematic review and meta-analysis.	**Same as above.**	P68

P: Prevent deterioration

Change	Section	Type of change	Relevant key recommendation	Page number
P1 Risk factor reduction ➢ P1.2.5 Electronic cigarettes (e-cigarettes)				
14	Nicotine e-cigarettes are an unapproved product, meaning that unlike other forms of nicotine replacement therapy, they have not been assessed by the TGA for safety, quality and efficacy. The Australian Government have announced that from 1 October 2021, further restrictions aimed at reducing access to the use of nicotine e-cigarettes among adolescents and young adults will be introduced while making them available for supporting smoking cessation. The arrangements include requiring a valid prescription to import nicotine e-cigarettes and liquids containing nicotine.	Australian government announcement regarding restrictions for e-cigarettes from 1 October 2021.	**Smoking cessation is the most important intervention to prevent the worsening of COPD** [evidence level II, strong recommendation].	P105-106
	P2.2 Pneumococcal immunisation			
15	Pneumococcal immunisation is recommended for all patients with COPD. Pneumococcal immunisation with conjugated vaccines covering 13 virulent serotypes (13vPCV) is highly effective in preventing community-acquired pneumococcal pneumonia in older adults (Bonten 2015).	Minor wording changes at the beginning of section.	**Vaccination reduces the risks associated with influenza and pneumococcal infection.** [evidence level I, strong recommendation]	P111
16	For those with newly diagnosed COPD who have never received pneumococcal immunisation: a first dose of 13vPCV (conjugated vaccine) is recommended at diagnosis followed by up to two additional doses of 23vPPV regardless of age. The number of lifetime doses of 23vPPV is now limited to 2 doses for all people who are recommended to receive 23vPPV. The doses of 23vPPV received in the past are also counted when deciding how many more are required. If a person has already received at least two doses based on previous recommendations, no further doses of 23vPPV are to be given. In the current national immunization program (NIP) patients under the age of 65 years with COPD and chronic emphysema **are not** included in the risk conditions for National Immunisation Program (NIP) funded pneumococcal vaccination. Consequently, they are not eligible for reimbursement. The NIP provides funding for 13vPCV followed by 23vPCV vaccine for Aboriginal and Torres Strait Islander adults 50 years and over. Please see The Australian Immunisation Handbook for further details.	New wording regarding interpretation of the recommendations in the Australian Immunisation Handbook.		P106-107

Change	Section	Type of change	Relevant key recommendation	Page number
P10 Oxygen therapy ➢ *Nocturnal oxygen therapy*				
17	***Nocturnal oxygen therapy:*** A large multicentre randomised controlled trial of nocturnal oxygen therapy versus air delivered via concentrator or sham concentrator (the so-called INOX trial) was performed in patients with COPD who did not fulfil criteria for LTOT (Lacasse 2020). Exclusion criteria included smoking cessation less than 6 months previously, significant obstructive sleep apnoea (AHI>15), BMI>40, known left heart failure and bronchiectasis. Inclusion criteria included desaturating to SPO2<90% for at least 30% of the recording time on nocturnal oximetry. Recruitment to this trial was stopped early because of recruitment and retention difficulties after n=243 patients, of a planned n=600, had undergone randomisation. At three years of follow up there was no difference between the groups in the composite endpoint of death from any cause or a requirement for long-term oxygen therapy as defined by the Nocturnal Oxygen Therapy Trial (NOTT) criteria in the intention-to-treat population. Although this trial was underpowered, based on these results and those of two previous studies by Fletcher et al (Fletcher 1992) and Chaouat et al (Chaouat 1999) current evidence does not support the prescription of nocturnal oxygen therapy to improve survival or slow disease progression in patients with COPD. However, the confidence intervals around the pooled treatment effects from a meta-analysis of these three studies performed by the authors of this recent INOX trial and presented as supplementary to this study concluded that the confidence limits around these outcomes are wide, and clinically significant effects are plausible [evidence level I]. More research is needed. In the meantime, some patients with hypoxaemia during sleep may benefit from nocturnal oxygen therapy. Nocturnal hypoxaemia should be considered in patients whose arterial gas tensions are satisfactory when awake, but who have daytime somnolence, polycythaemia or right heart failure. Oxygen may be indicated for patients whose nocturnal arterial oxygen saturation repeatedly falls below 88%. Sleep apnoea should be excluded and treated independently.	New wording and citation added discussing multi-centre randomised controlled trial.	**Long-term oxygen therapy has survival benefits for COPD patients with hypoxaemia** [evidence level I, strong recommendation].	P113-114

D: Develop a plan of care

Change	Section	Type of change	Relevant key recommendation	Page number
18	Changes throughout section, particularly with regard to Chronic disease self-management.	Re-arranged content to most relevant sub-section, additional wording and citations included.	**Good chronic disease care anticipates the wide range of needs in patients with COPD.** [evidence level I, strong recommendation]	P116-130

X: Manage eXacerbations

Change	Section	Type of change	Relevant key recommendation	Page number
	X3.2 Non-invasive ventilation			
19	Hartley et al used a derivation cohort of 489 patients to derive a mortality prediction score for patients with an exacerbation of COPD and hypercapnic respiratory failure receiving NIV. The NIVO score was then validated in a group of 733 patients from across 10 hospitals in England and Wales. The NIVO score consisted of 6 measures that should be available at the bedside (see below). The area under the curve form predicting mortality was 0.79. The score also allowed for mortality risk stratification - see table below. The NIVO score performed better in this patient group than all other mortality prediction scores tested. Use of this score may assist clinicians, patients and their carers in making decisions regarding acute non-invasive ventilation (Hartley 2021) [evidence level III].	New citiation and wording added to the end of existing section.	**Non-invasive ventilation (NIV) is effective for patients with rising paCO2 levels.** [evidence level I, strong recommendation]	P148