

COPD-X Summary of Changes V2.60, December 2019

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 December 2019 meetings of the COPD-X Guidelines Committee.

Implications for Clinical Practice

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

C. Confirm diagnosis and assess severity

Treatable Traits is a new treatment paradigm proposed for the management of people with airway diseases. The treatment approach has been suggested as a way to progress precision or personalised medicine in COPD and asthma (Agusti 2017, Agusti 2016, McDonald 2019b). Patients are first assessed through a detailed clinical history and identification of airway disease risk factors (e.g. smoking history, history of allergies, occupational exposures, family history, respiratory disease in early life); spirometry and measures of airway inflammatory biomarkers, including exhaled nitric oxide fraction (FeNO) and blood eosinophils. These assessments will indicate a high or low probability of the presence of an airway disease (Agusti 2016).

Following this confirmation, it is recommended that each individual undergoes a multidimensional assessment to identify treatable traits and an individualised treatment plan is implemented based on the presence of traits.

In order to be considered a trait, the following criteria should be met. Traits should be identifiable using a trait identification marker, clinically relevant and modifiable (McDonald 2019b).

Traits are grouped into three domains – pulmonary and extrapulmonary traits and behaviours/ risk-factors. While overall management according to treatable traits is a concept, the treatment of each individual trait is supported in most cases through RCT evidence. A proof of concept clinical trial in patients with COPD demonstrated that the treatable traits approach can lead to significant improvements in health related quality of life and inflammatory biomarkers (McDonald 2013) with similar results in an RCT in people with severe asthma (McDonald 2019a).

C2.3 Spirometry

In a Danish study (Katsimigas 2019) of opportunistic screening for COPD carried out in symptomatic smokers and ex-smokers (n=6,710), BMI <25 kg/m² and BMI >35 kg/m², increasing age and an increasing number of pack-years smoked were all important predictors for COPD (diagnosed in 17.7% in this study). GPs should target these patients for case finding to facilitate early diagnosis and initiate early interventions.

O. Optimise Function

O4.3 Biologic therapies

Inclusion of new paragraph discussing trials of benralizumab:

Large trials of benralizumab in patients with moderate COPD and frequent exacerbations despite dual or triple therapy found no differences in annual rates of COPD exacerbations in patients treated with benralizumab compared with placebo, and no associations between baseline eosinophil counts and treatment effect (Criner 2019a). In a further pre-specified analysis of the combined GALATHEA and TERRANOVA studies of benralizumab (Criner 2019b), a variety of statistical techniques were used to identify “efficacy associated factors” in the two studies. These hypothesis-generating analyses were interpreted as suggesting that a subpopulation of patients with COPD, frequent exacerbations during treatment with triple therapy and higher eosinophil counts might benefit from benralizumab 100 mg every 8 weeks. Unlike in asthma, there is no role for the use of biologic therapies in COPD.

O7.2 Cardiac disease

Addition of a paragraph discussing troponin I levels:

In a population with stable COPD and cardiovascular risk or disease, high sensitivity troponin I levels were associated with increased cardiac events and mortality. This effect was seen at troponin I >5ng/L; well below the threshold for diagnosis of coronary events (Adamson 2018) [evidence level III-2].

O7.2.2 Safety of beta-blockers

A prospective randomised trial of metoprolol to prevent exacerbations in moderate to severe COPD (Dransfield 2019) reported no benefit after early termination for futility and potential safety concerns about increased respiratory symptoms and severe exacerbations in the active treatment group. Patients with heart failure and recent ischaemic heart disease were excluded. The trial's outcome is plausible, but the study target population was unlikely to benefit. Due to the patient selection, these results should only be applied to patients who did not have a therapeutic indication for beta-blockers. Prospective data for COPD patients with cardiac disease are still needed.

O7.3 Osteoporosis

A systematic review of 58 studies (8,753 COPD patients) found a mean prevalence of 38% (95% CI 34 to 43) for osteoporosis in COPD patients, with increasing odds ratios for osteoporosis associated with lower BMI and sarcopenia (Chen 2019).

O9.2 Lung volume reduction surgery and bronchoscopic interventions

Section shortened.

O10. Palliative and supportive care

Palliative care

Data from a single-centre retrospective Australian study (Smallwood 2018), demonstrated that in the last two years of life, only 18% of patients with severe COPD accessed specialist palliative care, with 6% prescribed opioids as outpatients, despite most having severe chronic breathlessness. Similarly, only 5% wrote an advance directive.

Pharmacological management of breathlessness – opioids and benzodiazepines

A retrospective single-centre study (Taverner 2019) found over use of antibiotics, occurred commonly at the end of life in patients with COPD dying in hospital.

P: Prevent deterioration

No changes.

D: Develop a plan of care

D3. Self-management

In 2019, Aboumatar et al reported an RCT that recruited patients admitted to hospital with an acute exacerbation of COPD, or patients who had a previous diagnosis of COPD who were hospitalised and were receiving treatment for an increase in COPD symptoms (Aboumatar 2019). Patients (n=240) were randomised to a three-month intervention that involved, 1. A transition support aimed at preparing patients and caregivers for discharge and ensuring they understood the post discharge plan of care, 2. Individualised COPD self-management support to help patients take medications correctly, recognise exacerbations signs and follow action plans, practice breathing exercises and energy conservation techniques, maintain an active lifestyle, seek help as needed, and stop smoking, and 3. Facilitated access to community programs and treatment services. The intervention was delivered by COPD nurses. Usual care involved a general transition coach to follow the patient for 30 days after discharge, with a focus on adherence to the discharge plan, and connecting to outpatient care. The intervention resulted in an increased number of COPD related acute events per participant at 6 months compared to usual care (difference, 0.68 (95% CI 0.22 to 1.15)). There were no differences observed in health status measured by the St George's Respiratory Questionnaire (SGRQ) at 6 months (difference 5.18 (95% CI -2.15 to 12.51)).

Overall COPD self-management programs appear to improve health-related quality of life. The effect of these interventions on exacerbations remains unclear. Studies have reported positive outcomes, whilst others have reported increased rates of exacerbations associated with self management interventions (Aboumatar 2019). Due to the heterogeneity of the study designs, setting and outcomes, and conflicting results we are unable to make recommendations regarding the essential elements of a COPD self-management program.

Written Action Plans

A multicentre RCT (Lenferink 2019) (n=201) evaluated the effect of patient-tailored symptom-based written action plans embedded within a multi-disease self management intervention on COPD exacerbation days compared to usual care in patients with COPD and one or more comorbidity. Patients were given written action plans to prompt management of both

COPD exacerbations and comorbidities (congestive heart failure (CHF), ischaemic heart disease (IHD), anxiety, depression and diabetes), together with a self management education programme. No difference in the primary outcome of COPD exacerbation days/patient/year was observed (intervention median 9.6 versus usual care 15.6 days); (Incidence Rate Ratio (IRR) 0.87, 95% CI 0.54 to 1.30). There were however observed differences in the secondary outcome of duration of COPD exacerbations, in favour of the intervention (8.1 versus 9.5 days). There was no difference in overall health-related quality of life (HRQoL) between groups, and the intervention group reported poorer emotion function on the Chronic Disease Respiratory Questionnaire (CRQ) compared to usual care.

X: Manage eXacerbations

DECAF is a 30-day mortality prediction score for COPD admissions (Steer 2012). DECAF was derived with data from 920 consecutive patients admitted with a COPD exacerbation from two neighbouring hospitals in the UK. COPD had been confirmed on spirometry. The five strongest predictors of mortality that comprise the score are extended MRC Dyspnoea Score, eosinopenia, consolidation, acidemia, and atrial fibrillation. The score showed high discrimination for mortality with an area under the receiver operator characteristic curve = 0.86, 95% CI 0.82 to 0.89. A DECAF score of 3 predicts a 27.2% 30-day mortality risk. Echevarria et al examined the performance of the DECAF score in 2,645 patients with an admission of COPD across 6 hospitals in the UK and reported a similarly high performance for mortality prediction (Echevarria 2019).

X3.7 Discharge planning

Inclusion of Lung Foundation Australia resource *Managing a COPD Exacerbation Checklist*.

References

- ABOUMATAR, H., NAQIBUDDIN, M., CHUNG, S., CHAUDHRY, H., KIM, S. W., SAUNDERS, J., BONE, L., GURSES, A. P., KNOWLTON, A., PRONOVOST, P., PUTCHA, N., RAND, C., ROTER, D., SYLVESTER, C., THOMPSON, C., WOLFF, J. L., HIBBARD, J. & WISE, R. A. 2019. Effect of a Hospital-Initiated Program Combining Transitional Care and Long-term Self-management Support on Outcomes of Patients Hospitalized With Chronic Obstructive Pulmonary Disease: A Randomized Clinical Trial. *Jama*, 322, 1371-1380.
- ADAMSON, P. D., ANDERSON, J. A., BROOK, R. D., CALVERLEY, P. M. A., CELLI, B. R., COWANS, N. J., CRIM, C., DIXON, I. J., MARTINEZ, F. J., NEWBY, D. E., VESTBO, J., YATES, J. C. & MILLS, N. L. 2018. Cardiac Troponin I and Cardiovascular Risk in Patients With Chronic Obstructive Pulmonary Disease. *J Am Coll Cardiol*, 72, 1126-1137.
- AGUSTI, A., BAFADHEL, M., BEASLEY, R., BEL, E. H., FANER, R., GIBSON, P. G., LOUIS, R., MCDONALD, V. M., STERK, P. J., THOMAS, M., VOGELMEIER, C., PAVORD, I. D. & ON BEHALF OF ALL PARTICIPANTS IN THE, S. 2017. Precision medicine in airway diseases: moving to clinical practice. *Eur Respir J*, 50.
- AGUSTI, A., BEL, E., THOMAS, M., VOGELMEIER, C., BRUSSELLE, G., HOLGATE, S., HUMBERT, M., JONES, P., GIBSON, P. G., VESTBO, J., BEASLEY, R. & PAVORD, I. D. 2016. Treatable traits: toward precision medicine of chronic airway diseases. *Eur Respir J*, 47, 410-9.
- CHEN, Y. W., RAMSOOK, A. H., COXSON, H. O., BON, J. & REID, W. D. 2019. Prevalence and Risk Factors for Osteoporosis in Individuals With COPD: A Systematic Review and Meta-analysis. *Chest*.
- CRINER, G. J., CELLI, B. R., BRIGHTLING, C. E., AGUSTI, A., PAPI, A., SINGH, D., SIN, D. D., VOGELMEIER, C. F., SCIURBA, F. C., BAFADHEL, M., BACKER, V., KATO, M., RAMIREZ-VELEGAS, A., WEI, Y. F., BJERMER, L., SHIH, V. H., JISON, M., O'QUINN, S., MAKULOVA, N.,

- NEWBOLD, P., GOLDMAN, M. & MARTIN, U. J. 2019a. Benralizumab for the Prevention of COPD Exacerbations. *N Engl J Med*, 381, 1023-1034.
- CRINER, G. J., CELLI, B. R., SINGH, D., AGUSTI, A., PAPI, A., JISON, M., MAKULOVA, N., SHIH, V. H., BROOKS, L., BARKER, P., MARTIN, U. J. & NEWBOLD, P. 2019b. Predicting response to benralizumab in chronic obstructive pulmonary disease: analyses of GALATHEA and TERRANOVA studies. *Lancet Respir Med*.
- DRANSFIELD, M. T., VOELKER, H., BHATT, S. P., BRENNER, K., CASABURI, R., COME, C. E., COOPER, J. A. D., CRINER, G. J., CURTIS, J. L., HAN, M. K., HATIPOGLU, U., HELGESON, E. S., JAIN, V. V., KALHAN, R., KAMINSKY, D., KANER, R., KUNISAKI, K. M., LAMBERT, A. A., LAMMI, M. R., LINDBERG, S., MAKE, B. J., MARTINEZ, F. J., MCEVOY, C., PANOS, R. J., REED, R. M., SCANLON, P. D., SCIURBA, F. C., SMITH, A., SRIRAM, P. S., STRINGER, W. W., WEINGARTEN, J. A., WELLS, J. M., WESTFALL, E., LAZARUS, S. C. & CONNETT, J. E. 2019. Metoprolol for the Prevention of Acute Exacerbations of COPD. *N Engl J Med*.
- ECHEVARRIA, C., STEER, J. & BOURKE, S. C. 2019. Comparison of early warning scores in patients with COPD exacerbation: DECAF and NEWS score. *Thorax*, 74, 941-946.
- KATSIMIGAS, A., TUPPER, O. D. & ULRİK, C. S. 2019. Opportunistic screening for COPD in primary care: a pooled analysis of 6,710 symptomatic smokers and ex-smokers. *Int J Chron Obstruct Pulmon Dis*, 14, 1633-1638.
- LENFERINK, A., VAN DER PALEN, J., VAN DER VALK, P., CAFARELLA, P., VAN VEEN, A., QUINN, S., GROOTHUIS-OUDSHOORN, C. G. M., BURT, M. G., YOUNG, M., FRITH, P. A. & EFFING, T. W. 2019. Exacerbation action plans for patients with COPD and comorbidities: a randomised controlled trial. *Eur Respir J*.
- MCDONALD, V. M., CLARK, V. L., CORDOVA-RIVERA, L., WARK, P. A. B., BAINES, K. J. & GIBSON, P. G. 2019a. Targeting Treatable Traits in Severe Asthma: A Randomised Controlled Trial. *Eur Respir J*.
- MCDONALD, V. M., FINGLETON, J., AGUSTI, A., HILES, S. A., CLARK, V. L., HOLLAND, A. E., MARKS, G. B., BARDIN, P. P., BEASLEY, R., PAVORD, I. D., WARK, P. A. B., GIBSON, P. G., PARTICIPANTS OF THE TREATABLE TRAITS DOWN UNDER INTERNATIONAL, W. & TREATABLE TRAITS DOWN UNDER INTERNATIONAL WORKSHOP, P. 2019b. Treatable traits: a new paradigm for 21st century management of chronic airway diseases: Treatable Traits Down Under International Workshop report. *Eur Respir J*, 53.
- MCDONALD, V. M., HIGGINS, I., WOOD, L. G. & GIBSON, P. G. 2013. Multidimensional assessment and tailored interventions for COPD: respiratory utopia or common sense? *Thorax*, 68, 691-4.
- SMALLWOOD, N., ROSS, L., TAVERNER, J., JOHN, J., BAISCH, A., IRVING, L. & PHILIP, J. 2018. A Palliative Approach is Adopted for Many Patients Dying in Hospital with Chronic Obstructive Pulmonary Disease. *Copd*, 15, 503-511.
- STEER, J., NORMAN, E. M., AFOLABI, O. A., GIBSON, G. J. & BOURKE, S. C. 2012. Dyspnoea severity and pneumonia as predictors of in-hospital mortality and early readmission in acute exacerbations of COPD. *Thorax*, 67, 117-21.
- TAVERNER, J., ROSS, L., BARTLETT, C., LUTHE, M., ONG, J., IRVING, L. & SMALLWOOD, N. 2019. Antimicrobial prescription in patients dying from chronic obstructive pulmonary disease. *Intern Med J*, 49, 66-73.