Asthma–COPD overlap

KEY POINTS

Many adults have features of both asthma and chronic obstructive pulmonary disease (COPD). This is described as asthma–COPD overlap.

Asthma–COPD overlap is not a single disease, but is likely to have many underlying causes. It can develop in smokers, ex-smokers or non-smokers, particularly at older ages.

Patients with asthma–COPD overlap are at higher risk than patients with either condition alone, with more symptoms, more flare-ups, greater need for health care utilisation, and higher mortality.

Asthma–COPD overlap should be considered in adults when they have a history of asthma or have asthma-like symptoms, and spirometry before and after bronchodilator shows expiratory airflow limitation that is not completely reversible.

Specialist referral may be needed if there is doubt about the diagnosis, and to optimise treatment.

Treatment of patients with asthma–COPD overlap involves long-term inhaled corticosteroid (ICS) treatment to reduce the risk of asthma flare-ups. Most patients should also have a trial of a long-acting beta$_2$ agonist (LABA) and/or long-acting muscarinic antagonist (LAMA).

The use of LABAs or LAMAs without concomitant ICS should be avoided in patients with any features of asthma, or a history of asthma, because this increases the risk of hospitalisation and death.

Management also includes treatment of comorbid conditions, smoking cessation, adequate physical activity, pulmonary rehabilitation, regular vaccinations, self-management education including an up-to-date written action plan, and regular follow-up.

Asthma and COPD are heterogeneous conditions, each with several different underlying causes. The definitions of asthma and COPD are not mutually exclusive, and a significant proportion of adults with obstructive respiratory disease have clinical features of both conditions.

Distinguishing between typical asthma (e.g. childhood-onset allergic asthma) and typical COPD (e.g. emphysema in a heavy smoker) is straightforward.[1] However, it can be difficult to distinguish COPD from asthma in adults who have features of both conditions.[2, 3] These people are described as having asthma–COPD overlap. Asthma–COPD overlap is now recognised as an important clinical problem.[1, 3, 4]

Asthma–COPD overlap is not a single, well-defined disease entity, but includes a range of airway disease phenotypes with different causal mechanisms (Figure 1).[3, 5] It can be considered as positioned within a spectrum of chronic obstructive respiratory disease.[6]

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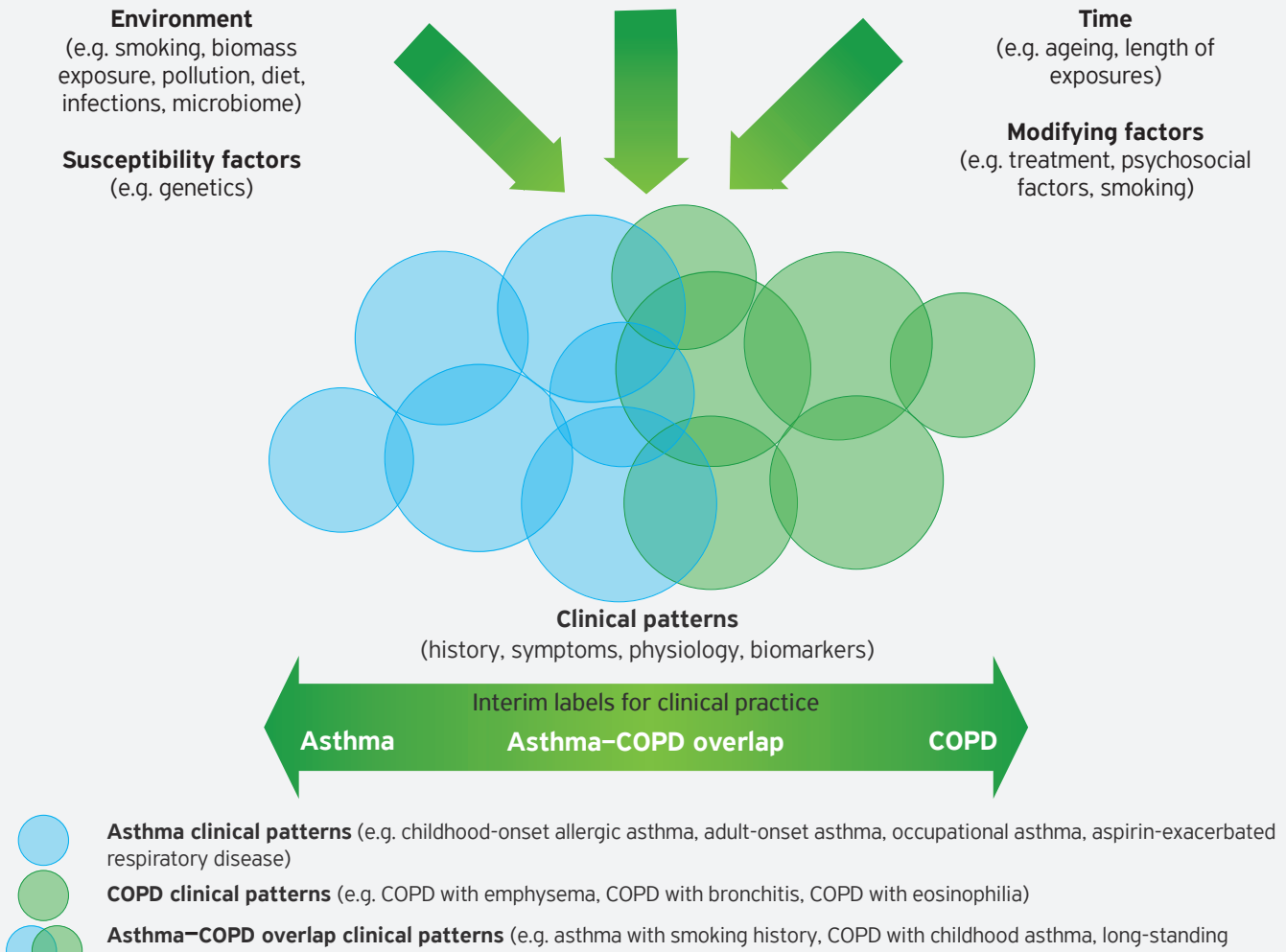
Figure 1. Development of asthma, COPD and asthma–COPD overlap



Adapted from Reddel (2015)[1]

Clinical presentations of asthma–COPD overlap

Coexisting features of both asthma and COPD have been described in:[4, 7-9]

- people with current asthma (allergic or non-allergic) who have had significant exposure to tobacco smoke
- people with longstanding asthma or late-onset asthma who have become persistently short of breath over time
- people with a significant smoking history and symptoms consistent with COPD who also have a history of childhood asthma
- people who present in middle age or later with shortness of breath, with a history of childhood asthma but no or few symptoms in between, and little smoking history.

In practice, asthma–COPD overlap is identified in clinical practice by the features that it shares with both asthma and COPD.[3] Research show that people with asthma–COPD overlap may have airway eosinophilia, neutrophilia, or a mixed pattern of airway inflammation, and may have systemic inflammation.[5]

People with asthma–COPD overlap often have poor disease outcomes, including:[3, 6, 9-12]

- high need for health care services
- worse quality of life, more wheezing, dyspnoea, cough and sputum production, and more frequent and severe respiratory exacerbations and hospitalisations, than people with COPD or asthma alone
- worse lung function demonstrated by spirometry than those with COPD alone, despite lower average exposure to tobacco smoke.

It is important to identify people with asthma–COPD overlap, because they are at higher risk than patients with asthma or COPD alone, and because they should be treated differently from people with COPD or asthma alone.

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Asthma management guidelines and COPD management guidelines make opposing safety recommendations: in asthma, long-acting bronchodilators should never be used without ICS, while in COPD, treatment should start with long-acting bronchodilators without ICS.

There is very limited evidence to guide pharmacological treatment for people with asthma–COPD overlap,[3] because these patients are excluded from most major pharmacologic studies of asthma or COPD treatment.[1,13] The few available studies sampled from relevant populations have used different definitions of asthma–COPD overlap.[14]

This information paper contains interim advice for health professionals, until firm guidelines can be developed from future research in this group of patients. Based on current understanding and evidence, a key safety precaution is to ensure that patients with any features of asthma receive regular ICS treatment.

Prevalence

Prevalence estimates for asthma–COPD overlap differ, depending on the definition used and whether the sample is population-based or hospital-based. Overall, approximately 20% of patients with obstructive airway disease have been diagnosed with both asthma and COPD:[5] 12–55% of patients with a primary diagnosis of COPD and 13–61% of those with a primary diagnosis of asthma.[2, 11, 15] If only spirometric criteria are used, the prevalence is much higher (approximately 50% of those aged over 50 years).[2, 16]

The coexistence of incompletely reversible expiratory airflow limitation (characteristic of COPD) and increased expiratory airflow variability (characteristic of asthma) is common among middle-aged adults with respiratory symptoms, especially people aged 65 years and over.[17]

Diagnosis

Diagnosis is based on the probability of asthma or COPD, according to the presence of clinical features of either.[3] If the diagnosis is unclear, consider referral to a respiratory physician.

History, clinical findings and spirometry

Based on history, physical examination and other investigations, identify features typical of asthma and typical of COPD (Figure 2).

Typical features of history include chronic or recurrent cough, sputum production, dyspnoea, wheezing, recurring acute lower respiratory tract infections, exposure to tobacco smoke or other airborne pollutants, a previous diagnosis of asthma or COPD, and the use of inhaled respiratory medicines.[3] Lung auscultation can be normal or there may be wheeze.[3]

If several features of both are present and neither is strongly favoured, manage according to recommendations for asthma–COPD overlap.

Spirometry

Perform spirometry before and after bronchodilator. If spirometry demonstrates expiratory airflow limitation that is not completely reversible (Table 1), consider the possibility of COPD (if risk factors such as smoking), or asthma–COPD overlap (with or without a history of smoking, if there are also any features of asthma).

Other investigations

Other investigations may be necessary to assess respiratory and other comorbidities. For more information, refer to *COPD-X Concise Guide for Primary Care*[18] (available at copdx.org.au) and the *Australian Asthma Handbook* (asthmahandbook.org.au).

RISK FACTORS FOR DEVELOPING FIXED AIRFLOW LIMITATION IN ASTHMA[2, 19, 20, 21, 22, 23]

Among people with asthma, having one or more of these factors might increase the chance of developing fixed airflow limitation, but no factor is essential.

Modifiable factors
Smoking
Occupational asthma
Exposure to respiratory irritants such as industrial dusts and chemical fumes
Lack of ICS treatment for asthma

Demographics
Male sex
Ageing

History
Hospital admission for severe respiratory infection before age 2 years
Asthma diagnosis as a child
Long-term asthma
Adult-onset asthma
History of smoking (even low pack–years)
Chronic mucus hypersecretion

Findings on investigation
Low baseline FEV_1
Atopy

FEV_1: forced expiratory volume in 1 second; ICS: inhaled corticosteroid

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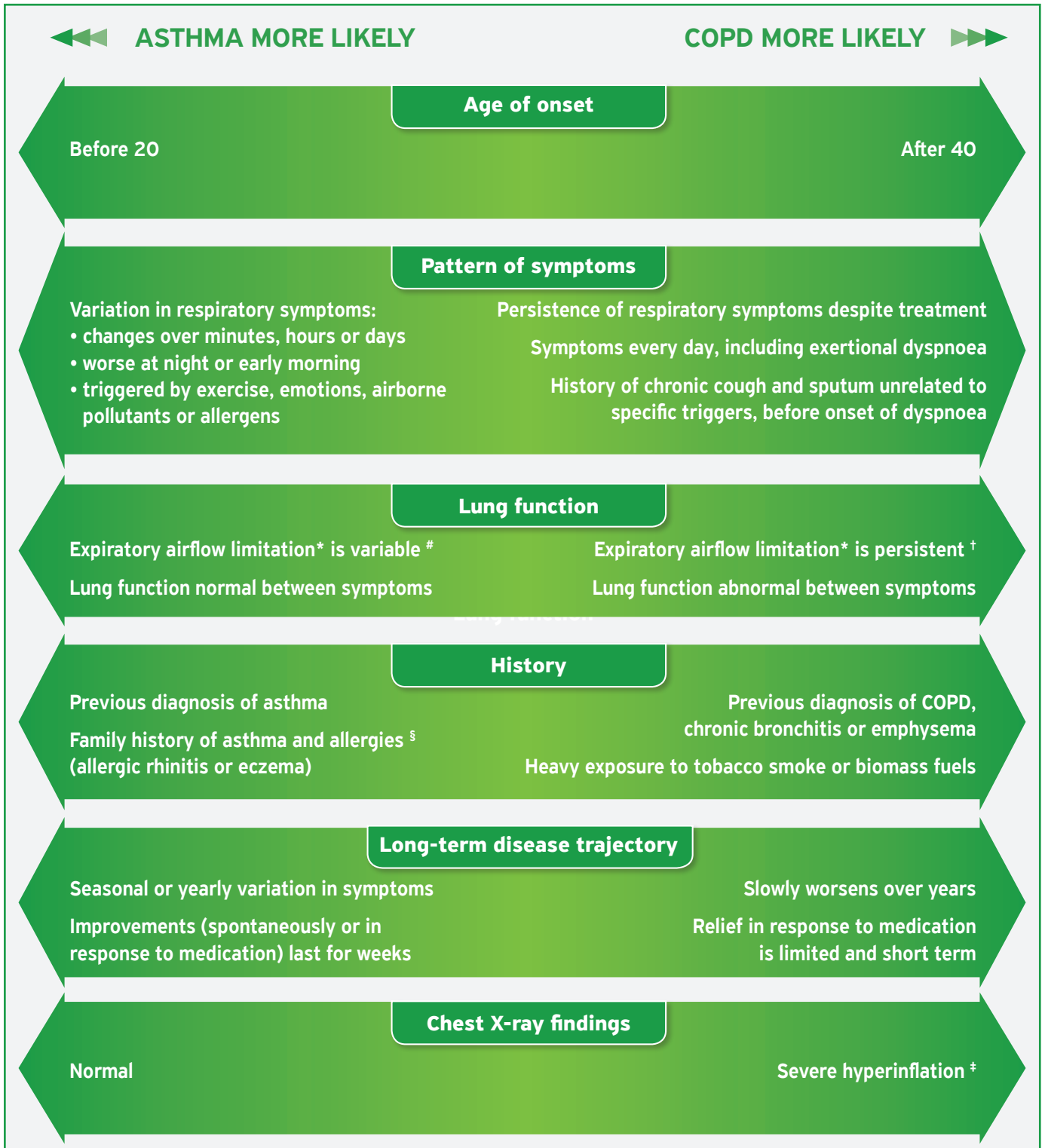
Figure 2. Features that, if present, favour asthma or COPD (continued on page 5)



Features that, when present, increase the probability of either asthma or COPD. None of these features is essential to make the diagnosis of asthma or COPD, with the exception of persistent airflow limitation for making the diagnosis of COPD. Absence of any of these features does not rule out asthma or COPD.

Adapted from GINA and GOLD (2017)[3]

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Figure 2. Features that, if present, favour asthma or COPD (continued from page 4)

* Expiratory airflow limitation: indicated by a reduced ratio of forced expiratory volume in one second (FEV_1) to forced vital capacity (FVC) on spirometry (FEV_1/FVC less than the lower limit of normal, i.e. less than the 5th percentile of normal population). Typical FEV_1/FVC values derived from population studies are > 0.75 in people aged 40–59 years and > 0.70 in people aged 60–80 years.[24]

\# Variable expiratory airflow limitation: variation beyond the range seen in healthy populations. It is indicated in adults by any of the following:[24]

- a clinically important increase in FEV_1 (change in FEV_1 of at least 200 mL and 12% from baseline) 10–15 minutes after administration of bronchodilator
- clinically important variation in lung function (at least 20% change in FEV_1) when measured repeatedly over time (e.g. spirometry on separate visits)
- a clinically important increase in lung function (at least 200 mL and 12% from baseline) after ≥ 4 weeks' treatment trial with an ICS
- clinically important variation in peak expiratory flow (diurnal variability of more than 10%, calculated over 1–2 weeks as the average of daily amplitude per cent mean)
- a clinically important reduction in lung function (decrease in FEV_1 of at least 200 mL and 12% from baseline on spirometry, or decrease in peak expiratory flow rate by at least 20%) after exercise (formal laboratory-based exercise challenge testing uses different criteria for exercise-induced bronchoconstriction)
- a clinically important reduction in lung function (15–20%, depending on the test) during a test for airway hyperresponsiveness (exercise challenge test or bronchial provocation test) measured by a respiratory function laboratory.

The greater the variations, or the more occasions excess variation is seen, the more confidently the diagnosis of variable expiratory airflow limitation consistent with asthma can be made.

† Persistent expiratory airflow limitation is indicated by reduced post-bronchodilator FEV_1/FVC*

§ Lack of history of atopy does not preclude the presence of non-allergic asthma

‡ Chest X-ray may be normal in a patient with COPD

Table 1. Interpreting spirometry findings in adults

Finding	Consistent with		
	Asthma	COPD	Asthma–COPD overlap
Normal FEV_1/FVC before or after bronchodilator	Yes	No	No*
Abnormal lung function (post-bronchodilator reduced FEV_1/FVC and FEV_1 < lower limit of normal)	Yes#	Yes	Yes
Airflow limitation with greater bronchodilator reversibility than in healthy population (Post-bronchodilator FEV_1 increase ≥ 12% and 200 mL from baseline)	Yes‡	Yes	Yes
Marked bronchodilator reversibility (FEV_1 increase ≥ 12% and 400 mL from baseline)	Yes	Possible but unusual†	Possible§

FEV_1/FVC: ratio of forced expiratory volume in one second (FEV_1) to forced vital capacity (FVC), either before or after bronchodilator

* Normal FEV_1/FVC is not consistent with COPD unless there is other evidence of chronic non-reversible expiratory airflow limitation.[3]

\# This finding is consistent with asthma that is poorly controlled or measured during a flare-up, or can be seen in some patients with longstanding asthma.

‡ The greater the variation, and the more times variation is seen, the more likely the diagnosis of asthma. However, some patients with longstanding asthma may develop persistent airflow limitation.

† Marked reversibility strongly favours asthma and is generally inconsistent with COPD, but does not rule out asthma–COPD overlap.[3]

§ This finding may be seen in patients with asthma–COPD overlap, or occasionally in COPD, especially when FEV_1 is low.[3, 13]

Treatment

KEY RECOMMENDATIONS

If there are any features or history of asthma, prescribe regular, long-term ICS treatment to reduce the risk of asthma flare-ups.

Consider adding a long-acting bronchodilator (LAMA or LABA) if symptoms and/or flare-ups are not well controlled. Options include:

- an ICS plus a LABA (in a single inhaler, if possible)
- an ICS plus a LAMA
- the combination of an ICS, a LAMA and a LABA (with at least two of the agents in a single inhaler).

Provide all patients with as-needed short-acting beta agonist (SABA).

Reassess and repeat spirometry 6–8 weeks later.

Do not prescribe LABAs or LAMAs for patients with asthma–COPD overlap unless they are also using long-term ICS. Use combination inhalers if possible, to prevent patients taking long-acting bronchodilators without ICS.[24] If no combination product is available for the desired combination, carefully explain to the patient that it is very important that they continue taking the ICS.

Advise patients to follow their action plan or get medical advice within 24 hours if they develop symptoms suggestive of a lower respiratory tract infection (e.g. such as fever and/or increased sputum production and/or increased shortness of breath).

Identify and manage comorbidities and other risk factors for flare-ups (e.g. heart disease).

Provide an action plan and update it regularly.

Inhaled corticosteroid treatment (essential)

Treatment is based on regular ICS at low-to-moderate doses (see Australian Asthma Handbook for definition of doses).[3] ICS treatment is essential to reduce the risk of potentially life-threatening asthma flare-ups, even if asthma symptoms appear mild.[3] In a well-conducted case-control study, patients with COPD who had a history of asthma had a significantly lower risk of hospitalisation or death if they were started on treatment with ICS/LABA combination therapy than with LABA alone.[25]

Long-acting bronchodilators

The addition of a LAMA or LABA (Table 3) to ICS is needed in most cases.[3] Some patients may benefit from the combination of all three classes.[26]

LABAs and LAMAs should not be used by people with asthma or asthma–COPD overlap unless they are also taking an ICS (either in combination or separately).

If possible, minimise the number of different types of inhaler devices to avoid confusion about inhaler technique. More information on inhaler technique is available from: National Asthma Council Australia, Lung Foundation Australia

Other treatments

Pulmonary rehabilitation is effective for people with symptomatic COPD.[27, 28] Supervised exercise training may help improve asthma symptoms and quality of life in people with asthma–COPD overlap, including older people.[29]

Comorbid medical conditions are common among people with coexisting asthma and COPD. Comorbidities should be assessed and managed individually.[7, 30]

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Table 3. Long-acting bronchodilators for asthma–COPD overlap

Class	Dosing frequency	Agent	Brand name
ICS–LABA combinations	Once daily	Fluticasone furoate + vilanterol	*Breo Ellipta* #
	Twice daily	Budesonide + formoterol	*Symbicort Rapihaler* *Symbicort Turbuhaler*
	Twice daily	Fluticasone propionate + formoterol	*Flutiform*
	Twice daily	Fluticasone propionate + salmeterol	*Fluticasone and Salmeterol Cipla* *Seretide Accuhaler* *Seretide MDI*
LABAs *	Once daily	Indacaterol	*Onbrez Breezhaler*
	Twice daily	Formoterol	*Oxis* *Foradile*
	Twice daily	Salmeterol	*Serevent Accuhaler*
LAMAs *	Once daily	Glycopyrronium	*Seebri Breezhaler*
	Once daily	Tiotropium	*Spiriva* *Spiriva Respimat*
	Once daily	Umeclidinium	*Incruse Ellipta*
	Twice daily	Aclidinium	*Bretaris Genuair*
LABA–LAMA combinations *	Once daily	Indacaterol + glycopyrronium	*Ultibro Breezhaler*
	Once daily	Olodaterol + tiotropium	*Spiolto Respimat*
	Once daily	Vilanterol + umeclidinium	*Anoro Ellipta*
	Twice daily	Formoterol + aclidinium	*Brimica Genuair*

*** Important! Ensure that patient is also using regular long-term ICS. LABAs and LAMAs should not be used by people with asthma or asthma–COPD overlap unless they are also taking an ICS, in combination or separately.**

Only the 100/25 mcg dose of fluticasone furoate/vilanterol is approved by the Therapeutic Goods Administration (TGA) for treatment of COPD. The higher dose (200/25 mcg) is not approved by the TGA for the treatment of COPD, so it should not be used in people with asthma–COPD overlap.

High doses of ICS (alone or in combination) are not recommended in patients with COPD and should therefore be used with caution in patients with asthma–COPD overlap, because of the risk of pneumonia.

Refer to PBS status before prescribing.

Holistic management

Management should also include smoking cessation, treatment of comorbid conditions, physical activity, pulmonary rehabilitation, vaccinations, self-management (including a regularly updated action plan) and regular follow-up.[3] Action plan templates are available for asthma and for COPD. Choose an asthma action plan or COPD action plan depending on the patient's dominant clinical features.

Respiratory tract infections should be monitored carefully because people with asthma–COPD overlap have high morbidity rates and because ICS treatment (particularly fluticasone propionate) is associated with increased risk of non-fatal pneumonia in people with COPD.[31] Most of the available evidence is from patients treated with fluticasone propionate. Increased pneumonia rates have also been observed in studies of patients with COPD using fluticasone furoate/vilanterol. The higher dose of fluticasone furoate/vilanterol (*Breo Ellipta* 200/25 mcg) is not TGA-approved for patients with COPD, so it should not be used in patients with asthma–COPD overlap.

Specialist referral

Specialist referral should be considered for patients with atypical symptoms or symptoms that suggest an alternative diagnosis, persistent symptoms or flare-ups despite treatment, or complex comorbidities.

References

1. Reddel HK. Treatment of overlapping asthma-chronic obstructive pulmonary disease: Can guidelines contribute in an evidence-free zone? *J Allergy Clin Immunol Pract* 2015; 136: 546-552.
2. Bateman ED, Reddel HK, van Zyl-Smit RN, Agusti A. The asthma-COPD overlap syndrome: towards a revised taxonomy of chronic airways diseases? *Lancet Respir Med* 2015; 3: 719-728.
3. Global Initiative for Asthma, Global Initiative for Obstructive Lung Disease. *Diagnosis and initial treatment of asthma, COPD and asthma-COPD overlap.* Updated April 2017. Global Initiative for Asthma and Global Initiative for Obstructive Lung Disease; 2017.
4. Gibson PG, Simpson JS. The overlap syndrome of asthma and COPD: what are its features and how important is it? *Thorax* 2009; 64: 728-735.
5. Gibson PG, McDonald VM. Asthma-COPD overlap 2015: now we are six. *Thorax* 2015; 70: 683-691.
6. Tho NV, Park HY, Nakano Y. Asthma-COPD overlap syndrome (ACOS): A diagnostic challenge. *Respirology* 2016; 21: 410-418.
7. McDonald VM, Higgins I, Gibson PG. Managing older patients with coexistent asthma and chronic obstructive pulmonary disease: diagnostic and therapeutic challenges. *Drugs Aging* 2013; 30: 1-17.
8. Reed CE. Asthma in the elderly: diagnosis and management. *J Allergy Clin Immunol* 2010; 126: 681-687.
9. Gelb AF, Christenson SA, Nadel JA. Understanding the pathophysiology of the asthma-chronic obstructive pulmonary disease overlap syndrome. *Curr Opin Pulm Med* 2016; 22: 100-105.
10. Nielsen M, Barnes CB, Ulrik CS. Clinical characteristics of the asthma-COPD overlap syndrome – a systematic review. *Int J Chron Obstruct Pulmon Dis* 2015; 10: 1443-1454.
11. Alshabanat A, Zafari Z, Albanyan O, et al. Asthma and COPD Overlap Syndrome (ACOS): A Systematic Review and Meta Analysis. *PloS one* 2015; 10: e0136065.
12. Lange P, Halpin DM, O'Donnell DE, MacNee W. Diagnosis, assessment, and phenotyping of COPD: beyond FEV(1). *Int J Chron Obstruct Pulmon Dis* 2016; 11 Spec Iss: 3-12.
13. Woodruff P, van den Berge M, Boucher R, et al. ATS-NHLBI Asthma COPD Overlap (ACO) Workshop Report. *Am J Respir Crit Care Med* 2017; IN PRESS.
14. Slats A, Taube C. Asthma and chronic obstructive pulmonary disease overlap: asthmatic chronic obstructive pulmonary disease or chronic obstructive asthma? *Ther Adv Respir Dis* 2016; 10: 57-71.
15. Wurst KE, Kelly-Reif K, Bushnell GA, et al. Understanding asthma-chronic obstructive pulmonary disease overlap syndrome. *Respir Med* 2016; 110: 1-11.
16. Weatherall M, Travers J, Shirtcliffe PM, et al. Distinct clinical phenotypes of airways disease defined by cluster analysis. *Eur Respir J* 2009; 34: 812-818.
17. Gibson PG, McDonald VM, Marks GB. Asthma in older adults. *Lancet* 2010; 376: 803-813.
18. Abramson M, Frith P, Yang I, et al. *COPD-X concise guide for primary care.* Brisbane: Lung Foundation Australia; 2017.
19. Lange P, Parner J, Vestbo J, et al. A 15-year follow-up study of ventilatory function in adults with asthma. *N Engl J Med* 1998; 339: 1194-1200.
20. Ulrik CS. Outcome of asthma: longitudinal changes in lung function. *Eur Respir J* 1999; 13: 904-918.
21. Baur X, Sigsgaard T, Aasen TB, et al. Guidelines for the management of work-related asthma. *Eur Respir J* 2012; 39: 529-545.
22. O'Byrne PM, Pedersen S, Lamm CJ, et al. Severe exacerbations and decline in lung function in asthma. *Am J Respir Crit Care Med* 2009; 179: 19-24.
23. Shirtcliffe P, Marsh S, Travers J, et al. Childhood asthma and GOLD-defined chronic obstructive pulmonary disease. *Intern Med J* 2012; 42: 83-88.
24. National Asthma Council Australia. *Australian Asthma Handbook* Version 1.2 [Website]. Melbourne: National Asthma Council Australia; 2016. Available from: www.asthmahandbook.org.au.
25. Gershon AS, Campitelli AM, Croxford R, et al. Combination long-acting B-agonists and inhaled corticosteroids compared with long-acting B-agonists alone in older adults with chronic obstructive pulmonary disease. *J Am Med Assoc* 2014;312: 1114-1121
26. Barnes PJ. Therapeutic approaches to asthma-chronic obstructive pulmonary disease overlap syndromes. *J Allergy Clin Immunol Pract* 2015; 136: 531-545.
27. Yang I, Dabscheck E, George J, et al. *The COPD-X Plan: Australian and New Zealand guidelines for the management of chronic obstructive pulmonary disease 2016*. Version 2.48: Lung Foundation Australia; 2016. Available from: http://copdx.org.au/copd-x-plan/.
28. Global Initiative for Chronic Obstructive Lung Disease (GOLD). *Global strategy for the diagnosis, management and prevention of COPD.* GOLD; 2016.
29. Turner S, Eastwood P, Cook A, Jenkins S. Improvements in symptoms and quality of life following exercise training in older adults with moderate/severe persistent asthma. *Respiration* 2011; 81: 302-310.
30. McDonald VM, Simpson JL, Higgins I, Gibson PG. Multidimensional assessment of older people with asthma and COPD: clinical management and health status. *Age Ageing* 2011; 41: 42-49.
31. Kew KM, Seniukovich A. Inhaled steroids and risk of pneumonia for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2014; Issue 3.

More information

For more information, including patient resources and support, health professional publications and training, and inhaler technique how-to videos, visit:

nationalasthma.org.au
lungfoundation.com.au

Treatment guidelines:

- *Australian Asthma Handbook* asthmahandbook.org.au
- *The COPD-X Plan: Australian and New Zealand guidelines for the management of COPD* copdx.org.au
- *COPD-X Concise Guide for Primary Care* copdx.org.au

Evidence-based publications from National Asthma Council Australia:

- *Inhaler technique for people with asthma or COPD* Information paper for health professionals
- *Asthma & COPD medications chart*
- *Spirometry quick reference guide*

Evidence-based publications from Lung Foundation Australia:

- *Stepwise Management of Stable COPD*
- *Primary Care Respiratory Toolkit*
- *COPD Action Plan*

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