National Asthma Council Australia

AUSTRALIAN ASTHMA HANDBOOK

VERSION 2.0

CLINICAL ISSUES

Chronic obstructive pulmonary disease (COPD)

This PDF is a print-friendly reproduction of the content included in the *Clinical Issues – COPD* section of the *Australian Asthma Handbook* at **asthmahandbook.org.au/clinical-issues/copd**

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ABBREVIATIONS

CFC	chlorofluorocarbon
COPD	chronic obstructive pulmonary disease
COX	cyclo-oxygenase
DXA	dual-energy X-ray absorptiometry
ED	emergency department
EIB	exercise-induced bronchoconstriction
FEV_1	forced expiratory volume over one second
FEV_6	forced expiratory volume over six seconds
FSANZ	Food Standards Australia and New Zealand
FVC	forced vital capacity
GORD	gastro-oesophageal reflux disease
HFA	formulated with hydrofluroalkane propellant
ICS	inhaled corticosteroid
ICU	intensive care unit
IgE	Immunoglobulin E
IL	interleukin
IU	international units
IV	intravenous
LABA	long-acting beta$_2$-adrenergic receptor agonist
LAMA	long-acting muscarinic antagonist
LTRA	leukotriene receptor antagonist
MBS	Medical Benefits Scheme
NHMRC	National Health and Medical Research Council
NIPPV	non-invasive positive pressure ventilation
NSAIDs	nonsteroidal anti-inflammatory drugs
OCS	oral corticosteroids
OSA	obstructive sleep apnoea
PaCO	carbon dioxide partial pressure on blood gas analysis
PaO	oxygen partial pressure on blood gas analysis
PBS	Pharmaceutical Benefits Scheme
PEF	peak expiratory flow
pMDI	pressurised metered-dose inhaler or 'puffer'
PPE	personal protective equipment
SABA	short-acting beta$_2$ -adrenergic receptor agonist
SAMA	short-acting muscarinic antagonist
SaO_2	oxygen saturation
SpO_2	peripheral capillary oxygen saturation measured by pulse oximetry
TGA	Therapeutic Goods Administration

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DISCLAIMER

Chronic obstructive pulmonary disease (COPD) and asthma

Overview

Asthma and COPD are quite distinctive and readily distinguishable from each other when they occur in their most characteristic forms. However, many adult patients show features of both these conditions.

The possibility of COPD as an alternative diagnosis and the possibility of asthma–COPD overlap should be considered during diagnostic investigation of respiratory symptoms in adults, particularly in smokers, ex-smokers and older adults.

Current asthma guidelines and COPD guidelines make contrasting recommendations for pharmacotherapy, based on differing safety findings in each population. Asthma guidelines generally recommend inhaled corticosteroids for most adults and recommend against long-acting $beta_2$ agonist without concomitant or combination inhaled corticosteroid therapy, whereas COPD guidelines recommend a long-acting $beta_2$ agonist as initial treatment and inhaled corticosteroids only for patients with more severe disease. Special considerations are therefore needed when a patient has features of both diagnoses.

In this section

Diagnostic considerations

Diagnostic considerations when COPD is a possibility

http://www.asthmahandbook.org.au/clinical-issues/copd/diagnostic-considerations

Managing asthma–COPD overlap

Management considerations for patients with asthma–COPD overlap

http://www.asthmahandbook.org.au/clinical-issues/copd/managing-asthma-copd-overlap

Diagnostic considerations when COPD is a possibility

▶ Go to: *The COPD-X Concise Guide for Primary Care*

Recommendations

Consider the possibility of COPD as an alternative diagnosis or asthma–COPD overlap in patients with respiratory symptoms and any of the following risk factors:

- **current smoking or history of smoking and age 35 years and over**
- **exposure to environmental tobacco smoke or other smoke**
- **age 55 years and over**
- **longstanding asthma.**

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Gibson *et al.* 2010[1]
- Guerra, 2009[2]
- Abramson *et al.* 2012[3]

If spirometry before and after bronchodilator demonstrates airflow limitation that is not completely reversible in an adult with risk factors for COPD, consider the possibility of COPD, even if the person has never smoked.

Table. Spirometry findings in asthma, COPD and asthma–COPD overlap

Finding	*Consistent with*		
	Asthma	**COPD**	**Asthma–COPD overlap**
Normal FEV_1/FVC before of 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 200mL from baseline)	**Yes** ‡	**Yes**	**Yes**

Finding	*Consistent with*		
	Asthma	**COPD**	**Asthma–COPD overlap**
Marked bronchodilator reversibility (**FEV_1 increase ≥ 12% and 400mL 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.**

 # 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.

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

Sources

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. Available from: http://ginasthma.org/gina-reports**

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; 196:375-381. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28636425**

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How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Abramson *et al.* 2012[3]

If an adult has risk factors for COPD, spirometry before and after bronchodilator demonstrates airflow limitation that is not completely reversible, and other diagnostic tests do not confirm asthma, start a treatment trial with an inhaled corticosteroid and repeat spirometry 6–8 weeks later.

After the trial of inhaled corticosteroid treatment, the diagnosis of asthma is supported if pre-bronchodilator spirometry shows that airflow limitation has resolved, or if spirometry before and after bronchodilator demonstrates airflow limitation that is fully reversible.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Identify patients with characteristics strongly favouring either asthma or COPD. If several features of both are present and neither is strongly favoured, manage according to recommendations for asthma–COPD overlap. If the diagnosis is unclear, consider referral to a specialist respiratory physician.

Table. Features that, when present, favour asthma or COPD

Clinical feature **(if measured/relevant)**	*Asthma more likely*	*COPD more likely*
Age of onset	**Before 20**	**After 40**
Pattern of symptoms	**Variation in respiratory symptoms:** • **changes over minutes, hours or days** • **worse at night or early morning** • **triggered by exercise, emotions, airborne pollutants or allergens**	**Persistence of respiratory symptoms despite treatment** **Symptoms every day, including exertional dyspnoea** **History of chronic cough and sputum unrelated to specific triggers, before onset of dyspnoea**
Lung function	**Expiratory airflow limitation* is variable#** **Lung function normal between symptoms**	**Expiratory airflow limitation* is persistent†** **Lung function abnormal between symptoms**
History	**Previous diagnosis of asthma** **Family history of asthma and allergies§ (allergic rhinitis or eczema)**	**Previous diagnosis of COPD, chronic bronchitis or emphysema** **Heavy exposure to tobacco smoke or biomass fuels**
Long-term disease trajectory	**Seasonal or yearly variation in symptoms** **Improvements (spontaneously or in response to medication) last for weeks**	**Slowly worsens over years** **Relief in response to medication is limited and short term**
Chest X-ray	**Normal**	**Severe hyperinflation‡**

Features that, when present, increase the probability of either typical asthma or typical 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.

*** 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.**

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

- **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 exclude non-allergic asthma.

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

Adapted from

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. Available from: http://ginasthma.org/gina-reports**

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Note: It is clinically important to identify asthma features because, in patients with features of both asthma and COPD, (1) treatment should always include an inhaled corticosteroid to reduce risk of flare-ups and asthma-related death, and (2) the use of long-acting $beta_2$ agonist or long-acting muscarinic antagonist without concomitant inhaled corticosteroid should be avoided to reduce the risk of flare-ups and asthma-related death.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

More information

Risk factors for COPD

Smoking is the most important risk factor for COPD.[4] Current national COPD guidelines recommend that COPD should be considered in all smokers and ex-smokers over 35 years, and in all patients with other smoking-related diseases.[4]

The other main risk factors for COPD include:[4, 2, 1]

- exposure to environmental tobacco smoke
- occupational exposure to dusts and fumes
- exposure to biological dust, diesel exhaust
- exposure to smoke from biomass fuels
- genetic predisposition ($alpha_1$ antitrypsin deficiency) interacting with environment (e.g. smoking)

Other risk factors for fixed (irreversible or incompletely reversible) airflow limitation include:[1]

- inadequate maximal lung function achieved in early life (e.g. due to untreated asthma or severe asthma in early childhood, premature birth, or bronchopulmonary dysplasia)
- ageing
- longstanding asthma.

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Diagnosis of COPD

The main symptoms of COPD are:[4]

- breathlessness
- cough
- sputum production.

Patients often attribute breathlessness to ageing or poor cardiopulmonary fitness. A persistent cough, typically worse in the mornings with mucoid sputum, is common in smokers.

Other common symptoms of COPD include chest tightness, wheezing, fatigue and airway irritability.[4]

The clinical diagnosis of COPD is usually based on clinical presentation (e.g. breathlessness on exertion, productive cough), together

with both the following:[4, 5]

- a history of smoking or exposure to other noxious agents
- post-bronchodilator FEV_1/FVC < 0.7 (or < lower limit of normal).

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Asthma–COPD overlap

Distinguishing between typical allergic asthma (childhood-onset allergic asthma) and typical COPD (emphysema in a heavy smoker) is straightforward.[6] However, it can be difficult to distinguish COPD from asthma in adults who have features of both conditions.[7, 8]These people are described as having asthma–COPD overlap.[7, 6, 9]

Asthma–COPD overlap is not a single, well-defined disease entity, but includes a range of airway disease phenotypes with different causal mechanisms.[7, 10] Features of both asthma and COPD have been described in:[9, 11, 12, 13]

- 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 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.

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

Please view and print this figure separately: http://www.asthmahandbook.org.au/figure/show/108

People with asthma–COPD overlap often have poor disease outcomes, including:[7, 1415, 16, 17]

- high need for healthcare 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.

Features of asthma, COPD and asthma–COPD overlap

If several features of both asthma and COPD are present and neither condition is strongly favoured, respiratory disease should be managed according to recommendations for asthma–COPD overlap.

Table. Features that, when present, favour asthma or COPD

Clinical feature **(if measured/relevant)**	*Asthma more likely*	*COPD more likely*
Age of onset	Before 20	After 40
Pattern of symptoms	Variation in respiratory symptoms: • changes over minutes, hours or days • worse at night or early morning • triggered by exercise, emotions, airborne pollutants or allergens	Persistence of respiratory symptoms despite treatment Symptoms every day, including exertional dyspnoea History of chronic cough and sputum unrelated to specific triggers, before onset of dyspnoea
Lung function	Expiratory airflow limitation* is variable# Lung function normal between symptoms	Expiratory airflow limitation* is persistent† Lung function abnormal between symptoms

Clinical feature **(if measured/relevant)**	*Asthma more likely*	*COPD more likely*
History	Previous diagnosis of asthma Family history of asthma and allergies[§] (allergic rhinitis or eczema)	Previous diagnosis of COPD, chronic bronchitis or emphysema Heavy exposure to tobacco smoke or biomass fuels
Long-term disease trajectory	Seasonal or yearly variation in symptoms Improvements (spontaneously or in response to medication) last for weeks	Slowly worsens over years Relief in response to medication is limited and short term
Chest X-ray	Normal	Severe hyperinflation[‡]

Features that, when present, increase the probability of either typical asthma or typical 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.

* 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.

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

- 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 exclude non-allergic asthma.

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

Adapted from

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. Available from: http://ginasthma.org/gina-reports

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Table. Spirometry findings in asthma, COPD and asthma–COPD overlap

Finding	*Consistent with*

	Asthma	COPD	Asthma–COPD overlap
Normal FEV_1 /FVC before of 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 200mL from baseline)	Yes ‡	Yes	Yes
Marked bronchodilator reversibility (FEV_1 increase ≥ 12% and 400mL 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.

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.

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

Sources

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. Available from: http://ginasthma.org/gina-reports

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; 196:375-381. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28636425

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Treatment for patients with asthma–COPD overlap

Inhaled corticosteroid treatment at low–moderate doses is essential to reduce the risk of potentially life-threatening flare-ups, even if asthma symptoms appear mild or infrequent.[7, 18]

Most patients also need treatment with a long-acting bronchodilator (either long-acting $beta_2$ agonist or long-acting muscarinic antagonist) in addition to an inhaled corticosteroid. Long-acting $beta_2$ agonists and long-acting muscarinic antagonists should not be used by people with asthma or asthma–COPD overlap unless they are also taking an inhaled corticosteroid (either in combination or separately).

Table. Long-acting bronchodilators for asthma–COPD overlap

Class	*Dosing*	*Agent*	**Brand name**
ICS–LABA combinations	Once daily	Fluticasone furoate + vilanterol	*Breo Ellipta 100/25 microg*† • Do not prescribe 200/25 microg formulation#
	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*

- * 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)
- Advise patients/carers that inhalers should be stored below 30°C and should not be left in cars.

† The inhaler must be discarded 1 month after opening the package and removing device from tray. When first opened, patients

should write the discard date on the label in the space provided. If stored in the refrigerator, inhaler should be taken out and allowed to return to room temperature for at least an hour before use.

‡ The inhaler must be discarded 6 weeks after opening after opening the package and removing device from tray. When first opened, patients should write the discard date on the label in the space provided. If stored in the refrigerator, inhaler should be taken out and allowed to return to room temperature for at least an hour before use.

Only the 100/25 microg dose of fluticasone furoate/vilanterol is TGA-approved for treatment of COPD. The higher dose (200/25 microg) is not TGA-approved 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.

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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.[7]

▶ Go to: *Asthma action plans*
Go to: *COPD action plans*

Respiratory tract infections should be monitored carefully because people with asthma–COPD overlap have high morbidity rates and because ICS treatment is associated with increased risk of non-fatal pneumonia in people with COPD.[19] Most of the available evidence is from patients treated with fluticasone propionate, particularly at higher doses. 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 microg) is not approved for patients with COPD, so it should also not be used in patients with asthma–COPD overlap.

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.

▶ Go to: National Asthma Council Australia's *Asthma–COPD overlap* information paper

For information on diagnosis and management of COPD, refer to the COPD-X Concise Guide for Primary Care.[20]

▶ Go to: Lung Foundation Australia's *COPD-X Concise Guide for Primary Care*

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Definition of variable expiratory airflow limitation

Most of the tests for variable expiratory airflow limitation are based on showing variability in FEV_1. While reduced FEV_1 may be seen with many other lung diseases (or due to poor spirometric technique), a reduced ratio of FEV_1 to FVC indicates airflow limitation.[21] Normal FEV_1/FVC values derived from population studies vary,[22, 23] but are usually greater than:[22]

- 0.85 in people aged up to 19 years
- 0.80 in people aged 20–39 years
- 0.75 in people aged 40–59 years
- 0.70 in people aged 60–80 years.

In children, it is less useful to define expiratory airflow limitation according to a specific cut-off for FEV_1/FVC ratio, because normal values in children change considerably with age.[23]

Some spirometers provide predicted normal values specific to age group. If these are available, a FEV_1/FVC ratio less than the lower limit of normal (i.e. less than the 5th percentile of normal population) indicates airflow limitation.

Variable expiratory airflow limitation (beyond the range seen in healthy populations) can be documented if any of the following are recorded:

- a clinically important increase in FEV_1 (change in FEV_1 of at least 200 mL and 12% from baseline for adults, or at least 12% from baseline for children) 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 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 increase in lung function (at least 200 mL and 12% from baseline) after a trial of 4 or more weeks of treatment with an inhaled corticosteroid

- clinically important variation in peak expiratory flow (diurnal variability of more than 10%)
- 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.

Notes

Patients referred to a respiratory function laboratory may be asked not to take certain medicines within a few hours to days before a spirometry visit.

A clinically important increase or decrease in lung function is defined as a change in FEV_1 of at least 200 mL and 12% from baseline for adults, or at least 12% from baseline for children, or a change in peak expiratory flow rate of at least 20% on the same meter.[24, 21] A clinically important increase in FVC after administering bronchodilator may also indicate reversible airflow limitation, but FVC is a less reliable measure in primary care because FVC may vary due to factors such as variation in inspiratory volume or expiratory time.

The finding of 'normal' lung function during symptoms reduces the probability that a patient has asthma, but a clinically important improvement in response to bronchodilator or inhaled corticosteroid can occur in patients whose baseline value is within the predicted normal range.

The greater the variation in lung function, the more certain is the diagnosis of asthma. However, people with longstanding asthma may develop fixed airflow limitation.

Reversibility in airflow limitation may not be detected if the person is already taking a long-acting $beta_2$ agonist or inhaled corticosteroid.

Airflow limitation can be transient and does not necessarily mean that the person has asthma (e.g. when recorded during a severe acute infection of the respiratory tract). Ideally, airflow limitation should be confirmed when the patient does not have a respiratory tract infection. Reduction in lung function during a respiratory tract infection with improvement in lung function after its resolution, commonly occurs in people with asthma, but can also be seen in patients with COPD or in healthy people without either asthma or COPD.[25,26]

▶ Go to: National Asthma Council Australia's *Spirometry Resources*
Go to: National Asthma Council Australia and Woolcock Institute *Peak Flow Chart*

References

1. Gibson PG, McDonald VM, Marks GB. Asthma in older adults. *Lancet*. 2010; 376: 803-813. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20816547
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Management considerations for patients with asthma–COPD overlap

Recommendations

For patients with features of COPD and any features of asthma, prescribe regular long-term inhaled corticosteroids (at a low dose, if possible, or at the lowest effective dose) to reduce the risk of serious flare-ups, even if asthma symptoms appear to be mild or infrequent.

- **Monitor closely for lower respiratory tract infections, and advise patients to get medical advice immediately if they develop symptoms of a lower respiratory tract infection.**

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- Abramson *et al.* 2012[1]
- GINA and GOLD, 2017[2]
- NACA, 2017[3]

Consider adding a long-acting bronchodilator (long-acting muscarinic antagonist [anticholinergic] or LABA), if symptoms and/or flare-ups are not well controlled. Options include:

- **combination inhaled corticosteroid/long-acting beta$_2$ agonist in a single inhaler (or separate inhalers if the preferred combination is not available in a single inhaler)**
- **concomitant treatment with an inhaled corticosteroid and a long-acting muscarinic antagonist (anticholinergic)**
- **the combination of an inhaled corticosteroid, a long-acting muscarinic antagonist and a long-acting beta$_2$ agonist (with at least two of the agents in a single inhaler).**

Ensure all patients have a short-acting beta$_2$ agonist to use as needed for symptom relief.

Table. Long-acting bronchodilators for asthma–COPD overlap

Class	*Dosing frequency*	*Agent*	**Brand name**
ICS–LABA combinations	**Once daily**	**Fluticasone furoate + vilanterol**	*Breo Ellipta 100/25 microg*† • **Do not prescribe 200/25 microg formulation#**
	Twice daily	**Budesonide + formoterol**	*Symbicort Rapihaler* *Symbicort Turbuhaler*
	Twice daily	**Fluticasone propionate + formoterol**	*Flutiform*

Class	*Dosing frequency*	*Agent*	**Brand name**
	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*

- *** 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)**
- **Advise patients/carers that inhalers should be stored below 30°C and should not be left in cars.**

† The inhaler must be discarded 1 month after opening the package and removing device from tray. When first opened, patients should write the discard date on the label in the space provided. If stored in the refrigerator, inhaler should be taken out and allowed to return to room temperature for at least an hour before use.

‡ The inhaler must be discarded 6 weeks after opening after opening the package and removing device from tray. When first opened, patients should write the discard date on the label in the space provided. If stored in the refrigerator, inhaler should be taken out and allowed to return to room temperature for at least an hour before use.

 # Only the 100/25 microg dose of fluticasone furoate/vilanterol is TGA-approved for treatment of COPD. The higher dose (200/25 microg) is not TGA-approved 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.

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Note: The use of separate inhalers for concomitant treatment with an inhaled corticosteroid and a long-acting bronchodilator (long-acting beta$_2$-agonist or long-acting muscarinic antagonist) in patients with asthma–COPD overlap should be avoided due to the risk of selective non-adherence with the inhaled corticosteroid. 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 inhaled corticosteroid, to reduce the risk of hospitalisation or death.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Abramson *et al.* 2012[1]

Consider pulmonary rehabilitation for patients with asthma–COPD overlap, manage comorbidities, and provide advice on physical activity, vaccinations, and self-management. Provide a written action plan. Choose an asthma action plan or a COPD action plan template, depending on the person's dominant clinical features.

▶ **Go to:** *Written asthma action plan templates*
Go to: *COPD action plan templates*

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Advise patients to follow their action plan or get medical advice within 24 hours if they develop symptoms that suggest a lower respiratory tract infection (e.g. fever, increased sputum production, worsening shortness of breath).

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Consider specialist referral for patients with atypical symptoms or symptoms that suggest an alternative diagnosis, persistent symptoms or flare-ups despite treatment, or complex comorbidities.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

More information

Asthma–COPD overlap

Distinguishing between typical allergic asthma (childhood-onset allergic asthma) and typical COPD (emphysema in a heavy smoker) is straightforward.[4] However, it can be difficult to distinguish COPD from asthma in adults who have features of both conditions.[2, 5]These people are described as having asthma–COPD overlap.[2, 4, 6]

Asthma–COPD overlap is not a single, well-defined disease entity, but includes a range of airway disease phenotypes with different causal mechanisms.[2, 7] Features of both asthma and COPD have been described in:[6, 8, 9, 10]

- 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 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.

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

Please view and print this figure separately: http://www.asthmahandbook.org.au/figure/show/108

People with asthma–COPD overlap often have poor disease outcomes, including:[2, 1112, 13, 14]

- high need for healthcare 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.

Features of asthma, COPD and asthma–COPD overlap

If several features of both asthma and COPD are present and neither condition is strongly favoured, respiratory disease should be managed according to recommendations for asthma–COPD overlap.

Table. Features that, when present, favour asthma or COPD

Clinical feature **(if measured/relevant)**	*Asthma more likely*	*COPD more likely*
Age of onset	Before 20	After 40
Pattern of symptoms	Variation in respiratory symptoms: • changes over minutes, hours or days • worse at night or early morning • triggered by exercise, emotions, airborne pollutants or allergens	Persistence of respiratory symptoms despite treatment Symptoms every day, including exertional dyspnoea History of chronic cough and sputum unrelated to specific triggers, before onset of dyspnoea
Lung function	Expiratory airflow limitation* is variable[#] Lung function normal between symptoms	Expiratory airflow limitation* is persistent[†] Lung function abnormal between symptoms
History	Previous diagnosis of asthma Family history of asthma and allergies[§] (allergic rhinitis or eczema)	Previous diagnosis of COPD, chronic bronchitis or emphysema Heavy exposure to tobacco smoke or biomass fuels
Long-term disease trajectory	Seasonal or yearly variation in symptoms Improvements (spontaneously or in response to medication) last for weeks	Slowly worsens over years Relief in response to medication is limited and short term
Chest X-ray	Normal	Severe hyperinflation[‡]

Features that, when present, increase the probability of either typical asthma or typical 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.

* 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.

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

- 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 exclude non-allergic asthma.

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

Adapted from

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. Available from: http://ginasthma.org/gina-reports

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Table. Spirometry findings in asthma, COPD and asthma–COPD overlap

Finding	*Consistent with*		
	Asthma	**COPD**	**Asthma–COPD overlap**
Normal FEV_1 /FVC before of 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 200mL from baseline)	Yes ‡	Yes	Yes
Marked bronchodilator reversibility (FEV_1 increase ≥ 12% and 400mL 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.

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.

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

Sources

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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; 196:375-381. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28636425

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Treatment for patients with asthma–COPD overlap

Inhaled corticosteroid treatment at low–moderate doses is essential to reduce the risk of potentially life-threatening flare-ups, even if asthma symptoms appear mild or infrequent.[2, 15]

Most patients also need treatment with a long-acting bronchodilator (either long-acting $beta_2$ agonist or long-acting muscarinic antagonist) in addition to an inhaled corticosteroid. Long-acting $beta_2$ agonists and long-acting muscarinic antagonists should not be used by people with asthma or asthma–COPD overlap unless they are also taking an inhaled corticosteroid (either in combination or separately).

Table. Long-acting bronchodilators for asthma–COPD overlap

Class	*Dosing frequency*	*Agent*	**Brand name**
ICS–LABA combinations	Once daily	Fluticasone furoate + vilanterol	*Breo Ellipta 100/25 microg*† • Do not prescribe 200/25 microg formulation#
	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*

Class	*Dosing frequency*	*Agent*	**Brand name**
	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*

- * 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)
- Advise patients/carers that inhalers should be stored below 30°C and should not be left in cars.

† The inhaler must be discarded 1 month after opening the package and removing device from tray. When first opened, patients should write the discard date on the label in the space provided. If stored in the refrigerator, inhaler should be taken out and allowed to return to room temperature for at least an hour before use.

‡ The inhaler must be discarded 6 weeks after opening after opening the package and removing device from tray. When first opened, patients should write the discard date on the label in the space provided. If stored in the refrigerator, inhaler should be taken out and allowed to return to room temperature for at least an hour before use.

Only the 100/25 microg dose of fluticasone furoate/vilanterol is TGA-approved for treatment of COPD. The higher dose (200/25 microg) is not TGA-approved 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.

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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.[2]

▶ Go to: *Asthma action plans*
Go to: *COPD action plans*

Respiratory tract infections should be monitored carefully because people with asthma–COPD overlap have high morbidity rates and because ICS treatment is associated with increased risk of non-fatal pneumonia in people with COPD.[16] Most of the available evidence is from patients treated with fluticasone propionate, particularly at higher doses. 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 microg) is not approved for patients with COPD, so it should also not be used in patients with asthma–COPD overlap.

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.

▶ Go to: National Asthma Council Australia's *Asthma–COPD overlap* information paper

For information on diagnosis and management of COPD, refer to the COPD-X Concise Guide for Primary Care.[17]

▶ Go to: Lung Foundation Australia's *COPD-X Concise Guide for Primary Care*

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Definition of variable expiratory airflow limitation

Most of the tests for variable expiratory airflow limitation are based on showing variability in FEV_1. While reduced FEV_1 may be seen with many other lung diseases (or due to poor spirometric technique), a reduced ratio of FEV_1 to FVC indicates airflow limitation.[18] Normal FEV_1/FVC values derived from population studies vary,[19, 20] but are usually greater than:[19]

- 0.85 in people aged up to 19 years
- 0.80 in people aged 20–39 years
- 0.75 in people aged 40–59 years
- 0.70 in people aged 60–80 years.

In children, it is less useful to define expiratory airflow limitation according to a specific cut-off for FEV_1/FVC ratio, because normal values in children change considerably with age.[20]

Some spirometers provide predicted normal values specific to age group. If these are available, a FEV_1/FVC ratio less than the lower limit of normal (i.e. less than the 5th percentile of normal population) indicates airflow limitation.

Variable expiratory airflow limitation (beyond the range seen in healthy populations) can be documented if any of the following are recorded:

- a clinically important increase in FEV_1 (change in FEV_1 of at least 200 mL and 12% from baseline for adults, or at least 12% from baseline for children) 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 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 increase in lung function (at least 200 mL and 12% from baseline) after a trial of 4 or more weeks of treatment with an inhaled corticosteroid
- clinically important variation in peak expiratory flow (diurnal variability of more than 10%)
- 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.

Notes

Patients referred to a respiratory function laboratory may be asked not to take certain medicines within a few hours to days before a spirometry visit.

A clinically important increase or decrease in lung function is defined as a change in FEV_1 of at least 200 mL and 12% from baseline for adults, or at least 12% from baseline for children, or a change in peak expiratory flow rate of at least 20% on the same meter.[21, 18] A clinically important increase in FVC after administering bronchodilator may also indicate reversible airflow limitation, but FVC is a less reliable measure in primary care because FVC may vary due to factors such as variation in inspiratory volume or expiratory time.

The finding of 'normal' lung function during symptoms reduces the probability that a patient has asthma, but a clinically important improvement in response to bronchodilator or inhaled corticosteroid can occur in patients whose baseline value is within the predicted normal range.

The greater the variation in lung function, the more certain is the diagnosis of asthma. However, people with longstanding asthma may develop fixed airflow limitation.

Reversibility in airflow limitation may not be detected if the person is already taking a long-acting $beta_2$ agonist or inhaled corticosteroid.

Airflow limitation can be transient and does not necessarily mean that the person has asthma (e.g. when recorded during a severe acute infection of the respiratory tract). Ideally, airflow limitation should be confirmed when the patient does not have a respiratory tract infection. Reduction in lung function during a respiratory tract infection with improvement in lung function after its resolution, commonly occurs in people with asthma, but can also be seen in patients with COPD or in healthy people without either asthma or COPD.[22,23]

▶ Go to: National Asthma Council Australia's *Spirometry Resources*
Go to: National Asthma Council Australia and Woolcock Institute *Peak Flow Chart*

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