Considering chronic obstructive pulmonary disease as an alternative or concomitant diagnosis in an adult with known or suspected asthma, and managing asthma in a person with coexisting COPD
ABBREVIATIONS

CFC  chlorofluorocarbon
COPD  chronic obstructive pulmonary disease
COX  cyclo-oxygenase
ED  emergency department
EIB  exercise-induced bronchoconstriction
FEV₁  forced expiratory volume over one second
FVC  forced vital capacity
FSANZ  Food Standards Australia and New Zealand
GORD  gastro-oesophageal reflux disease
HFA  formulated with hydrofluorocarbon propellant
ICS  inhaled corticosteroid
ICU  intensive care unit
IgE  immunoglobulin E
IV  intravenous
LABA  long-acting beta₂-adrenergic receptor agonist
LAMA  long-acting muscarinic antagonist
LTRA  leukotriene receptor antagonist
MBS  Medical Benefits Scheme
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
PaO₂  oxygen partial pressure on blood gas analysis
PBS  Pharmaceutical Benefits Scheme
PEF  peak expiratory flow
pMDI  pressurised metered-dose inhaler or ‘puffer’
SABA  short-acting beta₂-adrenergic receptor agonist
LAMA  long-acting muscarinic antagonist
TGA  Therapeutic Goods Administration

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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

- **Managing asthma-COPD overlap**
  - Management considerations for patients with 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
- Guerra, 2009
- Abramson et al. 2012

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.

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

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 the diagnosis is unclear, consider referral to a specialist respiratory physician.
Note: It is clinically important to identify asthma features because, in patients with features of both asthma and COPD, treatment should include an inhaled corticosteroid to reduce risk of flare-ups, and the use of long-acting beta2 agonist or long-acting muscarinic antagonist without concomitant inhaled corticosteroid should be avoided to reduce risk of adverse effects.

How this recommendation was developed
Adapted from existing guidance
Based on reliable clinical practice guideline(s) or position statement(s):

- Abramson et al. 2012

More information

Risk factors for COPD

Smoking is the most important risk factor for COPD. 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.

The other main risk factors for COPD include:

- 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 (alpha1 antitrypsin deficiency) interacting with environment (e.g. smoking)

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

- 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.

Diagnosis of COPD

The main symptoms of COPD are breathlessness, cough and 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 symptoms, such as chest tightness, wheezing, fatigue and airway irritability are common.

The clinical diagnosis of COPD is usually based on clinical presentation (e.g. breathlessness, productive cough), together with both the following:

- a history of smoking or exposure to other noxious agents
- post-bronchodilator FEV1/FVC < 0.7 (or < lower limit of normal) together with FEV1 < 80% of the predicted value.

Coexisting asthma and COPD

There is a subgroup of patients with longstanding asthma who do not demonstrate reversible airflow limitation. Asthma that begins later in life often shows a component of irreversible or incompletely reversible airflow limitation (also called ‘fixed airway obstruction’), due to airway remodelling and stiffening of the chest wall. The same may be seen in patients with a history of severe asthma in childhood.

Correspondingly, there is a subgroup of patients with COPD who demonstrate significant (though incomplete) bronchodilator response and meet the diagnostic criteria for variable airflow limitation in asthma. Most patients with COPD show some reversibility of airflow limitation with bronchodilators, and the degree of reversibility can vary from visit to visit.

Overlap of asthma and COPD is fairly common among older patients attending primary care:

- In a Dutch analysis of GP patient lists, approximately 10% of patients using an inhaled medication had both COPD and asthma as assessed by an independent pulmonologist.
• In a Belgian survey of 26 GPs, 30% of patients with asthma and 38% with COPD had their diagnosis changed to the combination of asthma and COPD following re-examination.9
• In a New Zealand population study, over 50% of people older than 50 years with airflow limitation showed some degree of overlap of asthma and COPD.10

COPD is an important comorbidity and can lead to under-diagnosis of asthma in older people.1 In older people, COPD and asthma can be difficult to distinguish because both disorders have similar manifestations despite potentially different causes and underlying abnormalities.1 Current Australian guidelines for the diagnosis and management of COPD recommend referral to a specialist respiratory outpatient service for patients with a clinical diagnosis of COPD in whom asthma cannot be excluded.3 Risk factors for coexisting asthma and COPD include ageing, longstanding asthma, and smoking. The coexistence of incompletely reversible airflow limitation (characteristic of COPD) and increased airflow variability (characteristic of asthma) is common among people with respiratory symptoms aged 65 years and over, and even among those over 50 years.1,5
The coexistence of asthma and COPD in older patients is not always due to cigarette smoking.7 In some people, persistent airflow limitation may develop as a complication of long-term asthma.1,9

Is it asthma, COPD or both?
The main symptoms of chronic obstructive pulmonary disease (COPD) are breathlessness, cough and sputum production. Chest tightness, wheezing and airway irritability are also common. Patients often attribute breathlessness to ageing or poor cardiopulmonary fitness.3
The definitions of asthma and COPD overlap, and asthma and COPD frequently coexist in people aged 65 years and over.1 Comorbid COPD is often misdiagnosed as asthma in older people,1 and vice versa.

►See: Chronic obstructive pulmonary disease (COPD) and asthma
See: Asthma in older adults
For information on diagnosis and management of COPD, refer to the COPD-X Concise Guide for Primary Care.11
The Global Initiative for Asthma (GINA) and Global Initiative Obstructive Lung Disease (GOLD) recommend the following stepwise approach for adults presenting with respiratory symptoms:12

1. Identify whether the patient has clinical features of, or is at risk of, chronic airway disease. This may be suggested by the clinical history and physical examination.
2. Identify features that favour a diagnosis of typical asthma or typical COPD. If several features of both are present, asthma-COPD overlap is likely.
3. Perform spirometry to confirm airflow limitation.
4. Start treatment, selected according to whether the assessment favoured the single diagnosis of asthma, the single diagnosis of COPD, or asthma-COPD overlap.
5. Refer for specialist assessment and other investigations, if necessary.

Definition of variable expiratory airflow limitation
Most of the tests for variable expiratory airflow limitation are based on showing variability in FEV1. While reduced FEV1 may be seen with many other lung diseases (or due to poor spirometric technique), a reduced ratio of FEV1 to FVC indicates airflow limitation.13 Normal FEV1/FVC values derived from population studies vary,14,15 but are usually greater than:14
• 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 FEV1/FVC ratio, because normal values in children change considerably with age.15
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. 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 β$_2$ 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.

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

References

5. 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. Available from: http://thorax.bmj.com/content/64/8/728.full


Management considerations for patients with asthma-COPD overlap

Recommendations

For patients with asthma-COPD overlap, prescribe long-term inhaled corticosteroids (at a low dose, if possible, or at the lowest effective dose) to reduce the risk of asthma flare-ups.

- 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

For patients with asthma-COPD overlap, consider treatment with both an inhaled corticosteroid and a long-acting bronchodilator, as (either of):

- 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) agent such as tiotropium.

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 should be avoided if possible, even if the person also has COPD. 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.

**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

In addition to prescribing inhaled corticosteroids in combination with long-acting bronchodilators, manage coexisting asthma and COPD according to the individual’s clinical features, comorbidities and response to treatment.

- Do not prescribe a long-acting bronchodilator (beta\(_2\) agonist or muscarinic antagonist) without an inhaled corticosteroid in these patients.

**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):

- McDonald et al. 2012
Coexisting asthma and COPD

There is a subgroup of patients with longstanding asthma who do not demonstrate reversible airflow limitation. Asthma that begins later in life often shows a component of irreversible or incompletely reversible airflow limitation (also called 'fixed airway obstruction'), due to airway remodelling and stiffening of the chest wall. The same may be seen in patients with a history of severe asthma in childhood.

Correspondingly, there is a subgroup of patients with COPD who demonstrate significant (though incomplete) bronchodilator response and meet the diagnostic criteria for variable airflow limitation in asthma. Most patients with COPD show some reversibility of airflow limitation with bronchodilators, and the degree of reversibility can vary from visit to visit.

Overlap of asthma and COPD is fairly common among older patients attending primary care:

- In a Dutch analysis of GP patient lists, approximately 10% of patients using an inhaled medication had both COPD and asthma as assessed by an independent pulmonologist.
- In a Belgian survey of 26 GPs, 30% of patients with asthma and 38% with COPD had their diagnosis changed to the combination of asthma and COPD following re-examination.
- In a New Zealand population study, over 50% of people older than 50 years with airflow limitation showed some degree of overlap of asthma and COPD.

COPD is an important comorbidity and can lead to under-diagnosis of asthma in older people. In older people, COPD and asthma can be difficult to distinguish because both disorders have similar manifestations despite potentially different causes and underlying abnormalities.

Current Australian guidelines for the diagnosis and management of COPD recommend referral to a specialist respiratory outpatient service for patients with a clinical diagnosis of COPD in whom asthma cannot be excluded.

Risk factors for coexisting asthma and COPD include ageing, longstanding asthma, and smoking. The coexistence of incompletely reversible airflow limitation (characteristic of COPD) and increased airflow variability (characteristic of asthma) is common among people with respiratory symptoms aged 65 years and over, and even among those over 50 years.

The coexistence of asthma and COPD in older patients is not always due to cigarette smoking. In some people, persistent airflow limitation may develop as a complication of long-term asthma.

Is it asthma, COPD or both?

The main symptoms of chronic obstructive pulmonary disease (COPD) are breathlessness, cough and sputum production. Chest tightness, wheezing and airway irritability are also common. Patients often attribute breathlessness to ageing or poor cardiopulmonary fitness.

The definitions of asthma and COPD overlap, and asthma and COPD frequently coexist in people aged 65 years and over. Comorbid COPD is often misdiagnosed as asthma in older people, and vice versa.

For information on diagnosis and management of COPD, refer to the COPD-X Concise Guide for Primary Care. The Global Initiative for Asthma (GINA) and Global Initiative Obstructive Lung Disease (GOLD) recommend the following stepwise approach for adults presenting with respiratory symptoms:

1. Identify whether the patient has clinical features of, or is at risk of, chronic airway disease. This may be suggested by the clinical history and physical examination.
2. Identify features that favour a diagnosis of typical asthma or typical COPD. If several features of both are present, asthma-COPD overlap is likely.
3. Perform spirometry to confirm airflow limitation.
4. Start treatment, selected according to whether the assessment favoured the single diagnosis of asthma, the single diagnosis of COPD, or asthma-COPD overlap.
5. Refer for specialist assessment and other investigations, if necessary.

Management of coexisting asthma and COPD

- Long-acting beta₂ agonists or long-acting muscarinic antagonists should not be prescribed without an inhaled corticosteroid in patients who have both asthma and COPD, or who have COPD with some features of asthma.
- For patients with both asthma and COPD, treatment should always include inhaled corticosteroids to reduce the risk of flare-ups.

Coexisting asthma and COPD should be managed according to the individual’s clinical features and response to treatment, and monitored by comprehensive ongoing assessment.⁵

Although back-titration of pharmacological treatment is a core principle of asthma management, there is insufficient evidence about the role of back-titration in patients with coexisting asthma and COPD. However, treatment decisions should always balance potential benefits with potential risks of treatment.

Pulmonary rehabilitation is effective for people with symptomatic COPD.¹² Pulmonary rehabilitation is also effective for people with asthma who experience persistent breathlessness, those who are physically inactive, and those with anxiety or depression.¹³

Supervised exercise training may help improve asthma symptoms and quality of life in people with coexisting asthma and COPD, even in older people.¹⁴

Comorbid medical conditions are common among people with coexisting asthma and COPD. Comorbidities should be assessed and managed individually.²,³

Assessment and management of asthma self-management skills must take into consideration comorbidity associated with COPD or ageing (e.g. impaired cognition, reduced manual dexterity and impaired vision).²,³

Pneumonia risk with inhaled corticosteroids in patients with COPD

In people with COPD, the risk of pneumonia is increased by the use of regular inhaled corticosteroids.¹⁵,¹⁶,¹⁷,¹⁸ Most of the available evidence is from patients treated with fluticasone propionate.¹⁸,¹⁹,²⁰,²¹,²²,²³ Increased pneumonia rates have also been observed in studies of patients with COPD using fluticasone furoate/vilanterol.²⁴ The higher dose of fluticasone furoate/vilanterol (Breo Ellipta 200/25 mg) is not indicated for patients with COPD.

Increased risk of pneumonia with inhaled corticosteroids has not been established in patients with asthma.²⁴,²⁵ However, the risk of pneumonia in patients with co-existing asthma and COPD is unknown, so caution is advised, particularly if high doses are being considered.

Definition of variable expiratory airflow limitation

Most of the tests for variable expiratory airflow limitation are based on showing variability in FEV₁. While reduced FEV₁ may be seen with many other lung diseases (or due to poor spirometric technique), a reduced ratio of FEV₁ to FVC indicates airflow limitation.²⁶ Normal FEV₁/FVC values derived from population studies vary,²⁷,²⁸ but are usually greater than:

- 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 FEV₁/FVC ratio, because normal values in children change considerably with age.²⁸

Some spirometers provide predicted normal values specific to age group. If these are available, a FEV₁/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 FEV₁ (change in FEV₁ 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.
- A clinically important increase in lung function (change in PEFR of at least 200 mL and 12% from baseline) 10–15 minutes after administration of bronchodilator.
- 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.

Reversibility in airflow limitation may not be detected if the person is already taking a long-acting beta₂ 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, acute infection of the respiratory tract). Ideally, airflow limitation should be confirmed when the patient does not have a respiratory tract infection.

Airflow limitation during symptoms reduces the probability that a patient has asthma, but a clinically important increase or decrease in lung function is defined as a change in FEV₁ 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. 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.

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Notes

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References

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. Available from: http://thorax.bmj.com/content/64/8/728.full

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


