VERSION 1.2

CLINICAL ISSUES

COMORBIDITIES

Considering and managing comorbid conditions in people with asthma, including gastro-oesophageal reflux disease, mental illness, obesity, allergic rhinitis, obstructive sleep apnoea

ABOUT

This PDF is a print-friendly reproduction of the content included in the Clinical issues - Comorbidities section of the Australian Asthma Handbook at asthmahandbook.org.au/clinical-issues/comorbidities

Please note the content of this PDF reflects the Australian Asthma Handbook at publication of Version 1.2 (October 2016). For the most up-to-date content, please visit asthmahandbook.org.au

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ABBREVIATIONS

CFC  chlorofluorocarbon  LAMA  long-acting muscarinic antagonist
COPD chronic obstructive pulmonary disease  LTRA leukotriene receptor antagonist
COX  cyclo-oxygenase  MBS Medical Benefits Scheme
ED emergency department  NIPPV non-invasive positive pressure ventilation
EIB exercise-induced bronchoconstriction  NSAIDs nonsteroidal anti-inflammatory drugs
FEV1 forced expiratory volume over one second  OCS oral corticosteroids
FVC forced vital capacity  OSA obstructive sleep apnoea
FSANZ Food Standards Australia and New Zealand  PaCO carbon dioxide partial pressure on blood gas analysis
GORD gastro-oesophageal reflux disease  PaO oxygen partial pressure on blood gas analysis
HFA formulated with hydrofluoralkane propellant  PBS Pharmaceutical Benefits Scheme
ICS inhaled corticosteroid  PEF peak expiratory flow
ICU intensive care unit  pMDI pressurised metered-dose inhaler or ‘puffer’
IgE Immunoglobulin E  SABA short-acting β2-adrenergic receptor agonist
IV intravenous  LAMA long-acting muscarinic antagonist
LABA long-acting β2-adrenergic receptor agonist  TGA Therapeutic Goods Administration

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ENDORSEMENT

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- The Royal Australian College of General Practitioners (RACGP)
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- The Thoracic Society of Australia and New Zealand (TSANZ)

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Comorbid conditions and asthma

Overview

The most common comorbid conditions in people with asthma are rhinosinusitis, gastro-oesophageal reflux disease (GORD), mental illness (e.g. depression, anxiety and panic disorders), chronic infections and obstructive sleep apnoea. The prevalence of comorbidities is high among people with severe asthma.1

Figure. Conditions that may affect asthma symptom control, risk or management
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▶ For information on rhinosinusitis or allergic rhinitis, see Allergies and asthma
For information on COPD, see Chronic obstructive pulmonary disease (COPD) and asthma

In this section

GORD
Asthma and gastro-oesophageal reflux disease

Mental illness
Asthma and mental illness, including depression, anxiety disorder and panic disorder
https://www.asthmahandbook.org.au/clinical-issues/comorbidities/mental-illness

Obesity
Asthma and obesity

Other comorbidities
Asthma and other comorbid conditions, including allergic rhinitis and obstructive sleep apnoea
https://www.asthmahandbook.org.au/clinical-issues/comorbidities/other-comorbidities

References

Figure. Conditions that may affect asthma symptom control, risk or management

GORD: gastro-oesophageal reflux disease; OSA: obstructive sleep apnoea; COPD: chronic obstructive pulmonary disease

Adapted from: Boulet LP. Influence of comorbid conditions on asthma. *Eur Respir J.* 2009; 33: 897-906. Available from: [http://erj.ersjournals.com/content/33/4/897.long](http://erj.ersjournals.com/content/33/4/897.long)
Asset ID: 68
Gastro-oesophageal reflux disease and asthma

Recommendations

In adults with asthma, manage reflux symptoms and gastro-oesophageal reflux disease according to current guidelines for reflux disease, but do not advise patients that drug treatments for reflux will improve asthma control.

How this recommendation was developed
Evidence-based recommendation (Grade B)
Based on systematic literature review
Clinical question for literature search:
Does GORD treatment/therapy (H2-receptor antagonists, proton pump inhibitors, anti-reflux surgery, acid suppressive therapy) improve asthma control in people with asthma (adults/children) who have a clinical diagnosis of GORD?
Key evidence considered:
- Chan et al. 2011
- Ekstrom et al. 1989
- Goodall et al. 1981
- Jiang et al. 2003
- Nagel et al. 1988
- Sharma et al. 2007
- Sontag et al. 2003

See: Systematic review of GORD treatment and asthma outcomes

For adults with asthma who have uncontrolled gastro-oesophageal reflux disease, offer referral for specialist assessment (including assessment for anti-reflux surgery).

How this recommendation was developed
Evidence-based recommendation (Grade C)
Based on systematic literature review
Clinical question for literature search:
Does GORD treatment/therapy (H2-receptor antagonists, proton pump inhibitors, anti-reflux surgery, acid suppressive therapy) improve asthma control in people with asthma (adults/children) who have a clinical diagnosis of GORD?
Key evidence considered:
- Sontag et al. 2003

See: Systematic review of GORD treatment and asthma outcomes

In children and adolescents with asthma, manage reflux symptoms and gastro-oesophageal reflux disease according to current age-appropriate guidelines for reflux disease, but do not advise parents or patients that drug treatments for reflux will improve asthma control.

How this recommendation was developed
Evidence-based recommendation (Grade C)
Based on systematic literature review
Clinical question for literature search:

*Does GORD treatment/therapy (H₂-receptor antagonists, proton pump inhibitors, anti-reflux surgery, acid suppressive therapy) improve asthma control in people with asthma (adults/children) who have a clinical diagnosis of GORD?*

Key evidence considered:

- Holbrook et al. 2012
- Khorasani et al. 2008
- Stordal et al. 2005

See: *Systematic review of GORD treatment and asthma outcomes*

Do not use proton pump inhibitors to manage uncontrolled asthma symptoms in children or adults who do not have a diagnosis of gastro-oesophageal reflux disease.

**How this recommendation was developed**

*Based on selected evidence*

Based on a limited structured literature review or published systematic review, which identified the following relevant evidence:

- Chan et al. 2011

More information

### Gastro-oesophageal reflux disease links with asthma

The majority of patients with asthma report symptoms of gastro-oesophageal reflux disease or an abnormal result on the 24-hour oesophageal pH test. Among children treated in referral clinics, the prevalence of gastro-oesophageal reflux disease is higher among those with asthma than those without asthma, but the causal link is unclear.

Asthma may contribute to gastro-oesophageal reflux disease via changes in intrathoracic pressure or the effects of asthma medicines on the gastro-oesophageal sphincter. Gastro-oesophageal reflux disease may contribute to bronchoconstriction through various mechanisms (e.g. vagally mediated reflexes, increased airway hyperresponsiveness, chronic microaspiration of gastric fluid into the airways, or airway neurogenic inflammatory responses). Although the presence of gastro-oesophageal reflux disease is generally thought to worsen asthma control, the precise effect of gastro-oesophageal reflux disease on asthma is unclear.

### Effects of gastro-oesophageal reflux disease treatment on asthma

#### Adults with gastro-oesophageal reflux disease

In adults with asthma and a diagnosis of gastro-oesophageal reflux disease, treatment with a proton pump inhibitor (esomeprazole, lansoprazole, omeprazole, pantoprazole or rabeprazole) produces a small increase in lung function and improves quality of life. There is insufficient evidence from randomised controlled clinical trials to determine whether proton pump inhibitor treatment improves asthma symptoms in patients with gastro-oesophageal reflux disease. The combination of a proton pump inhibitor and domperidone may improve lung function and asthma symptoms in adults with asthma and gastro-oesophageal reflux disease.

Earlier small studies of H₂-antagonists (conducted before proton pump inhibitors became the standard first-line medical treatment for gastro-oesophageal reflux disease) reported inconsistent effects of ranitidine and cimetidine on lung function and other asthma outcomes. In patients with a history of asthma symptoms related to reflux symptoms, H₂-antagonist treatment may reduce night-time symptoms and reliever requirement.

A small study reported that antireflux surgery was more effective than ranitidine for improving asthma symptoms in adults with asthma and gastro-oesophageal reflux disease.
Children with gastro-oesophageal reflux disease

Limited evidence from randomised controlled clinical trials suggests that proton pump inhibitor treatment (lansoprazole, omeprazole) does not improve asthma in children with gastro-oesophageal reflux disease.\(^8,10\) Clinical trials have not investigated the effects of reflux treatment on asthma in children aged 5 years and under.

Subclinical gastro-oesophageal reflux disease

Subclinical or undiagnosed gastro-oesophageal reflux disease is sometimes thought to contribute to asthma symptoms or poorly controlled asthma, leading to the hypothesis that reflux treatment may be useful in asthma treatment. However, clinical trial findings do not support this strategy:

- In adults with asthma but without confirmed gastro-oesophageal reflux disease, proton pump inhibitor treatment achieves a small increase in lung function that is unlikely to be clinically important.\(^1\)
- In children with poorly controlled asthma but no symptoms of gastro-oesophageal reflux disease, lansoprazole treatment did not improve asthma symptom or lung function, but was associated with increased adverse events (mainly respiratory infections).\(^8\)

References

Mental illness and asthma

Recommendations

In patients with moderate-to-severe asthma or asthma that is difficult to control, screen for depression, panic disorder and anxiety disorder, and offer comprehensive assessment, treatment or referral as appropriate.

 questões 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):

- Alvarez and Fitzgerald, 2007¹
- Boulet, 2009²
- Lavoie et al. 2011³
- Parry et al. 2012⁴
- Theoharides et al. 2012⁵
- Weinberger and Abu-Hasan, 2007⁶

Consider hyperventilation as an alternative or coexisting diagnosis when investigating asthma-like symptoms.

 questões 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):

- Weinberger and Abu-Hasan, 2007⁶

Consider potential effects of oral corticosteroids on mental health when prescribing, monitoring treatment response or when assessing adherence during flare-ups.

 questões How this recommendation was developed

Consensus

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

More information

Prevalence of mental illness among people with asthma

Epidemiological studies show that anxiety, depression and panic disorders are more common among people with asthma than in the general population:²,⁷

- A large international population study found that, compared with those without asthma, people with asthma were approximately 1.6 times more likely to have a depressive disorder, approximately 1.5 times more likely to have an anxiety disorder, and approximately 1.7 times more likely to have an alcohol use disorder."
Population studies have shown a higher prevalence of major depressive episodes among adolescents with asthma than adolescents without asthma.\textsuperscript{9} Depression and anxiety disorders are common among people with severe asthma and may be either a consequence of, or a contributor to asthma.\textsuperscript{2} Data from a prospective birth cohort suggest that there is a positive correlation between the risk of mental health problems and asthma severity in children and adolescents.\textsuperscript{10}

Population studies also suggest higher rates of behavioural problems in children with asthma than the general population.\textsuperscript{11} Several studies have shown an association between asthma and attention-deficit hyperactivity disorder in children and adolescents.\textsuperscript{12}

**Effects of mental illness on asthma**

Psychological factors may trigger asthma symptoms and affect patients’ asthma symptom perception, but also may influence medication compliance.\textsuperscript{2} Anxiety, depression and personality disorders have been thought to be risk factors for near-fatal asthma, but the association is unclear.\textsuperscript{1} Psychological factors may trigger asthma symptoms.\textsuperscript{2} High levels of asthma-related fear and panic can exacerbate asthma symptoms.\textsuperscript{4} However, anxiety and hyperventilation attacks can also be mistaken for asthma.\textsuperscript{6}

Data from a cohort study of patients with asthma attending a specialist asthma clinic suggest that comorbid generalised anxiety disorder is associated with worse asthma morbidity (poorer overall asthma control, increased bronchodilator use, and worse asthma quality of life) than patients with asthma overall.\textsuperscript{3} Several studies have reported an association between stress (socioeconomic status, interpersonal conflicts, emotional distress, terrorism) and asthma flare-ups.\textsuperscript{5} The mechanism is not yet understood, but may involve circulating adrenaline levels, altered sensitivity to corticosteroids, or mast cell activation.\textsuperscript{5}

Psychological factors may influence adherence to the treatment regimen.\textsuperscript{2} The experience of euphoria or dysphoria during oral corticosteroid therapy\textsuperscript{13} may influence a person’s adherence to their written asthma action plan and could lead to delays in seeking medical care during flare-ups.

**Hyperventilation and asthma**

Attacks of hyperventilation can be confused with asthma symptoms in people with asthma and in those without asthma.\textsuperscript{6} Some patients with asthma who experience hyperventilation attacks cannot readily distinguish the sensation of dyspnoea associated with hyperventilation from that associated with their asthma.\textsuperscript{6}

**Screening for depression**

There is a range of validated screening tools that can be used to identify symptoms of mental illness, including depression and anxiety. For adults, asking two simple screening questions in primary care can help identify those who need further investigation for depression:\textsuperscript{14}

*Over the past 2 weeks, have you felt down, depressed or hopeless?*

*Over the past 2 weeks, have you felt little interest or pleasure in doing things?*

A list of screening and assessment tools appropriate for adolescents and young adults is included in beyondblue’s *Clinical practice guidelines: Depression in adolescents and young adults* (2010).\textsuperscript{15}

Go to: beyondblue information for health professionals and patients

**Effects of mental health treatments on asthma**

Few randomised controlled clinical trials have investigated whether specific treatments for depression or anxiety in people with asthma can improve symptom control or overall function:\textsuperscript{7} In one placebo-controlled antidepressant trial, improvement in depression was associated with improvement in asthma control, irrespective of treatment received.\textsuperscript{16}

Other studies have reported psychosocial benefits with various interventions:

- In highly anxious patients with asthma, a brief cognitive behavioural intervention may reduce asthma-specific fear.\textsuperscript{4}
- Asthma self-management education and asthma monitoring (either written information and frequent follow-up, or more intensive coaching) has been associated with improvement in quality of life, particularly among patients with depressive symptoms.\textsuperscript{17}
Physical activity (aerobic training) has been associated with improvement in anxiety and depression in people with asthma.  

Systemic corticosteroids: psychiatric effects

Systemic corticosteroids can have a range of psychological effects. Large doses of prednisone or prednisolone can cause mood and behavioural changes, including nervousness, euphoria or mood swings, psychotic episodes including manic or depressive states, paranoid states and acute toxic psychoses. These adverse effects can occur in people without a previous history of psychiatric illness. Systemic corticosteroid treatment has been associated with elevated mood and reduction in depression among patients with asthma. With long-term prednisone or prednisolone therapy, initial mood changes appear to stabilise over time.

Montelukast for adults and adolescents: psychiatric effects

Post-marketing surveillance reports led to concerns about a possible association between leukotriene receptor antagonist use and suicide risk. A recent case-control study reported a statistically significant association between the use of leukotriene receptor antagonists and suicide attempts in people aged 19–24 years. However, this association was no longer statistically significant after adjusting for potential confounding factors, including previous exposure to other asthma medicines and previous exposure to other medicines associated with suicide.

Montelukast for children: warning parents about potential psychiatric adverse effects

Montelukast is generally very well tolerated. However, post-marketing surveillance reports suggested a slight increase in the rate of psychiatric disorders that was possibly associated with use of leukotriene receptor antagonists in children; this association may have been confounded by asthma severity and concomitant medication. Montelukast use has also been associated with suicidal ideation, but a recent nested case-control study concluded that children with asthma aged 5–18 years taking leukotriene receptor antagonists were not at increased risk of suicide attempts. Behavioural and psychiatric adverse effects were rare in clinical trials. The Thoracic Society of Australia and New Zealand advises that it is prudent to mention to parents the potential association of montelukast with behaviour-related adverse events when commencing treatment, and to cease therapy if such adverse events are suspected.

Go to: TGA’s safety update on montelukast and neuropsychiatric risks

Psychological interventions for asthma

Various psychological interventions have been evaluated for patients with asthma who do not have a diagnosis of mental illness. A systematic review of psychological interventions for adults with asthma found that: relaxation therapy reduced the use of relievers; cognitive behavioural therapy improved asthma-related quality of life; bio-feedback therapy may improve peak expiratory flow rate.

A systematic review assessing whether psycho-educational interventions improve health and self-management outcomes in adults with severe or difficult asthma found that positive effects observed were mainly short term. However, studies were generally poor quality.

References


Obesity and asthma

Recommendations

For obese patients with a previous diagnosis of asthma, perform or arrange spirometry to obtain objective measurement of lung function, and confirm the diagnosis by demonstrating variable airflow limitation.

**Table. Confirming the diagnosis of asthma in a person using preventer treatment**

Please view and print this figure separately: https://www.asthmahandbook.org.au/table/show/9

**How this recommendation was developed**
- Adapted from existing guidance
  - Based on reliable clinical practice guideline(s) or position statement(s):
    - Global Initiative for Asthma, 2012

Advise people with asthma who are obese that weight loss might help control their asthma.

**How this recommendation was developed**
- Consensus following inconclusive literature search
  - Based on clinical experience and expert opinion, after systematic literature review yielded insufficient evidence for an evidence-based recommendation: studies that met the inclusion criteria were not suitable for consideration due to unreliability (e.g. small number of participants, inappropriate study design or unacceptable risk of bias).
  - Clinical question for literature search:
    - Does weight loss improve asthma control in overweight/obese patients with asthma?
    - Does a weight loss intervention or program (e.g. diet, exercise, physical activity) improve asthma outcomes in obese/overweight patients (adults/children) with asthma, compared with usual care?
    - Does surgically induced weight loss (e.g. gastric bypass, gastric banding, bariatric surgery) improve asthma outcomes in obese patients with asthma, compared with usual care?
  - See: Systematic review of weight loss and asthma outcomes

Recommendation informed by the following source:
- Adeniyi and Young, 2012

Support obese or overweight people with asthma to lose weight by following current national guidelines for the management of obesity and overweight, including referral for bariatric surgery, if indicated.

**How this recommendation was developed**
- Consensus following inconclusive literature search
  - Based on clinical experience and expert opinion, after systematic literature review yielded insufficient evidence for an evidence-based recommendation: studies that met the inclusion criteria were not suitable for consideration due to unreliability (e.g. small number of participants, inappropriate study design or unacceptable risk of bias).
  - Clinical question for literature search:
    - Does weight loss improve asthma control in overweight/obese patients with asthma?
Advise patients that weight loss of as little as 5–10% in obese or overweight people with asthma may result in clinically important improvement in asthma control and quality of life.

In obese patients, monitor the effect of asthma treatment using objective measures of lung function (spirometry), to avoid escalating asthma treatment unnecessarily.

More information

**Obesity links with asthma**

**Prevalence and mechanisms**

Obesity (defined as BMI ≥ 30 kg/m²) is associated with an increased prevalence of asthma. Increased rates of obstructive sleep apnoea or gastro-oesophageal reflux disease among obese people do not entirely explain the higher rates of symptoms and morbidity seen in obese people with asthma, compared people with asthma who have a normal BMI.

Asthma in obese patients appears to be a specific phenotype, associated with changes in lung function caused by breathing at low lung volumes, a systemic inflammatory process, and a reduced response to asthma medicines. Obesity reduces chest wall compliance, which results in reduced lung volumes, increased work of breathing and increased energy and oxygen costs of breathing.

**Considerations for diagnosis and assessment**

Obese people with asthma report more dyspnoea and asthma-like symptoms than non-obese patients. Respiratory symptoms associated with obesity can mimic asthma.
In obese patients it is especially important to confirm a previous diagnosis of asthma by objective measures of variable airflow limitation.1

**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.12 Normal FEV₁/FVC values derived from population studies vary,13, 14 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.14 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
- clinically important variation in lung function (at least 20% change in FEV₁) when measured repeatedly over time (e.g. spirometry on separate visits)
- a clinically important reduction in lung function (decrease in FEV₁ 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 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.15, 12 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 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, commonly occurs in people with asthma, but can also be seen in patients with COPD or in healthy people without either asthma or COPD.16, 17

Go to: National Asthma Council Australia’s [Spirometry Resources](#)
Go to: National Asthma Council Australia and Woolcock Institute [Peak Flow Chart](#)

**Asthma management in obese patients**
Effects of obesity on asthma control

Among people with asthma, BMI predicts asthma control, independent of airway inflammation, lung function and airway hyperresponsiveness.\(^1\)

Obese people may have a reduced response to inhaled corticosteroids, compared with non-obese people.\(^1\), \(^19\), \(^20\), \(^21\) However, inhaled corticosteroids are still effective in obese people.\(^22\) Compared to people with normal BMI, people with BMI > 40 may take longer to achieve peak FEV\(_1\); after starting preventer treatment.\(^21\)

There is also some evidence of a reduced response to montelukast among obese patients, but findings are not consistent.\(^20\), \(^21\)

Effects of weight loss interventions on asthma

The true effects of weight loss in people with asthma cannot be determined reliably, because many clinical trials assessing the effects of weight loss intervention on asthma have been poorly designed or reported, and have a high risk of bias.\(^2\)

Systematic reviews of weight loss trials in people with asthma show that – regardless of the weight loss intervention – weight loss in people with asthma who are obese or overweight may improve asthma symptoms and reduce reliever requirement.\(^2\), \(^4\) However, weight loss has not been shown to achieve clinically important improvement in lung function.\(^2\)

Some recent case series studies have found that adults who underwent bariatric surgery (various procedures) were able to reduce their inhaled corticosteroid dose.\(^5\), \(^6\)

In an Australian clinical trial comparing a dietary intervention, an exercise intervention, and a combination of these for obese adults with asthma, asthma control improved in the diet and combination groups.\(^7\) Regardless of the method of weight loss, 5–10% weight loss was associated with a clinically important improvement in asthma control in 58% of patients, and improvement in quality of life in 83% of patients.\(^7\)

In a small study in Australian children, a dietary weight loss intervention was associated with improvement in lung function, compared with baseline.\(^3\)

References


Table. Confirming the diagnosis of asthma in a person using preventer treatment

<table>
<thead>
<tr>
<th>Clinical profile</th>
<th>Lung function</th>
<th>Interpretation or action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Typical variable respiratory symptoms</strong></td>
<td>Variable airflow limitation demonstrated</td>
<td>Consistent with asthma diagnosis.</td>
</tr>
<tr>
<td></td>
<td>Variable airflow limitation not demonstrated</td>
<td>Obtain historical documentation of variable airflow limitation if possible.</td>
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<td></td>
<td></td>
<td>If not available, test again (either of):</td>
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<td></td>
<td></td>
<td>• Repeat lung function test during and after symptoms</td>
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<td></td>
<td></td>
<td>• Withhold bronchodilator treatment for required time then repeat spirometry before and 10–15 minutes after salbutamol.</td>
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<td></td>
<td>If diagnosis still not confirmed, consider bronchial provocation (challenge) test.</td>
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<tr>
<td></td>
<td></td>
<td>Note: a negative challenge test would not rule out asthma in a person taking inhaled corticosteroids.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consider referral to a specialist respiratory physician to confirm the diagnosis.</td>
</tr>
<tr>
<td><strong>Current respiratory symptoms</strong></td>
<td>Fixed (irreversible or incompletely reversible) airflow limitation (post-bronchodilator FEV₁/FVC &lt; lower limit of normal for age and FEV₁ &lt;80% predicted)</td>
<td>Obtain historical documentation of variable airflow limitation if possible.</td>
</tr>
<tr>
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<td>Ask about age at onset of symptoms and whether there were typical asthma symptoms earlier in life.</td>
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<td>Consider alternative (or additional) diagnosis (e.g. COPD in adults).</td>
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<tr>
<td></td>
<td></td>
<td>Consider referral to a specialist respiratory physician to confirm the diagnosis, if lung function does not improve after 3-6 months of treatment with inhaled corticosteroids.</td>
</tr>
<tr>
<td><strong>Few respiratory symptoms</strong></td>
<td>Variable airflow limitation not demonstrated</td>
<td>Obtain historical documentation of variable airflow limitation if possible.</td>
</tr>
<tr>
<td>Clinical profile</td>
<td>Lung function</td>
<td>Interpretation or action</td>
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If not available, consider back-titrating preventer by one step:†

- Reduce inhaled corticosteroid dose by 50%.
- 2–3 weeks later reassess lung function by spirometry before and 10–15 minutes after salbutamol.
- If still no evidence of variable airflow limitation, consider stopping preventer treatment (with close monitoring) and repeating spirometry another 2–3 weeks later.

If preventer is ceased and symptoms do not return at 2–3 weeks, review within 6 months.

Table applies to patients taking maintenance inhaled corticosteroid or combination inhaled corticosteroid/long-acting beta<sub>2</sub> agonist

§ When spirometry is performed as a diagnostic test, inhaled bronchodilators should be withheld before the test. Withholding times vary between medicines:

- at least 4 hours for short-acting beta<sub>2</sub> agonists (e.g. salbutamol, terbutaline) and short-acting muscarinic antagonists (e.g. ipratropium)
- at least 12 hours for preventers containing long-acting beta<sub>2</sub> agonists for which twice-daily dosing is recommended (e.g. formoterol, salmeterol)
- at least 24 hours for long-acting muscarinic antagonists (e.g. aclidinium, glycopyrronium, tiotropium) and preventers containing long-acting beta<sub>2</sub> agonists with once-daily dosing (e.g. fluticasone furoate plus vilanterol).

Note: Requested withholding times may vary between centres that conduct formal lung function testing.

† For patients using inhaled corticosteroid/long-acting beta<sub>2</sub> agonist combinations, reduce the dose of inhaled corticosteroid component by 50%. For those already using the lowest possible dose of inhaled corticosteroid/long-acting beta<sub>2</sub> agonist combination, consider switching to low-dose inhaled corticosteroid or stopping preventer.

Before stepping down, document the patient’s current asthma status and risk factors, and ensure that the person has a written asthma action plan and an appointment for asthma review.
Other comorbidities and asthma

Recommendations

Identify and manage co-occurring allergic rhinitis in adults and children with 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):

- de Groot et al. 2012
- Kersten et al. 2012
- Pawankar et al. 2009
- Price et al. 2005
- Thomas et al. 2005
- Wallace et al. 2008

Consider the possibility of upper airway dysfunction as an alternative or coexisting diagnosis in adults and children with 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):

- Benninger et al. 2011
- Deckert and Deckert, 2010
- Weinberger and Abu-Hasan, 2007
- Morris and Christopher, 2010

Consider the possibility of coexisting obstructive sleep apnoea in people with asthma, particularly in those who are also obese. Offer referral for investigation as appropriate.

*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):

- Alkhalil et al. 2008
- Alkhalil et al. 2009
- Boulet, 2009
- Dixon et al. 2011
- Ross et al. 2012
- Teodorescu et al. 2010
- Teodorescu et al. 2012

1 de Groot et al. 2012
2 Kersten et al. 2012
3 Pawankar et al. 2009
4 Price et al. 2005
5 Thomas et al. 2005
6 Wallace et al. 2008
7 Benninger et al. 2011
8 Deckert and Deckert, 2010
9 Weinberger and Abu-Hasan, 2007
10 Morris and Christopher, 2010
11 Alkhalil et al. 2008
12 Alkhalil et al. 2009
13 Boulet, 2009
14 Dixon et al. 2011
15 Ross et al. 2012
16 Teodorescu et al. 2010
17 Teodorescu et al. 2012
For adults with obstructive sleep apnoea or children with sleep-disordered breathing, offer specialist referral.

**How this recommendation was developed**

**Consensus**

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

For Aboriginal and Torres Strait Islander children, routinely ask about coughing (frequency and quality), even if parents or carers do not mention cough.

**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):

- Morey *et al.* 2013

Consider the possibility of other chronic lung disease (e.g. bronchiectasis, chronic suppurative lung disease, pneumonia and COPD) as an alternative or coexisting diagnosis in Aboriginal and Torres Strait Islander adults and children with respiratory symptoms, particularly in remote regions.

**How this recommendation was developed**

**Adapted from existing guidance**

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

- Chang *et al.* 2008

In older patients, consider whether the presence of other common comorbid conditions (e.g. obesity, gastro-oesophageal reflux disease, obstructive sleep apnoea syndrome, osteoporosis, hypertension, cardiovascular disease) or their treatments may affect asthma control, increase the potential for drug–interactions, or affect the person’s ability to self-manage their 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

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**More information**

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**Upper airway dysfunction**

Upper airway dysfunction is intermittent, abnormal adduction of the vocal cords during respiration, resulting in variable upper airway obstruction. It often mimics asthma and is commonly misdiagnosed as asthma. It can cause severe acute episodes of dyspnoea that occur either unpredictably or due to exercise. Inspiratory stridor associated with vocal cord dysfunction is often described as ‘wheezing’, but symptoms do not respond to asthma treatment.

Upper airway dysfunction can coexist with asthma. People with asthma who also have upper airway dysfunction experience more symptoms than those with asthma alone and this can result in over-treatment if vocal cord dysfunction is not identified and managed appropriately.
Upper airway dysfunction probably has multiple causes. In some people it is probably due to hyperresponsiveness of the larynx in response to intrinsic and extrinsic triggers. Triggers can include exercise, psychological conditions, airborne irritants, rhinosinusitis, gastro-esophageal reflux disease, and medicines.

Upper airway dysfunction should be considered when spirometry shows normal FEV₁/FVC ratio in a patient with suspected asthma or symptoms do not respond to short-acting beta₂ agonist reliever. The shape of the maximal respiratory flow loop obtained by spirometry may suggest the diagnosis. Direct observation of the vocal cords is the best method to confirm the diagnosis of upper airway dysfunction.

**Allergic rhinitis and asthma: links**

**Prevalence, aetiology and symptoms**

Asthma and allergic rhinitis frequently coexist. At least 75% of patients with asthma also have rhinitis, although estimates vary widely.

Allergic rhinitis that starts early in life is usually due to a classical IgE hypersensitivity. Adult-onset asthma or inflammatory airway conditions typically have more complex causes. Chronic rhinosinusitis with nasal polyps is not a simple allergic condition and generally needs specialist care.

Symptoms and signs of allergic rhinitis can be local (e.g. nasal discharge, congestion or itch), regional (e.g. effects on ears, eyes, throat or voice), and systemic (e.g. sleep disturbance and lethargy). Most people with allergic rhinitis experience nasal congestion or obstruction as the predominant symptom. Ocular symptoms (e.g. tearing and itch) in people with allergic rhinitis are usually due to coexisting allergic conjunctivitis.

Patients may mistake symptoms of allergic rhinitis for asthma. Allergic rhinitis is sometimes more easily recognised only after asthma has been stabilised.

► Go to: National Asthma Council Australia’s *Allergic Rhinitis and Asthma* information paper

**Effects on asthma**

The presence of allergic rhinitis is associated with worse asthma control in children and adults.

Both rhinitis and asthma can be triggered by the same factors, whether allergic (e.g. house dust mite, pet allergens, pollen, cockroach) or non-specific (e.g. cold air, strong odours, environmental tobacco smoke). Food allergies do not cause allergic rhinitis. Most people with allergic rhinitis are sensitised to multiple allergens (e.g. both pollens and house dust mite), so symptoms may be present throughout the year. Pollens (e.g. grasses, weeds, trees) and moulds are typically seasonal allergens in southern regions, but can be perennial in tropical northern regions. Pollen calendars provide information on when airborne pollen levels are likely to be highest for particular plants.

► Go to: ASCIA’s *Pollen Calendar*

**Allergic rhinitis and asthma: treatment**

**Intranasal corticosteroids**

Intranasal corticosteroids are effective in reducing congestion, rhinorrhea, sneezing and itching in adults and children with allergic rhinitis, and are also effective against ocular symptoms associated with allergic rhinitis.

Intranasal corticosteroids are more effective in reducing nasal symptoms than other treatments, including oral H₁-antihistamines and montelukast, and are at least as effective as intranasal H₁-antihistamines. The use of intranasal corticosteroids in patients with concomitant allergic rhinitis and asthma may improve asthma control.

Intranasal corticosteroids are generally well tolerated in long-term use. In patients with asthma already taking inhaled corticosteroids, the intranasal corticosteroid dose should be taken into account when determining the total daily corticosteroid dose.

Patients need careful training to use intranasal sprays correctly. Detailed information and instructional videos for health professionals and patients are available on the National Asthma Council Australia website.

► Go to: National Asthma Council Australia information on intranasal delivery technique, including *How-to* videos

**Antihistamines**

Intranasal antihistamines reduce all symptoms of allergic rhinitis. Some have a more rapid onset of action than intranasal corticosteroids. Intranasal antihistamines are as effective as newer, less sedating oral H₁-antihistamines, but are generally less effective than intranasal corticosteroids for the treatment of allergic rhinitis.
Second-generation, less sedating oral H1-antihistamines (e.g. cetirizine, desloratadine, fexofenadine, levocetirizine or loratadine) are effective in managing allergic rhinitis symptoms of rhinorrhea, sneezing, nasal itching and ocular symptoms, but are less effective for congestion. They are also effective for managing co-occurring ocular symptoms of allergy.

**Specific allergen immunotherapy**

Specific allergen immunotherapy (desensitisation) is effective in reducing allergic rhinitis symptoms (See separate topic).

► Go to: ASCIA’s Allergen Immunotherapy fact sheet for patients

**Decongestants**

Intranasal decongestants have a limited role in the management of allergic rhinitis because they should only be used for very short courses (up to 5 days maximum). Repeated or long-term use can cause rebound swelling of nasal mucosa necessitating dose escalation (rhinitis medicamentosa), with a risk of atrophic rhinitis.

► Go to: National Asthma Council Australia’s Allergic rhinitis treatments chart

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**Comorbidity in older adults**

Many older people with asthma also have multiple comorbidities and complex healthcare needs. Common conditions in older people that may affect asthma control include:

- obesity
- gastro-oesophageal reflux disease
- obstructive sleep apnoea syndrome and other sleep disorders
- osteoporosis (vertebral fractures can impair respiratory capacity)
- cardiovascular disease (some medicines may worsen asthma).

The presence of diabetes can affect decisions about the use of systemic corticosteroids, while heart disease or anaemia can mimic symptoms.

There is limited clinical trial evidence to guide asthma management in older people with common comorbid conditions, because most asthma treatment trials have excluded people with these conditions. Guidelines for one disease condition may have to be modified for older people with multiple chronic diseases to avoid potential adverse effects including drug–drug interactions.

Common age-related problems such as cognitive impairment, poor eyesight, hearing loss, poor coordination or osteoarthritis can affect a person’s ability to use inhaler devices correctly.

Medicare items for chronic disease management (e.g. GP Management Plans, Team Care Arrangements, Multidisciplinary Care Plans) apply to patients with asthma.

► Go to: Australian Government Department of Health

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**Obstructive sleep apnoea and asthma**

**Links with asthma**

The risk of obstructive sleep apnoea is higher among people with asthma than in the general population. Obstructive sleep apnoea is associated with upper and lower airway inflammation. Pharyngeal inflammation in obstructive sleep apnoea may promote upper airway collapse.

Obstructive sleep apnoea syndrome is an independent risk factor for asthma flare-ups. In adults, unrecognised obstructive sleep apnoea may contribute to persistent asthma daytime or night-time asthma symptoms, based on cohort study evidence.

In obese adults, obstructive sleep apnoea may contribute to poor asthma control.

Obstructive sleep apnoea may also interact with gastro-oesophageal reflux disease to affect asthma control in adults.

In children, sleep-disordered breathing in children appears to be a risk factor for severe asthma, independent of obesity.

**Effects of obstructive sleep apnoea treatment on asthma**
Continuous positive airway pressure (CPAP) may improve asthma in adults with concomitant obstructive sleep apnoea syndrome. Among children with obstructive sleep apnoea, asthma control (measured by frequency of acute asthma flare-ups, reliever use, and asthma symptoms) may improve after adenotonsillectomy. Tonsillectomy or adenotonsillectomy is indicated in the management of upper airway obstruction in children with obstructive sleep apnoea.

**Respiratory disease in Aboriginal and Torres Strait Islander peoples**

Morbidity and mortality from respiratory diseases among Aboriginal and Torres Strait Islander people is higher than among non-Indigenous Australians across all age groups and regions. Among Aboriginal and Torres Strait Islander people living in remote areas, the rate of hospitalisation for respiratory disease is approximately three times the rate among Aboriginal and Torres Strait Islander people living in major cities. However, from 1997 to 2010 there was a 39% reduction in deaths due to respiratory disease among Aboriginal and Torres Strait Islander people.

Detection, diagnosis and management of asthma may be complicated by increased rate of respiratory infections and chronic lung disease in rural remote Aboriginal and Torres Strait Islander communities.

- Approximately 30% of Aboriginal and Torres Strait Islander people report respiratory problems.
- Chronic cough in Aboriginal and Torres Strait Islander children may be under-reported because it is so common that it is considered normal by parents and caregivers.
- Pneumonia and COPD are the most common causes of hospitalisation for respiratory disease among Aboriginal and Torres Strait Islander people. The prevalence of COPD among Aboriginal and Torres Strait Islander people cannot be accurately estimated. The rate of death due to COPD among Aboriginal and Torres Strait Islander people is five times the rate among non-Indigenous Australians.
- The prevalence of bronchiectasis is disproportionately high in remote Aboriginal communities, particularly in Central Australia, but is under-diagnosed. High-resolution computed tomography of the chest is necessary to diagnose bronchiectasis in adults. In Aboriginal and Torres Strait Islander adults, it may be difficult to distinguish between asthma, COPD and bronchiectasis. Bronchiectasis is associated with relatively rapid decline in lung function.
- Chronic suppurative lung disease is highly prevalent among Aboriginal and Torres Strait Islander children in remote communities. The diagnosis of chronic suppurative lung disease is made in children who have symptoms and signs of bronchiectasis without radiographic features of bronchiectasis. In Aboriginal and Torres Strait Islander children, it may be difficult to distinguish between asthma and bronchiectasis or chronic suppurative lung disease.
- Protracted bacterial bronchitis is often misdiagnosed as asthma, but can also co-occur with asthma. Protracted bacterial bronchitis might precede chronic suppurative lung disease, but this is not yet well understood. Inadequate treatment of protracted bacterial bronchitis might put Aboriginal and Torres Strait Islander children at risk for chronic suppurative lung disease. Recurrent episodes of protracted bacterial bronchitis that does not resolve after treatment (e.g. a 14-day course of antibiotics) require investigation for chronic suppurative lung disease, bronchiectasis and aspiration.

| See: Diagnosing asthma in children |
| Go to: Multidisciplinary consensus group position statement Management of bronchiectasis and chronic suppurative lung disease in Indigenous children and adults from rural and remote Australian communities |
| Go to: Thoracic Society of Australia and New Zealand and Lung Foundation Australia position statement Chronic suppurative lung disease and bronchiectasis in children and adults in Australia and New Zealand |

**Notes**

† Chronic suppurative lung disease is defined as a clinical syndrome of respiratory symptoms and signs due to chronic endobronchial suppuration, including continuous, wet or productive cough > 8 weeks, with or without other features (e.g. exertional dyspnoea, symptoms of reactive airway disease, recurrent chest infections, growth failure, clubbing, hyperinflation or chest wall deformity).

‡ Bronchiectasis is diagnosed in patients with both chronic suppurative lung disease and the presence of radiological features on a chest high-resolution computed tomography scan.

**Non-respiratory comorbidity among Aboriginal and Torres Strait Islander peoples**

Aboriginal and Torres Strait Islander peoples have a high burden of chronic diseases that may affect asthma control and management, including:

- diabetes
- cardiovascular disease
- kidney disease
• ear disease
• mental health problems.

See: Comorbid conditions and asthma

References
