Evidence-based guideline on the primary care management of asthma

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This is an updated version of the first North of England Asthma Guideline1,2 and summarizes the full guideline.3 This paper presents all the recommendations within the guideline and, where these are new or substantially altered from the original version, it also presents a summary of the supporting evidence.

The aims and methods of development (summarized in Box 1) of this guideline are unchanged from the original version, to which readers are directed for more detail. The research questions raised during the development of this guideline are shown in Box 2.

Drugs used in the treatment of asthma

Compliance
Recommendation:

- Compliance with treatment is important and should be checked regularly, especially if symptom control is poor or treatment is about to be increased (D).

Inhaled short-acting beta₂ agonists
Recommendations:

- Inhaled short-acting beta₂ agonists should be used on an ‘as required’ basis to relieve symptoms (B).
- They should be used before exercise in patients who have exercise-induced bronchospasm (A).
- As there is no good evidence of clinically important differences between different inhaled short-acting beta₂ agonists, patients should be treated with the cheapest preparation that they can effectively use (D).

Inhaled long-acting beta₂ agonists
Recommendations:

- Most patients treated with inhaled long-acting beta₂ agonists will be controlled satisfactorily on 50 μg twice daily of salmeterol or 12 μg twice daily of eformoterol. If used in higher doses, attention must be paid to side effects (A).
- If patients’ symptoms are not controlled on up to 1000 μg of beclomethasone daily (or equivalent), then regular inhaled long-acting beta₂ agonists should be added to their treatment (A).
- Treatment with an inhaled short-acting beta₂ agonist should be continued on an ‘as required’ basis (B).
- Inhaled long-acting beta₂ agonists should be used in preference to sodium cromoglycate or oral bronchodilators (A).
- As there is no good evidence of clinically important differences between different inhaled long-acting beta₂ agonists, patients should be treated with the cheapest preparation that they can effectively use (D).

In one short-term evaluation, salmeterol was as safe as an inhaled short-acting beta₂ agonist (I).5 Inhaled long-acting beta₂ agonists produce significant bronchodilatation for 12 hours (I).6,7 They produce little additional effect beyond twice daily dosages of 12 μg of eformoterol or 50 μg of salmeterol but the side effects of salmeterol increase (I).6,8–11 Salmeterol and eformoterol have an equivalent bronchodilator effect over 12 hours, but eformoterol appears to have a faster onset of action (I).12 Twice daily inhaled long-acting beta₂ agonists are more effective than inhaled short-acting beta₂ agonists used four times daily (as a metered dose inhaler or a powder) in studies of populations where a proportion (usually a majority) of patients were also on prophylactic treatment (I).13–22 In studies where all patients were on...
Box 1  The search strategy, categories of evidence and strength of recommendations

The search strategy and synthesizing the literature

We searched the electronic databases MEDLINE, EMBASE and the Cochrane Database of Reviews (1994–1997) using a combination of subject heading and free text terms aimed at locating systematic reviews, meta-analyses and randomized trials. The search was backed up by the expert knowledge and experience of group members. The quality of relevant studies retrieved was assessed and, from relevant papers, the information was synthesized qualitatively.

Categories of evidence
I: evidence from meta-analysis of randomized controlled trials or from at least one randomized controlled trial
II: evidence from at least one controlled study without randomization or at least one other type of quasi-experimental study
III: evidence from non-experimental descriptive studies, such as comparative studies, correlation studies and case–control studies
IV: evidence from expert committee reports or opinions and/or clinical experience of respected authorities

Strength of recommendation
A directly based on category I evidence
B directly based on category II evidence or extrapolated recommendation from category I evidence
C directly based on category III evidence or extrapolated recommendation from category I or II evidence
D directly based on category IV evidence or extrapolated recommendation from category I, II or III evidence

Box 2  Research questions

Short-acting beta₂ agonists
What is the relative place of regular and p.r.n. dosing with short-acting beta₂ agonists?

Inhaled corticosteroids
What is the lowest dose of inhaled corticosteroids at which patients benefit from the addition of long-acting beta₂ agonists?
When and how quickly should inhaled corticosteroids be decreased?
Is it effective to increase the dose of inhaled corticosteroids during intercurrent illnesses?
How safe are inhaled corticosteroids and what is the significance of changes in serum cortisols?
Is there a role for using inhaled corticosteroids as first line therapy?

Leukotriene antagonists
What is the appropriate place of leukotriene antagonists in a therapeutic sequence?

Complementary therapy
What is the appropriate role of complementary therapies in the treatment of asthma?

Patient education and self-management
The cost-effectiveness of different self-management plans needs to be evaluated in a pragmatic community-based randomized controlled trial.
Is there a learning effect from the use of peak flow meters on symptom perception and control?
What is the role of peak flow in predicting outcome in acute situations in UK primary care?
Which patients should be monitored with regular peak expiratory flow rate measurements and when?
prophylactic treatment, use of an inhaled long-acting beta₂ agonist improved control (I)²³–²⁶ and in one study patients could decrease their dose of inhaled corticosteroids and still experience benefit (I).²⁷ In one study, patients on 1000 µg of beclomethasone or equivalent benefited from the addition of an inhaled long-acting beta₂ agonist rather than an increase in the dose of inhaled corticosteroid (I).²⁸ In studies where a proportion (usually a majority) of patients are on prophylactic treatment, the addition of an inhaled long-acting beta₂ agonist produced more improvement across a range of parameters than addition of sodium cromoglycate, oral terbutaline or theophylline (I).²⁹–³²

**Inhaled anti-inflammatory agents**

**Inhaled corticosteroids**

Recommendations:

- Patients requiring more than two to three doses a day of inhaled short-acting beta₂ agonists should be treated with inhaled corticosteroids (A).
- Inhaled corticosteroids should usually be used on a twice daily (rather than once or four times daily) basis (B).
- If symptoms are not controlled on twice daily dosing and there is concern about the total daily dose, then increasing the dosage frequency to four times daily but at the same total daily dose should be tried (A).
- If patients’ symptoms are not controlled on up to 1000 µg of beclomethasone daily (or equivalent), regular inhaled long-acting beta₂ agonists should be added (A).
- If symptoms are not controlled on standard doses (up to a daily equivalent of 1000 µg beclomethasone) plus the addition of regular inhaled long-acting beta₂ agonists, higher doses of inhaled corticosteroids should be used up to a daily equivalent of 2000 µg beclomethasone (D).
- A one to three month period of stability should be shown before slow stepwise reduction of inhaled corticosteroids is undertaken, decreasing the dose approximately 25–50% at each step (D).
- As there is no good evidence of clinically important differences between differing inhaled corticosteroids, patients should be treated with the cheapest inhaled corticosteroid that they can effectively use and which controls their symptoms (D).

**Other inhaled anti-inflammatory agents**

Recommendation:

- Nedocromil or sodium cromoglycate may be useful in occasional patients as an adjunct to inhaled steroids, or as an alternative in those patients who cannot tolerate or do not wish to take inhaled corticosteroids. They should be considered as a second line treatment to inhaled corticosteroids (B).

**Leukotriene antagonists**

Recommendation:

- The appropriate therapeutic position of leukotriene antagonists is not clear (D).

In patients on no other anti-inflammatory medication, leukotriene antagonists are more effective than placebo in terms of improvements in spirometry, inhaled short-acting beta₂ agonist use and reported symptoms (I). In studies where patients are also on inhaled corticosteroids, leukotriene antagonists may have a corticosteroid-sparing effect (I).³³–⁴²

**Drug delivery devices**

Recommendations:

- Health care professionals advising patients should use the cheapest drug delivery device which the patient can use and comply with effectively (D).
- Patients should initially be treated with a metered dose inhaler (MDI) (D).
- If patients cannot co-ordinate the activation of an MDI, then a large-volume spacer device should be added (C).
- Large-volume spacer devices should be used with inhaled drugs when the aim is to deal with problems co-ordinating the use of an MDI or to increase the effectiveness of inhaled drugs without increasing the dose. Additionally, they should be used with high-dose inhaled corticosteroids to decrease oral candidiasis (A).
- Patients who cannot use an MDI plus large-volume spacer should be treated with the cheapest powder or automatic aerosol inhaler that they can comply with (D).
- Patients who find an MDI plus large-volume spacer difficult to carry round during the day because of its bulk should be treated with the cheapest powder or automatic aerosol inhaler that they can comply with for daytime use (D).
- In acute situations, large-volume spacer devices are an effective alternative to nebulizers for delivering high-dose bronchodilators (A).

**Inhaler technique**

Recommendations:

- Health care professionals should ensure that patients can use their inhalers adequately (D).
- Inhaler technique should be re-checked whenever control is in doubt (D).

**Oral bronchodilators**

Recommendation:

- Oral bronchodilators should be considered as second line therapy to the use of inhaled bronchodilators and corticosteroids together (A).
**Drug sequencing**

A suggested sequence for treatment is shown in Figure 1.

**Recommendations:**

- The trigger to increasing treatment at all stages is when symptom control is not good [the British Thoracic Society Guidelines define good control as: minimal (ideally no) chronic symptoms; minimal (infrequent) exacerbations; minimal need for relieving bronchodilators; no limitations on activities] (D).
- Compliance should be checked before any treatment increase (D).
- A one to three month period of stability should be shown before slow stepwise reduction in treatment is undertaken, decreasing the dose of inhaled corticosteroid by approximately 25–50% at each step (D).

**Non-drug treatment**

**Acupuncture, homeopathy and yoga**

**Recommendation:**

- Patients should not be treated solely with acupuncture, yoga or homeopathy (A).

There is no good evidence of any therapeutic benefit from acupuncture (I), homeopathy (I) or yoga (I). In the one identified study of yoga, bronchial reactivity decreased.

![Sequencing treatment algorithm](image)
Exacerbations of asthma

Recommendations:

- Patients with an exacerbation of asthma should be treated with oral corticosteroids; there currently is no good evidence to suggest using high-dose inhaled corticosteroids as an alternative (A).
- Prednisolone should be given at dosages of 30–40 mg daily and continued until the episode has resolved, symptoms are controlled and lung function has returned to previous best levels. While seven days' treatment will often be sufficient, it may need to be continued for up to 21 days (B).
- Oral corticosteroids do not need to be tapered; they can be stopped from full dosages. In patients on maintenance oral steroids, reduction should be to their pre-exacerbation dose rather than stopping (D).
- In patients experiencing an exacerbation, inhaled short-acting beta2 agonists can usually be delivered as effectively by spacer as by nebulizer (A).
- Inhaled therapy should be used in preference to intravenous beta2 agonists in the treatment of exacerbations of asthma (A).
- In patients given an inhaled short-acting beta2 agonist via a spacer device, clinicians should consider repeat doses at 30–60 minutes; re-assessment of such patients is important (A).

Oral corticosteroids are effective in the treatment of exacerbations of asthma; oral administration is as effective as intravenous or intramuscular (I).[^49][^50] Used in short courses, oral corticosteroids are safe; they produce very low rates of gastrointestinal bleeding. The greatest risk is in those with a past history of gastrointestinal bleeding or taking anti-coagulants (III).[^51] One underpowered study showed no advantage of high-dose inhaled steroids over oral steroids in treating exacerbations of asthma (I).^[^52]

Inhaled aminophylline offers little benefit over beta2 agonists in the treatment of acute asthma (I).[^53][^54] Nebulized salbutamol is more effective than intravenous salbutamol in the treatment of acute asthma (I).[^55] Spacer devices can be as effective as nebulizers in delivering drugs for the treatment of acute asthma (I).[^56] In patients given a short-acting beta2 agonist via a spacer, their short-term spirometry improves more if the initial dose is repeated after 30–60 minutes (I).[^57] Adding ipratropium to salbutamol produces little additional benefit in terms of spirometry (I).[^58][^59]

Allergen-specific immunotherapy may be appropriate for selected patients but it is not currently a primary care treatment (A).

Methods aimed at reducing exposure to house dust mite allergens seem to be ineffective in producing significant clinical benefit (I).[^62] Allergen-specific immunotherapy reduces asthma symptoms and medication requirements, but has no consistent effect upon lung function. It reduces allergen-specific bronchial hyper-reactivity to a greater extent than non-specific bronchial hyper-reactivity (I).[^63]

Smoking and smoking cessation

Recommendations:

- The current smoking status of all patients should be known (D).
- While there is no one strategy that is effective for all, patients’ strategies should be centred around both advice and support from a health professional, and nicotine replacement therapy in those who are motivated to quit (A).
- Advice and strategies should be tailored to individual circumstances (D).
- Patients should avoid passive smoking (D).

Brief advice from a health professional and nicotine replacement therapy can both help patients stop smoking (I).[^64][^65]

Patient education and self-management

Recommendations:

- Patients should be offered education about their condition and its management (A).
- Self-management education which involves a written action plan, self-monitoring and regular medical review should be offered to adults with asthma (B).
- The routine home use of peak flow meters for self-management is not mandatory (A).

Patient education is capable of improving knowledge and morbidity, and beneficially altering behaviour (I).[^66] A self-management package incorporating regular review, self-monitoring and individualized written action plans may be more effective than limited education in reducing morbidity and resource use (I).[^67]

Precipitants

**Allergen avoidance and allergen-specific immunotherapy**

Recommendations:

- Mite reduction methods should not be recommended routinely (A).

Referral

**Referral to a chest physician**

Recommendations:

Referral to a respiratory physician is appropriate for:

- Patients in whom there is diagnostic doubt (D).
- Patients with possible occupational asthma (D).
- Patients who present a problem in management (D).
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References


Barnes NC, Pujet JC. Prenalukast, a novel leukotriene receptor antagonist: results of the first European, placebo controlled, multicentre clinical study in asthma. *Thorax* 1997; **52**:523–527.


Slater CH, Linder SH. A reassessment of the additive scoring of health practices. *Med Care* 1988; **26**:1216–1227.

