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How should patients be assessed?

What are the treatment options?

How can outcomes be improved?

THE UK HAS ONE OF THE HIGHEST PREVALENCE RATES FOR ASTHMA IN THE WORLD WITH AROUND 1 in 12 (4.3 million) adults affected.[1] Depending on the exact definition used the vast majority of asthma is considered to be mild to moderate (i.e. symptoms and exacerbation frequency controlled without the need for high-dose asthma therapy) and is therefore managed predominantly in primary care.

However, it is widely acknowledged that asthma is an umbrella term covering a multitude of phenotypes, within which symptoms, airway inflammation and bronchial hyperreactivity vary over time. As such no single test performed at one specific time point can definitively confirm or refute the diagnosis.

Asthma guidelines may contain complex diagnostic pathways[2] (see figure 1, p14), suggesting multiple investigations, some of which remain uncommon in primary care (e.g. exhaled nitric oxide)[2] and even when followed may not result in a clear diagnosis being made for a significant proportion of individuals.[3] This coupled with the fact that a number of other conditions (including non-respiratory causes) may also present with wheeze, cough, chest tightness and episodic breathlessness means there are simultaneous concerns about both the over- and under-diagnosis of asthma. However, what is clear from the UK-based National Review of Asthma Deaths (NRAD) report *Why asthma still kills* is that most patients who died were actually considered to have mild to moderate asthma, with 57% of fatal cases not under specialist care at the time of their death.[4]

'Most patients who died were considered to have mild to moderate asthma, with 57% of fatal cases not under specialist care at the time of death'

MANAGEMENT

Pharmacological treatment

The *Why asthma still kills* report highlighted that in cases of fatal asthma there was widespread underuse of inhaled corticosteroids (ICS) — 80% of patients did not receive monthly treatment — and an overreliance on short-acting beta-agonists (SABA).[4] In the most extreme case, one patient »

Box 1

The Royal College of Physicians three questions to identify individuals with good, recent symptomatic control of asthma

In the past month:
- Have you had difficulty sleeping because of your asthma symptoms (including cough)?
- Have you had your usual asthma symptoms during the day (cough, wheeze, chest tightness, or breathlessness)?
- Has your asthma interfered with your usual activities (e.g. housework, work/school, etc)?

NB No to all three questions indicates good control

'Significant over-reliance on reliever medication and underuse of inhaled corticosteroids is a key reason for poor outcomes in mild to moderate asthma'

who died had received 113 reliever inhalers in the previous 12 months.[4]

It is easy to understand why those with mild to moderate disease might forgo regular maintenance therapy and instead rely solely on as required reliever treatment. However, this may mask deteriorating symptoms while allowing the accumulation of critical airway inflammation, risking a life-threatening deterioration which may be sudden. In the National Review of Asthma Deaths, 45% of those who suffered a fatal asthma attack died without seeking medical assistance or before emergency medical care could be provided.[4] The joint BTS/SIGN guideline therefore no longer considers SABA inhalers an appropriate monotherapy apart from in those few individuals with very occasional short-lived wheeze[5] (and there is debate about whether such cases should be classed as asthma at all).

Asthma is an inflammatory airways disease and should therefore always be treated with a steroid-containing inhaler. All other treatments (including SABA) should be considered additional to inhaled corticosteroids.

Confusingly, national guidelines diverge on the recommended initial add-on therapy to regular low-dose ICS. BTS/SIGN suggests adding in a long-acting beta-agonist (LABA) in the form of a combination inhaler,[5] which may help to avoid non adherence with steroids and is modestly superior in reducing oral corticosteroid-treated exacerbations[6] when compared with the NICE recommendation of an oral leukotriene receptor antagonist. However, the latter may be more cost effective in those patients in whom it works.[2]

Both guidelines suggest considering a maintenance and reliever therapy (MART) regimen before [NICE], or after [BTS/SIGN] progressively escalating the dose of the ICS component of treatment.[2,5]

A MART regimen allows a single ICS/LABA combination inhaler to be used both regularly as a preventer and in between as required as a quick acting reliever. Individuals using a MART regimen receive escalating inhaled steroid therapy automatically when their symptoms increase and this form of management has been shown to reduce unplanned admissions while actually decreasing total steroid burden overall.[7] Only certain ICS/LABA devices and strengths are licensed to be used in this way and in those that are the total number of daily doses may vary by product.

Care must be taken in those sub groups where there is poor correlation between symptoms and airway inflammation – individuals who regularly use their inhalers for episodes of dysfunctional breathing or anxiety may, on a MART regimen, be inadvertently exposing themselves to high-doses of ICS, something that increases the risk of pneumonia.[8]

Use of separate LABA inhalers, which are unlicensed for asthma, is considered unsafe and has been linked to an increased risk of asthma-related death.[9,10] The majority of mild to moderate asthma would be expected to respond prior to the need for high-dose ICS-containing products ± a fourth agent (e.g. long-acting muscarinic receptor antagonist or theophylline), the need for which heralds more difficult or severe asthma and onward referral should be considered.

Consideration must also be given to de-escalation of treatment where possible. It is important to discuss with individuals who have been well controlled for at least three months about reducing treatment. Withdraw oral ± inhaled adjuncts to ICS therapy where possible; aim to reduce any steroid-containing product by no more than 25-50% at a time until the lowest ICS-containing maintenance regimen achievable is found.[11]

'Consideration must also be given to de-escalation of treatment where possible'

NICE guidance still suggests that there is a group of patients that might be treated with SABA alone and while it is clear that this is intended to be suitable for only a very small minority of individuals[2] this has proved a controversial decision in light of the NRAD report,[4] particularly as a large-scale Scandinavian study has shown that early implementation of preventer therapy in primary care reduces mortality.[12] Data is beginning to emerge to suggest that reliever inhalers may not be required at all in some forms of mild asthma.[13]

Both major UK guidelines draw attention to the need to check inhaler technique and reinforce good concordance with treatment.[2,5]

'Pregnant women should be informed that uncontrolled asthma is by far the greatest risk to their developing fetus'

Importantly, treatment should be continued during pregnancy as large-scale studies have failed to show any increase in congenital malformations associated with asthma therapy. Pregnant asthma patients, a third of whom will experience worsening symptoms during pregnancy, should be informed that uncontrolled asthma is by far the greatest risk to their developing fetus.[5]

Other medication

Consider whether coprescribed medications may be impacting on asthma

control particularly beta-blockers (even cardioselective ones) and NSAIDs. Cough induced by ACE inhibitors may be mistaken for worsening asthma symptoms. Sensitivity to aspirin is also common, particularly in patients with comorbid nasal polyps, with some series suggesting this impacts on > 20% of cases.[14] If ongoing antiplatelet therapy is still indicated, clopidogrel may be a suitable alternative, particularly as its anti-leukotriene effects have been shown to attenuate airway hyperresponsiveness in animal models.[15]

Non-pharmacological treatment

While triggers should be identified, forms of aeroallergen avoidance, particularly those aimed at decreasing exposure to house dust mite, have not been shown to be an effective method of improving asthma control and should not be routinely recommended.[5]

Significant weight loss in obese asthma patients may be beneficial,[16] as with any respiratory condition patients often become fearful of getting breathless and restrict their physical activity leading to weight gain and deconditioning which further exacerbate their symptoms.

Up to one in five asthma patients smoke. Smoking is associated with poorer control and higher use of oral corticosteroids[17] and was another preventable factor highlighted in the NRAD report.[4]

Assessment

According to the BTS/SIGN guideline individuals with well controlled asthma:

- Should not have bothersome symptoms in the day or night
- Require little/no reliever medication
- Do not suffer exacerbations
- Have preserved lung function

Control should be achieved without significant side effects from treatment.[5] Assessment should consider both current symptomatic impact as well as future risk of asthma. Over time patients may become accustomed to ongoing symptoms and fail to complain about less than adequate control. The RCP three questions are a quick, simple and clinically useful screening tool to identify individuals with good recent symptomatic control[18] (see box 1, p12).

Exacerbation frequency, lung function (spirometry or peak expiratory flow rates) and possibly exhaled nitric oxide readings[19] may help to identify individuals at higher future risk and these factors alone may prompt consideration of a need to increase treatment or seek specialist advice in otherwise seemingly well controlled individuals. Men with late-onset asthma in particular may have low symptom perception but high levels of airway inflammation.[20] We feel that exhaled nitric oxide monitoring may be particularly useful to guide the management of this group although there is not yet an established evidence base to support this.

SELF-MANAGEMENT

Helping patients to understand the need for ongoing use of ICS-containing maintenance therapy, even after symptoms abate is of the utmost importance. Patients are often shocked when told that their blue inhaler does not treat asthma.

‘Patients are often shocked when told that their blue inhaler does not treat asthma’

Non concordance with treatment is widespread. Even among patients attending tertiary level asthma services more than a third were found to collect less than half of their medications.[21]

Education on self-management delivered in a primary care setting can be effective in improving asthma control and preventing unplanned use of healthcare services particularly when supported by a written personalised asthma action plan (PAAP).[5] Such plans are fundamental to improving self-management. They should include details of a patient’s maintenance regimen and also what specific actions to take in response to deteriorating asthma control, such as temporarily increasing the ICS component of treatment or using oral steroids. PAAPs may be triggered by either increasing symptoms or decreasing peak flow readings compared with an individual’s predicted or, if known, actual best.

An example of an action plan using a traffic light system is available to download free of charge from the Asthma UK website, (see figure 2, p15). Once individualised, patients should be encouraged to take a picture of their PAAP on their mobile phone so it is readily available to them.

As well as understanding what they should be taking for their asthma and when, patients must also be shown how to use their treatments and their inhaler technique reassessed at every contact with a healthcare professional. Matching devices or using combination inhalers as far as possible when multiple inhaled therapies are required may help avoid unintentional non-adherence, as studies have shown that patients with respiratory conditions who cannot use their inhalers properly experience poorer disease control and more severe exacerbations.[22]

REFERRAL

A wide range of national and international recommendations exist on which patients should be referred to secondary care,[23] in general we feel the main determinants include the factors shown in table 1, below.

Non-referral of individuals requiring secondary care input has been highlighted as an avoidable factor in cases of fatal asthma.[4] Data, soon to be published, from a retrospective national database study suggest that although »

Table 1

Criteria for referral to secondary care

Diagnostic uncertainty or atypical features

Clinical findings: Crepitations, inspiratory or monomorphic wheeze, clubbing, persistent breathlessness, copious sputum production. Rapidly progressive course; significant extra-pulmonary/systemic symptoms

Investigations: Chest X-ray changes, restrictive spirometry, marked or persistent eosinophilia

Coexisting conditions complicating asthma control: Overlapping COPD; vocal cord dysfunction; bronchiectasis; nasal polyposis. Pregnancy if associated with deteriorating control or significant problems during previous gestational periods

Possibility of hypersensitivity to inhaled material

Including cases of suspected: Hypersensitivity pneumonitis; occupational asthma; work-aggravated asthma; reactive airways dysfunction syndrome (that follows a single high-volume exposure to an irritant)

Treatment and exacerbations

Need for high-dose ICS to control symptoms: Refer patients at any stage of treatment in the following circumstances:

- More than two courses of systemic corticosteroids/year required
- Presentation to emergency care providers more than once in the past 12 months
- Following any asthma-related hospital admission

Patients who have suffered even a single life-threatening asthma attack at any point in the past should be under specialist supervision

Figure 1

NICE recommendations for interpreting test results for adults with symptoms suggestive of asthma[2]

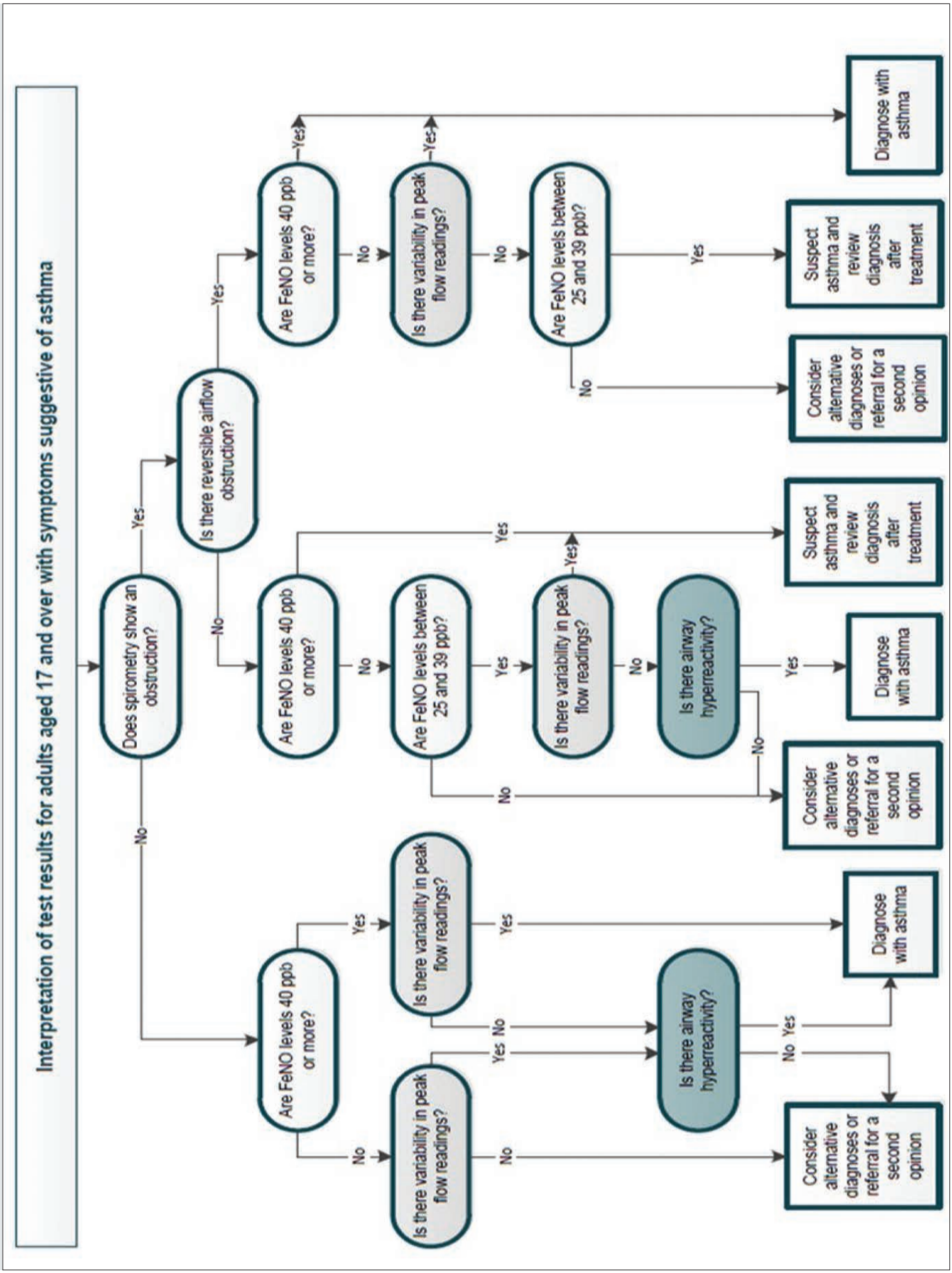


Figure 2

Asthma UK adult asthma action plan using the traffic light system. The template can be downloaded free from the Asthma UK website: www.asthma.org.uk

Every day asthma care:

My asthma is being managed well:

- With this daily routine I should expect/aim to have no symptoms.
- If I've not had any symptoms or needed my reliever inhaler for at least 12 weeks, I can ask my GP or asthma nurse to review my medicines in case they can reduce the dose.
- My personal best peak flow is: ____

My daily asthma routine:

My preventer inhaler (insert name/colour):

I need to take my preventer inhaler every day even when I feel well

I take ____ puff(s) in the morning

and ____ puff(s) at night.

My reliever inhaler (insert name/colour):

I take my **reliever** inhaler only if I need to

I take ____ puff(s) of my reliever inhaler if any of these things happen:

- ★ I'm wheezing
- ★ My chest feels tight
- ★ I'm finding it hard to breathe
- ★ I'm coughing

Other medicines and devices (eg spacers) I use for my asthma every day:

When I feel worse:

My asthma is getting worse if I'm experiencing any of these:

- My symptoms are coming back (wheeze, tightness in my chest, feeling breathless, cough).
- I am waking up at night.
- My symptoms are interfering with my usual day-to-day activities (eg at work, exercising).
- I am using my reliever inhaler three times a week or more.
- My peak flow drops to below: ____

URGENT! If you need your reliever inhaler more than every four hours, you're having an asthma attack and you need to take emergency action now.

What I can do to get on top of my asthma now:

If I haven't been using my preventer inhaler, I'll start using it regularly again or if I have been using it...

Increase my preventer inhaler dose to ____ puffs ____ times a day until my symptoms have gone and my peak flow is back to my personal best.

Take my reliever inhaler as needed (up to ____ puffs every four hours).

I carry my reliever inhaler with me when I'm out.

URGENT! See a doctor or nurse within 24 hours if you get worse at any time or you haven't improved after seven days.

Other advice from my GP about what to do if my asthma is worse (eg SMART/MART or rescue steroid tablets):

In an asthma attack:

I'm having an asthma attack if I'm experiencing any of these:

- My reliever inhaler is not helping or I need it more than every four hours.
- I find it difficult to walk or talk.
- I find it difficult to breathe.
- I'm wheezing a lot or I have a very tight chest or I'm coughing a lot.
- My peak flow is below: ____

What to do in an asthma attack

1. **Sit up straight** – try to keep calm.
2. **Take one puff of your reliever inhaler (usually blue)** every 30 - 60 seconds, up to a maximum of 10 puffs.
3. **If you feel worse** at any point OR you don't feel better after 10 puffs call 999 for an ambulance.
4. **Repeat step 2 after 15 minutes** while you're waiting for an ambulance.

After an asthma attack:

See your GP within 48 hours to make sure you're not at risk of another attack. If you get worse see them urgently. Finish any medicines they prescribe you, even if you start to feel better. If you don't improve after treatment, see your GP urgently.

What to do in an asthma attack if I'm on SMART/MART:

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key points

SELECTED BY

Dr Peter Saul
GP with an interest in respiratory medicine, Wrexham and Associate GP Dean for North Wales, UK

The UK has one of the highest prevalence rates for asthma in the world with around 1 in 12 (4.3 million) adults affected. Depending on the exact definition used the vast majority of asthma is considered to be mild to moderate (i.e. symptoms and exacerbation frequency controlled without the need for high-dose asthma therapy) and managed predominantly in primary care.

The UK-based National Review of Asthma Deaths found that most patients who died were actually considered to have mild to moderate asthma, with 57% of fatal cases not under specialist care at the time of death. In cases of fatal asthma there was widespread underuse of inhaled corticosteroids (ICS) — 80% of patients did not receive monthly treatment — and an overreliance on short-acting beta-agonists (SABA).

The joint BTS/SIGN guideline no longer considers SABA inhalers an appropriate monotherapy apart from in those few individuals with very occasional short-lived wheeze. Asthma is an inflammatory airways disease and should always be treated with a steroid-containing inhaler. All other treatments including SABA should be considered additional to ICS.

Guidelines diverge on the recommended initial add-on therapy to regular low-dose ICS; BTS/SIGN suggests adding in a long-acting beta-agonist (LABA) in the form of a combination inhaler, which may help to avoid non adherence with steroids and is modestly superior in reducing oral corticosteroid-treated exacerbations when compared with the NICE recommendation of an oral leukotriene receptor antagonist. Both guidelines draw attention to the need to check inhaler technique and reinforce good concordance with treatment.

According to the BTS/SIGN guideline individuals with well controlled asthma: should not have bothersome symptoms in the day or night; should require little or no reliever medication; should not suffer exacerbations; and have preserved lung function. Education on self-management, in primary care, can be effective in improving asthma control and prevent unplanned use of healthcare services particularly when supported by a written personalised asthma action plan. As well as understanding what they should be taking for their asthma and when, patients must also be shown how to use their treatments and their inhaler technique reassessed at every contact with a healthcare professional. Reducing exposure to house dust mite, has not been shown to be an effective method of improving asthma control. Significant weight loss in obese asthma patients may be beneficial. Smoking is associated with poorer control and higher use of ICS.

Referral to secondary care should take place when there is diagnostic uncertainty or atypical features, the possibility of hypersensitivity to inhaled material or concerns over treatment or exacerbations. Patients who have suffered even a single life-threatening asthma attack should be under specialist supervision.

Box 2

Good practice points in mild to moderate asthma

- Interrogate asthma registry datasets to identify individuals not receiving ICS-containing treatment – such patients need their diagnosis or treatment reviewing urgently
- Ensure all patients have been taught to use their inhaler correctly and reassess this whenever possible – where feasible match device types, use combination inhalers and avoid blanket switching to other products
- Ensure all asthma patients have an individualised personal asthma action plan and audit this regularly
- Assess prescription pick-up rates in any patient with deteriorating control, prior to any escalation in regular treatment or referral to secondary care
- Consider how frequently reliever medication should be issued – short-acting beta-agonists do not modify disease course and overreliance on them is associated with fatal asthma

a significant proportion of asthma patients fulfill referral criteria, only a small percentage of eligible patients are actually sent for a specialist opinion and even then after some considerable delay. Whether there is adequate capacity to see all eligible patients in secondary care remains unclear.

IMPROVING OUTCOMES

We have highlighted relatively simple methods that may lead to significantly improved asthma outcomes, particularly the need to ensure regular ICS-containing products are taken as well as the use of written action plans to support self-management. Furthermore, in the *Why asthma still kills* report the following additional recommendations were made:[4]

- GP practices should have a named clinical lead for asthma
- Structured asthma reviews should take place at least annually

The report also suggested that patients prescribed > 12 short-acting reliever inhalers in a year should be called for urgent review.[4] However, a well controlled asthma patient should have infrequent need of SABA – a blue inhaler should last almost a year if used no more than twice a week. We are aware of some primary care teams therefore issuing reliever medication quarterly rather than monthly, making a clinical review necessary for those patients requiring more than four blue inhalers a year and helping to reinforce the importance of maintenance therapy. Likewise patients on a MART regimen who regularly order extra inhalers should be called for a review. Other services routinely check pick-up rates for ICS before escalating treatment or referring to secondary care.

CONCLUSION

Mild to moderate asthma is very common and generally its impact and future risk can be managed extremely well with simple interventions. However, this patient group may be prone to an acceptance of suboptimal control and underestimate the potential for sudden deterioration of their condition if management is not adhered to. As with other chronic conditions huge potential gains are achievable with simple interventions that could be achieved using expertise and systems already in place in primary care (see box 2, above).

Competing interests
Dr Gareth Jones has received honoraria from Astra-Zeneca, GSK, Pfizer and NAPP.
Dr Fatima Khalid has no competing interests.

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Useful information

BTS/SIGN asthma guideline (2016)
www.brit-thoracic.org.uk/standards-of-care/guidelines/btssign-british-guideline-on-the-management-of-asthma

NICE asthma guideline. NG80. (2017)
www.nice.org.uk/guidance/ng80

Comparing BTS/SIGN and NICE recommendations
A comparison of the differences between the BTS/SIGN and NICE asthma guidelines
blogs.bmj.com/thorax/files/2017/12/BTS-SIGN-and-NICE-Asthma-guidelines.pdf

Asthma UK
A downloadable asthma action plan template can be found at:
www.asthma.org.uk/globalassets/health-advice/resources/adults/adult-asthma-action-plan.pdf

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