Poorly controlled and severe asthma: triggers for referral for adult or paediatric specialist care – a PCRS pragmatic guide

This pragmatic guide has been developed by an expert group led by Dr Steve Holmes a GP based in Shepton Mallet, Somerset and including: Binita Kane, Manchester University Foundation Trust, Manchester; Angela Pugh and Alison Whittaker, University Hospital of Llandough Cardiff & Vale University Health Board; Ruth McArthur, Macintosh Practice, East Kilbride, Glasgow; and Will Carroll University Hospital of the North Midlands, Stoke-on-Trent

Asthma is a chronic respiratory disease that can range from mild to severe in severity. The severity of the condition can change during the year and throughout a person’s life, and all patients are at risk for periodic exacerbations that can themselves range from mild to severe and even life-threatening events. Consequently, asthma management is an ongoing and dynamic intervention, and treatment needs to be continually reviewed and tailored to the patient’s current level of asthma severity.

It is important to make the distinction between patients with poorly controlled asthma and those with severe asthma, as patients with severe asthma not responding to optimal therapy available in the primary care setting require a different management approach. Poorly controlled asthma (sometimes also referred to as difficult asthma) may be the result of poor adherence to prescribed medication, poor inhaler technique for inhaled medications, the presence of other comorbid conditions (eg, rhinitis) or, indeed, to an incorrect diagnosis. Adherence to prescribed medication can be challenging to measure in clinical practice and involves collecting a prescription, filling the prescription at the pharmacy, attempting to use the medication as prescribed (dose and frequency) and, finally, in the case of an inhaled medication, using the inhaler correctly. A cut-off of 80% adherence for requesting and filling prescriptions may be a relevant and useful way of deciding on a patient’s level of adherence in practice. Patients should be supported to achieve at least 80% adherence to their prescribed medication. Those patients with poorly controlled asthma despite >80% adherence may require further evaluation and medication review.

The National Institute for Health and Care Excellence (NICE) defines uncontrolled asthma as:5

- 3 or more days a week with symptoms; or
- 2 or more days a week with required use of a short-acting beta agonist (SABA) for symptomatic relief; or
- 1 or more nights a week with awakening due to asthma

The European Respiratory Society (ERS) and American Thoracic Society (ATS) joint guidelines define uncontrolled asthma as:6

- Poor symptom control: eg, Asthma Control Questionnaire (ACQ) score that is consistently >1.5 or an Asthma Control Test (ACT) score <20
- Frequent exacerbations defined as ≥2 courses of oral corticosteroids (OCS) of more than 3 days’ duration in the previous year
- Serious asthma exacerbation requiring hospitalisation
- Airflow limitation (forced expiratory

Key facts:

- Asthma UK suggests that an estimated 5.4 million individuals are living with asthma in the UK.1
- Someone has a potentially life-threatening asthma attack in the UK every 10 seconds and 185 people are admitted to hospital every day.1
- The number of asthma-related deaths in England and Wales has barely changed in the last 20 years from 1,268 in 2001 to 1,320 in 2017.2
- The picture is similar in Scotland with 101 deaths in 2001 and 126 in 2017.3
- The cost of caring for individuals with asthma now exceeds £1.1 billion each year, the majority of these being spent on prescription medications and primary care consultations.4

Asthma UK suggests that an estimated 5.4 million individuals are living with asthma in the UK.1
volume in 1 second (FEV$_1$) <80% predicted following a withhold of both SABA and LABA)

Severe asthma is increasingly regarded as a distinct disease entity and may be driven by different inflammatory pathways from those driving asthma in the majority of patients. For these patients, alternative treatments are needed that target different inflammatory pathways to those targeted by inhaled and OCS. The British Thoracic Society (BTS) and the Scottish Intercollegiate Guidelines Network (SIGN) define severe asthma as >2 asthma attacks a year or persistent symptoms with SABA use more than twice a week despite specialist-level therapy of asthma and comorbidities. The ERS/ATS joint guidelines define severe asthma as requiring medications suggested for Global Initiative for Asthma (GINA) steps 4 and 5 (high dose ICS + LABA or LTRA/theophylline) for the previous year or systemic corticosteroids for at least 6 of the previous 12 months to prevent asthma becoming uncontrolled, or which remains uncontrolled despite this therapy. Where available, these patients should be referred to specialist asthma centres as they may require biologics, bronchial thermoplasty or immunosuppressant therapy.

Patients with severe asthma are estimated to account for around 3.6% of all asthma patients, equating to around 200,000 individuals in the UK. The proportion of patients whose asthma is poorly controlled is less apparent, not least because patients themselves may not recognise that their level of symptom control is not as good as it could be. Asthma UK estimates that there are around 1 million individuals in the UK with difficult asthma (17% of the total asthma population).

Both groups of patients are at increased risk for severe, potentially life-threatening asthma attacks, making it imperative to identify them, optimise their treatment and refer them for specialist review as appropriate.

When should we refer our asthma patients for specialist review?

When asthma control is not achieved, a review of the patient’s medication, their inhaler technique, exposure to triggers and their general health (to identify any comorbid conditions or aggravating problems such as smoking) is warranted. When treatment with readily available medications has been optimised in terms of both dose and adherence, the diagnosis confirmed, and other confounding conditions ruled out or managed effectively, and the patient remains symptomatic, the patient should be considered for specialist review (Figure 1).

BTS/SIGN recommend referral for specialist evaluation for patients whose diagnosis is unclear, who have suspected occupational asthma, or who have a poor response to treatment (Table 1).

The UK National Review of Asthma Deaths (NRAD), following a detailed review of 195 asthma-related deaths, recommends that patients who require ≥3 courses of OCS for exacerbations in the past year or those on the level of treatment where three asthma medications have not obtained control or in people who are on regular oral steroid treatment must be referred for specialist review. NRAD also

<table>
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<th>Table 1: BTS/SIGN recommendations for referral of patients with asthma to specialist services</th>
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<td><strong>Adults</strong></td>
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<tr>
<td>Diagnosis is unclear</td>
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<tr>
<td>Poor response to asthma treatment</td>
</tr>
<tr>
<td>Suspected occupational asthma (symptoms that improve when the patient is not at work, adult-onset asthma and workers in high-risk occupations)</td>
</tr>
<tr>
<td>Severe/life-threatening asthma attack requiring hospitalisation</td>
</tr>
<tr>
<td>Patient or parental anxiety or need for reassurance</td>
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Figure 1 The Asthma UK ideal pathway to specialist care for patients with difficult or severe asthma.
How can we determine when our asthma patient needs specialist referral?

Identifying patients at increased risk for a severe/potentially life-threatening asthma attack before they experience a severe event and referring these patients for specialist review has the potential to reduce the number of asthma-related deaths each year. Proactively identifying patients with poorly controlled asthma also has the potential to improve symptom control and quality of life for the estimated 200,000 individuals with difficult or severe asthma in the UK.5

A major challenge is that, while these patients are likely to be experiencing daily symptoms, their symptom burden may have become normalised for them and they might consider that they are managing those symptoms effectively with what is in fact overuse of their rescue SABA therapy.12

The patient who comes to clinic

Generally, asthma is most appropriately managed in the primary care setting with regular structured clinical review at least once a year, using a validated tool to assess symptom burden (eg, Asthma Control Test (ACT), Control of Allergic Rhinitis and Asthma Test (CARAT), CARAT KIDS), along with assessment of medication use and inhaler technique, among other areas.

NICE guidance on monitoring asthma

NICE recommendations for monitoring asthma control are shown in Table 2.5

The patient who does not come to clinic

More challenging is the patient who does not attend clinic for their annual review or when they experience symptom worsening. This may be because they fail to recognise that their symptoms are not well controlled, that they are overusing their rescue SABA inhaler and that this overuse is a sign of poor asthma control.13

A Europe-wide survey of 8,000 patients with asthma conducted in 2012 revealed that almost half (45%) of those questioned had uncontrolled asthma at the time of the survey and 44% had required oral OCS for asthma in the previous 12 months.13 Of concern was the observation that 75% of those who had required OCS for their asthma in the previous 12 months did not regard their asthma as serious.13 In practical terms, if a patient does not attend a clinic in general practice where it is often much closer than a local hospital and often has wider hours of variability, it is unlikely they would attend a tertiary specialist asthma clinic.

The prescriber is responsible for any prescriptions, so it should be incumbent
upon the practice to make (and document) every attempt to engage these patients constructively and encourage them to attend. Practical and escalating steps may include:

- A written communication (letter, email, text message) with each prescription and a further communication within 7–14 days of a prescription fill.
- Follow-up telephone calls – one from reception and a further call from a clinician if needed.
- An alert/s to the dispensing pharmacist who can also be asked to encourage the patient to make an appointment with the GP.

Rescue SABA overuse as an indicator of poor control

An objective factor that could be assessed to measure the level of symptoms is a review of prescription refill frequency for rescue SABA medication. Overuse of rescue SABA inhalers is known to be associated with poor asthma control as well as an increased risk for exacerbations, hospitalisation and death. This may provide an indication of poor adherence to prophylactic treatment if prescriptions are requested less frequently than expected, but may also reveal an over-reliance on rescue SABA medication if prescriptions are requested more frequently than expected.

A recent study of 10 GP practices in North Glasgow found that 5% of patients who received at least one prescription for a reliever or prevention inhaler in the previous 12 months could be defined as SABA overusers (≥13 SABA inhalers in the past 12 months). There are currently no formal guidelines on which to define a threshold for rescue SABA overuse based on prescription frequency. Indeed, a recent survey of a panel of GPs and hospital physicians found that the threshold for acceptable SABA use varied between 0.5 (100 doses) and 12 SABA inhalers (2,400 doses) per year. If we consider this in terms of daily SABA doses, this would range from 0.3 reliever doses per day to 6.6 reliever doses per day (Table 3).

Collection of medical records data including reliever use, healthcare utilisation, lung function and smoking status, among other risk factors, can effectively identify patients at risk of recurrent asthma attacks. While routine collation of all such data may be beyond the capacity of an individual general practice when such data are available, they can be particularly helpful in identifying ‘at-risk’ individuals. For those at risk, written communication can be useful.

An example of a letter that could be sent to a patient identified as filling prescriptions for ≥6 rescue SABA inhalers over a 12-month period is shown in Box 1.

For patients identified as potentially poorly controlled through filling prescriptions for more than a predefined number of rescue SABA inhalers, as outlined above, a review of prescription fill rates for ICS or ICS/LABA should also be undertaken.

Educating patients to monitor their symptoms and recognise poor control

Educating patients on what is poorly controlled asthma may encourage them to attend clinical with worsening symptoms. Not all patients with worsening symptoms will require specialist referral, but all should have their current medication reviewed and their inhaler technique and their medication adherence and symptoms assessed.

An example of a simple algorithm that may be useful to empower patients to recognise poor asthma control in the context of rescue SABA inhaler use is shown in Figure 2. This could be used as a visual

### Table 3: Metrics to evaluate short-acting beta agonist (SABA) use and define overuse

<table>
<thead>
<tr>
<th>Number of rescue SABA inhalers prescribed per year</th>
<th>Available reliever doses per inhaler</th>
<th>Average reliever dose per day over 365 days</th>
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<tbody>
<tr>
<td>1</td>
<td>200</td>
<td>0.6 reliever doses every day (1 reliever dose every 2 days)</td>
</tr>
<tr>
<td>6</td>
<td>1200</td>
<td>3.3 reliever doses every day</td>
</tr>
<tr>
<td>12</td>
<td>2400</td>
<td>6.6 reliever doses every day</td>
</tr>
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### Box 1 Example letter that could be sent to a patient filling prescriptions for ≥6 rescue SABA inhalers over a 12-month period

Dear [Patient Name]

You have asked for a repeat prescription for your asthma ‘blue’ reliever inhaler. As your use of reliever medication is in the high-risk category, we would like to offer you an appointment to discuss your use of medication. Please could you arrange an appointment to see your usual GP or nurse who helps you to manage your asthma. You can also speak to one of the reception team to help you make an appointment.

With kind regards
Pragmatic guidance

All patients with asthma should undergo a clinical review at least every 12 months.

There is some evidence that telephone review for people who are well controlled is acceptable\(^{17,18}\) and, if not controlled, a clinician telephoning may be sufficient to encourage the patient to attend.

For patients who do not attend for their scheduled clinical review, a review of prescription requests for rescue SABA and OCS prescriptions should be undertaken followed by a significant and escalating effort to try to engage these patients constructively. Each prescription should be accompanied by an attempt to get the patient to attend with written communications, follow-up telephone calls (one from reception and a further call from a clinician if needed). The dispensing pharmacists should also be alerted that the patient has been asked to attend for review and can also be asked to encourage the patient to make an appointment with their GP.

- Indicator for rescue SABA overuse may be ≥6 inhalers prescribed in the previous 12 months as a trigger for an invitation for a clinical review
- Trigger for an urgent invitation for a clinical review may be an OCS prescription for asthma exacerbation in the previous 12 months

All patients should receive a personal action plan that provides specific guidance on how to recognise poor asthma control and what to do if asthma control is worsening. Poor control would be:

- 3 or more days a week with symptoms; or
- 2 or more days a week with required use of a rescue SABA inhaler for symptomatic relief; or
- 1 or more nights a week with awakening due to asthma

Include graphical or written guidance on the level of SABA inhaler use that should prompt a patient to attend for a medication review in the patient’s personal action plan.

A patient should be referred for specialist review when:

- The diagnosis of asthma is unclear
- Their asthma remains poorly controlled despite optimal treatment with, and adherence to, medications readily available in primary care
- Occupational asthma is suspected
- The patient has received ≥2 courses of OCS for exacerbations in the past year
- The patient has received more than 12 reliever inhalers in a year (and the amount does not look like reducing)\(^{7,19}\)
- The patient has experienced a severe/life-threatening asthma attack, attended the Emergency Department or been hospitalised with asthma in the last year\(^{7,19}\)

A clinician should be prepared to refer for a more specialist opinion (tertiary level) if, despite secondary care specialist review, the patient and clinician agree that care and improvement does not match their expectations.
guide during a consultation or included as part of a personal action plan.

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References

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