Asthma Guidelines in Practice – A PCRS-UK Consensus

Asthma Guidelines in Practice – A PCRS-UK Consensus was commissioned to provide clarity on aspects of diagnosis, management and monitoring of asthma that are uncertain due to differences between current national guidelines. The article has been written by Dr Luke Daines (GP and Academic Clinical Fellow, University of Edinburgh), in conjunction with GP colleagues, Duncan Keeley, Kevin Gruffydd Jones, Steve Holmes and nurse colleagues, Val Gerrard and Carol Stonham. It is based on the recently published PCRS-UK briefing paper (see https://pcrs-uk.org/sites/pcrs-uk.org/files/BriefingAsthmaGuidelines_V3.docx). This article focuses on mild/moderate asthma, for severe asthma please see British Thoracic Society/ Scottish Intercollegiate Guideline Network. 2016. British Guideline on the Management of Asthma. Available from: http://www.sign.ac.uk/assets/sign153.pdf

Introduction

Asthma is a chronic respiratory condition affecting an estimated 5.4 million people in the UK.[1] Individuals with asthma suffer from wheeze, shortness of breath, cough and chest tightness, limiting everyday activities and fulfilment of roles at home and work.[2]

In the UK, public sector spending for asthma exceeds £1.1 billion each year, with the majority of costs (74%) arising from prescriptions and the estimated 6.4 million primary care consultations that occur each year.[3] Evidence-based management can maintain good day-to-day control for most people with asthma and substantially reduce the risk of asthma attacks.[2]

UK specific national guidelines for asthma management are now available from two sources: the National Institute for Health and Care Excellence (NICE) and British Thoracic Society / Scottish Intercollegiate Guideline Network (BTS/SIGN).[2,4] Whilst the BTS/SIGN guideline covers all aspects of asthma care, the NICE guideline concentrates on diagnosis, monitoring and chronic management. Although broadly similar in methodology, NICE include a thorough health economic evaluation, which other guidelines do not.[4] Subsequently differences in management recommendations can occur if there is little or no clinical difference between interventions.

Recommendations for the diagnosis of asthma also differ between NICE and BTS/SIGN guidelines.[2,4] Achieving a clear consensus for the best diagnostic strategy for asthma is a particular challenge as on top of economic and implementation considerations, the definition of asthma is also evolving.[4] Traditionally a diagnosis of asthma was based on symptoms and demonstration of variable obstructive airflow on lung function testing.[2,5] Yet, more recent definitions of asthma include airway inflammation and airway hyper-responsiveness to incorporate the subtypes of asthma identified through recent research on genetics and pathophysiological mechanisms.[2] This changing understanding of asthma has delivered new ways in which to test and treat for asthma subtypes and may in the future lead to asthma being 'deconstructed' into distinct 'treatable traits'.[5,6] Until then, a clear pragmatic way forward is needed to guide clinicians in non-specialist settings, where most asthma cases are diagnosed.[6]

Rationale for PCRS-UK consensus

In response to the uncertainty faced by many primary care clinicians in light of conflicting recommendations from national guidelines, this article developed by PCRS-UK members, aims to provide a clear, concise and pragmatic view on the diagnosis, management and monitoring of asthma in primary care. This article does not attempt to reproduce all the details contained in each guideline, but instead focuses on the areas that vary substantially between NICE and BTS/SIGN versions, offering a workable solution.

Recommendations

Asthma diagnosis

There is no definitive gold standard test which can categorically confirm or refute the diagnosis of asthma. Therefore, the diagnosis of asthma is made clinically following a structured clinical assessment; a careful integration of evidence from a wide variety of sources.[2,4] Key components of a structured clinical assessment include a detailed history, examination, review of the patient's clinical records and previously completed investigation results (e.g. peak expiratory flow, spirometry, blood eosinophils from a full blood count).

When taking a history, ask about wheeze, shortness of breath, cough and chest tightness, the most suggestive symptoms of asthma.[2,4] Symptoms usually occur in episodes with no (or minimal) symptoms between episodes.[2] Combinations of symptoms (particularly wheeze, cough and shortness of breath) occurring in episodes are more useful for identifying asthma than individual symptoms, particularly in children.[7] Ask about variability in symptoms through the day and between seasons. Clarify any triggers that provoke or worsen symptoms,[4] and in adults, check specifically for work-related factors. Remember to enquire about personal or family history of other atopic conditions such as allergic rhinitis or eczema.[4] Information from the patient clinical record, including previous respiratory illnesses, treatments and responses and previous examination findings (particularly wheeze heard on chest auscultation by a health professional) can further build the clinical picture.

On auscultation of the chest, asthmatic wheeze tends to be end-expiratory, scattered and polyphonic. Consider alternative diagnoses if wheeze is never heard during symptomatic episodes (Box 1). Remember that respiratory examination may well be normal in an asymptomatic individual, so it is important not to exclude asthma solely on examination findings.[4] In addition to a respiratory examination, check the throat for enlarged tonsils, and look out for other signs of atopic disease such as eczema or rhinitis.

Following a structured clinical assessment, the BTS/SIGN guideline recommends weighing up the probability that the individual has asthma based on three categories: high, medium and low.[2]

If a patient (whether adult or child) has all of the following typical clinical features, they are considered to have a high probability of asthma:[2]

- Recurrent episodes of symptoms ('attacks')
- Wheeze confirmed by a healthcare professional
- A personal or family history of atopy
- A past record of variable airflow obstruction
- No features to suggest an alternative diagnosis (Box 1).

If there is any doubt, the diagnosis should be considered as intermediate probability. Adults and children who have none of the typical features of asthma or whose symptoms are suggestive of an alternative diagnosis have a low probability of asthma.[2] The probability of asthma informs the next steps in the diagnostic work up as demonstrated in (Figure 1).

Even with a careful structured clinical assessment and diagnostic work up, the diagnosis of asthma can be challenging, particularly due to the variable nature of symptoms and lung function over time and the heterogeneity of presentation. Primary care is ideally placed to collect, record and appraise the information required to make an asthma diagnosis and provide continuity to allow repeated assessments over time so that treatment response and natural variation can be evaluated. Consequently, a diagnostic strategy based on repeated clinical assessments, supported by objective clinical tests (including peak expiratory flow monitoring) and sensitively using trials of initiating and discontinuing therapy is recommended as a practical way forward.

It is important to refer to specialist services in cases of doubt or difficulty (Box 2).

Whilst investigating asthma, and until a diagnosis is confirmed, use the code 'suspected asthma'.[2,4] Once a diagnosis of asthma has been made, record the basis for the decision in a single entry in the person's medical records, alongside the coded diagnostic entry. The diagnosis of asthma should ideally be revisited and checked regularly – especially when you first take over the care of a patient thought to have asthma. Good documentation is strongly recommended as the variable nature of asthma can lead to individuals experiencing long periods without symptoms, leading patients and clinicians to question the original diagnosis.[8]

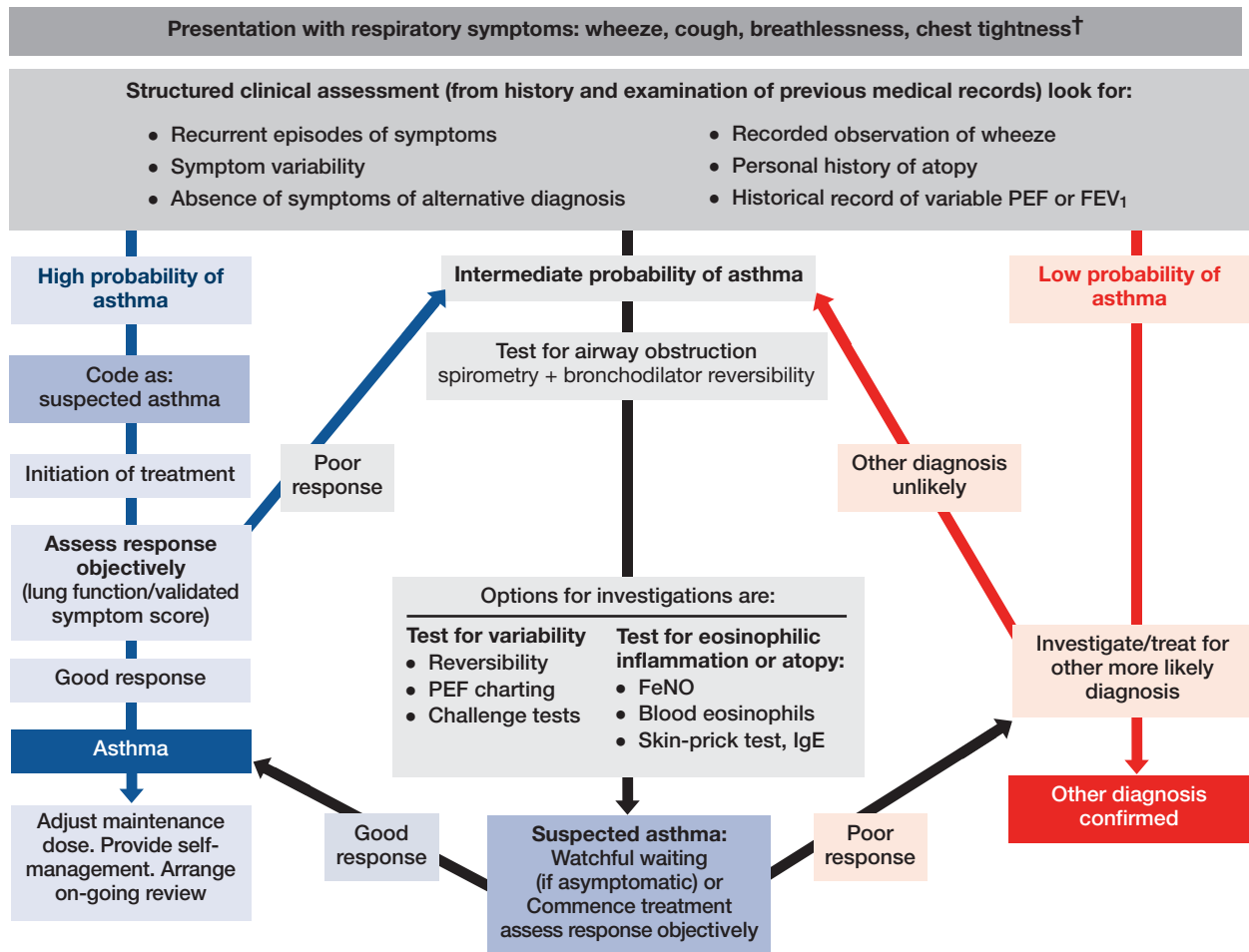| Box 1. Clinical features to suggest an alternative diagnosis to asthma in adults (from BTS/SIGN 2016)[2]	
No airflow obstruction	
Predominant cough with no lung function abnormality	Chronic cough syndromes; pertussis
Prominent dizziness, light-headedness or peripheral tingling	Dysfunctional breathing
Recurrent severe 'asthma attacks' without objective evidence to confirm	Vocal cord dysfunction
Mostly nasal symptoms without lung function abnormality	Rhinitis
Postural and food related symptoms, predominant cough	Gastro-oesophageal reflux disease
Orthopnoea, paroxysmal nocturnal dyspnoea, peripheral oedema, pre-existing cardiac disease	Cardiac failure
Crackles on auscultation	Pulmonary fibrosis
With airflow obstruction	
Significant smoking history (i.e. over 30 pack-years), age of onset over 35 years	COPD
Chronic productive cough with no wheeze or breathlessness	Bronchiectasis*, inhaled foreign body*, obliterative bronchiolitis, large airway stenosis
New onset in smoker, systemic symptoms, weight loss, haemopthysis	Lung cancer*, sarcoidosis*
* may also be associated with non-obstructive spirometry	

Figure 1. Diagnostic algorithm for individuals presenting with symptoms suggestive of asthma (from BTS/SIGN; 2016)[2]

Presentation with respiratory symptoms: wheeze, cough, breathlessness, chest tightness†

Structured clinical assessment (from history and examination of previous medical records) look for:

- Recurrent episodes of symptoms
- Symptom variability
- Absence of symptoms of alternative diagnosis
- Recorded observation of wheeze
- Personal history of atopy
- Historical record of variable PEF or FEV_1

High probability of asthma

Intermediate probability of asthma

Low probability of asthma

Code as: suspected asthma

Test for airway obstruction
spirometry + bronchodilator reversibility

Initiation of treatment

Poor response

Other diagnosis unlikely

Assess response objectively
(lung function/validated symptom score)

Good response

Options for investigations are:

Test for variability
- Reversibility
- PEF charting
- Challenge tests

Test for eosinophilic inflammation or atopy:
- FeNO
- Blood eosinophils
- Skin-prick test, IgE

Investigate/treat for other more likely diagnosis

Asthma

Good response

Poor response

Adjust maintenance dose. Provide self-management. Arrange on-going review

Suspected asthma:
Watchful waiting (if asymptomatic) or Commence treatment assess response objectively

Other diagnosis confirmed

† In children under 5 years and others unable to undertake spirometry in whom there is a high or intermediate probability of asthma, the options are monitored initiation of treatment or watchful waiting according to the assessed probability of asthma

Objective tests

Objective tests should be done in all patients old enough to perform them, as part of an initial diagnostic assessment to support a confident diagnosis of asthma. Increasing the quality and availability of objective testing across healthcare is an important policy priority. Understanding that each diagnostic test available for asthma has strengths and limitations is therefore valuable in order to use tests most effectively to build up sufficient evidence so that a differential diagnosis can be confirmed or refuted correctly.

Tests for demonstrating variability in airflow obstruction

A defining feature of asthma is variable airflow obstruction caused by airway bronchoconstriction. Yet, demonstrating variable airflow obstruction can be a challenge as airway physiology may be normal when an individual with asthma is asymptomatic. This is reflected in estimates for the negative predictive value of spirometry in adults and children which varies between 18 and 54%, indicating that more than half of patients who have a negative result (non-obstructive spirometry) will have asthma.[9]

Therefore, relying on objective tests of airflow obstruction completed only at a single point of time risks missing asthma, particularly if the patient is asymptomatic at the time of testing. Instead, testing for variable airflow obstruction should be repeated over time.

In primary care, peak expiratory flow monitoring and spirometry with bronchodilator reversibility testing are recommended measures to demonstrate variable airflow obstruction. When interpreting spirometry, BTS/SIGN recommend the use of lower limit of normal for FEV_1/FVC ratio (instead of the fixed ratio of 70%) in order to avoid the substantial under diagnosis in children and over diagnosis of obstruction in older people.[2,10] Although sometimes undervalued, peak expiratory flow monitoring can provide useful measurements. The value of PEF monitoring as an important initial test in the assess-

Box 2. Reasons for specialist referral (from BTS/SIGN)[2]	
Adults	**Children**
Referral for tests not available in primary care	
Diagnosis unclear	Diagnosis unclear
Suspected occupational asthma (symptoms that improve when patient is not at work, adult-onset asthma and workers in high-risk occupations)	
Poor response to asthma treatment	Poor response to monitored initiation of asthma treatment
Severe/life-threatening asthma attack	Severe/life-threatening asthma attack
'Red-flags' and indicators of other diagnoses	
Prominent systemic failure (myalgia, fever, weight loss)	Failure to thrive
Unexpected clinical findings (e.g. crackles, clubbing, cyanosis, cardiac disease, monophonic wheeze or stridor)	Unexpected clinical findings (e.g. focal signs, abnormal voice or cry, dysphagia, inspiratory stridor)
Persistent non-variable breathlessness	Symptoms present from birth or perinatal lung problem
Chronic sputum production	Excessive vomiting or posseting
Unexplained restrictive spirometry	Severe upper respiratory tract infection
Chest X-ray shadowing	Persistent wet or productive cough
Marked blood eosinophilia	Family history or unusual chest disease
	Nasal polyps
Patient or parental anxiety or need for reassurance	

ment of asthma was discussed in the Spring 2017 edition of *Primary Care Respiratory Update* see https://pcrs-uk.org/peak-flow-and-microspirometry-support-diagnosis.

Tests for demonstrating eosinophilic inflammation

A positive Fractional Exhaled Nitric Oxide (FeNO) test indicates the presence of eosinophilic inflammation, providing supporting (rather than conclusive) evidence for an asthma diagnosis. PCRS-UK produced a guide to FeNO testing in its Spring 2016 issue of *Primary Care Respiratory Update* – see https://pcrs-uk.org/feno-testing.   A recent systematic review of the accuracy of FeNO in diagnosing asthma in adults and children reported a pooled sensitivity of 65% and specificity of 82%, indicating that FeNO has a higher potential for ruling in as opposed to ruling out the diagnosis of asthma.[11] In adults, a FeNO reading of 40ppb or more should be regarded as a positive test.[2,4] Accurate interpretation of a FeNO result requires an understanding of the potential confounding factors that may produce false positive and false negative results (Box 3), and must be made in the clinical context of the individual patient.

NICE (2017) recommendations for the role of FeNO in the diagnosis of asthma are very different to those advocated by BTS/SIGN.[2,4] Given the limitations of FeNO, a central role in

the diagnostic work up of all people suspected of asthma, as advocated by NICE, seems over emphasised and may lead to unintended consequences. Currently, FeNO is not widely available in UK primary care, therefore, if FeNO is perceived as a required test, referrals to secondary care may increase, adding to the workload in specialist settings, and potentially de-skilling clinicians in primary care. Cost may be a barrier for individual practices adopting FeNO, as ongoing consumables are required in addition to an initial investment. A future solution might be for practices to pool resources and develop a locality based diagnostic service, as successfully implemented in the Netherlands, and currently being trialled in the UK.[4,14]

Despite these concerns, there are clear benefits to be gained from using FeNO, which could be realised if appropriately implemented. For instance, if an individual has an intermediate probability of asthma following a structured clinical assessment, a positive FeNO test increases the probability of asthma, providing further supporting evidence to confirm or refute a diagnosis. The BTS/SIGN recommendations for using FeNO in diagnosing asthma are therefore endorsed, until an optimal diagnostic pathway for UK practice is demonstrated.

Diagnosis in children

Confirmation of variable airflow obstruction by objective

Box 3. Factors that may confound the accuracy of FeNO in making an asthma diagnosis[2,12,13]

Increased levels in men, tall people, and those with a diet high in nitrates (e.g. spinach, broccoli).

Increased levels in individuals with allergic rhinitis exposed to an allergen (even without respiratory symptoms)

Increased levels in those with rhinovirus infection (inconsistent effect in those with asthma)

Lower levels observed in children (N.B. accordingly a lower reference range is used)

Reduced levels in cigarette smokers

Reduced levels by inhaled or oral steroids

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demonstration of peak flow monitoring or spirometry with reversibility is desirable in children old enough to perform these tests. However, the use of spirometry is not well established in children in primary care and additional training may be needed to ensure accurate results. If using FeNO in children aged 5-16 years of age, a result of 35ppb or more is regarded as a positive test.[2,4]

In children under 5 years of age, a diagnosis of asthma is based on establishing the probability of asthma after an initial structured clinical assessment.[2] If the probability of asthma is high, a trial of an inhaled corticosteroid (ICS) using a dosage of 400micrograms/day beclomethasone or equivalent may be considered.[15] If a child is started on a trial of treatment, it should last for 6 – 8 weeks, and stopped at the end of the trial.[2,15] If the child has had no response to treatment, and the medication has been taken, the diagnosis of asthma is unlikely.[15] If symptoms improve with ICS but recur when stopped, then settle again with reintroduction of treatment, a diagnosis of asthma can be made.[15] Where diagnostic doubt persists   referral for specialist assessment should be considered (Box 2).

Asthma management

Management of asthma should be patient centred; encouraging and supporting self-management, and making treatment decisions in partnership with the individual. This should include promoting non-pharmacological approaches including weight control, encouraging physical activity and addressing tobacco dependency. Supported self-management, which includes the provision of an asthma action plan, improves individual asthma control whilst reducing visits to unscheduled care.

ICS are regarded as the foundation of asthma pharmacological treatment.[2,10] Therefore, a regular (low dose) ICS with a short-acting beta-agonists (SABA) as required is the recommended first line maintenance treatment for adults and children with asthma. Overuse of SABAs is well established as a risk factor for fatal asthma.[16] Close monitoring of short-acting beta-agonist use is

advocated to ensure no more than 12 inhalers a year are used. If asthma is really well controlled a SABA inhaler containing 200 doses should last for three months.

Prescribing inhalers by brand name and device ensures that patients receive the inhaler that the prescriber intends for them. Prescribing a generic inhaler, or not specifying the device should be avoided as it may result in a patient receiving an inhaler they have not been taught to use. In addition, spacers should be prescribed with metered dose inhalers to increase the efficacy of drug delivery.

Add-on therapies

NICE and BTS/SIGN have different advice for the choice of first-line add-on treatment to low-dose ICS. Long-acting beta-agonists (LABA) are the more familiar add-on therapy in line with BTS/SIGN recommendations, and are more effective than leukotriene receptor antagonists (LTRA) in reducing the number of exacerbations.[4,17] LABA's are prescribed in combination inhalers with ICS which does improve the likelihood of adherence to an additional medication, and reduces the risk of harm from using LABA as monotherapy.[18]

NICE recommend LTRA as the first-line add-on therapy because the marginal superiority in efficacy of LABA (noted in adults)[17] is outweighed by its greater cost.[4] As an oral medication, LTRA's may offer an advantage for some for whom an inhaler is impractical. LTRA also offer treatment benefit for those with allergic rhinitis. Therefore, in line with a value based health care approach,[19] PCRS-UK recommend LTRA as the first line add-on therapy to ICS. Effectiveness and tolerability should be reviewed in 4-6 weeks. If LTRA is found ineffective, it should be withdrawn, as adding a LABA on top of a LTRA removes any cost advantage.

Ultimately the decision to opt for LTRA or LABA as initial add-on therapy should be made after a discussion between clinician and patient and should take consideration of other factors including patient preference, adherence (including the potential for additional prescription costs), concomitant diseases (e.g. rhinitis) and risk of exacerbation. Furthermore, there is no need to change the medication of patients who are already well controlled on LABA/ICS.

In children, the use of a paediatric low dose ICS with LTRA as first line add-on treatment is recommended. If this combination is ineffective then switch the LTRA for a LABA.

Asthma monitoring

Primary care is best placed to monitor asthma by staff who are trained, competent and confident, and should be completed regularly (at least annually in stable patients with a definite diagnosis) as a pre-planned appointment but also opportunistically. A more frequent review may be necessary when a diagnosis is first made, or for those with poor asthma control. At each review, asthma control, lung function, asthma attacks, oral corticosteroids and absence from work or school

Box 4. Common causes of poor asthma control
Incorrect diagnosis. Or co-morbidity that has been missed
Lack of medication adherence
Current treatment is unsuitable
Under-use of ICS. Or overuse of SABAs
Inappropriate inhaler technique
Failure to use a spacer with ICS delivered by a metered dose inhaler
Smoking (active or passive) – ideally use a carbon monoxide meter to monitor smoking
Exposure to occupational triggers
Seasonal or environmental factors
Psychosocial reasons, including ideas and concerns about asthma / treatment

should be recorded in the notes. Asthma control should be assessed using the validated asthma control questionnaire or asthma control test, and are recommended over the Royal College of Physicians three questions which has greater value as a screening test for poor control. Peak flow or spirometry (or both) should be used to assess lung function. If asthma control is sub-optimal check for and address the common causes of asthma control listed in Box 4.

Currently there is insufficient evidence from real-life primary care to support using FeNO routinely to monitor asthma control. However, it may be an option to support asthma management in people who are symptomatic despite using ICS as it can help to identify poor adherence.

As well as during a routine review, inhaler technique should be observed and errors in technique corrected at every opportunity when there is a deterioration in asthma control; when the inhaler is changed; and if the patient requests a check.

Conclusions

The presence of multiple guidelines for asthma care is unhelpful, creating uncertainty for clinicians and potentially leading to inconsistencies in the care of individual patients.

From the outset of NICE's proposal to develop guidelines for asthma PCRS UK has argued for retaining a single comprehensive and regularly updated asthma guideline for the four nations of the UK.[20] We have restated this call repeatedly to NICE, BTS/SIGN and NHS England.

A return to a single asthma guideline developed through the collaboration of NICE and BTS/SIGN, would allow the

strengths of both organisations to be drawn upon to produce clear and consistent recommendations.

In the meantime, we have proposed clear guidance to address particular concerns over conflicting aspects of asthma diagnosis, management and monitoring that will support non-specialists to continue providing high quality asthma care.

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