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Smokers with asthma: how can we help them to stop?

- Even in the UK, where there are well-established tobacco-control policies, there is a slowdown in the reduction in smoking prevalence and we encounter an increasing number of harder-to-treat smokers.
- Smoking places a major burden on healthcare services; for example, it is responsible for 28% of hospital admissions in the UK.
- Self-reported smoking is just as prevalent among people with asthma as those without.

Smoking impacts the development and management of asthma.

- Smoking and second-hand/passive smoking increase the risk of developing asthma.
- Smokers with asthma:
  - have decreased asthma control
  - are at increased risk of exacerbations and death
  - experience an increase in asthma severity

How should people with asthma who smoke be managed in the primary care setting?

- In clinical practice, there is a false assumption that the link between smoking and asthma is well understood.
- Therefore, smoking is sometimes not taken into account when developing a PAAP.
- Smokers with asthma should be provided with at least the same support as the general population to stop smoking.
- Initiatives are underway to raise awareness and provide practical guidance for PCPs. One such initiative has been piloted by the London Respiratory Network.

London Respiratory Network recommended support mechanisms for smokers with asthma.

Tobacco-dependence drug therapies for people with asthma who smoke

- There is a need to consider the evidence for specific regimens in smokers with asthma to ensure the optimal treatment choice is made.
- Pharmacological therapy for smokers with asthma needs to be considered on a case-by-case basis. Step 2 ICS may not be sufficient due to the impact of tobacco smoke on ICS pharmacokinetics. The use of smoking-cessation therapies should be considered before stepping up to avoid excessive and unnecessary high-dose ICS.

Improving the ‘Stop Smoking’ strategy to help people with asthma to stop smoking

- Effective clinician–patient collaboration is paramount for smokers with asthma, and there is a need for the clinician to acknowledge that teamwork is important during reviews.
- This teamwork approach is important for motivating people with asthma to stop smoking.

Practical recommendations to support people with asthma to stop smoking

- Identify the smoking prevalence and burden within your practice.
- Be aware of your practice Stop Smoking Champion, or appoint one.
- Make exhaled CO testing part of your asthma annual review. Have a conversation about smoking after the test, not before.
- Ensure your team has the correct training to aid motivational support for patients who want to stop smoking.

CO testing measures the level of exhaled CO. It helps the PCP and the patient to monitor progress, aiding either reduction in or stopping smoking.

- Identify smokers as being at high risk for more severe symptoms, accelerated decline in lung function, and impaired short-term response to ICS.
- Discuss the impact of smoking on asthma as often as possible.
- Plan tobacco-dependence therapy according to the reported smoking status, CO level, and minutes to first tobacco after waking.
- Prior to stepping up asthma treatment, offer guideline-recommended support to stop smoking.
- Ensure stopping smoking is included as a treatment option in PAAPs and other educational materials.

Tools for motivating patients to stop smoking

- CO testing measures the level of exhaled CO. As CO is usually undetectable after 24 hours of smoking, it acts as a useful marker for regular smoking.
- CO is easy to measure using a portable device that is similar in price to a high-quality electronic blood pressure monitor.
- The levels of CO are provided in a digital format, providing a numerical value that the PCP can share with the patient.
  - The digital format is a useful motivational tool, as it helps the PCP and the patient to monitor progress, aiding either reduction in or stopping smoking.
- Generally, 9 ppm is the highest acceptable level of CO in non-smokers. In practice, any value above 5 ppm suggests exposure to tobacco smoking.
- Nevertheless, it should not be assumed that raised CO levels indicate exposure to tobacco smoke. It is important to engage the patient in a conversation to rule out other causes of raised CO levels, such as a faulty gas boiler.

Key point: Motivating smokers with asthma to stop should be a priority for PCPs and be part of routine asthma management.
A closer look at biomarkers in asthma: is FeNO the way forward?

- Biomarkers have received increasing attention in recent years
- FeNO testing measures the level of exhaled nitric oxide in a breath sample and can be conducted using a number of different portable devices
  - However, few primary care centres have access to these devices
- FeNO is a non-invasive biomarker of inflammation, and high levels of FeNO are commonly associated with eosinophilic asthma
  - FeNO can also be associated with conditions such as atopy and allergic rhinitis
- There is still controversy surrounding the role and relevance of FeNO in asthma management
  - It is most likely to find a role as a marker of exacerbation risk and as a predictor of ICS treatment response, rather than as a means of diagnosing asthma per se
- There is also increasing evidence that the blood eosinophil count can provide complementary information to other diagnostic approaches

Inflammatory markers used to distinguish between asthma and other respiratory diseases
- FeNO
- Atopy markers, such as IgE
- Blood eosinophil count
- Sputum inflammatory cell analysis (relevant in the research context rather than clinical practice)

The value of FeNO as a tool to support the diagnosis and management of asthma was discussed at ERS 2016 and in recent publications

Studies supporting FeNO measurement
- FeNO provides information about outcomes that really matter, such as exacerbation risk and the likely benefit of ICS treatment, rather than arbitrary disease labels
- Tailoring asthma medications based on FeNO levels compared with normal primary care practice (based on clinical symptoms) decreases the frequency and severity of asthma exacerbations
- When used in combination with current treatment guidelines, adding FeNO measurement to standard asthma care has been shown to increase quality of life and provide cost savings related to asthma management, including lower costs for asthma medications

Studies questioning FeNO measurement
- A meta-analysis has shown conflicting evidence on the benefits of FeNO in asthma management
- More research is needed to establish the best way to use FeNO, particularly in primary care

Key point: Although the GINA strategy states that FeNO has not been fully established as a useful diagnostic tool for asthma, it may still have a role to play in disease management and remains a hot topic of debate among asthma experts.

ERS = European Respiratory Society; FeNO = fractional exhaled nitric oxide; GINA = Global Initiative for Asthma; ICS = inhaled corticosteroids; IgE = immunoglobulin E.
Looking to the future: new studies on biologics in asthma

- A one-size-fits-all approach to treating asthma can leave many with sub-optimal asthma control. This realisation has led to a growing appreciation of the heterogeneity that exists within the pathophysiology of asthma.

- Biologics are predominantly targeted for use in the difficult-to-treat population with severe, persistent eosinophilic asthma (GINA Step 5).

- Although patients with severe asthma are managed by hospital specialists, PCPs have an important role to play in their management, and should be aware of these new therapies.
  - In particular, they should look for patients with recurrent exacerbations and raised markers of eosinophilic airway inflammation (i.e. raised blood eosinophil count, high FeNO).

- Nucala® (mepolizumab) and Cinqaero® (reslizumab) are EU-approved biologics for the treatment of severe asthma. Both have a large positive impact on exacerbation risk.

The advancement of biologics in asthma was highlighted at ERS 2016, with the publication of two pivotal Phase III trials for the new IL-5 receptor inhibitor, benralizumab:

**SIROCCO trial**
- **Biologic:** Benralizumab
- **Patient population:** Severe, uncontrolled asthma with blood eosinophilia*, aged 12–75 years (N=1,204)
- **Endpoints:** Annual exacerbation rate, pre-bronchodilator FEV₁, and total asthma symptom score
- **Results:** At Week 48, the group receiving benralizumab achieved a significantly greater decrease in annual exacerbations, reduced asthma symptoms, and improved lung function compared with the placebo group.
- **Safety:** Adverse events were similar in both groups.
- **Conclusion:** In this Phase III study, benralizumab showed clinical benefit in all parameters measured in people with severe, uncontrolled eosinophilic asthma.

**CALIMA trial**
- **Biologic:** Benralizumab
- **Patient population:** Severe, uncontrolled eosinophilic asthma†, aged 12–75 years (N=1,306)
- **Endpoints:** Annual exacerbation rate, pre-bronchodilator FEV₁, and total asthma symptom score
- **Results:** At Week 56, the group receiving benralizumab achieved a significantly greater decrease in annual exacerbations, reduced asthma symptoms, and improved lung function compared with the placebo group.
- **Safety:** Adverse events were similar in both groups.
- **Conclusion:** In this Phase III study, benralizumab showed clinical benefit in all parameters measured in people with severe, uncontrolled eosinophilic asthma.

Key point: With the increasing evidence for biologics in patients with severe persistent asthma, more patients will be seen in primary care who are being treated with these agents; therefore, PCPs need to know how to manage these patients.

ERS = European Respiratory Society; FeNO = fractional exhaled nitric oxide; FEV₁ = forced expiratory volume in 1 second; GINA = Global Initiative for Asthma; ICS = inhaled corticosteroids; IL = interleukin; LABA = long-acting β₂-agonists; PCPs = primary care physician.

Achieving a differential asthma diagnosis: practical guidance

- The recently published BTS/SIGN 2016 guidelines outline a practical approach for making a differential asthma diagnosis. However, there is no definitive evidence to inform the most appropriate approach for making an asthma diagnosis in the clinical setting. An asthma diagnosis can be difficult because:
  - the diagnosis of asthma is clinical; there is no single symptom, sign, or test that is diagnostic
  - asthma is, by definition, a variable condition and there will be times when the patient is asymptomatic and tests are negative. Results when patients are asymptomatic can be compared with those when they are symptomatic
- A new and potentially promising approach is to focus on traits that can be identified and treated. Airflow limitation and eosinophilic airway inflammation are thought to be the most important.

Key point: Asthma is a clinical diagnosis. Therefore, it is important to use a structured approach to clinical assessment, determining probabilities, and monitoring initial treatment. It is also vital to record the basis on which a diagnosis has been made.

### Decision support

1. Presentation with respiratory symptoms
   - Wheeze
   - Cough
   - Breathlessness
   - Chest tightness

2. In the initial structured clinical assessment, ask about and look for a record of the following:
   - Recurrent episodes of symptoms
   - Symptom variability
   - Recorded observation of wheeze assessed by a primary care physician
   - Family or personal history of other atopic conditions, such as allergic rhinitis
   - Absence of history to suggest an alternative diagnosis, such as smoking history or weight loss
   - Previous record of variable PEF or FEV1
   - Raised biomarkers of eosinophilic airway inflammation (i.e. blood eosinophil count)

3. Decide on an approach based on the probability of an asthma diagnosis

   **High probability**
   - Record the patient as likely to have asthma and start a monitored course of treatment (typically 6 weeks of ICS)
   - Assess the patient's status by providing a validated symptom questionnaire and/or a lung function test
   - Confirm and record the diagnosis of asthma (based on good symptoms and an objective response to treatment)
   - **If response to treatment is good:**
     - Confirm the asthma diagnosis
     - Adjust the maintenance dose, provide self-management support and a PAAP, and set up ongoing reviews
   - **If response to treatment is poor:**
     - Investigate other more likely diagnoses

   **Intermediate probability**
   - Test for variable airway obstruction using spirometry and a bronchodilator reversibility test or a challenge test
   - Check for eosinophilic inflammation (e.g. with FeNO) or evidence of atopy (e.g. skin prick testing)
   - If asthma is suspected, the options are:
     - Carry out watchful waiting if asymptomatic
     - Commence a monitored course of treatment, repeating lung function tests and objective measures of asthma control
   - **If response to treatment is good:**
     - Confirm the asthma diagnosis
   - **If response to treatment is poor:**
     - Investigate other more likely diagnoses

   **Low probability**
   - Investigate or treat for other more likely diagnoses

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1. BTS = British Thoracic Society; FeNO = fractional exhaled nitric oxide; FEV1 = forced expiratory volume in 1 second; ICS = inhaled corticosteroid; PAAP = personalised asthma action plan; PEF = peak expiratory flow; SIGN = Scottish Intercollegiate Guideline Network.