

## Editorial

## Tailoring asthma therapies using FeNO: can a new objective measure help more people to gain control and reduce over-treatment?

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Despite being one of the most common long-term diseases worldwide [1], asthma is notoriously difficult to get under control for many people with the condition. Changes to an individual's treatment regimen are usually made using a stepwise approach, guided by factors such as frequency of symptoms, rescue medication use, and asthma attacks [2,3]. Treatment is stepped up if control is deemed to be inadequate and stepped down if control is good. However, even in countries with high levels of access to health care that is free at the point of need, control remains poor. A recent survey of approximately 8000 people with asthma in 11 European countries found that nearly half of the respondents had uncontrolled asthma, and for a further third their asthma was only partially controlled. [4] Conversely, there is evidence that some people with asthma are being overtreated, or even misdiagnosed, and are therefore exposed unnecessarily to the side effects associated with therapy. [5,6]

As a result of this mismatch between the therapy people with asthma need and the therapy they receive, there is growing interest in objective measures to guide both diagnosis and management of asthma. One such strategy involves measuring the amount of a specific gas, nitric oxide (NO), when a person exhales. This is known as the fractional exhaled nitric oxide (FeNO). FeNO is a marker of airway inflammation caused by eosinophils and associated with allergy. [7] Eosinophilic airway inflammation accounts for over 50% of asthma cases (allergic asthma), and this type of asthma responds better to treatment with steroids. [7]

FeNO may offer a simple non-invasive method for diagnosing eosinophilic asthma and for guiding the stepping-up and -down of inhaled corticosteroids (ICS), the mainstay of asthma treatment. In 2011 the American Thoracic Society issued strong guidance to healthcare professionals in the United States advocating the clinical use of FeNO, at the time based on only low-to-moderate-quality evidence. [8]

In 2006, 2008, and 2009 Cochrane Reviews produced and updated a Cochrane Review examining the evidence from randomized controlled trials investigating whether using FeNO to guide asthma management is more effective than the established methods, such as clinical guidelines. More recently, this review has been split to look at adults and children separately. The review in adults has been published and includes seven trials, which compare the use of FeNO with clinical guidelines, the asthma Control Questionnaire score, or a combination of symptoms, lung function, and physical examination. [9] Despite five years passing since the American Thoracic Society recommendation, the evidence from trials remains somewhat inconclusive.

Pooled data from five studies involving over 1000 adults showed that the number of participants experiencing an asthma attack was lower in the FeNO group (odds ratio 0.60, 95% confidence interval 0.43 to 0.84). However, severe exacerbations requiring hospitalization occurred so rarely in the included trials that the authors could not be sure whether the use of FeNO to guide management had an impact on these most serious and costly exacerbations. In addition, no clear between-group difference was detected for asthma control, health-related quality of life, symptoms, or initial dose of ICS. Different FeNO thresholds and dose adjustment algorithms were used in the trials, hampering interpretation, and some trials implemented a ceiling dose of ICS to prevent relentless increases in response to persistently elevated FeNO, perhaps due to concomitant therapy. Importantly, the authors also noted that the included studies did not report any cost analysis of using FeNO.

So, what can we conclude? The crucial question is whether FeNO offers an advantage over using symptoms and measures such as peak flow to tailor asthma treatment. Can FeNO improve control for some, by triggering an appropriate ICS dose increase, while reducing over-treatment for others? Largely the case is not yet closed. Tailoring treatment on the basis of FeNO measurement is only going to have an impact if the myriad other obstacles to good control, including adherence to inhaled steroids, inhaler technique, and appropriate self-management, are tackled and improved simultaneously.

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## Declarations of interest

The authors have completed the [ICMJE form for disclosure of potential conflicts of interest](http://www.cochrane.org/ICMJE) (form available upon request). CC was an author on an earlier Cochrane Review on FeNO, and he checked the data entry for the version of the review mentioned in the editorial. The authors declare no other conflicts of interest.

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