

Fractional exhaled nitric oxide monitoring in paediatric asthma management

BACKGROUND AND ADVANTAGES OVER EXISTING TECHNOLOGY

An annual review is recommended for children with asthma but objective measures of control are lacking.¹ Monitoring exacerbations and a symptom score are both suggested, but the widely used Children's Asthma Control Test (C-ACT) has a positive predictive value of only 46.7% for asthma exacerbations at the recommended score of <24/27.² Additional tests such as peak expiratory flow or spirometry have not been shown to improve quality of life or symptom scores compared with symptom-based management.³ Fractional exhaled nitric oxide (FeNO) may provide additional information, such as quantifying eosinophilic airway inflammation to identify patients more likely to benefit from an adjustment in their inhaled corticosteroid (ICS) regimen over other treatment options.

DETAILS OF TECHNOLOGY

The National Institute for Health and Care Excellence (NICE) has evaluated three portable, hand-held devices that measure exhaled nitric oxide, produced in proportion to inflammation in the lungs: NObreath, NIOX VERO, and NIOX MINO.¹ The devices cost between £1794–£2540, plus £4.93–£9.35 per test for the sensor and filter. Each is accurate to +/-5 ppb (parts per billion) and tend to be precise to <10% of the measured value. Child-friendly versions are available and FeNO monitoring has been shown to be reproducible and feasible in children aged ≥4 years.

PATIENT GROUP AND USE

FeNO levels may help targeted optimisation of ICS dosing in children. In particular, FeNO could help decide whether children aged ≥5 years with suboptimal asthma control, despite treatment with very low-dose ICS, are more likely to benefit from increasing ICS dose versus the addition of a long-acting bronchodilator.

Impact of FeNO-guided asthma monitoring compared with conventional monitoring

The authors identified nine relevant randomised controlled trials, all conducted in secondary care with between 47 and 546 participants, and with a range of asthma severities.^{4–12}

Impact on number of exacerbations. Two studies found FeNO-guided management was associated with fewer participants requiring oral steroids for asthma exacerbation relief. In one, the proportion of children receiving ≥1 course was 6/31 with FeNO-guided management compared with 15/31 in the control ($P=0.017$)⁴ and, in the second, 32.1% (95% CI = 25.3 to 36.7) with FeNO-guided management compared with 42.0% (95% CI = 35.1 to 47.4) in the control ($P=0.014$).⁵ A third defined an exacerbation by deterioration in clinical symptoms and found there were 18/46 in children with FeNO-guided management and 35/46 in the control ($P=0.02$).⁶ In a fourth, no significant difference was found in oral steroid courses between groups ($P=0.60$).⁷ The remaining study that collected data on asthma exacerbations reported a longitudinal reduction in mean exacerbation frequency with FeNO-guided management, but did not perform any formal comparisons with guideline-based management.⁸

Impact on inhaled corticosteroid prescriptions. Four studies reported a significantly higher final ICS dose in the FeNO group of between 100 mcg to 200 mcg above that in the comparator.^{4–6,9} Three of these showed a reduction in exacerbations as described earlier, suggesting appropriately targeted ICS use has a therapeutic effect.^{4–6} Two studies saw a similar decrease in ICS dose in both arms^{10–11} and two showed no change in dose in either arm.^{7,12} In these four studies there was no significant change in exacerbation frequency or measures of asthma control. One study showed a reduction in exacerbations in the FeNO arm

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Submitted: 27 February 2017; **Editor's response:** 8 March 2017; **final acceptance:** 5 April 2017.

©British Journal of General Practice 2017; 67: 531–532.

DOI: <https://doi.org/10.3399/bjgp17X693449>

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without a change in ICS dose, but no change in exacerbation incidence in the comparator arm, despite an increase in ICS dose.⁸

The FeNO threshold to step up treatment varied widely from 10 ppb to 50 ppb and there was an association between this threshold value and the subsequent ICS dose. Four of the five studies using a threshold of ≤ 20 ppb saw an increase in ICS dose in the FeNO group.^{4–6,9} The four studies using a FeNO threshold of ≥ 25 ppb all saw either a reduction or no change in ICS dose and no change in outcomes between groups.^{7,10–12}

Impact on asthma-related quality of life. Four studies assessed this using either the Paediatric Asthma Quality of Life Questionnaire (PAQLQ), the Paediatric Asthma Caregiver Quality of Life Questionnaire (PACQLQ),^{4,10–12} or both.^{4,11} None showed a significant difference between the FeNO and comparator groups.

Cost-effectiveness. An economic evaluation based in the Netherlands comparing FeNO to web-based monitoring and standard care showed the FeNO-based strategy could potentially be a cost-effective way to monitor childhood asthma.¹³ From a healthcare perspective, the FeNO-based strategy was 20% likely to be the most cost-effective at a willingness-to-pay threshold of €40 000/QALY. From a societal perspective, the FeNO-based strategy was favoured over a wide range of values and had the highest chance (83%) of being most cost-effective at a willingness-to-pay threshold near €40 000/QALY.¹³

GUIDELINES AND RECOMMENDATIONS

NICE and the Scottish Intercollegiate Guidelines Network (SIGN) recommend FeNO alongside other investigations to help correctly identify asthma when there is diagnostic uncertainty or to guide treatment where patients remain symptomatic despite ICS.¹ They suggest there is currently insufficient evidence to support FeNO for routine childhood asthma monitoring and recommend further research.¹ The American Thoracic Society reports that FeNO may have benefits over more established tests such as FEV1 reversibility in identifying eosinophilic airway inflammation and patients likely to benefit from ICS. Benefits could include monitoring therapeutic response to ICS and helping identify non-adherence to treatment to improve asthma control.¹⁴

WHAT THIS TECHNOLOGY ADDS

There remains a lack of adequately powered,

well-designed studies demonstrating a benefit from FeNO measurement to support its routine use for childhood asthma monitoring. Further evidence is required to standardise a protocol for FeNO use and help researchers reach consensus on its role. However, if the optimal decision thresholds and role of FeNO could be established, its ease of use, portability and reproducibility would make it a potentially important tool in primary care. The RCTs here suggest it has the potential to reduce asthma exacerbations by appropriate targeting of increased ICS dose. Long term, a targeted strategy for asthma treatment with adequate doses of ICS and a subsequent reduction in exacerbations may be cost-effective due to reduced costs of hospitalisation and serious complications.

METHODOLOGY

Standardised methodology was applied in writing this report, using prioritisation criteria and a comprehensive, standardised search strategy, and critical appraisal. The search aimed to identify randomised controlled trials comparing FeNO-guided management to alternative models of care in children with asthma in a primary care or hospital outpatient setting. Details of the methods and search strategy can be found at <https://www.oxford.dec.nihr.ac.uk/reports-and-resources/horizon-scanning-reports/>.

Funding

This article presents independent research funded by the National Institute for Health Research (NIHR) Diagnostic Evidence Co-operative Oxford. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, or the Department of Health. The study sponsors had no role in the design, analyses or reporting of the study. The researchers retained complete independence in the conduct of this study.

Provenance

Freely submitted; externally peer reviewed.

Competing interests

The authors have declared no competing interests.

Acknowledgements

The authors would like to thank Nia Roberts for helpful discussions.

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