

THE ECONOMIC CASE FOR FRACTIONAL EXHALED NITRIC OXIDE (FENO) IN THE MANAGEMENT OF ASTHMA

Summary of the recent evidence

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1.0 BACKGROUND

1.1 This report summarises the recent evidence on the health economic impact on the use of Fractional Exhaled Nitric Oxide (FeNO) in the management of asthma.

2.0 METHODOLOGY

2.1 A search was undertaken of the literature for papers, reviews etc, written in English dating up to 2021. Papers from other countries have been quoted where there was no UK literature available. A total of 36 papers and NICE (National Institute for Health and Care Excellence) guidance/Technology Assessment were reviewed.

2.2 The search focused on the health economic impact on the use of Fractional Exhaled Nitric Oxide (FeNO) in the management of asthma

2.3 Databases searched included: Medline, PubMed, Embase and the NICE website

3.0 FRACTIONAL EXHALED NITRIC OXIDE (FeNO)

3.1 Fractional Exhaled Nitric Oxide (FeNO) is a specific biomarker in the type 2 immune inflammatory response in asthma.

3.2 The type 2 inflammatory response results in the production of nitric oxide from the epithelial cells in the airways which is then released in the expired breath.

3.3 FeNO is recommended by NICE as an option to help diagnose asthma in adults and children by identifying people who are likely to respond to treatment with inhaled corticosteroids (ICS). It is not recommended for routine monitoring of asthma although it can be used to monitor people who are symptomatic despite using inhaled corticosteroids¹

3.4 NICE has approved three devices for the measurement of FeNO concentration in breath samples for the diagnosis and monitoring of asthma (NIOX MINO, NIOX VERO and NObreath)²

3.5 NIOX VERO – can be used by both adults and children and needs a 10 second exhalation of breath to measure FeNO concentration. The device is battery powered and is designed to be a service and calibration free system.²

3.6 NObreath – this device measures exhaled nitric oxide and requires 12 seconds of exhalation of breath in adults and in seconds in children.²

3.7 NIOX MINO – this device is now not available having been replaced by NIOX VERO³

3.8 There is another device the Bosch Healthcare Solutions Vivatmo pro available which is used as a point of care intervention for professional use.²

4.0 COST EFFECTIVENESS OF FeNO MEASUREMENT IN THE MANAGEMENT OF ASTHMA

4.1 This report summarises the evidence from papers, conference abstracts etc that have been published from 2018 onwards when the NICE review of Diagnostics Guidance (DG) 12: ‘Measuring fractional exhaled nitric oxide concentration in asthma: NIOX MINO, NIOX VERO and NObreath’ was published³. Earlier papers are noted if they are relevant

4.2 Evidence assessed in the review of DG12: ‘Measuring fractional exhaled nitric oxide concentration in asthma: NIOX MINO, NIOX VERO and NObreath, by NICE in 2019 concluded that *‘FeNO has only a small effect, or no effect, on clinical outcomes when compared with current practice or alternative strategies for monitoring asthma’*³.

4.3 A systematic review on the economic evaluation of NIOX MINO, NIOX VERO and NObreath concluded that using FeNO measurement could have value in diagnostic and management settings (the incremental cost-effectiveness ratio (ICER) of using FeNO in children being approximately £45,200 per QALY and in adults an ICER of £2100 per QALY). However there were assumptions about changes in use of inhaled corticosteroids over time, the number of nurse visits for FeNO monitoring and duration of effect plus limitations in the evidence base⁴

Diagnosis and management

4.4 A German evaluation of the use of FeNO in the diagnosis and management of asthma showed that using FeNO measurement for diagnosis alone cost €38 compared to standard diagnostics (€26). However, in patients with mild to severe asthma FeNO measurement resulted in cost savings of €30 per patient per year whilst in the more severe population this saved €160 per patient⁵.

4.5 An American study examining the impact of FeNO monitoring on the cost effectiveness of asthma management compared with management without the use of FeNO found that FeNO measurement in conjunction with standard care decreased the annual expenditure per patient (\$2228) and increased the QALY per patient per year (0.844) compared with standard care alone (\$2,637 and 0.767). The authors concluded that FeNO monitoring to guide the management of asthma was cost effective, resulted in increased QALYs and reduced healthcare costs⁶.

4.6 A Dutch study compared the effects of managing adults with partly controlled asthma, controlled asthma and FeNO-driven controlled asthma on medication use in the primary care setting. Asthma medication use was significantly lower in the partly controlled and FeNO-driven controlled asthma strategies compared to the controlled asthma strategy (medication costs for partially controlled asthma \$452, controlled asthma \$551 and FeNO-driven controlled asthma \$456). The FeNO-driven controlled asthma strategy had the highest probability (86%) of cost-effectiveness at \$50,000/QALY (partially controlled asthma (2%) and controlled asthma (12%)). There was no difference in the severe exacerbation rate.

The authors conclude that managing controlled asthma using FeNO measurement is the preferred strategy as it reduced medication use and associated costs while maintaining symptom control and quality of life in primary care⁷.

4.7 The cost-effectiveness of using FeNO as a biomarker to identify patients with moderate to severe asthma who were likely to respond to omalizumab was examined in an American study. The results showed that the per patient costs for FeNO plus omalizumab was \$10,943 and for omalizumab only was \$13,703 for the trial period of one year. The expected cost per responder to omalizumab as identified by FeNO monitoring was \$4,326 compared to \$7,786 for omalizumab only. The authors conclude that using FeNO measurement to identify people with asthma who would respond to omalizumab decreased the patient cost by nearly 50%^{8,9}.

4.8 A Dutch Randomised Controlled Trial compared the cost-effectiveness of web-based monthly monitoring, 4 monthly monitoring of FeNO and standard care of children with asthma. Whilst there were no statistically significant differences between the three management strategies in terms of quality-adjusted life years (QALY) and costs, the web-based strategy had a 77% chance of being most cost effective at € 40,000/QALY from a healthcare (healthcare costs and travel) perspective and the FeNO -based strategy had an 83% chance of being most cost-effective at € 40,000/QALY from a societal (healthcare costs, travel plus loss of productivity) perspective compared to standard care. The authors conclude that as clinical outcomes also favoured the web-based and FeNO management strategies, these would be useful additions to standard care^{10,11}.

Devices and healthcare resources costs in the UK

4.9 A review of the Diagnostics Guidance (DG) 12: 'Measuring fractional exhaled nitric oxide concentration in asthma: NIOX MINO, NIOX VERO and NObreath' by NICE in 2019³ reported that the healthcare resources costs had decreased since the publication of DG 12 in 2014. However, these costs were based on the treatment of asthma that has changed since the publication of the guidance and therefore was uncertainty about the medical management of the average patient.

Resource cost parameter	Sources	Cost in DG12	Current cost
Primary care GP visit	PSSRU (2012 and 2017)	£43.00	£37.00
Primary care practice nurse visit	PSSRU (2012)	£13.69	Unknown
Secondary care respiratory medicine outpatient visit	NHS reference cost (2011-2012 and 2015-2016)	£204.29	£154.77
Secondary care laboratory visit	NHS reference cost (2011-2012 and 2015-2016)	£203.29	£133.56

From NICE: Review of DG12 (2019)³

4.10 The same review reported that the costs of the devices had changed; the NIOX VERO instrument having increased marginally above inflation although consumable costs were below inflation; and the NObreath monitor and consumables having reduced in value in real terms (with the exception of the costs for the device replacement being unknown)

Item	Cost in DG12	Current cost	Difference (% change)
Costs associated with NIOX VERO			
NIOX VERO Instrument ^a	£2,100.00	£2,640.00	£540 (+26%)
Test kit ^b (1000 tests)	£4,200.00 (£4.20 per test)	£4,580.00 (£4.58 per test)	£380 (+9%)
Test kit ^b (500 tests)	£2,200.00 (£4.40 per test)	£2,290.00 (£4.58 per test)	£90 (+4%)
Test kit ^b (300 tests)	£1,500.00 (£5 per test)	£1,510.00 (£5.03 per test)	£10 (<1%)

Item	Cost in DG12	Current cost	Difference (% change)
Costs associated with NObreath			
NObreath FeNO nitric oxide monitor ^c	£1,995.00	£1,795.00	-£200 (-10%)
NObreath mouthpieces ^d (box of 50)	£195.00 (£3.90 per mouthpiece)	£150.00 (£3 per mouthpiece)	-£45 (-23%)
^a The instrument is also available in various combination with the test kit consumables ^b Contains a sensor for the required number of tests and 1 consumable filter for each test ^c Package comes complete with Bedfont NObreath FeNO Monitor, NObreathFLO mouthpiece attachment, an interpretation chart and 3 x AA batteries. ^d Mouthpieces are required to be purchased separately. The only pack size available on the Intermedical website is 50.			

From NICE: Review of DG12 (2019)³

Healthcare Setting

Primary care

4.11 A Spanish study evaluating the cost-effectiveness of FeNO monitoring of adults with asthma in primary care showed that adding this measurement to standard asthma care resulted in saving €62.53 per patient per year and improved the QALY by over 0.026 per patient per year¹². The main drivers to cost reduction was due to reduction in hospitalisations of people with severe asthma and reduction in consumption of inhaled corticosteroids¹³

4.12 Two German studies compared the costs of FeNO-assisted therapy with standard asthma care in the primary care setting. It was assumed for the calculation of the costs that

90% of patients are seen by a general practitioner and 10% by a specialist as well as the cost of the FeNO test (€21.17 - in one study¹⁴ and €25 - in the other¹⁵ . The direct care costs for standard care were €571.56 and for the FeNO based therapy ranged from €522.93¹⁴ - €538.25¹⁵ per patient per year

Secondary care

4.13 A German study evaluating the impact of using FeNO to monitor asthma showed that compared to standard testing, although FeNO measurement placed an additional cost, the routine use of the test resulted in cost savings of €2 (year 1) to € 25 (year 5) per asthma patient through the optimizing of asthma medication. If hospitalisation, physician visits and standard tests are taken into account the savings increased to €4 (year 1) to €31 (year 5). The authors conclude that the use of FeNO measurement has an impact on medication optimisation as well as hospitalisations due to severe exacerbations¹⁶

4.14 An American study which analysed the Medicare database relating to people who had been hospitalised or attended the Emergency Department (ED) for their asthma found that 97% needed these services for an asthma-related event did not have FeNO monitoring. For those who did receive FeNO monitoring only 46% required in-patient or ED care for their asthma. Asthma-related charges for people who did not have FeNO were \$16.21 per patient compared to those who did, \$6.46 per patient¹⁷.

4.15 An observational study examining the cost-effectiveness of the use of FeNo in the management of asthma in the outpatient setting found that treatment was altered in more than one third of patients, specifically augmentation of medication in 20% and medication decreases in 16% of patients. The use of FeNO in addition to standard care was estimated to save \$629 per patient per annum^{18,19}.

CONCLUSIONS:

In the papers that have been summarised above the following conclusions can be made:

- The health economic data arise from European and American studies
- FeNO monitoring has an impact on increasing the Quality Adjusted Life Years and decreasing healthcare costs through the management of symptoms leading to fewer exacerbations, reduced hospitalisations and reduced used of inhaled corticosteroids. FeNO monitoring has been shown to identify patients with moderate to severe asthma who are likely to respond to biologic therapy (omalizumab)
- There need to be more studies conducted in the UK context to obtain a better picture of the health economic impact of FENO monitoring

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