

Original article

An economic evaluation of NIOX MINO airway inflammation monitor in the United Kingdom

Background: Fractional exhaled nitric oxide (FE_{NO}), a marker of eosinophilic airway inflammation, is easily measured by noninvasive means. The objective of this study was to determine the cost-effectiveness of FE_{NO} measurement using a hand-held monitor (NIOX MINO), at a reimbursement price of £23, for asthma diagnosis and management in the UK.

Methods: We constructed two decision trees to compare FE_{NO} measurement with standard diagnostic testing and guideline recommendations for management. For asthma diagnosis, we compared FE_{NO} measurement with lung function and reversibility testing, bronchial provocation and sputum eosinophil count. For asthma management, we evaluated the impact on asthma control, including inhaled corticosteroid use, exacerbations and hospitalizations, of monitoring with FE_{NO} measurement *vs* symptoms and lung function as in standard care. Resource use and health outcomes were evaluated over a 1-year time frame. Direct costs were calculated from a UK health-care payer perspective (2005 £).

Results: An asthma diagnosis using FE_{NO} measurement cost £43 less per patient as compared with standard diagnostic tests. Asthma management using FE_{NO} measurement instead of lung function testing resulted in annual cost-savings of £341 and 0.06 quality-adjusted life-years gained for patients with mild to severe asthma and cost-savings of £554 and 0.004 quality-adjusted life-years gained for those with moderate to severe asthma.

Conclusions: Asthma diagnosis based on FE_{NO} measurement with NIOX MINO alone is less costly and more accurate than standard diagnostic methods. Asthma management based on FE_{NO} measurement is less costly than asthma management based on standard guidelines and provides similar health benefits.

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The costs of asthma to the United Kingdom National Health Service (UK NHS) were estimated at £750 million per year in 2000 (1) and to the UK overall, at over £2.3 billion per year in 2004 (2). Economic evaluations of asthma therapies and management strategies are thus an important component of decisions regarding best approaches to asthma care. Because a disproportionate share of asthma costs is attributable to patients with poorly controlled asthma (3–5), strategies aimed at improving asthma control could reduce costs as well as improve quality of life (QoL) of patients with asthma.

Asthma is characterized pathophysiologically by variable airway obstruction, airway inflammation and airway hyperresponsiveness. Assessments of airway inflammation can complement lung function testing for diagnosing and monitoring asthma; these include bronchial biopsy, bronchoalveolar lavage, induced sputum analysis and measurement of fractional exhaled nitric oxide (FE_{NO}). FE_{NO} is a marker of eosinophilic airway inflammation

that correlates well with other measures of airway eosinophilia, such as sputum eosinophilia (6, 7), and can aid in asthma diagnosis as well as management (8–11).

The measurement of FE_{NO} differs from other means of assessing airway inflammation as it is noninvasive and easily performed and gives immediate and reproducible results (6, 12). Once primarily a research tool, measuring FE_{NO} is now more accessible to clinicians because of the development of an inexpensive hand-held FE_{NO} monitor (NIOX MINO®; Aerocrine AB, Solna, Sweden) (13, 14).

In the present day health economic environment, clinical tests must prove not only to be reliable and reproducible but also cost-effective. Our prior cost-effectiveness analysis of NIOX MINO in Germany found that, as compared with standard diagnostic and management procedures in that country, FE_{NO} measurement alone offered improved accuracy at slightly increased cost

(€12 more per patient) for asthma diagnosis and similar health benefits at lower cost for asthma management (15). The objective of this study was to determine the cost-effectiveness of FE_{NO} measurement, using NIOX MINO, as compared with common clinical practice, for diagnosis and management of asthma in the UK.

Methods

Economic models

We constructed two decision-tree models, one for asthma diagnosis and one for asthma management, using decision analysis software (TreeAge Pro 2006; TreeAge Software, Inc., Williamstown, MA, USA). A decision tree is a structured representation of alternative strategies, probabilities of subsequent events and ultimate outcomes (16). The use and cost of each strategy, as well as associated outcomes, such as diagnostic accuracy, are derived from the medical literature appropriate for the country under

study, for incorporation into the model and subsequent calculation of cost-effectiveness.

For asthma diagnosis, we compared FE_{NO} measurement with standard diagnostic tests used in UK clinical practice, including lung function and reversibility testing, bronchial provocation and sputum eosinophil count (Fig. 1). In the base-case analysis, we compared FE_{NO} measurement individually with each test. In addition, we ran separate analyses comparing (1) FE_{NO} measurement against reversibility plus peak expiratory flow (PEF) charting and (2) FE_{NO} measurement combined with lung function testing against standard care. For each diagnostic test, our model incorporated the assumption that a patient could receive a positive or negative diagnosis of asthma and, subsequently, that this was a true or false diagnostic determination, as based on the sensitivity and specificity of each test (Fig. 1A).

For asthma management, we constructed a decision tree to capture the impact on asthma outcomes of monitoring with FE_{NO} measurement vs lung function testing as recommended by asthma management guidelines (17, 18). We analysed the impact of the two strategies on the following outcomes, as depicted in Fig. 1B, using a 1-year time frame, for the two management strategies:

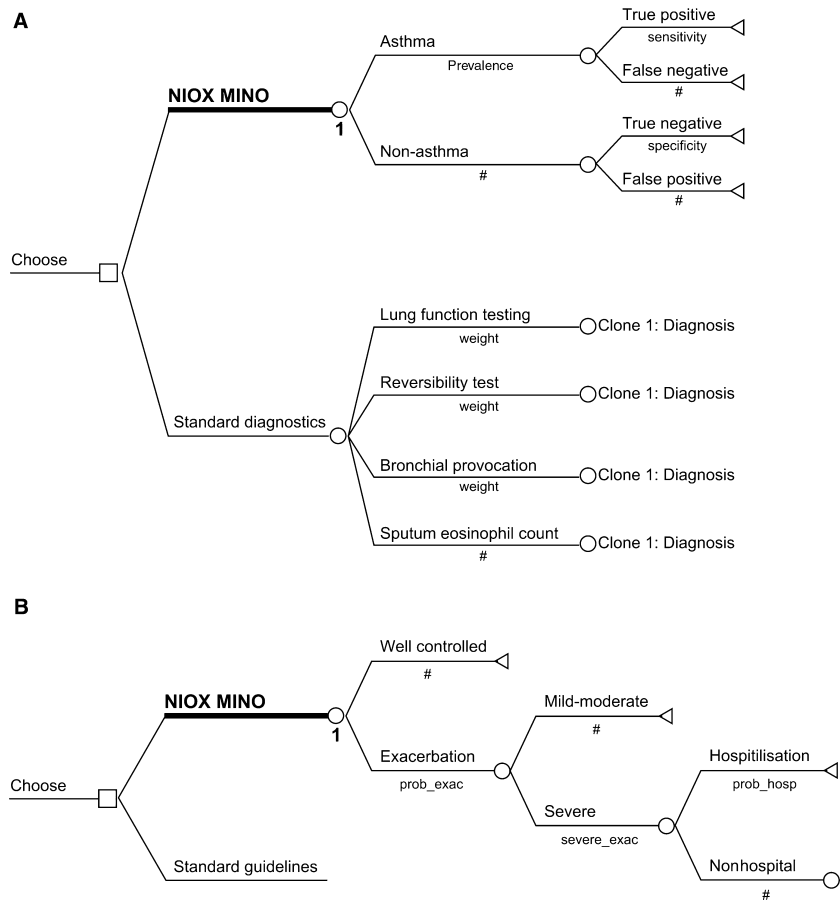


Figure 1. (A, B) Structure of economic model for evaluation of FE_{NO} measurement (NIOX MINO) in asthma diagnosis (A) and management (B). The decision trees represent the different results after asthma diagnosis or management with FE_{NO} measurement using NIOX MINO compared with standard methods. For each of the standards, a dynamic copy (clone) of the possible events is linked to the branches after NIOX MINO. For asthma diagnosis, results are influenced by underlying disease prevalence, test accuracy and relative frequency of test use. The key outcomes in asthma management are successful control and exacerbations; these are related to different levels of medical resource use and quality of life.

1. Successful control of asthma
 - a. With standard inhaled corticosteroid (ICS) dose or
 - b. With reduced ICS dose
2. Asthma exacerbation, categorized as
 - a. Mild to moderate, which was defined as requiring short-acting β_2 -agonist, or
 - b. Severe, which was defined as requiring oral corticosteroids, and
 - i. Requiring hospitalization or
 - ii. Possible to manage on an outpatient basis.

Data sources

Most published studies to date used a stationary chemiluminescence analyser for measuring FE_{NO} . More recently, comparisons of the stationary device and the portable electrochemical NIOX MINO analyser have shown good correlation and clinically acceptable agreement between measurements made using these two devices, for both adults and children, with asthma and without (13, 14, 19). Thus, we have applied data from chemiluminescence analyser studies in the economic analyses for NIOX MINO. Our main analysis (base case), as per the data sources, included nonsmoking adult patients with mild to severe asthma as seen in both primary and secondary care.

Data sources for asthma diagnosis. The selection of diagnostic tests for comparison with FE_{NO} measurement was based on information in the UK asthma guidelines (20). To avoid making assumptions about the sensitivity and specificity of likely combinations of diagnostic tests, as these data are not available, partly due to lack of a definite gold standard, we estimated frequency weights for each test, according to the relative use of each test in the UK, as per UK guidelines (20). The commonly used diagnostic methods were weighted as follows:

1. Lung function testing using PEF charting (PEF measurements taken at two visits 2 weeks apart): relative frequency weight, 48.5%.
2. Reversibility testing (percentage change in forced expiratory volume in 1 s [FEV_1] 10 min after administration of 200 μ g inhaled salbutamol): relative frequency weight, 48.5%.
3. Bronchial provocation using methacholine airway responsiveness (provocative concentration of methacholine causing > 20% fall in FEV_1 [PC_{20}]): relative frequency weight, 2.5%.
4. Sputum eosinophil count: relative frequency weight, 0.5%.

The sensitivity and specificity of each diagnostic test were derived from three published papers (Table 1), identified by a systematic review of the literature and selected to develop the most conservative model (6, 11, 21). Smith et al. (6) assessed the diagnostic utility of FE_{NO} measurement for 47 patients referred to a pulmonary function laboratory for possible asthma. The sensitivity and specificity of the standard diagnostic tests listed above were taken from an observational study by Hunter et al. (21), who compared their accuracy in 69 patients with asthma, 21 controls, and 20 patients with an asthma diagnosis who were found to have an alternative explanation for their symptoms. For the analysis comparing FE_{NO} measurement with reversibility plus PEF charting, we used the highest sensitivity and specificity of the two tests and the sum of their costs. Finally, data for the use of FE_{NO} measurement in conjunction with FEV_1 – a proxy for FE_{NO} measurement plus PEF charting, as these data were not available – was derived from a review of recent studies evaluating the diagnostic accuracy of FE_{NO} measurement (11).

Table 1. Sensitivity and specificity of diagnostic tests for asthma as incorporated in the decision-making model

Test	Sensitivity (%)	Specificity (%)	Source
FE_{NO} (flow rate 50 ml/s; > 20 ppb)	88	79	Smith et al. (6)
FE_{NO} (flow rate 50 ml/s; > 33 ppb) + FEV_1 < 80% predicted	94	93	Smith and Taylor (11)
PEF A%M > 21.6%	43	75	Hunter et al. (21)
Reversibility test: FEV_1 > 2.9% improvement after salbutamol	49	70	Hunter et al. (21)
Bronchial provocation: methacholine PC_{20} < 8 mg/ml	91	90	Hunter et al. (21)
Sputum eosinophil count > 1%	72	80	Hunter et al. (21)

FE_{NO} , exhaled nitric oxide; FEV_1 , forced expiratory volume in 1 s; PEF A%M, maximum within-day peak expiratory flow amplitude mean percentage (calculated from PEF measured twice daily over 14 days as the best of three blows); PC_{20} , provocative concentration of methacholine causing > 20% fall in FEV_1 .

We made the assumption that the proportion of symptomatic patients with a positive diagnosis of asthma would be 36%, as in the study of Smith et al. (6), in which asthma was diagnosed for 17 of the 47 patients. In addition, we made the assumption that patients who received a false diagnosis would require at least one additional outpatient visit to receive a correct diagnosis.

Data sources for asthma management. The data for cost analyses of FE_{NO} measurements in asthma management were drawn from three prospective randomized controlled trials that used levels of inflammatory markers, either induced sputum eosinophil counts (22, 23) or FE_{NO} (10), to guide management decisions for asthma (Table 2). We were able to include the two studies using induced sputum as a management measure because sputum eosinophil counts and FE_{NO} are significantly correlated across a wide range of patients with asthma, provided they are nonsmokers (7). We assumed the proportion of severe exacerbations requiring an outpatient visit and number of severe exacerbations per year to be as in the Formoterol and Corticosteroids Establishing Therapy (FACET) study (24, 25). The FACET study defined mild and severe

Table 2. Parameters from published studies as incorporated in the asthma management model

Parameters	Value	Source
<i>Baseline event probabilities</i>		
Exacerbation risk during 1 year	71%	Jayaram et al. (23)
Proportion of exacerbations that are severe	23%	Jayaram et al. (23)
Hospitalization for severe exacerbation	23%	Green et al. (22)
Proportion of severe exacerbations requiring outpatient visit	75%	Andersson et al. (24)
Mean no. severe exacerbations/year (overall population)	2	Jayaram et al. (23) and Tattersfield et al. (25)
Mean no. severe exacerbations/year (moderate-severe asthma)	4	Green et al. (22)
<i>Impact of FE_{NO} management</i>		
Reduction in ICS dose	42%	Smith et al. (10)
Relative risk reduction of exacerbation	29%	Jayaram et al. (23)
Relative risk reduction of hospitalization for severe exacerbation	83%	Green et al. (22)

FE_{NO} , exhaled nitric oxide; ICS, inhaled corticosteroid.

exacerbations, the primary study endpoints, similarly to the other studies included in our model (10, 22, 23).

Table 2 summarizes the parameters used in our asthma management model. Other assumptions used in the base case were as follows:

1. The average patient was at step 3 and above (i.e. received an inhaled corticosteroid and long-acting β_2 -agonist for maintenance asthma therapy), as per Global Initiative for Asthma (GINA) and British asthma guidelines (17, 18).
2. Our results apply only to nonsmoking patients.
3. Visits to monitor asthma control, using FE_{NO} measurement and asthma management guidelines, were scheduled four times per year.
4. The population included patients with mild to severe asthma, as in the study by Jayaram et al. (23) and only the risk reduction for any exacerbation was applied.

Costs and utilities

Our economic evaluations were conducted from a UK health-care payer perspective (pounds sterling [£] 2005) and included changes in resource use, namely, the direct medical costs, including costs of diagnostic tests, outpatient visits, hospitalizations and treatment, as available from published data (Table 3) (26–28). Drug costs were calculated, using public prices and generic products, from average dosages across recommended dose ranges for usual maintenance and rescue therapies for asthma.

We derived utilities for asthma control level from the study by Szende et al. (29), who investigated the relationship between level of asthma control and health-related QoL using the Euro-QoL EQ-5D, a generic QoL instrument (30, 31). Utilities serve as the preference weights within the model to calculate quality-adjusted life-years (QALYs). EQ-5D values were converted to utilities using standard

conversion algorithms relevant to the UK population (32). Of 228 adult patients with asthma, those with good asthma control had a utility value of 0.93 (anchored at 0 [death] to 1 [full health]); values for mildly reduced control, moderately reduced control, and poor control, were 0.76, 0.65 and 0.52, respectively. For our model, we defined successfully controlled patients as having good control, those with an exacerbation not requiring hospitalization as having moderately reduced control, and those requiring hospitalization as having poor control.

Sensitivity analyses

We performed numerous one-way sensitivity analyses to examine the robustness of both diagnostic and management models. In addition, we examined a second scenario, including patients with moderate to severe asthma, as in the study by Green et al. (22) and applied the risk reduction for hospitalizations instead of asthma exacerbations. Finally, we examined the use of NIOX MINO in conjunction with lung function testing, as compared with standard testing, for both asthma diagnosis and management.

Results

Cost-effectiveness results for the base case

The cost of an asthma diagnosis made using NIOX MINO was £29 per patient, or £43 less than when using standard diagnostic tests (£72 per patient).

For patients with mild to severe asthma, the cost of management with NIOX MINO was £341 less per patient per year, as compared with lung function testing (£666 vs £1007), when used as per asthma management guidelines (17, 18). Use of NIOX MINO provided a small incremental improvement of 0.059 QALYs, namely, 0.785 vs 0.726.

Sensitivity analyses

Asthma diagnosis. The cost of using NIOX MINO in combination with FEV₁ was £42 more per patient than using standard diagnostic tests (Table 4). In the other sensitivity analyses, NIOX MINO remained cost-saving compared with standard diagnostics when different parameters in the model were varied, with one exception, namely, if the reimbursement price for NIOX MINO were increased by 200%, it would cost £3 per patient more than standard diagnostics alone (Table 4).

Asthma management. For managing patients with moderate to severe asthma, the cost savings seen with NIOX MINO over lung function testing increased to £554 per patient per year, and NIOX MINO remained the dominant strategy with a small incremental improvement in QALYs (Table 5). These results were consistent in all sensitivity analyses except when adding NIOX MINO to lung function testing, which accrued an additional cost of £17 per patient per year at an incremental cost-effectiveness ratio (ICER) of £279 per QALY (Table 5 and online table).

Table 3. Unit costs used in the decision-making models for asthma diagnosis and management in the UK (2005 prices)

Cost item	Cost (£)	Source
<i>Tests</i>		
NIOX MINO	22.90	Aerocrine, AB
Peak flow charting for 2 weeks (two visits)	89.27	NHS reference costs, 2005 (28)
Reversibility test	29.27	NHS reference costs, 2005 (28)
Bronchial provocation	48.50	NHS reference costs, 2005 (28)
Sputum eosinophil induction	48.50	NHS reference costs, 2005 (28)
<i>Visits</i>		
Outpatient visit to general practitioner	30.00	Unit costs of health and social care 2005 (26)
Outpatient visit to lung specialist	44.00	Unit costs of health and social care 2005 (26)
Hospitalization for asthma	2231.45	NHS reference costs, 2005 (28)
<i>Treatment</i>		
Maintenance therapy (1 year) with long-acting β_2 -agonist	359.84	British national formulary 51 (27)
Maintenance therapy (1 year) with inhaled corticosteroid	109.00	British national formulary 51 (27)
Rescue therapy (1 week) with short-acting β_2 -agonist	7.38	British national formulary 51 (27)
Rescue therapy (1 week) with oral prednisone	5.13	British national formulary 51 (27)

NIOX MINO, exhaled nitric oxide measurement.

Table 4. Sensitivity analyses for selected parameters in the asthma diagnosis model

Variation in model parameters	Cost (£)		
	NIOX MINO	Standard diagnostics	Cost saving with NIOX MINO
<i>Variation in test sensitivity (all tests)</i>			
–50%	35	76	40
+10%	29	72	43
<i>Variation in test specificity (bronchoprovocation and sputum only)</i>			
–50%	39	81	42
+10%	28	71	43
<i>Asthma prevalence in tested population (base case, 36%)</i>			
10%	30	70	40
50%	29	74	45
90%	28	78	50
<i>NIOX MINO cost (base case, £23)</i>			
–50%	18	72	54
+200%	75	72	–3
<i>Cost of standard tests</i>			
+50%	29	72	43
+100%	29	102	72
+150%	29	131	102
+200%	29	161	131
<i>Number of added visits for false diagnosis (base case, one visit)</i>			
Two visits	36	86	50
Four visits	49	113	63
<i>Scenario</i>			
NIOX MINO vs reversibility + PEF charting	29	131	102
NIOX MINO + FEV ₁ vs standard tests	115	72	–42

FEV₁, forced expiratory volume in 1 s.

Discussion

Results of our economic analysis indicate that measurement of FE_{NO} using NIOX MINO is a cost-effective alternative to standard testing for both asthma diagnosis and management in the UK. The cost of an asthma diagnosis made using FE_{NO} measurement was £43 less per patient, including the cost of false diagnoses, as compared with standard diagnostic tests. Asthma management using FE_{NO} measurement instead of lung function testing was a dominant strategy, resulting in annual cost-savings of £341 and 0.06 QALYs gained for patients with mild to severe asthma and cost-savings of £554 and 0.004 QALYs gained for those with moderate to severe asthma.

Varying our assumptions in the sensitivity analyses gave results consistent with the base-case analysis for both asthma diagnosis as well as management, indicating that the base-case models are robust. For asthma diagnosis, the cost of FE_{NO} measurement with NIOX MINO would have to triple to result in slightly greater costs (£3 more per patient) than with standard testing.

Otherwise, NIOX MINO remained less expensive than standard diagnostic tests when we varied multiple parameters, including test sensitivity, specificity and costs. In addition, the cost of NIOX MINO was £102 less than the commonly used combination of reversibility testing followed by PEF charting (the latter added when reversibility testing is equivocal). Similarly, for asthma management, in the sensitivity analyses FE_{NO} measurement with NIOX MINO remained the dominant strategy in most cases.

In clinical practice, a diagnosis of asthma is typically made on the basis of history and physical findings, ideally supported by lung function and airway hyperresponsiveness testing (20). Thus, it is likely that, in practice, FE_{NO} measurement will be used in conjunction with other tests rather than as their replacement. We examined this scenario and found that the combination of FE_{NO} measurement plus lung function testing increased costs for diagnosing asthma by £42. The usefulness of this combination is supported by results of a recent study in which measurement of FE_{NO}, used in conjunction with spirometry, improved diagnostic confidence and therapeutic decision-making with regard to 94% of patients with nonspecific respiratory symptoms presenting in primary care (33).

The combination of FE_{NO} plus lung function testing for managing asthma was a hypothetical scenario, as there are no clinical studies from which to obtain precise data for the model. Use of this combination for managing asthma resulted in an incremental cost of £17 per patient per year and 0.059 QALYs gained, amounting to an incremental cost-effectiveness ratio of £279/QALY.

The findings of economic modelling are dependent on the assumptions contained in the model. Our goals in constructing our models were to compare FE_{NO} measurement with strategies recommended by BTS guidelines and used in clinical practice in the UK today (rather than with ideal practice without FE_{NO} measurement), as we believe these are the most relevant economic comparisons. We aimed to reflect the situation in a primary care setting, where most asthma is managed in the UK, as well as to use conservative assumptions to reach a conservative estimate of the cost-effectiveness of NIOX MINO in the UK. Our findings are thus specific to the UK.

Factors that are likely to be different between countries that could affect costs include the pattern of diagnostic tests as well as asthma treatments. In Germany, confirmation of an asthma diagnosis is often performed by office-based pulmonary specialists who use a battery of tests, including spirometry. In our analyses for Germany, to be conservative, we chose to use the cost of only spirometry (reimbursed at €8), and we found that asthma diagnosis based on FE_{NO} measurement alone (using NIOX MINO) offered improved accuracy at a cost of €12 more per patient

Table 5. Sensitivity analyses for selected assumptions and parameters in the asthma management model

	QALY						
	Cost (£)		Incremental cost (£)	Effect (QALY)		Incremental effect	ICER (£/QALY)
	NIOX MINO	Standard		NIOX MINO	Standard		
Moderate–severe asthma	628	1181	–554	0.730	0.726	0.004	Dominant
1-year baseline risk of exacerbation of 0.35 (base case, 0.71)	589	915	–326	0.857	0.83	0.027	Dominant
Utility for moderate control of 0.76 (base case, 0.65)	666	1007	–341	0.835	0.8	0.035	Dominant
No. monitoring visits/year – mild–severe asthma (base case, four visits)							
Two visits/year	620	828	–208	0.785	0.726	0.059	Dominant
Six visits/year	712	1185	–473	0.785	0.726	0.059	Dominant
No. monitoring visits/year – moderate–severe asthma (base case, four visits)							
Two visits/year	582	1003	–421	0.73	0.726	0.004	Dominant
Six visits/year	673	1360	–687	0.73	0.726	0.004	Dominant
NIOX MINO cost – mild–severe asthma							
–50%	620	1007	–387	0.785	0.726	0.059	Dominant
+50%	712	1007	–295	0.785	0.726	0.059	Dominant
NIOX MINO cost – moderate–severe asthma							
–50%	582	1181	–599	0.73	0.726	0.004	Dominant
+50%	673	1181	–508	0.73	0.726	0.004	Dominant
ICS dose reduction – mild–severe asthma (base case, 42%)							
10%	683	1007	–324	0.785	0.726	0.059	Dominant
80%	645	1007	–362	0.785	0.726	0.059	Dominant
ICS dose reduction – moderate–severe asthma (base case, 42%)							
10%	638	1181	–543	0.73	0.726	0.004	Dominant
80%	616	1181	–565	0.730	0.726	0.004	Dominant
Relative risk reduction for exacerbation – mild–severe asthma (base case, 29%)							
10%	707	1007	–300	0.747	0.726	0.021	Dominant
50%	621	1007	–386	0.828	0.726	0.102	Dominant
Relative risk reduction for hospitalization – moderate–severe asthma (base case, 83%)							
10%	869	1181	–312	0.727	0.726	0.001	Dominant
100%	571	1181	–610	0.731	0.726	0.005	Dominant
Scenario: NIOX MINO + lung function vs. Lung function (added costs)*	1023	1007	17	0.785	0.726	0.059	279

ICER, incremental cost-effectiveness ratio; ICS, inhaled corticosteroid; QALY, quality-adjusted life-year.

*There are no data available on changes in resource use when NIOX MINO is added to lung function testing in asthma management; thus, this is purely a hypothetical scenario.

than spirometry alone, while treatment decisions based on FE_{NO} measurement were less costly than those based on asthma management guidelines and provided similar health benefits (15).

There is currently no gold standard for diagnosing or managing asthma (17); moreover, comparative data on clinical testing for asthma are few. For our analyses, we derived sensitivity and specificity data for FE_{NO} measurement from the study by Smith et al. (6) and for PEF charting and other diagnostic testing from the study by Hunter et al. (21). While this resulted in an indirect comparison, the higher sensitivity and specificity values for

PEF charting, and the low FEV_1 reversibility cut point (2.9%), as reported by Hunter et al. (21), relative to other studies (6, 34), represented a conservative approach to the analysis. The management model applied risk reductions with FE_{NO} management from a population including patients with mild asthma (23), while the reductions were greatest in moderate to severe asthma, thus underestimating the benefits and again representing a conservative approach.

We were unable to examine asthma diagnosis and management strategies in a single economic model because data linking an improved diagnosis to treatment

outcomes are not available. Moreover, the comparators and assumptions differed between the two models.

In the management model, the effect of FE_{NO} measurement on ICS dose was based on patients treated in primary care (10), while the impact on exacerbations was based on patients treated in secondary care (22, 23). We included both parameters in the model, thus assuming a mixed population utilizing both primary and secondary care resources. The follow-up periods in these studies were 1–1.5 years; a longer time frame might have allowed better stabilization of asthma control through seasonal fluctuations and thus better outcome assessments.

For the management model, we used the only data, to our knowledge, linking utilities to levels of asthma control (29). While this approach allowed us to calculate outcomes in terms of QALYs, a measure that can be compared across economic studies, it is associated with some uncertainty, both because of the difficulty in assessing the impact of exacerbations and hospitalizations on QoL and because of limited sensitivity of the EQ-5D for patients with mild asthma (29). Nonetheless, we believe that the slight gain in QALYs seen with FE_{NO} measurement for asthma management indicates at least a similar health effect to that of lung function testing.

Most economic analyses in asthma have examined alternatives for pharmacological therapy, while the cost-effectiveness of clinical tests for asthma has been little studied (35), and we found no other relevant comparators for the present study other than our German cost-effectiveness analysis (15). It would have been of interest to examine costs associated with the limited performance (sensitivity, specificity, reliability and validity) of existing measures; these data, however, are not available. We did

not include indirect costs of asthma in our analyses because there are no applicable data on the impact of FE_{NO} measurement on indirect costs. Moreover, this is not required by UK payers. It is possible, however, that inclusion of indirect costs would strengthen our findings because of the added cost of lost productivity associated with asthma exacerbations and hospitalizations.

The application of FE_{NO} measurement in clinical practice can play an important role in diagnosing and assessing airway disease (12). This role will become better characterized with further study, in particular to define threshold values and cut-off points, use of individualized FE_{NO} profiles and use of differential flow analysis for identifying sites of airway inflammation (12, 36). With regard to cost-effectiveness, the results of our model need to be verified in practice, ideally prospectively and for a real-life primary care population, as only a small proportion of outpatients with asthma are eligible for enrolment in the typical randomized clinical trial (37, 38).

Our findings support the cost-effectiveness of FE_{NO} measurement for diagnosing and monitoring asthma in UK clinical practice. With the availability of a hand-held monitor (NIOX MINO), FE_{NO} measurement is now a practical alternative in day-to-day practice, as testing is noninvasive and simple to perform. In addition, FE_{NO} results can complement other findings, such as lung function testing, to provide a more complete picture of airway status.

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