

Contents	
Guidelines	1
FeNO Benefits	1

Fraction of Exhaled Nitric Oxide

Guidelines

A European Respiratory Society technical standard: exhaled biomarkers in lung disease

Horváth I, Barnes PJ, Loukides S, Sterk PJ, Högman M, Olin AC, Amann A, Antus B, Baraldi E, Bikov A, Boots AW, Bos LD, Brinkman P, Bucca C, Carpagnano GE, Corradi M, Cristescu S, de Jongste JC, Dinh-Xuan AT, Dompeling E, Fens N, Fowler S, Hohlfeld JM, Holz O, Jöbbsis Q, Van De Kant K, Knobel HH, Kostikas K, Lehtimäki L, Lundberg J, Montuschi P, Van Muylem A, Pennazza G, Reinhold P, Ricciardolo FLM, Rosias P, Santonico M, van der Schee MP, van Schooten FJ, Spanevello A, Tonia T, Vink TJ. Eur Respir J. 2017 Apr 26;49(4). pii: 1600965

Global strategy for asthma management and prevention 2017

2017 GINA (Global Initiative for Asthma) Report

British guideline on the management of asthma: SIGN Clinical Guideline 141, 2014

James DR, Lyttle MD, 2014 Archives of Disease in Childhood - Education and Practice 2016;101:319-322.

Measuring fractional exhaled nitric oxide concentration in asthma

NICE diagnostics guidance 12. Issued: April 2014

An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FENO) for clinical applications.

Dweik RA, Boggs PB, Erzurum SC, Irvin CG, Leigh MW, Lundberg JO, Olin AC, Plummer AL, Taylor DR; American Thoracic Society Committee on Interpretation of Exhaled Nitric Oxide Levels (FENO) for Clinical Applications. Am J Respir Crit Care Med. 2011 Sep 1;184(5):602-15. doi: 10.1164/rccm.9120-11ST.

ATS/ERS recommendations for standardized procedures for the online and offline measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide, 2005.

American Thoracic Society; European Respiratory Society. Am J Respir Crit Care Med. 2005 Apr 15;171(8):912-30.

ATS workshop proceedings: exhaled nitric oxide and nitric oxide oxidative metabolism in exhaled breath condensate.

Silkoff PE, Erzurum SC, Lundberg JO, George SC, Marcin N, Hunt JF, Effros R, Horvath I; American Thoracic Society; HOC Subcommittee of the Assembly on Allergy, Immunology, and Inflammation. Proc Am Thorac Soc. 2006 Apr;3(2):131-45.

FeNO Benefits

Utilising Exhaled Nitric Oxide Information to Enhance Diagnosis and Therapy of Respiratory Disease - Current Evidence for Clinical Practice and Proposals to Improve the Methodology

Marieann Högman, Lauri Lehtimäki, Anh Tuan Dinh-Xuan. Expert Rev Respir Med 11 (2), 101-109. 2017 Jan 20.

The extended NO analysis to estimate NO parameters will continue to be a tool for the specialist lung or respiratory physiology clinic. It needs a fast responding analyzer and accurate flow measurements to give correct estimations. There are many patient categories that can benefit of these estimations and especially for the alveolar NO. The development of NO analyzers with other techniques than chemiluminescence is welcome mostly in the primary care. Exhaled NO is here to stay, but it needs to be used in the right patient to give good guidance for diagnosis and treatment evaluation.

Exhaled nitric oxide in the diagnosis of asthma in adults: a systematic review.

Harnan SE, Essat M, Gomersall T, Tappenden P, Pavord I, Everard M, Lawson R. Clin Exp Allergy. 2017 Mar;47(3):410-429.

FeNO50 had variable diagnostic accuracy even within subgroups of studies with similar characteristics. Diagnostic accuracy, optimal cut-off values and best position for FeNO50 within a pathway remain poorly evidenced.

Fractional exhaled nitric oxide for the management of asthma in adults: a systematic review

Munira Essat, Sue Harnan, Tim Gomersall, Paul Tappenden, Ruth Wong, Ian Pavord, Rod Lawson, and Mark L. Everard. Eur Respir J. 2016 Mar; 47(3): 751–768.

FeNO guided management showed no statistically significant benefit in terms of severe exacerbations or ICS use, but showed a statistically significant reduction in exacerbations of any severity.

Measurement of exhaled nitric oxide concentration in asthma: a systematic review and economic evaluation of NIOX MINO, NIOX VERO and NObreath.

Health Technol Assess. 2015 Oct;19(82):1-330. doi: 10.3310/hta19820. Harnan SE, Tappenden P, Essat M, Gomersall T, Minton J, Wong R, Pavord I, Everard M, Lawson R.

“The economic analysis indicates that FeNO monitoring could have value in diagnostic and management settings. The diagnostic model indicates that FeNO monitoring plus bronchodilator reversibility dominates many other diagnostic tests. FeNO-guided management has the potential to be cost-effective, although this is largely dependent on the duration of effect.”

Exhaled nitric oxide to predict corticosteroid responsiveness and reduce asthma exacerbation rates.

Donohue JF, Jain N. Respir Med. 2013 Jul;107(7):943-52.

Until recently, there has been no point-of-care tool for use in assessing the underlying airway inflammation associated with asthma. However FeNO testing has emerged as a non-invasive, inexpensive, reliable indicator of corticosteroid-responsive Th2-mediated inflammation for use in the assessment and management of asthma. Does FeNO assist clinicians in treatment decision making such as initiating or increasing ICS therapy, and can these decisions have a beneficial impact on asthma outcomes? Taking into account the accumulated evidence, including the data from new analyses in this paper, the answer to both questions is “yes.”

Methods of NO detection in exhaled breath.

Cristescu SM, Mandon J, Harren FJ, Meriläinen P, Högman M. J Breath Res. 2013 Mar;7(1):017104.

Monitoring exhaled NO has a significant contribution in disease diagnosis and monitoring treatment efficiency, especially in asthma and some lung-related diseases. The knowledge of NO biology achieved was used to provide guidelines for NO measurements. A proper selection of the clinical scenarios in combination with a proper methodology for monitoring NO that includes a suitable detection method in combination with a trustable standardization procedure and proper determination of the NO parameters will definitely improve the confidence in using exhaled NO in other clinical applications.

Exhaled nitric oxide (FeNO) as a non-invasive marker of airway inflammation.

Munakata M. Allergol Int. 2012 Sep;61(3):365-72.

FeNO is a very useful diagnostic tool and control monitoring maker of asthma. Usefulness of FeNO in asthma management is probably better than spirogram, induced sputum, and AHR test, because of its non-invasiveness, effort independency, measurement simplicity, and reproducibility. Although the FeNO analyzer has not been approved as a medical device, it will be widely used as a convenient clinical tool for asthma management in the near future in Japan.

Clinical aspects of using exhaled NO in asthma diagnosis and management.

Ludviksdottir D, Diamant Z, Alving K, Bjermer L, Malinovschi A. Clin Respir J. 2012 Oct;6(4):193-207. doi: 10.1111/crj.12001.

In several studies, FE(NO) measurements provided additional information on aspects of asthma including phenotyping, corticosteroid-responsiveness and disease control. Thus, if correctly applied and interpreted, FE(NO) can aid asthma diagnosis, identify patients at risk of exacerbation and support customized treatment decisions. A simple and reliable tool to quantify peripheral nitric oxide will further aid to identify patients with small airways inflammation.

Use of exhaled nitric oxide measurement to identify a reactive, at-risk phenotype among patients with asthma.

Dweik RA, Sorkness RL, Wenzel S, Hammel J, Curran-Everett D, Comhair SA, Bleecker E, Busse W, Calhoun WJ, Castro M, Chung KF, Israel E, Jarjour N, Moore W, Peters S, Teague G, Gaston B, Erzurum SC; National Heart, Lung, and Blood Institute Severe Asthma Research Program. Am J Respir Crit Care Med. 2010 May 15;181(10):1033-41.

Grouping of asthma by FeNO provides an independent classification of asthma severity, and among patients with severe asthma identifies the most reactive and worrisome asthma phenotype.

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

Price D, Berg J, Lindgren P; Allergy. 2009 Mar;64(3):431-8

Asthma diagnosis based on FENO measurement with NIOX MINO alone is less costly and more accurate than standard diagnostic methods. Asthma management based on FENO measurement is less costly than asthma management based on standard guidelines and provides similar health benefits.

A technical report on exhaled nitric oxide measurement: asthma monitoring in athletes.

Grob NM, Laskowski D, Dweik RA. J Breath Res. 2008 Sep;2(3):37027. doi: 10.1088/1752-7155/2/3/037027.

Exercise training in asthmatics was associated with a decrease (improvement) in NO levels but no significant change in FEV(1) and PEF. This suggests that exhaled NO levels may be more sensitive to changes in the airway as a result of exercise than traditional pulmonary function testing.

Nitric oxide as a clinical guide for asthma management.

Taylor DR. J Allergy Clin Immunol. 2006 Feb;117(2):259-62.

In practice, F(E)NO measurements are useful in the management of severe or difficult asthma. High and low F(E)NO levels in symptomatic patients provide the clinician with information that enables active eosinophilic airway inflammation to be included or excluded. Either outcome is helpful in decision making. F(E)NO measurements complement the use of other tests in asthma, but more work is required to determine reference values and cut-points for appropriate interpretation.

Exhaled nitric oxide measurements: clinical application and interpretation.

Taylor DR, Pijnenburg MW, Smith AD, De Jongste JC. Thorax. 2006 Sep;61(9):817-27.

FENO measurements offer a step forward in the assessment of airways disease. As an "inflammometer", FENO provides the clinician with hitherto unavailable information regarding the nature of underlying airway inflammation, thus complementing conventional physiological testing, including the measurement of AHR. FENO measurements are easy to perform, reproducible, and technically less demanding than induced sputum analysis. They are unreliable in current smokers and, when used diagnostically, in patients who have been taking inhaled or oral steroids recently.

Exhaled nitric oxide: a predictor of steroid response.

Smith AD, Cowan JO, Brassett KP, Filsell S, McLachlan C, Monti-Sheehan G, Peter Herbison G, Robin Taylor D. Am J Respir Crit Care Med. 2005 Aug 15;172(4):453-9

FENO measurements greater than 47 ppb provide a means of predicting steroid response in patients with undiagnosed respiratory symptoms. Assessing airway inflammation is of more practical value than diagnostic labeling when considering the potential usefulness of inhaled anti-inflammatory therapy.

The use of exhaled nitric oxide concentration to identify eosinophilic airway inflammation: an observational study in adults with asthma.

Berry MA, Shaw DE, Green RH, Brightling CE, Wardlaw AJ, Pavord ID. Clin Exp Allergy. 2005 Sep;35(9):1175-9.

This value of exhaled NO would seem to be the best for identifying significant eosinophilic airway inflammation. It is applicable to a wide range of non-smoking patients with asthma; exhalation flow does not alter the ability of exhaled NO concentration to detect a sputum eosinophilia.

Exhaled nitric oxide predicts asthma exacerbation.

Harkins MS, Fiato KL, Iwamoto GK. J Asthma. 2004 Jun;41(4):471-6.

FeNO appears to be a clinically useful tool to assess disease control in this population.

Diagnosing asthma: comparisons between exhaled nitric oxide measurements and conventional tests.

Smith AD, Cowan JO, Filsell S, McLachlan C, Monti-Sheehan G, Jackson P, Taylor DR. Am J Respir Crit Care Med. 2004 Feb 15;169(4):473-8. Epub 2003 Nov 25.

Our study confirms the overall superiority of FeNO measurements and induced sputum analysis in the diagnosis of asthma compared with conventional tests. FeNO measurements are quick and easy to perform and may be readily incorporated into routine pulmonary function test procedures. This advance offers the possibility that a diagnosis of asthma may be performed more easily and confirmed with much greater confidence than has been possible to date.

Relations between exhaled nitric oxide and measures of disease activity among children with mild-to-moderate asthma.

Covar RA1, Szefler SJ, Martin RJ, Sundstrom DA, Silkoff PE, Murphy J, Young DA, Spahn JD. J Pediatr. 2003 May;142(5):469-75.

FE(NO) may be a complementary tool to current practice guidelines in assessing asthma control and medication response.

The predictive value of exhaled nitric oxide measurements in assessing changes in asthma control.

Jones SL, Kittelson J, Cowan JO, Flannery EM, Hancox RJ, McLachlan CR, Taylor DR. Am J Respir Crit Care Med. 2001 Sep 1;164(5):738-43.

We conclude that eNO measurements are as useful as induced sputum analysis and AHR in assessing airway inflammation, with the advantage that they are easy to perform.