Comparative validation of handheld fractional exhaled nitric oxide measurements

van Deelen, Sanne; Tramper-Stranders, Gerdien A.; Hendriks, Rudi W.; Reinders, Marcel J.T.; Braunstahl, Gert Jan

DOI
10.1080/17434440.2025.2499652

Publication date
2025

Document Version
Final published version

Published in
Expert Review of Medical Devices

Citation (APA)
van Deelen, S., Tramper-Stranders, G. A., Hendriks, R. W., Reinders, M. J. T., & Braunstahl, G. J. (2025). Comparative validation of handheld fractional exhaled nitric oxide measurements. *Expert Review of Medical Devices*, *22*(6), 643-650. https://doi.org/10.1080/17434440.2025.2499652

Expert Review of Medical Devices

ISSN: 1743-4440 (Print) 1745-2422 (Online) Journal homepage: www.tandfonline.com/journals/ierd20

Comparative validation of handheld fractional exhaled nitric oxide measurements

Sanne van Deelen, Gerdien A. Tramper-Stranders, Rudi W. Hendriks, Marcel J. T. Reinders & Gert-Jan Braunstahl

To cite this article: Sanne van Deelen, Gerdien A. Tramper-Stranders, Rudi W. Hendriks, Marcel J. T. Reinders & Gert-Jan Braunstahl (2025) Comparative validation of handheld fractional exhaled nitric oxide measurements, Expert Review of Medical Devices, 22:6, 643-650, DOI: 10.1080/17434440.2025.2499652

To link to this article: https://doi.org/10.1080/17434440.2025.2499652

EXPERT REVIEW OF MEDICAL DEVICES
2025, VOL. 22, NO. 6, 643–650
https://doi.org/10.1080/17434440.2025.2499652

Taylor & Francis
Taylor & Francis Group

ORIGINAL RESEARCH

Comparative validation of handheld fractional exhaled nitric oxide measurements

Sanne van Deelen [a,b,c], Gerdien A. Tramper-Stranders[d], Rudi W. Hendriks[b], Marcel J. T. Reinders[c] and Gert-Jan Braunstahl[a,b]

[a]Department of pulmonology, Franciscus Gasthuis & Vlietland, Rotterdam, Netherlands; [b]Department of pulmonology, Erasmus MC, Rotterdam, Netherlands; [c]Pattern recognition & bioinformatics, Delft University of Technology, Delft, Netherlands; [d]Department of pediatrics, Franciscus Gasthuis & Vlietland, Rotterdam, Netherlands

ABSTRACT

Background: Fractional exhaled nitric oxide (FeNO) is a noninvasive method to determine the degree of airway inflammation. Handheld devices such as the Vivatmo Me are used for home monitoring. Differences were found between the Vivatmo Me and standard measurements with the NIOX VERO. Therefore, we aimed to determine the accuracy of the Vivatmo Me for FeNO measurements.

Methods: Adult patients with an appointment for FeNO-measurement according to regular care, were invited to perform the FeNO measurement with both devices. From these measurements the FeNO values were compared, and the device user-friendliness was determined.

Results: One hundred and sixty-four patients were included. The number of attempts needed for a successful measurement and the failure rate were higher with the Vivatmo Me. Although the measurements were highly correlated, a significant difference ($p < 0.001$) was found between FeNO values measured with both devices. From the Vivatmo measurements, 32% did not fall within the claimed accuracy ranges. A linear correction on the FeNO values reduced this number.

Conclusion: Our findings indicate that the Vivatmo Me does not comply with the claimed accuracy of clinical FeNO measurements and the measurement is challenging to perform. By applying the proposed correction, the comparative validity of the FeNO measurement improves and therefore its clinical usefulness.

ARTICLE HISTORY
Received 30 December 2024
Accepted 18 April 2025

KEYWORDS
Asthma; asthma-COPD-overlap syndrome; chronic obstructive pulmonary disease; fractional exhaled nitric oxide; handheld devices

1. Introduction

Fractional exhaled nitric oxide (FeNO) is a measure of the concentration nitric oxide (NO) in exhaled air and is used to determine the degree of inflammation in the airways [1]. NO is formed in the lungs by three different NO-synthase (NOS) enzyme isoforms. Neuronal NOS (nNOS/NOS1) and endothelial isoform NOS (eNOS/NOS3) are activated by mediators of damaged tissue. Inducible isoform NOS (iNOS/NOS2) is activated by bacterial products or inflammatory cytokines. Many patients with asthma have an increased expression of iNOS, which causes increased release of NO in the lungs, and therefore bronchoconstriction, inflammation and remodeling [2,3]. Currently, FeNO measurements are mostly used as noninvasive marker in asthma [1]. The American Thoracic Society (ATS) recommends FeNO measurements for asthma patients with regard to (1) detecting eosinophilic inflammation, (2) predicting a possible treatment response to corticosteroids, (3) monitoring airway inflammation to determine corticosteroid treatment, and (4) revealing therapy non-adherence [4]. Asthma patients with a low FeNO measurement (<25 ppb) most likely have no eosinophilic inflammation type and probably have a poor response to corticosteroids. A moderate FeNO value (25–50 ppb) should be related to clinical context. High FeNO values (>50 ppb) correspond to an eosinophilic inflammation type (type 2 inflammation), risk of an asthma exacerbation and a good treatment response to corticosteroids and biological therapies [1,4,5]. Besides the use in asthma treatment, FeNO measurements are increasingly used in other diseases including chronic obstructive pulmonary disease (COPD) [1]. During a FeNO measurement (independent of the measurement device) the following should be taken into account: (1) excluding nasal NO [6], (2) the flow of the exhaled air [6], (3) excluding nonspecific influences, such as spirometry measurements prior to a FeNO measurement, airway and anti-inflammatory medication, respiratory tract infections, tobacco and food (nitrate-rich food increases the NO-measurement) [1,5,7].

FeNO measurement devices are often stationary, or not portable. Therefore, FeNO measurements are mostly limited to a planned appointment at the lung function department in a hospital. With regard to home-monitoring, research or easily accessible FeNO measurement during a consultation with a physician, a smaller and portable device could provide a resolution. Multiple portable FeNO measurement devices are available, for example the Vivatmo Me of Bosch Healthcare Solutions GmbH. However, before such alternative devices can be used in clinical practice, we need to have insights in accuracy and user-friendliness. To this end, we

CONTACT Sanne van Deelen s.vandeeleen@franciscus.nl Department of Pulmonology, Franciscus Gasthuis & Vlietland, Kleiweg 500, Rotterdam 3045 PM, Netherlands

Supplemental data for this article can be accessed online at https://doi.org/10.1080/17434440.2025.2499652

performed a side-by-side comparison with the current standard measurement method, the NIOX VERO. No validation or comparative studies regarding the Vivatmo Me have been published to date. However, the NIOX VERO is commonly used, and is validated in multiple researches [8,9]. Therefore, our aim was to determine the accuracy of the Vivatmo Me for FeNO measurements in patients with (suspected) asthma, COPD or asthma-COPD-overlap syndrome (ACOS), compared to the NIOX VERO.

2. Patients and methods

This prospective cross-sectional validation study was performed in Franciscus Gasthuis & Vlietland hospital in The Netherlands. The study was ethically approved by the hospital scientific board, additional assessment of the regional medical ethical committee was waived due to the noninvasive character of the study. Patients over 16 years old (due to device settings of 10 second measurements from the age of 16 [7,10]) with (suspected) asthma, COPD, or ACOS, with an appointment for a NO-measurement according to regular care, were asked to participate in the study. Informed consent had to be signed before inclusion.

The patients were asked to use two devices to determine the FeNO value, the Vivatmo Me (Bosch Healthcare Solutions GmbH, Waiblingen, Germany) and the NIOX VERO (NIOX group, Oxford, UK). The order of the measurements with both devices were randomized. Measurements with the NIOX VERO were performed according to the hospital protocols (maximal 8 attempts). There is no limitation on the number of attempts per patient by the manufacturer. According to the manufacturer's instructions, measurements with the Vivatmo Me can be performed with a maximum of 5 attempts (maximum 5 attempts per mouthpiece and maximum 15 minutes out of the packaging [10]). After a successful attempt, no further attempts are measured, resulting in a single outcome per patient. If a patient had no successful measurement (no outcome measure shown on the device screen) within the maximum number of attempts, the measurement was marked as failed on that device. For each patient a new unopened mouthpiece was used. The measurements were performed with the standard duration setting for adults of 10 seconds. The minimum value displayed on both devices is "5 ppb -LOW-" or "<5 ppb," so a value between 0 and 5 ppb cannot be determined more precisely. To prevent outliers or artifacts in the data, patients were screened for confounding factors according to standard hospital protocol regarding FeNO measurement. The confounding factors were heavy exercise (<1 h ago), eating (<1 h ago), drinking (<1 h ago), smoking (<1 h ago), airway infection (<2 weeks ago), airway medication and hay fever symptoms at the moment of the measurement. These confounders should be taken into account for the clinical interpretation. Both devices are equally influenced by the presence of any confounders, therefore it should not affect a comparison of outcome measures.

2.1. Statistical analysis

In total 164 patients needed to be included for a power of 95%, with an alpha of 5%, assuming the difference in accuracy between the outcomes measured with both devices is at least 10%. Based on whether the data followed a normal distribution, the patient- and clinical characteristics were described as mean values with standard deviation or median values with interquartile range, and categorical variables are described as percentages. All statistical analyses have been performed with Python (version 3.9.5, Python Software Foundation, https://www.python.org/).

2.1.1. User friendliness

The user-friendliness of the Vivatmo Me was assessed. This includes the failure rate of the measurements, and the average needed number of attempts to succeed a measurement. The mean attempts for a successful measurement per device were compared to determine the difference in difficulty of the measurement. The failure rate is the percentage of measurements that failed (no successful measurement in 5 attempts). The failure rate of the Vivatmo Me was compared with the failure rate of the NIOX VERO. The reason for failing the measurements were marked with the following reasons: (1) Device is not working (e.g. system error), (2) performance of the patient is insufficient (not able to keep a constant flow), (3) number of attempts is too much for the patient (according to the patient or lung function analyst), or (4) other reasons. In order to determine if failing occurs more within certain age categories, the number of successful and failed measurements and the failure rate per age category was analyzed.

2.1.2. Comparison of FeNO outcomes

The outcomes of the Vivatmo Me were compared to FeNO values obtained with the NIOX VERO. Within this study, the NIOX VERO is seen as the standard measurement device. The primary outcome was the percentage of deviation of the FeNO value measured with the Vivatmo Me, as proportion to the deviation per range according to Bosch Healthcare Solutions GmbH: For measurements below 50 ppb, a fixed threshold of 5 ppb was used. For measurements of 50 ppb or higher, a threshold of 10% was applied, and for measurements of 160 ppb or higher, a threshold of 15% was used (5 ppb < 50 ppb, 10% ≥50 ppb, 15% for ≥160 ppb) [10]. Similarly, the average measured FeNO value per device was given. Also, the percentage of values within the clinical ranges (<25 ppb, 25–50 ppb, and ≥50 ppb) were given to observe the distribution in clinical context. The not-normally distributed FeNO value data measured with both devices were tested on significant difference with the Wilcoxon-signed-rank-test. The correlation between the measurements with both devices and the strength of this correlation was expressed with a Pearson correlation coefficient. To confirm that randomization did not influence the outcome of the measurement, the differences between the measurements per starting device were compared with a Mann-Whitney-U-Test. To confirm that the number of attempts did not influence the FeNO value, the median and the distribution of FeNO values measured with the Vivatmo Me per needed number of attempts were determined. The clinical ranges with cutoffs on 25 and 50 ppb were also used to identify false positives and false negatives. A scatter plot of the FeNO values measured with the NIOX VERO against the values measured with the Vivatmo Me was

made to observe the distribution of the data and to determine a possible trendline in the deviation of the Vivatmo Me compared to the NIOX VERO. Within the scatterplot outliers were defined as outside double the accuracy ranges (10 ppb < 50 ppb, 20% ≥50 ppb, 30% for ≥160 ppb). A linear trendline was found with polynomial fitting. The FeNO values measured with the Vivatmo Me were corrected by this linear trend and again analyzed on significant difference, and false positives and negatives. With these outcomes, the influence of the correction could be expressed.

3. Results

In total 164 patients were included. The final study population included patients between 21 and 91 years of age. The median age of the included patients was 56 years (Table 1). More females (65%) than males were included. From all patients, 88% had (or were suspected having) asthma, 7% COPD and 5% ACOS.

3.1. User friendliness

In the complete group ($N = 164$), 48 had a failed measurement with one or both the devices. Patients needed on average 1.61 attempts on the NIOX VERO and 3.28 attempts on the Vivatmo Me for a successful measurement. From the failed measurements, 45 patients failed only the Vivatmo Me measurement, one patient only the NIOX VERO measurement, and two patients failed the measurement on both devices. The Vivatmo Me had a failure rate of 29%, whereas the NIOX VERO had a failure rate of 2%. The reason for the failed measurements were for most (46 patients) an insufficient performance (not able to keep a constant flow), and for two patients it was decided by the researcher and lung function analyst that the number of attempts was too much for the patient. Patients with a failed measurement had an average age of 59.5 years compared to 53.1 years in the successful measurement group. Looking at the median FeNO values measured with the NIOX VERO, all the successful measurements have a median of 18.5 ppb (IQR: LOW-28.5) and the measurements that were failed by the Vivatmo Me (but successful with NIOX VERO) 26.0 ppb (IQR: 3.00–49.0). Figure 1 shows the number of successful and failed measurements measured with the Vivatmo Me and the failure rate per age category. Showing an increase in failure rate after the age of 70 years.

3.2. Comparison of FeNO outcomes

The FeNO values measured with the Vivatmo Me had a median value of 15.0 ppb (IQR: LOW-34.3). Those measured with the NIOX VERO had a median value of 18.5 ppb (IQR: LOW-28.5) (Figure 2(a)), being significantly different (Wilcoxon signed-rank test, $p < 0.001$). The FeNO values measured with both devices had an overall Pearson correlation coefficient of $r = 0.96$. Within the clinical ranges the correlation coefficients are: $r = 0.77$ (<25 ppb), $r = 0.70$ (25–50 ppb) and $r = 0.91$ (≥50 ppb). Figure 2(b) shows that 32% of the successful measurements (37/116 patients) were outside the expected accuracy range (an accuracy of 5 ppb < 50 ppb, 10% ≥50 ppb, 15% for ≥160 ppb).

From the 116 successful measurements (i.e. successful on both devices), 62 patients started with the Vivatmo Me and 54 with the NIOX VERO. The randomization group starting with NIOX had a median difference between the two devices of 3.0 ppb (IQR: −3.0–9.0) and the group starting with Vivatmo had a similar median difference of 3.0 ppb (IQR: −0.75–6.75), resulting in no differences in outcome measurements between the two randomization groups ($p = 0.532$). No correlation was found between the median FeNO values measured with the Vivatmo Me and the necessary number of attempts to succeed the measurement (Figure 3).

In clinical practice of asthma treatment, FeNO values are labeled low (<25 ppb), moderate (25–50 ppb) and high (≥50 ppb) [4]. Of the successful NIOX VERO measurements, 59% were in the clinical range below 25 ppb, 25% between 25–50 ppb and 16% above 50 ppb. In Figure 4, the number of measurements in each clinical range is shown for measurements with the NIOX VERO and with the Vivatmo Me. The FeNO values obtained with the Vivatmo Me showed two overestimations and five underestimations when considering the

Table 1. Demographics of the total study population, and of the subgroup with successful measurements and subgroup with failed measurements. A successful measurement is a measurement that was successfully performed on both measurement devices.

	All measurements	Successful measurements	Failed measurements
N	164	116 (70%)	48 (29%)
Age (years)	Mean: 56.0 SD: ± 24.5	Median: 53.1 IQR: 37.4–68.8	Median: 59.5 IQR: 43.8–75.2
Sex			
Male	58 (35%)	42 (36%)	16 (33%)
Female	106 (65%)	74 (64%)	32 (67%)
Diagnosis			
Asthma	144 (88%)	102 (88%)	42 (88%)
*COPD**	11 (7%)	7 (6%)	4 (8%)
*ACOS***	9 (5%)	7 (6%)	2 (4%)
FeNO* questionnaire**			
Exercise <1 h	6 (4%)	4 (3%)	2 (4%)
Food <1 h	35 (21%)	23 (20%)	12 (25%)
Drinking <1 h	50 (30%)	36 (31%)	14 (29%)
Smoking <1 h	6 (4%)	4 (3%)	2 (4%)
*RTI**** *<2 weeks*	13 (8%)	8 (7%)	5 (10%)
Airway medication	132 (80%)	95 (82%)	37 (77%)
Allergic rhinitis	14 (9%)	7 (9%)	7 (15%)

*Chronic Obstructive Pulmonary disease, **Asthma-COPD Overlap Syndrome, ***Fractional Exhaled Nitric Oxide, ****Respiratory Tract Infection.

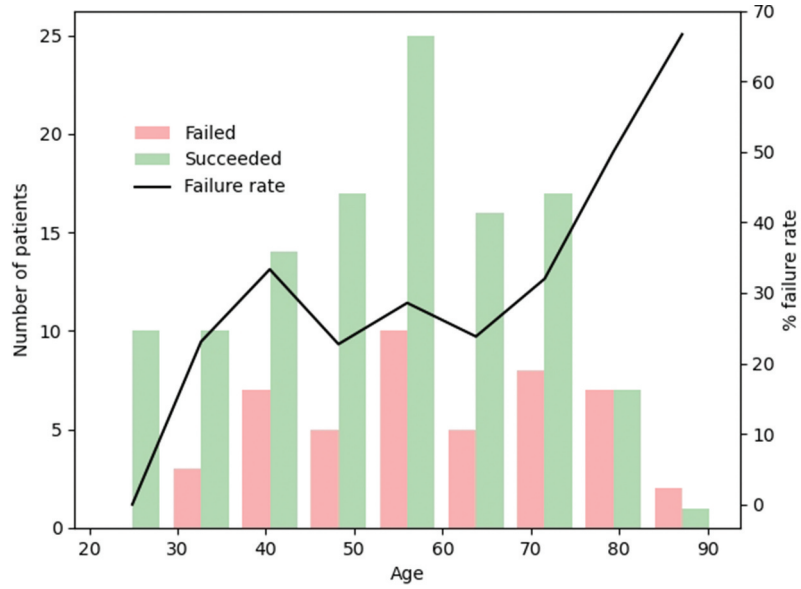

Figure 1. The histograms show the number of successful and failed measurements measured with the Vivatmo Me per age category in respectively green and red. The black line represents the failure rate in percentage (failed in age category/total in age category).

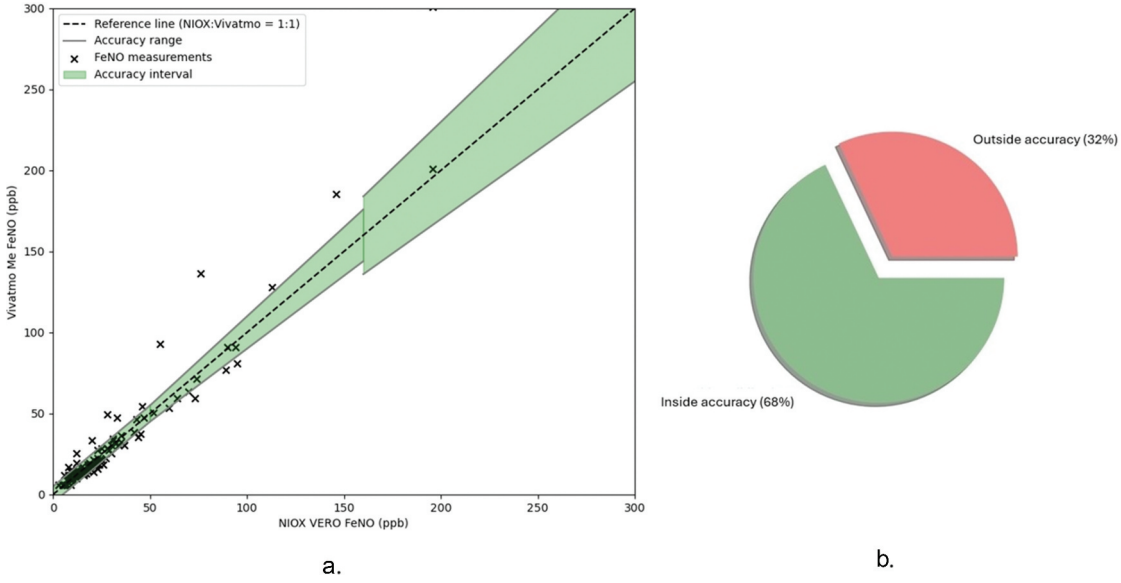

Figure 2. (a) FeNO values of the successful measurements measured with the NIOX VERO (median 18.5 ppb) against the FeNO values measured with the Vivatmo Me (median 15.0). The green areas display the accuracy ranges (5 ppb < 50 ppb, 10% ≥ 50 ppb, 15% for ≥ 160 ppb [7]). (b) Thirty-seven of the 116 successful measurements (32%) were outside the expected accuracy range.

clinical cutoff of 25 ppb compared to the NIOX VERO. One overestimation was outside the accuracy range, and three underestimations were outside the accuracy range. When considering the clinical cutoff value of 50 ppb, 1 overestimation and 1 underestimation were found, of which only the overestimation was outside the accuracy range.

3.3. Outcome correction

As can be seen in Figure 2(a), most of the measurements seemed to be below the reference line, indicating an underestimation of the FeNO value measured with the Vivatmo Me. To suggest a possible correction, a trend line was estimated. To do so, first, outliers were set as at least double the accuracy ranges (10 ppb < 50 ppb, 20% ≥50 ppb, 30% for ≥160 ppb) and removed from the data. With the remaining data a linear trend line (Vivatmo = 0.9913*niox −2.836) was estimated through linear regression (Figure 5). By correcting the data with the found linear trend line, the number of measurements outside the accuracy range was reduced from 32% to 22% (25 out of 116 measurements). No significant difference between the measurements with both devices was found after applying the correction (Wilcoxon rank-sign test, $p = 0.904$). After correction there were three overestimations and four

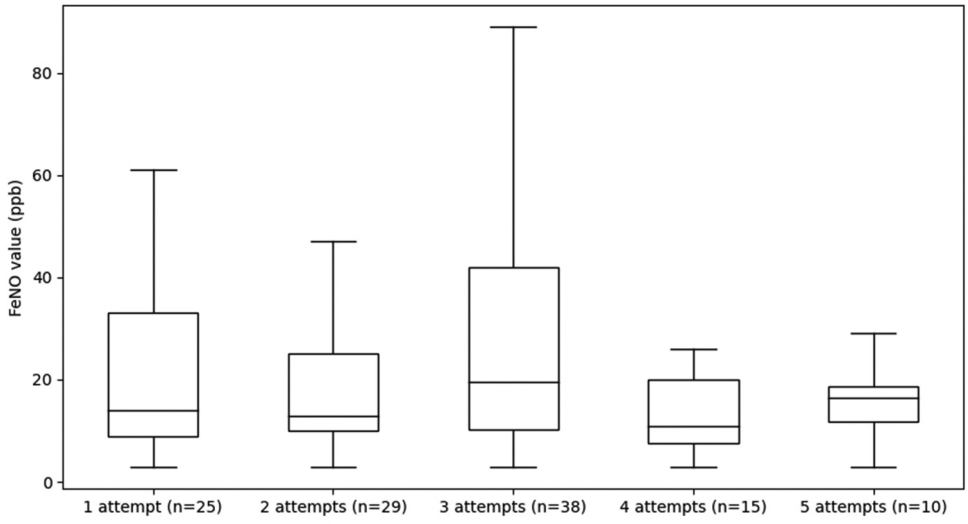

Figure 3. The median FeNO values measured with the Vivatmo Me for each number of attempts needed by the patient to succeed the measurement."n" shows number of patients in relation to number of attempts to succeed.

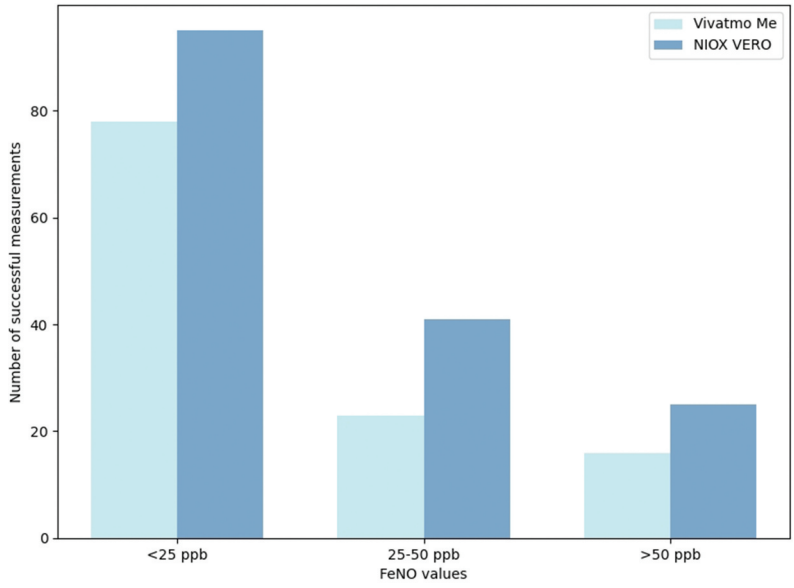

Figure 4. Number of successful measurements in each clinical range for measurements with the NIOX VERO and with the Vivatmo Me.

underestimations for measurements on the cutoff of 25 ppb, and 1 overestimation and 1 underestimation for measurements on the clinical cutoff of 50 ppb.

4. Discussion

This study investigated the comparative validity of FeNO measurements with the Vivatmo Me compared to the NIOX VERO. As FeNO is increasingly being used as a biomarker for asthma management, accuracy of different measurement methods, and thereby clinical utility, is important. The results show a high correlation, but also significant differences between the two devices. When applying the company-specified accuracy ranges, 32% of the successful measurements did not fall within these ranges.

The lower median FeNO value of the Vivatmo Me (as well as the point-by-point comparison as shown in Figure 2(a)) suggest a possible underestimation of the FeNO value by the Vivatmo Me. When correcting this trend linearly, the number of data points outside the claimed accuracy range reduced to 22%. We speculated that the underestimation of FeNO values measured with the Vivatmo Me was due to the number of attempts until successful measurement. However, this was not proven as there was no difference in FeNO values observed with an increase in number of attempts. Although there are no comparative validation studies found on the Vivatmo Me, research by Molino et al. showed lower FeNO measurements

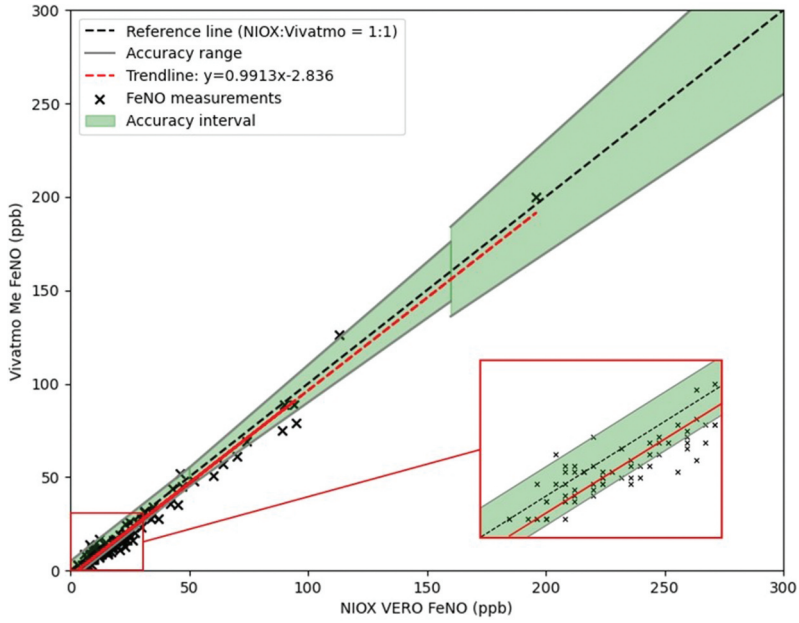

Figure 5. FeNO values measured with the NIOX VERO against the Vivatmo Me, excluding the outliers, and displaying a trend line of $y = 0.991\times - 2.836$. The red box highlights the data < 25 ppb and the green areas display the accuracy ranges (5 ppb < 50 ppb, 10% ≥ 50 ppb, 15% for ≥ 160 ppb.

with the Vivatmo Pro, the professional stationary device by Bosch Healthcare Solution GmBH, compared to the NIOX VERO [11]. These results are consistent with this research.

Whereas most of the data showed an underestimation of the FeNO value measured with the Vivatmo me, the outliers were mostly (9 out of the 10 outliers) an overestimation. The outliers were found in all 3 accuracy intervals and range from a FeNO value measured with the NIOX VERO from 12 to 196. Hence, physicians should be aware that if an outcome does not seem compliant with the clinical presentation, reassessment of the FeNO measurement is advised. This advice applies to all possible devices, but as proven in this study it should be especially considered when using the Vivatmo Me.

The cutoff FeNO values used in therapeutic decisions in asthma treatment are >25 ppb (moderate) and ≥50 ppb (high) [1,4]. Approaching these cutoff values, one can reason that it is more ethically sound to overestimate the FeNO value than underestimate. Underestimation could lead to undertreatment and, therefore, uncontrolled asthma. This will cause an increased disease burden and lower quality of life of the patient [12]. With the proposed correction on the Vivatmo Me FeNO values, the number of false negative categorizations decreases and overall the values are less underestimated than before correction. The correction will therefore provide a better outcome for clinical practice. In total 29% of the patients were not able to perform the FeNO measurement on the Vivatmo Me, whereas only 2% were not able to perform the measurement on the NIOX VERO. For most of the patients the reason for the failed measurement was insufficient performance of the patient (not able to keep a constant flow in the right flow-range). Also, from the successful measurements, patients needed more attempts on average with the Vivatmo Me than the NIOX VERO. Patients mentioned that they found the Vivatmo Me more difficult to use due to multiple reasons. One of the reasons is the feedback through the lightning on the Vivatmo Me. The NIOX VERO shows a scale on which patients can see how much harder or softer they have to blow in the device to get the right flow range. The Vivatmo Me only shows lights for an insufficient or excessive flow and does not show how much harder or softer the flow needs to be. Although there are also a few patients that perform better without this visual feedback, most patients profited from it. Other feedback given was that the range in which the flow was correct on the Vivatmo Me seemed smaller than the range on the NIOX VERO, making the Vivatmo Me more 'sensitive.' Contradictive, Beeh et al. showed that 95% of the 85 included patients rated the Vivatmo Me as neutral/somewhat easy to easy/very easy to handle (to learn and actually use the device) [13]. However, within the study of Beeh et al. patients within the age 18–74 (median = 48 years) were included. Since failing of the measurement is related to age, this could partly explain the different findings in device handling. The higher failure rate above 70 years old could mean that the Vivatmo Me is possibly not the right choice for patients above this age, which can be explained by loss in elastic recoil and alveolar attachments with aging, causing decreasing expiratory flows [14]. Moreover, patients with a higher FeNO, and thus active inflammation of the lungs, have more difficulty with execution of the measurement on the Vivatmo Me.

It could be argued that the discrepancy between the number of attempts allowed for each device (maximum of 5 attempts for the Vivatmo Me and 8 attempts for the NIOX VERO) may have influenced the number of successful measurements in the favor of measurements performed with NIOX VERO. However, only one patient exceeded the number of attempts with the NIOX VERO over the maximum number of attempts allowed with the Vivatmo Me. Notably, this was the only patient that failed the measurement with the NIOX VERO and succeeded the measurement with the Vivatmo Me. Therefore, the discrepancy in number of attempts allowed between the two devices did not influence the success rates.

Other parameters like sex, diagnosis and attributes of the FeNO questionnaire show roughly the same distributions

amongst the successful and failed measurement (as shown in Table 1), and therefore do not seem to have an influence on the chance of failing the measurement.

4.1. Strengths and limitations

The prospective cross-sectional study design ensured a varied study population with different ages, diseases and disease severity. The patients ranged from experienced in FeNO measurements to patients that had never done the measurement before. Randomization of the starting device ruled out the influence of a possible learning curve after first attempt. The power calculation of 95% ($n = 164$) was relatively high, since a power of 80% ($N = 94$) would also have been sufficient. Therefore, a success rate of 116 out of 164 is still adequate to statistically prove the found difference in accuracy between the measurement devices. Since FeNO is part of the standard follow-up of asthma patients and not (yet) for COPD, most of the patients had a (suspected) asthma diagnosis (88%). A limitation of this study is that FeNO values were mostly in the lower clinical range (<25ppb) than in the higher clinical ranges. Possibly more people were in a stable situation due to the use of inhalation corticosteroids and less people had uncontrolled asthma or COPD at the time of measurement, explaining the lower FeNO values. Another limitation is that patients that come in regularly for checkups have more experience in the FeNO measurement with NIOX VERO. This could cause a bias in the user-friendliness of the devices. However, some patients already had some experience with the Vivatmo Me. Lastly, this research is cross-sectional, therefore no statements can be made about the repeated measurements within one patient during a follow-up period. Hence, the quality of using the Vivatmo Me as a monitoring device cannot be assessed. Follow-up research focusing on the precision of the device is needed to provide information about the reliability in monitoring within individual patients, thereby providing insight into its clinical utility.

5. Conclusion

Although the FeNO measurements of the Vivatmo Me were highly correlated with the measurements of the NIOX VERO, a significant difference was found between them. Besides, the FeNO measurements with Vivatmo Me did not comply with the claimed accuracy ranges and were more difficult to perform for patients. By applying the proposed correction, the comparative validity of the FeNO measurement improved. With the correction applied, clinical assessment of the FeNO value with the Vivatmo Me is applicable since it is comparable with the validated NIOX VERO outcomes, however reassessment of FeNO measurements is advised in the case of discrepancies between the FeNO value and the clinical presentation.

Abbreviations

ACOS Asthma-COPD Overlap Syndrome
ATS American Thoracic Society
COPD Chronic Obstructive Pulmonary Disease
eNOS endothelial isoform Nitric Oxide
FeNO Fractional exhaled Nitric Oxide
iNOS inducible isoform Nitric Oxide
NOS Nitric Oxide Synthase
nNOS neuronal Nitric Oxide Synthase
OSAS Obstructive Sleep Apnea Syndrome
ppb parts per billion

Funding

This research was financed by fundings from Stichting Bevordering Onderzoek Franciscus (BOF), Dutch Lung Foundation and Sanofi Genzyme B.V.

Declaration of interest

The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Reviewer disclosures

Peer reviewers on this manuscript have no relevant financial relationships or otherwise to disclose.

Author contributions

Sanne van Deelen was involved in the conception and design, analysis and interpretation of the data and the drafting of the paper. Gerdien A. Tramper-Stranders, Rudi W. Hendriks, Marcel J.T. Reinders and Gert-Jan Braunstahl were involved in revising the paper critically for intellectual content and final approval of the version to be published.

Acknowledgments

Our appreciation goes to the lung function analysts of Franciscus Gasthuis & Vlietland for their collaboration during data collection of this research.

ORCID

Sanne van Deelen http://orcid.org/0009-0003-7452-6611

References

1. Horvath I, Barnes PJ, Loukides S, et al. A European respiratory society technical standard: exhaled biomarkers in lung disease. Eur Respir J. 2017;49(4):1700016. doi: 10.1183/13993003.00965-2016
2. Van der Vliet A, Eiserich JP, Cross CE. Nitric oxide: a pro-inflammatory mediator in lung disease? Respir Res. 2000;1(1):1–6. doi: 10.1186/rr14
3. Prado CM, Martins MA, Tiberio IFLC. Nitric oxide in asthma physiopathology. ISRN Inflamm. 2011;2011(1):832560. doi: 10.5402/2011/832560
4. Dweik RA, Boggs PB, Erzurum SC, et al. An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FENO) for clinical applications. Am J Respir Crit Care Med. 2011;184(5):602–615. doi: 10.1164/rccm.9120-11ST
5. American Thoracic Society, European Respiratory Society. ATS/ERS recommendations for standardized procedures for the online and offline measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide. Am J Respir Crit Care Med. 2005;171(8):912–930. doi: 10.1164/rccm.200406-710ST
6. Pavord ID, Deniz Y, Corren J, et al. Baseline FeNO independently predicts the dupilumab response in patients with moderate-to-severe asthma. J Allergy Clin Immunol Pract. 2023;11(4):1213–1220. doi: 10.1016/j.jaip.2022.11.043

7. Circassia AB. NIOX VERO Airway Inflammation Monitor gebruiksaanwijzing [Internet]. Oxford: Circassia AB; 2023. Available from: https://www.niox.com
8. National Institute for Health and Care Excellence. Measuring fractional exhaled nitric oxide concentration in asthma: NIOX MINO, NIOX VERO and NObreath [Internet]. London: National Institute for Health and Care Excellence; 2014. Available from: https://www.nice.org.uk/guidance/dg12
9. Alving K, Anolik R, Crater G, et al. Validation of a new portable exhaled nitric oxide analyzer, NIOX VERO®: randomized studies in asthma. Pulm Ther. 2017;3(1):207–218. doi: 10.1007/s41030-017-0032-8
10. Bosch Healthcare Solutions GmbH. Bosch Vivatmo Me gebruiksaanwijzing [Internet]. Waiblingen: Bosch Healthcare Solutions GmbH; 2022. Available from: https://www.vivatmo.com
11. Molino A, Fuschillo S, Mosella M, et al. Comparison of three different exhaled nitric oxide analyzers in chronic respiratory disorders. J Breath Res. 2019;13(2):026003. doi: 10.1088/1752-7163/ab0167
12. Lee LK, Obi E, Paknis B, et al. Asthma control and disease burden in patients with asthma and allergic comorbidities. J Asthma. 2018;55(2):208–219. doi: 10.1080/02770903.2017.1316394
13. Beeh K-M. Benefit of daily FeNO measurement in asthmatics over 12 weeks: adherence, handling and overall satisfaction in the FeNO@home observational study. In: Poster session presented at: ERS congress 2024; Vienna, Austria.
14. Neder JA, Berton DC, O'Donnell DE. Probing the old lung: challenges to pulmonary function testing interpretation in the elderly. J Bras Pneumol. 2022;48(5):e20220272. doi: 10.36416/1806-3756/e20220272