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Original Research



Exhaled breath condensate based breath analyser: Real-time thermofluidic standardisation of hydrogen peroxide for longitudinal COPD monitoring: a pilot investigation

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) remains a leading cause of morbidity and mortality worldwide, yet current monitoring strategies based on clinic spirometry and symptom reporting often fail to detect early exacerbations. Exhaled breath condensate (EBC) offers a non-invasive alternative; however, substantial variability in biomarker concentrations has limited its clinical translation.

This study aimed to quantify longitudinal variability of EBC hydrogen peroxide (H_2O_2) in healthy volunteers and COPD participants and to determine whether real-time correction for physiological sampling conditions could improve measurement consistency.

We developed a handheld EBC collection device integrating temperature and inspiratory flow sensors with an on-the-fly correction algorithm to compensate for temperature- and flow-dependent heat and mass transfer effects. In artificial breath experiments, the algorithm reduced measurement variability from 20% to 7%.

In a three-month longitudinal pilot study, 15 COPD participants and 15 healthy volunteers were assessed at monthly intervals (three visits per subject). H_2O_2 concentrations were significantly higher in COPD participants than in healthy controls ($p < 0.001$), and this difference was preserved after standardisation. After standardisation, month-to-month variation in healthy volunteers was no longer statistically significant. Electrochemical detection using a Prussian blue-based sensor showed good agreement with a fluorometric reference method, with 94.8% of measurements within the 95% limits of agreement, a mean bias of 0.112 μM, and a standard deviation of 0.41 μM. Most participants rated the device as easy and comfortable to use.

These findings support the technical feasibility of portable, standardised EBC H_2O_2 measurement. This approach warrants further evaluation in COPD studies.

1. Introduction

Chronic obstructive pulmonary disease (COPD) represents a significant global health burden, characterized by persistent airflow limitation and respiratory symptoms including dyspnea, chronic cough, and excessive sputum production. The disease follows a progressive trajectory, with patients initially presenting with mild symptoms such as intermittent coughing that gradually advances to substantial functional impairment affecting daily living activities [1].

The epidemiological impact of COPD is substantial both nationally and internationally. Within the United Kingdom, COPD ranks as the second most prevalent respiratory condition and constitutes the third leading cause of mortality, contributing to approximately 22,000 annual deaths. Globally, the disease was responsible for over 3 million deaths in 2021 and is currently the third leading cause of death, with projections estimating nearly 600 million individuals living with COPD by 2050, particularly among women and in low- and middle-income countries [2,3].

A substantial proportion of COPD-related healthcare costs arises from emergency visits and hospitalizations required for the management of exacerbations. There is a critical need to detect exacerbation events prior to the onset of symptoms, initiate timely therapeutic interventions, and thereby mitigate further deterioration of pulmonary function.

Current monitoring strategies for chronic obstructive pulmonary

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disease (COPD) rely predominantly on clinic-based spirometry assessments, including measurements of FEV1 progression and, in some cases, the FEV1/FVC ratio, as well as patient self-monitoring of symptoms [4]. However, real-world unsupervised home spirometry still faces implementation constraints, because only around 60% home sessions meet acceptability criteria, making data quality assurance and patient support critical for routine use in primary care [5]. Symptom based monitoring using symptom/CAT data from assisted with machine-learning models predicting acute exacerbation of COPD within 1–8 days achieved high negative predictive value (~98–99%) but very low positive predictive value (~5–7%), suggesting stronger utility for ruling out near-term exacerbation risk than for generating actionable alerts [6].

Nonetheless, remote monitoring has shown potential to reduce both the frequency and severity of COPD exacerbations. Current approaches under investigation include monitoring respiratory rate, electrocardiography (ECG), and arterial (or transcutaneous) carbon dioxide partial pressure ($PaCO_2$/$PtcCO_2$) [7].

Exhaled breath condensate (EBC) as a promising non-invasive diagnostic/monitoring approach. This methodology offers significant advantages for monitoring pulmonary inflammatory processes and biochemical activities while potentially providing insights into systemic disease manifestations beyond the respiratory system [8,9].

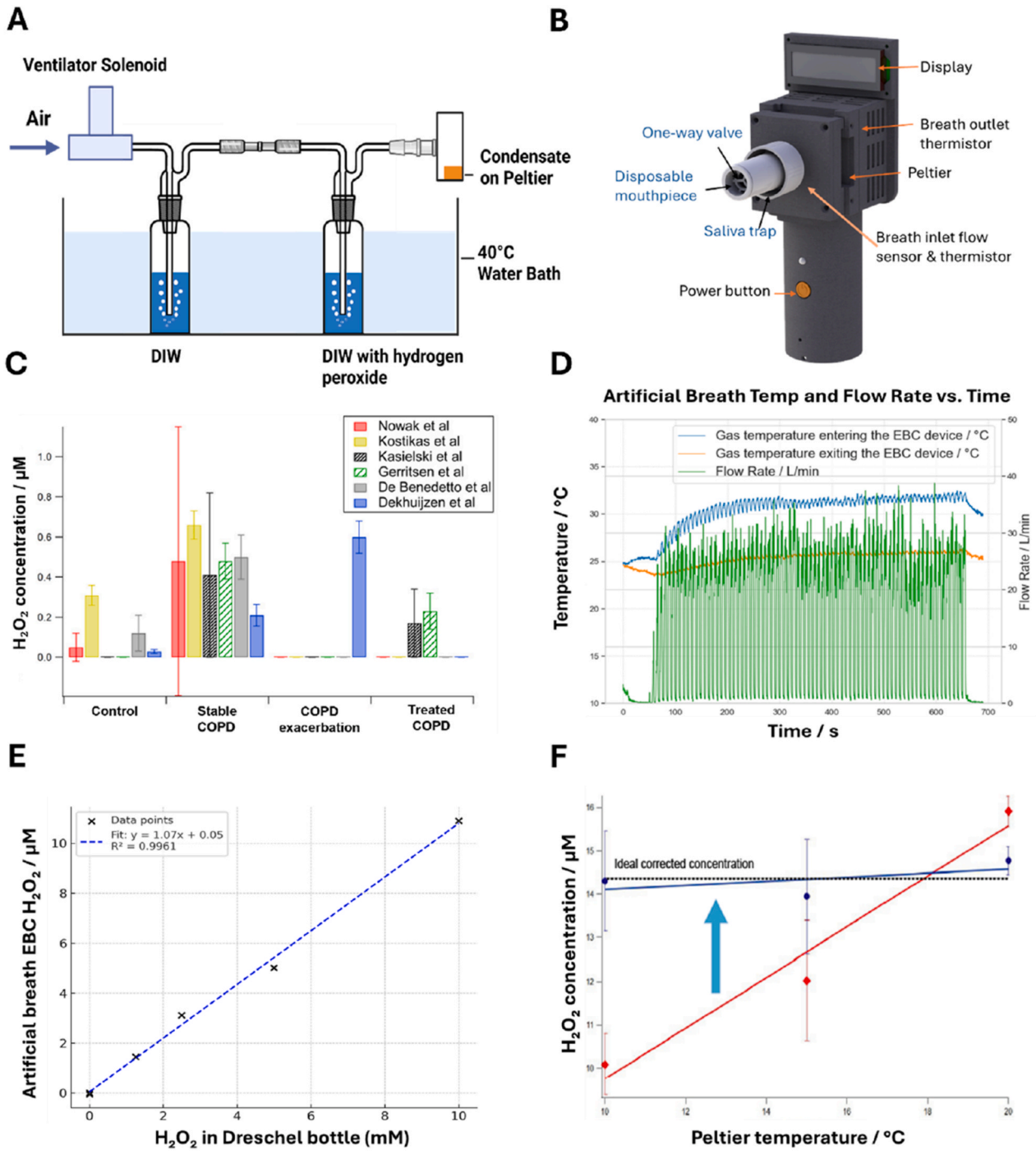


Fig. 1. A. Experimental setup for artificial breath, B. Handheld EBC collector, C. Variation of hydrogen peroxide concentration between different clinical studies, D. Flow rate and inlet, outlet temeparture of the artificial breath E. Correlation of Dreschel bottle hydrogen peroxide concentration to artificial breath hydrogen peroxide concentration, F. Analyte concentration before and after algorithm correction.

The composition of exhaled breath includes volatile compounds and water vapor that originate from the fluid lining of alveolar spaces, airways, and oral cavity through gas-phase diffusion, alongside aerosols from multiple parts of the airways. The EBC collection process involves cooling exhaled air to achieve dehumidification, resulting in a condensed liquid matrix. This biofluid contains numerous potential biomarkers, including non-volatile substances in the form of aerosols (cytokines, electrolytes, and adenosine) alongside volatile water-soluble molecules such as ammonia and hydrogen peroxide [9,10].

However, significant methodological challenges exist in EBC research, particularly regarding inter-study variability that extends beyond patient-specific factors. Liu and colleagues [11] conducted a comprehensive evaluation of various EBC collection systems, including RTube, Ecoscreen, and custom-built glass and silicon devices, revealing substantial discrepancies in analyte concentrations between platforms. Notably, NOx measurements from Ecoscreen devices were seven-fold higher compared to RTube systems.

Hydrogen peroxide represents a particularly relevant biomarker for COPD monitoring due to its biological origin and pathophysiological significance [12]. Activated inflammatory cells, including neutrophils, eosinophils, and macrophages, generate H_2O_2 through respiratory burst processes, producing reactive oxygen species as part of the inflammatory response [13]. The reported concentrations of H_2O_2 in the epithelial lining fluid of the lung range from micromolar to tens-micromolar levels, with COPD patients showing significantly elevated exhaled H_2O_2 concentrations compared to healthy controls [9].

Despite these promising findings and consistent disease stratification in both COPD and asthma, absolute H_2O_2 concentrations vary considerably across studies, as summarised for COPD patients in Fig. 1C [14–24]. This variability stems from two primary sources: **{1}** the inherent instability of hydrogen peroxide [25], which is highly susceptible to degradation influenced by storage conditions, container materials, and temperature fluctuations, and **{2}** inadequate thermal control during collection procedures, where temperature variations within individual breathing cycles, between successive breaths, across measurement sessions, and among different patients introduce significant and typically uncontrolled variations in the thermodynamic parameters (Henry's law constant, enthalpy of condensation etc.) In addition, whilst it is inevitable that change in gas velocity will cause changes in the convective and mass transport boundary layers, poorly defined flow conditions can lead to changes in the flow regime over a single breath and introduce significant secondary flows.

To address these limitations, our research focuses on three primary objectives: **{1}** establishing and maintaining consistent heat transfer characteristics and controlled convective boundary layer dimensions across a broad range of breathing velocities, **{2}** developing a standardization algorithm that incorporates real-time measurements of inlet/outlet temperatures and airflow velocities to minimize inter-measurement variability. **{3}** Clinical evaluation quantify longitudinal variability in EBC hydrogen peroxide (H_2O_2) levels in healthy and COPD subjects, and to evaluate whether real-time correction for physiological sampling conditions can improve measurement reliability.

2. Method

Artificial breath simulations were established using compressed air connected to a solenoid valve and two Dreschel bottles immersed in a water bath maintained at 40 °C, a temperature chosen to approximate exhaled breath temperature measured in the laboratory. The first Dreschel bottle filled with deionised water served solely for humidification and heating, while hydrogen peroxide solution in deionised was introduced into the second bottle. Polytetrafluoroethylene (PTFE) tubing was used throughout to minimize redox interactions between hydrogen peroxide and the tubing material.

Two analytical techniques for hydrogen peroxide quantification were compared: Amplex Red fluorometry [26] and a Prussian blue–based electrochemical sensor developed in our laboratory. The performance comparison of these methods has been reported previously [27] Amplex Red fluorimetry is an established method for determining low concentrations of H_2O_2 and sufficiently widely as a gold standard method, in the absence of suitably sensitive methods for low concentrations and small sample volumes [25].

The EBC collector used in this study was designed and manufactured in our laboratory jointly with Respire Diagnostics where details were published previously [27]. It includes thermistor sets (Murata NXFT15XV103FEAB050) to measure both the temperature of the exhaled breath and the temperature of the breath leaving the collector after the condensation process. The device also incorporates a flow sensor (IST FS7.0.1L.195) to measure the exhaled breath flow rate, which was pre-calibrated against a Sensirion SFM3000-200C.

For the clinical evaluation (IRAS project ID: 289549) of the EBC analyser, 15 healthy volunteers and 15 patients with COPD were recruited for longitudinal monitoring over three months. The COPD cohort comprised 15 participants: 5 mild, 7 moderate, and 2 severe cases, with 1 case not clearly classified from the screening Case Report Form (CRF); 14 participants were ex-smokers and 1 was recorded as a non-smoker. Participants were selected on the basis of a COPD diagnosis, being not current smokers, and having stable COPD at baseline, defined by no chest infection requiring antibiotics and/or oral steroids in the previous month, no recent change in maintenance inhaled therapy, and no exacerbation requiring emergency room treatment or hospitalisation within the previous four weeks.

The healthy volunteer cohort comprised 15 participants, of whom 12 were recorded as non-smokers and 3 as ex-smokers with minor past smoking history. Healthy volunteers were selected on the basis of being free of significant disease, aged 18 years or above, able to provide informed consent and comply with study procedures, and having no upper or lower respiratory infection within 3 weeks of baseline assessment.

For further cohort characteristics please refer to the Supplementary Information Tables 2 and 3

EBC samples were collected every month for each volunteer and analysed for H_2O_2 concentration before and after algorithmic correction. Breath temperature, exhalation period, and spirometry (FEV_1/FVC) were also measured during each visit. Additionally, a standard questionnaire was answered by each participant to determine their attitudes to the technology and its ease of use, in the context of the participants' familiarity with technology in everyday life. The questionnaire form is supplied in the Electronic Supplementary Information.

Exhaled breath condensate (EBC) was collected during quiet tidal breathing in accordance with the European Respiratory Society (ERS) technical standard for exhaled biomarkers [10]. Participants breathed into the EBC collection device for a total of 10 min, with a short rest after the first 5 min. A nose clip was not used because the prototype mouthpiece incorporates a one-way valve that permits exhalation into the condenser but prevents inhalation through the mouthpiece; consequently, continuous bidirectional mouth breathing through the device was not feasible at the time of clinical trial. An inhalation filter was not used because the device did not include a filter interface [28]. Samples were transported on ice packs and analysed on the same day, given the known instability of H_2O_2 in EBC.

In total, 45 H_2O_2 measurements were expected in each group (15 participants × 3 visits). However, due to instrument malfunction (leakage issue), complete H_2O_2 data were not available for all samples: 42 H_2O_2 values were obtained from healthy participants and 35 from patients with COPD. Similarly, breath temperature and exhalation period data were missing in 2 healthy participants and 1 COPD participant, also due to instrument sensor malfunction.

3. Result and discussion

3.1. Correction for thermofluid parameters

Exhaled breath condensate consists of moisture and biomarkers, where the process of EBC condensation can be considered as 1. Moisture condensation and 2. Biomarker transfer.

Moisture condensation can be simply modelled through the humidity difference between breath entering and exiting the collection device thus:

$$\dot{m}_{EBC} = \dot{m}_{breath}(\omega_{in} - \omega_{out})$$

Where $\dot{m}$ is the mass flow rate (kg s^{-1}) and ω is the specific humidity of the breath in kg H_2O(kg air)$^{-1}$. Humidity can be linked to breath temperature T (°C)with the following equations [29].

$$P_s = RH \times 610.162 \times \exp\left(\frac{17.291T}{T + 237.481}\right)$$

$$\omega_{breath} = 0.622 \times \frac{P_s}{P_{atmosphere} - P_s}$$

P_s is the saturation pressure (pa) at a known RH (relative humidity), T (breath temperature in °C), $P_{atmosphere}$ is the atmospheric pressure (pa). Mass transfer of analyte into EBC the mass transfer resistance can be in either:

I. Gas-phase mass transfer
II. Liquid phase mass transfer

Two-resistance theory was adopted to study the mass transfer. The overall transfer coefficient, for species A transferring from gas phase to liquid phase the coefficient is given by:

$$\frac{1}{k_{overall}} = \frac{1}{k_G} + \frac{1}{K_H k_L}$$

$k_{overall}, k_G, k_L$ are the overall, gas phase, and liquid phase mass transfer coefficient respectively. K_H is the Henry's law constant in unit $molm^{-3}Pa^{-1}$. For large Henry's law constant species, the equation would simply reduce to:

$$k_{overall} \sim k_{gas}$$

Since it is impractical to measure the partial pressure of the analyte due to low its value, the mass transfer coefficient can be determined from boundary layer-based mass transport analysis, where the non-dimensional numbers, the Sherwood number (Sh), Reynolds number (Re), and Schmidt number (Sc) were adopted, defined below:

$$Re = \frac{4\dot{V}_{breath}}{\pi d \nu}$$

$$\overline{k_{gas}} = \frac{\overline{Sh} \times D_{gas}}{d}$$

$$\overline{Sh} = f(Re, Sc)$$

V_{breath} is the volumetric flow rate of breath (m^3s^{-1}), d is the characteristics length of the flow (m), and ν is the kinematic viscosity (m^2s^{-1}) The Sherwood number can be found through theoretical or empirical analysis, for instance, laminar flow over a parallel plate has an averaged Sherwood number given by:

$$Sh_L = 0.664(Re_L)^{\frac{1}{2}}(Sc)^{\frac{1}{3}}$$

With the assumption of breath being an ideal gas, the mass transfer ordinary differential equation (ODE) can be written as

$$\frac{dP}{dr} = \frac{P \times k_{overall} \times (2\pi r)}{\dot{V}_{breath}}$$

Where P is the partial pressure of the analyte (pa) r is the radial dimension (m). The number of molecules transferred can then be modelled as

$$n = k_{overall} \times \frac{P}{R_{gas}T} \times \pi r^2$$

Where n is the number of molecules in mol, R_{gas} is the universal gas constant ($Jmol^{-1}K^{-1}$). The concentration of the condensate can then be determined from below, where $\rho_{condensate}$ is the density of condensate (kgm^{-3}) and $m_{condensate}$ is the mass of the condensate in kg

$$[Analyte] = \frac{n\rho_{condensate}}{m_{condensate}}$$

4. Implementation of on-the-fly standardisation on device

Although the calculation showed a similar trend to the experimental results, however the concentration differs by 10 fold. This could be due to loss of hydrogen peroxide during the experiment. Nonetheless if we define a standard, the percentage change of the theory and the experiment matched well as shown in Table 1.Therefore, a standardisation algorithm with defined standard device operation parameters can be implemented to obtain a correction factor. Standard device operation parameters are defined as follows in Table 2. A correction factor (CF) can be determined

$$CF = \frac{[H_2O_2]_m}{[H_2O_2]_s} = \frac{\frac{\dot{N}_{H2O2,m} \times \rho_{condensate}}{\dot{m}_{condensate,m}}}{\frac{\dot{N}_{H2O2,s} \times \rho_{condensate}}{\dot{m}_{condensate,s}}} = \frac{\frac{\dot{N}_{H2O2,m}}{\dot{m}_{condensate,m}}}{\frac{\dot{N}_{H2O2,s}}{\dot{m}_{condensate,s}}}$$

4.1. Artificial breath experiment

An artificial breath experiment was established, as depicted in Fig. 1A, to evaluate the effectiveness of the standardization algorithm for breathing pattern flow. Fig. 1B showcases the EBC collector developed in our laboratory and employed in the study, while Fig. 1D presents the measured flow rate and temperature profiles of the artificial breath entering and exiting the collector for the artificial breath experiments. As shown in Fig. 1E, the hydrogen peroxide concentration measured in the artificial breath exhibited a strong linear correlation with the hydrogen peroxide concentration within the Dreschel bottle. Notably the 95% confidence limit includes zero, showing no significant offset between Dreschel bottle concentration and measured concentration. Finally, Fig. 1F reveals that application of the correction algorithm reduced the relative standard deviation of the measurements from 20% to 7%, underscoring its capability to substantially improve measurement precision. Statistical analysis revealed that before correction, the hydrogen peroxide concentration was significantly dependent on collection temperature ($F(2,6) = 20.76$, $p = 0.0020$). After applying the correction algorithm, this dependence became statistically insignificant ($F(2,6) = 0.33$, $p = 0.73$), confirming that temperature effects were effectively removed.

Table 1
Percentage of (hydrogen peroxide concentration at a condensation temperature) divided by (hydrogen peroxide concentration at standard temperature, 20 °C), data adapted from Fig. 1F.

Peltier temperature (°C)	Theory	Experiment
10	66%	61%
15	79%	75%
20	100%	100%

Table 2
Standard defined for standardisation algorithm.

Standard device operation parameters	Value
Inlet breath temperature (°C)	35.0
Breath volumetric flow rate (l/min)	3
Outlet breath temperature[a] (°C)	29.5

[a] outlet breath temperature is theoretically calculated from Peltier temperature of 20 °C.

4.2. Clinical study

A key aim of our preliminary clinical evaluation was to test the variability of measured hydrogen peroxide concentrations. Three samples were collected on three successive visits close to one calendar month apart. Variations for any one individual were more important that the group (healthy volunteers or COPD patients). Variations in concentration were expected to be greater in the patient group than the healthy volunteer group.

Pooling data across the three collection months, we obtained EBC volumes of 346 ± 83 μL for COPD patients and 382 ± 117 μL for healthy individuals, with no statistically significant difference between groups (Fig. 2A) .

By analysing all samples collectively across the three months, as shown in Fig. 3A and B, without consideration of temporal variation, hydrogen peroxide concentrations in EBC were significantly higher in COPD patients than in healthy individuals, both before and after correction as shown in Table 3 (n = 34 for COPD and 42 for healthy, $p = 3.25 \times 10^{-4}$ and 4.42×10^{-3} respectively).

Standardisation reduces the variance associated with insufficient control of thermofluid parameters, which represents the primary conclusion of this study. In the present case, a significant difference is observed between COPD patients and healthy volunteers, both with and without correction. Nevertheless, the observed concentration variations—approximately 10% of the mean—are consistent with the discrepancies reported across many published studies and may, at least in part, explain the variation in reported levels.

From a clinical perspective, the main value of the correction algorithm at this stage is improvement in within-subject measurement repeatability, by reducing variability introduced by differences in exhalation flow and breath temperature between visits. The data also suggest some benefit for between-subject comparability, insofar as standardisation reduces non-biological sampling variation without obscuring the separation between healthy and COPD groups. These findings provide a basis for further investigation of whether this degree of correction could support clinical decision-making, including exacerbation detection or treatment monitoring.

The Prussian blue-based electrochemical sensor demonstrated strong agreement with the reference fluorometric method (Fig. 2C; n = 58. 94.8% of data within 95% confidence limits of the mean), with a mean bias of 0.112 μM, standard deviation of differences of 0.41 μM, proportional bias of 0.51, and 95% limits of agreement from −0.69 to 0.91 μM. Given the biological variability in EBC H_2O_2 (COPD: 0.282 ± 0.289 μM; healthy: 0.101 ± 0.105 μM), the observed agreement is sufficient to demonstrate fitness for purpose both clinical and research use.

Whilst variations are expected in the COPD group, due to variations in the condition and the disease progression, repeated samples from individual healthy volunteers are expected to be more consistent in the absence of respiratory disease. This was tested over three successive repeats over three months. Repeated-measures ANOVA, summarised in Table 4, revealed that, prior to thermal fluidic correction, month-to-month variation was significant in healthy volunteers (p = 0.0143) but became non-significant after correction (p = 0.2681). In the COPD group, variation was non-significant both before (p = 0.3623) and after correction (p = 0.3426). Additionally, we measured breath temperature

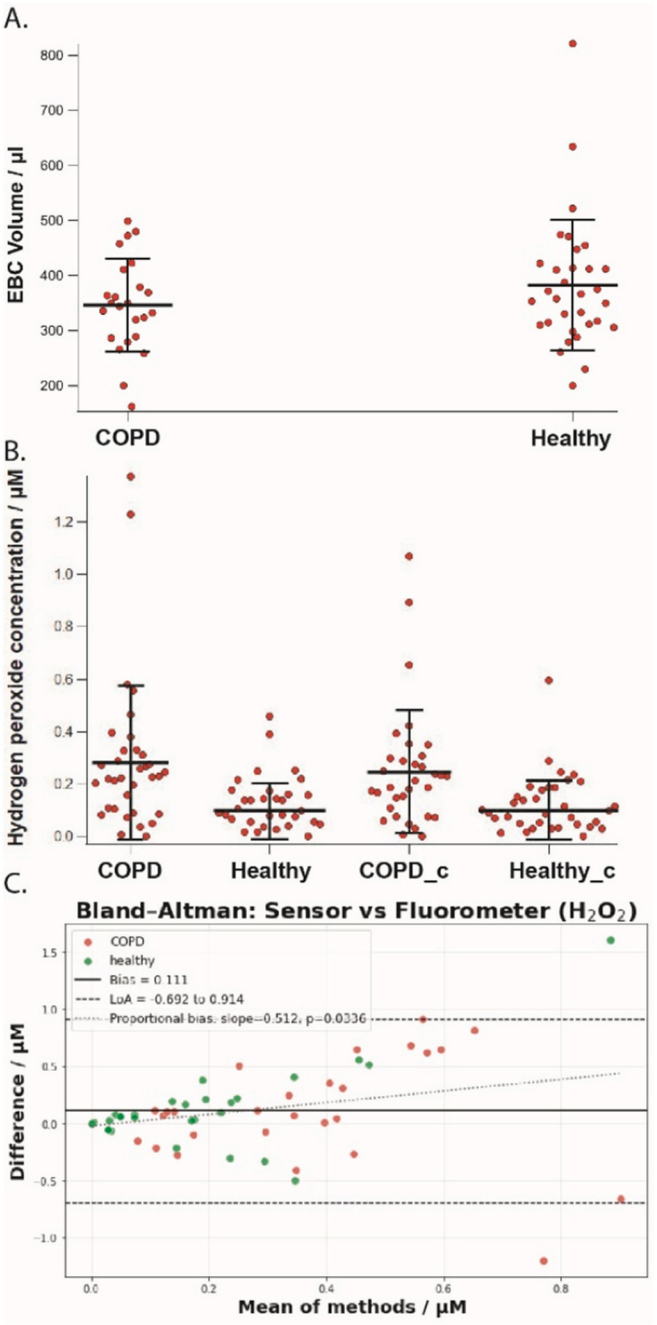


Fig. 2. A. EBC volume collected from COPD and healthy patient, B. Hydrogen peroxide concentration in EBC for COPD and healthy, before and after correction, C. Bland and Altman plot of the disposable hydrogen peroxide sensor v. s. fluorometer.

(p = 0.973 for healthy and p = 0.172 for COPD) and exhalation duration (p = 0.181 for healthy and p = 0.477 for COPD) and found no significant month-to-month changes in either the COPD or healthy volunteer groups (See Fig. 3C and D). Similarly, no significant month-to-month changes were observed in spirometer-measured FEV_1/FVC ratios as shown in Fig. 3E (p = 0.370 for healthy and p = 0.150 for COPD).

Mixed ANOVA, summarised in Table 5, revealed a significant between-group effect (COPD vs. healthy) for hydrogen peroxide concentrations in exhaled breath condensate, both before correction ($p = 4.28 \times 10^{-4}$) and after correction ($p = 8.13 \times 10^{-4}$). A significant group difference was also observed for exhalation duration ($p = 7.75 \times 10^{-3}$) and spirometer-measured FEV_1/FVC ratios

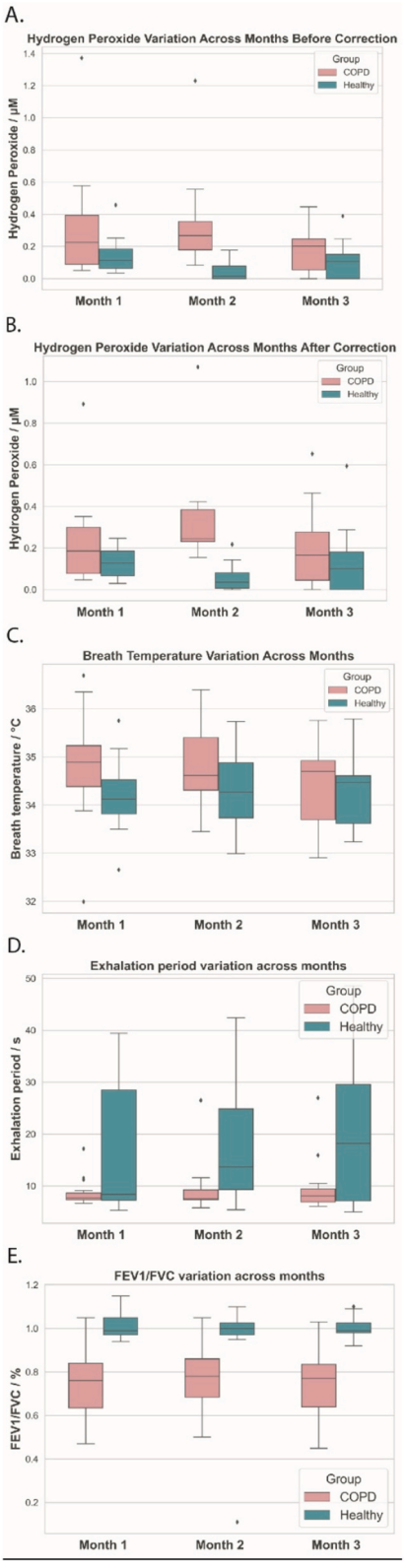


Fig. 3. A. COPD and healthy patient EBC hydrogen peroxide variation across 3 successive monthly visits B. COPD and healthy patient EBC hydrogen peroxide variation across 3 successive monthly visits after standardisation with correction factor C. Breath temperature variation across3 successive monthly visits D. Exhalation period variation across 3 successive monthly visits E. Spirometry FEV1/FVC variation across 3 successive monthly visits.

Table 3
Concentration of hydrogen peroxide in EBC before and after standardisation.

	COPD/μM	Healthy/μM
Mean	0.282	0.101
Std.	0.289	0.105
Mean after standardisation	0.248	0.101
Std. after standardisation	0.230	0.110

Table 4
p-value of rmANOVA analysis for month to month variations.

p-value of rmANOVA	Healthy	COPD
Hydrogen peroxide before correction	**0.0143**	**0.3623**
Hydrogen peroxide after correction	**0.2681**	**0.3426**
Breath temperature	**0.9728**	**0.1716**
Exhalation period	**0.4769**	**0.181**
FEV1/FVC	**0.3702**	**0.1499**

Table 5
p-value of mixed ANOVA analysis across groups.

p-value of mixed ANOVA	Healthy vs COPD
Hydrogen peroxide before correction	$\mathbf{4.28 \times 10^{-4}}$
Hydrogen peroxide after correction	$\mathbf{8.13 \times 10^{-4}}$
Breath temperature	**0.151**
Exhalation period	$\mathbf{7.75 \times 10^{-3}}$
FEV1/FVC	$\mathbf{2.91 \times 10^{-5}}$

($p = 2.91 \times 10^{-5}$). In contrast, no significant between-group difference was detected for breath temperature ($p = 0.151$).

These findings suggest that the correction algorithm primarily improves the stability of repeated measurements over time, particularly in individuals in whom true biological change is expected to be limited. In other words, the algorithm appears to reduce variability caused by sampling conditions rather than altering the underlying biological signal. This is relevant for future longitudinal or home-based applications, where uncontrolled variation in breathing pattern and sampling conditions is likely to be greater than in supervised research visits.

Several limitations should be acknowledged. First, this was a pilot study with a relatively small sample size, which limits statistical precision and generalisability. Second, missing measurements due to sample leakage and sensor malfunction were not negligible and may have affected estimates of variability and longitudinal stability. Although the findings support technical feasibility and improved measurement consistency, they do not yet establish clinical utility for longitudinal monitoring, exacerbation detection, or treatment guidance. Further validation in larger cohorts, together with continued technical refinement to reduce data loss, will be needed before broader clinical application can be considered.

4.3. *Qualitative patient research*

Fig. 4A shows that approximately 25% of COPD patients are late adopters of new technology. However, more than 90% of COPD patients report being comfortable using a medical device at home to monitor their condition. These findings suggest that effective patient education and clear instructions will be essential to facilitate the adoption of future COPD-monitoring devices.

From Fig. 4B we found that the device was generally easy to use and comfortable across both patient groups. However, opinions differed regarding the difficulty of breathing into the device for 5 min: COPD patients reported it as more challenging, with a p-value of 0.0237 indicating a statistically significant difference compared to healthy participants. Thus, based on these results, future iterations of the collection device will be designed to condense sufficient EBC volume

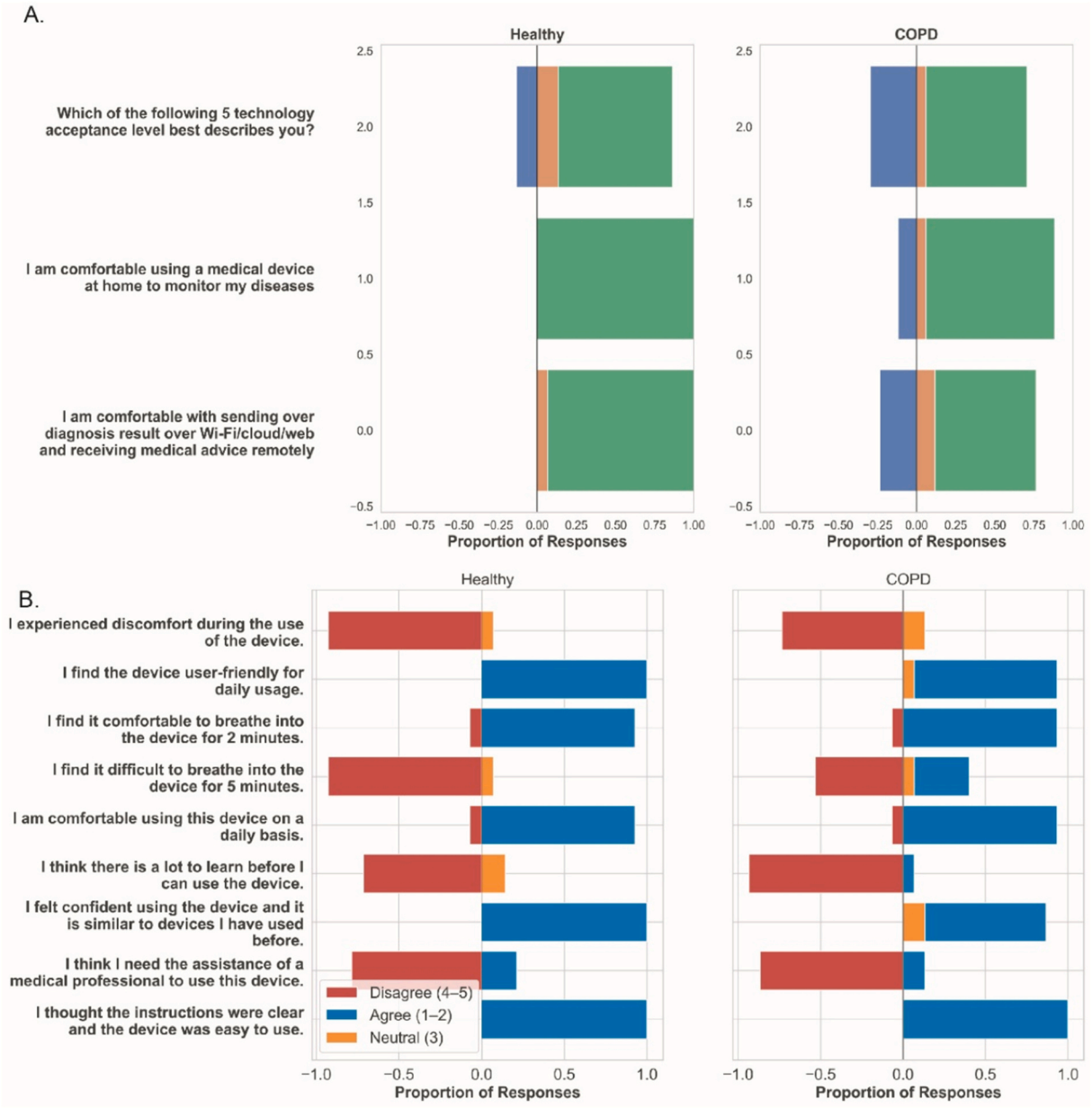


Fig. 4. A. Likert scale of volunteers willingness to adopt home-based point of care medical device. B. Likert scale analysis of user-friendliness and overall usability feedback of the device among Healthy and COPD participants, (1 = strongly agree, 5 = strongly disagree).

within 2 min, thereby reducing patient discomfort and minimizing barriers to device adoption.

5. Conclusions

Exhaled breath condensate collection combined with a real-time standardization algorithm offers a robust framework for monitoring oxidative stress in COPD. By compensating for breath temperature and flow variations, the proposed algorithm reduced measurement variability from 20 % to 7 % in artificial breath tests and enabled consistent correction across operating temperatures.

In a three-month clinical pilot study, hydrogen peroxide concentrations remained significantly higher in COPD patients than healthy volunteers both before and after correction, confirming the biomarker's diagnostic value. Standardization eliminated month-to-month fluctuations in healthy subjects and did not mask disease-related differences, while the disposable Prussian blue sensor delivered comparable performance to fluorometry.

Patient feedback indicated high acceptability for home use, although reducing the exhalation time from five to 2 min may improve comfort.

Overall, these findings support the technical feasibility of a portable, sensor-integrated EBC analyser with on-the-fly thermofluidic correction and suggest that standardisation may improve the reliability of hydrogen peroxide measurements in EBC research settings. The present findings warrant further study to establish whether this analyser alongside with the correction algorithm can contribute to clinical decision-making, including exacerbation detection and treatment monitoring.

Future work will also prioritise redesign of the mouthpiece to allow bidirectional tidal breathing through the device and integration of an inspiratory filter interface, improving standardisation of EBC sampling and alignment with ERS technical recommendations.

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CRediT authorship contribution statement

Yu-Chih Chen: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Writing – original draft. **Shulin Zhang:** Data curation, Formal analysis, Investigation. **ShaoKai Hong:** Funding acquisition, Investigation, Writing – review & editing. **Sally Meah:** Investigation, Project administration, Resources. **Martyn F. Biddiscombe:** Project administration. **Omar S. Usmani:** Resources, Supervision, Writing – review & editing. **Danny O'Hare:** Funding acquisition, Project administration, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmed.2026.108813.

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