



# ARTP

Association for  
Respiratory Technology  
& Physiology

## INSIDE THIS ISSUE:

FIRST WORD

3

A WORD FROM THE CHAIR

4

ON THE BLOWER

6

HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH  
DYSFUNCTIONAL BREATHING REFERRED TO A  
CARDIOPULMONARY EXERCISE TESTING SERVICE

12

THE PREVALENCE OF PATIENTS ATTENDING FOR REVERSIBILITY  
TESTING FROM PRIMARY CARE REFERRALS WITH NORMAL  
SPIROMETRY THAT FULFIL THE CRITERIA FOR GOLD MILD COPD

18

INTRA-DEVICE REPEATABILITY OF THE NIOX-VERO HANDHELD  
FRACTIONAL EXHALED NITRIC OXIDE MONITOR

24

PROJECT FIZZY

28

FRESH AIR

32

REFRESHER

42

TOP FORUM

44

# inspire



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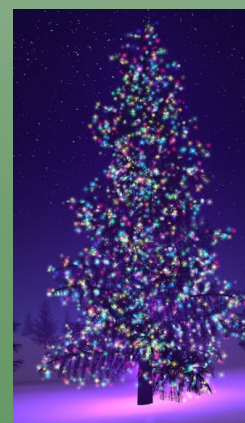
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# FIRST WORD

VOLUME 20, ISSUE 3. DECEMBER 2019



Hello and early Seasonal Greetings to you all. This cracker of an issue (sorry) continues the hitherto unsuspected festive tradition of high-quality respiratory physiology and technology content.

What do we have under the tree? Well, there are articles by three of the four authors who were recipients of ARTP Travel Grants to attend the recent European Respiratory Society congress. The first concerns Dysfunctional Breathing and Quality of Life and the second, regarding reversibility, segues nicely with this issue's 'Fresh Air' column, presented on behalf of ARTP Research and Innovation Committee. See if you agree that the author HAS put the "cat amongst the pigeons". The third article explores a test of exhaled Nitric Oxide and could save you (and your finance department) money! Such conference grants are one of the benefits on offer for being an ARTP member (for the others, see <http://artp.org.uk/en/about-artp/bursary.cfm>).

We have an update on an interesting project from just next door to me, which uses latest technology, big data, children's love of gaming and a sprinkling of Microsoft to try to improve physiotherapy techniques and perhaps verify which are the most effective. Several of these themes we shall no doubt increasingly see emerging in the imminent future.

After these it is time to unwrap the presents we know about—the regular features; the aforementioned 'Fresh Air', 'Top Forum' - highlighting a particularly busy ARTP forum over the past four months. Topics such as alternative measures for height, amplitude and variability of oximetry dips, hypoxic challenge tests and remote monitoring of CPAP are included, the latter featuring a mention of Brexit, which is a subject I am sure will impact on all of us, including perhaps the manufacturers. 'On the Blower' has the latest equipment and manufacturer news and 'Refresher' looking particularly like those sweets of yesteryear (???) gives a quick summary of recent news and social media 'stuff'. A Word from the Chair highlights some exciting long term projects coming to post-festive fruition.

Did anyone manage the summer cryptic crossword? Answers are at the back.

My thanks to all the contributors and of course the Editorial committee for their help with this issue and over the past year. I wish them and you a Merry Christmas and a Happy New Year. ARTP conference 2020 is just around the corner —please come and let me know if you have any ideas for future editions of **INSPIRE** or how you think it can be improved.

**Aidan Laverty**



# A WORD FROM THE CHAIR



Welcome to the December edition of **Inspire**! The darker nights herald the onset of winter, but the wet weather that we've had recently is more like a monsoon season; I hope no one has been too badly affected by flooding in recent weeks.

Many of you will have attended the BTS Winter meeting in London that was held recently, with many ARTP members presenting their research work. With BTS 2019 barely over, preparations are already under way for the BTS 2020 program. ARTP has an exciting opportunity to submit a symposium proposal for the BTS 2020 conference, so if you have a session that you would love to see and an idea of speakers that could present, please contact me or any members of the ARTP Board and we can support you with the proposal. Deadlines are tight for this and all symposia submissions need to be in before 6th January 2020, so get your thinking caps on!

This edition of Inspire promises to be an excellent read with a terrific range of articles that will hopefully take your mind off the chaos and confusion that is the current political state of the UK! They range from a thorough review of the ongoing issues around assessing the reversibility response from Dr. Adrian Kendrick to the issues around the assessment of COPD using GOLD guidelines or standardised residuals from Sara Macarthur and the team at the Royal Infirmary of Edinburgh. Our paediatric colleagues (and non-paediatric too!) will find Project Fizzyo of interest; this looks at how remote monitoring technology can be used to improve the treatment and management of patients with cystic fibrosis.

Your ARTP Board has continued to work on delivering the new website, which should be ready to launch before we attend Conference in January! This exciting development should provide a one-stop portal to access a much wider range of ARTP information, services and benefits, so keep a look out for the launch date. Another thing to look forward to is the eagerly awaited update to the ARTP Guidelines. I would personally like to extend my thanks to everyone who has worked so hard to prepare this extensive document, with special thanks going to Keith Butterfield, Dr Karl Sylvester and Professor Martin Miller for putting the final touches to them. ARTP plan to provide every Lung Function Department with a copy of the guidelines and publish them in a peer reviewed journal to ensure they can be accessed as widely as possible.

## [ BTS 2020 ]

ARTP has an exciting opportunity to submit a symposium proposal for the BTS 2020 conference, so if you have a session that you would love to see and an idea of speakers that could present, please contact me or any members of the ARTP Board and we can support you with the proposal. DEADLINE 6th January 2020



Talking of the [ARTP Conference](#), the ARTP Events Committee are putting the final touches to what we hope will be an educational program with something for everyone – the most current version is available on the [website](#) and the calibre of the speakers and sessions promises to be superb. We have a number of manufacturers specialist sessions, a dedicated sleep and paediatric track and an Early Careers session on both days. We are also pleased to announce that we had a record number of scientific abstracts submitted to the ARTP Research Committee, which has enabled us to present an exciting and stimulating poster discussion and thematic poster session. The entertainment program promises to be as fun-packed as ever, with the Gala dinner and awards ceremony to close the whole event and we look forward to seeing you there.

The New Year will ring in a number of changes from the ARTP Education Committee, who are working incredibly hard on developing a new format for the Professional Examinations, which will ensure that the quality in training and education that is the hallmark of ARTP is maintained. The ARTP Education and Training Courses 2020 brochure is almost ready for publication and demand is sure to be high, with many courses already having a waiting list, so book early! The courses have been developed by the ARTP education committee to inform, support and develop all healthcare professionals working in and around the respiratory and sleep environment. Not content with all of this, ARTP Education has a number of other exciting educational developments in the pipeline for 2020, so watch this space for updates!

As always, I'd really love to hear your feedback and suggestions for what you would like from [your](#) ARTP.

Wishing you and your loved ones the best of the season's festivities and hoping you all enjoy some well-deserved time away from work. I look forward to seeing many of you at the upcoming annual Conference in Birmingham; please register for conference as soon as you can. I really hope you enjoy this edition of Inspire. Until next time, feel free to contact me at [chair@artp.org.uk](mailto:chair@artp.org.uk).

Matt Rutter  
Alan Moore  
Prof. Brendan  
Cooper

# ON THE BLOWER

This edition of 'On the blower' has the latest product updates from Intermedical, Drive Devilbiss, Pari and S-Med.

## *Manufacturers Survey*

*A big thank you to everyone who took the time to complete this years manufacturers survey. We have had another tremendous response and I look forward to announcing the winners at the ARTP conference in Birmingham.*

## PRODUCT UPDATES:

CLICK ON MANUFACTURER LOGOS TO BE TAKEN TO THEIR WEBSITES



Intermedical are pleased to announce that they have signed a distributor agreement with Ventica®, part of Revenio Group Corporation, a health tech group based in Finland.

Ventica® System provides physicians and physiologists with a reliable, quantitative assessment of asthmatic children aged 5 years and younger. The non-invasive measurements are performed overnight while the child is sleeping at home in their own bed.

Ventica® calculates variability in night-time tidal breathing and is based on a novel application of impedance pneumography, indirectly measuring relative lung volume changes and derived flow rate profiles during breathing using chest electrode configuration.

The Ventica® Recorder is set up by a physiologist or physician. The parents are educated on the use of the device. At home, parents place the electrodes near the child's armpits. Alternatively, the electrodes can be placed by the healthcare professional during the office visit.

After gathering a full night's measurement data, Ventica® is used to identify a child's expiration phases during restful sleep. Proprietary software then calculates the correlation coefficients between all identified expiratory flow-volume curves. The final result of the analysis is the child's Expiratory Variability Index (EVI), a single number score which accurately and reliably indicates an individualised level of respiratory variability which is displayed on a simple report.





## Drive DeVilbiss Healthcare Introduce the iGo2 Portable Oxygen Concentrator

Drive DeVilbiss Healthcare are excited to announce the launch of the iGo2 Portable Oxygen Concentrator (POC).

Built upon a 130-year-old legacy of quality, the high performance iGo2 is the first of its kind to use patented SmartDose Technology, which automatically adjusts the dose of oxygen to a patients' breath rate. Consistently delivering more oxygen when needed eliminates the need to manually adjust oxygen settings. The iGo2 also offers a standard PulseDose delivery mode alongside SmartDose.

The iGo2 features a protective, rugged overmould for an added layer of protection, and a Pressure-Vacuum Compressor System (PVSA) that removes nitrogen and humidity to reduce sieve bed wear and extend the time before the unit needs to be replaced. The POC also features a sensitive conserver trigger (0.05 cm H<sub>2</sub>O) that detects patient breathing at lower pressures.

Weighing just 2.2kgs, the lightweight and easy-to-carry iGo2 promotes a more active lifestyle. The battery and LCD screen are located on top of the unit and can be accessed while in the over-the-shoulder carry case. Other features include a rechargeable battery and AC/DC adaptors for easy charging wherever the user goes.

The iGo2 has a 3 year limited warranty and is Federal Aviation Administration (FAA) compliant for in-flight use.

To learn more about the iGo2 POC please go to [www.igo2poc.com](http://www.igo2poc.com)



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## PARI Medical Ltd is celebrating its 25th Anniversary this year

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Mal Apter, Country Manager says "At PARI our mission is to improve the lives of those affected by respiratory diseases and those who provide care to them. Through the continued dedication of the team here in the UK and with the support of our colleagues throughout the world, we aim to ensure that our customers can continue to rely on PARI, long into the future."







## RXiBreeze – a portable home use CPAP solution

Until now, PORTABLE CPAP such as the Z1 & Transcend devices have purportedly been a poor imitation of the home CPAP product. Not intuitive, varying degrees of difficulty with set up, settings and use, noisy with higher noise levels, stability and delivery fluctuations. But now the RXiBreeze offers portability with all the functionality of the major home CPAP device currently on offer. The difference? Is in the detachable main console for travel, no need to buy a secondary expensive unit.

### Features:

- 13+ hr Battery, Main Console Clicks on Top into Position
- HME filters to Enhance Humidification During Travel
- Bluetooth Wireless iPOM SpO<sub>2</sub> Watch for Monitoring\*
- Smart Phone Connectivity
- iMatrix Software

\* Sold separately



### Home or Away:

The new RXiBreeze has been designed using the highest industrial grade hardware platform and implementing ResVent's high performance blower, coupled with touch screen sensitivity that is equal to the latest smart phones and a comprehensive data management system, the RXiBreeze opens up CPAP devices not only to a new level but a new era.



### Advantages:

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## S-Med Ltd – S-News

### Domino V3.0



S-Med are pleased to announce the latest release of our DOMINO Software. This new version brings together the different versions of DOMINO and DOMINOlite into one version. Domino V3.0 has been completely rewritten from the ground up and is now fully 64-bit compatible and also certified to run on Windows 10. We will be rolling this out across the country in the next few months.

Key features include:

- ◇ Full support for SOMNOtouch, SOMNOscreen and SOMNO HD hardware for both ambulatory and on-line recordings
- ◇ New Custom Report Designer with Export to MS Word .DOCX format
- ◇ Full support for our Home Sleep Camera for ambulatory recordings with synchronised Video. It is now also possible to fully edit video recorded on the HSC
- ◇ Anonymisation of recording folders to comply with GDPR regulations

In order to run DOMINO V3.0, you will need a computer running a 64-bit version of Windows.

Please contact us if you are interested in upgrading and we will provide you with details of computer requirements.

As always, software updates continue to be free of charge!





**VITALOGRAPH would like to wish all of the ARTP membership a very Merry Christmas and a prosperous New Year!**

2019 has been an exciting year for Vitalograph and 2020 promises to be even better, especially for our loyal current customers and prospective new partners as we roll out new solutions and services.

This year's ARTP conference at the Hilton Doubletree in Glasgow was a busy one for us as we held exclusive interactive demonstrations of our planned PFT equipment and software. Our workshops were fully booked, and feedback shows they were a huge success. With that in mind, we would like to let you know that we plan on holding two workshops again at next year's conference in Birmingham, keep an eye out for further details in the coming weeks – you won't be disappointed!

We invite you to come talk to us, visit our stand and book into our workshops for a taste of what the future holds and a true alternative to the status quo. If you are unable to come to the conference or would like a personal conversation please contact us on 01280 827110, email us at [sales@vitalograph.co.uk](mailto:sales@vitalograph.co.uk) or visit our website [www.vitalograph.co.uk](http://www.vitalograph.co.uk).

## Health related quality of life in patients with dysfunctional breathing referred to a cardiopulmonary exercise testing service.

Julia Rogers

Wrexham Meilor  
Hospital, Wrexham

### Introduction

Dysfunctional breathing (DB) is a disorder characterised by an abnormal pattern of breathing. One proposed definition is '*an alteration in the normal biomechanical patterns of breathing that result in intermittent or chronic symptoms which may be respiratory and/or non-respiratory*'<sup>1</sup>. Symptoms of DB include shortness of breath at rest, unusual shortness of breath during exercise, dizziness, chest pain, tingling, sighing, 'air hunger' and general fatigue<sup>2</sup>. There is currently no 'gold standard' diagnostic method for DB. Cardiopulmonary exercise testing (CPET) can help to identify abnormal respiratory patterns associated with DB, such as hyperventilation, frequent sighing and irregular rate and volume of respiration (Barker and Everard, 2015)<sup>1</sup>. CPET can also help to identify other disorders that may be causing the patient's symptoms e.g. ischaemic heart disease. Anecdotally, discussion with patients with DB at our centre has often revealed a high degree of functional limitation and anxiety about their symptoms. Chenivesse et al<sup>3</sup> hypothesise that quality of life (QOL) may be reduced in DB due to a number of factors including limited recognition by the medical profession, as well as exercise intolerance and unpleasant breathlessness at low exercise intensity. This study aimed to measure health related QOL in DB using the Short Form 36 Health Survey (SF-36) and to compare our results to Welsh normal values extracted from the 2015 Welsh Health Survey (WHS). Ethical approval for the study was granted by the London – Surrey Research Ethics Committee in January 2018.

## Methods

CPET data was collected using a calibrated computer based exercise system (Ultima Cardio2 CPET system, Medgraphics) and an electromagnetically braked cycle ergometer (Ergoselect 200, Medgraphics). In order to assess if an exercise response was abnormal or not, we compared the response to a predicted 'normal' response, using the nine-panel plot described by Wasserman et al<sup>4</sup> and a set of reference values.

Reference values for CPET are subject to a number of limitations relating to the precision of the values, methodological defects and selection bias<sup>5</sup>. We consider these limitations when assessing the response to CPET and the result taken in context with clinical symptoms, co-morbidities and the patient's current level of exercise.

We measured health related QOL using a previously validated questionnaire, the SF-36 version 2<sup>6</sup>. The questionnaire is a generic measure of health status and provides an eight-scale profile of health and well-being. We chose a generic questionnaire as there is currently not a condition-specific questionnaire designed for those with dysfunctional breathing, and it would enable us to compare scores across different conditions. The eight dimensions measured by the SF-36 are physical functioning, role limitations (physical), bodily pain, general health perceptions, energy and vitality, social functioning, role limitations (emotional) and mental health. There are also two summary scores that can be calculated: physical health component summary score and mental health component summary score<sup>7</sup>.

Age (years) - mean (range)	61 (31-88)
Male/Female ratio	6/5
BMI (kg/m <sup>2</sup> ) – mean (range)	31 (22-37)

Table 1—Patient Characteristics

We recruited eleven patients. All patients completed a symptom limited CPET. We elected not to use physiological markers of maximal effort in our study but relied on symptom limitation as reported by the patient. This was because, in our clinical experience, many patients with DB stop exercising before reaching these points because they are limited by the sensation of breathlessness and we did not want to exclude these patients from the study, especially as they were likely to be the worst affected by the condition. To classify a test as showing DB the CPET response had to be normal or in keeping with known co-morbidities, show an erratic pattern of breathing and symptoms reported correlating with their usual symptoms. Figures 1 and 2 are of ventilatory equivalents and end- tidal partial pressures of oxygen and carbon dioxide against time. These were used to aid in the identification of an abnormal pattern of breathing.



Figure 1. Dysfunctional patterns of breathing

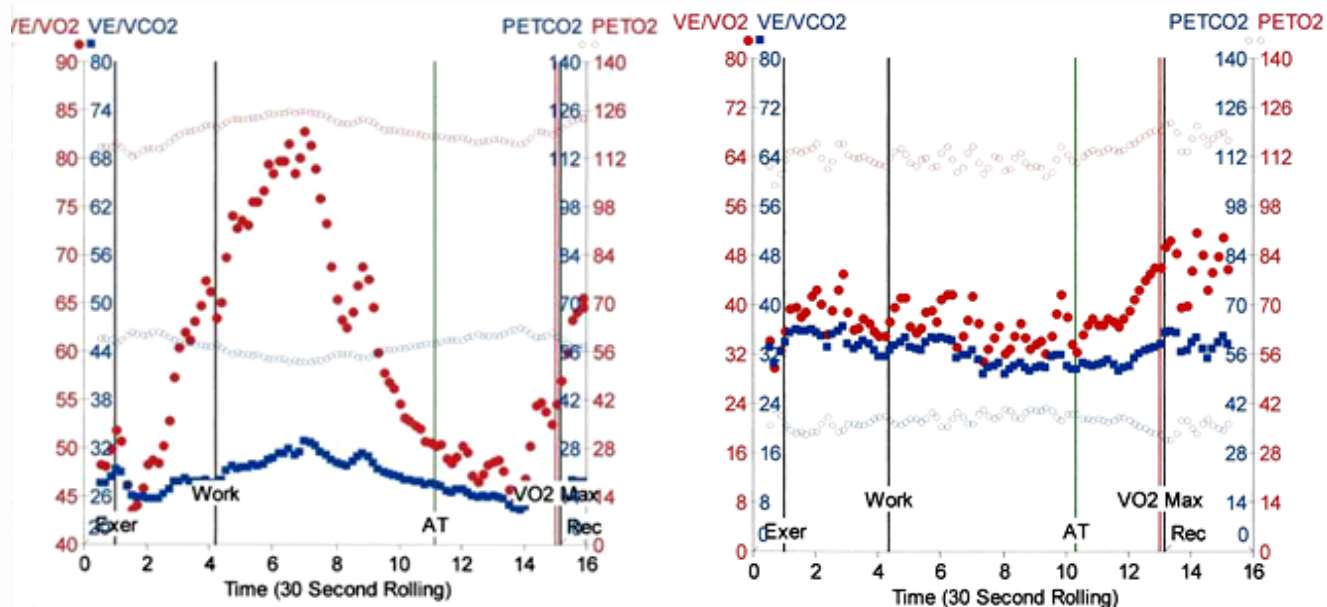
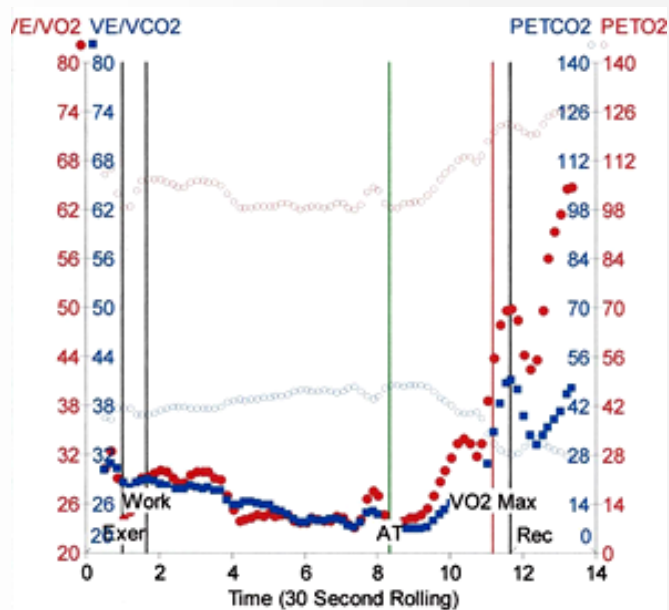


Figure 2. Non-dysfunctional breathing



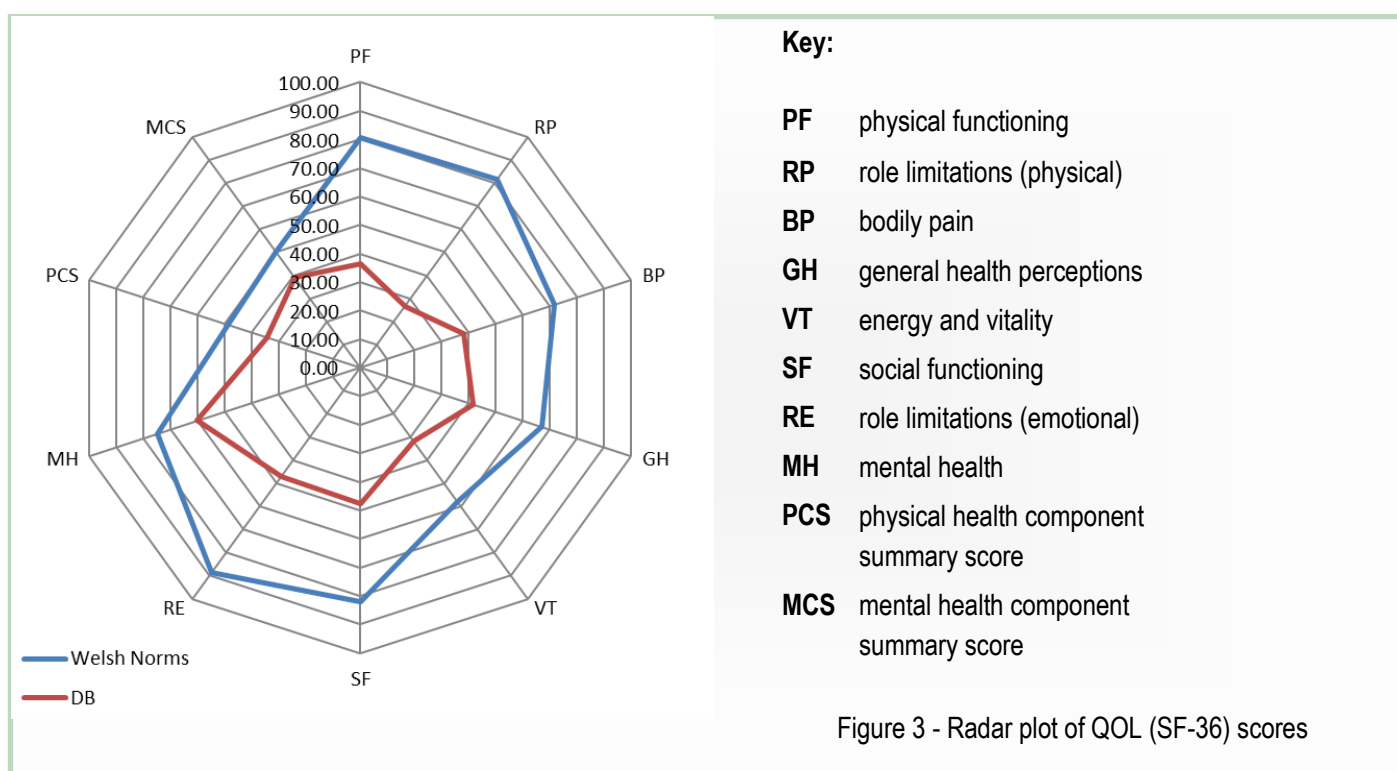
## Results

VO <sub>2</sub> peak % predicted	88.7 (20.0)
V <sub>E</sub> /VCO <sub>2</sub> slope	28.9 (5.1)
Respiratory rate at VO <sub>2</sub> peak	40.7 (6.3)
Breathing reserve at VO <sub>2</sub> peak (% predicted)	40.5 (14.5)
Heart rate at VO <sub>2</sub> peak	123.8 (32.0)
VO <sub>2</sub> /work rate slope	11.6 (1.0)

Table 2 - Main CPET results - (mean/SD)

The reason for stopping testing was breathlessness in eight patients and leg fatigue in three.

Breathlessness would be an expected sensation in patients with DB. The patients that stopped due to leg fatigue may experience DB sensations more at a lower level of exercise, although none of the patients had DB that completely normalised after the AT. Seven patients achieved a  $\text{VO}_2$  peak of greater than 80% of their predicted value (considered normal). Four patients did not achieve this but had no other detectable abnormalities during CPET other than the presence of an erratic breathing pattern. It is likely that most of the patients had some degree of deconditioning; many cite a 'slowing down' due to their symptoms of breathlessness and this may partly account for the reduction in  $\text{VO}_2$  peak in these patients. Seven of the participants had current co-morbidities (e.g. mild bronchiectasis, mild left ventricular dysfunction) or had a serious event in their medical history (e.g. myocardial infarction, pulmonary embolism) although these were considered by the referring physician to be either resolved or out of proportion to their symptoms. One of these patients had a previous diagnosis of moderate COPD (chronic obstructive pulmonary disease) however, their transfer factor for carbon monoxide was within normal limits and they were considered to be disproportionately breathless; this patient was found to hyperventilating throughout CPET. Overall, four patients were considered to be hyperventilating with high respiratory rates throughout CPET, associated with a raised  $\text{VE}/\text{VCO}_2$  slope. In the absence of pathology causing ventilation perfusion mismatching this can be due to an increase in dead space ventilation caused by taking fast, shallow breaths. Measurement of  $\text{PaCO}_2$  by arterial blood sampling can help to distinguish between these<sup>8</sup>; unfortunately, we do not have arterial blood gas sampling available to us at our centre so we highlight this caveat in any report where ventilatory equivalents are abnormal.



## QOL scores

Figure 3 is a Radar plot showing differences between means between our patient group with DB and North Welsh normal values (age 30+) taken from the 2015 WHS. SF-36 domains are presented as mean scores ranging from 0-100. Zero represents the worst possible QOL with 100 the best possible QOL in that domain.

## Discussion

Our study has found that our patients with DB have a significantly lower QOL in all domains of the SF-36 than Welsh normal values. We cannot attribute the reduced QOL in whole to DB in our patient population because of the many factors that can affect this concept; however, we can hypothesise why DB may reduce QOL in our patients. The largest differences are in RP and RE. Limitations in physical activity could be caused by the sensation of breathlessness, the main complaint in most individuals with DB. Physical deconditioning may be a contributory factor as DB symptoms cause patients to be less active than they may have been previously. Emotional distress can occur due to physical limitations and uncertainty over diagnosis. The smallest difference is in the MH (mental health) domain. This is surprising, as we would have expected a more adverse effect on mental health caused by the physical and emotional role limitations that our patient group has. This finding may be because the SF-36 cannot adequately investigate mental health using a small number of questions, or that mental health is not as affected in our patient group as we might initially have thought. It is not clear why bodily pain is higher in our patient group. Only one patient reported a potential confounding factor (osteoarthritis). It may be that accessory respiratory muscle use and muscular imbalances are present, causing pain and discomfort. Chest pain and cramp is also a feature of DB and this could be a contributory cause. Reduced vitality could be explained by tiredness or fatigue brought on by the unpleasant sensation of breathlessness. Use of accessory muscles of respiration can increase the work of breathing and cause discomfort. Social functioning could be affected if patients feel that they cannot engage in social activities due to their symptoms. It may be that DB sufferers also find difficulty in explaining their symptoms to others in social situations due to a lack of clear diagnosis and a lack of awareness of the condition. If there is uncertainty around diagnosis and potential progression of symptoms this is also likely to have an adverse effect on QOL. Our results are comparable in many of the SF-36 domains to that found in conditions such as moderate COPD<sup>9</sup> and symptomatic congestive heart failure<sup>10</sup>.

## **Conclusion**

Our study has found that patients with a dysfunctional pattern of breathing identified using CPET and clinical symptoms have a reduced quality of life in all SF-36 domains. Although our sample was small and probably at the more severe end of the DB spectrum symptomatically, this highlights the potential impact on sufferers and the need for recognition and treatment of the condition.

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The prevalence of patients attending for reversibility testing from primary care referrals with normal spirometry that fulfil the criteria for GOLD mild COPD (chronic obstructive pulmonary disease).

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Edinburgh

### Introduction

COPD has a high mortality and morbidity rate and is often underdiagnosed<sup>1</sup>. It has been estimated that the third leading potential cause of misdiagnosis of COPD was spirometry errors<sup>2</sup>. To ensure quality and aid diagnosis, the Respiratory Physiology Service in Edinburgh has a pathway whereby general practitioners and prescribing nurses in primary care can directly refer patients for reversibility testing if they are querying whether the patient has COPD. Within the service pulmonary function tests are interpreted using standardised residuals but when interpreting primary care reports GOLD COPD guidelines are used<sup>3</sup>. A cut off of FEV<sub>1</sub>/FVC ratio <70% is used to determine airflow obstruction but this may overestimate COPD prevalence in older patients<sup>3</sup>. For older patients a ratio <70% may be within the normal range thus leading to potential confusion.



## Aims

Do patients attending for reversibility testing that fulfil the criteria for GOLD mild COPD have normal ventilatory capacity based on standardised residuals (SRs)?

## Methods

Patients from a primary care referral source with clinical details of potential COPD performed baseline spirometry at the Respiratory Physiology Service, Edinburgh, using a Vitalograph Alpha, measuring FEV<sub>1</sub>, FVC, VC and PEF. Then 2.5mg Salbutamol was administered via nebuliser if deemed necessary (as per the NHS Lothian direct access pathway, see Figure 1). Patients that were now non-symptomatic and above predicted values did not have salbutamol administered. Post-bronchodilator spirometry was performed 20 minutes later and the results interpreted using GOLD COPD criteria (Table 1) and also SRs (ECCS predicted equations were used).

GOLD Classification	FEV/VC ratio %	FEV % predicted	Comment on AFO
GOLD 1	< 70 (symptomatic) or < LLN	80 and >	Mild
GOLD 2	< 70	50-79	Moderate
GOLD 3	< 70	30-49	Severe
GOLD 4	< 70	< 30	Very Severe

Table 1. GOLD criteria for classification of COPD

(adapted from [https://goldcopd.org/wp-content/uploads/2018/11/GOLD-2019-POCKET-GUIDE-FINAL\\_WMS.pdf](https://goldcopd.org/wp-content/uploads/2018/11/GOLD-2019-POCKET-GUIDE-FINAL_WMS.pdf)).

Baseline and post bronchodilator results based on SRs:

1. Normal (all SRs between -1.65 to 1.65)
2. Suggestive of Restriction (SR low FEV<sub>1</sub>, VC but ratio within normal range)
3. Mild obstruction (low ratio >-1.65 and FEV<sub>1</sub> normal or <-2.5)
4. Moderate obstruction (low ratio >-1.65 and FEV<sub>1</sub> between -2.5 and -3.5)
5. Severe obstruction (low ratio >-1.65 and FEV<sub>1</sub> >-3.5)

Post-bronchodilator results based on GOLD severity definitions:

1. Normal
2. Suggestive of restriction
3. Mild obstruction
4. Moderate obstruction
5. Severe obstruction
6. Very severe obstruction

Patients were excluded if they could not perform reproducible spirometry. The results were collated from 10/01/18 to 10/07/18, separated into 4 distinct groups and analysed. The groups were:

**1:** normal spirometry, above predicted values, **2:** post-bronchodilator results showing normal SRs but mild COPD using GOLD criteria, **3:** different post-bronchodilator classification to GOLD and **4:** post-bronchodilator SRs that concur with GOLD.

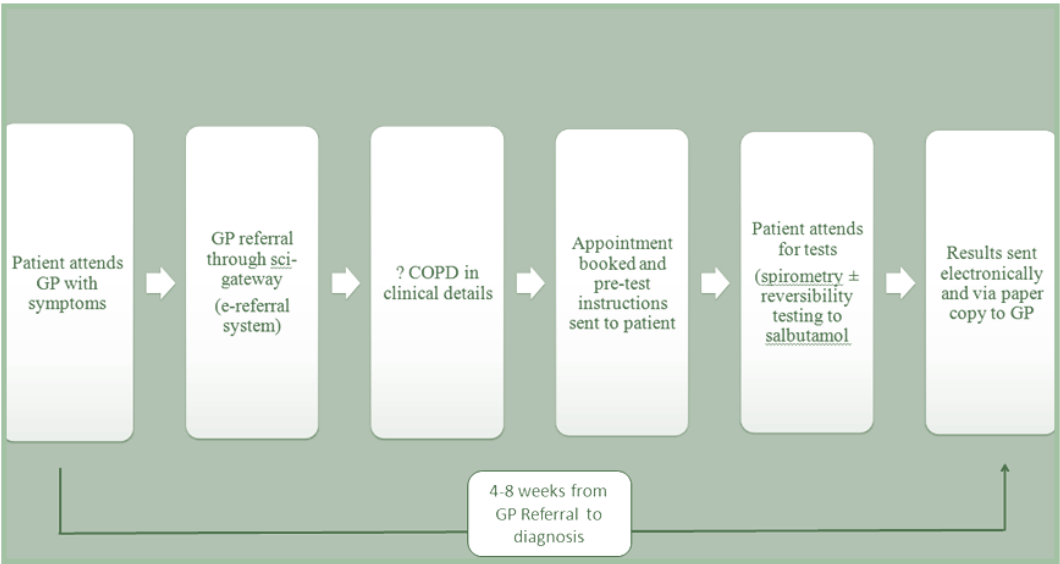


Figure 1: NHS Lothian Respiratory Physiology GP direct access pathway for patients with potential COPD

Results

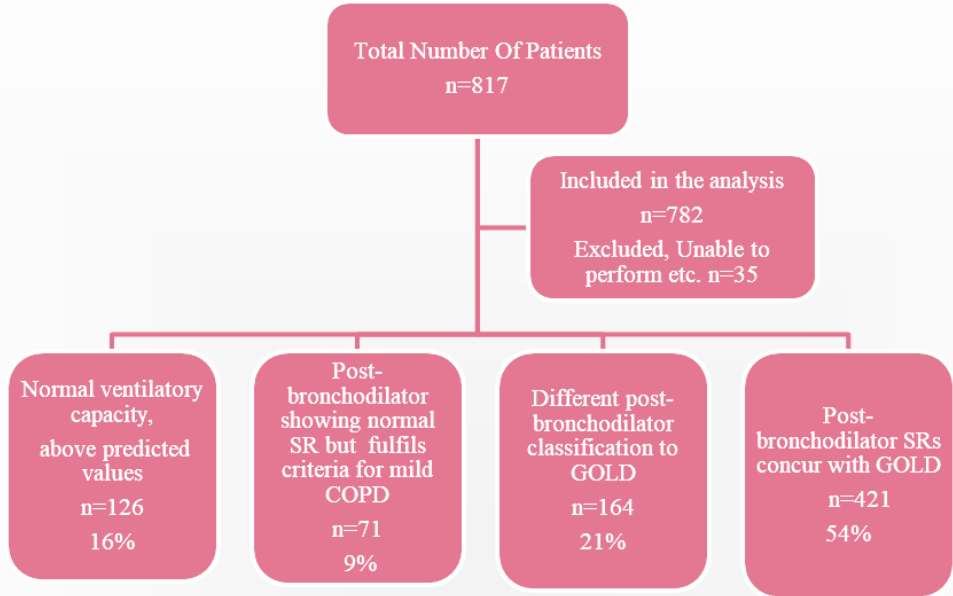


Figure 2: Results summary

Used Inhalers (n=14)	Unable To Perform (n=14)	Other (n=7)
	Including: <ul style="list-style-type: none"><li>* Due to stroke (2)</li><li>* Due to cough (2)</li><li>* ?Max effort (1)</li></ul>	<ul style="list-style-type: none"><li>* Angina (1)</li><li>* Deaf: no result even with BSL interpreter (1)</li><li>* Inappropriate behaviour and language throughout test (1)</li><li>* Had baseline test but did not want salbutamol nebuliser (1)</li><li>* Nervous (1)</li><li>* Patient inebriated (1)</li><li>* Unable to comprehend test (1)</li></ul>

Table 2: Reason for Exclusion

		Total (n=782)	Normal Spirometry, Above Predicted Values (n=126, 16%)	Post- bronchodilator showing Normal SR but Mild COPD (n=71, 9%)	Different Post- bronchodilator Classification to GOLD (n=164, 21%)	Post- bronchodilator SRs Concur with GOLD (n=421, 54%)
<b>Gender</b>	M	358	45	42	84	187
	F	424	81	29	80	234
<b>Age years</b>	Mean	62	61	67	66	56
	Range	31-94	31-93	47-85	43-89	31-94
<b>Smoking History</b>	Y	437	65	30	97	245
	X	304	53	35	64	152
	N	41	8	6	3	24
<b>BMI kg/m<sup>2</sup></b>	Range	17-55	17-51	20-38	16-46	17-55
	<18.5	16	2	0	10	4
	18.5-24.9	192	28	16	49	99
	25-29.9	250	50	26	48	126
	30-39.9	288	38	29	52	169
	≥40	36	8	0	5	23

Table 3: Patient demographics

## Discussion

More female patients than males attended for appointments which is in keeping with other published literature<sup>4</sup> and also seems to reiterate the findings that women are more likely to develop COPD even with a lesser cigarette exposure than men<sup>5</sup>. The average age of patients attending was 62 years which is in keeping with the British Lung foundation statistics for people newly diagnosed with COPD (>40 years)<sup>6</sup>. The vast majority of patients attending for testing were smokers or ex-smokers (n=741) which is unsurprising as this is a well established risk factor for the development of COPD<sup>7</sup>. A smaller number of patients (n=41) were non-smokers but it has been show that fumes, dust, air pollution and genetic disorders can also cause COPD<sup>7</sup>.

## Conclusion

9% of patients attending for reversibility testing had results that would fulfil the GOLD criteria for mild COPD but are normal using SRs.

Results should be interpreted with other clinical risk factors and symptoms to avoid misdiagnosis<sup>3</sup>.

In the service an additional comment is now added to the reports to highlight this issue (Although post bronchodilator results would support a diagnosis of COPD using GOLD criteria please note the FEV<sub>1</sub>/VC ratio exceeds lower limit of normal or can be normal for this patient).

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## Intra-device repeatability of the NIOX-VERO handheld fractional exhaled nitric oxide monitor

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### Abstract

#### Background

The fraction of exhaled nitric oxide has increasingly been used as a non-invasive biomarker of airway inflammation. Current European Respiratory Society recommendations from 1999 state that repeated exhalations are performed until two nitric oxide values agree at the 5% level. In the preceding years, there has been marked advancements in exhaled nitric oxide measurement devices using electrochemical sensors. However, while the intra-repeatability of the NIOX-MINO has been investigated, such data have been largely obtained with subjects without a respiratory condition and not using the NIOX-VERO device. **Objective:** The objective of the current study was to determine the feasibility of only obtaining a single fraction of exhaled nitric oxide measurement by assessing the intra-repeatability of the NIOX-VERO, with a sample representative of the population referred for respiratory assessment by the paediatric respiratory medicine service at the Evelina London Children's Hospital; due to the relatively high cost to number of sensor uses ratio. **Methods:** Four-hundred and twenty-one datasets were included (aged 4–17 years) of patients who had paired fraction of exhaled nitric oxide measurements using the NIOX-VERO. The intra-repeatability of the paired fraction of exhaled nitric oxide measurements were analysed using a one-way repeated measures analysis of variance test. **Results:** No significant difference was observed between the first and second paired fraction of exhaled nitric oxide measurements ( $p = 0.153$ ). **Conclusions:** The findings of the current study go further to support the use of a single fraction of exhaled nitric oxide measurement within clinical practice.

## Introduction

Reliable measurement of the fraction of exhaled nitric oxide (FeNO) is an important tool that has been increasingly used within respiratory medicine as a biomarker of eosinophilic airway inflammation<sup>1</sup>. The fraction of exhaled nitric oxide (FeNO) has increasingly been used as a non-invasive biomarker of airway inflammation.

While the intra-repeatability of the NIOX-MINO has been investigated using an electrochemical sensor, such data have been largely obtained with subjects without a respiratory condition<sup>2</sup>. Also, to our knowledge, the intra-device repeatability of the NIOX-VERO device (Figure 1) has not previously been investigated.

In addition, the sensor of the NIOX-VERO is time-limited and the number of times measurements are



Figure 1. The NIOX-VERO device.

repeated adds to the operational cost of obtaining FeNO measurements. The American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines for measuring FeNO state that two measurements should be taken, unless under financial constraints, when one measurement is acceptable<sup>3</sup>.

Within the Evelina London's Respiratory team, two FeNO measurements are currently taken per test, equating to ~1600 separate measurements per year. The cost of one FeNO measurement can be up to £10.61. Therefore, the total annual cost of the FeNO test within the Evelina London is ~ £16976.

To improve the cost effectiveness of obtaining FeNO measurements and for the application of the measurement in wider healthcare settings under tighter financial constraints, the current study aimed to determine the intra-repeatability of the NIOX-VERO with a sample representative of the patients referred for respiratory assessment by the paediatric respiratory medicine service at the Evelina London Children's Hospital. Given that the ATS/ERS guidelines recommend two consecutive measurements, we also aimed to determine the feasibility of reducing the recommended two measurements to one, to substantially reduce the financial cost of performing the test.

Method

Four-hundred and twenty-one datasets were included (aged 4–17 years) of patients who had had paired FeNO measurements using the NIOX-VERO.

FeNO measurements were taken prior to any other respiratory test performed on their visit, as measurements have shown to be reduced following spirometry<sup>4</sup>.

The intra-repeatability of the paired fraction of exhaled nitric oxide measurements were analysed using a one-way repeated measures analysis of variance test.

Results

No significant difference was observed between the first and second paired FeNO measurements ( $p = 0.153$ ) (Table 1).

Comparison of the two FeNO measurements for the NIOX-VERO device revealed strong agreement between the two measurements (Figure 2). There was little bias towards either of the two FeNO measurements being higher, suggesting strong intra-device repeatability. There was also a strong correlation shown between both of the recorded FeNO measurements (Figure 3).

	Bias	95% limits of agreement
FeNO Measurements 1 & 2	-0.08	-10.43 – 10.28

Table 1. Bias and 95% limits of agreement between the two consecutive FeNO measurements. .

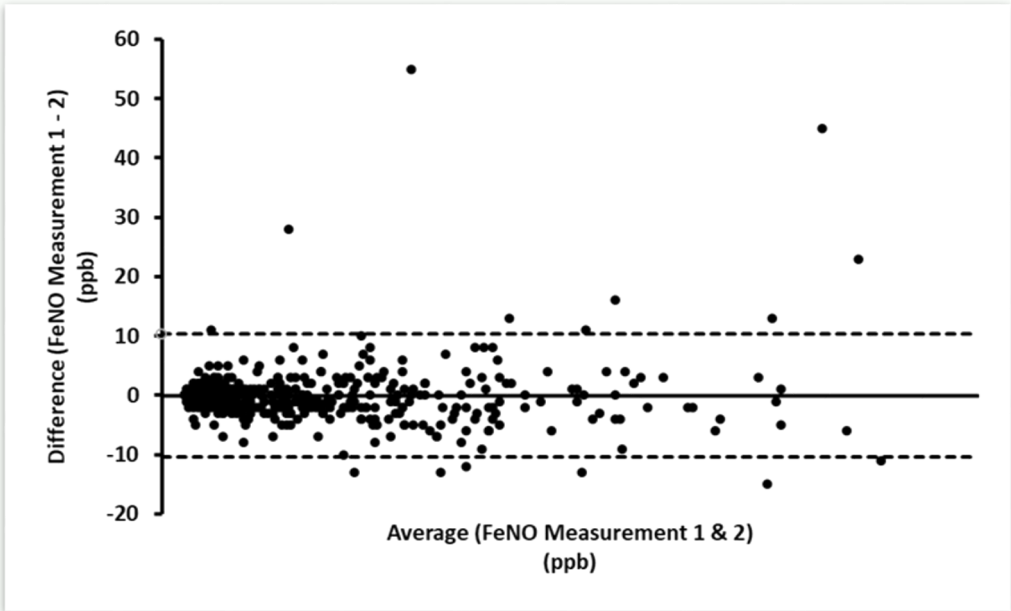
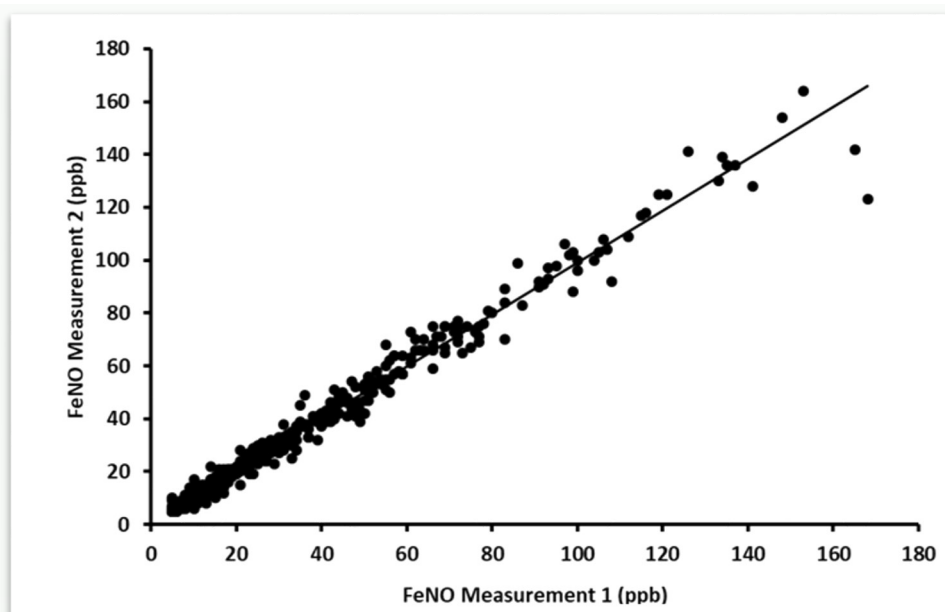


Figure 2. Bland–Altman plots showing the agreement between two consecutive FeNO measurements.



**Figure 3.** Correlation between two consecutive FeNO measurements.

## Discussion

This study is the first to examine the intra-device repeatability of the NIOX-VERO handheld fractional exhaled nitric oxide monitor in a cohort of paediatric patients under the care of our department. We have demonstrated no significant differences in the first and second paired FeNO measurements. The first and second paired measurements were also strongly correlated with one another.

Although ATS/ERS guidelines for measuring FeNO recommend collecting two measurements per test<sup>3</sup>, data from the current study suggests that performing two sequential FeNO measurements can be reduced to a single measurement without affecting the validity of the test outcome when assessing a paediatric population. Therefore, this study provides a significant financial incentive to those using the NIOX-VERO device to reduce their number of measurements to a single measurement. (~50% or £8488 per year).

## Conclusion

We have demonstrated strong intra-device repeatability in the NIOX-VERO device when used clinically in a paediatric population, going further to support the use of a single FeNO measurement within clinical practice. There was strong agreement between two consecutive FeNO measurements, suggesting that significant financial savings can be gained from performing one measurement without compromising the validity of results obtained in a clinical setting. Further research could consider whether a similar conclusion can be drawn from an adult cohort.

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# Project Fizzyo

Remote monitoring and gamification of physiotherapy for children with cystic fibrosis

When people with CF were asked what the top priorities should be for research in cystic fibrosis (CF), reducing the treatment burden was found to be the top priority<sup>1</sup> and when asked which treatment they think is the greatest burden they said airway clearance physiotherapy<sup>2</sup>.

Physiotherapy is an integral part of treatment for people with CF. Airway clearance physiotherapy usually involves breathing a certain way or through a device a set number of times to create pressure or vibrations in the lungs which can help move mucus so that it can be coughed up. Most people with CF do this every single day. Because of the active nature of physiotherapy, blinding someone to what they are doing is not possible, so as such there is limited good quality evidence to guide physiotherapy prescription for people with CF<sup>3</sup>. Treatment is based on physiological principles but not good quality experimental evidence.

There are a wide variety of airway clearance techniques (ACT) and devices routinely used by people with CF (PwCF) including devices that provide positive expiratory pressure (PEP) and PEP with oscillation (OPEP, e.g. Acapella). However the long term clinical effects of different devices and prescriptions remain unknown. Device choice and prescription is mainly driven by patient and practitioner preference. Until recently there was no way to tell how often and what techniques PwCF were doing at home, so optimising treatment for individuals was difficult.

**Project Fizzyo** This is where Project Fizzyo comes in:  
(<https://youtu.be/gm1pi6K1kS4>)

Is there something we can do to improve treatment prescription, and make physiotherapy less of a burden, less boring?

Project Fizzyo is the first study of its kind to investigate using remote monitoring of physiotherapy and the gamification of regular treatments in children and young people with cystic fibrosis.

The remote monitoring of physical activity for the study is done using Fitbits. Using extended API access records of continuous heart rate and foot step data up to 16 months data per child are available. This will be the largest physical activity dataset in children with CF to date.



Image of a child wearing a Fitbit and a Fizzyo ACT sensor on an Acapella ACT device.

Emma Raywood,

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Remote monitoring of airway clearance was not possible with a commercially available sensor. Along with collaborators from Microsoft UK and UCL, we designed a bespoke pressure sensor to attach to a number of existing ACT devices. When designing the sensor it had to be easy to clean, durable and simple to use. The sensor can, as well as recording treatments, be used to control computer games. The aim of the games is to make ACTs more enjoyable and therefore to reduce treatment burden. Gaming for spirometry is already widely used to encourage children to do the best technique and to keep them engaged.

### Spirometry



Using the ACT sensor to control games meant a different approach had to be taken. For ACT physiotherapy the games needed to encourage a regular pattern of breathing in cycles or sets, rather than one maximal exhalation, the player needs to be able to pause for cough/huff without being penalised and the player shouldn't be able to cheat by doing short or no breaths. The gaming framework and especially the calibration of the games took most of the focus for development, making games that work for someone aged 6 years old and someone aged 16 proved to be challenging! In the backend, we also provide a whole set of achievements, high score tables along with the critical analytics services for capturing the breath data captured from the gameplay, all to give better feedback to the players as they progress in the games

The games are all designed in Unity (<https://unity.com>) and are open source (<https://github.com/Fizzyo>). The idea being other developers (maybe even you!) and people with CF can develop their own ideas and build their own games.



Screenshots of some of the available bespoke Fizzyo ACT games

Participants are enrolled in the study for 16 months each, sending daily Fitbit and ACT data via apps on a computer tablet. The study is observational; we did not modify physiotherapy prescription or advise any changes to activity patterns. Gaming is available for the middle 8 months only (interrupted time series design). This means we can measure a baseline without gaming and see if any changes occur when gaming is introduced, when the games are removed we can see if the games are required to sustain any changes in patterns.

We now are fully recruited and have over 130 children, from 3 London paediatric CF centres, daily using remote monitoring sensors and playing the Fizzyo games. Data collection for project Fizzyo is due to continue until late 2020.

Due to the large amount of data generated by remote monitoring, plus electronic patient records (EPR) Project Fizzyo already has a large dataset. Traditional data analysis methods are not sufficient. As such the GOSH digital research environment (DRE, <https://www.goshdrive.com>) is vital for Fizzyo data analysis. It is a data storage and analysis platform which allows de-identified clinical records to be reconciled with data from elsewhere (such as data from the Fitbit and ACT sensor) and analysed by data scientists or researchers in R within a secure environment.

Working with the DRE team and programmers at Microsoft we have developed a data pipeline to process the raw pressure and Fitbit signals for machine learning and unsupervised clustering analyses. We can start to investigate treatment and activity profiles and how they relate to different clinical outcomes. We can use this large and powerful data set to, for the first time, improve and personalise physiotherapy prescription.

## Preliminary results

We have started to analyse the physical activity patterns and the breath data during treatments with and without gaming, and we are starting to see some patterns.

The data is as yet unpublished so we describe the results below.

From the Fitbit data we can see variability in activity profiles. Many of the children are not meeting the 60 minutes a day moderate to vigorous physical activity (MVPA) advised in the government guidelines for all children, whereas others regularly exceed this. We can also start to see strong activity trends and patterns, such as that younger children do more physical activity at break and lunch times than older children. When this dataset is fully analysed it will help to define how activity trackers can be used to monitor and prescribe exercise for children and young people with CF (CYPwCF) in the future. This will help identify which behaviour patterns are associated with the best clinical profiles and personalise advice.

From the ACT data we have found that though all children are given similar instructions on breath length and pressure during ACT there is a large range of what they are actually doing. With some devices having shorter harder breaths than other which are longer and less forceful. We have also been able to see that gaming can modify technique with some participants demonstrating longer blows more in the advised therapeutic range during gaming and some showing more regular adherence to prescribed treatments.

We will investigate how long any behaviour changes are sustained for and if they have an effect on other parameters. When this data set is analysed it will improve the prescription of ACT and we can for the first time start to look at the differences between devices and prescriptions along with associated clinical outcomes to personalise ACT prescription.

# Future Directions

As we want to look at reducing burden of treatment patient feedback is hugely important. So far feedback has been generally positive with parents and children really engaged in the idea and clinical physiotherapists keen to be involved. We are working with our participants to improve the Fizzyo app and sensor as well as the games to ensure it is relevant to what they want.

If we are able to prove there are benefits to the frequency and/or quality of treatments with gaming it is essential we develop this idea further and make it available to more people. This kind of gaming technology has great potential to be applied to other treatments and other conditions. Furthermore the type of analysis we are doing with electronic patient records and machine learning should be used more widely in healthcare and the benefits passed onto patients to improve their lives.

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## Project Fizzyo

### Remote monitoring and gaming for physiotherapy

"His blows are much **better** and it's much quicker when he is playing the game"

"It shows by playing the games he is **working harder** than yesterday"

"It takes **longer to do treatment** when she plays the games **because she wants to** get a high score"

"The games are a **bit boring**"

"She **wasn't bothered** about the games but we got her to have a go and I can see how they can **really help**"

"Even after only a few days, when it works, the game we've tried (the Qubi one) does seem to **encourage good physio**."

"Her technique used to be bad so this has definitely **made an improvement** in her breaths"

James Stockley

ARTP Chair of  
Research and  
Innovation

## Fresh air



Dear Reader, Welcome to 'Fresh Air'. These articles are designed to communicate novel trends in research, innovation and clinical practice from both respiratory and sleep sciences. We aim not only to provide an interesting read but also to incite conversation within the ARTP community that we hope will continue to drive the evolution of physiological practice.

On behalf of the Research and Innovation Committee, we are delighted to present an update on bronchodilator reversibility testing written by **Dr Adrian Kendrick**, a Consultant Clinical Scientist and Senior Lecturer at the University Hospitals Bristol. Dr Kendrick provides expert insight into our current understanding of reversibility testing and proposes a novel approach using evidence-based physiology.

**Dr. Adrian Kendrick**

Consultant Clinical Scientist,  
Department of Respiratory Medicine,  
University Hospitals Bristol

**Putting the Cat  
amongst the Pigeons!**

## Background

This short review will revisit one of the thorns in the side of respiratory measurement – the most appropriate method for the assessment of the bronchodilator response (BDR).

Respiratory tests are used to assess the response of the airways to inhaled bronchodilators. In a patient with no symptoms and normal lung function, there may still be some change in FEV<sub>1</sub> after administering a bronchodilator<sup>1-4</sup>. In many laboratories, the response to bronchodilators is only assessed if the ratio of FEV<sub>1</sub> to VC or FVC (whichever is largest<sup>5</sup>) is <70% or if the referring physician remembers to request it! The 70% value is highly questionable as in men over 36 years and women over 46 years, lower limit of normal for the FEV<sub>1</sub>/VC ratio is <70% due to the normal ageing process<sup>6</sup>.

## Indications for Bronchodilator Response (BDR) Assessment

The indications for performing reversibility studies are -

- Confirm diagnosis of asthma
- Determine reversibility of airway obstruction demonstrated by a reduced FEV<sub>1</sub>/VC ratio or other indicators of flow limitation
- Evaluate alternative drug regimens in patients with known hyper-reactive airways
- Reverse bronchospasm induced by bronchial challenge tests
- Disability determination when the FEV<sub>1</sub> is < 70% predicted
- Pre-operative evaluation when airway obstruction is present
- Evaluation of new inhaled bronchodilator agents
- Clinical trial protocol requirements

Post bronchodilator FEV<sub>1</sub> is also used in the diagnosis of COPD and the determination of the patient's prognosis.

## Factors Influencing the Response

Many factors influence the measured response to an inhaled bronchodilator –

### Severity and nature of baseline obstruction

This determines if the expected response should be large or small. In asthma, the response to bronchodilators may differ according to the severity of the condition. In mild or moderate asthma, considerable improvement may be seen, but severe asthma may be resistant to bronchodilator therapy due to the nature of the airways.

Using the criteria of  $> 12\%$  and  $+200$  mL to define BDR, a patient who has an increase in  $FEV_1$  from 0.90 L to 1.017 L ( $+13\%$  and  $+0.117$  L) would not fulfil the criteria, whilst a patient with an increase in  $FEV_1$  from 2.75 L to 3.108 L ( $+13\%$  and  $+0.358$  L) would. Hence the magnitude of the baseline value will affect the potential classification of a patient meeting the required criteria.

### Class of bronchodilator agent used

Very large responses to  $\beta_2$ -adrenoceptor stimulants are usually only seen in patients with asthma (with a response of  $>50\%$  often seen in asthmatics), a lesser response is usually seen in more chronic asthmatics and in patients with COPD<sup>4</sup>.

### Dose of bronchodilator

The dose administered is often the standard recommended dose for that particular agent, e.g. two puffs of a terbutaline inhaler. Higher doses are delivered by a nebuliser or an MDI plus spacer to establish with certainty if a response is present. There is some evidence that giving higher doses as a routine, without increasing the risks of side-effects may be more beneficial, i.e. 200 mg vs 400 mg of salbutamol.

### Mode of aerosol generation and technique of inhalation

Although the proportion of bronchodilator drug deposited in the airways is approximately the same for both MDIs and nebulisers; the latter deliver a much higher dose and may therefore reflect the maximum obtainable reversibility. Spacer attachments when used with an MDI can increase drug deposition in the airways and therefore increase the potential response to a bronchodilator.

### Timing of test in relation to maximal action of drug

With most  $\beta_2$ -adrenoceptor stimulants, a maximal response is achieved about 20 minutes after administration, though if necessary, the test could be delayed for longer as the effect lasts for around 2 hours.

Anticholinergic agents have a slower onset of action, so the post-bronchodilator tests can be performed 45 minutes after administration. Appreciable bronchodilation should have occurred by then, but a maximum effect may not be seen until 2 - 3 hours later.

### Possible residual effect of previous bronchodilator drug use

Baseline airway obstruction will be affected by previous bronchodilator therapy, whether taken by inhalation or orally. Ideally, therefore, all short acting bronchodilators (both inhaled and oral preparations) should be withheld, based on their pharmacokinetics, for a suitable period before testing is commenced within the laboratory. This should be as long as possible and reflect the duration of action of the drugs in question. However, in some patients it may be impossible for them to withhold their inhaled bronchodilators for any length of time. Thus, it is important that clear instructions are given to the patient concerning bronchodilator use on the day of attendance at the laboratory. In reality, although the pharmacokinetics and pharmacodynamics would dictate longer periods of time, based on the drug half-life, a more pragmatic approach needs to be taken as outlined in the recently published ATS/ERS Spirometry guidelines<sup>7</sup>.



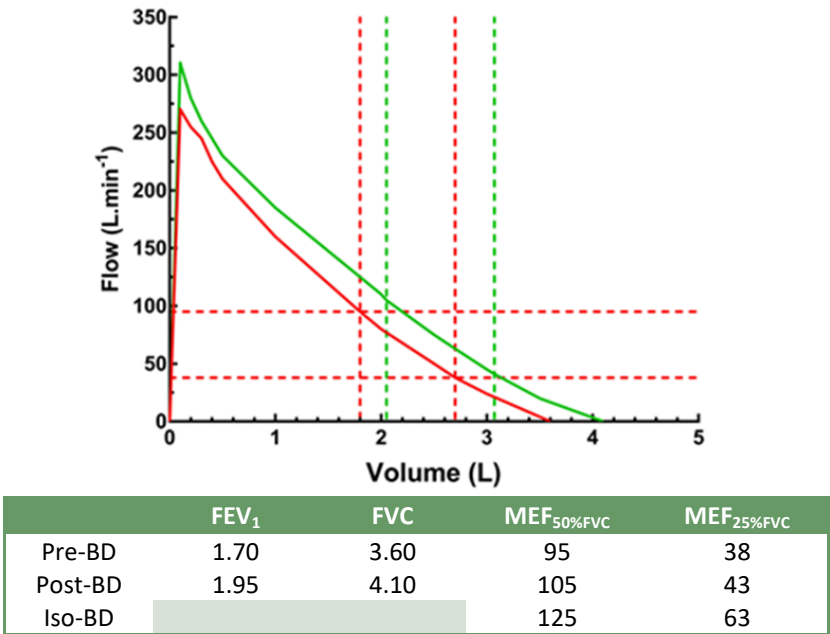


Methods of Assessing Response to Bronchodilators

The most often applied tests and variables are those obtained during a forced expiratory manoeuvre after a full inspiration (FEV<sub>1</sub> and FVC). Although inspiration to total lung capacity may induce a transient increase in bronchomotor tone in most asthmatics, these tests have the advantage that they are reproducible and relatively easy to perform.

It is important to note that many patients with chronic bronchitis, emphysema and COPD will have little or no response in FEV<sub>1</sub> post-bronchodilator but may have a more detectable change in FVC and/or VC<sup>8-12</sup>. Basically, in these patients there is a decrease in the FRC/TLC ratio – i.e. a reduction in the degree of hyperinflation, so the patient finds it easier to breathe as they are now on the slightly steeper part of the lung compliance curve, where the work of breathing is reduced<sup>13</sup>.

Maximal expiratory flow-volume curves are often used to assess the response to inhaled bronchodilators. After bronchodilation, there may be expansion of the whole of the maximal expiratory and inspiratory flow-volume curve with improvement throughout in maximal flows and in FVC. Changes in expiratory flows of MEF<sub>50%FVC</sub> and MEF<sub>25%FVC</sub> (synonymous with the North American FEF<sub>50</sub> and FEF<sub>75</sub>, respectively) are often observed, although these flow rates are affected by the FVC, which may increase<sup>8</sup>. Comparison of the flows can only be undertaken if the volume point from which the Pre-BD flow rate is used to assess changes at the same volume point Post-BD. This is known as the iso-volume point (Figure 1). This simple technique has not been widely adopted by equipment suppliers. Patients may have little or no change in FEV<sub>1</sub> pre- to post-BD, but their flow rates within the smaller airways are improved, potentially resulting in a reduction in their symptoms.



**Figure 1** Pre- and Post-BD (green line) flow-volume curves showing the importance of correctly reporting the flows at MEF<sub>50%FVC</sub> and MEF<sub>25%FVC</sub>. There is an increase in FEV<sub>1</sub> of +250 mL (+14.7%). The FVC also increases by +500 mL (+13.9%). Using the equivalent MEF<sub>50%FVC</sub> and MEF<sub>25%FVC</sub>, there is minimal increase in the flow rates of +10.5% and +13.2%. If the Iso-BD points are taken, which represent the changes in the respective flow rates at the Pre-BD volumes (red vertical dashed lines), then the increases in the respective flows are 31.5% and 65.8% indicating that there is potentially clinically significant improvement in small airway function.



## Expression of Results

The methods of expressing the bronchodilator response can influence the interpretation of the statistical, as well as the clinical significance of the response. There is currently no clear, established standard definition of what constitutes a BDR.

Different criteria for BDR positivity include the Global Initiative for Chronic Obstructive Lung Disease (GOLD)<sup>14</sup>, American Thoracic Society (ATS)<sup>15</sup>, American College of Chest Physicians (ACCP)<sup>16</sup>, major criteria of the Spanish definition of asthma-COPD overlap syndrome<sup>17</sup>, criteria compatible with ACOS in the Global Initiative for Asthma (GINA)<sup>18</sup>, European Respiratory Society (ERS)<sup>19, 20</sup>, the National Institute of Clinical Excellence (NICE)<sup>21</sup>, the BTS guidelines<sup>22, 23</sup>, the joint ATS/ERS guidelines<sup>24</sup> and the current BTS/ARTP guidelines<sup>25</sup>. Some of the criteria for expressing positivity are shown in Table 1.

Guidelines	Ref	Recommendations
ATS (1991)	15	$\geq 12\%$ and $> 200$ mL increase (FEV <sub>1</sub> or FVC)
Quanjer et al (1993)	19	$\Delta$ FEV <sub>1</sub> $> 9\%$ predicted value
BTS/ARTP (1994)	25	160 mL increase in FEV <sub>1</sub> ; 330 mL increase in VC
Siafakas et al (1995)	20	$\Delta$ FEV <sub>1</sub> $> 10\%$ predicted value
BTS/SIGN (2003)	22	$\geq 200$ mL + $\geq 15\%$ increase in FEV <sub>1</sub> from baseline
NICE (2004)	21	$\Delta$ FEV <sub>1</sub> $> 400$ mL
ATS/ERS (2005)	24	$> 12\%$ predicted FEV <sub>1</sub> and $> 200$ mL
GOLD (2007)	18	$> 200$ mL + $> 12\%$ increase in FEV <sub>1</sub> from baseline
BTS/SIGN (2012)	23	$\Delta$ FEV <sub>1</sub> $> 400$ mL
Ward et al (2015)	28	FEV <sub>1</sub> $> 8\%$ predicted
Quanjer (2017)	11	$> +8.0\%$ predicted in FEV <sub>1</sub> from baseline $> +0.78$ in z-Score in FEV <sub>1</sub> from baseline $> +0.64$ in z-Score in FVC from baseline
ATS/ERS (2019)	7	The % change and absolute change in FEV <sub>1</sub> and FVC compared with pre-bronchodilator values are reported. The change in FEV <sub>1</sub> as a %pred FEV <sub>1</sub> or as z-scores avoids sex and height bias.
Aggarwal et al. (2019)	26	$\geq 12\%$ and $> 200$ mL increase (FEV <sub>1</sub> or FVC)

Table 1 Bronchodilator reversibility criteria recommendations from various organisations



More recently, Quanjer has highlighted the use of both the z-score and the %predicted as potentially better ways of determining the BDR<sup>11</sup>. There is clearly a need for clarity, as the most informative way of expressing the results is currently not clear<sup>27</sup>. Another important aspect of the assessment of the BDR is how this relates to disease outcomes and potential survival<sup>9, 12, 28, 29</sup>. These criteria used over time are calculated as per Table 2.

<b><u>Absolute Change (ml) from Pre-bronchodilator Value</u></b>
Post-bronchodilator FEV <sub>1</sub> – pre-bronchodilator FEV <sub>1</sub> (mL)
<b><u>Percentage of Initial Pre-bronchodilator Value (% Initial)</u></b>
$\frac{(\text{Post BD FEV}_1 - \text{Pre BD FEV}_1) \times 100}{\text{Pre BD FEV}_1}$
<b><u>Percentage of Predicted (% Predicted)</u></b>
$\frac{(\text{Post BD FEV}_1 - \text{Pre BD FEV}_1) \times 100}{\text{Predicted FEV}_1}$
<b><u>Percentage of Possible Reversibility (% Possible)</u></b>
$\frac{(\text{Post BD FEV}_1 - \text{Pre BD FEV}_1) \times 100}{\text{Predicted FEV}_1 - \text{Post BD FEV}_1}$
<b><u>ECCS Recommended</u></b>
$\frac{(\text{Post BD FEV}_1 - \text{Pre BD FEV}_1) \times 100}{\Sigma (\text{Pre-BD FEV}_1 - \text{Post BD FEV}_1)/2}$
<b><u>Change in z-score</u></b>
$\Delta z\text{FEV}_1 = \text{Post}, z\text{FEV}_1 - \text{Baseline}, z\text{FEV}_1$
$\Delta z\text{FVC} = \text{Post}, z\text{FVC} - \text{Baseline}, z\text{FVC}$

Table 2. Different calculations of bronchodilator response (BDR). Although FEV1 is stated in the majority of calculations below, the FVC or VC could be equally substituted into many of these.

**Bronchodilator Reversibility Criteria**

The controversies that exist with reference to the expression of results also apply to the determination of what constitutes a clinically or statistically significant response to inhaled bronchodilators. Whatever evidence is taken to be indicative of significant reversibility, this should in all instances, be based on the reproducibility of the pre- and post-measurements made. Poor bronchodilator response may be related to inadequate drug deposition due to poor inspiratory effort or inhalation technique. Some individuals may show a paradoxical response to bronchodilator therapy with flows or volumes actually decreasing. Decreased responses may also be related to effort fatigue from multiple forced expiratory manoeuvres.

Previous practice was to express the change as a percent of the baseline value, leading to sex and size bias in the results as the lower the baseline value the easier it is to achieve a given threshold percentage change. The use of an absolute threshold is either the sole criteria or added to the percentage change. This biases the outcome towards male sex being responders. To overcome these issues it has been proposed that change should be expressed as percent of the subject’s predicted value or as change in z-score so as to be free from sex and size bias<sup>11, 28</sup>.

A change in FEV<sub>1</sub> of > 8% of predicted has been shown to be associated with a subsequent survival advantage that would favour a diagnosis of asthma and active treatment<sup>28</sup>. A change in z-score of > +0.78 is proposed as a clinically meaningful change<sup>11</sup> and an improvement of FVC post-BD of > +0.64 was more pronounced in those with the most severe airflow obstruction, suggesting a clinically important relief of hyperinflation.

Ideally, therefore the BD response should be expressed as  $\Delta$ z-Score for both FEV<sub>1</sub> and FVC with the % predicted response being an acceptable alternative<sup>7, 11, 28</sup>.

To add to this discussion, Fortis et al (2019)<sup>12</sup> has suggested dividing the response of BDR in COPD into 4 categories;

1. No-BDR – no response in either FEV<sub>1</sub> or FVC
2. FEV<sub>1</sub>-BDR – BDR in FEV<sub>1</sub> response only, but none in FVC
3. FVC-BDR – BDR in FVC, but none in FEV<sub>1</sub>
4. Combined-BDR – BDR in both FEV<sub>1</sub> and FVC

The divisions into the 4 classifications are based on ATS/ERS criteria<sup>24</sup>. The conclusion of this study is that BDR in both FEV<sub>1</sub> and FVC indicates a COPD phenotype with asthma-like characteristics and is clinically

### Limitations of Assessing the Bronchodilator Response

The following are the main limitations of assessing the bronchodilator response in patients with respiratory disease. It is not a comprehensive list but serves to highlight important points:

1. Individuals may vary in their response to bronchodilators - 20% - 30% of responsive patients may respond to one agent but not another.
2. Expressing results in terms of percentage change after the delivery of an inhaled bronchodilator relates to the degree of baseline airway obstruction.
3. Increase in FEV<sub>1</sub> or FVC of < 8% is generally within the variability of the measurements and may represent normal reduction in vagally mediated bronchomotor tone. A value of > 8% suggests possible asthma and should be treated.
4. Failure to demonstrate a significant response to a single drug on one occasion does not preclude clinical response and further assessment may be required. The use of very strict criteria (20% increase in FEV<sub>1</sub> plus 400 mL) defines a specific population that is highly likely to have asthma. Responses less than 15% predicted do not exclude the possibility of asthma, nor the possibility that they will have a good symptomatic outcome to vigorous treatment. The decision to treat patients is on clinical grounds rather than laboratory results.
5. Results from patients not performing acceptable or reproducible FVC manoeuvres should be interpreted with caution. Bronchodilator response may need to be evaluated clinically *in lieu* of acceptable spirometry e.g. the patient who coughs during baseline measurements may improve post-bronchodilator delivery. Alternatively, other methods of assessing response that require considerably less effort, such as airways resistance measurements, may be an acceptable alternative if available.

6. Ideally, the response to inhaled bronchodilator should be compared to the response observed when placebo alone is delivered although in reality this may not be possible.
7. A failure to obtain the desired response in relation to FEV<sub>1</sub> alone should not preclude patients from treatment if there is a clearly significant improvement in the FVC. This illustrates the probability of the patient being less hyperinflated ( $\downarrow$ FRC/TLC) and hence will likely have a reduction in the work of breathing. The patient will perceive an improvement in breathing and their symptoms may be reduced.

### Does it really make that much difference?

To illustrate the potential differences and the known confounding factors are severity and sex bias, Table 3 shows the effects of using the various criteria outlined above on five subjects with differing baseline FEV<sub>1</sub> and FVC. On the assumption that we use z-scores to physiologically and statistically represent normality or abnormality then it is completely logical to use z-scores to define BDR<sup>11</sup>. It is also important to understand changes in the small airways measures, such as MEF25%FVC as this may contribute to improvements in the symptomatic response of the patient. This can only be done if suppliers of equipment correctly analyse the pre- and post-BD flow-volume curves using the iso-volume point.

	1	2	3	4	5
	FEV <sub>1</sub>				
Pre-FEV <sub>1</sub>	0.77	1.15	2.15	0.98	3.55
Post FEV <sub>1</sub>	1.23	1.27	2.68	1.01	4.05
Pred FEV <sub>1</sub>	2.34	3.09	3.60	1.84	4.00
Absolute	0.46	0.12	0.53	0.03	0.50
% Initial	59.74	10.40	24.60	3.10	14.10
% Pred	19.70	3.88	14.70	1.63	12.50
% Possible	41.44	6.59	57.61	3.61	10.0
Pre-z-Score	-4.13	-3.80	-2.84	-2.26	-0.98
Post-z-Score	-2.92	-3.56	-1.80	-2.18	+0.10
$\Delta$ z-Score	+1.21	+0.24	+1.04	+0.08	+1.08
	FVC				
Pre-FVC	1.85	1.95	3.45	1.75	4.65
Post FVC	2.45	2.65	4.12	2.05	4.75
Pred FVC	2.78	3.92	4.51	2.24	4.95
% Pred	21.58	17.86	14.86	13.39	2.02
Pre-z-Score	-2.16	-3.23	-1.74	-1.14	-0.49
Post-z-Score	-0.77	-2.08	-0.64	-0.44	-0.33
$\Delta$ z-Score	+1.39	+1.15	+1.10	+0.70	+0.16

Table 3 Utilisation of the various methods of expressing the results of assessment of the bronchodilator response as shown in Table 2. Volumes are given in litres



However, the recommendations on what is deemed a positive BDR are generally based on statistical rather than clinical criteria. The physiological data obtained form part of the overall picture. A BDR that appears to not meet the recommended criteria may still be clinically important, particularly in a patient with poor lung function who states that they are symptomatically better<sup>30, 31</sup>. Changes in the FEV<sub>1</sub> of 5% to 10% from the baseline FEV<sub>1</sub> is regarded as clinically meaningful<sup>32</sup>, whilst a BDR change in FEV<sub>1</sub> of > 8% predicted suggested an optimal survival advantage<sup>28</sup>.

Ideally, the criteria used for a positive BDR in routine clinical practice should be related to the clinical outcomes, and include data on the number of exacerbations, the number of hospitalisations, and the often overlooked, yet highly important quality of life<sup>33</sup>. Furthermore, how respiratory impairment is categorised causes issues, as the percent predicted FEV<sub>1</sub> leads to age bias. This could be overcome if only we all started using z scores<sup>34</sup>. However, at present that seems to be elusive, with perhaps the exception of the new ATS/ERS spirometry guidelines<sup>7</sup> which indicates how we should be reporting the BDR.

Generally, the primary emphasis is still based on the BDR using FEV<sub>1</sub>. Yet, there is clearly an improvement in the FVC response in the presence of airflow limitation and it is essential that this is accounted for in defining clinical outcomes as a reduction in the level of hyperinflation will have significant beneficial effects on dyspnoea, exercise performance, and gas exchange. Including the FVC response increases the number of positive responses in those with airways obstruction by > 50%, and is particularly relevant in

## Conclusions

This review has attempted to highlight some of the issues in assessing the BDR. Confusion still remains as to how to report the change, with even current spirometry guidelines lacking consensus<sup>7, 26</sup>. We need to change our approach to ensure that we are reliably reporting the BDR in terms of physiology and statistics<sup>7, 11, 28</sup> and in relation to the immediate BDR and the potential of long-term survival. It is also important that we have, clinically, a better understanding in terms of the quality of life of the patients whom we are assessing and managing in both primary and secondary care, taking a more holistic approach than perhaps we do at the moment. Finally, we need to sort out the criteria for defining severity of the disorder in a more appropriate way<sup>34</sup>!

To achieve this will require a massive sea-change, lots of re-education and probably not happen in my lifetime – but I can hope!

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## A round-up of ARTP forum discussions since the August issue.

### Title: Ulna length or arm span to measure height?

Date: 02/08/2019

*Question: Does anyone use ulna length to measure height or stick to arm span for patients unable to stand?*

Replies: A leading paediatric physiologist described how arm-span was used for patients with scoliosis but ulna length for patients with muscle weakness and cerebral palsy who are unable to fully stretch their arms. The equations used were: For males, Height (cm) =  $4.605U + 1.308A + 28.003$  ( $R^2 = 0.96$ ), For females, Height (cm) =  $4.459U + 1.315A + 31.485$  ( $R^2 = 0.94$ ). Where U = Ulna Length (cm), A = age (years). Reference - Gauld L et al. Developmental Medicine & Child Neurology 2004, 46: 475–480.

The physiologist suggested setting up a multi-site research study whereby standing height, ulna height and arm span was recorded in children and several physiologists demonstrated an interest in this.



### Title: Sleep Study/Oximetry Reports

Date: 10/09/2019

*Question: We are trying to align sleep investigation reporting in two hospitals where one uses a 3% dip rate and the other 4% (AASM 2012 v AASM 2007). Which Guidelines do other centres use?*

Replies: This question, which has appeared on the forum several times previously, received a large number of responses.

Indeed, two physiologists reported using 3% dip with one highlighting they used a combination of 3% dips and a 30% decline in airflow for scoring a hypopnoea. In contrast, two other physiologists reported using 4 % dips along with 30 % reduction in airflow. One of these physiologists stated this was because the AASM state 3% dips should only be used when sleep staging is present.

Furthermore, it initiated an interesting debate on the significance of using desaturations to diagnose OSA. One physiologist suggested the AASM recommendations were designed to maximise reimbursement in the USA and using them in the UK could greatly underestimate the AHI which is used to diagnose OSA. Indeed, he raised the question, "Can you explain physiologically why someone who is in reasonably good health except for OSA should desaturate by 3% with 30% drop in airflow?".

Another physiologist approached the question from a different angle and suggested undertaking a research study to better understand how the choice of guideline used would affect the management/care of patients rather than just the diagnosis. He suggested identifying how many of those patients who were diagnosed with OSA using 3% dips but wouldn't have been using 4% dips received a symptomatic benefit from using CPAP.



### Title: HCT/Fly Assessment - Services/Private Patient Provision?

Date: 12/09/2019

*Question: Background: A patient was discharged from chest clinic 2 years ago with a positive HCT. He recently informed his airline he requires inflight*

*oxygen but they stated his 2 year old HCT was insufficient and now require SpO2 on room air and on 4L/min O2.*

*However, the consultant declined to respond to the airline as the patient is not currently under his care and neither his GP or private clinic provide such a service. Have other services experienced this? Do you offer "Fly Assessment" paper work and HCT and a PP procedure? Or, are GP's in other areas happy to refer people as NHS patients to secondary care?*

Replies: One reply suggested funding for HCTs on the NHS could be a postcode lottery with some Trusts seeing it as a "basic necessity" and others viewing this as a "luxury add-on". Since it is unlikely their lungs have improved, their previous HCT will not either, but a specialist review should occur. Another physiologist was in agreement that a consultant review should take place as the required level of supplemental oxygen could have increased. They stated their department did not accept GP referrals for a HCT and recommended the results are valid for 6 months if infection clear for 6 weeks and a re-test if they develop a chest infection between "passing" and flying.

### **Title: Treating Tracheomalacia with CPAP**

Date: 20/09/2019

*Question: How do we assess the efficacy of the CPAP in tracheomalacia. Is symptomatic improvement of breathlessness and ease of sputum expectoration enough? Some key points from the clinic letter were: Bronchoscopy showed a 50-75% tracheal and main bronchi obstruction on expiration. PEEP of 5 cmH2O obliterated expiratory dynamic airway closure. Stenting inappropriate. Recommend CPAP to improve expectoration and lung recruitment for breathlessness.*

Replies: There was one very useful reply where the physiologist reported anecdotal evidence that these patients with either co-existent OSA or airflow

limitation experienced changes in oxygen saturation. Therefore, they suggested a limited channel sleep study to investigate any objective improvement. They also stated that most of the research they could find was case studies limited to using CPAP during exercise, or acute exacerbations.

### **Title: Consent form for remote monitoring of CPAP**

Date: 16/10/2019

*Question: Does anyone use a consent form that the patient signs agreeing to the use of remote monitoring for CPAP?*

Replies: One physiologist explained that with Philips Dream Mapper Software the patient has to provide consent when downloading it and thus GDPR is covered. Another physiologist attached an example of a consent form provided by ResMed.

In contrast, one physiologist reported that their Information Governance team informed them consent was not required because they were already entitled to process patient data under the remit of providing direct care. Nonetheless, there was an obligation to inform patients that third party software/hardware was being used. The department delivered this information to patients via leaflets, which stated the lawful basis for processing their data.

Finally, one physiologist described how the hospital trust may have to enter into a data sharing agreement with the third party which has to be signed off by your Trust's Caldicott Guardian (Medical Director).

### **Title: Oximetry Delta Index**

Date: 16/10/2019

*Question: A student project is comparing the use of 4% oxygen desaturation index (ODI) to the*



***delta-12 index in the diagnosis of OSA.  
Does anyone routinely use the delta index  
when looking at oximetry traces?***

Replies: One physiologist stated they always used delta index as a marker of variability in the signal from oximetry. However, another physiologist reported rarely using it because of a lack of evidence. Nonetheless, they discussed the individuals who developed or adopted it often had very smart ideas so a study to re-validate this index in multi-channel sleep studies would be beneficial. However, it was highlighted by one physiologist that a potential concern of this index was that measurements between ear and finger may show a difference of up to 3-4 %.

Finally, a very useful response discussed how the Delta 12 index may be used more in paediatrics and provided a useful reference. Hill et al., Home oximetry to screen for obstructive sleep apnoea in Down syndrome. Arch Dis Child. 2018 Oct;103(10):962-967.

***Title: A No-Deal Brexit - Perish the Thought!***

Date: 20/10/2019

***Question: The physiologist raised a concern that in the case of a no-deal Brexit they might not be able to continue using software that stored patient data outside the UK. They suggested transferring personal data to or from the EU may become unlawful. This could have implications for CPAP/NIV services using telemedicine.***

Replies: This question received only a limited response, is it possible that

physiologists are bored of Brexit!? However, a useful response came from a leading CPAP/NIV company who provided a copy of a statement they were issuing to Hospital Trusts in regards to post-Brexit data management.

“Data collected by [Care Orchestrator/EncoreAnywhere/DreamMapper] in the UK is stored (processed) in [Ireland/France]. Post-BREXIT this “processing” will potentially involve a cross-border transfer from the UK to an EEA country. The UK’s Information Commissioner Office (ICO) has confirmed that transfers of data from the UK to the EEA will not be restricted in the event of no-deal BREXIT....”



**Title: Mask Re-issue**

Date: 21/10/2019

***Question: Do other hospitals make patients buy their own mask when damaged or neglected sooner than say 10-12 months?***

Replies: One physiologist stated that they do not make patients buy replacements unless they break a lot where they would reassess and re-emphasize the importance of care etc. They work on the basis that masks should last 9-12 months with care and attention.

Another physiologist explained they had experienced different approaches at various hospitals. In one department, masks were replaced upon request but this proved costly as patients weren’t careful with their equipment/masks. In another department patients were informed they would only get one mask a year but actually masks were still replaced if needed. The physiologist attached a poster from a recent conference providing some evidence on the

implications of sticking to the 1 mask per year procedure. Another useful response highlighted the need to maintain a good database to track how many masks patients are using. However, not one of the physiologists responding to this question stated patients were actually made to buy their own replacements.



[illegible]

## August 2019 'NO PRIZES' SOLUTION

## Across

2. Short Czech in pain regrouped to aid interpretation? (1, 5)
6. Sounds like multiple pretty boys are meditating over RPG, yah? Sleep recording (15)
8. Hide the device for nose or face (4)
9. Reorganised part to make a great organisation! (4)
11. Sounds like turn is boring for sleep feature (7)
12. Knots amulet transformed to help asthma control (11)
13. Special Japanese Maple to help with medication? (6)
14. Freedom of transport initially provides test technique (3)
16. Walk boldly, alternatively for high-pitched breathing (7)
17. Still battling at church tower but lead others to breathe regardless (7)
19. See 12 down
20. Previous icy rain but breathe out now (6)

## Down

1. This Gen-X brief year old is essential to breathe (6)
3. Imports rye muddles in LFT (10)
4. Brit shorn with concoction for a tight squeeze? (19)
5. Much ado over almost poisonous creates lack of vital gas (7)
6. This derived sleep parameter may create the ultimate spinster (5, 7, 4)
7. Sleep pattern creates GP harmony (9)
8. Religious service with disorganised em, retrospect detects gas. (4, 12)
10. Disorganised grizzly perhaps plus article inspires (7)
12. Pammi spends for colloquial muscle strength measurement (4, 3, 4)
15. It's the skin of a bullock in a compound ain't it mate? (5)
17. Hernial transplant provides respiratory relief (7)





## ARTP 2020 Birmingham

16th - 17th January

[Hilton Birmingham Metropole](#)

ARTP are delighted to be bringing the conference to the heart of England in January 2020. With a prime location on the NEC complex, Hilton Birmingham Metropole is a 5-minute walk from Resorts World Arena and entertainment complex and the new Bear Grylls Adventure.

The ARTP Events' committee is working hard putting together an exciting educational programme and social events to match so keep an eye on the website for more information.