December 2018 VOLUME 19, ISSUE 3

ARTP | Association for Respiratory Technology & Physiology

Inspire

INSIDE THIS ISSUE:

www.artp.org.uk

ARTP Association for Respiratory Technology & Physiology

ARTP EXECUTIVE Council

Dr James Hull	President
Dr Karl Sylvester	Chair
Julie Lloyd	Vice Chair
Mike Lang	Treasurer
Cara Roberts	Secretary
Ken Hutchinson	Non-Executive Director (HR)
Mark Hubbocks	Executive Director (Finance)
Ricky Harwood	Non-Executive Director (Patient)
Position vacant	Non-Executive Director (Medical)

ARTP EXECUTIVE Board

Dr Karl Sylvester	Chair
Julie Lloyd	Vice Chair
Mike Lang	Treasurer
Cara Roberts	Secretary
Chris Jones	Communications
Dr Vicky Cooper	Sleep co-chair
Sara Parsons	Sleep co-chair
Kelly Pauley	Events
Ian Cliff	Standards
Joanna Shakespeare	Education
Claire Stacey	Workforce
Paul Burns	Paediatrics

ARTP EDITORIAL BOARD

Aidan Laverty	Inspire Editor
Suhilla Hashimi	Inspire Deputy Editor
Alison Butler	S-news Editor
Dr Andrew Robson	
Prof Brendan Cooper	
Keith Butterfield	
Nigel Clayton	
Dr Karl Sylvester	
Chris Jones	
Martyn Bucknall	
Kimberley Lewis	
Katie Bayfield	

ALL ARTP CORRESPONDENCE TO:

ARTP Administrator, Executive Business Support Ltd., Unit E1 City Wharf, Davidson Road, Lichfield, Staffordshire WS14 9DZ

Tel: 01543 442141

Fax: 0121 355 2420

e-mail: admin@artp.org.uk

ENQUIRIES TO THE EDITOR or ARTICLES FOR SUBMISSION:

Please contact the Editor, Aidan Laverty Inspire@artp.org.uk

INSPIRE is published three times per year: 1st April, August, December. Deadline for articles two weeks prior to publication.

ADVERTISING RATES Please contact ARTP Administration for more information on admin@artp.org.uk or see the ARTP website http://www.artp.org.uk/en/about-artp/admin/advert-rates.cfm

FIRST WORD

VOLUME 19, ISSUE 3. DECEMBER 2018

CHRISTMAS is the time for giving and I must confess to being overwhelmed with being given so many articles for this issue. ARTP members have approached me with ideas to improve *Inspire* and some of these have been introduced in this issue.

We have a round-up of the ARTP forum—that resource which many of us use and is now to be compiled between issues as *'Top Forum'*. Although not strictly 'new', the rather recent *'Fresh Air'* has been expanded, now with closer links to ARTP Research and Innovation committee with the aim of stimulating feedback and conversation. My hope is that both of these will become regular features in *Inspire*, to sit alongside *'On the Blower'* and *'Word from the Chair'*, not to mention *'From the museum'*.

The winners of ARTP grants to attend the recent ERS conference have also been busy in sending their articles—definitely the fastest response since I have been Editor. You can read two of these research articles *here*, with the remainder, each sleep-related, held over for the next issue or in S-NEWS.

Unfortunately I could not attend the always informative ARTP National Strategy Day this year but one of the presentations, concerning the ARTP National Research survey results, has been written up *here*.

Accreditation is becoming increasingly important for laboratories so what prevents them from applying? University Hospital Birmingham were recently successful in becoming accredited and there is an interview with their lead *here* with tips to help others who are thinking of starting the process.

The Global Lung Initiative (GLI) Project continues apace to incorporate reference equations for ever more of our standard tests. A timely update is provided here.

I wish to thank all the contributors for their input. I would also particularly like to thank all members of the Editorial committee who have helped so much this year with their proof reading and suggestions for improvements. Thank you also to ARTP members who have suggested ideas for articles and provided feedback (of any sort!). The only item on which feedback was not received was the crossword in the August issue—I can only assume no one completed it—answers are at the back!

My best wishes for a Merry Christmas and a Happy 2019, which begins with the *ARTP Annual conference* in January so I hope to see you there. Feel free to let me know your ideas as to how *Inspire* can be improved upon.

Aidan Laverty

A WORD FROM THE CHAIR

Dr. Karl Sylvester

ARTP Honorary Chair

It is with great pride at ARTP's achievements over the last 6 years, and with more than a hint of sadness, that I write my last ever ***Word from the Chair***. I have thoroughly enjoyed my time as ARTP's Honorary Chair and am immensely grateful to colleagues and friends both from within and external to ARTP who have continued to build on the great work of previous Chairs. The drive and enthusiasm of individuals who also work within busy, clinically demanding services, is outstanding.

Many of you may be unaware of the work that your ARTP committees undertake on your behalf and to some extent that is a failing on our part for not communicating this better to you. As a profession we are not as good as other colleagues at shouting about how good we are at what we do. We are a humble group who prefer to get on with the great work you all do for the benefit of our patients. However, we have great communication resources and none better than ***Inspire*** which continues to improve, evolve and develop into a great resource for ARTP members. Under the leadership of our Inspire Editor, Aidan Laverty and with your continued feedback this publication adapts to the on-going changes and demands within respiratory physiology and assists in driving up standards within respiratory and sleep science.

Speaking of driving up standards, it's great to see another department from the UK gaining IQIPS accreditation as part of a wider all-physiology accreditation. Well done Queen Elizabeth Hospitals, Birmingham. May there be many more to follow in yours and Coventry & Warwickshire Hospitals' footsteps. Read more about this achievement later on in this publication.

Following on the communications theme, ARTP are currently in the process of updating and revamping our website. We are conscious that the current website could do with a little brightening up and making content much easier to find in a quicker timescale. Chris Jones, Communications Chair, is leading on this piece of work. This is a big investment for ARTP but one that we believe is more than worth it. The website is our face to the wider healthcare community. It needs to be inviting and easy to navigate so people visit on a regular basis, have a better understanding of what we do and want to engage and get involved. Expect an update in Spring/Summer 2019.

ARTP has many associations with other organisations from within the healthcare sector around the UK and beyond. Currently our most important association is as part of the Taskforce for Lung Health **https://www.blf.org.uk/taskforce**. This is a collaboration of 29 professional body and patient representative organisations from around the UK. The aim of the taskforce, when originally setup, was to create a 5-year strategy to improve the nation's lung health. This includes prevention, better diagnosis, disease management and end-of-life care for patients with lung disease. A number of recommendations on how to achieve the aims have been developed. It was clear early on in the discussions that to achieve the aims of the taskforce there would be a requirement to have a more robust workforce. Evidence for this was supplied by many of the professional body organisations and ARTP provided our evidence through the workforce survey **http://www.artp.org.uk/en/about-artp/artp-reports.cfm/Workforce-Survey-2018**.

During the development of this document it was announced that respiratory will finally be a clinical priority for NHS England in its long term strategy. The Taskforce recommendations will now feed into this workstream. This is a long term strategy so we don't expect to see immediate changes but we have a voice and influence with the aim to improve our services for the future benefit of patients and the public.

I would like to finish by letting you know that ARTP continue to drive up standards in all areas of respiratory and sleep science, particularly in education and professional development. Expect to see great and important changes to our examinations process, new national competency certificates in other areas of respiratory and sleep, ARTP accreditations plus fabulous member benefit events that will truly further justify your membership of this great organisation.

May I wish you all the very best in your futures and great success. Look forward to seeing you in Glasgow for what promises to be another fabulous educational and networking opportunity.

Slán agus beannacht

Karl

ARTP ERS 2018 TRAVEL GRANT WINNER

Measuring Forced Vital Capacity in Idiopathic Pulmonary Fibrosis

Suhani Patel
(s.patel1@rbht.nhs.uk)

Pulmonary Rehabilitation and Muscle Research Group, Royal Brompton & Harefield NHS Foundation Trust, Harefield, Middlesex UB9 6JH

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive fibrotic lung disease, with a median survival from diagnosis of 2-5 years[1, 2] and no curative treatment. The prognosis of IPF is worse than some lung cancers[3]. Over 30,000 people live with IPF in the UK, with 5000 new cases per year[4]. Frequently reported symptoms include cough, shortness of breath, and fatigue[5-7]. Disease progression is heterogeneous with some patients experiencing a continuous slow decline, while others experience episodes of significant deterioration interspersed with periods of clinical stability[2]. There is significant interest in outcomes and clinical endpoints in IPF due to the emergence of licensed pharmacological treatments in routine clinical care, and an expanding pipeline of future therapeutic products.

A wide range of physiological, imaging and patient-reported outcomes can be used to assess severity and monitor disease progression in IPF. However, each have their own potential limitations. Monitoring by high-resolution CT scanning, for example, exposes the patient repeatedly to ionising radiation, and there may be inter-individual variability in reporting. Field walking tests, such as the six-minute walk, requires long, straight courses that can be difficult to accommodate in some clinical settings, and patient performance can be influenced by factors outside of the lungs (e.g. musculoskeletal problems).

By far the most commonly used outcome measure in IPF is forced vital capacity (FVC). There are several reasons why it is an attractive measure. FVC is widely agreed as the physiological measure that best reflects disease progression and worsening fibrosis[8]. It is cheap and readily available, and when there is consistency of equipment, training and calibration, FVC is reliable. FVC correlates with other markers of disease severity (e.g. fibrosis scored on CT scans[9], six-minute walk distance[10], transfer factor of the lung for carbon monoxide (TL_{CO})[11]). Longitudinal decline in FVC is consistently associated with disease progression and worse prognosis[12]. Unsurprisingly, change in FVC is the primary outcome measure in many interventional studies of patients with IPF. Indeed, the two drug treatments licenced for use in IPF (pirfenidone and nintedanib) were approved due to their effects on slowing of FVC decline[13, 14].

However, the use of FVC does have potential limitations. Not all patients with IPF can perform the test, due to either cough or discomfort during the manoeuvres. The evidence from clinical trials suggests that this is a noticeable problem, even in selected trial populations with milder disease. In pirfenidone trials, FVC data was missing in up to 13% of patients at 6 months, and 19% of patients at 12 months, in addition to the 11% and 22% of patients that did not survive to the 6- and 12-month timepoints[13]. Similarly, in the INPULSIS-1 and INPULSIS-2 trials which evaluated the use of nintedanib in patients with IPF, FVC was not recorded in 17% of patients at 1 year, in both the active and placebo groups[14]. Patients included in these therapeutic studies have had relatively well preserved FVC (>50% of predicted values). There is no data regarding FVC performance in patients with more advanced IPF, but it is plausible that a significant proportion experience discomfort, even distress, such that they are unable to perform the measure within acceptable technical standards.

Missing values have implications for both trial design and data analysis. For example, some patients participating in trials are observed to have stable FVC prior to death. This may be due to sudden deterioration not captured by interval spirometry. One way to counter this problem is increasing the frequency of FVC measurements such that slopes of change can be calculated. A recent study investigating the value of home-based daily spirometry as an outcome measure in IPF demonstrated that patients with a rapid decline in absolute value of FVC had worse prognosis. However, of the 50 patients recruited onto the study, 13 (26%) discontinued testing by a year, with 11 (22%) discontinuing before 6 months. The reasons for stopping testing at home included intolerance of the procedure, or distress caused by observing deterioration in spirometry readings[15].

A further difficulty with FVC is reproducibility and the interpretation of change values. Even in healthy individuals with normal lung function, FVC can vary as much as 5-9% between measurements[16]. International spirometry guidelines allow a within-test variation of 6% in lung volumes of up to 2.5L (between manoeuvre variation of ≤0.150L)[17]. For those with a lung volume less than one litre, a difference of 10% is considered acceptable variation[17]. Yet, after utilising a variety of different methods, du Bois and colleagues estimated the minimum clinically important difference of FVC in IPF to lie between 2-6%[18]. Therefore, interpreting the clinical significance of a small change in FVC is challenging in an individual patient.

Are there other lung function tests that can act as an alternative or as an adjunct to FVC measurements in IPF? Transfer factor (TL_{CO}) at baseline is predictive of 5-year mortality with a moderate strength correlation found between TL_{CO} %predicted and survival time (r=0.557), with TL_{CO} <40% predicted being associated with poorer prognosis (HR 2.70 (95% CI 1.46 – 4.99)[1, 19]. A change in TL_{CO}, like FVC, has also been associated with worse prognosis in IPF, with a 15% drop considered significant[11]. However, many of the performance issues with FVC also apply to TL_{CO}. There is often missing data[19], and recent conference abstract data reported that 23% of patients with IPF were unable to perform TL_{CO} [20], with reduced inspiratory capacity often the cause of poor technique. The use of TL_{CO} as a study outcome is hampered by inherent variability of the test, with TL_{CO} harder to standardise across centres than FVC.

There is a growing interest in novel non-volitional measures of lung function, such as structured light plethysmography[21], and the forced oscillation or impulse oscillometry techniques[22]. The benefits of such effort-independent measures are the ability to obtain results from symptomatic patients, as well as those that have difficulty performing the manoeuvres required for traditional lung function tests. However, there is very limited experience of these measures in patients with IPF, and further work is needed to establish the sensitivity, validity, responsiveness and prognostic value of these non-volitional measures. Until then FVC, and change in FVC, remains the lung function measurement of choice in IPF. Some of the weaknesses associated with using FVC as a primary outcome measure can be minimized by a combination of rigorous quality control and frequent calibration of standardised equipment.

References

1. Collard HR, King TE, Bartelson BB, Vourlekis JS, Schwarz MI, Brown KK. Changes in Clinical and Physiologic Variables Predict Survival in Idiopathic Pulmonary Fibrosis. 2003: 168(5): 538-542.
2. Ley B, Collard HR, King Jr TE. Clinical course and prediction of survival in idiopathic pulmonary fibrosis. American journal of respiratory and critical care medicine 2011: 183(4): 431-440.
3. Goldstraw P, Chansky K, Crowley J, *et al.* The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. Journal of Thoracic Oncology 2016: 11(1): 39-51.
4. Navaratnam V, Fleming K, West J, Smith C, Jenkins R, Fogarty A, Hubbard R. The rising incidence of idiopathic

pulmonary fibrosis in the UK. Thorax 2011: thx. 2010.148031.

5. Key AL, Holt K, Hamilton A, Smith JA, Earis JE. Objective cough frequency in Idiopathic Pulmonary Fibrosis. Cough 2010: 6(1): 4.

6. Swigris JJ, Stewart AL, Gould MK, Wilson SR. Patients' perspectives on how idiopathic pulmonary fibrosis affects the quality of their lives. Health and quality of life outcomes 2005: 3(1): 1.

7. Yount SE, Beaumont JL, Chen S-Y, Kaiser K, Wortman K, Van Brunt DL, Swigris J, Cella D. Health-related quality of life in patients with idiopathic pulmonary fibrosis. Lung 2016: 194(2): 227-234.

8. du Bois RM, Nathan SD, Richeldi L, Schwarz MI, Noble PW. Idiopathic pulmonary fibrosis: lung function is a clinically meaningful endpoint for phase III trials. American journal of respiratory and critical care medicine 2012: 186(8): 712-715.

9. Xaubet A, Agustí C, Luburich P, Roca J, MontÓn C, Ayuso MC, BarberÁ JA, Rodriguez-Roisin R. Pulmonary function tests and CT scan in the management of idiopathic pulmonary fibrosis. American journal of respiratory and critical care medicine 1998: 158(2): 431-436.

10. Lederer DJ, Arcasoy SM, Wilt JS, D'ovidio F, Sonett JR, Kawut SM. Six-minute-walk distance predicts waiting list survival in idiopathic pulmonary fibrosis. American journal of respiratory and critical care medicine 2006: 174(6): 659-664.

11. Peelen L, Wells AU, Prijs M, Blumenthal JP, Van Steenwijk RP, Jonkers RE, Peek N, Bresser P. Fibrotic idiopathic interstitial pneumonias: mortality is linked to a decline in gas transfer. Respirology 2010: 15(8): 1233-1243.

12. Zappala C, Latsi P, Nicholson A, Colby TV, Cramer D, Renzoni E, Hansell D, Du Bois R, Wells A. Marginal decline in forced vital capacity is associated with a poor outcome in idiopathic pulmonary fibrosis. European Respiratory Journal 2010: 35(4): 830-836.

13. Raghu G, Johnson WC, Lockhart D, Mageto Y. Treatment of idiopathic pulmonary fibrosis with a new antifibrotic agent, pirfenidone: results of a prospective, open-label Phase II study. American journal of respiratory and critical care medicine 1999: 159(4): 1061-1069.

14. Richeldi L, du Bois RM, Raghu G, Azuma A, Brown KK, Costabel U, Cottin V, Flaherty KR, Hansell DM, Inoue Y. Efficacy and safety of nintedanib in idiopathic pulmonary fibrosis. New England Journal of Medicine 2014: 370(22): 2071-2082.

15. Russell A-M, Adamali H, Molyneaux PL, Lukey PT, Marshall RP, Renzoni EA, Wells AU, Maher TM. Daily home spirometry: an effective tool for detecting progression in idiopathic pulmonary fibrosis. American journal of respiratory and critical care medicine 2016: 194(8): 989-997.

16. Dowson L, Mushtaq M, Watts T, Shurvinton J, Gooch R, Hayton R, Jones J, Perks W. A re-audit of pulmonary function laboratories in the West Midlands. Respiratory medicine 1998: 92(9): 1155- 1162.

17. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, Crapo R, Enright P, van der Grinten CPM, Gustafsson P, Jensen R, Johnson DC, MacIntyre N, McKay R, Navajas D, Pedersen OF, Pellegrino R, Viegi G, Wanger J. Standardisation of spirometry. European Respiratory Journal 2005: 26(2): 319-338.

18. Du Bois RM, Weycker D, Albera C, Bradford WZ, Costabel U, Kartashov A, King Jr TE, Lancaster L, Noble PW, Sahn SA. Forced vital capacity in patients with idiopathic pulmonary fibrosis: test properties and minimal clinically important difference. American journal of respiratory and critical care medicine 2011: 184(12): 1382 -1389.

19. Hamada K, Nagai S, Tanaka S, Handa T, Shigematsu M, Nagao T, Mishima M, Kitaichi M, Izumi T. Significance

of pulmonary arterial pressure and diffusion capacity of the lung as prognosticator in patients with idiopathic pulmonary fibrosis. Chest 2007: 131(3): 650-656.

20. Bryce M, Oates K, Chivers G, Parfrey H. Determining why patients with idiopathic pulmonary fibrosis (IPF) have difficulty performing gas transfer. Eur Respiratory Soc, 2013.

21. de Boer W, Lasenby J, Cameron J, Wareham R, Ahmad S, Roach C, Hills W, Iles R. SLP: A Zero- Contact Non-Invasive Method for Pulmonary Function Testing. In: BMVC; 2010; 2010. p. 1-12.

22. Smith H, Reinhold P, Goldman M. Forced oscillation technique and impulse oscillometry. European Respiratory Monograph 2005: 31: 72.

ARTP ERS 2018 TRAVEL GRANT WINNER

The comparison of Functional Residual Capacity measured by Body Plethysmography and Multiple Breath Washout in schoolchildren with Cystic Fibrosis

Mollie Riley
(Mollie.Riley@gosh.nhs.uk)

Lung Function Laboratory

Great Ormond Street Hospital for Children NHS Foundation Trust | London WC1N 3JH

Introduction

Cystic fibrosis (CF) is a multi-organ, genetic disorder that presents with a range of clinical phenotypes. Although outcomes have substantially improved, CF is life-limiting with progressive respiratory decline as the predominant reason for mortality[1].

Lung function testing plays a crucial role in CF longitudinal monitoring[2]. Plethysmography uses gas compression properties to measure static lung volumes[3]. However, the test requires considerable co-operation to perform which is beyond many preschool children[4]. Multiple breath washout (MBW) is an alternative method for measuring lung volumes[5], being easy to perform, applicable across the paediatric range and sensitive to detecting early CF lung disease[6]. The main outcome measure of MBW is the Lung Clearance Index (LCI). LCI is the number of lung volume turnovers required to clear a marker gas to 1/40th of its starting concentration[5]. An upper limit of normality of 8.2 has previously been validated at this site[8] and found to be appropriate. Plethysmography and MBW both measure functional residual capacity (FRC). FRC measured by plethysmography (FRC_{pleth}) represents all intrathoracic gas volume including poorly ventilated areas[7]. However, FRC measured by MBW (FRC_{mbw}) measures only the communicable regions[5].

Aims and Objectives

The aim of this study is to compare the FRC measurements obtained from Plethysmography and MBW in CF school children and therefore, assess the clinical usefulness of performing both techniques at CF annual review. Jensen et al., performed a similar study and found good agreement between FRC_{pleth} and FRC_{mbw} measured by N_2 washout in CF children, however this study had just 30 children who performed both tests[9]. The secondary aim is to determine whether there is a difference in the FRC comparison for CF children with normal and abnormal lung function (defined by spirometry and lung clearance index (LCI)).

Methods

Data was collected from CF children aged 6-17 years who had attended an annual review between October 2015 and March 2017. MBW measurements were obtained using the Exhalyzer D® washout device with Nitrogen (N_2) as the 'washout' gas. MBW and plethysmography were performed on patients that passed the local protocol criteria (Figure 1). At GOSH, patients <8 years of age have MBW irrespective of spirometry. Patients >8 years will only have MBW if spirometry is within the normal range.

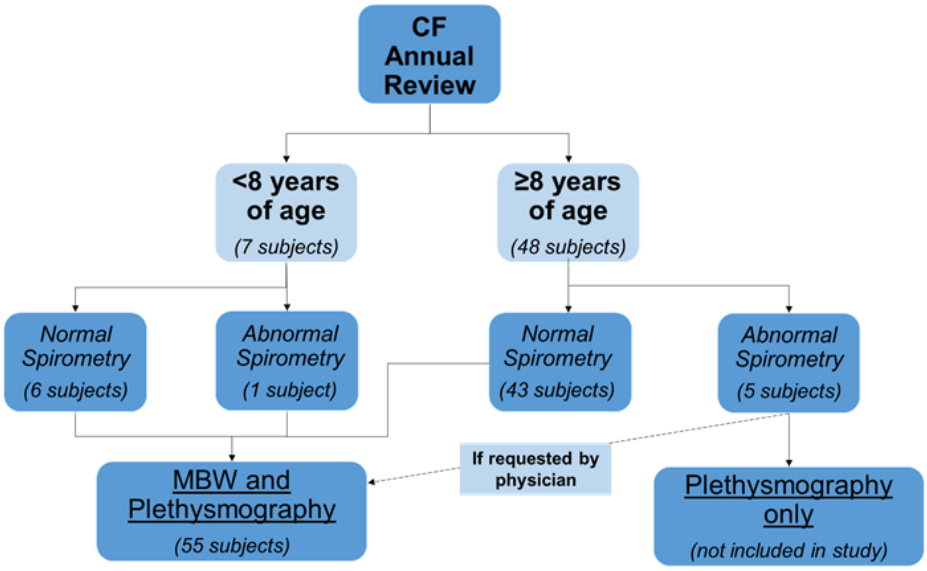


Figure 1: MBW local protocol and the number of study subjects in each category.

Results

75 patients passed the MBW local protocol criteria and attempted to perform MBW, plethysmography and spirometry at annual review. 20 children were excluded; 16 children had no plethysmography result and 4 children did not produce technically acceptable MBW runs. Results were obtained in 55 clinically well CF patients with a median age of 11.2 years. There were 30 (54%) male subjects and the majority (87%) of the cohort were Caucasian. The study sample had a reduced BMI of 17.48kg/m^2 classified as underweight. 49 children (89%) had normal spirometry results and 6 (11%) had abnormal spirometry <=1.64 z-scores. All 6 children with abnormal spirometry showed an obstructive defect. A larger proportion of children (73%) were classed as abnormal (>8.2 by the LCI).

Variable	Median (IQR) or Mean ±SD*	Range
FRC_{pleth} (L)	1.67(0.81)	0.91-3.56
FRC_{mbw} (L)	1.58(0.88)	0.91-3.41
FEV_1 (L)	1.99(0.97)	0.80-4.85
FEV_1 z-score	-0.59±0.86	-3.17-1.73
LCI	9.52(3.13)	6.60-18.54

*Table 1: Descriptive statistics. * Where data was parametric results were presented as mean ±SD rather than median (interquartile range (IQR)).*

A Wilcoxon test showed no significant difference between functional residual capacity (FRC) as measured by plethysmography and when measured by MBW (p=0.062).There was a strong positive linear correlation between FRC_{pleth} and FRC_{mbw} (R^2=0.84) as shown in Figure 2. However, no pattern was observed when analysing the different groups, possibly due to the small number of abnormal subjects classified by spirometry.

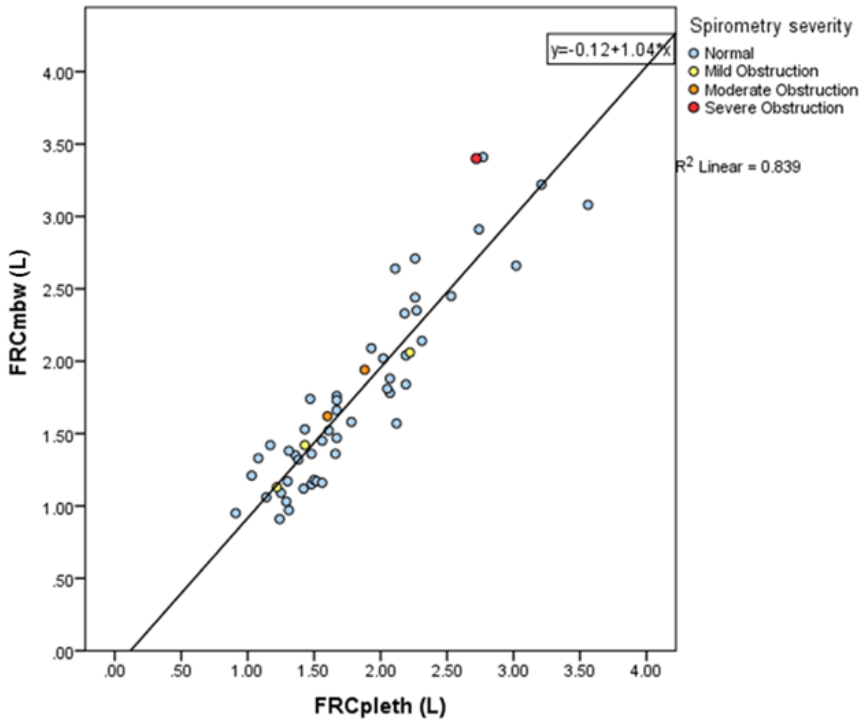


Figure 2: Relationship between FRC_{mbw} and FRC_{pleth} (L). Patients are grouped by spirometry results as shown on key.

Although, correlation shows that FRC_{pleth} and FRC_{mbw} are strongly related, it does not show that the two values agree. It is important to also assess the agreement between FRC_{pleth} and FRC_{mbw} as data that poorly agrees can produce high correlations[8].

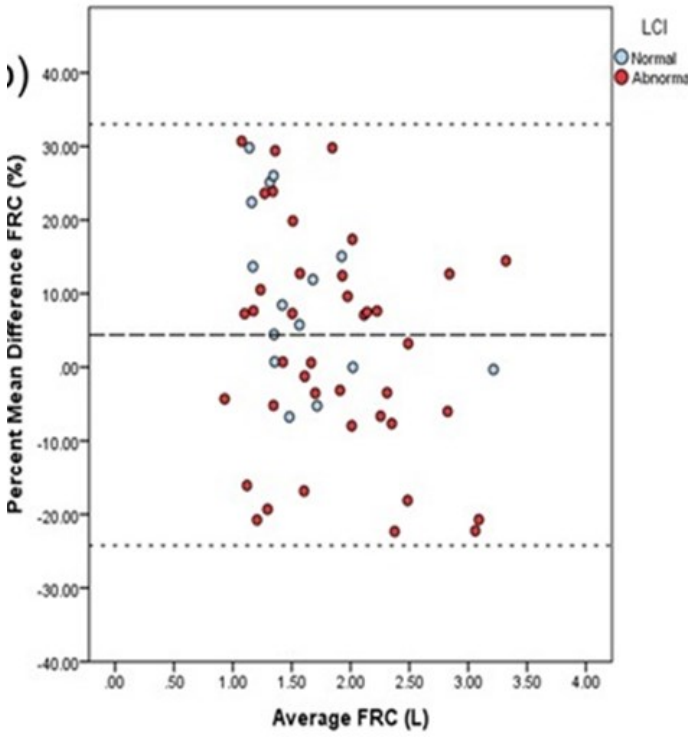


*Figure 3: Bland Altman plot of percentage mean difference ((FRC_{pleth}-FRC_{mbw} / meanFRC) *100)(%) vs mean FRC(L). Patients grouped according to LCI results shown on key. The dashed lines represent the mean difference/bias line, and the dotted lines represent the LoA (mean difference+/1.96SD) for the whole CF cohort.*

Bland-Altman analysis showed no systematic bias between tests; the percentage mean difference was 4.39%. However, the limits of agreement were wide (-24 to 33%). Similarly to spirometry results, there is no clear pattern

of patients with an abnormal LCI; with respect to both positive and negative percentage difference and throughout the range of FRC.

Conclusion

This is the first study, at our tertiary paediatric hospital to compare FRC measured by body plethysmography and the new commercially available MBW N_2 system.

In conclusion, although comparing FRC between plethysmography and MBW in children with CF is subject to methodological and physiological differences, such as peripheral trapped gas and tissue N_2 excretion, in this study, we found that CF patients show on average no difference between FRC_{pleth} and FRC_{mbw} with no clear tendency for higher values in one method over the other. It can also be said that it was very difficult to explore any differences in the FRC comparison for CF children with normal/abnormal spirometry. As a result of the local protocol there were a small number of children with airflow obstruction.

Although, one method was not more useful in measuring FRC than the other, this study has highlighted the usefulness of performing both tests at annual review in order to gain an overall clinical picture of lung function in CF children. Ultimately, spirometry and the LCI measure different aspects of airway dysfunction

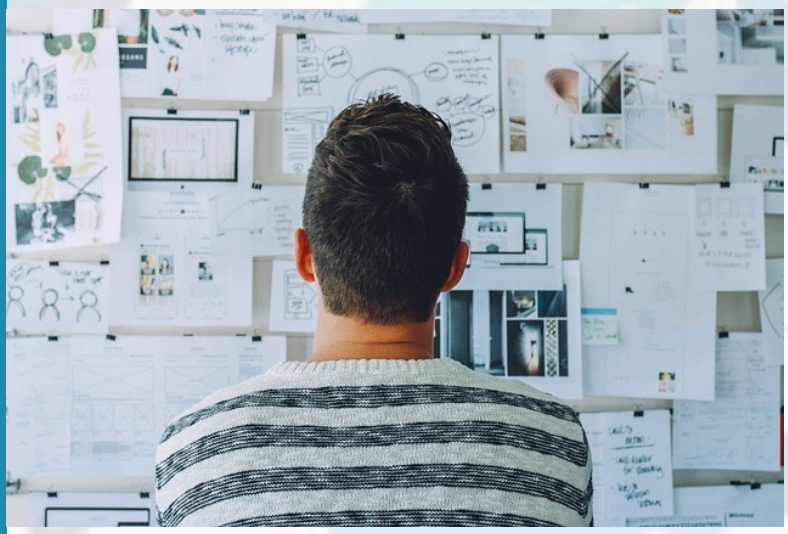
References

1. Rosenblatt, R.L. (2009) 'Lung Transplantation in Cystic Fibrosis,' Respir Care, 54, (6), pp. 777–786.
2. Davies, J.C. Alton, E. Bush, A. (2007) 'Cystic Fibrosis,' BMJ, 335, 1255. doi: 10.1136/bmj.39391.713229.AD.
3. Seung Lee, J. Lee, S.M. Lee, S.W. Seo, J.B. Huh, J.W. Oh, Y-M. Lee, S-D. (2014) 'Clinical utility of Computed Tomographic Lung Volumes in patients with Chronic Obstructive Pulmonary Disease,' Respiration, 87, pp. 196–203. doi: 10.1159/000355097.
4. Wanger, J. Clausen, J.L. Coates, A. et al., (2005) 'ATS/ERS Task force on standardisation of lung function testing: standardisation of the measurement of lung volumes,' Eur Respir J, 26, pp. 511–522. doi: 10.1183/09031936.05.00035005.
5. Robinson, P.D. Latzin, P. Verbanck, S. Hall, G.L. Horsley, A. Gappa, M. Thamrin, C. Arets, H. Aurora, p. Fuchs, S.I. King, G.G. Lum, S. Macleod, J. Paiva, M. Pillow, J.J. Ranganathan, S. Ratjen, F. Singer, F. Sonnappa, S. Stocks, J. Subbarao, P. Thompson, B.R. Gustafsson, P.M. (2013) 'Consensus statement for inert gas washout measurement using multiple and single-breath tests: ERS/ATS Consensus Statement,' Eur Respir J, 44, pp. 507-522. doi: 10.1183/09031936.00069712.
6. Aurora, P. Bush, A. Gustafsson, P. Oliver, C. Wallis, C. Price, J. Stroobant, J. Carr, J. Stocks, J. (2005) 'Multiple-Breath Washout as a Marker of Lung Disease in Preschool Children with Cystic Fibrosis,' ATS, 171(3). doi: 10.1136/thx.2009.132100.
7. West, J.B. (2011) Respiratory Physiology: The Essentials (Respiratory Physiology: The Essentials). 9th edn. United Kingdom: Lippincott Williams and Wilkins.
8. Raywood, E. Duncan, J. Wade, A. Stocks, J. Bush, A. Aurora, P. (2015) 'Validation of commercial devices for measurement of lung clearance index (LCI) and functional residual capacity (FRC) in school-aged children,' European Respir J, 46, PA4148. doi: 10.1183/13993003.congress-2015.PA4148.
9. Jensen, R. Stanojevic, S. Gibney, K. Salazar, J.G. Gustafsson, P. Subbarao, G. Ratjen, F. (2013) 'Multiple Breath Nitrogen Washout: Alternative to Mass Spectrometry,' PloS ONE 8 (2), e56868. Doi: 10.1371/ journal.pone.0056868.
10. Bland, J.M. Altman, D.G. (1986) 'Statistical methods for assessing agreement between two methods of clinical measurement,' Lancet, 1 (8476), pp. 307-310.

2018 ARTP National Research Survey Results

Gavin Comber
Gavin.Comber@uhnm.nhs.uk
Respiratory Clinical Scientist
Lung Function Laboratories
University Hospitals of North Midlands
County Hospital
Stafford
ST16 3SA

Research, audit and innovation are a fundamental element of healthcare sciences and indeed the NHS as a whole. It is an area that the NHS constitution states will lead to the highest level of excellence and is something that comes in many forms, for many reasons.



Within the ARTP membership, its importance is rated very highly with an average score of 8 out of 10 and yet there are a number of barriers that we as a profession must overcome in order to incorporate research into the normal working life of a healthcare scientist.

With this in mind, The ARTP Research & Innovation committee invited all departments to complete a survey detailing current research activity and the barriers they face in conducting more. This article will show the results of this survey as well as exploring what can be done to improve the current situation.

Responses were collected from 67 departments around the UK comprising of paediatric, adult, respiratory, sleep, small and large services.

What research is going on within UK Respiratory and Sleep departments?

It is important to determine what research is taking place in departments around the country in order to not only determine any areas for improvement but to highlight examples of services who have successfully incorporated research and audit into day-to-day working. (**Figure 1**)

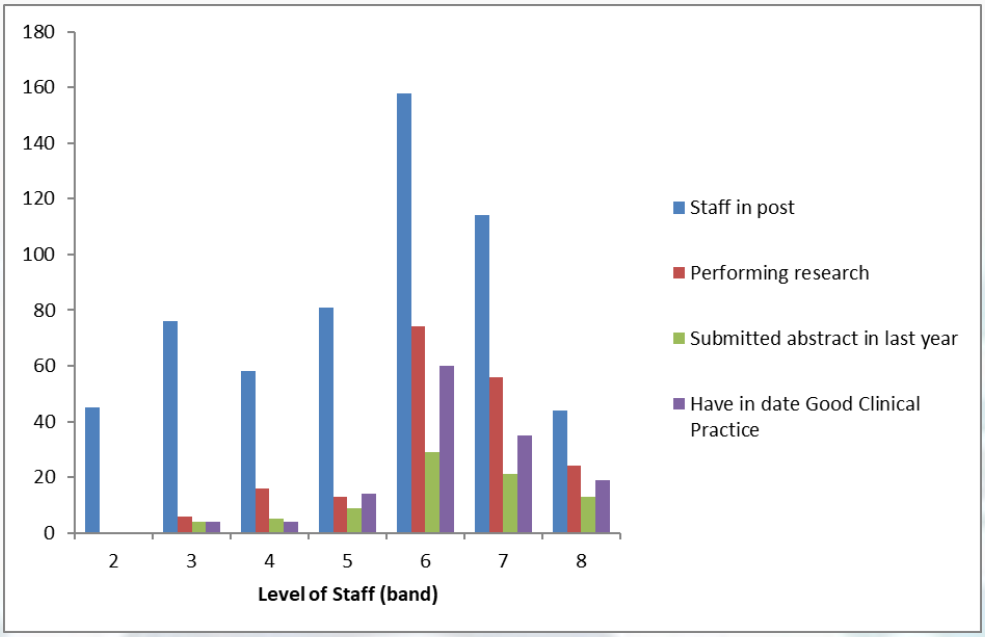


Figure 1. The breakdown of current research activity compared to number of staff currently employed within respiratory and sleep physiology services.

The data illustrates research and audit is primarily performed by bands 6+ however still only includes 50% for each particular banding. Of those staff performing research, there are varying levels of staff submitting work to conferences in the form of an abstract, as shown in **Table 1**.

	Performing Research	Submitted Abstract	GCP trained
Band 2	0%	0%	0%
Band 3	8%	67%	67%
Band 4	28%	31%	25%
Band 5	16%	69%	100%
Band 6	47%	39%	81%
Band 7	49%	38%	63%
Band 8	55%	54%	79%

Table 1. *Percentages of staff performing research, submitting abstracts and have in-date GCP training by band.*

Of the staff performing research, a number do not have valid, in-date Good Clinical Practice (GCP) training but more on that later.

Whilst it is no surprise that research activity is heavily weighted towards the higher banded staff, it is important to understand the implications of this. As a profession there is a national shortage of graduate physiologists coming through the Practitioner Training Programme (PTP). As a result it is feasible that departments begin to relook at the traditional "*grow your own*" approach by training staff bands 2-4 so that they can become registered respiratory and sleep physiologists. This requires application to either RCCP or AHCS through their respective equivalence processes. Within their applicant guidance, both require evidence of research and/ or presentation of work. Therefore, if we wish to help staff develop and progress, they need to be involved within research/audit and learn about the underpinning processes such as when to seek ethical approval.

As we all know, a lot of research activity departments are involved in relates to supporting students with their academic research projects comprising of PTP, STP and sometimes PhD level work. Whilst undeniably important to ensure high quality staff are joining the profession, this does cause additional strain on a department to provide adequate time and support (**Figure 2)**.

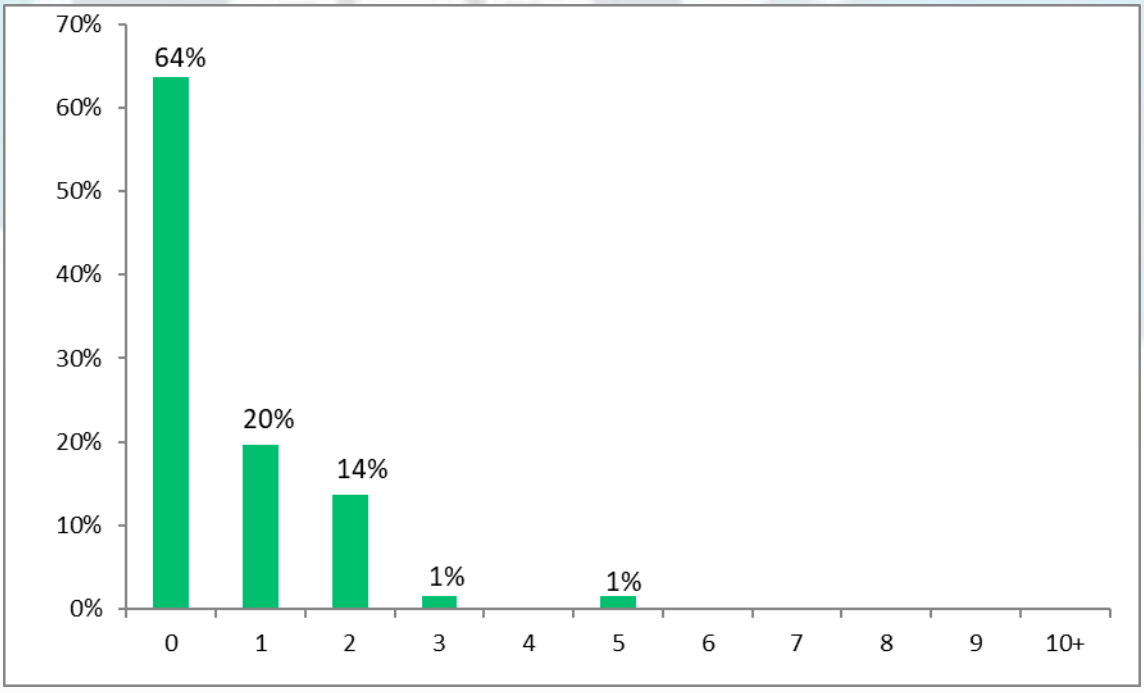


Figure 2. *The percentage of students supported with research in each department.*

The third area of research requiring time and staff to help support is commercial. This may be large respiratory medication trials (hopefully with a suitable financial incentive) or routine follow-up testing of patients on non-respiratory trials. See **Figure 3**.

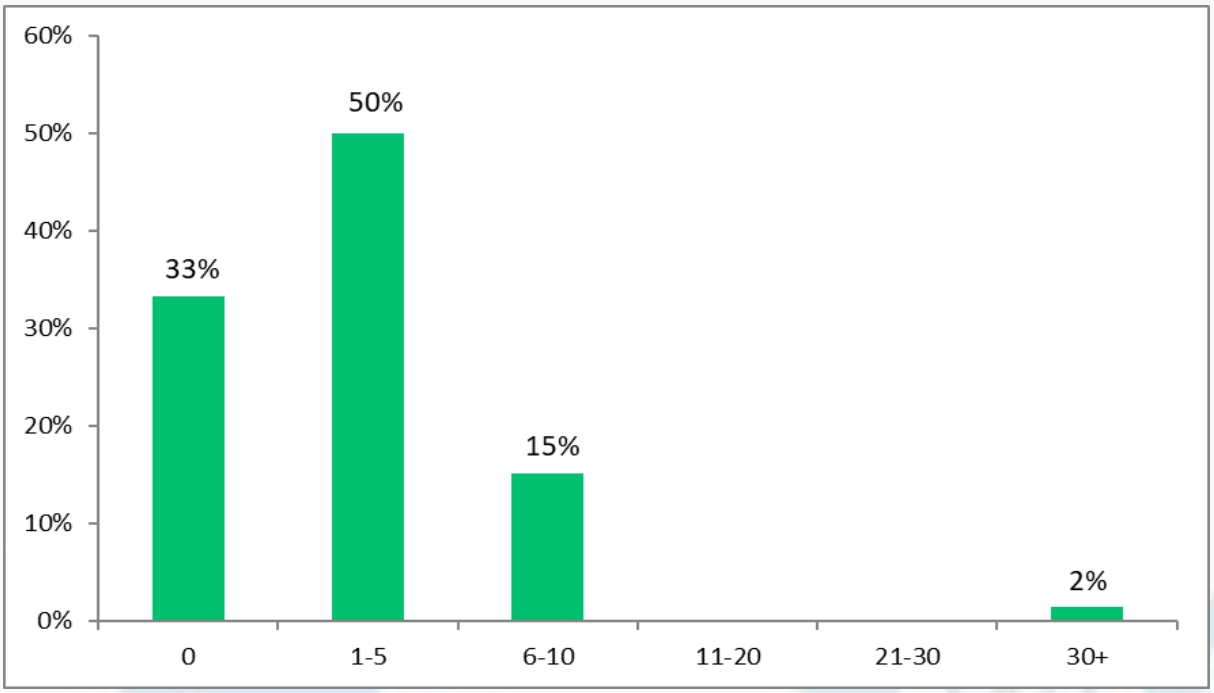


Figure 3. Current percentage of commercial research trials being supported.

Why perform research?

The reasons for performing research and audit is extensive and **Figure 4** shows some of the most common. Survey responders report the importance of research as 8/10. This echoes the sentiments of the UK policy framework for health and social care research who report that "*the quality of current care may be higher in organisations that take part in, adopt a learning culture and implement research findings*".

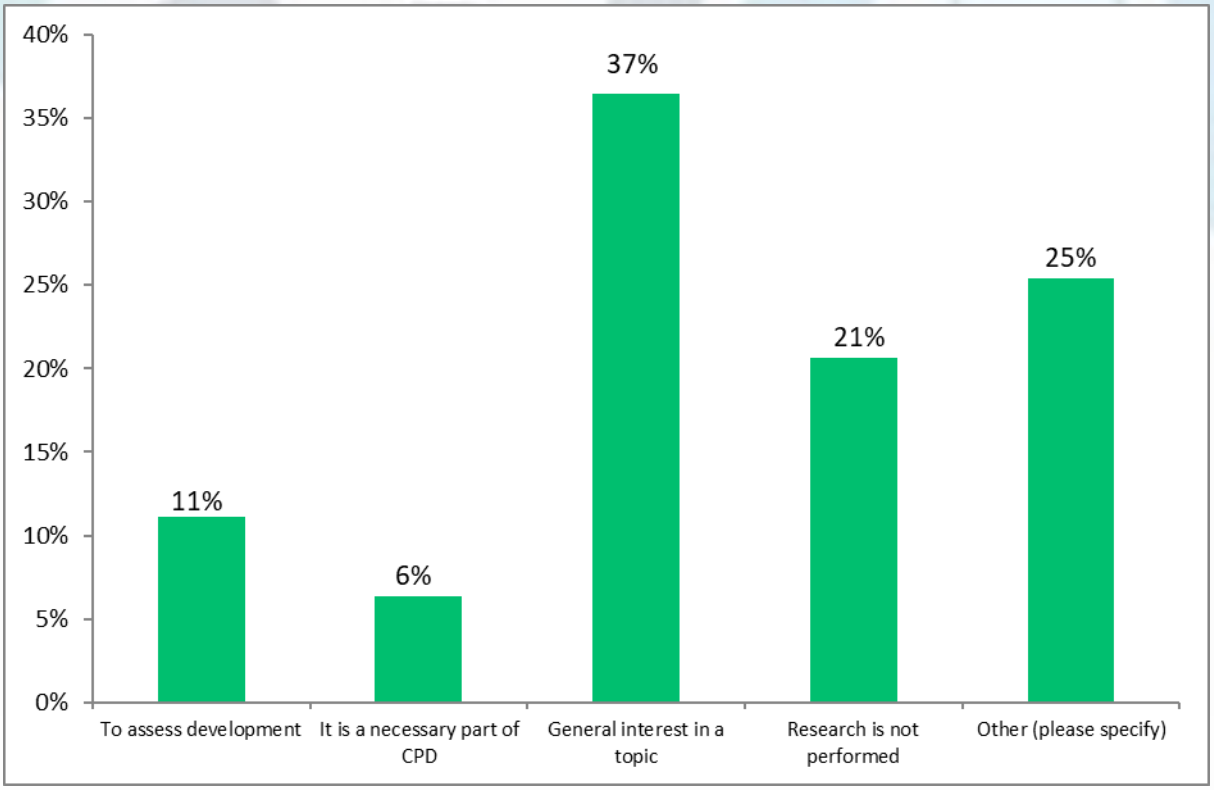


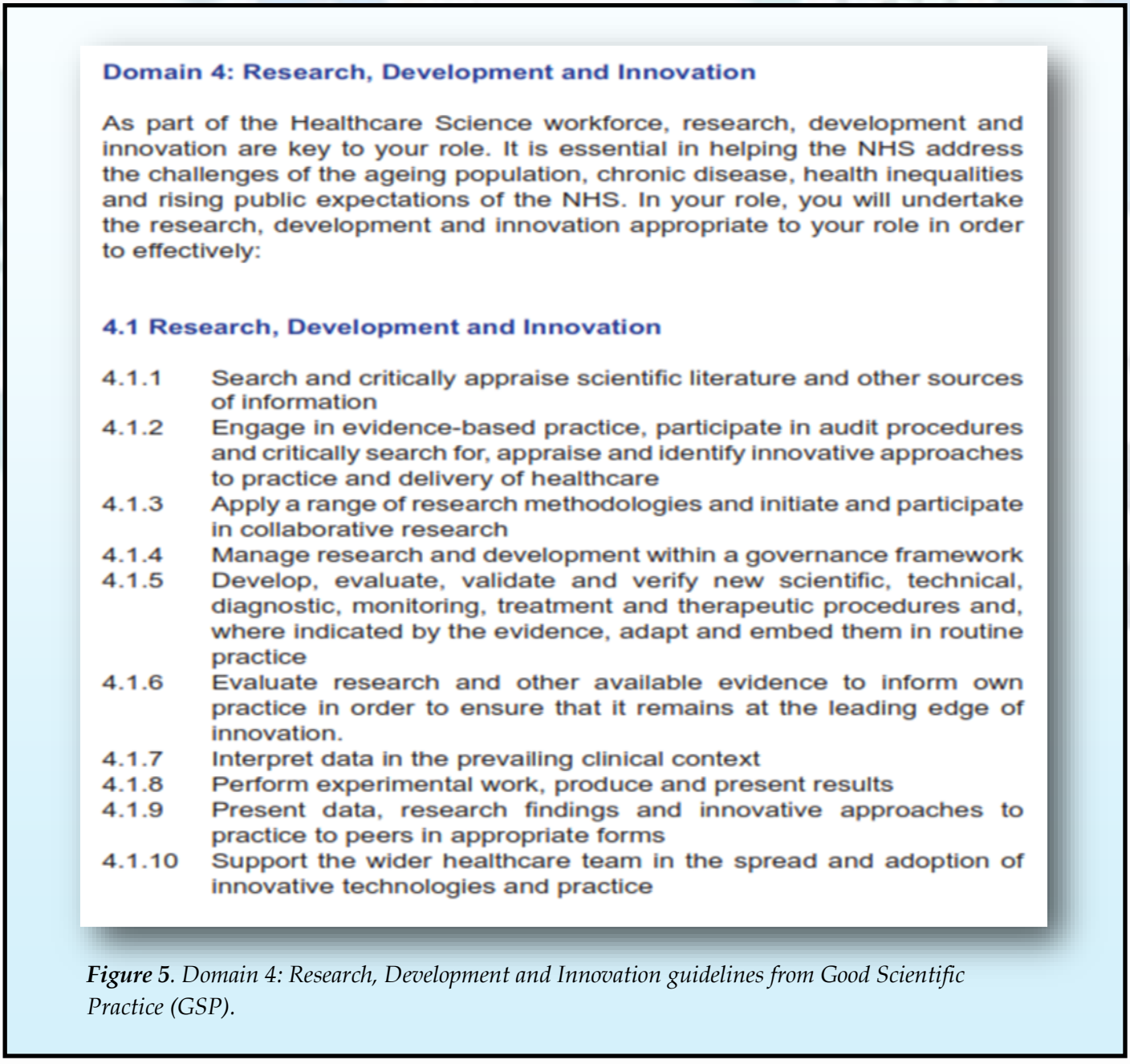
Figure 4. *Most common reasons for performing research*

General interest in a particular topic is the stand out reason for performing research however the important areas to note are that only 11% of departments use research to help support and monitor developmental service changes and 21% do not perform any research.

Other areas in which research and audit can prove extremely beneficial include:

- Improving patient care through quality improvement projects and innovation
- Aid in the development of services to streamline pathways or increase capacity
- Give staff a sense of contribution to the wider healthcare provision through joint working
- Justify and add weight to current or future business cases.

Further to the above, research is a crucial part of Good Scientific Practice (GSP) which all physiologists/healthcare scientists should be adhering to. GSP sets out 5 key areas or domains which form the basis of our day-to-day roles to ensure high quality, safe services.



Domain 4: Research, Development and Innovation

As part of the Healthcare Science workforce, research, development and innovation are key to your role. It is essential in helping the NHS address the challenges of the ageing population, chronic disease, health inequalities and rising public expectations of the NHS. In your role, you will undertake the research, development and innovation appropriate to your role in order to effectively:

4.1 Research, Development and Innovation

4.1.1	Search and critically appraise scientific literature and other sources of information
4.1.2	Engage in evidence-based practice, participate in audit procedures and critically search for, appraise and identify innovative approaches to practice and delivery of healthcare
4.1.3	Apply a range of research methodologies and initiate and participate in collaborative research
4.1.4	Manage research and development within a governance framework
4.1.5	Develop, evaluate, validate and verify new scientific, technical, diagnostic, monitoring, treatment and therapeutic procedures and, where indicated by the evidence, adapt and embed them in routine practice
4.1.6	Evaluate research and other available evidence to inform own practice in order to ensure that it remains at the leading edge of innovation.
4.1.7	Interpret data in the prevailing clinical context
4.1.8	Perform experimental work, produce and present results
4.1.9	Present data, research findings and innovative approaches to practice to peers in appropriate forms
4.1.10	Support the wider healthcare team in the spread and adoption of innovative technologies and practice

***Figure 5**. Domain 4: Research, Development and Innovation guidelines from Good Scientific Practice (GSP).*

Improving Quality in Physiological Services (IQIPS) is at the forefront of department accreditation as a recognised aspect of Care Quality Commission (CQC) assessments within hospital settings. A significant aspect of gaining accreditation involves being able to show that services are being continually monitored via audits with services being improved as a result of findings as part of an on-going audit cycle. There is so much importance placed on having successful CQC visits and their subsequent rating of a hospital that it may be possible to gain much needed support for devoting additional time to research and audit, even in the face of ever increasing clinical demands on services.

Barriers to research?

Despite the numerous reasons to be performing research, there are numerous barriers that prevent it from happening. These reasons need to be fully understood before anything can change.

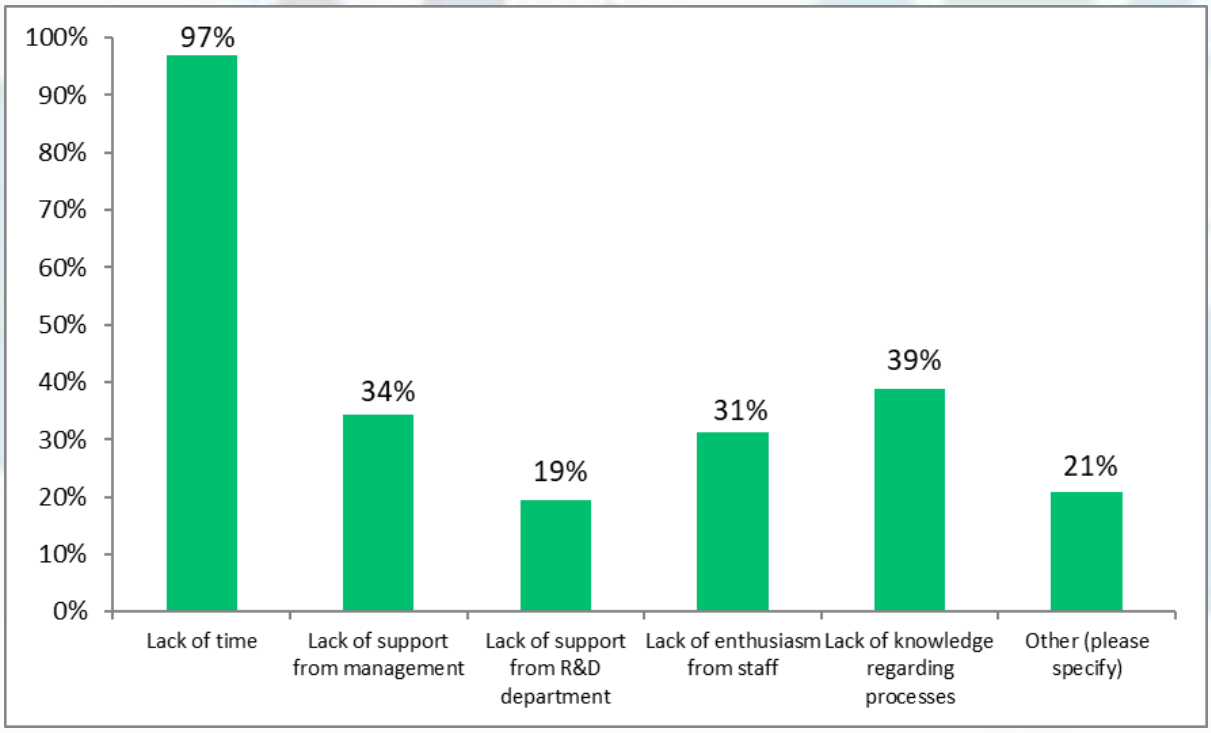


Figure 6. *Barriers to performing research*

Given the pressures the NHS is currently facing, it is no surprise that 97% of responders list lack of time as a reason for not performing research. Due to different pressures and service provisions across departments, there is no easy, "*one size fits all*" solution. It is however vitally important that departments look at how research can be best incorporated into their work load. Research and audit may not benefit the patients seen or being seen today however it may have significant benefit to hundreds or thousands that are to follow.

What next?

Changing current practices and increasing research activity across UK departments is not going to be a short process and the ARTP Research & Innovation Committee are keen to look at the best way of providing support to those who need it. There are however a number of things that can be implemented now to help going forward.

Research should be an all-inclusive area of work and not restricted to the higher bands. It is

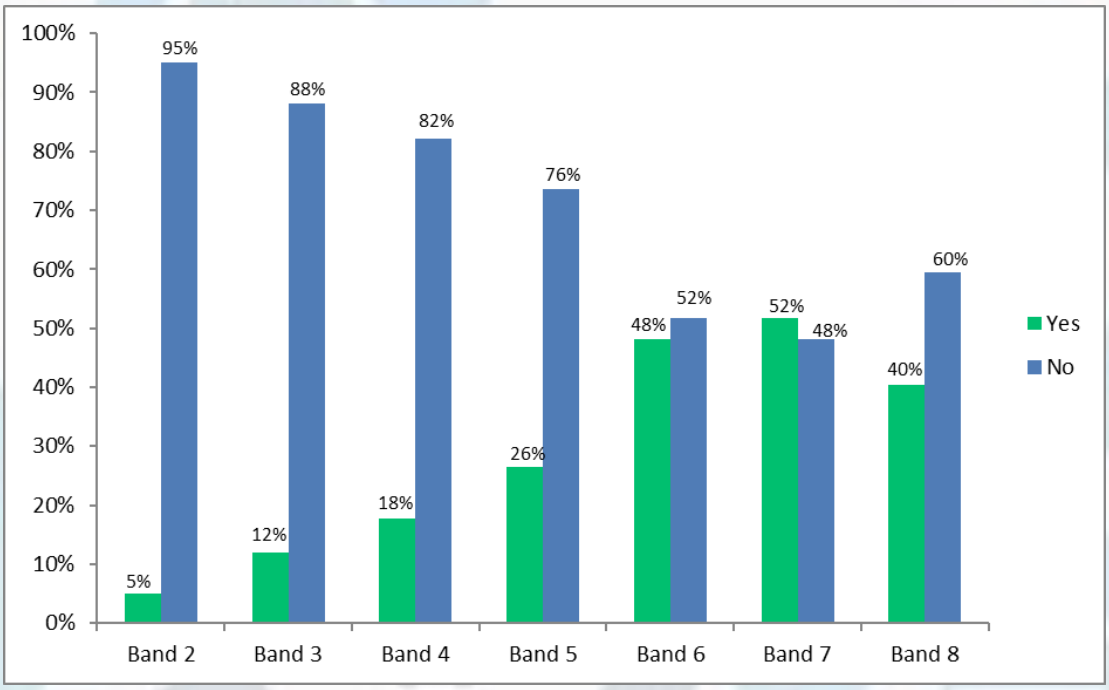


Figure 7. *The percentage of staff that have research included within their annual review.*

likely that there are a various members of staff bands 2-4 who have never performed research and will require a lot of help. However, they do not necessarily have to be included from start to finish. It may simply be in the form of data collection to begin with which could help give an insight into what research involves, eventually prompting an interesting question of their own. This being said, there are numerous lower banded staff with great capabilities and experience of research and statistics. These members of staff should not be prevented from engaging in research purely because of their banding.

Research and Innovation should be included in all new job descriptions and personal development reviews (PDRs). Much like the research activity being performed primarily by bands 6+, so is the expectation.

It is a difficult discussion as to whether or not research and audit should be a compulsory part of a physiologist's role as we know there are many who have little interest or experience in this.

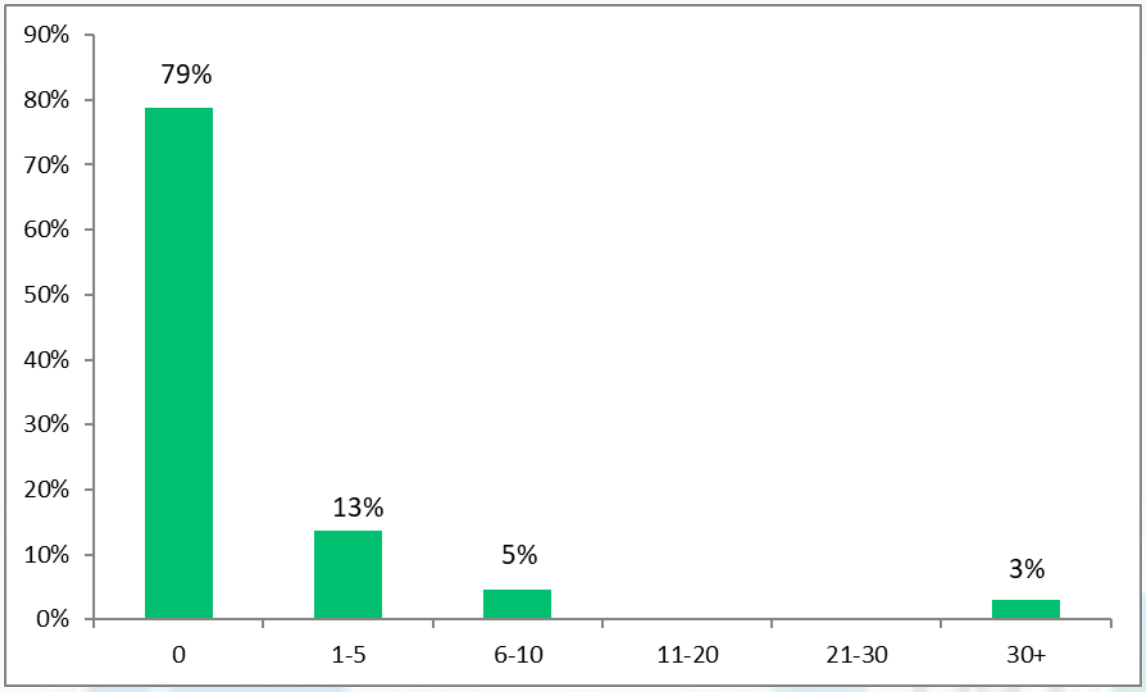


***Figure 8**. Average number of protected hours given to staff to perform research per month*

However, consider this; should a member of staff be exempt from performing clinical duties that are banding-appropriate purely because it is disliked or not fully understood?

Having Research and Innovation included in this way may help to prevent criticism from management when staff are provided time away from direct patient care to enable data collection or analysis. It also helps to create a department ethos where research is just another part of the job.

With this in mind, when research is to be performed, designated protected time is necessary to ensure the member of staff can concentrate and has sufficient time to complete the analysis. We can see that not many departments are able to provide regular protected time however 24% of departments do manage it.

We need to assess what lessons can be learnt from these departments that may be applicable to other services in providing protected time without compromising their clinical workload.

Everyone involved in research should have in-date GCP training. This is a free course run by the National Institute for Health in Research (NIHR) which can be undertaken either face-to-face or on-line. After the initial introduction, a refresher is required every two-three years and provides invaluable lessons regarding how research should be conducted. It also works as great evidence of CPD. More information can be found at https://www.nihr.ac.uk/our-research-community/clinical-research-staff/learning-and-development/national-directory/good-clinical-practice/

Take home message

Research is an area that should be applicable to all; just at different levels and involvements. If you are a manager and have staff interested in research, this should be encouraged. For everyone else, if you want to get involved, discuss this with your manager and see what is possible.

The 2018 ARTP National Research Survey has yielded some very useful results that the Research & Innovation Committee will be looking at using to increase participation in research and to make resources available. The exact manner in which this will happen is too early to say however watch this space!

Vitalograph®

Your cardio-respiratory partner

Introducing

THE FUTURE OF PULMONARY FUNCTION TESTING SOFTWARE AND EQUIPMENT

Don't miss out on our two exciting and educational workshops

- **EXCLUSIVE PREVIEW**
  Future Product Demonstration
- What are the implications of the 2017 ERS/ATS standards for **DLCO measurement** and **rapid gas analysers**?

Booking Essential, places are limited

Exclusively at the ARTP 2019 Conference in Glasgow

Visit our stand for more information

56056_1

The Respiratory/Sleep Department at University Hospital Birmingham gains IQIPS Accreditation

The Respiratory and Sleep Unit at the University Hospital of Birmingham (UHB) has recently become accredited by the United Kingdom Accreditation Service (UKAS) for meeting the IQIPS standards. Well done to the team!

Maxine Goring, the IQIPS lead for Respiratory/Sleep at UHB discusses IQIPS Accreditation with Martyn Bucknall (ARTP Lead for Accreditation).

Accreditation is not mandatory, so why did your service decide to work towards IQIPS Accreditation?

We always thought that we had a well-run department which was very patient focused and offered excellent care but that it would be beneficial to undertake external accreditation in order to provide documented evidence from an external provider that this was the case.

What were the 3 major barriers in working through the IQIPS process and how did your service overcome these?

1 & 2. Understanding the IQIPS Standards and Time. Initially it takes time to understand specifically what the standards are looking for and what evidence you can provide but as you progress this does become easier. Instead of having to search for evidence you will find things in your normal daily practice which you can use as evidence. For example, emails from consultants or staff meeting minutes. You do not necessarily need to create evidence, it probably already exists and if it doesn't creating it will only make your service better.

3. Staff were concerned about getting answers wrong and being watched by the assessors whilst performing their duties. We promoted the Standards in an informal setting and there was an A-Z of what you should know about accreditation prior to the inspection.

How important is engaging the whole respiratory/sleep teams in delivering IQIPS?

The whole team of physiologists had to be engaged for a successful application, inspectors will review your service as a whole and can speak to any member of staff so everyone needed to be involved in the process.

I know your service is large, but what advice would you give to other services, especially smaller services who might be thinking about working towards accreditation?

Go for it, by working through the standards and collating evidence it highlights areas which could be improved and can make processes more streamlined which is ultimately beneficial to the department.

I talk to many services who are keen on applying for accreditation, but down to time, workload and resource they feel this is not achievable – what would your advice be?

Once you start you probably find that most of the evidence you need is already available either at a departmental level i.e. Standard Operating Procedures or in Trust policies i.e. Health and Safety policies.

Difficult question – but if you had to estimate how many hours of time were dedicated to achieving accreditation, what would your estimate be? How long did the process take?

I cannot estimate how much this was as it was not just myself alone who worked on achieving accreditation. When we first commenced the process it was a departmental decision and progress was

slow, but once the Trust Board decided to support the process and with the help of a Trust Diagnostic Services Accreditation Lead (Debra Balderson) the physiology services had fortnightly meetings lasting an hour. Here, ideas and interpretation of the standards were discussed and deadlines were set. We assisted each other and where support was required from other non-clinical departments the process was more streamlined. For example instead of all 7 departments approaching the patient experience team individually asking for the same information the patient experience team would attend this meeting periodically.

What were the advantages (and challenges) of working with the other physiology disciplines within your Trust?

The advantages were that you get to know people in other areas, where you all have the same questions/ concerns and these can be addressed and discussed to find the most appropriate and standardised solution. Plus they may already have documents which are applicable to your service too or may just need slight alteration to be applicable to your service saving time when it is precious. Another bonus now is that we always have a point of contact in the other physiology departments and if we have any queries they will assist or if they can't they will know someone who will.

How supportive were your Trust Board, and how did they support the accreditation process?

Initially it was decided departments could make their own decisions as to whether to apply for accreditation, however it was then decided that all physiological services must be accredited. Once the final decision was made support was available.

What service improvements did your service make during the journey through accreditation? Were there any quick wins?

The patient experience team worked with departments to create a process which would easily cover most of the patient experience domain. We always conducted the friends and family test but the team specifically designed another questionnaire for patients to completely cover the patient experience standards and on an annual basis for one month all patients are asked to complete this and a formal report is compiled. Patient information was a quick win area, ideally as a department you will create your own but if this isn't a fully stocked patient information board from external sources may suffice.

Early days, but what are the benefits to date of being an accredited service?

A sense of achievement and pride and a confidence in the services we provide. We have gone through a "culture change" where service problems are tackled and solved and not ignored or avoided by everyone in the team.

Any other points?

Appointing one person to coordinate inter-departmental IQIPS processes and jobs really made the process more effective. Because this was a multi-physiology IQIPS process (the first in the UK!). Having the "external" coordinator was essential to streamline the procedures and processes.

More details on IQIPS Accreditation can be found at https://www.ukas.com/services/accreditation-services/physiological-services-accreditation-iqips/

McDermott, dry bellows, digital spirometer with calibrating weight and orifice, 1980 Garw Electronic Instruments, Glamorgan, South Wales

This 6V, battery operated, low resistance dry bellows spirometer was used extensively in epidemiological field studies from the 1970s to the 1990s. The example shown is a rigid frame model but another model with collapsible legs was available to increase its portability. The initial models of the spirometer displayed the FEV_1 (or $FEV_{0.75}$) and FVC. A later, digital version was developed that recorded volume expired in 10ms increments and displayed additionally the PEF, MEF_{50} and MEF_{75}. The data could be processed to replay the flow-volume curve at a reduced speed on any cheap, slow responding XY printer. In addition, the increments could be stored digitally on a magnetic cassette tape for later processing in the laboratory. The spirometer was excellent for recording Helium-Oxygen flow volume curves and for generating off-line moments analysis applied to the spirogram (Mean Transit Time, Moments Ratio etc).

Spirometer display showing tumblers for program setting (upper one), setting the time interval for the FEV (lower left hand) and BTPS temperature correction (lower right hand). The socket below the upper tumbler links to an XY plotter to print the flow-volume curve in delayed time. The jack plug socket marked 'record' provides an output to the cassette recorder.

Image showing the bellows expanded vertically.

An Update on The Global Lung Function Initiative: Reference data for all lung function tests

Jane Kirkby PhD, Sheffield Children's Hospital

Background:

Lung function tests are used in a variety of settings. The correct interpretation of LFT results relies on applying standardised tests and protocols to ensure accurate results are obtained, and then comparison to appropriate reference values obtained from a population of healthy individuals of the same age, height, sex and ethnic group. The Global Lung Function Initiative (GLI) was established in 2005 and aimed to collate lung function outcomes and generate global lung function reference values. In 2012 the Global Lung Function Initiative (GLI) Task Force published the "Multi-ethnic reference values for spirometry for the 3-95 year age range: the global lung function 2012 equations"[1] and more recently, in 2017 they published the "Official ERS technical standards: Global Lung Function Initiative reference values for the carbon monoxide transfer factor for Caucasians." [2] This article summarises these two papers, and discusses the practical implications of using them and updates on the ongoing GLI-Lung Volume project.

Summary of the GLI-2012 spirometry reference equations:

The GLI-spirometry team identified and contacted authors who had published spirometry reference data and asked them to submit the data.

- After exclusions (e.g. due to missing data on ethnicity) 97,759 records of healthy non-smokers (55.3% females) aged 2.5 to 95 years were combined
- Reference equations were derived for healthy individuals from 3-95 years for:
    - o Caucasians (n=57,395)
    - o African Americans or 'Black'(n=3,545)
    - o North East Asians (e.g. North China and Korea) (n=4,992) and
    - o South East Asians (e.g. South China, Thailand, Malaysia etc.) (n=8,255)
- Predicted values and their lower limit of normal (LLN) were presented
- On average, FEV_1 and FVC were found to be reduced by ~ 14% in Black individuals, 11% and 3% in those from S.E and N.E Asia respectively and by 7% in those classified as 'other' or of mixed ethnicity
- FEV_1 and FVC between ethnic groups differed proportionally from that in Caucasians, such that FEV_1/FVC remained virtually independent of ethnic group
- For individuals not represented by these four groups, or of mixed ethnic origins, a composite equation taken as the average of the above equations is provided to facilitate interpretation until a more appropriate solution is developed

Latest Updates: T_{LCO} Equations

Continuing on from the success of the GLI-spirometry project, the GLI team moved its focus to T_{LCO}. The GLI team identified papers that published T_{LCO} data in healthy individuals after the year 2000 and contacted the authors to share their data with the GLI-T_{LCO} task force. The recent ERS T_{LCO} guidelines identified several methodological aspects (e.g. changes in equipment, software and measurement techniques) that may mean that some of the previously published reference values for T_{LCO} may no longer be appropriate[3]. The aim of GLI-T_{LCO} was to collate contemporary T_{LCO} data from healthy individuals and derive GLI reference values for TLCO measurements.

Summary of the GLI-T_{LCO} reference equations:

- Data from 19 centres in 14 countries were collected
- A total of 12660 T_{LCO} measurements from asymptomatic, lifetime non-smokers were submitted and outliers were identified and excluded
- Reference values for healthy individuals aged 5 to 85 years were derived for T_{LCO}, carbon monoxide transfer coefficient (K_{CO}) and alveolar volume (V_A)
- 85% of the submitted data were from Caucasians, therefore reference values were developed for Caucasians only
- Details about the equipment and methodology used were collected
- All data were uncorrected for haemoglobin (Hb) concentration
- All data were adjusted to the inspiratory oxygen partial pressure at standard barometric pressure (PB; 760 mmHg or 101.3 kPa)

Where can I find more information about GLI-spirometry or GLI-T_{LCO}?

The European Respiratory Society has recently taken over hosting the GLI website. The website contains free software for interpreting either individual results or batch conversion of results and also has a list of several independent publications that validate the GLI-spirometry equations. It also contains desktop calculators in which you can type in values to verify your results. Please see the ERS website for further information: : **https://www.ers-education.org/guidelines/global-lung-function-initiative/tl,co-tools.aspx**.

.

Ongoing Project: GLI-Lung Volumes

The GLI-Lung Volume project commenced in 2016 and hopes to be completed in 2019. It has undergone a similar format as the GLI-spirometry and GLI-T_{LCO}, with the team identifying publications with lung volume reference data and contacting the authors to submit data. So far they have gathered ~13000 data points using plethysmography, Nitrogen washout and He dilution. Comparison of the spirometry data submitted with the lung volume data has been compared with GLI-spirometry reference equations and revealed an excellent fit, indicating reliable data. These are currently being reviewed with the view to develop the reference equations in 2019. Further information will be announced in the new year.

Practical implications of switching to GLI:

Will the clinical interpretation change when applying the GLI-2012 equations?

Inevitably there will be differences between the predicted values in different studies, and the choice of reference equation has been shown to have important implications on interpretation. The biggest change in interpretation will occur in the young and the elderly, as previous reference data were compiled using small sample sizes and the within-subject variability in these age groups was not considered properly. Spirometry results calculated using the GLI-2012 equations may therefore differ by large amounts, particularly in very short/tall subjects. When using trend reports, it is essential to recalculate all previous results with the same reference equations. See: https://www.ers-education.org/guidelines/global-lung-function-initiative/faq/validation-studies-of-the-gli-2012-equations-and-impact-of-implementation-on-clinical-interpretation-of-measurements.aspx

How do I implement the equations?

There is a list on the website of manufacturers that provide the spirometry equations. It is important to note that this is a voluntary list, therefore if your manufacturer isn't on the list, you should contact your manufacturer. The majority of manufacturers are now able to implement GLI-spirometry equations as they have now been available for 6 years, however the more recent GLI-T_{LCO} equations are still being implemented into software and may not yet be available. If you are unsure how to get these equations contact your manufacturer directly. Do not rely on the default reference equations within the lung function software.

Should I wait until reference data for all lung function outcomes are available?

It is important to note that it is common practice for manufacturers to stitch together reference data from different sources. The previously recommended ECCS reference data was collected and combined over a number of years and did not represent the entire population (the very young, the elderly, women and non-Caucasians were not adequately included in the reference data) and manufacturers often combined lung function outcomes from ECCS with other reference data to ensure all lung function outcomes had a "predicted value." Until further reference data is available we recommend using GLI- spirometry and GLI-T_{LCO} reference equations and combine with your previous lung volume reference equations until the new lung volume reference equations are ready.

How do I define ethnicity?

The GLI-spirometry work revealed proportional reductions in FVC and FEV_1 (thus no difference in FEV_1/FVC) in different ethnic groups. These differences are thought to be due to variations in body proportions across ethnic groups, with those from Black ethnic origin having longer leg and shorter thorax in comparison to Caucasian ethnic origin. Five ethnic groups were identified for spirometry (see **Table 1**).

Group	Country/region
Caucasian	Europe, Israel, Australia, USA, Canada, Mexican Americans, Brazil, Chile, Mexico, Uruguay, Venezuela, Algeria, Tunisia
Black	African American
South East Asian	Thailand, Taiwan and China (including Hong Kong) south of the Huaihe River and Qinling Mountains
North East Asian	Korea and China north of the Huaihe River and Qinling Mountains

Table 1: Different ethnic groups for interpreting spirometry

In addition to the countries listed, it would be reasonable to apply the group reference equations to others with geographic or ethnic proximity. Thus the Caucasian equations could be used for any person having origins in any of the original peoples of Europe, the Middle East, or North Africa and for any non-indigenous person of South America. Similarly, the South East Asian equations may be reasonably extended throughout that region. The fifth set of equations, "Other", is made up as a combination of the four groups above, which may be applied as a first approximation to individuals not represented by one of the groups or who are of mixed ethnicity. This should be noted in the report and results interpreted with awareness of increased uncertainty. This will be similar to what was done prior to the publication of GLI reference equations, whereby a 10-15% deduction may have been applied with a comment to interpret with caution.

Although not perfect the GLI-spirometry ethnic groups improve on what was seen previously and should be used wherever possible. The GLI-T_{LCO} reference equations did not collect enough data to devise ethnic specific equations, however from the data obtained no major differences were observed. Currently we recommend using GLI-T_{LCO} reference data for all ethnic groups.

Conclusion:

The Global lung function Initiative is the largest collection of lung function reference data to date. Data collection for all lung function tests is ongoing, interested groups may submit additional data at any time. Further information can be found on the ERS-GLI website:

https://www.ers-education.org/guidelines/global-lung-function-initiative.aspx

References:

1) Multi-ethnic reference values for spirometry for the 3-95yr age range: the global lung function 2012 equations Quanjer et al, *Eur Resp J* 2012
2) Official ERS technical standards: Global Lung Function Initiative reference values for the carbon monoxide transfer factor for Caucasians, Stanojevic et al, *Eur Resp J* 2017
3) 2017 ERS/ATS standards for single-breath carbon monoxide uptake in the lung. Graham et al, *Eur Resp J* 2017.

Matt Rutter

Alan Moore

Prof. Brendan Cooper

ON THE BLOWER

This edition of 'On the blower' has the latest product updates from Intermedical, nSpire health, Remserve and Vyaire.

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 Glasgow.

MR

PRODUCT UPDATES

intermedical http://www.intermedical.co.uk/

Intermedical are delighted to announce the launch of the New NOBreath FeNO Monitor. The 2nd Generation NObreath is the only FeNO device to bring unlimited testing capabilities. *The NObreath has built-in patient test compliance, full -colour touchscreen with easy-to-use interfacing and onscreen motivational exhalation guides, adjustable flow settings and memory for data storage as well as PC software. It has an ergonomic design which is fully portable and incorporated with SteriTouch® technology for optimum infection control. The NOBreath also has low ongoing service and maintenance costs and low cost consumables.*

Our ndd range continues to provide free software updates on all devices. The EasyOne Air now facilitates direct printing to HP printers. New features allow for the graphic trending of selected parameter including Z scores and external parameters such as FeNO. The EasyOne Air was used with great success at the Health Lungs for Life lung function screening in downtown Paris at the recent ERS. More than 800 members of the public attended and were screened using the EasyOne Air.

Following on from the success of the Resmon Pro FOT device, we are pleased to announce the launch of the Resmon Diary for use by COPD patients at home. Ten tidal breathes per day is all that is required for the tele-monitoring of severe COPD patients. The data is sent via 3G to a secure website which is then assessed by a consultant or physiologist. If an exacerbation is likely, a warning is given and the patient can be provided with appropriate treatment to avoid the exacerbation occurring thereby avoiding a hospital admission and potentially lengthy stay. This methodology has already been extensively tested in the Chromed multi-centre trial which was published in AJRCCM in March of this year (Am J Respir Crit Care Med. 2018 Sep 1;198(5):620-628).

Intermedical are pleased to be partnering Dolby Vivisol in this venture and are in the process of establishing initial UK trial sites. These will examine the practicalities of using FOT for home monitoring and will seek to measure patient outcomes and cost savings for the NHS.

NSPIRE HEALTH

http://www.nspirehealth.com/

Introducing Iris IQ™ PFT Department Management Solution including Quality Management, Business Analytics and new Testing Standards.

Thank you for recognising nSpire Health as the 2018 ARTP Lung Function Manufacturer of the Year. This upcoming year we will be showcasing our newest Iris IQ™ software modules at the ARTP conference.

Peer literature and laboratory assessments of current PFT practices show that up to 50% of all spirometry and pulmonary function test results do not meet the minimally viable quality standards for interpretation. This leads to an increased rate of misclassifications and misdiagnoses when diagnosing and monitoring patients' lung disease.

Until now, industry has not helped you solve this problem. Quality and department level management processes cost too much and take too long. nSpire Health is committed to providing you with the tools you need to produce PFT results that meet or exceed ERS minimum standards so clinicians can make clinical decisions based on complete and accurate information, ultimately providing better care to your patients at a substantially lower cost. Iris IQ™ helps eliminate misclassifications of test results while permitting you to detect smaller physiological changes over time. The product works with all manufacturers devices across the healthcare system and is designed to grow as your service needs grow, easily adding new or replacement instruments, or workstations supporting new features and capabilities over time.

- ◊ *New levels of device performance for FVC, Plethysmography and DLCO*
- ◊ *Automated PFT Department Quality Management*
- ◊ *Web-based Workflow Automation, Training and Corrective Action Tools with Analytics for Clinical Data Management, Clinical Operations Management, and Asset Management*

Stop by our stand at ARTP to see how Iris IQ™ can help you eliminate misclassifications and improve quality of care.

Matt Rutter

Alan Moore

Prof. Brendan Cooper

ON THE BLOWER

RemServe E-Mail: info@remservemedical.com t:0844 815 7088 f:0844 815 7158

Continuously striving to provide the absolute pinnacle in quality services to the NHS and its patients with our main focus being toward Obstructive Sleep Apnoea.

At RemServe Medical we continuously take steps to innovate the market with new products sourced from every corner of the globe. We want to continue to grow a range of products that perfectly balances patient comfort, service efficiency, product quality and keeping the overall cost to the NHS down.

We are really excited to exhibit new innovative products and take a special interest in the Paediatric side of OSA. We found many instances of a small nasal mask being used as a full face mask for a Paediatric patient which led us to investing in a full Paediatric line of masks including the NeoQ neo-natal masks, the Cirri-Mini nasal and the FitMax Total Face.

Not only are we looking at masks that cover neonatal paediatrics from a weight of less than 5 kilos up to over 8 kilos before being moved on to a paediatric mask that ranges from 0 to 8 years old. We are also attempting to keep ahead of the issues that are presented with treating younger patients. One of the main issues is "headgear" are keeping it on the patients' head without them becoming uncomfortable.

We don't just look at the bare minimum that a patient requires in order to be treated for a sleep disorder (like OSA); we are driven to work with the NHS to improve compliance across the board. This includes looking at comfier headgear, new ways of keeping CPAP equipment clean – eliminating pesky household smells that can be absorbed by filters and looking at more serious issues like bacterial and mould spores to help prevent patients' contracting a lung infection or in more serious cases – Pneumonia.

On top of the growing range of products that we supply to the NHS, we also appreciate that there is a gap in the market for products that some sleep clinics are unable to budget for. Some patients may have pressure sores or skin irritation from their mask cushion which is why we stock "Aftercare" products including mask-liners and other products like tube wraps to help prevent condensation in the tubing.

But it's not always about what products we have available to offer you, we also take the time to assess each sleep service on an individual basis and will even attempt to source new or alternative products that you may need or to help to reduce costs. We are always happy to work with the NHS in any way that we can.

https://www.vyaire.com/intl

Nothing is more critical to human life than air. When the ability to breathe is compromised, quality of life suffers. This is what drives Vyaire Medical, to create respiratory diagnostic equipment, that strives for higher levels of accuracy and patient friendliness than ever before.

With that, Vyaire Medical is pleased to announce the latest member of our Vyntus® family. The ***Vyntus® ONE****. Vyaire Medical has designed Vyntus® ONE to be effortless for clinicians and people-friendly for patients. Vyntus ONE is incredibly capable with a modular design that possesses an impressive array of features. It is designed to make your tests more accurate, less intrusive and less stressful for patients.*

Powered by SentrySuite® software, the reliable Vyntus ONE offers you the following applications:

- ***Standard measurements for Pulmonary Function Testing*** *(using our Ultrasonic Flow Sensor and Flow Path Valve eDemand)*
- ***Standard measurements for Cardiopulmonary Exercise Function Testing*** *(using Digital Volume Transducer for the CPET measurements)*
- ***Many optional measurements and features*** *to accommodate the wide range of patients and tests carried out in your busy lab today*

Come, visit us at the ARTP in Glasgow 31st January -1st February 2019 (stand 9), and see our latest Vyntus family member for yourself.

Edward Parkes

Suhila Hashimi

Fresh air

Dear Reader,

*Welcome to '**Fresh Air**'. This section is orientated around highlighting the latest trends in research and innovation from both respiratory and sleep sciences. The aim of this evolving feature is to not only provide you with what we hope is an interesting read; but also to provide you with a topic of conversation with your colleagues, far and wide, that may lead to on-going research. Dr Chris Earing has written an interesting article on the control of breathing and asks us all, as we sit and read this edition of **Inspire**, is breathing inherent, learnt or both?*

Edward Parkes

ARTP Chair of Research and Innovation Committee

With my new-born son in one arm and my daughter pulling on the other, I am privileged to get the ball rolling and begin with what is, I admit, an easier topic for me as it is after all skirting around my research background. I hope you enjoy reading and I certainly look forward to contributing further articles in the near future.

Dr Chris Earing

ARTP Research and Innovation Committee

The control of breathing inherited, learnt or both?

The rhythm of the breathing is the role of the brainstem central pattern generator which receives input from many divergent sources related to the state of the organism, including emotional, sleep-related, environmental and motor activity states, and more basic sensory inputs from mechano- and chemoreceptors located in lung and airway tissues and the bloodstream[1]. Ventilation is tightly controlled via an important feedback control system, consisting of the central and peripheral chemoreceptors. These work to keep $PaCO_2$ and plasma pH remarkably constant with the presence of normal kidney function[2,3]. Figure 1 illustrates the interaction between central and peripheral chemoreceptors which operate through the central pattern generator to bring about ventilation.

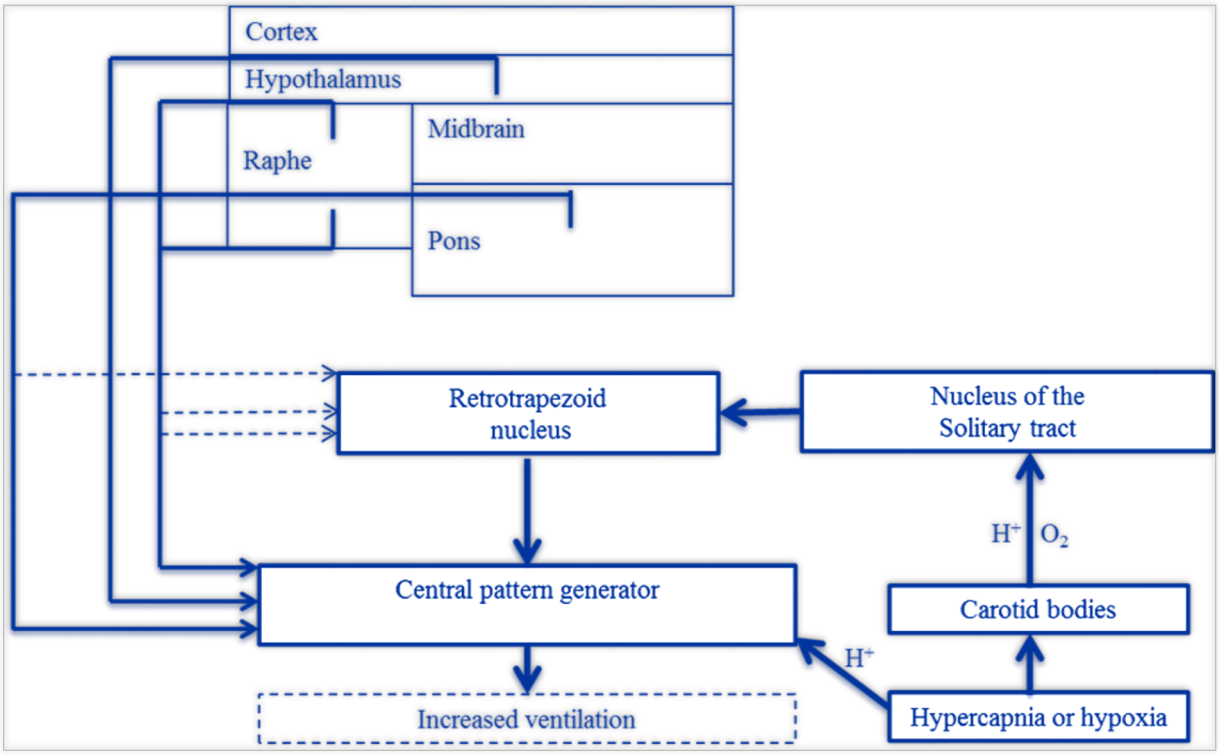


Figure 1. Showing the interaction between the central and peripheral chemoreceptors operating through a common respiratory controller located in the RTN. Adapted from Guyenet (2010).

Based on the reaction theory for ventilatory control, CO_2 stimulates the central chemoreceptors through liberating H^+ ions resulting in decreased pH[4]. Based on this theory, the central chemoreceptors detect the resulting acidosis and respond by increasing ventilation to help maintain arterial pCO_2 within a few mmHg of the steady-state (~40 mmHg) regardless of the metabolic production of CO_2 and level of vigilance[5,6,7,8]. It is recognised that the carotid bodies (peripheral chemoreceptors) are polymodal receptors (meaning respond to several different forms of sensory stimuli) that are responsible for detecting a variety of circulating stimuli including O_2, CO_2 and H^+ ions in addition to K^+, noradrenaline, temperature, osmolality, glucose and insulin[9,10]. The peripheral chemoreceptors particularly respond to hypoxia when PaO_2 falls below 70 mmHg[11]. It is now more widely accepted that the peripheral and central chemoreceptors do not act as entirely separate entities but interact with each other. It has been revealed that the stimulation of the peripheral chemoreceptors enhances the slope of the central CO_2

ventilatory response and inhibition of the carotid bodies reduces the slope of the central CO_2 response[9,12].

Previously a large proportion of research literature assessed the ventilatory response to hypercapnia and hypoxia separately. Individuals react with different sensitivities to increased CO_2 and there is a large divide in research findings, as to whether one acquires their ventilatory sensitivity through inheritance, learning or an interaction of both[13,14].

Research in support of inheritance include Saunders *et al*.[14] finding a strong significant relationship between CO_2 ventilatory sensitivity in young swimmers and their siblings, with swimming training not related to such findings. Our research with Scuba divers discussed later also found no such correlation between diving experience and the ventilatory response to CO_2 rebreathing and inhalation. We however did not look at inheritance[15]. In contradiction, Scoggin *et al*.[16] found no relationship between the ventilatory response of regional/national endurance runners and their families.

Congenital central hypoventilation syndrome (CCHS) is a rare genetically inherited disorder. In 2003, paired-like homeobox2B (PHOX2B) was identified as the disease-defining gene for CCHS. Alveolar hypoventilation is most profound during non-rapid eye movement (NREM) sleep, but is also present to a milder degree during Rapid eye movement (REM) sleep and wakefulness[17,18].

Interestingly, though, some patients who lack chemosensitivity (e.g. patients with CCHS) have a normal exercise hyperpnea (increased ventilation in response to exercise)[19,20,21,22]. This supports the view that learning processes shape the control of breathing with the observation that chemical feedback cannot fully account for the increase in ventilation at the onset of exercise.

Somjen[23] hypothesised the brain learns through a process of trial and error from as early as infancy and proposed a feedforward control, a learned process by which the brain knows exactly the amount of CO_2 produced and anticipates the corresponding ventilation rate to avoid any changes in arterial blood gases.

Is the ventilatory response adaptable? Research findings within Ysbyty Gwynedd/Bangor University:

Wood *et al*[13] found repeated bouts of exercise paired with simultaneous CO_2 inhalations modified the normal ventilatory response to exercise leading to the ideology that the ventilatory response to CO_2 is closely matched by learning and memory.

Previously within Bangor University and ongoing in Ysbyty Gwynedd we have investigated the ventilatory response to CO_2 in two populations. A healthy population of experienced scuba divers versus non-diving matched controls[15] and patients with obstructive sleep apnoea (*this research is currently still ongoing*).

Hypercapnia-induced symptoms are not uncommon amongst scuba divers ranging from a mild to severe headache, to increased risk of decompression illness, unconsciousness and death underwater. This increased incidence occurs as a result of a combination of factors including intentional 'skip breathing' or unintentional hypoventilation, the use of a semi-closed or closed circuit rebreather and the performance of vigorous physical exertion with both diving depth and water current[24,25,26].

Over time we have performed a series of investigations with experienced scuba divers compared to non-diving controls. We identified throughout that experienced scuba divers had a lower ventilatory response to CO_2; we also found this when CO_2 rebreathing was performed during cycling on ergometer at workload estimated to be relevant to scuba diving[27]. The CO_2 ventilatory response slope was not significantly modified by the exercise within both groups. There still though remains no agreement in

the research literature on the influence of exercise on ventilatory sensitivity[28,29,30,31,32,33].

Based on CO_2 rebreathing complete with analysed capillary blood samples (Table 1) we identified at 5% inspired CO_2 the non-diving controls tended to respond whereas experienced scuba divers responded later at around the 6% inspired CO_2.The analysed capillary blood samples revealed significant CO_2 retention in the scuba divers during CO_2 rebreathing but not on room air (normocapnic and normoxic condition). The two groups were also found to not differ in their CO_2 retention with the accumulation of more than 7% inspired CO_2, suggesting that both groups had reached their peak ventilatory response to the pCO_2. We used these findings to guide our CO_2 concentrations with scuba divers and our future research with patients with obstructive sleep apnoea.

	Ambient	5%	6%	7%
pH				
Scuba	7.40 ± 0.02	7.36 ± 0.02**	7.34 ± 0.01**	7.32 ± 0.02
Control	7.40 ± 0.02	7.38 ± 0.02	7.37 ± 0.02	7.33 ± 0.3
pCO_2 (mm Hg)				
Scuba	43.18 ± 2.40	47.73 ± 2.28**	49.43 ± 2.23**	53.20 ± 2.20
Control	41.55 ± 1.57	44.72 ± 1.74	45.80 ± 1.48	51.14 ± 4.22
HCO3std (mmol/L)				
Scuba	26.01 ± 0.91	25.45 ± 0.80	24.97 ± 0.81	25.46 ± 1.29
Control	25.71 ± 0.95	25. 70 ± 0.71	25.56 ± 0.78	25.33 ± 0.93
BE (mmol/L)				
Scuba	1.44 ± 1.16	0.57 ± 1.03	-0.04 ± 1.03	0.60 ± 1.64
Control	1.05 ± 1.21	0.90 ± 0.91	0.70 ± 0.99	0.42 ± 1.19
THbc (g/dL)				
Scuba	13.91 ± 0.80	13.93 ± 0.85	14.26 ± 0.91	14.42 ± 1.03
Control	13.93 ± 0.85	13.65 ± 1.01	13.88 ± 0.98	14.06 ± 0.84

Table 1. *Capillary blood gas parameters during ambient and resting CO2 rebreathing.*

*Where significantly different means between the two groups, ** = p <0.01. Abbreviations: standard bicarbonate (HCO3std) , base excess (BE), total haemoglobin (THbc).*

In the final study we examined respiratory drive of the groups using four different gas mixtures balanced with N_2 (ambient air; 25% O_2 /6% CO_2; 13% O_2; 13% O_2/6% CO_2) to assess the combined response to hypercapnia and moderate hypoxia. To our knowledge this was the first study to investigate the possible contribution of the peripheral chemoreflex for the divers altered ventilatory response. The ventilatory response to CO_2 in the hypoxic and hyperoxic conditions between the two groups were unchanged, suggesting the altered ventilatory response in experienced divers is a central adaptation.

As mentioned before in each study no correlation was found between the ventilatory response and diving experience, a finding which is in agreement with other studies[34,35]; this leads to the suggestion that the changes in the ventilatory response to CO_2 is either achieved in a comparably short time or that the sensitivity is inherited or both acquired through learning and inherited with individuals whom are sensitive to CO_2 and not likely to continue diving as a leisure or professional activity. Walterspacher *et al*.[36] postulated successful breath hold diving is dependent on the magnitude of trainable adaptation to increased CO_2 levels as well as genetics. Apnoea training, involving repeated breath holds with short recovery periods, have also been shown to increase the time in withstanding the respiratory drive, contributing to prolonged breath hold duration. Adaptations have been shown to occur in a short time amongst clinical populations which may also further increase our understanding of the modification of the ventilatory adaptation amongst scuba divers. In clinical populations abnormal breathing patterns, with CO_2 retention during waking and especially in sleep has been documented in neurodegenerative diseases such as Parkinson's disease, amyotrophic lateral sclerosis, post-polio syndrome with bulbar involvement and multiple system atrophy. All have been linked to deficits in neurons within the pre-Bötzinger complex, pontine raphe and adjacent areas[9,37]. These are all areas believed to play roles in chemoreception.

Patients with Chronic Obstructive Pulmonary Disease (COPD) have also been reported to have an attenuated ventilatory response to hypercapnia/hypoxia[38,39]. Unfortunately, however, in COPD it is difficult to determine whether the reduced ventilatory response is due to impaired respiratory central drive, as the ventilatory response is correlated with the mechanical limitations of COPD[39,40].

Patients with sleep apnoea are frequently exposed to nocturnal bouts of hypoxia and hypercapnia during apnoeic related events which have also been implicated to induce alterations in the response of the central and peripheral chemoreceptors[41]. One theory is this is a progressive adaptation involving "resetting" of the receptors of the integrative neurons in the brainstem to a different sensitivity threshold[42,43]. It is also plausible that there is a pathogenic role of inflammation which mediates the upregulation of the renin-angiotensin system in the carotid body causing over activity in the chemoreflex[44,45].

An alteration in the ventilatory response may cause an increase in the collapsibility of the upper airway. An increase in the ventilatory drive would activate the upper airway muscles and promote patency whereas a reduction in ventilatory drive would relax the upper airway muscles and facilitate closure[46]. Other researchers also speculate that a heightened responsiveness may contribute to respiratory control instability potentially leading to periodic breathing and further airway obstruction via increased loop gain whereas blunted responsiveness may prolong apnoea duration due to lowering of the arousal reflexes[42].

Currently our latest doctorate student is coming towards the end of data collection within Ysbyty Gwynedd. We

have presented some preliminary findings at conference however the experiments are still ongoing with the recruitment of a larger number of patients and controls for comparison. Therefore, it would be premature to present such findings here.

In conclusion:

It is widely debated in the research literature as to whether the ventilatory response is learnt, inherited or an interaction of both. This current analysis reports evidence of both inheritance with similar ventilatory responses reported amongst close family members in some studies however not always. Our data from experienced scuba divers support that if learning does take place it is achieved in a comparably short time with no correlation found between the ventilatory response and the number of dives. It is likely a question which warrants further investigation. If there is an acquired component then this might open up potential benefits of certain interventions designed to alter the ventilatory response as an advantage to improve clinical outcomes in certain clinical populations.

References

1. Bellingham, M.C. 1998, "Driving respiration: the respiratory central pattern generator", Clinical and Experimental Pharmacology & Physiology, vol. 25, no. 10, pp. 847-856.
2. Ogoh, S., N. Hayashi, M. Inagaki, P.N. Ainslie & T. Miyamoto 2008, "Interaction between the ventilatory and cerebrovascular responses to hypo- and hypercapnia at rest and during exercise", Journal of Physiology, vol. 586, no. 17, pp. 4327-4338.
3. Miyamoto, T., M. Inagaki, H. Takaki, T. Kawada, Y. Yanagiya, M. Sugimachi & K. Sunagawa 2004, "Integrated characterization of the human chemoreflex system controlling ventilation, using an equilibrium diagram", European Journal of Applied Physiology, vol. 93, no. 3, pp. 340-346.
4. Loeschcke, H.H. 1982, "Central chemosensitivity and the reaction theory", Journal of Physiology, vol. 332, pp. 1-24.
5. Guyenet, P.G., Stornetta, R.L. & Bayliss, D.A. 2010, "Central respiratory chemoreception", Journal of Comparative Neurology, vol. 518, no. 19, pp. 3883-3906.
6. Nattie, E. & Li, A. 2009, "Central chemoreception is a complex system function that involves multiple brain stem sites", Journal of applied physiology, vol. 106, no. 4, pp. 1464-1466.
7. Nattie, E. 1999, "brainstem chemoreceptors and breathing", Progress in Neurobiology, vol. 59, no. 4, pp. 299-331.
8. Feldman, J.L., Mitchell, G.S. & Nattie, E.E. 2003, "Breathing: rhythmicity, plasticity, chemosensitivity", Annual Review of Neuroscience, vol. 26, pp. 239-266.
9. Dempsey, J.A. & Smith, C.A. 2014, "Pathophysiology of human ventilatory control", The European respiratory journal, vol. 44, no. 2, pp. 495-512.
10. Kumar, P. & Bin-Jaliah, I. 2007, "Adequate stimuli of the carotid body: more than an oxygen sensor?", Respiratory physiology & neurobiology, vol. 157, no. 1, pp. 12-21.
11. Nattie, E. 2006, "Why do we have both peripheral and central chemoreceptors", Journal of applied physiology, vol. 100, no. 1, pp. 9-10.
12. Blain, G.M., Smith, C.A., Henderson, K.S. & Dempsey, J.A. 2010, "Peripheral chemoreceptors determine the respiratory sensitivity of central chemoreceptors to CO2", The Journal of physiology, vol. 588, no. 13, pp. 2455-71.
13. Wood, H.E., Fatemian, M. & Robbins, P.A. 2003, "A learned component of the ventilatory response to exercise in man", The Journal of physiology, vol. 553, no. Pt 3, pp. 967-974.
14. Saunders, N.A., Leeder, S.R. & Rebuck, A.S. 1976, "Ventilatory response to carbon dioxide in young athletes: a family study", The American Review of Respiratory Disease, vol. 113, no. 4, pp. 497-502.
15. Earing, C.M.N., McKeon, D.J. & Kubis, H. 2014, "Divers revisited: The ventilatory response to carbon dioxide in experienced scuba divers", Respiratory medicine, vol. 108, no. 5, pp. 758-765.
16. Scoggin, C.H., Doekel, R.D., Kryger, M.H., Zwillich, C.W. & Weil, J.V. 1978, "Familial aspects of decreased hypoxic drive in endurance athletes", Journal of applied physiology: respiratory, environmental and exercise physiology, vol. 44, no. 3, pp. 464-468.
17. Ramanantsoa, N. & Gallego, J. 2013, "Congenital central hypoventilation syndrome", Respiratory physiology & neurobiology, vol. 189, no. 2, pp. 272-279.
18. Tanizawa, K. & Chin, K. 2018, "Genetic factors in sleep-disordered breathing", Respiratory investigation, vol. 56, no. 2, pp. 111-119.
19. Gozal, D. & Harper, R.M. 1999, "Novel insights into congenital hypoventilation syndrome", Current opinion in pulmonary medicine, vol. 5, no. 6, pp. 335-338.
20. Gozal, D. & Simakajornboon, N. 2000, "Passive motion of the extremities modifies alveolar ventilation during sleep in patients with congenital central hypoventilation syndrome", American journal of respiratory and critical care medicine, vol.

162, no. 5, pp. 1747-1751.

21. Shea, S.A., Andres, L.P., Shannon, D.C., Guz, A. & Banzett, R.B. 1993, "Respiratory sensations in subjects who lack a ventilatory response to CO2", Respiration physiology, vol. 93, no. 2, pp. 203-219.

22. Gallego, J., Nsegbe, E. & Durand, E. 2001, "Learning in respiratory control", Behavior modification, vol. 25, no. 4, pp. 495-512.

23. Somjen, G.G. 1992, "The missing error signal - regulation beyond negative feedback", News in Physiological Sciences, vol. 7, pp. 184-185.

24. Cheshire, W.P. & Ott, M.C. 2001, "Headache in divers", Headache, vol. 41, no. 3, pp. 235-47.

25. Eynan, M., Arieli, R. & Adir, Y. 2005, "Response to CO2 in novice closed-circuit apparatus divers and after 1 year of active oxygen diving at shallow depths", Journal of applied physiology (Bethesda, Md.: 1985), vol. 98, no. 5, pp. 1653-1659.

26. Morrison, J.B., Florio, J.T. & Butt, W.S. 1978, "Observations after loss of consciousness under water", Undersea biomedical research, vol. 5, no. 2, pp. 179-187.

27. Ainsworth, B.E., Haskell, W.L., Herrmann, S.D., Meckes, N., Bassett, D.R., Jr, Tudor-Locke, C., Greer, J.L., Vezina, J., Whitt-Glover, M.C. & Leon, A.S. 2011, "2011 Compendium of Physical Activities: a second update of codes and MET values", Medicine and science in sports and exercise, vol. 43, no. 8, pp. 1575-1581.

28. McConnell, A.K. & Semple, E.S. 1996, "Ventilatory sensitivity to carbon dioxide: the influence of exercise and athleticism", Medicine and science in sports and exercise, vol. 28, no. 6, pp. 685-691.

29. Clark, T.J. & Godfrey, S. 1969, "The effect of CO2 on ventilation and breath-holding during exercise and while breathing through an added resistance", The Journal of physiology, vol. 201, no. 3, pp. 551-566.

30. Cummin, A.R., Alison, J., Jacobi, M.S., Iyawe, V.I. & Saunders, K.B. 1986, "Ventilatory sensitivity to inhaled carbon dioxide around the control point during exercise", Clinical science (London, England : 1979), vol. 71, no. 1, pp. 17-22.

31. Kelley, M.A., Owens, G.R. & Fishman, A.P. 1982, "Hypercapnic ventilation during exercise: effects of exercise methods and inhalation techniques", Respiration physiology, vol. 50, no. 1, pp. 75-85.

32. Martin, B.J., Weil, J.V., Sparks, K.E., McCullough, R.E. & Grover, R.F. 1978, "Exercise ventilation correlates positively with ventilatory chemoresponsiveness", Journal of applied physiology: respiratory, environmental and exercise physiology, vol. 45, no. 4, pp. 557-564.

33. Miyamura, M., Yamashina, T. & Honda, Y. 1976, "Ventilatory responses to CO2 rebreathing at rest and during exercise in untrained subjects and athletes", The Japanese journal of physiology, vol. 26, no. 3, pp. 245-254.

34. Florio, J.T., Morrison, J.B. & Butt, W.S. 1979, "Breathing pattern and ventilatory response to carbon dioxide in divers", Journal of applied physiology: respiratory, environmental and exercise physiology, vol. 46, no. 6, pp. 1076-1080.

35. Froeb, H.F. 1961, "Ventilatory response of scuba divers to CO2 inhalations", Journal of applied physiology, vol. 16, pp. 8-10.

36. Walterspacher, S., Scholz, T., Tetzlaff, K. & Sorichter, S. 2011, "Breath-hold diving: respiratory function on the longer term", Medicine and science in sports and exercise, vol. 43, no. 7, pp. 1214-1219.

37. Schwarzacher, S.W., Rub, U. & Deller, T. 2011, "Neuroanatomical characteristics of the human pre-Botzinger complex and its involvement in neurodegenerative brainstem diseases", Brain : a journal of neurology, vol. 134, no. Pt 1, pp. 24-35.

38. Fahey, P.J. & Hyde, R.W. 1983, ""Won't breathe" vs "can't breathe". Detection of depressed ventilatory drive in patients with obstructive pulmonary disease", Chest, vol. 84, no. 1, pp. 19-25.

39. Xu, F., Zhuang, J., Wang, R., Seagrave, J.C. & March, T.H. 2007, "Blunted ventilatory response to hypoxia/hypercapnia in mice with cigarette smoke-induced emphysema", Respiratory physiology & neurobiology, vol. 158, no. 1, pp. 5-13.

40. Cherniack, R.M. & Snidal, D.P. 1956, "The effect of obstruction to breathing on the ventilatory response to CO2", The Journal of clinical investigation, vol. 35, no. 11, pp. 1286-1290.

41. Cooper, V.L., Pearson, S.B., Bowker, C.M., Elliott, M.W. & Hainsworth, R. 2005, "Interaction of chemoreceptor and baroreceptor reflexes by hypoxia and hypercapnia - a mechanism for promoting hypertension in obstructive sleep apnoea", Journal of Physiology (London), vol. 568, no. 2, pp. 677-687.

42. Verbraecken, J., De Backer, W., Willemen, M., De Cock, W., Wittesaele, W. & Van de Heyning 1995, "Chronic CO2 drive in patients with obstructive sleep apnea and effect of CPAP", Respiration physiology, vol. 101, no. 3, pp. 279-287.

43. Guilleminault, C. & Cummiskey, J. 1982, "Progressive improvement of apnea index and ventilatory response to CO2 after tracheostomy in obstructive sleep apnea syndrome", The American Review of Respiratory Disease, vol. 126, no. 1, pp. 14-20.

44. Fung, M.L., Tipoe, G.L. & Leung, P.S. 2014, "Mechanisms of maladaptive responses of peripheral chemoreceptors to intermittent hypoxia in sleep-disordered breathing", Sheng li xue bao : [Acta physiologica Sinica], vol. 66, no. 1, pp. 23-29.

45. Lam, S., Liu, Y., Ng, K., Lau, C., Liong, E.C., Tipoe, G.L. & Fung, M. 2012, "Chronic intermittent hypoxia induces local inflammation of the rat carotid body via functional upregulation of proinflammatory cytokine pathways", Histochemistry and cell biology, vol. 137, no. 3, pp. 303-17.

46. Wellman, A., Malhotra, A., Jordan, A.S., Stevenson, K.E., Gautam, S. & White, D.P. 2008, "Effect of oxygen in obstructive sleep apnea: role of loop gain", Respiratory physiology & neurobiology, vol. 162, no. 2, pp. 144-151.

Did you like this article? Do you have any comments?

You can discuss these with the author at Christopher.earing@wales.nhs.uk f you have any ideas on what would be a suitable topic for a future article then please contact Edward Parkes, ARTP Chair of Research and Innovation Committee at Edward.Parkes@uhcw.nhs.uk.

More fresh air

Recent tweets that have inspired

Aspergillus and progression of lung disease in children with cystic fibrosis
https://thorax.bmj.com/content/early/2018/10/01/thoraxjnl-2018-211550?papetoc

Consequences of long-term oral corticosteroid therapy and its side-effects in severe asthma in adults: a focused review of the impact data in the literature
http://erj.ersjournals.com/content/52/4/1800703?ctkey=shareline

Wheezing Exacerbations Predicted by Allergen Sensitization and Exposure
https://www.pulmonologyadvisor.com/allergies/wheezing-allergens-sensitization-exposure-inhaled-corticosteroids/article/810571/?utm_campaign=Relevant++News&utm_content=79120832&utm_medium=social&utm_source=twitter

Secondhand aerosol exposure associated with increased risk of asthma attack in teens, study suggests.
https://www.medpagetoday.com/pulmonology/asthma/75984?utm_campaign=Relevant%20%20News&utm_content=79109315&utm_medium=social&utm_source=twitter

Infant growth and childhood respiratory health: how long is the road to preventive measures?
https://thorax.bmj.com/content/early/2018/09/28/thoraxjnl-2018-212341?papetoc=

Toxic air at the door of the NHS
https://www.blf.org.uk/take-action/campaign/nhs-toxic-air-report

Inhaler Technique Education and Exacerbation Risk in Older Adults with Asthma or Chronic Obstructive Pulmonary Disease: A Meta-Analysis
https://onlinelibrary.wiley.com/doi/10.1111/jgs.15602

Patterns, trends and determinants of e-cigarette use in 28 European Union Member States 2014–2017
https://www.sciencedirect.com/science/article/pii/S0091743518302597?via%3Dihub

"How astrophysics could transform the treatment of cystic fibrosis and other rare diseases" — http://theconversation.com/how-astrophysics-could-transform-the-treatment-of-cystic-fibrosis-and-other-rare-diseases-104449

Share your tweets with Suhilla Hashimi, Inspire Deputy Editor at Suhilla.Hashimi@gstt.nhs.uk

FeNO testing at just **£3.50 per patient**

NObreath® 2

Cost-effective, accurate and reliable FeNO testing.
Launching January 2019.

Visit our stand at ARTP Glasgow

intermedical
CARDIO RESPIRATORY

sc@intermedical.co.uk | 01732 522444

Harry Griffin

Top Forum

Since becoming a member of ARTP in 2014 I have found the ARTP forum to be an invaluable learning tool. It is a great platform to ask the country's leading respiratory and sleep physiologists for advice. This can be clinical, such as interpreting a tricky diagnostic test or service related, such as selecting the correct tariffs. The ARTP Forum is open to all ARTP members and is especially useful for junior members to pick the brains of those more experienced physiologists, recently referred to on the forum as 'Wise Owls' or 'Permanently Confused Pigeons'.

If you are already a member of the forum then the term 'like London busses' may spring to mind. There are weeks when your inbox receives nothing from the forum and then others when there are simply too many to keep up with. We thought it might be useful to have a regular section in Inspire that summarises some of the key posts. We hope you think it is a useful feature but please let us know either way.

NICE Pirfenidone Reference Values (24.07.2018)

The question: *Which reference equations were used to calculate FVC % predicted in either the ASCEND or CAPACITY trials? The underlying question being raised, was whether different reference ranges might affect who is prescribed anti-fibrotics (e.g. Perfenidone)?*

The responses: Several physiologists responded and clearly this is an area of concern for our profession. Indeed, if you have been to any recent ERS conferences you will have seen several presentations on this topic.

The general consensus on the forum was that NHANES reference ranges were used for the ASCEND trial. Several very useful articles covering this topic were highlighted. This included a great review article by Amy Taylor-Gonzalez in the August 2016 edition of Inspire, titled: *The use of lung function data in NICE pathways and guidance to ascertain eligibility for treatment on the NHS. A call for more respiratory physiologists to become involved in the review process.*

Further reading included, *Patient Eligibility for anti-fibrotic therapy in idiopathic pulmonary fibrosis can be altered by use of different sets of reference values for calculation of FVC percent predicted. K.Ward, T.M. Maher, S. Ward, F. Chua, A. Wells et al. Resp Med 120 (2016) 131-133.*

EIA – bike protocol (27.07.2018)

The question: *Does anyone use a bike for exercise induced asthma testing and if so, what is your protocol?*

The responses: It was suggested that exercise intensity should be increased over three minutes to raise the HR to 80% of predicted max and then sustained for eight minutes. Titrating the exercise intensity could help maintain the desired HR. However, it was highlighted that laboratory cycling may not be sensitive at identifying EIA and running whilst breathing dry and/or cold air would be better. Furthermore, a Mannitol test might be more sensitive and reading Sandy Anderson's research on this topic would be beneficial.

TLCO measurements (31.07.2018)

The question: *ARTP exam paperwork states inspiration on gas transfer test should be within 1.5-2 seconds. What effect does too fast an inspiration have on TL_{CO}?*

The responses: This question certainly ruffled the feathers of a few 'wise owls' who provided detailed responses on the physiological effects of varying inspiratory speeds.

Several physiologists stated they ask patients to inspire as fast as possible. This is in keeping with the 2017 ATS/ERS standards paper which states "the inspiration must be rapid" and that "DL_{CO} calculations assume instantaneous lung filling". However, one physiologist explained that 1.5-2 seconds was chosen because it was fast but not too fast to significantly alter intrathoracic pressures that would affect V/Q relationships.

Transvasin (06.08.2018)

The question: *There appears to be a national shortage of transvasin, what are other people using as alternative?*

The responses: A regular topic on the Forum but physiologists were able to offer several alternative methods. These included Deep heat cream, Capsaicin cream (Zacin 0.025% w/w - Cephalon) or a nitrile glove with water warmed to a specified, safe temperature.

CPET interpretation help (20.08.2018)

The question: *CPET results were provided and advice was sought for why the AT was so high?*

The responses: Help was offered by several CPET experts and an agreement was reached on why the AT was high. This was a great example of how the forum can be used to directly improve patient care. A more significant outcome of this post was the discussions that followed regarding setting up regional MDTs to discuss interesting CPET cases.

CPAP / NIV / APAP machines (29.08.2018)

The question: *The HSE and MHRA recommend annual electrical safety testing for CPAP / NIV / APAP machines and this NHS trust is considering a 50k external contract. What does your department offer?*

The responses: One reply detailed how a medical engineer would perform an electrical safety test, pressure and humidifier check every two years during the patients' follow up physiologist led clinic appointment. However, another physiologist stated "Class 2 electronic devices do not need routine testing. Contact the manufacturer for written confirmation of this fact".

'NO PRIZES' CRYPTIC CROSSWORD

Answers to 'No Prizes', August 2018 issue:

Across: 3. RESEARCH 5. CPAP 7. NOSECLIP 10. TRACHEA 12. PERFUSION 13. OBESITY 16. CANNULA 19. THERAPY 21. TB 21. CYSTIC

Down: 1. LARYNGEAL 2. HISTAMINE 4. PERTUSSIS 6. PHYSICIAN 8. VIRUS 9. LABORATORY 11. BRONCHOSCOPY 14. TRACHEOSTOMY 15. INTERSTITIAL 17. BREATHING 18. HYPOXIC

ARTP Association for Respiratory Technology & Physiology

ARTP ANNUAL CONFERENCE 2019
THURSDAY 31ST JANUARY - FRIDAY 1ST FEBRUARY 2019

The Executive Board of ARTP are thrilled to bring the annual conference to all parts of the United Kingdom (where it is practically possible to do so and appropriate venues exist) and so we are delighted to announce that the 2019 Conference will returning to Glasgow. This promises to be a superb conference filled with engaging speakers, covering topics from a range of physiology and new innovations including sessions on breathlessness, treatment of sleep disordered breathing, combating infection in respiratory disease and paediatric session around the topic of respiratory assessment in the non-respiratory child.

http://www.artp.org.uk/en/meetings/artp-annual-conference-2019/index.cfm