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AO 001

**COMPARISON OF ESTIMATING ELASTIC RECOIL FROM OESOPHAGEAL BALLOON AND THE FORCED OSCILLATION NILSEN K<sup>1,2,4</sup>, THOMPSON B<sup>1,2</sup>, CHAPMAN D<sup>4,6</sup>, THIEN F<sup>2,3</sup>, KING G<sup>4,5</sup>, TONGA K<sup>4,5</sup>, THAMRIN C<sup>4,5</sup>**

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**Introduction/Aim.** Loss of elastic recoil occurs with aging as well as in diseases such as emphysema and asthma. The gold standard method of measuring elastic recoil involves an oesophageal balloon to estimate transpulmonary pressure (Ptp); however, the test is invasive and thus of limited clinical use. This study aims to examine a new method of assessing elastic recoil using the forced oscillation technique (FOT), an easy-to-perform, emerging lung function test in the clinical setting.

**Methods.** Subjects with asthma (n = 16) and healthy controls (n = 17) completed spirometry and plethysmography before insertion of an oesophageal balloon. Subjects then performed inspiratory capacity manoeuvres during which Ptp and FOT were simultaneously obtained. The relationship between transrespiratory pressure, FOT reactance and lung volume was used to calculate a surrogate measure of Ptp. The Colebatch equation  $V = A - Be^{(-kP)}$  was then used to model the relationship between volume (expressed as %predTLC) and Ptp derived from both methods, and the agreement between the two models compared in terms of k (compliance) and B/A ratio (measure of elastic recoil). We also examined differences between controls and asthma.

**Results.** There was no difference in k ( $0.026 \pm 0.022$  vs  $0.029 \pm 0.014$ ,  $P = 0.23$ ) between the two models, while bias was seen in B/A ( $61.4 \pm 18.6$  vs  $78.3 \pm 18.3$ ,  $P < 0.01$ ). There were no differences in k or B/A between controls and asthma, however change in FEV1 post-bronchodilator was negatively correlated with B/A ( $r^2 = 0.57$ ,  $P < 0.001$ ) in asthma.

**Conclusion.** FOT provides a promising surrogate for elastic recoil that is easy to implement into clinical practice. Using this technique, we suggest that increase of elastic recoil may contribute to the loss of reversibility in asthma.

**CONTROLLED VS UNCONTROLLED BREATHING PROTOCOL IN ADULTS USING MULTIPLE BREATH NITROGEN WASHOUT (MBNW) TO MEASURE VENTILATION HETEROGENEITY**

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**Introduction/Aim.** Multiple Breath Nitrogen Washout (MBNW) provides indices of ventilation heterogeneity, which may help detect and quantify early onset of small airway dysfunction. Two protocols are commonly used: uncontrolled tidal breathing vs 1-L controlled tidal volume breathing. We aimed to determine if the two protocols provided equivalent MBNW indices in healthy adults, and compared FRC obtained from both protocols against plethysmographic FRC. We also examined factors contributing to any observed differences.

**Method.** Healthy individuals with a smoking history <5pk yrs, performed both the 1-L controlled breathing and uncontrolled tidal breathing protocols, in randomised order, on the Eco Medics Exhalizer<sup>®</sup> D system, according to ATS/ERS criteria. Indices from each protocol were extracted from the pooled results 3 trials per session: FRC, LCI (lung clearance index), Scnd and Sacin (ventilation heterogeneity primarily in the conductive and acinar airways, respectively). For the uncontrolled protocol, Scnd and Sacin were corrected for tidal volume. The two protocols were compared using paired-t tests, correlations, and Bland-Altman plots.

**Results.** Data from 13 (8 males) individuals (age range 19-51 yrs, mean  $\pm$  SD BMI  $23 \pm 2.56$ , FEV<sub>1</sub>% pred  $102.15 \pm 15.7$  FEV<sub>1</sub>/FVC  $84.4 \pm 6.92$ ) are presented. FRC measurements between the two methods were highly correlated ( $r = 0.98$ ,  $P < 0.0001$ ). There were no significant differences between the two methods for FRC, Scnd and LCI, while Sacin was higher using the 1-L controlled protocol (paired t-test,  $P = 0.009$ ). However, Bland-Altman plots revealed significant proportional bias, i.e. the differences in FRC and Sacin between the two protocols depended on their magnitudes ( $P = 0.0158$  and  $P < 0.0001$ , respectively). Furthermore, the 1-L controlled protocol increasingly overestimated FRCpleth in individuals with larger FRCpleth ( $P = 0.030$ ).

**Conclusion.** Lung volume and ventilation heterogeneity assessed using the two protocols may not be comparable in taller individuals. These preliminary results will aid in the ongoing standardisation efforts for MBNW, which are critical for its clinical application, and form a basis for future comparisons in patients with lung disease.

**Key Words:** Multi-Breath Nitrogen Washout (MBNW), FRC, Protocols  
**Nomination for New Investigator Award: Yes Grant Support: No**

### VENTILATION MEASUREMENTS FROM HYPERPOLARIZED <sup>3</sup>HE MAGNETIC RESONANCE IMAGING ARE A MARKER OF AIRWAY CLOSURE IN SUBJECTS WITH AIRFLOW OBSTRUCTION

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**Introduction/Aim.** Images from Hyperpolarised <sup>3</sup>He magnetic resonance imaging (<sup>3</sup>He MRI) provide exquisite detail of gas distribution across the lung. What is lacking is functional information from these images. In this study we examine the percentage of ventilated lung from <sup>3</sup>He MRI and compare these with measurements of ventilation heterogeneity and markers of airway closure.

**Methods.** Subjects with asthma (n = 10), fixed airflow obstruction (n = 9) and healthy controls (n = 10) attended two testing sessions. On visit one, full pulmonary function assessment (both pre and post methacholine challenge) was conducted. Measurements performed were: spirometry, plethysmography, multiple breath washout (MBW) and the forced oscillation technique (FOT). On visit two, <sup>3</sup>He MRI scans were conducted pre and post methacholine challenge. The percentage of voxels above 0.15 of the maximum voxel intensity was used to calculate the percentage of ventilation.

**Results.** Measurements of the percentage of ventilated lung from <sup>3</sup>He MRI scans were significantly reduced in subjects with asthma by  $-12.3 \pm 10.1$  (percent ventilation) ( $P < 0.001$ ) and in subjects with fixed airflow obstruction by  $-12.9 \pm 7.3$  (percent ventilation) ( $P = 0.015$ ), post methacholine. This reduction in percentage ventilation from <sup>3</sup>He MRI was positively correlated with a FOT marker of airway closure and a MBW maker of ventilation heterogeneity in the conducting region of the lung, in both asthma ( $X_{rs} 6\text{Hz}$ ,  $r^2 = 0.54$ ,  $P < 0.01$  and  $\text{Scand}$ ,  $r^2 = 0.31$ ,  $P < 0.01$ ) and fixed airflow obstruction ( $X_{rs} 6\text{Hz}$ ,  $r^2 = 0.28$ ,  $P < 0.01$  and  $\text{Scand}$ ,  $r^2 = 0.29$ ,  $P < 0.01$ ). Subjects with fixed airflow obstruction had a significantly higher pre methacholine value of Sacin ( $0.21 \pm 0.1 \text{ L}^{-1}$  vs  $0.11 \pm 0.03$ ,  $P = 0.04$ ), which was also correlated ( $r^2 = 0.79$ ,  $P < 0.01$ ) with decreased percentage ventilation.

**Conclusion.** <sup>3</sup>He MRI scans enable remarkable visualisation of airway closure and ventilation heterogeneity. Measurements of percentage ventilation from <sup>3</sup>He MRI scans are associated with physiological markers of airway closure and ventilation heterogeneity in subjects with airflow obstruction.

#### Grant Support:

NHMRC project grant 606994.

### CONCORDANCE OF BRONCHODILATOR RESPONSE (BDR) IN ASTHMA AND COPD

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**Introduction/Aim.** BDR is clinically important in obstructive airways diseases. The concordance between spirometry and Forced Oscillation Technique (FOT) BDR is unknown. We aim to determine the concordance in BDR between spirometry and FOT in asthma & COPD.

**Method.** A retrospective analysis of 117 asthmatic and 42 COPD patients who had performed spirometry and FOT, pre and post-400ug Salbutamol. Respiratory resistance ( $R_{rs5}$ ) and reactance ( $X_{rs5}$ ) at 5Hz were calculated from 3x30s acquisitions from FOT. A positive BDR in spirometry is defined as changes in  $\text{FEV}_1$  or  $\text{FVC} \geq 12\%$  and 200 mL and in FOT as a percentage(%) change in  $R_{rs5} < 31.5\%$  or  $X_{rs5} > 43.5\%$  of baseline; or an absolute decrease in  $R_{rs5} > 1.40 \text{ cmH}_2\text{O/L/s}$  or an absolute increase in  $X_{rs5} > 0.56 \text{ cmH}_2\text{O/L/s}$  from baseline. Concordance in BDR was assessed using Cohen's kappa statistic.

#### Results:

	n	Age(yrs) $\pm$ SD	FEV1% <sub>PRED</sub>	FEV1/FVC(%)	Subjects with Positive BDR		
					Spirometry	FOT (%change)	FOT (absolute)
Asthma	117	61.9 $\pm$ 16.9	76.6 $\pm$ 19.3	63.5 $\pm$ 11.6	20 (17%)	23 (20%)	41 (35%)
COPD	42	68.7 $\pm$ 10.6	47.9 $\pm$ 19.4	43.7 $\pm$ 13.2	9 (21%)	0 (0%)	11 (26%)

Concordance between Spirometry & FOT (Cohen's Kappa)				
	Spiro vs FOT (absolute)	Spiro vs FOT (%change)	FEV1 vs R5 (absolute)	FEV1 vs X5 (absolute)
Asthma	0.26	0.40	0.49	0.29
COPD	0.21	0.00	0.29	0.30

In asthma, the absolute change in  $X_{rs5}$  was a more sensitive measure of BDR than  $R_{rs5}$  or spirometry (35%, 12% and 17%, respectively); and similarly in COPD (26%, 5% and 21%, respectively).

**Conclusion.** In both asthma and COPD, BDR concordance is weak between spirometry and FOT, with  $X_{rs5}$  being the most sensitive indicator of BDR.

**Key Words:** Forced Oscillation Technique, Spirometry, Asthma, Bronchodilator, COPD

**Nomination for New Investigator Award: Yes Grant Support: No**

AO 005

AO 006

## DOUBLE DIFFUSION METHOD FOR EVALUATING $D_{LCO}$ AND $D_{LNO}$ IN HEALTH AND COPD

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**Introduction/Aim.**  $D_{LCO}$  measures gas transfer capacity of the lung and is used for evaluation and progression of lung diseases including chronic obstructive pulmonary disease (COPD). Measurement of nitric oxide diffusing capacity ( $D_{LNO}$ ) helps disentangle the effects of alveolar membrane function vs pulmonary vasculature on gas transfer. The relationship between  $D_{LCO}$  and  $D_{LNO}$  has been established in health, but is relatively unknown in COPD. We sought to examine the relationship in health and COPD. We also investigated equivalence of gas transfer indices using 5-s and standard 10-s breathholds.

**Methods.** Healthy and COPD subjects performed two sets of two manoeuvres in randomised order, according to international guidelines, on two Medisoft systems (Leeds, United Kingdom): standard  $D_{LCO}$  protocol 10-s breathhold using BodyBox and 5-s breathhold using HypAir double diffusion, which simultaneously measures  $D_{LCO}$  and  $D_{LNO}$ .

**Results.** 15 healthy (6 males, age  $33.3 \pm 10.1$  yrs (SD), BMI  $25 \pm 3$ ) and 4 COPD subjects (3 males, age  $62.3 \pm 8.5$  yrs, BMI  $26 \pm 4$ ) were analysed. There was a strong correlation between  $D_{LNO}$  and  $D_{LCO}$  in healthy ( $r = 0.93$ ,  $P < 0.01$ ) and COPD subjects ( $r = 0.98$ ,  $P < 0.02$ ). The  $D_{LNO}/D_{LCO}$  ratios in health were  $4.8 \pm 0.34$  and COPD  $5.5 \pm 0.47$  ( $P = 0.02$ ). There were no significant differences between 5-s and 10-s protocols in  $D_{LCO}$ ,  $K_{CO}$  and  $V_A$  (paired t-test  $P = 0.13$ ,  $0.20$ , and  $0.28$  respectively). Similarly, there were no difference between breathhold protocols in  $K_{CO}$  and  $V_A$  in COPD subjects (paired t-test  $P = 0.15$ ,  $0.36$  respectively), however, more COPD subjects are needed to conclude differences in  $D_{LCO}$  ( $P = 0.06$ ). Intra-session repeatability and test-to-test measurement error in healthy subjects were 1.3, 3.5 for  $D_{LCO}$  and 5.0, 13.8  $\text{mL}\cdot\text{min}^{-1}\cdot\text{mmHg}^{-1}$  for  $D_{LNO}$ .

**Conclusion.** Preliminary analyses reveal no differences in  $D_{LCO}$ ,  $K_{CO}$  and  $V_A$  between breathhold protocols in health, but a difference in COPD.  $D_{LNO}/D_{LCO}$  between health and COPD differed significantly, although  $D_{LNO}/D_{LCO}$  varied between COPD patients. These results will help towards determining the potential utility of  $D_{LNO}$ .

**Key Words:**  $D_{LCO}$ ,  $D_{LNO}$

**Nomination for New Investigator Award**

**Grant Support:** N/A

## RELATIVE PREVALENCE OF VENTILATORY LIMITATION IN MALE AND FEMALE ADOLESCENT ATHLETES AT PEAK EXERCISE

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**Introduction/Aim.** Exercise induced dyspnoea (EID) is commonly attributed to exercise induced asthma in healthy children and adolescents with other causes being overlooked. Ventilatory limitation, presenting as expiratory flow limitation (EFL) and/or ventilation close to TLC, may account for EID. This study aimed to investigate the prevalence and severity of ventilatory limitation at peak exercise and its association with EID in adolescent athletes.

**Method.** 42 subjects (20 males and 22 females, mean age  $14.4 \pm 1.8$  yrs) completed pulmonary function tests and a cardiopulmonary exercise test using the standardised exponential exercise protocol. Tidal flow-volume loops were recorded during exercise and compared to the maximal flow-volume loop. A novel technique was used to assess EFL [1]. The minimum distance between the tidal and maximal flow-volume loops was assigned an arbitrary unit less number termed the flow reserve index (FRI). If tidal flow-volume loops surpass and continue beyond the maximal flow-volume loop the FRI is  $<0.05$  and becomes increasingly negative, indicating EFL. Subjects with FRI  $<0.05$  or inspiratory reserve volume  $<10\%$  of FVC were classified as demonstrating a ventilatory limitation. Dyspnoea at peak exercise was assessed using the modified Borg dyspnoea scale. Unpaired student T-tests calculated  $P$ -values, significance was set at  $P < 0.05$ .

**Results.** Males had a significantly lower FRI compared to females ( $-0.12 \pm 0.27$  vs  $0.18 \pm 0.38$ ,  $P = 0.01$ ). Ventilatory limitation during exercise was observed in 80% of males and 68% of females. Peak Borg dyspnoea scores exhibited an inverse relationship with FRI of subjects with EFL (Pearson's  $r = -0.40$ ).

**Conclusion.** Our findings suggest ventilatory limitation during exercise, in particular EFL, is more common in males compared to females and is associated with increased EID.

**Key Words:** Dyspnoea, Expiratory flow limitation

**Nomination for New Investigator Award:** Yes

**Grant Support:**

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**REFERENCES**

[1] Ellyett, K. (2019). "A new method for the investigation of flow limitation," in *TSANZSRS Annual Scientific Meeting 2019*, Gold Coast, 2019

### HYPERCAPNIC VENTILATORY RESPONSE AND AIRWAY OCCLUSION PRESSURE AT 100 MILLISECONDS IN HEALTHY PEOPLE

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**Introduction.** Hypercapnic Ventilatory Response (HCVR) and Airway Occlusion Pressure at 100 milliseconds (P0.1) measures the respiratory chemo-sensitivity and drive. However, robust normative data are lacking. Previous studies have utilised a low number of participants or are outdated, rendering interpretation of results difficult.

**Aim.** To generate a reliable and accurate predicted range for HCVR with P0.1 in a healthy population.

**Method.** Prospective recruitment of healthy participants for the HCVR with P0.1 test. Ventilation (Ve) and P0.1 were measured and plotted against end tidal carbon dioxide (P<sub>et</sub>CO<sub>2</sub>). Participants with a history of smoking or respiratory disease and incomplete tests were excluded. Spirometry, to assess lung function, was performed. Participants with abnormal spirometry results were excluded. The slope (gradient) and intercept of Ve/P<sub>et</sub>CO<sub>2</sub> and P0.1/P<sub>et</sub>CO<sub>2</sub> were calculated and Forward Stepwise Linear Regression analysis was used to determine parameters predictive of these values. Parameters entered into the predictive model included age, gender, height, weight and spirometry.

**Results.** 40 subjects (17 females) were recruited. Mean age was 31.4 ± 7.4 years (SD). Mean FEV1 and FVC percent predicted were 98.5 ± 10.5% (SD) and 99.3 ± 18.1% (SD), respectively. Mean P0.1/P<sub>et</sub>CO<sub>2</sub> gradient was 0.51 ± 0.39 (SD) and mean P0.1/P<sub>et</sub>CO<sub>2</sub> intercept was 38.2 ± 6.19 (SD). Mean Ve/P<sub>et</sub>CO<sub>2</sub> gradient was 2.51 ± 1.23 (SD) and mean Ve/P<sub>et</sub>CO<sub>2</sub> intercept was 37.3 ± 4.40 (SD). Using Forward Stepwise Linear Regression for data analysis, the parameters age, gender, height, weight and spirometry were all excluded as predictors of the slope and intercept of Ve/P<sub>et</sub>CO<sub>2</sub> and P0.1/P<sub>et</sub>CO<sub>2</sub>.

**Conclusion.** HCVR with P0.1 results in a normal population show a wide confidence interval. These results cannot be predicted by patient demographics or spirometric parameters. The recruitment of subjects for the current study is ongoing.

#### Nomination for New Investigator Award

**Key words:** Hypercapnic Ventilatory Response, Airway Occlusion Pressure

### CORRELATIVE ANALYSIS OF GOLD CLASSIFICATION OF COPD SEVERITY FROM FEV<sub>1</sub> % PREDICTED AND COPD ASSESSMENT TEST

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**Introduction/Aim.** Airflow limitation in Chronic Obstructive Pulmonary Disease (COPD) is confirmed by spirometry according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. This has recently been uncoupled from COPD severity. Severity is identified by symptom, exacerbation and patient history. The aim of this study is to consider whether COPD Assessment Test (CAT), an eight question, self-reported summary of symptom burden, offers insight to COPD severity considering the airflow limitation. We hypothesise current interpretation of CAT to be of limited clinical benefit in assessment of COPD where a score 10+ demonstrates severity promotion (A–B; C–D).

**Method.** 115 Participants were allocated into five groups including a Control group; Mild; Moderate; Severe and Very Severe COPD GOLD classification of airflow limitation utilising GLI 2012 predicted data. After administration of salbutamol, Spirometry was measured for the calculation of FEV<sub>1</sub> (% predicted) followed by the COPD Assessment Test. Regression analysis and single factor ANOVA was applied to determine statistical significance.

**Results.** There is poor correlation between spirometry and CAT measures in a population of COPD patients as seen in Table 1. This is the case with the cohort and in each group with statistical significance except the "Very Severe" group (P = 0.515).

Table 1 Comparative results across groups for FEV<sub>1</sub> % predicted and CAT

	n (male)	Age ± SD	FEV % pred. ± SD	CAT ± SD	R <sup>2</sup>	P
Control	17 (6)	56.9 ± 10.2	103.4 ± 10.7	9.0 ± 7.5	0.0201	<0.01
Mild	22 (11)	64.6 ± 9.5	91.0 ± 13.2	15.3 ± 6.7	0.0636	<0.01
Moderate	27 (12)	65.2 ± 10.4	63.0 ± 8.2	18.8 ± 9.6	0.1366	<0.01
Severe	28 (15)	68.0 ± 7.9	39.0 ± 5.0	22.5 ± 6.9	0.01	<0.01
Very severe	21 (9)	65.0 ± 7.6	23.1 ± 3.9	22.0 ± 6.6	0.0245	0.515
Cohort	115 (53)	56.9 ± 10.2	61.2 ± 30.0	18.2 ± 8.8	0.204	<0.01

**Conclusion.** We suggest re-evaluation of the cut off for higher severity using CAT.

**Key Words:** COPD; COAD; GOLD; Spirometry; CAT

**Nomination for New Investigator Award:** Yes

**Grant Support:** N/A

AO 009

AO 010

### DELAYED VO<sub>2</sub> RECOVERY IS ASSOCIATED WITH REDUCED TRANSPLANT FREE SURVIVAL IN HEART FAILURE

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**Introduction.** Impaired peak oxygen uptake (VO<sub>2</sub>) is an established prognostic marker in heart failure (HF) and utilised to support decision for cardiac transplantation<sup>1</sup>. VO<sub>2</sub> recovery delay (VO<sub>2</sub>RD) post cardiopulmonary exercise testing (CPET) has been investigated to further understand physiologic demand and prognosis in HF patients<sup>2</sup>.

**Aim.** Determine the incidence of VO<sub>2</sub>RD in heart failure patients undergoing CPET for investigation of HF and the relationship between VO<sub>2</sub>RD and 12-month outcomes.

**Method.** A retrospective analysis of the results of CPETs performed in 52 patients with confirmed heart failure performed between July 2015 and June 2017. VO<sub>2</sub>RD, defined as time for VO<sub>2</sub> to decline below peak VO<sub>2</sub> following cessation of exercise and peak VO<sub>2</sub> overshoot (VO<sub>2</sub>OS), where VO<sub>2</sub> increases during the recovery phase, were used as measures for oxygen recovery kinetics. All patients were reviewed 12 months after their CPET.

**Results.** 12 patients had a normal VO<sub>2</sub> recovery post CPET while 40 patients showed a delayed VO<sub>2</sub> recovery.

	Transplant-free survival (n = 32)	Transplantation/ deceased (n = 20)
Normal Post CPET VO <sub>2</sub> Recovery	9	3
Post CPET VO <sub>2</sub> RD	10	4
Post CPET VO <sub>2</sub> OS	13	13

38% of patients (n = 20) died or underwent cardiac transplantation at review. 85% of these patients experienced delayed VO<sub>2</sub> recovery compared to 72% of those that remained alive and transplant-free.

**Conclusion.** Delayed post CPET VO<sub>2</sub> recovery with VO<sub>2</sub>RD or VO<sub>2</sub>OS is easily identifiable and may prove useful for further stratification of heart failure. Further data analysis will focus on VO<sub>2</sub>RD as a predictor of cardiac limitation to exercise and prognosis in heart failure.

**REFERENCES.** 1. Mehra MR, Kobashigawa J, Starling R, et al. *J Heart Lung Transplant* 2006; 25:1024-42.

2. Bailey CS, Wooster LT, Buswell M, et al. *J Am Coll Cardiol HF* 2018; 6:329-39.

**Key Words:** Cardiopulmonary Exercise Test, Heart Failure

**Nomination for New Investigator Award:** Yes

### LUNG FUNCTION CHANGES WITH INITIATION OF NON-INVASIVE VENTILATION IN CHILDHOOD DUCHENNE MUSCULAR DYSTROPHY

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**Introduction/Aim.** The use of non-invasive ventilation (NIV) support in children has increased rapidly over the past decade. The aim of this study was to describe and analyse lung function (LF) changes with initiation of NIV in children with Duchenne Muscular Dystrophy (DMD), and assess for differences between Steroid Users and Steroid Naïve subjects.

**Method.** A retrospective clinical audit of children with DMD who were initiated on NIV in the past ten years was conducted. Serial LF data was collected for individuals throughout adolescence, including the period before and following NIV initiation.

**Results.** Twenty-nine males with DMD started NIV during the ten year study period. Nine subjects were using steroids, with a median age of commencement of 6 years (IQR 2.5, range 4-8). The median age that NIV was initiated was 14.66 years (IQR 2.35, 10.47-17.96) with no significant differences in initiation seen between Steroid Users vs. Steroid Naïve groups. Lung function is better (FVC z-score -3.26 vs -5.41,  $P < 0.02$ ) and the rate of decline is slower (FVC z-score -0.58 vs -0.68,  $P < 0.001$ ) in Steroid Users, compared to those who are Steroid Naïve. The median rate of decline in FVC z-score prior to NIV initiation was -0.72 z-score pa (95% CI -0.79, -0.64, SE 0.04,  $P < 0.01$ ) and following NIV initiation it was -0.46 z-scores pa (95% CI -0.54, -0.38, SE 0.04,  $P < 0.01$ ). This reduction in rate of decline following NIV initiation was significantly different,  $P < 0.001$ . The rate of decline in FVC is significantly reduced following NIV initiation in the steroid Naïve group, but increased in the Steroid User group and this reaches significance for z-scores ( $P < 0.001$ ) and % predicted values ( $P < 0.001$ )

**Conclusion.** The rates of decline in FVC are higher in boys with DMD prior to NIV than they are following NIV initiation. Long-term steroid use did not affect the age of NIV initiation in this cohort. However, Steroid Naïve patients have lower LF, and an increased rate of decline in LF prior to NIV initiation, which slows following NIV initiation.

**Key Words:** Lung function, Spirometry, Non-Invasive Ventilation, Duchenne Muscular Dystrophy

**Nomination for New Investigator Award**

**Grant Support:** None



### THE EMPEY INDEX PREDICTS UPPER AIRWAY OBSTRUCTION IN CHILDREN

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**Introduction.** Reduced PEF in relation to FEV<sub>1</sub> is associated with upper airway obstruction (UAO) in children. Children can present with tracheal stenosis, vocal cord dysfunction, subglottic stenosis, tracheo-bronchomalacia or persisting laryngomalacia. Stridor may be present. Bronchoscopy is often performed for diagnosis, monitoring and treatment. Forced expiration measured with spirometry, provides the Empey Index (EI) (FEV<sub>1</sub> (ml) / PEF (L/min)), also expressed as the Expiratory Disproportion Index (EDI), (EI x 6). The usual cut-off for EI is 10. EI is raised in adults with UAO.

**Aim.** To show the sensitivity of EI in identifying UAO in children.

**Method.** A cohort of children with physician diagnosed UAO were identified between Aug 2016 and Aug 2018. EI was calculated in all retrospective spirometry measures for the entire cohort. Those with unacceptable spirometry by the ATS/ERS criteria were excluded. The defined EI cut-off of 10 was applied with a Bayesian analysis. Longitudinal data were further explored for interventions where available.

**Results.** 2350 patients, 1294 male, (mean ± SD) age = 11.0 ± 3.6 yrs, were tested. 41 children with UAO were identified. 29 male, age = 11.6 ± 3.5 yrs. 12 spirometries were excluded due to technique, leaving 29 tests to be analysed. 20 male, age 11.3 ± 3.1 yrs.

	UAO (1.2%)	No UAO (98.8%)
EI Positive	27 (93%)	38 (1.6%)
EI Negative	2 (7%)	2283 (98.4%)
Total	29	2321

EI measured in children using the cut-off index 10 has a Sensitivity 0.93, Specificity 0.98, PPV 0.41, NPV 0.99 for identifying UAO. Analysis of longitudinal data from 16 individuals revealed, improvements in the EI with surgical intervention to UAO.

**Conclusion.** EI is a sensitive and specific test measure for UAO, and should be reported whenever UAO is suspected. Further investigation of its usefulness in measuring severity and monitoring progress is warranted.

**Key Words:** Empey Index, Upper Airway Obstruction.

**Nomination for New Investigator Award** No

**Grant Support:** Nil

### EFFECT OF ADOPTING GLI REFERENCE EQUATIONS ON THE INTERPRETATION OF T<sub>L</sub>CO

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**Introduction/Aim.** The recently published T<sub>L</sub>CO reference equations from the Global Lung Initiative (GLI) provide an opportunity to adopt a current, all-age, widely applicable set of reference equations. The aim of this study was to document the effect of changing to GLI from commonly utilised reference equations on the interpretation of T<sub>L</sub>CO results.

**Method.** 33,863 sets of T<sub>L</sub>CO results (48% female, 88% Caucasian, 97% >18 yrs) from clinical pulmonary function laboratories within three Australian public hospitals were analysed. Mean predicted values were calculated using GLI and other commonly used reference equations. The proportion of patients with a T<sub>L</sub>CO below the lower limit of normal (LLN) were calculated for each of these equations.

**Results.** Mean predicted values for T<sub>L</sub>CO using the GLI equations were slightly lower for adults (-1.5 to -3.7 ml/min/mmHg) and similar for children (-1.2 to +0.7 ml/min/mmHg) compared to the other reference equations. The LLN for T<sub>L</sub>CO was comparable across all equations, with the exception of Roca (-3.2 ± 1.9 ml/min/mmHg). These minor differences however resulted in altered rates of reduced T<sub>L</sub>CO for adults (+2.4 to -23.2%), but with no change for children (<0.4%).

	Reference equations	T <sub>L</sub> CO < LLN
Adult	Roca	59.2%
	ECSC	42.2%
	Miller	33.6%
	GLI	36.0%
Children	Kim (<18 yrs)	89.1%
	Cotes (<18 yrs)	89.4%
	GLI (<18 yrs)	89.1%

Result classification changed (abnormal to normal) more frequently for adult females than males, particularly when moving from Roca to GLI equations (32% of females vs 15% of males).

**Conclusion.** This analysis of a clinical dataset shows that the adoption of GLI T<sub>L</sub>CO reference equations in adults will result in altered interpretation depending on the equations previously used and to a greater extent in females. The effect on interpretation in children is negligible. This analysis will facilitate implementation of the 2017 GLI T<sub>L</sub>CO reference equations into clinical practice.

**Key Words:** Reference equations, T<sub>L</sub>CO, lung function

AO 013

AO 014

### CLINICAL IMPLICATIONS OF ADOPTING THE 2017 GLOBAL LUNG INITIATIVE CARBON MONOXIDE TRANSFER FACTOR REFERENCE VALUES

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**Introduction/Aim.** The 2017 Global Lung Initiative all-age carbon monoxide transfer reference values is the largest collection of normative DLCO data, using data from 12,639 subjects aged between 4.5 and 91 years. The aim of this study was to assess the implications of adopting the GLI equations in a clinical dataset.

**Method.** Of the 20,441 gas transfer tests successfully performed between 2011-2017 at a tertiary hospital respiratory department, 14,808 were unique subjects aged over 18 years and included in the analysis. The frequency of normal DLCO results (as defined by a DLCO > LLN) was assessed using the GLI equations and compared to commonly-used European Community of Steel and Coal (ECSC) and Miller reference sets. The size of the change in absolute DLCO predicted values was quantified, and the predicted VA using the GLI equations was compared to the ECSC TLC.

**Results.** 47% of subjects were above the GLI DLCO LLN, while 39% and 51% were above the ECSC and Miller LLN, respectively. The mean change between ECSC and GLI predicted DLCO was  $-1.69\text{ml/min/mmHg} \pm 1.11$  (st dev), while the mean change between Miller and GLI was  $-1.20\text{ml/min/mmHg} \pm 1.14$  (st dev). 722 subjects had a predicted VA higher than their ECSC predicted TLC.

**Conclusion.** Depending on the lung volume reference equations used, a small subset of patients may have physiologically impossible combinations of reference values. However, despite being generally lower than previous DLCO reference values, the GLI equations will yield clinically comparable interpretations in the majority of patients.

**Key Words:** Reference values, gas transfer, DLCO, GLI  
**Nomination for New Investigator Award:** N/A

**Grant Support:** N/A

### PREVALENCE OF VCD IN ASTHMA AND COPD AND ASSOCIATION WITH TRACHEAL INSTABILITY

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**Introduction/Aim.** Limited attention has been paid to laryngeal and tracheal ('middle airway') dysfunction in asthma and COPD. We have demonstrated that vocal cord dysfunction (VCD) can be detected in up to 20% of symptomatic asthma but this has never been studied in COPD. Moreover, excessive dynamic airway collapse (EDAC) occurs frequently in COPD (Leong, Resp Res, 2017) and in asthma (unpublished observations), thus it is possible that laryngeal instability and dysfunction predispose to VCD. The aim of current studies was to determine the prevalence of VCD and EDAC in symptomatic asthma and COPD and to examine links between VCD and EDAC.

**Methods.** Patients with symptomatic asthma ( $n = 125$ ) and COPD ( $n = 101$ ) suspected of having VCD (total  $n = 226$ ) as well as healthy control individuals ( $n = 35$ ) were assessed using dynamic 320-slice CT larynx and trachea. VCD was diagnosed only if detected during inspiration using a validated algorithm described by Low et al. (AJRCCM 2011). EDAC was diagnosed by CT if tracheal area during expiration was <50% of maximal tracheal area during inspiration. Groups were compared using appropriate statistical methods.

**Results.** VCD and EDAC were absent in controls. VCD was diagnosed in 50/226 (22.1%) cases and EDAC in 58/226 (25.7%) overall. VCD was present in asthma in 18/125 (14.4%) patients and in 32/101 (31.6%) patients with COPD ( $P < 0.01$ ). EDAC was detected in asthma in 22/125 (17.6%) and in 36/101 (35.6%) cases with COPD ( $P < 0.01$ ). Both VCD and EDAC together occurred in only 18/226 (8.0%) cases; more often in COPD (13/101, 12.9%) than in asthma (5/125, 4%;  $P < 0.01$ ).

**Conclusion.** Surprisingly VCD was more frequently detected in COPD than in asthma and more patients had EDAC. However, a minority of patients with VCD had coexisting EDAC suggesting that a pathological link between VCD and tracheal dysfunction may be unlikely. These observations merit further study.

**Grant Support:**

Monash Lung and Sleep Institute

AO 015

AO 016

## A NEW METHOD FOR THE INVESTIGATION OF FLOW LIMITATION

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**Introduction/Aim.** Conventional measurements taken from forced vital capacity (FVC) and tidal (TV) flow volume loops at rest and during exercise are routinely recorded. However conventional methods of quantifying flow limitation from these recordings do not adequately describe the limitations to flow nor do they adequately reflect the severity of flow limitation that can evolve during exercise. We aimed to develop a new technique to quantify flow limitation from tidal loops recorded both during exercise and rest to allow for more objective measures of flow limitation.

**Method.** A method using vector analysis and flow-volume integration was developed to determine the extent of expiratory flow reserve or flow deficit. This method calculates the minimum vector between the FVC and the TV loop (i.e. the minimum distance between the two loops) named the flow reserve index (FRI). Calculation of integrals of the flow-volume loop spaces provides objective quantification of breathing reserves and/or breathing deficits.

**Results.** This method has been used to analyse of flow volume loops during exercise in young athletes, which has shown that the FRI is inversely proportional to the Borg dyspnoea scores (Pearson's  $r = -0.40$ ).

**Conclusion.** This new technique allows for quantification of flow limitations at rest and during exercise. When this technique was applied to young athletes the severity of exertional dyspnoea was directly correlated with the degree of ventilatory limitation. Utilisation of data obtained from this technique allows for a better understanding of ventilatory limitations and allows for more informed interventions to avoid these limitations particularly when un-utilised flow volume space is present, in both health and disease.

**Key Words:**

spirometry, flow limitation,

**Nomination for New Investigator Award**

**Grant Support:**

## EXPERIMENTAL MODULATION OF MOOD BY ACOUSTIC STIMULATION AND ITS EFFECT ON EXERTIONAL DYSPNOEA

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**Introduction/Aim.** Dyspnoea is a debilitating symptom across a range of pathological conditions (e.g. cardiopulmonary, neuromuscular, cancer and obesity) and is often associated with anxiety and depression. Recent reports indicate that experimental viewing of standardised mood-modulating stimuli with pleasant/unpleasant images (International Affective Picture System-IAPS) decreases/increases dyspnoea perception in both healthy and clinical population. The current study investigated the effect of mood-modulating acoustic sounds (International Affective Digitized Sounds-IADS system) on exertional dyspnoea in healthy subjects. Unlike IAPS, IADS offers a feasible approach for integration into activities of daily living and rehabilitation programs, but its effect on dyspnoea has not been explored.

**Method.** Following familiarisation, 18 healthy participants (age 21-49 year) attended three experimental sessions on separate days, performing two 5-min treadmill exercises tests separated by a 30-min rest-interval on each day. During each visit, participants listened to either a positive, negative or neutral set of IADS sound clips and rated their levels of dyspnoea (intensity and bother) during the first exercise test and their mood during the second. Heart rate (HR), ventilation ( $V_E$ ), oxygen uptake ( $VO_2$ ) carbon dioxide output ( $VCO_2$ ), respiratory frequency ( $f_R$ ) and tidal volume ( $V_T$ ) were measured during each exercise test.

**Results.** During the last 2-min of exercise, mood valence (1-9) ratings were significantly lower when listening to the negative (mean  $\pm$  SE =  $3.0 \pm 0.4$ ) compared to the positive sounds  $6.7 \pm 0.3$ ,  $P < 0.001$ ). Both dyspnoea (0-10) intensity ( $4.0 \pm 0.5$ ) and dyspnoea bother ( $3.1 \pm 0.5$ ) when listening to negative IADS were significantly higher compared to positive IADS ( $3.2 \pm 0.3$ ,  $P = 0.013$  and  $1.6 \pm 0.2$ ,  $P = 0.006$ ). HR,  $VO_2$  and  $V_T$  did not differ significantly between three mood states ( $P > 0.05$ ) while  $V_E VCO_2$  and  $f_R$  were significantly higher in the negative, compared to positive, mood state ( $P < 0.05$ ).

**Conclusion.** These findings suggest that positive auditory mood modulation can alleviate exertional dyspnoea in healthy individuals and advocates for further research involving clinical population to explore to feasibility of mood modulation in reducing exertional dyspnoea in chronic clinical conditions.

**Key Words:**

Dyspnoea, Mood, IADS, Treadmill Exercise, Cardiopulmonary Disease

**Grant Support:**

Griffith University New Researcher Grant awarded and the National Health and Medical Research Council Grant APP597411

AO 017

AO 018

### NASAL HIGH FLOW THERAPY AND SUPPLEMENTAL OXYGEN DOES NOT AUGMENT EXERCISE PERFORMANCE IN COPD

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**Introduction/Aim.** Nasal high flow therapy (NHFT) is an emerging treatment for a range of respiratory conditions. There is confounding evidence regarding the utility of NHFT during exercise and COPD. We have recently shown no performance improvement nor attenuated stress using NHFT (no oxygen) during a walk test in patients with COPD<sup>1</sup>. It is not known whether the addition of supplemental oxygen into NHFT circuit would improve performance. The purpose of this study was to evaluate the effect of oxygen during NHFT on exercise performance in patients with COPD. The primary hypothesis: Supplemental oxygen will improve walk distance during NHFT.

**Method.** Fifteen subjects with COPD performed two randomised six minute walk tests (6MWT) 30 minutes apart. NHFT was used in both tests (45 L/min, 37°C) either with room air (RA), or with 2 L/min oxygen (O<sub>2</sub>). Subjects were blinded to the gas conditions. Pulse oximetry, respiratory rate, and dyspnoea scores were recorded. Paired t-tests (student/Wilcoxon matched-pairs) were used to assess differences between conditions.

**Results.** There was no difference in the mean 6MWT distance (RA = 416 ± 86m, O<sub>2</sub> = 419 ± 86m (SD)) between conditions. The mean SpO<sub>2</sub> during the 6MWT was significantly higher in the O<sub>2</sub> condition ( $P < 0.001$ ). There were no significant differences in mean pulse rate, mean respiratory rate and end-test dyspnoea scores between conditions.

**Conclusion.** In this cohort of COPD patients, the addition of oxygen into the NHFT circuit had no effect on exercise performance despite improved oxygenation. This suggests that walk performance in this group is linked to ventilatory limitations rather than availability of oxygen to the working muscles.

#### REFERENCE

1. Kelly et al, NHFT: The effect on exercise performance in COPD. ERS congress, 2018.

**Key Words:** Nasal high flow therapy, COPD, oxygen, six minute walk test.

**Nomination for New Investigator Award:** NA

**Grant Support:** None

### BENRALIZUMAB IMPROVES SMALL AIRWAY FUNCTION RAPIDLY IN PATIENTS WITH SEVERE EOSINOPHILIC ASTHMA

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**Introduction/Aim.** Benralizumab, an anti-interleukin 5 receptor  $\alpha$  monoclonal antibody, was recently approved in Australia for the treatment of severe eosinophilic asthma (SEA). Small airway function is abnormal in severe asthma contributing to the symptom burden. The effect of benralizumab on small airway function has not been described. We sought to describe changes in ventilation heterogeneity, a marker of small airway function, in patients commencing benralizumab.

**Method.** All patients with SEA despite high-dose inhaled corticosteroids/long-acting  $\beta$ 2-agonists had the following measurements at baseline (week 0) and one month after commencing benralizumab (week 4): 5-item Asthma Control Questionnaire (ACQ-5), spirometry, and multiple breath nitrogen washout to derive measures of ventilation heterogeneity in the conducting airways ( $S_{\text{cond}}$ ) and more distal acinar airways ( $S_{\text{acin}}$ ). All other asthma treatment was unchanged. Paired t-test and Pearson's correlations were performed.

**Results.** To date, 10 patients (6 males), mean  $\pm$  SD age 53  $\pm$  23 yrs, BMI 27  $\pm$  5.2 kg/m<sup>2</sup>, eosinophil count 0.9  $\pm$  0.4  $\times 10^9$ /L, FEV<sub>1</sub> 51  $\pm$  15 %predicted, FEV<sub>1</sub>/FVC ratio 50  $\pm$  12%. At week 4, eosinophil count was undetectable and ACQ-5 improved significantly (2.4  $\pm$  0.76 to 1.16  $\pm$  0.76,  $P = 0.001$ ). There was a significant improvement in  $S_{\text{cond}}$  (0.065  $\pm$  0.024 to 0.053  $\pm$  0.022,  $P = 0.002$ ) and a trend for improvement in  $S_{\text{acin}}$  (0.312  $\pm$  0.184 to 0.240  $\pm$  0.163,  $P = 0.06$ ) and FEV<sub>1</sub> (1.85  $\pm$  0.65 to 2.15  $\pm$  0.76L/s,  $P = 0.08$ ). The change in ACQ-5 correlated only with the change in  $S_{\text{acin}}$  ( $r = 0.66$   $P = 0.04$ ).

**Conclusion.** In this preliminary analysis, benralizumab significantly and rapidly improved symptom control after 4 weeks. The improvement in small airway function correlated with improved symptoms.

**Key Words:** MBNW, ACQ, benralizumab, eosinophilic Asthma, ventilation heterogeneity

**Grant Support:** N/A

AP 001

AP 002

### A SERVICE EVALUATION REVIEW OF CHILDREN'S HEALTH QUEENSLAND PATIENTS HAVING RESPIRATORY FUNCTION TESTS IN REGIONAL AND REMOTE CLINICS

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**Introduction/Aim.** Serial lung function testing is an important tool for monitoring disease progression and intervention efficacy. The Queensland Children's Hospital (QCH) Respiratory Laboratory provides a lung function testing service (predominantly spirometry) for children who attend regional and remote specialist paediatric clinics operated through Indigenous Respiratory Outreach Care. Among children who received respiratory paediatric specialist care in an outreach setting, we aimed to (a) evaluate the change in spirometry values and (b) determine if these changes differed between disease profiles.

**Method.** In this retrospective study, children were included if they were medically reviewed and had performed spirometry at outreach clinics for a period  $\geq 12$  months. Global Lung Function Initiative (GLI) predicted values were used for all patients; the GLI "Other" ethnicity category was used for Indigenous patients. In this preliminary analysis, we compared FEV<sub>1</sub>%pred, FVC%pred and FEV<sub>1</sub>/FVC% at first visit to an outreach clinic (baseline) with the best values within 12 months from their most recent clinic. Comparisons were made for whole cohort, and for sub-groups of those with confirmed diagnoses of asthma and bronchiectasis. Paired Wilcoxon signed rank test was used for comparison.

**Results.** The eligible cohort (n = 190) consisted of 115 males and 75 females, 142 of whom identified as Indigenous. The mean age at first visit was 7.4 yrs ( $\pm 2.8$  SD). The mean time from first visit to best recent visit was 29mth (range 3 to 84mth). The table below presents baseline and best recent spirometry data.

**Conclusion.** There was significant improvement in spirometric lung function in children attending outreach specialist paediatric respiratory service for the whole cohort. The improvement was also significant in the sub-group of children with asthma. While there was no significant improvement in children with bronchiectasis, no deterioration occurred.

**Key Words:** Paediatric, respiratory function, outreach

### PATIENT-REPORTED HEIGHTS RESULT IN CHANGES TO SPIROMETRY REFERENCE VALUES AND SEVERITY CLASSIFICATION

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**Introduction.** Sex, height and age are important variables used to determine appropriate reference values for spirometry. When measuring standing height is not possible, an alternative method of obtaining height must be used. Identification documents and patient-reported heights have been shown to correspond closely with measured heights in patients requiring spirometry<sup>1</sup>.

**Aim.** To determine whether patient-reported height is an appropriate substitute for measured height and to assess the accuracy of using patient-reported height to calculate reference values for spirometry.

**Method.** Subjects (n = 214) were new and review patients (age 65  $\pm$  14 years; 109 females) presenting for lung function tests at a tertiary hospital. Height was measured using a stadiometer, with the patient's head in the Frankfort horizontal plane, and an estimated height obtained from simple verbal prompts.

A paired t-test was used to assess difference between FEV<sub>1</sub>%Predicted using measured and patient-reported height and a chi-squared test was used to assess changes of severity classification.

**Results.** Significant differences were found between measured and patient-reported heights ( $P < 0.01$ ), changes to severity classification ( $\chi^2 = 594.60$ ,  $P < 0.01$ ), changes to normal/abnormal classification ( $\chi^2 = 594.61$ ,  $P < 0.01$ ) and FEV<sub>1</sub>% Predicted ( $P < 0.01$ ). 39 results (18%) had a change in severity classification when using patient-reported height. Patient-reported height resulted in changes to FEV<sub>1</sub>%Predicted as large as 27% and differences between patient-reported and measured height of up to 15cm were observed.

**Conclusion.** Using patient-reported height to determine spirometry reference values may result in a misclassification of severity and is not a reliable source.

**REFERENCES.** 1 Capderou A, Berkani M, Becquemin M-H, Zelter M. Reconsidering the arm span-height relationship in patients referred for spirometry. *Eur Respir J* 2011; 37: 157-163.

**Key Words:** Spirometry, height, reference values

**Nomination for Young Investigator Award –**

**Grant Support: –**

	Whole group (n = 190)			Asthma (n = 115)			Bronchiectasis (n = 39)		
	Base Median (IQR)	Recent Median (IQR)	P	Base Median (IQR)	Recent Median (IQR)	P	Base Median (IQR)	Recent Median (IQR)	P
FEV <sub>1</sub> (%pred)	93.8 (19.6)	98.4 (17.5)	<0.001	96.4 (19.6)	100.6 (17.0)	0.009	91.7 (22.5)	93.7 (15.5)	0.257
FVC (%pred)	94.5 (18.4)	100.3 (17.5)	0.002	96.8 (18.3)	101.9 (18.1)	0.011	91.6 (17.0)	94.6 (14.0)	0.253
FEV <sub>1</sub> /FVC (%)	88.4 (11.3)	87.2 (7.0)	0.098	88.2 (10.7)	87.2 (6.4)	0.119	89.7 (11.9)	87.7 (7.3)	0.396

Base = Baseline, Recent = Best Recent, IQR = Interquartile Range

**REDUCING POST BRONCHODILATOR SPIROMETRY ASSESSMENT WAITING TIME**

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**Introduction/Aim.** The ATS/ERS criteria for spirometry assessment has long stated that post bronchodilator spirometry be measured 10-15 minutes after bronchodilator administration. This study examines the feasibility of using a shorter post bronchodilator assessment time to detect a clinically significant bronchodilator response.

**Method.** A random sample of patients attending a public hospital respiratory laboratory had baseline spirometry performed to ATS/ERS criteria then repeated measures at 5 minutes and 10 minutes post bronchodilator administration ( 400ug salbutamol via mdi and spacer). The scientist performing spirometry was blinded to the patient's suspected or known diagnosis. Results were assessed for a clinically significant bronchodilator response and whether there would be a difference in clinical outcome with measurements taken at the 5 minute and 10 minute time points.

**Results.** 450 sequential patients attending the laboratory were screened. 100 were found to have highly reproducible spirometry (best and next best FEV1 within 50 mL) and were included in this analysis. In this random sample 65% (65) were found to have no significant bronchodilator response (<200 mL and <12% increase from baseline) at either the 5 minute or 10 minute time points. The remaining 35% (35) were found to have had a significant bronchodilator response by the 10 minute time point and of those, 30 had demonstrated a significant improvement by the 5 minute time point. A binary proportional analysis found a very good level of agreement with 85.7% of the responders correctly identified at the 5 minute time point. The remaining 14.3% of responders at the 10 minute time point had achieved a 9-11.4% improvement from baseline by 5 minutes.

**Conclusion.** In this cohort the majority of patients with a clinically significant bronchodilator response had demonstrated this improvement by 5 minutes. It is therefore feasible to perform repeat spirometry after 5 minutes and if a clinically significant result is achieved then no further testing is required. Patients who demonstrate an improvement of >9% after 5 minutes should be retested after an additional 5 minutes, in keeping with the current ATS-ERS guidelines

**Key Words:**

Spirometry, bronchodilator response, ATS/ERS criteria, salbutamol

**Nomination for New Investigator Award**

**Grant Support:** Nil

**SICKLE CELL DISEASE AND LUNG FUNCTION. A CASE STUDY**

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**Introduction.** Sickle Cell Disease (SCD) is a congenital disease in which the phenotype for red blood cells becomes sickle in shape. It has multiple organ pathological effects, however a large factor for mortality/morbidity in these patients are the effects on the lungs, historically restrictive defects with lowered CO diffusing capacity (DLCO) are associated with patients with history of Acute Chest Syndrome (ACS)- ACS is a vaso occlusive crisis when pulmonary infiltrates for example sicklised cells, accumulate within the vessels of the lung turning it opaque (Miller, A. and Gladwin, M 2012) and severe enough episodes can become fatal if not properly monitored. The aim of this case study is to review the lung function in a patient diagnosed with Sickle cell disease along with a recent literature review.

**Method.** Review Lung function in case study, compare published literature, and conduct literature review.

**Results.** Case study Lung function & Literature review

Case study Lung function & Literature review				
GENDER	MALE	PREDICTED		
AGE	26 years	n/a		
BMI	26.37	n/a		
FVC	2.38L (59% Predicted)	4.03L		
FEV1	1.97L (56% Predicted)	3.51L		
FEV1/FVC	83%	83%		
DLCO ADJ	21.7 mL/mmHg/Min (75% Predicted)	29.0 mL/mmHg/Min		
DLVA ADJ	7.04 mL/mHg/Min/L (133% Predicted)	5.30 mL/mmHg/Min/L		
VA	3.08L (56%% Predicted)	5.46L		
Study	FVC (SCD) (Mean)	DLCO (Mean) performed	Age (Mean)	ACS history
Arikoglu, et al (2018)	94.8% ±14.5	no	15	N=30 (51.7%)
Sylvester et al (2003)	1.5L SD =0.5	no	10	N=7 (9.14%)
Klings et al (2006)	84.37% ± 16.01	Yes DLCO ADJ: 61.74% ± 19.93	30.7	37%

**Discussion.** Compared to control groups/known normal values, the SCD group showed lower FVC overall especially as the age of the groups increased, a limited study on 38 patients by Chambellan et al., (2015) found an inverse correlation to DLCO and Hospitalisation due to ACS, and concluded that DLCO testing could be used as a tool to manage ACS incidents.

**Conclusion.** Recent published literature suggests that abnormal lung function is consistent in this group of patients. However, there is a lack of data on the measurement of spirometry and diffusing capacity just prior to an ACS incident. Screening using Lung function testing may be useful in the management and prevention of ACS.

**Key Words:** Sickle Cell Disease, Acute Chest Syndrome, Restriction. Diffusing capacity.

### COPD PATIENTS PRESCRIBED ONLY AMBULATORY OXYGEN HAVE SUB-OPTIMAL ADHERENCE TO OXYGEN THERAPY

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**Introduction.** Ambulatory oxygen may be prescribed in COPD patients who have a preserved resting PaO<sub>2</sub> above 60mmHg, but demonstrate desaturation of SpO<sub>2</sub> below 88% on exertion while breathing room air. However, recent evidence indicates that patients with COPD prescribed ambulatory oxygen only, have little to no improvement in quality of life or exercise capacity. We hypothesised that these patients would have suboptimal adherence to their oxygen therapy.

**Aim.** Our aim was to assess whether current COPD patients on ambulatory oxygen only were using oxygen therapy as prescribed.

**Method.** Data from two tertiary hospitals was analysed to obtain a cohort of COPD patients currently receiving ambulatory oxygen only. Compliance data (previous 6 months) was obtained from the State Wide Equipment program based on monthly cylinder usage. Patients were categorised as: Non-compliant (did not fill their prescriptions at all), partially-compliant (completed some of their prescription) and compliant (completed all their prescriptions over the period investigated).

**Results.** In this cohort 36.2% (21/58) of COPD patients were compliant with their oxygen as prescribed by their physician. 29.3% (17/58) were partially-compliant and 34.5% (20/58) were non-compliant.

COPD Cohort	Male	Female
Gender (%)	52	48
Age (yrs)	78 (60-91)	75 (61-93)
FEV1 (%pred)	43 (15-69)	41 (16-93)
FER (%)	41 (25-61)	43 (22-68)
TLCO (%pred)	38 (17-62)	34 (15-72)
SpO <sub>2</sub> (nadir)	84 (77-87)	83 (76-87)

**Conclusion.** Compliance rates in this real world clinical cohort indicate that a significant number of patients do not use their oxygen as prescribed. This is consistent with evidence that COPD patients prescribed ambulatory oxygen only do not derive any clinical benefit.

**Key Words:** COPD, Ambulatory oxygen, Compliance

### LUNG FUNCTION DOES NOT PREDICT SEVERITY OF SHUNT FRACTION IN PATIENTS AWAITING ORTHOTOPIC LIVER TRANSPLANT

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**Introduction.** Current guidelines for Orthotopic Liver Transplant (OLT) assessment recommend screening for Hepatopulmonary Syndrome (HPS) on all candidates. As part of screening, all OLT candidates at Princess Alexandra Hospital perform spirometry, diffusion capacity of the lung for carbon monoxide (D<sub>L</sub>CO) and shunt fraction, which includes arterial blood gas (ABG). Current literature on HPS suggest OLT candidates are likely to present with reduced D<sub>L</sub>CO, increased shunt fraction and reduced room air ABG PaO<sub>2</sub> (<80 mmHg). However, there are limited data to confirm these assumptions.

**Aim.** Determine if a significant correlation exists between shunt fraction and lung function tests in patients awaiting OLT.

**Method.** Search of lung function database for OLT candidates between February 2007 and September 2018, who performed spirometry, D<sub>L</sub>CO and shunt fraction on the same visit. The probability of lung function predicting normal or increased shunt fraction was studied using two-by-two contingency tables.

**Results.** 330 patients (80 females) were included with mean age of 52.6 ± 10.0 years (SD). Mean shunt fraction was 5.6 ± 3.3%. Mean FEV1 %predicted, FVC %predicted and D<sub>L</sub>CO %predicted were 85 ± 18% (SD), 91 ± 18% (SD) and 72 ± 20% (SD), respectively. The table summarises the negative predictive value (NPV) and positive predictive value (PPV) of various lung function parameters detecting severity of shunt fraction.

Lung function	NPV	PPV
D <sub>L</sub> CO	34	24
FEV1	35	21
FVC	42	13

The low NPV suggests normal lung function is a poor predictor of normal shunt fraction whilst the low PPV suggests reduced lung function is a poor predictor of an increased shunt fraction. Therefore, the probability of having a normal or increased shunt fraction cannot be determined using lung function.

**Conclusion.** A normal, or increased, shunt fraction cannot be predicted from lung function data in OLT candidates.

**Key words:** Orthotopic Liver Transplant, Shunt Fraction, Lung Function

### COMMUNITY SPIROMETRY COMPETENCY: ARE WE ACHIEVING BUY-IN AND MEETING OUR TARGETS

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**Introduction.** Christchurch Spirometry Course attendees are encouraged to submit 10 spirometry tests for competency assessment post course. Tests are assessed by a qualified Respiratory Physiologist against the ATS/ERS(2005) Spirometry Standards. Expectations are: 1) every attendee submits for competency assessment; 2) submissions are received within three months of course attendance; 3) submissions are marked within four weeks of receipt; 4) tests submitted have an appropriate technical comment regardless of test quality. An audit was performed to determine whether expectations were being met.

**Method.** All submissions between April 2015 and July 2018 were audited. Further investigations into test acceptability/repeatability, trial numbers, and technical commenting were made amongst the three main submitting groups: Occupational Health Nurses; Practice Nurses; and Canterbury Clinical Network (CCN) Practice Nurses whose testing is quality-oversighted by the Christchurch Respiratory Laboratory.

**Results.** 189 participants attended 17 spirometry courses between April 2015 and July 2018. 94 (50%) submitted for competency assessment. 53% submitted within three months and 89% within six months of course attendance (range 12–328 days). Time to mark was 24 ± 17.24 days (mean ± SD), with breaches of the four-week target occurring when only one physiologist was available to mark submissions.

Spirometry quality statistics among professional groups:

Professional group	Acceptable and repeatable spirometry	Tests (n)	%Total tests	Average trials (n)	%Correct technical comment
Occupational health nurses	no	74	20%	5.2	38%
	yes	302	80%	4.1	93%
Practice nurses	no	25	18%	6.1	18%
	yes	115	82%	5.1	94%
CCN practice nurses	no	50	12%	7.2	52%
	yes	355	88%	6.2	98%

**Conclusion.** Half of course attendees did not apply for competency assessment and roadblocks to submission should be investigated. An expectation of submission within three months of a course is ideal but within six months appears more realistic. The four-week marking target was achieved when more than one physiologist was available to assess submissions. Technical commenting was poor when test criteria weren't met, highlighting this as an area for further training.

**Key Words:** community spirometry, spirometry course, competency

**Nomination for New Investigator Award:** No

**Grant Support:** Will be applying for a Travel Grant to the 2019 ASM although this may not be successful

### VE/VCO<sub>2</sub> SLOPE IN CPET IS AFFECTED BY METHOD SELECTION

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**Introduction.** A steep VE/VCO<sub>2</sub> slope measured during Cardio-Pulmonary Exercise Testing (CPET) is characteristic of increased dead space ventilation associated with diseases such as pulmonary vascular disease. Literature recommends calculating this slope between the commencement of load (WL) and the respiratory compensation point (VT<sub>2</sub>). Recent studies have shown VE/VCO<sub>2</sub> slope calculated from WL to peak exercise has a higher prognostic value for mortality within the heart failure group.

**Aim.** To assess the variability in VE/VCO<sub>2</sub> slope calculation between different methodologies.

**Method.** 100 CPET results from patients referred to a metropolitan lung function laboratory primarily for investigation of dyspnoea were retrospectively reviewed. The VE/VCO<sub>2</sub> slope was calculated from either: 1) WL to lactate threshold (VT<sub>1</sub>; where VE changes relative to VO<sub>2</sub> but not VCO<sub>2</sub>), 2) WL to VT<sub>2</sub>, 3) VT<sub>1</sub> to VT<sub>2</sub>, 4) using the first linear portion of the plot and 5) WL to peak exercise. All data selection was verified by two scientists. Data were analysed using one-way ANOVA and paired t-test.

**Results.** From this population (age: 50.5 ± 19.0 years (Mean ± SD), female gender: 56%), VT<sub>1</sub> and VT<sub>2</sub> were present in 90% of all tests.

Table 1 Comparison of the VE/VCO<sub>2</sub> slope between all methods

Method	Slope (Mean ± SD)	WL to VT <sub>1</sub>	WL to VT <sub>2</sub>	VT <sub>1</sub> to VT <sub>2</sub>	First linear portion
WL to VT <sub>1</sub>	28.7 ± 6.7	--	P = 0.068	P = 0.069	P = 0.403
WL to VT <sub>2</sub>	29.1 ± 6.3	P = 0.068	--	P = 0.085	P = 0.074
VT <sub>1</sub> to VT <sub>2</sub>	29.3 ± 6.3	P = 0.079	P = 0.385	--	P = 0.210
First linear portion	29.3 ± 6.3	P = 0.403	P = 0.058	P = 0.650	--
WL to peak exercise	35.2 ± 6.1	P < 0.00001	P < 0.00001	P < 0.00001	P < 0.00001

VE/VCO<sub>2</sub> slope calculated from WL to peak exercise is significantly different from all other methods. Remaining methods were not significantly different from each other

**Conclusions.** Calculating the slope from commencement of load to peak exercise results in a significantly higher VE/VCO<sub>2</sub> slope value in this population. This may result in an overestimation of abnormality when compared to other methods. It is important therefore to standardise and report the method of calculation for VE/VCO<sub>2</sub> slope to make appropriate clinical decisions.

**Key Words:** CPET, VE/VCO<sub>2</sub> slope

**Nomination for NIA:** No

**Grant Support:** Nil



**PRE-OPERATIVE ASSESSMENT FOR SCOLIOSIS SPINAL SURGERY IN PULMONARY FUNCTION LABORATORIES ACROSS AUSTRALIA AND NEW ZEALAND**

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**Introduction/Aim.** Royal Perth Hospital (RPH) currently promotes a *Choose wisely* campaign to reduce unnecessary tests being performed. Evaluation of pulmonary function in patients with scoliosis prior to spinal surgery aids in assessing potential post-operative pulmonary complications and surgical approach<sup>1</sup>. Comprehensive pulmonary function tests (PFT) are routinely performed at RPH in this patient group. We aimed to determine the PFTs performed as standard practice in this population across pulmonary function laboratories in Australia and New Zealand.

**Method.** SurveyMonkey<sup>®</sup> was used to survey pulmonary function laboratories. Questions determined whether laboratories offered testing in this population, the tests performed and whether follow-up tests are performed post-surgery.

**Results.** A total of 42 pulmonary function laboratories responded. Fourteen (33%) perform pre-operative PFTs in patients with scoliosis. Thirteen laboratories indicated the tests they perform. All perform spirometry (100%), 5 (38%) perform lung volume measurements, 2 (15%) measure diffusing capacity for carbon monoxide (DL<sub>CO</sub>), 1 (8%) laboratory measures sniff nasal inspiratory pressures and 1 (8%) laboratory performs peak cough flow and slow vital capacity (SVC). Only one laboratory repeats PFTs 6 weeks post-surgery.

**Conclusion.** Results of this survey contradict current practice at RPH. Spirometry, SVC, lung volume measurements, DL<sub>CO</sub> and maximal expiratory and inspiratory pressures are routinely performed in this patient group. This is a significantly greater number of tests compared to other laboratories across Australia and New Zealand. Spirometry is almost exclusively measured pre-operatively, with a small number of laboratories offering additional tests. The survey results suggest that RPH may be over servicing this patient group. This warrants further investigation to determine the clinical usefulness of providing comprehensive PFTs with the aim of reducing unnecessary tests and burden on patients and staff.

**Key Words:** Scoliosis, pre-operative, pulmonary function test

**Nomination for New Investigator Award:** No

**Grant Support:** Nil

**REFERENCE.** 1. Bullmann V, Schulte TL, Schmidt C *et al.*, Eur Spine J, 2013; 22:2, S164–S171

**AN AUDIT OF CURRENT PRACTICES: WHICH IS THE BEST METHOD OF PREDICTING A MAXIMAL WORKLOAD?**

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**Introduction/Aim.** Cardiopulmonary Exercise Tests (CPET) provide a global assessment of multi-organ system function. In order to obtain optimal results, an incremental workload resulting in a 10 (ideal 8-12) minute exercise test must be selected. This retrospective study aimed to determine the best method of predicting a maximal workload: equations which utilize anthropometric data or a Scientist-chosen W<sub>max</sub> derived from a workload increment based on a questionnaire and visual examination of the patient.

**Method.** Patients were referred to the laboratory for Cardiopulmonary assessment. The CPET included Spirometry and Maximal Voluntary Ventilation (MVV) in all, and used an incremental ramp protocol. For each CPET, 2 of 4 Scientists independently chose a workload protocol based on visual inspection of the patient and a questionnaire examining the patient's current level of physical fitness. The Scientist's decisions were averaged and multiplied by 10 to obtain predicted W<sub>max</sub>. The computer-predicted workload comes from a mix of Hansen-Sue-Wasserman (1984) equations and Jones Ergometer (1997) equations. The work increment was calculated as W<sub>max</sub> divided by 10 minutes.

**Results.** 40 patients aged 21-79 (M = 17, F = 23)

Sample Size	Mean Achieved workload ± SD (W)	Mean Scientist Predicted Workload ± SD (W)	Mean Computer Predicted Workload ± SD (W)	T-Test (Achieved vs. Scientist Predicted)	T-Test (Achieved vs. Computer Predicted)	Mean Differences (Achieved vs. Scientist Predicted)	Mean Differences (Achieved vs. Computer Predicted)
n=40	138 ± 87	136 ± 62	132 ± 55	p = 0.69	p = 0.46	2	6

The optimal test time was not achieved for 50% of the tests (37.5% < 8 minutes, 12.5% > 12 minutes). For 35% of tests the Scientist estimate of work increment was used, and of these 50% exercised < 8 minutes and 7.14% exercised > 12 minutes. For the remaining 65% of tests, the computed work increment was chosen whereby 30.8% < 8 minutes and 15.4% > 12 minutes.

**Conclusion.** Although this study demonstrated that there was no significant difference between the achieved workload and the workload predicted by the Scientist or computer, it revealed that the Scientist's prediction overestimated W<sub>max</sub> most often yielding an exercise test less than 8 minutes. Better methods of predicting a maximal workload are needed.

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Nomination for New Investigator Award: No Grant Support: No

### TROUBLESHOOTING THE TLCO SIMULATOR: EXPERIENCE FROM FIONA STANLEY HOSPITAL

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**Introduction/Aim.** Upon commissioning a new Pulmonary Physiology Laboratory, a Hans Rudolph T<sub>L</sub>CO Simulator was purchased to validate five testing systems. Raw data was in agreement across all systems; however, the EasyQC targets were inaccurate. The aim of this study was to determine the cause of this inaccuracy.

**Method.** The Simulator was used with varying settings applied and manual calculation of the data. Collaboration with other laboratories occurred and the variables were then sequentially manipulated to determine the source of error. 95 duplicate Simulator trials were performed using 3 test gases across 5 testing systems. After identifying the problem, a further 15 trials were performed.

#### Results.

- Tests performed with and without BTPS correction led to greater inaccuracy.
- Collaboration revealed similar problems and resulted in a decision to widen acceptability limits.
- Results from local inter-laboratory tests showed similar results from the test gases.
- Manual calculation of the T<sub>L</sub>CO result replicated EasyQC target values.
- Sequential manipulation of the data identified that a minute change in CO<sub>2</sub> was the fundamental cause of the inaccuracy (0.004% CO difference resulted in 2ml/min. mmHg T<sub>L</sub>CO difference).
- Correction for CO<sub>2</sub> cross-sensitivity using the infra-red analyser settings led to target values being obtained (5% CO<sub>2</sub> concentration in the 3 test gases).

T <sub>L</sub> CO difference from target (mL/min.mmHg)			
Test gas range	Before investigation (mean ± SD)	After investigation (mean ± SD)	P-value
Low	-1.61 ± 0.83	-0.33 ± 0.59	<0.001
Mid	-2.15 ± 0.78	-0.14 ± 0.51	<0.001
High	-2.36 ± 0.86	-0.19 ± 0.50	<0.001

**Conclusion.** T<sub>L</sub>CO Simulators are in common use across Australasia, with the majority not achieving the specified targets. Initial investigation focused on the EasyQC software calculations. Automatic offset of CO<sub>2</sub> cross-sensitivity during tidal breathing is enabled for subjects but tidal breathing using the T<sub>L</sub>CO Simulator is ambient air, hence manual CO<sub>2</sub> correction is required. We now achieve both precision and accuracy with the Simulator.

#### Key Words:

T<sub>L</sub>CO Simulator, EasyQC

Nomination for New Investigator Award

NilGrant Support:

Nil

### DIFFERENCES IN VALUES OF RESPIRATORY FUNCTION TEST PARAMETERS MEASURED USING THE SENSORMEDICS® V62J AUTOBOX (MASS FLOW SENSOR) AND THE MEDGRAPHICS® PLATINUM ELITE SERIES PLETHYSMOGRAPH SYSTEMS (PITOT TUBE FLOW SENSOR)

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**Aim.** To determine if there are significant differences in values of respiratory function test (RFT) parameters obtained on new equipment utilising different airflow technology (Medgraphics® Platinum Elite Series Plethysmograph [MGC]; pitot tube flow sensor) compared with existing equipment (SensorMedics® V62J Autobox [62]; mass flow sensor).

**Method.** 31 healthy volunteers were recruited to undergo RFT. Each subject performed spirometry, DLCO and plethysmography sequentially, (following ATS/ERS guidelines), on both sets of equipment (with order of testing randomly varied), on the same day. The difference in each lung function parameter (62 minus MGC) was calculated for each subject. Data were expressed as mean ±, -standard deviation (SD). *P* < 0.05 was significant.

**Results.** One subject's plethysmography results were excluded due to poor technique, resulting in a total of 30 data sets for plethysmography and 31 for both spirometry and DLCO.

Parameter	Mean Difference (62 minus MGC) ± SD (P-value)	Parameter	Mean Difference (62 minus MGC) ± SD (P-value)
FVC (L)	0.02 ± 0.15 ( <i>P</i> = 0.51)	IVC (L)	-0.18 ± 0.22 ( <i>P</i> < 0.001)*
FEV <sub>1</sub> (L)	-0.07 ± 0.09 ( <i>P</i> < 0.001)*	VC (L)	0.06 ± 0.15 ( <i>P</i> = 0.047)*
FEV <sub>1</sub> /FVC (%)	-2.2 ± 2.2 ( <i>P</i> < 0.001)*	TLC (L)	0.05 ± 0.28 ( <i>P</i> = 0.354)
FEF <sub>25-75%</sub> (L/sec)	-0.27 ± 0.17 ( <i>P</i> < 0.001)*	RV (L)	-0.01 ± 0.29 ( <i>P</i> = 0.869)
PEF (mL/mmHg/min)	0.34 ± 0.86 ( <i>P</i> = 0.037)*	RV/TLC (%)	-0.4 ± 4.00 ( <i>P</i> = 0.596)
DLCO (mL/min)	-1.56 ± 1.48 ( <i>P</i> < 0.001)*	FRC (L)	-0.04 ± 0.18 ( <i>P</i> = 0.235)
VA (L)	-0.22 ± 0.24 ( <i>P</i> < 0.001)*	ERV (L)	-0.05 ± 0.28 ( <i>P</i> = 0.345)

\* = significant difference observed

**Conclusion.** There were small but significant differences observed for all spirometry and DLCO parameters, with the exception of FVC. There were no clinically significant differences observed for plethysmographic lung volumes. Of those parameters with significant differences, the 62 measured a higher PEF, whilst the MGC measured a higher FEV<sub>1</sub>, FEV<sub>1</sub>/FVC, FEF<sub>25-75%</sub>, DLCO, VA and IVC. These differences may be related to different airflow measurement technology and should be considered when interpreting sequential respiratory function tests. We conclude that sequential RFTs should ideally be performed on the same equipment on each test occasion.

**Key Words:** Respiratory function test, mass flow sensor, pitot tube flow sensor.

**Grant Support:** Nil.

**TELEHEALTH MENTORING FOLLOWING CULTURALLY APPROPRIATE INDIGENOUS SPIROMETRY TRAINING PROGRAM MAY IMPROVE SPIROMETRY QUALITY**

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**Introduction.** Health workers (HW) trained through the Indigenous Health Worker Spirometry Training Program (STP) as part of the Indigenous Respiratory Outreach Care program (IROC) increase both the number of HW performing spirometry (spiro) and the quantity of spirometry tests performed<sup>#</sup>. Telehealth mentoring of HW in the months after STP was added to assist in establishing good spiro outcomes.

**Aim.** To assess the quality of spiro after training (Post STP) and compare it to the quality of spiro after telehealth mentoring (Post Tele STP).

**Method.** HW in Indigenous primary care attended a 2 day culturally appropriate STP. Spirometry tests performed after training and again after telehealth mentoring were submitted for quality assessment including patient demographics, test acceptability and repeatability and technical comment inclusion (a total score out of 8). The average quality test score was calculated for each HW portfolio and the mean  $\pm$  SD quality score was calculated for the group Post STP & Post Tele STP. Spiro quality feedback was returned to HW. A survey was sent to HW to investigate the perceived usefulness of the spiro quality feedback and the telehealth sessions.

**Results.** 17 HW submitted spiro tests Post STP & Post Tele STP (9 Indigenous). The increase in mean quality score after telehealth was not significant (Wilcoxon Rank  $P = 0.309$ ) even though 11 HW had an increase in spiro Quality score Post Tele STP.

	Quality score (n = 17)	
	Post STP	Post TeleSTP
Mean (SD)	5.15 (1.30)	5.48 (1.43)

Survey response rate = 45% (8/17). The telehealth session was *Helpful or Very Helpful* 100%(8/8). The spiro feedback Post Tele STP was *Helpful or Very Helpful* 100% (7/7).

**Conclusion.** There is a trend towards improved quality of spirometry after telehealth mentoring. Telehealth sessions & spiro quality feedback are useful when training HWs <sup>#</sup> *Respirology* (2018) 23 (Suppl. 1), 17

**Key Words:** Spirometry training, Indigenous primary care, telehealth

**Nomination for New Investigator Award:** No

**Funding:** Aboriginal & Torres Strait Islander Branch of Qld Health through IROC

<sup>#</sup> *Respirology* (2018) 23 (Suppl. 1), 17

**LUNG FUNCTION TESTING AFTER A RECENT MYOCARDIAL INFARCTION IS SAFE**

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**Introduction/Aim.** American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines suggest avoiding lung function tests within 1 month of a myocardial infarct (MI). Based on evidence from exercise testing, other recommendations suggest that testing 7 days after an MI would be safe. However currently there is no direct evidence describing complications from lung function testing within 7 days or 1 month of an MI. Since patients with a recent MI sometimes require pre-operative lung function testing, the aim of this study was to assess the safety of lung function testing performed after a recent MI.

**Method.** A retrospective search was performed identifying all in-patients having lung function tests performed within 30 days of MI, since 2010. The medical records were examined to identify if there were any immediate (within 24 hours) or short-term (after 24 hours) complications that could be related to the lung function tests.

**Results.** 172 patients were identified as having lung function tests with 30 days of an MI. The mean (SD) FEV1 was 2.21 (0.81)L. 114 of these patients had tests within 7 days of an MI. Five of the 172 patients had immediate complications (angina: 4, dyspnoea: 1) however only one of these was thought to be related to the lung function test (angina during testing). This patient was tested 18 days post MI. Seven patients had short-term complications after the lung function tests (angina: 4, acute pulmonary oedema: 2, dyspnoea: 1), however most of these patients had ongoing angina and none of the complications were thought to be a consequence of the testing itself.

**Conclusion.** Lung function testing after a recent MI was found to be safe in this group of in-patients. These findings may provide evidence for future lung function testing guidelines.

**Key Words:** spirometry, lung function testing, myocardial infarction.

AP 015

AP 016

### END-TIDAL GAS ANALYSIS IS NOT APPROPRIATE FOR THE CALCULATION OF DEAD SPACE VENTILATION DURING INCREMENTAL EXERCISE

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**Introduction/Aim.** The ratio of dead space to tidal volume ( $V_D/V_T$ ) falls with incremental exercise and a failure to do so, or an elevated value, can reflect gas exchange abnormalities. Optimal calculation of  $V_D/V_T$  requires  $PCO_2$  from invasive arterial blood gas (ABG) sampling. However,  $V_D/V_T$  is commonly measured using pressure of end-tidal exhaled gases (PET) as a non-invasive surrogate. While representative in health, PET may underestimate ABG in the presence of V/Q mismatch. A comparison between  $V_D/V_T$  calculated via ABG and PET was performed.

**Method.** Sequential data over 30 months from patients referred for a CPET using ramped cycle ergometry was collected.  $V_D/V_T$  was calculated from the Bohr equation using expired gases (Quark, Cosmed, Italy) that included either  $P_{ET}CO_2$  (PET) or  $PaCO_2$  (ABG). Values collected at rest and near maximum exercise were compared using two-tailed paired t-tests.  $V_E/VCO_2$  slopes  $\geq 35$  were considered abnormally elevated.

**Results.** 56 (29 female) subjects, mean (SD) age 58 (15) years, 27.3 (5.8) BMI were studied. 14 (25%) had an elevated  $V_E/VCO_2$  slope. In the whole cohort,  $V_D/V_T$  differed at rest ( $P = 0.0001$ ) but not at max exercise ( $P = 0.4$ ). Hence, the calculated change in  $V_D/V_T$  with incremental exercise differed significantly (0.13 (0.08) ABG vs -0.03 (0.04) PET ( $P = 0.0001$ )). ABG Vs PET  $V_D/V_T$  both at rest and at max exercise ( $P = 0.001$ ) were significantly different in those with an elevated  $V_E/VCO_2$  slope.

At max exercise, mean (SD) mmHg	$P_{ET}CO_2$	$PaCO_2$
All n = 56	34.4 (4.8)	34.3 (4.5)
$V_E/VCO_2 \geq 35$ n = 14	31.3 (2.1)	33.6 (5.0)
$V_E/VCO_2 < 35$ n = 42	35.4 (5.0)	34.5 (4.3)

**Conclusion.** These results confirm that PET underestimates arterial  $PCO_2$  in the presence of disease, consistent with the effects of V/Q mismatch. This reinforces the recommendation ABGs are used for the dynamic analysis of  $V_D/V_T$  in clinical CPET.

**Key Words:** CPET, ABG, dead space ventilation

**Grant Support:** Nil

### ACUTE INCREASE IN HAEMOGLOBIN CONCENTRATION DURING CLINICAL CARDIOPULMONARY EXERCISE TESTING

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**Introduction/Aim.** Arterial blood gas (ABG) analysis during incremental exercise allows improved accuracy of gas exchange assessment. We observed a consistent change in haemoglobin concentration ([Hb]) in ABG samples not well described in the literature. A retrospective analysis of [Hb] changes following incremental exercise was conducted to confirm and quantify this physiological response.

**Method.** Sequential data over 30 months from patients referred for clinical cardiopulmonary exercise testing (CPET) using ramped cycle ergometry were included. Studies with matched ABG samples taken at rest and near maximum exercise were compared using two-tailed paired t-tests. Association with haematological and gas exchange parameters were investigated with Pearson's correlation.

**Results.** 57 (30 female) subjects, mean (SD) age 58 (15) years, 27.3 (5.7) BMI were studied. Incremental exercise time was 8:54 (1:00) min: sec, with a respiratory exchange ratio (RER) 1.20 (0.11) and oxygen uptake 90 (23)% predicted at maximal exercise (108 (60) watts). [Hb] by co-oximetry (CoV of 1.2%) increased from 13.9 (1.3) g/dL at rest to 15.0 (1.3) near maximal exercise ( $P = 0.0001$ ,  $r = 0.96$ ). Measured lactate concentration ([La]) (CoV 8.1%) increased from 1.4 (0.7) mmol/L to 6.8 (2.1) and was associated with the %change in [Hb] ( $r = 0.61$ ,  $P = 0.0001$ ). The associations were extended to the primary CPET indicators of effort at maximal exercise including RER ( $r = 0.51$ ,  $P < 0.0001$ ).

**Conclusion.** We have quantified a consistent acute increase in [Hb] during incremental CPET in a clinical setting. This was associated with markers of effort. Potential mechanisms include altered plasma volume, splenic contraction or more rapid red cell transit through spleen. Increased [Hb] should improve  $O_2$  delivery.

**Key Words:** Haemoglobin, CPET

**Grant Support:** Nil

AP 017

**SUBOPTIMAL CARDIOPULMONARY EXERCISE TESTING  
QUALITY CONTROL PRACTICES ACROSS RESPIRATORY  
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**Introduction.** The current TSANZ Respiratory Function Laboratory Accreditation Standards were updated in July 2016. Some standards for accreditation previously listed as 'should' were updated to 'must', including those in relation to quality control (QC) of laboratory equipment. Laboratories applying for accreditation need to ensure they meet the standards of the July 2016 manual prior to the accreditation process.

**Aim.** Assess quality control practices for cardiopulmonary exercise testing (CPET) in respiratory laboratories across Australia and New Zealand.

**Method.** A web-based, multi-question survey was distributed to respiratory laboratory managers across Australia and New Zealand between May 2018 and October 2018. One response per laboratory was requested. Questions included TSANZ laboratory accreditation status, number of CPET performed over the past 5 years, modality used for CPET, calibration practices, biological and non-biological QC practices including number of biological controls used and frequency of CPET QC, and data analysis methods.

**Results.** 41 completed surveys were analysed. 15 responding laboratories do not perform CPET. 26 laboratories perform CPET and of those, 15 are accredited by TSANZ; 3 are accredited but not for CPET, and 8 are not accredited. 46% of laboratories do not perform QC on their CPET equipment (outside of routine pre-test calibration). 93% of laboratories that perform QC use non-biological and biological control methods. There is little consistency of QC methods, rationale or data analysis methods.

**Conclusion.** From the data collected, a significant proportion of TSANZ accredited laboratories performing CPET are not meeting current QC accreditation standards. It is unclear, at this stage, whether laboratories are unaware of the requirement for CPET QC or, the TSANZ accreditation process does not mandate this requirement.

**Key Words:** cardiopulmonary exercise testing, quality control, TSANZ Accreditation

TO 001

### DETERMINING THE IMPACT OF RESPIRATORY VIRUSES ON AT RISK PATIENT POPULATIONS

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**Introduction/Aim:** Respiratory viruses are ubiquitous and are known to cause acute disease in otherwise healthy individuals and may be associated with severe clinical outcomes in those with underlying chronic diseases. However, respiratory viruses do not always result in disease. The frequency and implications of asymptomatic carriage within at-risk patient populations remain poorly understood.

**Methods:** Multiple sample types were collected. Samples were processed, subjected to RNA extraction, cDNA synthesis and assayed using multiple uniplex PCRs for human rhinovirus, respiratory syncytial virus, influenza A and B, parainfluenza 1, 2, 3 and human metapneumovirus, the most common community acquired respiratory viruses (CARV). Clinical outcomes were analysed and compared with microbial detection.

**Results:** The exhaled breath methodology was compared to NPS, BAL and sputum, and correlated well with all modalities across patient populations. When the methodology was tested in patients with stable bronchiectasis and in ICU patients intubated for any reason, the major finding was the high rate of detection of CARV in the absence of other evidence suggestive of acute respiratory viral infection. In the transplant study, CARV were commonly detected in lung transplant patients and persisted for up to 21 weeks post transplantation. There was also no association between viral presence and development of acute cellular rejection.

**Conclusions:** These studies detail the development of a novel viral sampling methodology and its evaluation in a range of patient cohorts. They support the utility of a non-invasive method examining exhaled breath, to detect CARV. Both the bronchiectasis and the ICU study uncovered the high rate of CARV in at risk patients. The lung transplant study provides novel evidence that viruses are transplanted within the donor lung and remain detectable for many months after transplantation. This is the first study to outline the potential role of CARV as transient members of the human respiratory virome.

**Grant Support:** N/A

### TRANSCRIPTOMIC ANALYSIS OF PERIPHERAL BLOOD MONONUCLEAR CELLS FROM STABLE COPD PATIENTS REVEALS IMPORTANT IMMUNOMODULATORY CHANGES IN RESPONSE TO MESENCHYMAL STROMAL CELL INFUSION

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**Introduction and Aims:** We have previously demonstrated that mesenchymal stromal cell (MSC) infusion into patients with stable chronic obstructive pulmonary disease (COPD) elicited systemic immunological responses that target inflammatory pathways relevant to COPD, including reductions in circulating pro-inflammatory and oxidative stress biomarkers. Despite these findings, there is still a need to understand the pathways, and potential immune regulators that are targeted by MSCs in COPD.

**Methods:** MSCs were infused into patients with stable COPD (n = 9), and peripheral blood mononuclear cells (PBMCs) were isolated pre-infusion, 1 hour, 1 day, 2 days, 7 days post-infusion, followed by collection of PBMC 1 hour after a second infusion on the 7<sup>th</sup> day. RNA was extracted from PBMC and prepared for RNA sequencing. Global transcriptomic changes in PBMC were assessed using the weighted gene co-expression network analysis (WGCNA) pipeline.

**Results:** MSC infusion induced a transient differential gene expression that was highest after 1 day, but returned to baseline by 7 days. WGCNA identified a gene module that was enriched in pro-inflammatory genes (IL-1, TNF and IL-8) which was significantly downregulated following MSC infusion. Further network analysis identified IL-8 as a candidate regulator of this network. IL-8 production was also significantly reduced in the presence of MSC-conditioned media in PBMC culture.

**Conclusion:** We provide novel data showing MSC therapy in COPD patients induces transient changes following MSC infusion at the gene expression level, and identified IL-8 as a potential target of MSC-derived paracrine factors which may have significant implications in treating COPD. Exploration of MSC-mediated mechanisms that attenuate IL-8 may lead to the improvement of therapeutic strategies that involve MSCs and their secreted immunomodulating factors.

**Grant Support:** The project was funded by a national health and medical research council (NHMRC) grant.

### EFFICACY OF ORAL ANTIBIOTICS FOR NON-SEVERE-EXACERBATIONS OF BRONCHIECTASIS IN CHILDREN

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**Introduction:** Antibiotics are used routinely to treat bronchiectasis exacerbations. However, placebo-containing RCTs are lacking and, in non-severe (non-hospitalised) cases, antibiotics might be unnecessary since many exacerbations are virus-triggered. We tested our primary hypothesis that when treating a non-severe exacerbation in children with bronchiectasis, oral amoxicillin-clavulanate and azithromycin are superior to placebo for achieving resolution by day-14.

**Methods:** We conducted a multicentre, parallel-group, double-dummy, double-blind placebo-controlled RCT in 4 centres. When an exacerbation began, children were randomised to receive either amoxicillin-clavulanate (22.5 mg/kg bd)/placebo, azithromycin (5 mg/kg/day)/placebo or placebo/placebo for 14-days. Our primary outcome was exacerbation resolution (defined as 'return-to-baseline') by 14-days. Secondary outcomes were exacerbation duration, time-to-next exacerbation, cough-specific quality-of-life (PC-QoL), white blood cell count and CRP and FEV<sub>1</sub>. Nasal swabs were also collected.

**Results:** One-hundred-and-ninety-seven children were randomised (amoxicillin-clavulanate n = 63, azithromycin n = 67, and placebo n = 67). Their baseline characteristics were comparable. By day-14, exacerbations had resolved in 41/63, 41/67 and 29/67 of the 3 groups respectively. Compared to placebo, the relative-risk-of-resolution by day-14 was 1.50 (95% CI 1.08-2.09; number-needed-to-treat for benefit (NNTFB) = 5, 95%CI 3-21) and 1.41 (95% CI 1.01-1.97; NNTFB = 6, 95% CI 3-97) in the amoxicillin-clavulanate and azithromycin groups respectively. The median exacerbation duration was significantly shorter in the amoxicillin-clavulanate group (7 vs 10-days, *P* = 0.018) than placebo, but not for azithromycin (8 vs 10-days *P* = 0.242). There were no significant differences in time-to-next exacerbation, or changes in PC-QoL, white blood cell count, CRP or FEV<sub>1</sub>% between treatment days 1-14 in either active arm compared to placebo. At exacerbation onset, 57% of nasal swabs contained a respiratory virus.

**Conclusion:** Amoxicillin-clavulanate and azithromycin are both superior to placebo for treating non-severe exacerbations of bronchiectasis in children without *Pseudomonas aeruginosa*. Identifying those most likely to benefit from antibiotics is now a priority.

**Grant Support:** NHMRC project grant (1019834). NHMRC PG scholarship (VG). NHMRC practitioner fellowship (ABC).

### A SMARTPHONE APPLICATION FOR REPORTING SYMPTOMS IN ADULTS WITH CYSTIC FIBROSIS IMPROVES THE DETECTION OF RESPIRATORY EXACERBATIONS

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**Introduction/Aim:** In people with cystic fibrosis (CF), respiratory exacerbations impair lung function and health-related quality of life. Delayed identification can result in more severe exacerbations and worse outcomes. We developed a smartphone application (App) for adults with CF used to report symptoms to the CF team. We investigated the impact of this App in a 12-month randomised controlled trial on antibiotic use and other health outcomes.

**Methods:** Participants were randomised to the intervention or control group. The intervention group used the App weekly, or sooner if they felt their symptoms had worsened. The App comprised 12 yes/no questions relating to symptoms suggestive of an exacerbation, and two questions relating to emotional wellbeing. Participants were contacted by the nurse practitioner if they answered yes to any questions, and their care was triaged. The control group continued usual care. The primary outcome measure was the number of courses of intravenous antibiotics.

**Results:** Sixty participants (31 male, aged [mean ± SD] 31 ± 9 years, FEV<sub>1</sub> 60 ± 18% predicted) were recruited, with 29 (48%) allocated to the intervention group. There was no difference in the number of intravenous antibiotic courses (intervention 42 vs. control 30; incidence rate ratio [IRR] 1; 95% confidence interval [CI] 0.5 to 1.8), however there was an increase in the number of courses of oral antibiotics (intervention 71 vs. control 46; IRR 1.6; 95% CI 1.1 to 2.1). The median time to exacerbation requiring oral or intravenous antibiotics was 70 days in the intervention group, compared to 141 days in the control group (*P* = 0.02). No between-group differences were observed in other outcomes.

**Conclusion:** The weekly use of an App to report symptoms to the CF team reduced time to detect respiratory exacerbations that required antibiotics, and increased the use of oral antibiotics.

**Grant Support:** Sir Charles Gairdner Group Research Advisory Committee Grant.

### THE IMPACT OF AZITHROMYCIN THERAPY ON THE LUNG MICROBIOTA AND RESISTANCE IN THE AMAZES TRIAL COHORT

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**Introduction/Aim:** Azithromycin reduces exacerbations in adults with persistent symptomatic asthma.<sup>1</sup> However, owing to the pleiotropic properties of macrolides, unintended bacteriological consequences such as augmented pathogen colonisation or dissemination of antibiotic-resistant organisms can occur, calling into question the long-term safety of azithromycin maintenance therapy. We aimed to assess the effects of azithromycin on the airway microbiota, pathogen abundance, and carriage of antibiotic-resistance genes.

**Methods:** A combination of pooled-template shotgun metagenomic sequencing,<sup>2</sup> amplicon sequencing, whole genome sequencing (WGS), and quantitative PCR were performed on paired sputum samples from 61 participants (n = 34 placebo, n = 27 azithromycin) of the AMAZES trial: a 48-week, double-blind, placebo-controlled trial of thrice-weekly 500mg oral azithromycin in adults with persistent uncontrolled asthma. Bacterial taxonomy was assigned using QIIME, and resistance genes were identified by alignment to the Comprehensive Antibiotic Resistance Database (CARD).

**Results:** Azithromycin did not affect total bacterial load ( $P = 0.37$ ). However, azithromycin significantly decreased the microbiota diversity ( $P = 0.026$ ) and significantly reduced absolute load of *Haemophilus influenzae* ( $P < 0.0001$ ). Azithromycin did not significantly affect *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* or *Moraxella catarrhalis*. Of the 89 antibiotic resistance genes detected, macrolide resistance genes (*erm*(B), *erm*(F), *msr*(E), *mef*(A), and *meI*) and tetracycline resistance genes (*tet*(M) and *tet*(W)) were increased significantly. Culture-based azithromycin sensitivity, followed by WGS, identified viridians streptococci as the carrier of these transmissible resistance genes, with tetracycline resistance genes carried on the same transposable element as macrolide resistant genes.

**Conclusion:** The potential for macrolide therapy to substantially increase resistance carriage or provide a selective advantage for macrolide-tolerant respiratory pathogens within the airway microbiota is cause for concern. However, we observed no significant increase in bacterial load, no significant increase in abundance of respiratory pathogens, and increase in resistance was largely confined to commensal streptococci. Furthermore, the significant reduction in *H. influenzae* identifies a potential mechanism of action for azithromycin.

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### TEMPORAL VARIABILITY OF FORCED OSCILLATION MECHANICS FROM HOME TELEMONITORING IS RELATED TO SYMPTOMS AND QUALITY OF LIFE AND CHANGES BEFORE ACUTE EXACERBATIONS IN COPD

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**Introduction/Aim:** Studies on the utility of home telemonitoring in chronic obstructive pulmonary disease (COPD) for early detection and management of acute exacerbations (AECOPD) have produced mixed results. Day-to-day variations in lung function show promising clinical utility in asthma, and might be beneficial in COPD also.

This study aimed to (i) evaluate the day-to-day variability of forced oscillation technique (FOT) measures from home telemonitoring in COPD and their relationship with symptoms and quality of life, and (ii) to examine the timing of changes in FOT variability measures and symptoms in relation to AECOPDs.

**Methods:** Daily home-measured total and within-breath FOT parameters (resistance (R) and reactance (X); Resmon Pro Diary, Restech srl, Milan, Italy), daily symptoms (electronic COPD Assessment Test, CAT) and 4-weekly quality of life (St. George's Respiratory Questionnaire, SGRQ) were obtained over 8-9 months. FOT variability was assessed using standard deviation (SD) and coefficient of variation (CV) over 7-day running windows. Linear mixed modelling was used to evaluate the relationship between FOT versus CAT and SGRQ. One-way repeated measures ANOVA (with post-hoc Dunnett's test) was used to examine changes in FOT and CAT within 14 days prior to AECOPD.

**Results:** Adherence of 16 enrolled COPD participants ( $69 \pm 9$  years, %predFEV1  $40.7 \pm 14.0$ ) was  $86.9 \pm 16.1\%$ . Of all FOT parameters, variability of inspiratory X (X<sub>insp</sub>SD) was related to both CAT (fixed effect estimate coefficient 1.56 (0.63-2.50 95% CI),  $P = 0.001$ ) and SGRQ (4.64 (0.17-9.11 95% CI),  $P = 0.04$ ). The relationship was consistent over 7, 10 and 14-day windows. Both X<sub>insp</sub>SD and mean CAT score over 7 days changed significantly 1 day before AECOPD ( $P = 0.03$  and  $P = 0.009$ , respectively); X<sub>insp</sub>CV changed earlier, i.e. 2 days prior to AECOPD ( $P = 0.009$ ).

**Conclusion:** Variability of FOT measures obtained by home telemonitoring reflects symptoms and quality of life in COPD, and may be a sensitive marker to detect AECOPD early.

**Grant Support:** NHMRC Postgraduate Scholarship, NHMRC Project Grant 1049560, Lung Foundation Australia / Boehringer Ingelheim COPD Research Top-Up Grant 2016



TO 007

TO 008

### A PROSPECTIVE COHORT STUDY OF HEALTH LITERACY AMONGST ATTENDEES OF A QUEENSLAND SLEEP DISORDERS CLINIC

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**Introduction/Aim:** Sleep disorders, particularly obstructive sleep apnoea (OSA) are common conditions amongst the Australian adult population. Of great significance is the 2-3 fold increase in all-cause mortality amongst individuals with severe untreated OSA.

Health Literacy is a multifaceted concept defined as 'The degree to which individuals have the capacity to obtain, process and understand basic health information and services needed to make appropriate health decisions'. Low individual health literacy is associated with higher rates of hospitalization and emergency care, and with higher rates of adverse outcomes. Using two validated questionnaires this study aimed to describe the baseline health literacy of a prospective cohort sleep clinic patients.

**Methods:** A prospective cross-sectional analysis at a single time point was conducted with all sleep disorders clinic patients being invited to participate. Patients were recruited through the weekly public sleep medicine clinic in accordance with approved HREC protocol. Patient demographics, sleep diagnostic information and results of a brief questionnaire were performed using the Short Form Rapid Estimate of Adult Literacy in Medicine (REALM-SF; 3 minutes to administer) and "3 Screening Questions" approach.

**Results:** 100 participants (50% male) with an average age of 59 years old (23-88 yrs) were recruited over a 3-month period. 18% had completed university education, with 37% having no further education beyond grade 10 schooling. 28% had inadequate health literacy on REALM-SF.

**Conclusion:** A third of patients seen through the clinic have inadequate health literacy as measured by the more specific tool REALM-SF. 40% of our cohort do not feel confident filling out medical forms all the time. Moving forward, the development of new documents providing health information needs to take into consideration that a large segment of our patient population do not feel comfortable with writing information and innovative approaches are needed.

**Grant Support:** •

### BARRIERS AND ENABLERS OF BRONCHIECTASIS MANAGEMENT: A PATIENT PERSPECTIVE

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**Introduction/Aim:** Bronchiectasis management impacts both patient and health service outcomes. Little is known about what patients think about current bronchiectasis management. This study aims to identify what are the barriers and enablers to bronchiectasis management from a patient perspective

**Methods:** A quantitative questionnaire using a 7 point Likert scale rating to statements about bronchiectasis management and a qualitative one-on-one interview about their experiences with condition management and engagement with health professionals was conducted with 14 bronchiectasis patients. Participants interviewed included nine moderate and five severe bronchiectasis patients with a mean age of 71 years  $\pm$ 9.9 (range 40-83). Questionnaires were analysed in excel. Transcripts were typed verbatim and coded under categories of the theoretical domains framework using NVIVO software.

**Results:** Questionnaire results reveal that patients consider their bronchiectasis as slightly well managed with a mean reported value of  $4.8 \pm 1.8$ . Patients believe that they received enough education to self-manage had a mean reported value of  $5.6 \pm 1.5$ . Patients were less likely to actively seek more information about bronchiectasis with a mean reported value of  $4.1 \pm 2.5$ . Patients believe that improving bronchiectasis management should be a higher priority with a mean reported value of  $5.9 \pm 1$ .

Barriers to bronchiectasis management include late referral to multidisciplinary team, and lack of engagement with their health professional. Enablers to bronchiectasis management include working together with a multidisciplinary team of health professionals which includes chronic disease management and support, recognition of the patient's role in management and their heavy burden of disease.

**Conclusion:** Bronchiectasis patients rely heavily on health professionals for management guidance particularly in meeting their self-management learning needs. Health professionals need to consider the importance of early engagement with bronchiectasis patients and earlier referral to physiotherapists and respiratory nurses for chronic disease management, education and support.

**Grant Support:** Nil declarations

TO 009

TO 010

### GUIDELINE USE AND BEST PRACTICE IN COPD: A NURSING PERSPECTIVE

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**Introduction/Aim:** Guidelines to inform clinical management of Chronic Obstructive Pulmonary Disease (COPD) are regularly updated with the latest research evidence. Yet in Australia, COPD is a leading cause of morbidity and mortality, responsible for 1.3% of all hospital admissions. Importantly, studies highlight that up to 40% of patients do not receive guideline concordant care, which could contribute to COPD being ranked second in the country for avoidable hospital admissions. Nursing staff have an important role in the management of COPD patients within both the inpatient and outpatient setting. This study aims to identify the nursing perspective on perceived and actual barriers and facilitators for provision of guideline concordant care for people with COPD.

**Methods:** Qualitative one-on-one interviews and a nine point Likert scale questionnaire on COPD management were conducted with eight respiratory nurses (median age 46 years) treating COPD patients (13 median years) working in acute or outpatient respiratory services in the Central Adelaide Local Health Network. Interviews were conducted between May and August 2018. Transcripts were typed verbatim and coded using thematic analysis under the Theoretical Domains Framework with NVIVO software.

**Results:** Knowledge and use of COPD guidelines was not consistent across all respiratory nurses. Perceived barriers to deliver best practice care included: time restrictions, access to relevant information in COPD guidelines, assessing inhaler technique and patient access to written action plans and emergency packs. Enablers included: use of technology to access guidelines, patient compliance in self-management, access to specialist respiratory nurses and health professional education. The questionnaire identified a significant difference ( $P = 0.015$ ) between ward and specialist respiratory nurses in "sharing similar approaches to best-practice care" and "actively seeking information in COPD care".

**Conclusion:** Accessing specialist respiratory nurses and use of technology to complement nursing education should be encouraged to support implementation of best-practice COPD guidelines in patient care.

**Grant Support:** Nil

### EFFECTIVENESS OF AN EARLY DISCHARGE SERVICE FOR PATIENTS ADMITTED TO HOSPITAL WITH AN ACUTE COPD EXACERBATION: A PILOT PROGRAMME (RADS STUDY)

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**Introduction/Aim:** Hospital-in-the-home model of care has been shown to improve outcomes in patients with chronic obstructive pulmonary disease (COPD). However, local literature on nurse-led early discharge services for patients with acute exacerbations of COPD are limited. Aim of this study is to determine if patients with an acute exacerbation of COPD and enter an early discharge service with nurse-led community based recovery receive safe and cost-effective care.

**Methods:** All patients who were recruited to the Respiratory Acute Discharge Service (RADS) programme at Sunshine Coast University Hospital over a four months period from June to September 2018 were included. The criteria for the programme were: confirmed diagnosis of acute COPD exacerbation, mobile and able to self-care, adequate social circumstances, living in own residence, usual oxygen requirement and oxygen saturations >88%. The co-primary outcomes for this study were length of hospital days saved and rate of readmission within 30 days from discharge.

**Results:** A total of 97 patients (median age 72 years (range 42-95)) were included in the study. The mean FEV1% of the patients was 40.9% (SD 19.3). The median length-of-stay prior to discharge on the RADS programme was 2 days (range 0 to 5), compared to a previous average of 5.8 days. Patients were on the programme for a median of 4 days (range 1 to 6). A total of 265 hospital bed days were saved over the study period. Eleven patients (11.3% (95% CI 6.5-19.2%)) were re-admitted to hospital, of whom majority (64%) were due to recurrent symptoms. The rate of 30-day all-cause mortality for the study population was 2.1% ( $n = 2$ ).

**Conclusion:** Early supported discharge care model with nurse-led community based recovery after an acute exacerbation of COPD in selected patients is safe, and has the potential to provide greater flow through the hospital systems with cost effective care.

**Grant Support:** •

TO 011

TO 012

## HAS THE INTEGRATED RESPIRATORY NURSING SERVICE IN CANTERBURY MADE A DIFFERENCE?

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**Introduction/Aim:** In February 2017, the Integrated Respiratory Nursing Service (IRNS) project commenced. A newly developed algorithm outlined the referral pathway to the appropriate community respiratory nursing service via a single point of entry. This streamlined access to four providers and enabled a coordinated approach to patient education for those with complex chronic respiratory conditions. The single point of entry simplified the referral process, decreased duplication of referrals to different service providers and increased collaboration between four community respiratory nursing services and general practice.

**Aim of audit:** To review the referrals received ascertain if there was a reduction in Emergency Department presentations and hospitalisations for respiratory illness post intervention from the IRNS.

**Methods:** Data captured from the commencement date February 2017 until the end of March 2018 provided by the single point of entry coordinator, and from each nursing service using a standardised format via an excel spread sheet. The combined information provided results regarding referral numbers, Emergency Department visits (not admitted) and hospitalisations pre and post the referral intervention for coded for respiratory illness. 'Pre' defined as one calendar year prior to referral and 'Post' as one calendar year after referral.

**Results:** Total number of referrals seen by the IRNS totalled 162 for this period. The referrals showed a winter peak with 51 referrals in quarter three (July – September 2017). The number that have completed one year follow-up to date is 83 patients.

For this cohort:

- Emergency Department visits pre referral - 92, visits post referral - 43
- Hospitalisations pre referral - 275, visits post referral - 193
- Patients deceased since referral - 18

**Conclusion:** The results demonstrate the IRNS has decreased Emergency Department visits and respiratory hospitalisations. Data collection will continue as part of the on-going audit of the service. This audit does not look at the patients' experience. Future research is under development for a qualitative study to review this.

**Grant Support:** No grants obtained for this project.

## PHASE 3 INTERIM ANALYSIS: TEZACAFTOR/IVACAFTOR (TEZ/IVA) IN PATIENTS HETEROZYGOUS FOR F508DEL-CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR (CFTR) AND RESIDUAL FUNCTION (RF) MUTATION

MIDDLETON P<sup>1</sup>, FLUME P<sup>2</sup>, LEKSTROM-HIMES J<sup>3</sup>, FISCHER BINER R<sup>4</sup>, SIMARD C<sup>3</sup>, DOWNEY D<sup>5</sup>, ZHOU H<sup>3</sup>, OWEN C<sup>3</sup>, DE BOECK K<sup>6</sup>

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**Introduction/Aim:** EXTEND (NCT02565914) is an ongoing open-label study of TEZ/IVA, a CFTR modulator combination, in patients who completed participation in TEZ/IVA pivotal studies. Here we report an interim analysis of pooled safety data from EXTEND and efficacy data from patients heterozygous for *F508del* and an RF mutation.

**Methods:** Patients received TEZ 100 mg qd/IVA 150 mg q12h. The primary endpoint was safety; secondary endpoints included absolute change from baseline in ppFEV<sub>1</sub>, BMI and CF Questionnaire Revised (CFQR) respiratory domain score and number of pulmonary exacerbations (PEX). The safety set included all EXTEND patients on TEZ/IVA ≥48 weeks (n = 613); the efficacy set included patients who rolled over from EXPAND (NCT02392234), an 8-week crossover, placebo- and IVA-controlled, Phase 3 study in *F508del*/RF patients, and completed 16 weeks of TEZ/IVA in EXTEND (n = 226).

**Results:** Safety: mean (SD) TEZ/IVA exposure in 613 patients was 86.0 (21.3) weeks from start of active drug. 601 (98.0%) patients had ≥1 treatment-emergent adverse event (TEAE). Common TEAEs were infective PEX of CF (54.0%), cough (39.2%) and nasopharyngitis (25.4%). Serious TEAEs occurred in 194 patients (2.0% treatment related). Three (0.5%) patients discontinued due to TEAEs; no deaths occurred. Efficacy: TEZ/IVA-treated patients maintained improvements in ppFEV<sub>1</sub> and other endpoints up to 24 weeks; placebo- or IVA-treated patients from EXPAND receiving TEZ/IVA in EXTEND had improvements in ppFEV<sub>1</sub> and other endpoints consistent with results in EXPAND (Table).

LS mean (95% CI or SD)	Absolute change from baseline in efficacy endpoints at the average of weeks 4 and 8 in EXPAND and at extension week 16 in EXTEND					
	EXPAND at weeks 4 and 8 (average) <sup>a</sup>			EXTEND at week 16 <sup>b</sup>		
	Placebo (n=161)	IVA (n=156)	TEZ/IVA (n=161)	Placebo TEZ/IVA (n=80)	IVA TEZ/IVA (n=70)	TEZ/IVA TEZ/IVA (n=76)
ppFEV <sub>1</sub>	-0.3 (-1.2, 0.6)	4.4 (3.5, 5.3)	6.5 (5.6, 7.3)	4.8 (3.1, 6.5)	6.5 (4.7, 8.3)	7.8 (6.1, 9.6)
BMI, kg/m <sup>2c</sup>	0.18 (0.81)	0.47 (0.80)	0.34 (0.96)	0.61 (1.29)	0.67 (1.28)	0.94 (1.75)
CFQR (respiratory domain)	-1.0 (-2.9, 1.0)	8.7 (6.8, 10.7)	10.1 (8.2, 12.1)	9.8 (6.5, 13.1)	11.6 (8.0, 15.1)	11.5 (8.0, 14.9)
PEX, estimated event rate per year	0.63 <sup>d</sup>	0.29 <sup>d</sup>	0.34 <sup>d</sup>	0.38 <sup>d</sup>	0.26 <sup>d</sup>	0.22 <sup>d</sup>

<sup>a</sup>N for EXPAND represents patients exposed in both treatment period 1 and treatment period 2 in this crossover study design; <sup>b</sup>Baseline is the start of parent study (EXPAND); <sup>c</sup>Absolute change at week 8; <sup>d</sup>PEX analysis period includes through week 8 of study drug treatment; <sup>e</sup>PEX analysis period includes all time that a patient was on TEZ/IVA from the start of period 2 in the parent study (EXPAND) through week 16 in EXTEND

**Conclusion:** TEZ/IVA was well tolerated for ≥48 weeks; no new safety concerns were identified. Durable improvement across multiple endpoints was observed in *F508del*/RF patients.

**Grant Support:** Sponsored by Vertex Pharmaceuticals Incorporated.

TO 013

TO 014

## CYTOCHROME INTERACTIONS OF CYSTIC FIBROSIS MODULATORS AND RESULTING PLASMA CONCENTRATIONS

SCHNEIDER-FUTSCHIK E<sup>1</sup>

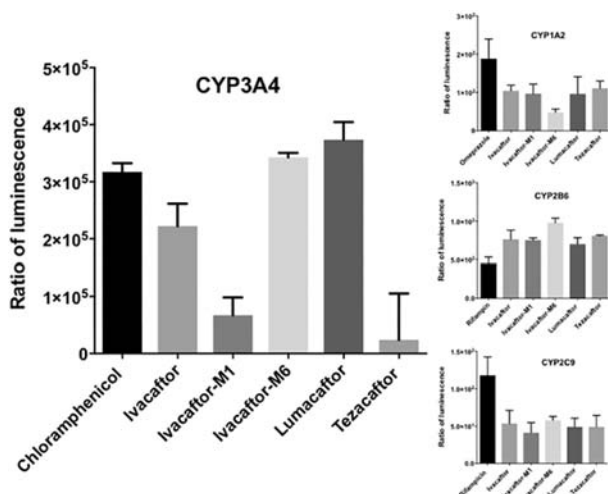
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**Introduction/Aim:** Since release of ivacaftor-lumacaftor combination for cystic fibrosis therapy several red-flags have been raised that highlight the clinical efficacy of this combination strategy maybe be limited due to antagonistic drug-drug interactions.

**Methods:** The effect of ivacaftor, its major metabolites M1 and M6, lumacaftor and the novel cystic fibrosis transmembrane conductance regulator (CFTR) modulator tezacaftor at 10 µg/mL on the enzymatic activity of the major xenobiotic metabolizing enzymes CYP1A2 and CYP3A4 as well as the minor enzymes CYP2B6 and CYP2C9 was assayed. The results were then compared to plasma concentrations of CF patients.

**Results:** Lumacaftor ( $3.74 \times 105 \pm 3.11 \times 104$  RLU), and ivacaftor-M6 ( $3.43 \times 105 \pm 7.61 \times 103$  RLU) markedly induced the activity of CYP3A4 (Figure). Ivacaftor ( $2.22 \times 105 \pm 3.94 \times 104$  RLU) showed a lower relative ratio of luminescence units compared to chloramphenicol ( $3.17 \times 105 \pm 1.55 \times 104$  RLU). Interestingly, ivacaftor-M1 ( $6.74 \times 104 \pm 3.09 \times 104$  RLU) and the novel CFTR modulator tezacaftor ( $2.40 \times 104 \pm 8.14 \times 104$  RLU) did not show CYP3A4 induction. In the CYP1A2 and CYP2C9 assay, all metabolites showed a decrease in the ratio of luminescence units compared to the controls omeprazole ( $1.88 \times 102 \pm 5.19 \times 101$  RLU), and rifampicin ( $1.18 \times 102 \pm 2.46 \times 101$  RLU), respectively. Ivacaftor, its major metabolites, lumacaftor and tezacaftor all showed slight increase in the ratio of luminescence units compared to the control rifampin ( $4.52 \times 102 \pm 8.06 \times 101$  RLU) with CYP2B6.

**Conclusion:** All in all, present findings would suggest that, lumacaftor and ivacaftor-M6 are strong inducers of CYP3A4, potentially reducing ivacaftor concentrations; ivacaftor itself induces CYP3A4 to some extent. Tezacaftor is not an CYP3A4 inducer and therefore not affecting ivacaftor concentrations.



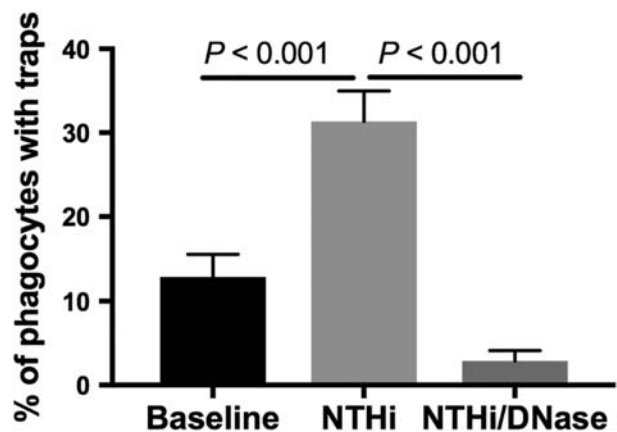
## EXTRACELLULAR TRAPS AS A THERAPEUTIC TARGET IN EARLY-STAGE CYSTIC FIBROSIS

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<sup>1</sup>Monash Children's Hospital, Melbourne, Australia, <sup>2</sup>Monash University, Melbourne, Australia, <sup>3</sup>Monash Lung and Sleep, Monash Medical Centre, Melbourne, Australia, <sup>4</sup>Murdoch Children's Research Institute, Melbourne, Australia, <sup>5</sup>Royal Children's Hospital, Melbourne, Australia, <sup>6</sup>The University of Melbourne, Melbourne, Australia

**Introduction/Aim:** A recent landmark study demonstrated that neutrophil elastase (NE) activity in bronchoalveolar (BAL) fluid in early infancy was associated with early persistent bronchiectasis in children with cystic fibrosis (CF)<sup>1</sup>. The mechanisms responsible for the expression of NE in early CF have not been well-defined. One potential relevant process is the formation of neutrophil and macrophage extracellular traps (NETs/METs), composed of extracellular DNA with co-expressed proteases including NE. Importantly, the expression of these extracellular traps can be dismantled by the addition of deoxyribonuclease (DNase), commercially available in recombinant form as inhaled dornase alpha. The aim of this study was to define the presence of NETs/METs in early CF.

**Methods:** BAL and serum samples were obtained from children aged 1-10 years undergoing flexible bronchoscopy and BAL for management of their lung disease; both from CF subjects and those without CF (disease controls). Cells from BAL were cultured onto cover slips. A proportion of the BAL cells were stimulated with the bacterium non-typeable *H. influenzae* (NTHi). DNase was also added. Extracellular trap expression was measured at each stage using confocal microscopy. NE activity was measured in BAL supernatant. DNA-complexes and inflammatory mediator production were assessed in the serum samples.



**Results:** Twenty subjects (10 CF, 10 control) have been assessed to date, with a median age of 3 years. In the CF subjects, there was prominent baseline expression of both NETs and METs expressing various pathogenic proteases including NE. In both CF and control subjects, the addition of NTHi *in vitro* increased trap expression, whilst this effect was abolished with the addition of DNase. Combined results of the 20 subjects are shown in the figure.

**Conclusion:** Phagocytic extracellular traps express proteases such as neutrophil elastase in early-life CF. The expression of these traps is dismantled by the addition of DNase.

### REFERENCE

[1] Sly P *et al.* Risk Factors for Bronchiectasis in Children with Cystic Fibrosis. *NEJM*, 2013;368:1963

**Grant Support:** 65 km for CF Foundation

TO 015

TO 016

### RESCUE OF CFTR FUNCTION IMPAIRED BY MUTATIONS IN EXON 15 IN CHILDREN WITH CYSTIC FIBROSIS

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**Introduction/Aim:** Over 2000 different mutations have been reported in patients with Cystic Fibrosis (CF) and found to occur in all *CFTR* exons and introns. Many mutations are not amenable to current therapies, and therefore new drugs must be developed. Antisense oligonucleotides (AOs) are synthetic nucleic acid analogues designed to anneal to selected splice motifs within pre-mRNAs. AO binding alters the recognition of the splice site by the spliceosome and therefore modulates exon selection. Exon 15 harbors ~40 mutations and exclusion of this exon will not disrupt the mRNA reading frame. We hypothesize by skipping exon 15 in patients with amenable mutations such as p.Phe861Leufs3, studied here, the induced isoform may retain residual function, therefore alter the course of disease.

**Methods:** AO sequences were initially optimised using 2'-O-Methyl modified bases on a phosphorothioate backbone (2OMe) and transfected using lipofectamine into primary airway epithelial cells (AEC) from non-CF (2.6 years M) and p.Phe861Leufs3/p.Phe508del CF children (4.1 years M). The most effective 2OMe AO sequence was re-synthesised as the clinically validated phosphorodiamidate morpholino (PMO) chemistry and any modification of protein shown by western blot. Resulting CFTR function was then measured using Ussing Chamber studies and air liquid interface (ALI) cell cultures.

**Results:** The 2OMe sequence produced 50% skipping in p.Phe861Leufs3/p.Phe508del CF airway epithelial cells. The PMO induced skipping of exon 15 from non-CF (49%) and p.Phe861Leufs3/p.Phe508del CF (88%) cells after 7 days in culture. Western blot illustrated the effect of exon 15 skipping on the induced CFTR protein expression. AEC grown at ALI then confirmed resultant CFTR function.

**Conclusion:** Exon 15 can be efficiently skipped from the *CFTR* transcript in both non-CF and CF-derived airway epithelial cells. We propose that exon skipping to remove disease-causing mutations in selected in-frame exons can improve function in amenable CF patients.

**Grant Support:** USCF, NHMRC

### THE CYSTIC FIBROSIS GUT MICROBIOME: A MAJOR RESERVOIR OF TRANSMISSIBLE ANTIBIOTIC RESISTANCE

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**Introduction/Aim:** Our ability to manage respiratory infections relies on continuing antibiotic efficacy. Antibiotic resistance arising within high exposure patients, such as those with cystic fibrosis (CF), can not only affect the management of chronic respiratory infections caused by specific pathogens, but can also act as a source of resistance dissemination through the horizontal movement of transmissible genes. While the gut microbiome is a potential major reservoir for antibiotic resistance, it is rarely considered in respiratory cohorts. We aimed to comprehensively define the intestinal resistome for a cohort of adult CF patients.

**Methods:** Shotgun metagenomic sequencing was performed on faecal samples from 19 CF patients attending the Mater Adult CF clinic and 16 healthy controls. Assembled genes were mapped to the Comprehensive Antibiotic Resistance Gene Database (CARD). *Klebsiella pneumoniae* and *Escherichia coli* isolates from CF faecal samples, and *Pseudomonas aeruginosa* isolates from CF sputum, underwent tobramycin (TOB) sensitivity testing and whole genome sequencing (WGS). TOB-sensitive *P. aeruginosa* isolates were co-cultured with TOB-resistant *K. pneumoniae* or TOB-resistant *E. coli* to determine element transmissibility.

**Results:** The faecal resistome differed significantly between CF patients and healthy adults (Pseudo-F = 4.675;  $P = 0.0004$ ). Of all the resistance genes, those that are transmissible between species were significantly higher in CF ( $P = 0.0027$ ) and their composition was significantly different (Pseudo-F = 6.9263;  $P < 0.0001$ ), compared to healthy. Notably, CF patients displayed significantly higher carriage of plasmid-mediated aminoglycoside-modifying genes ( $P < 0.0001$ ), consistent with widespread use of drugs such as TOB. TOB-resistant *K. pneumoniae* and *E. coli* isolated from CF faecal samples were found to harbour transmissible TOB-resistant genes *aac(6')-Ib'* and *aac(6')-Ib7*, which were also present in TOB-resistant *P. aeruginosa* from the same patients.

**Conclusion:** The CF gut microbiome is a major reservoir of transmissible resistance against antibiotics that are clinically important for the management of respiratory infections. Gut-derived TOB-resistance might reduce the efficacy of anti-pseudomonal treatment.

TO 017

TO 018

**PHASE 3 INTERIM ANALYSIS: TEZACAFTOR/IVACAFTOR (TEZ/IVA) IN PATIENTS HOMOZYGOUS FOR F508DEL-CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR (CFTR)**

**SMITH D<sup>1</sup>**, FLUME P<sup>2</sup>, LEKSTROM-HIMES J<sup>3</sup>, FISCHER BINER R<sup>4</sup>, SIMARD C<sup>3</sup>, DOWNEY D<sup>5</sup>, ZHOU H<sup>3</sup>, OWEN C<sup>3</sup>, DE BOECK K<sup>6</sup>

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**Introduction/Aim:** EXTEND (NCT02565914) is an ongoing open-label study of TEZ/IVA, a CFTR modulator combination, in patients who completed participation in TEZ/IVA pivotal studies. Here we report an interim analysis of pooled safety data from EXTEND and efficacy data from patients homozygous for *F508del*.

**Methods:** Patients received TEZ 100 mg qd/IVA 150 mg q12h. The primary endpoint was safety; secondary endpoints included absolute change from baseline in ppFEV<sub>1</sub>, BMI and CF Questionnaire Revised (CFQR) respiratory domain score and number of pulmonary exacerbations (PEX). The safety set included all EXTEND patients on TEZ/IVA ≥48 weeks (n=613); the efficacy set included patients who rolled over from EVOLVE (NCT02347657), a 24-week, placebo-controlled, Phase 3 study in *F508del/F508del* patients, and completed 24 weeks of TEZ/IVA in EXTEND (n = 459).

**Results:** Safety: mean (SD) TEZ/IVA exposure in 613 patients was 86.0 (21.3) weeks from start of active drug. 601 (98.0%) patients had ≥1 treatment-emergent adverse event (TEAE). Common TEAEs were infective PEX of CF (54.0%), cough (39.2%) and nasopharyngitis (25.4%). Serious TEAEs occurred in 194 patients (2.0% treatment related). Three (0.5%) patients discontinued due to TEAEs; no deaths occurred. Efficacy: TEZ/IVA-treated patients maintained improvements in ppFEV<sub>1</sub> and other endpoints up to 48 weeks; placebo patients from EVOLVE receiving TEZ/IVA in EXTEND had improvements in ppFEV<sub>1</sub> and other endpoints consistent with results in EVOLVE (Table).

Absolute change from baseline in efficacy endpoints through week 24 in EVOLVE and at extension week 24 in EXTEND				
LS mean (95% CI)	EVOLVE through week 24		EXTEND at week 24	
	Placebo (n=256)	TEZ/IVA (n=248)	Placebo TEZ/IVA (n=231) <sup>a</sup>	TEZ/IVA TEZ/IVA (n=228) <sup>b</sup>
ppFEV <sub>1</sub>	-0.6 (-1.3, 0.0)	3.4 (2.7, 4.0)	4.3 (3.3, 5.4)	3.4 (2.3, 4.5)
BMI, kg/m <sup>2c</sup>	0.12 (0.03, 0.22)	0.18 (0.08, 0.28)	0.25 (0.13, 0.38)	0.23 (0.11, 0.36)
CFQR (respiratory domain)	-0.1 (-1.6, 1.4)	5.0 (3.5, 6.5)	3.7 (1.5, 6.0)	3.1 (0.8, 5.3)
PEX, estimated event rate per year	0.99 <sup>d</sup>	0.64 <sup>d</sup>	0.65 <sup>e</sup>	0.72 <sup>e</sup>

<sup>a</sup>Based on EXTEND baseline for placebo--TEZ/IVA; <sup>b</sup>Based on EVOLVE baseline for TEZ/IVA--TEZ/IVA; <sup>c</sup>Absolute change at week 24; <sup>d</sup>PEX analysis period includes through week 24 of study drug treatment; <sup>e</sup>PEX analysis period includes all time that a patient was on TEZ/IVA from the start of the parent study (EVOLVE) through week 24 in EXTEND

**Conclusion:** TEZ/IVA was well tolerated for ≥48 weeks; no new safety concerns were identified. Durable improvement across multiple endpoints was observed in *F508del/F508del* patients.

**Grant Support:** Sponsored by Vertex Pharmaceuticals Incorporated.

**ASSESSING THE QUALITY OF CLINICAL CARE IN MANAGEMENT OF BRONCHIOLITIS**

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**Introduction/Aim:** Bronchiolitis is the most common cause of hospitalisation in children aged <2 years. Clinical practice guidelines (CPGs) suggest only supportive management without the need for any medications. We conducted an assessment of guideline adherence in the management of bronchiolitis in children at a sub-nationally representative level including across inpatient, emergency and ambulatory settings in Australia.

**Methods:** We searched for national and international Clinical Practice Guidelines (CPGs) relating to management of bronchiolitis in children and identified 16 recommendations which were formatted into 40 medical record audit indicator questions. A retrospective medical record review assessing compliance with the CPGs was conducted across three types of healthcare setting: hospital inpatient admissions, Emergency Department (ED) presentations, and general practice (GP) consultations in three Australian states for children aged ≤2 years receiving care in 2012 and 2013.

**Results:** Purpose-trained surveyors conducted 13,979 eligible indicator assessments across 796 visits for bronchiolitis at 119 sites. Guideline adherence for management of bronchiolitis was 77.3% (95% CI: 72.6-81.5) for children attending EDs, 81.6% (95% CI: 78.0-84.9) for inpatients and 52.3% (95% CI: 44.8-59.7) for children attending GPs. While adherence to some individual indicators was high, overall adherence to documentation of 10 indicators relating to history taking and examination was poorest and estimated at 2.7% (95% CI: 1.5-4.4). Indicators assessing avoidance of inappropriate tests and examinations, across all healthcare settings, found 92.6% adherence (95% CI: 87.5-96.1) however 40.6% (95% CI: 29.0-52.9) of children aged <12 months, with moderate bronchiolitis underwent blood tests or chest x-rays.

**Conclusion:** Guideline adherence was high for some assessments, and varied across different healthcare settings. There are opportunities to improve the management of bronchiolitis.

**Grant Support:** The research was funded as an Australian National Health and Medical Research partnership grant (APP1065898).

TO 019

TO 020

### VIDEO TESTIMONIALS MAY FACILITATE UNDERSTANDING OF AND REFERRAL TO PULMONARY REHABILITATION IN PEOPLE WITH CHRONIC RESPIRATORY DISEASE

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**Introduction/Aim:** 'Knowledge' and 'beliefs about consequences' influence uptake and completion of pulmonary rehabilitation (PR). Narrative video communication has improved understanding and uptake of treatments in other chronic conditions. This pilot aimed to understand the effect of video testimonials portraying the patient experience of PR on understanding and expectations of PR referral and uptake.

**Methods:** Individuals with stable chronic obstructive pulmonary disease (COPD) or interstitial lung disease (ILD) attending outpatient clinics were invited to answer a series of standard questions relating to their understanding of PR, and perceived benefits of PR, before and after viewing the video testimonials.

**Results:** Twenty-nine individuals (10 male; 2 ILD; mean (standard deviation (SD)) age 71(8) years) viewed the video testimonials and completed questionnaires. Seventeen individuals had previously heard of PR, but only 10 had participated. Prior to viewing the video 18 (62%) anticipated PR would be beneficial for them, and agreed that PR would be suitable for someone like themselves (mean (SD) 4 (1) on 5-point Likert scale). After viewing the video testimonials 24 participants (83%) identified with the patient experiences described in the video. Twenty three (79%) expected PR would be beneficial for them and felt they would be physically able to manage PR. Over half the participants (n = 15, 52%) requested further information about PR, with 8 participants (28%), all naive to PR, requesting referral to PR. Despite interest in attending PR, 45% of participants indicated that getting to centre-based PR sessions would be hard or somewhat hard.

**Conclusions:** Video testimonials about PR participation may improve patient understanding, or confirm previous knowledge, of what PR involves; and may facilitate acceptance of PR referral. Established travel and transport barriers to PR attendance remain evident and are not addressed by this strategy. Future analysis will assess PR uptake and attendance rates relative to video testimonial viewing.

**Grant Support:** Institute for Breathing and Sleep Education Grant. NSC is the holder of an NHMRC early career fellowship.

### A THEORY-BASED INTERVENTION FOR IMPROVED UPTAKE AND ADHERENCE TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE GUIDELINES IN THE HOSPITAL SETTING: AN INTERVENTION MAPPING APPROACH

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**Introduction:** Exacerbations of Chronic Obstructive Pulmonary Disease (COPD) present a costly burden to the healthcare system. Despite reduced exacerbation rates with provision of guideline concordant care, uptake and adherence to guideline recommendations are variable in clinical practice. Evidence is currently sparse and heterogeneous for the effectiveness of innovative, rigorously developed technology-based interventions targeting improved adherence to best-practice guidelines for inpatient management of COPD.

**Aim:** To rigorously design a technology-based intervention and accompanying implementation and evaluation plan to improve uptake and adherence to best-practice guidelines for the management of COPD in the hospital setting.

**Methods:** The six-step Intervention Mapping Framework (IM) was used to guide the development of a theory and evidence-based intervention. Step 1) needs assessment undertaken through literature review and qualitative input (multidisciplinary roundtable meetings); Step 2) performance and change objectives were formulated; Step 3) theory-based practical applications were identified and selected to address barriers to guideline uptake; Step 4) guideline intervention resources designed using input from multidisciplinary team. Implementation and evaluation (steps 5&6) design are in progress.

**Results:** The needs assessment identified the importance of integration of guidelines into daily workflow, simplicity and interactivity for future interventions. Change in the following determinants was deemed necessary to improve guideline concordant care: knowledge, attitudes, self-efficacy, skills and motivation. Following on from the first three steps, a technology-based intervention package was designed to be relevant and feasible in current clinical practice. Components of the package include: 1) electronic medical record integration; 2) ward-located flipchart embedded with mobile augmented reality technology; and 3) an extensive patient and practitioner education and user support program.

**Conclusion:** The IM Framework provided a comprehensive approach for the development of a rigorous theory and evidence-based intervention, specifically targeting behaviours that have been historically difficult to change around uptake and adherence to COPD guidelines in the hospital setting.

**PROGNOSIS OF ADULTS WITH IDIOPATHIC PULMONARY FIBROSIS WITHOUT EFFECTIVE THERAPIES: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Introduction/Aim:** Idiopathic pulmonary fibrosis (IPF) is a common interstitial lung disease with low survival. With scientific advances, diagnostic criteria for IPF have changed considerably in recent decades, potentially affecting estimates of prognosis. In addition to facilitating planning for healthcare delivery, reliable information about prognosis is essential for treatment decisions in individual patients. This review aimed to evaluate the survival of patients with IPF without effective therapies.

**Methods:** Relevant studies were identified by search of electronic databases and clinical trial registries, review of reference lists of included studies, and contacting authors of IPF international consensus statements. All cohort studies and the placebo arms of randomised controlled trials (RCTs) with  $\geq 12$ -month follow-up which assessed survival of IPF patients without effective therapies were included. Two reviewers independently evaluated studies for inclusion, assessed risk of bias and extracted data.

**Results:** Of the 12485 citations, 154 cohort studies and 16 RCTs published between 1972 and 2018, including participants from the Asia-Pacific, the Americas and Europe, were included. The diagnosis was made according to the 2011 ATS/ERS/JRS/ALAT Guideline for 38 studies, the 2000 ATS/ERS Consensus Statement for 56 studies and other criteria for 66 studies. The pooled proportions of mortality were 0.12 (95%CI: 0.09, 0.14; 59 studies, 25,314 participants) at 1 year and 0.61 (95%CI: 0.48, 0.73; 27 studies, 11,807 participants) at 5 years. The reported median overall survival ranged from 0.45 to 8.5 years, with a pooled mean survival of 3.4 years (19 studies, 1,334 participants). Subgroup analyses revealed significant differences in mortality rates according to diagnostic criteria, although heterogeneity was high.

Table: Pooled proportions of overall mortality at 1 year

	Number of studies	Number of participants	Proportion	95% CI	Heterogeneity
Overall	59	25314	0.12	0.09,0.14	$I^2 = 95\%$
2011 ATS/ERS/JRS/ALAT Guideline	14	2152	0.07	0.05,0.10	$I^2 = 72\%$
2000 ATS/ERS Consensus Statement	23	2048	0.10	0.05,0.16	$I^2 = 92\%$
Other criteria	22	21114	0.18	0.15,0.22	$I^2 = 92\%$

**Conclusion:** Collectively, the survival rates for patients with IPF without effective therapies were 86% at 1 year and 42% at 5 years. Although limited by significant heterogeneity in study design and population, findings from this review can inform treatment discussions with patients and comparisons for future studies with new therapies.

**Grant Support:** NHMRC Postgraduate Scholarship for Khor YH

**BIOMARKERS IN LUNG BIOPSIES: INSIGHTS FROM AUSTRALIAN IPF REGISTRY**

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**Introduction/Aim:** Provisional analysis of serum biomarkers from Australian IPF Registry patients identified candidate biomarkers for further study in lung tissue. Using these biomarkers, we sought to compare tissue levels in lung biopsy samples obtained from IPF patients with either rapidly progressive or stable disease.

**Methods:** Patients from the Australian IPF Registry who had surgical lung biopsies were identified and categorised into "decliners" (fall in FVC  $\geq 10\%$  or DLco  $\geq 15\%$  or death within 1 year from baseline) or stable. Using immunohistochemistry, lung tissue was stained from IPF patients for biomarkers of interest. Biomarkers studied were matrix metalloproteinase (MMP)-7, Osteopontin (OPN), CXCL13 and intracellular adhesion molecule-1 (ICAM-1). Computer-assisted image analysis was performed using a Leica DM 2500 microscope and Image Proplus V7 software. Data is represented as percentage staining. Quantitative analysis of biomarker staining and survival analyses were performed. Statistical analysis was performed using Stata/SE 15.1 and Prism 7.0d.

**Results:** 29 IPF patients were identified (Age:  $67 \pm 5.9$  years, FVC  $81.9 \pm 24.2\%$ , DLco  $52.7 \pm 15.1\%$ ). Fourteen out of the 29 patients (48%) were found to be rapid decliners and 15 (52%) had stable disease. All four biomarkers had significantly increased staining in the tissue of the rapid decliners compared to stable IPF patients [MMP-7 (stable:  $4.6 \pm 3.8$ , decliner:  $8.6 \pm 7.0$ ;  $P = 0.03$ ), ICAM-1 (stable:  $33.7 \pm 14.6$ , decliner:  $67.8 \pm 5.6$ ;  $P < 0.001$ ), CXCL13 (stable:  $12.1 \pm 7.4$ , decliner:  $17.7 \pm 8.1$ ;  $P = 0.03$  and OPN (stable:  $7.1 \pm 4.6$ , decliner:  $9.7 \pm 3.4$ ,  $P = 0.05$ )]. ICAM-1 was found to independently predicted transplant-free survival in a univariate cox analysis (HR = 1.04, 95% CI: 1.01 – 1.08,  $P = 0.01$ ).

**Conclusion:** We demonstrate a significant increase in candidate biomarkers quantified in the lung tissue of IPF patients with rapidly progressive disease compared to stable disease course. ICAM-1 was found to independently predict transplant-free survival. Further studies will be needed to evaluate the significance of these biomarkers in IPF lung tissue with larger cohorts.

**Grant Support:** NHMRC and Clifford Craig Foundation



TO 023

### SHARED EXPERIENCES, MUTUAL SUPPORT: PEER CONNECT SERVICE FOR PULMONARY FIBROSIS

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**Introduction:** People living with pulmonary fibrosis (PF) report unmet needs for information and support. Lung Foundation Australia (LFA) developed the Peer Connect Service to facilitate telephone support between people with PF across Australia. This project aimed to evaluate the resources required to deliver the Peer Connect Service, and to document the experiences of participants.

**Methods:** Number of matches undertaken over 12 months was recorded, along with the number of contacts between LFA staff and participants required to establish each match. People with PF who had participated in the Peer Connect Service took part in a semi-structured interview by telephone. Primary Peers (registered patient peers who agreed to initiate contact) and Secondary Peers (eligible patients who had sought a peer match) were interviewed. Thematic analysis was undertaken by two independent researchers.

**Results:** 60 peer matches were made, with a minimum of seven contacts from LFA staff to establish every match, mostly via telephone. Interviews were conducted with 32 participants with PF, consisting of 17 primary peers, 13 secondary peers and two who were both. Ages ranged from 53 to 89 years. A prominent theme was the value of shared experience, allowing information and emotional support needs to be met. Most participants perceived that Peer Connect provided mutual support, however a small number of Primary Peers had unmet support needs or were concerned that their phone calls were intrusive. Shared personal characteristics (eg gender, family background, hobbies) were important to the success of a match. Participants saw face-to-face contact with peers as highly desirable, whilst acknowledging the practical difficulties with achieving this.

**Conclusion:** The Peer Connect Service provides a unique opportunity for people with PF to share experiences and offer mutual support. This telephone matching model may be useful to provide peer support for individuals with rare diseases who are geographically dispersed.

**Grant Support:** NHMRC Centre of Research Excellence in Pulmonary Fibrosis (GNT 1116371)

Table 1. Biomarker concentration by ILD subgroup (shown as median (range) in ng/mL unless indicated)

Biomarker	No ILD			ILD		P-value IPF+SSc-ILD, n=442	ILD vs non-ILD
	HC n=30	SSc n=168	HC+SSc n=198	SSc-ILD n=270	IPF n=172		
<b>CCL18</b>	48.9 (9.64-172.3)	68.1 (14.5-459)	62.7 (9.64-459)	76.9 <sup>^</sup> (9.37-828)	59.8 (23.3-662)	83.5 <sup>#</sup> (9.37-828)	<0.001
<b>Ca15.3 (pg/mL)</b>	28.5 (5.99-62)	31.7 (4.41-452)	30.4 (4.41-452)	49.4 (4.14-965)	67.1 (7.03-770)	55 (4.14-965)	<0.001
<b>E-selectin</b>	24.1 (9.4-50.1)	35.2 (6.29-107)	32.9 (6.29-107)	37.4 (9.64-113)	39.0 (13.9-164)	38.2 (9.64-113)	<0.001
<b>ICAM</b>	378 (36.2-1405)	544 (48.5-2248)	528 (36.2-2248)	642 (19.7-2601)	732 <sup>β</sup> (195-2648)	666 <sup>Ω</sup> (19.7-2648)	<0.001
<b>MMP-3</b>	9.8 (4.3-26.6)	12.8 <sup>Σ</sup> (3.9-201)	11.6 <sup>θ</sup> (3.9-201)	12.8 <sup>∞</sup> (3.05-230)	17.7 <sup>Δ</sup> (4.9-119)	14.9 <sup>∅</sup> (3.06-230)	0.003
<b>MMP-7</b>	0.93 (0.47-2.28)	1.46 (0.39 -24.2)	1.36 (0.39-24.2)	2.02 (0.36-7.34)	2.54 (0.5-20.5)	2.24 (0.36-20.5)	<0.001
<b>SP-D</b>	7.78 (2.36-35.8)	21.6 <sup>β</sup> (3.30-152)	19.0 <sup>Φ</sup> (2.36-152)	35.4 <sup>∇</sup> (5.62-264)	55.7 <sup>δ</sup> (8.15-148)	42.9 <sup>Ψ</sup> (5.62-264)	<0.001

<sup>^</sup>n=269; <sup>#</sup>n=441; <sup>β</sup>n=171; <sup>Ω</sup>n=441; <sup>Δ</sup>n=170; <sup>Σ</sup>n=164; <sup>∞</sup>n=262; <sup>θ</sup>n=194; <sup>∅</sup>n=432; <sup>δ</sup>n=167; <sup>β</sup>n=167; <sup>∇</sup>n=264; <sup>Φ</sup>n=197; <sup>Ψ</sup>n=431  
7 biomarkers demonstrated higher serum levels in ILD (IPF+SSc-ILD) versus non-ILD patients (HC+SSc) – table 1. Ca15.3, ICAM, MMP-3, MMP-7 and SP-D also demonstrated elevated levels in IPF versus SSc-ILD ( $P < 0.05$ ), and Ca15.3, MMP-7 and SP-D distinguished SSc-ILD from SSc ( $P < 0.0001$ ).

### UTILITY OF SERUM BIOMARKERS TO DETECT ILD IN IDIOPATHIC PULMONARY FIBROSIS (IPF) AND SCLERODERMA-ASSOCIATED ILD (SSc-ILD)

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**Introduction:** Accurate prediction of disease progression and therapeutic response in interstitial lung disease (ILD) is lacking. Validation of candidate serum biomarkers remains limited by small, single-centre studies without longitudinal disease measures. We assessed the diagnostic role of 28 biomarkers in two large, multicentre cohorts of Australian idiopathic pulmonary fibrosis (IPF) and scleroderma-ILD (SSc-ILD) patients with prospective longitudinal data and linked sera.

**Methods:** The serum concentration of 28 biomarkers was evaluated using bead-based multiplex assays (SP-D, MMP-1/-3/-7/-12, periostin, CXCL13, CCL2, IL-6/-8, CXCL4/-10/-12, TGF-beta, Ca15.3, Endothelin 1, VEGF, Amphiregulin, TIMP1, CCL18, ICAM, VCAM, E-selectin) and ELISA (KL-6, fibulin-1, LOXL2). IPF and SSc patients were identified from the Australian IPF Registry and Scleroderma Cohort Study, including prospective, longitudinal clinical and outcome data and linked serum bio-banks. Sera was also obtained from non-smoking healthy controls.

**Results:** 640 patients (mean age 60 ± 13.7 years, 33% male, 52% ever smokers), including 172 IPF, 168 SSc, 270 SSc-ILD patients and 30 healthy controls were analysed. IPF patients were older (mean 70 ± 18 years) and more male predominant (70% male). SSc-ILD patients were less likely to be ever smokers (44%). FVC did not differ between groups (mean 2.68 ± 0.80L, 76 ± 12%pred). DLCO was lower in IPF patients versus SSc and SSc-ILD (mean 38, 64 and 58% respectively;  $P < 0.001$ ) and SSc-ILD compared with SSc ( $P = 0.003$ ).

**Conclusion:** We identified a panel of serum proteins able distinguish IPF and SSc-ILD from non-ILD patients; between ILD subtypes; and SSc with and without ILD. Further analysis is required to determine the relationship of biomarkers with disease severity and outcomes.

**Grant Support:** Lung Foundation Australia David Wilson PhD Scholarship. We would also like to acknowledge the Australian IPF Registry and Australian Scleroderma Interest Group.

### NINTEDANIB IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS: SAFETY AND TOLERABILITY

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**Introduction/Aim:** Nintedanib slows progression of idiopathic pulmonary fibrosis (IPF) by reducing the FVC decline rate. To characterize its safety and tolerability, we analyzed adverse events (AEs) in nintedanib-treated IPF patients based on pooled data from six clinical trials.

**Methods:** Data were pooled from patients treated with nintedanib 150 mg bid in the TOMORROW trial (NCT00514683) and/or its open-label extension (OLE) (NCT01170065), the INPULSIS trials (NCT01335464, NCT01335477) and/or their OLE (NCT01619085), and a Phase IIIb trial (NCT01979952) with a placebo-controlled period of up to 12 months followed by an open-label period of up to 12 months. Dose reductions to 100 mg bid and treatment interruptions were allowed. Event rates per 100 patient exposure-years were calculated.

**Results:** The analysis included 1126 patients. Mean (SD) nintedanib exposure was 27.7 ± 20.5 months; total exposure 2599 patient-years. The rates of AEs leading to permanent dose reduction and discontinuation were 12.8 and 23.8 events per 100 patient exposure-years, respectively. AE rates reported in the pooled population were generally lower than those in nintedanib-treated patients in the INPULSIS trials (Table). There were fewer bleeding events in the pooled population vs nintedanib-treated patients in the INPULSIS trials (9.3 vs 15.8 per 100 patient exposure-years, respectively).

	Pooled population		INPULSIS trials	
	Nintedanib (n = 1126)	Nintedanib (n=638)	Placebo (n=423)	
Diarrhoea	76.5	112.6	25.6	
Nausea	18.0	34.9	7.0	
Nasopharyngitis	15.1	19.6	22.0	
Bronchitis	14.5	15.5	15.0	
Cough	13.2	16.1	16.2	
Progression of IPF*	12.9	11.8	17.7	
Vomiting	11.2	17.1	2.7	
Upper respiratory tract infection	10.1	12.1	13.3	

Number of AEs per 100 patient exposure-years. AEs with rate >10 per 100 patient exposure-years in pooled population are shown.

\*Includes disease worsening and IPF exacerbations (MEDRA 'IPF' term).

**Conclusion:** Data from the largest set of nintedanib-treated patients with IPF analyzed to date demonstrated that nintedanib had a manageable safety and tolerability profile.

**Grant Support:** Boehringer Ingelheim

### ACUTE PHYSIOLOGICAL RESPONSES TO INTERVAL AND CONTINUOUS TRAINING IN ILD

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**Introduction/Aim:** Exercise training in pulmonary rehabilitation is an effective intervention for people with interstitial lung disease (ILD). However, a large proportion of those who participate are not attaining its benefit. Alternative training strategies to the current method of continuous exercise at moderate intensity may prove more effective in people with ILD. This study aims to compare the acute physiological effects of high intensity interval training (HIIT), moderate intensity interval training (MIIT) and moderate intensity continuous training (MICT) in people with ILD.

**Methods:** Six participants with ILD performed in random order three different cycle training protocols until volitional exhaustion, symptom limitation or desaturation (SpO<sub>2</sub> < 80%) after performance of a baseline cardiopulmonary exercise test. Training protocols were thirty second intervals alternating 100% peak work rate with unloaded cycling (HIIT), two minute intervals alternating between 80% and 40% peak work rate (MIIT) and continuous exercise at 60% peak work rate (MICT). The cycle tests were separated by a minimum of one week. Heart rate (HR), blood pressure, SpO<sub>2</sub>, oxygen uptake (VO<sub>2</sub>), minute ventilation (V<sub>E</sub>) and Borg scores for dyspnoea and fatigue were recorded.

**Results:** The MIIT protocol resulted in significantly higher VO<sub>2</sub>, HR and V<sub>E</sub> (Table 1) when compared to other exercise protocols. During MIIT, participants exercised at a higher percentage of VO<sub>2peak</sub> (Table 1) and were associated with more dyspnoea, leg fatigue and oxygen desaturation, although this was not statistically significant. There was no significant difference between HIIT and MICT protocols for the VO<sub>2</sub>, VE, HR, SpO<sub>2</sub>, leg fatigue or dyspnoea. However, HIIT was associated with a smaller volume of work.

**Conclusion:** Using HIIT for people with ILD may allow for a greater training load with similar levels of breathlessness and desaturation to traditional endurance training. Whereas MIIT appears to result in a greater physiological challenge suggesting it is a less effective training strategy.

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	HIIT	MIIT	MICT	P value	
	Mean (SD) at end of exercise			Intensity	Intensity x Time
Work Mins*%	1641 (905)	1914 (865)	2059 (697)	0.2	
WRPeak					
VO <sub>2</sub> L <sub>min</sub>	1.2 (0.4)	1.4 (0.5)	1.2 (0.4)	0.02	0.9
VE L <sub>Min</sub>	50 (11)	58 (12)	47 (10)	0.005	0.9
HR bpm	116 (20)	123 (20)	116 (19)	0.01	0.04
SpO <sub>2</sub> (%)	87 (3)	86 (2)	87 (3)	0.2	0.5
Dyspnoea (Borg)	4 (2)	5 (3)	3 (1)	0.2	
Leg Fatigue (Borg)	13 (4)	14 (5)	13 (5)	0.4	
VO <sub>2</sub> % pred	80 (15)	90 (17)	80 (16)	0.07	
HR % pred	84 (5)	89 (5)	88 (6)	0.06	

Data are estimated marginal means at end of exercise derived from Repeated measures Anova. P values are for intensity effect and intensityxtime interaction. % pred - percent of the peak VO<sub>2</sub> and HR achieved on CPET at end of exercise.

### DIFFERENCES IN CIRCULATING NUCLEIC ACIDS BETWEEN PATIENTS WITH STABLE AND PROGRESSIVE LUNG FUNCTION IN IPF

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**Introduction/Aim:** Idiopathic pulmonary fibrosis (IPF) is a progressive fibrotic disease characterised by dismal prognoses and therapeutic challenges. The pathogenesis of this disease remains elusive, and the long-term clinical outcome of IPF is heterogenous. We explored whether nucleic acids in circulation could predict differences between stable and progressive disease providing insights into the pathogenesis of IPF.

**Methods:** Patients from the Australian IPF Registry who consented to the blood substudy were categorised into 'stable' and 'progressors'. Plasma and peripheral blood mononuclear cells (PBMCs) were isolated from patient blood. Transcript expression from circulating RNA was compared between the groups by microarray, and the top targets with a minimum 2-fold difference were subsequently validated by droplet digital PCR (ddPCR). DNA and RNA were extracted from patient PBMCs and the RNA used for differential gene and transcript analysis by RNAseq, comparing transcriptome profiles between the two groups. The DNA was used to compare telomere length between 'stable' and 'progressive' IPF by quantitative PCR (qPCR).

**Results:** Analysis of the microarray data identified 8 transcripts in the plasma that were differentially expressed between the groups, and validation by ddPCR confirmed 2 of the 8 transcripts were significantly up-regulated in 'progressors' versus 'stable' IPF and healthy controls ( $P < 0.05$ ). The differentially expressed transcripts included *NT5C2* and *MIR6841*. The RNAseq data revealed no differences in transcriptome profiles between PBMCs isolated between the two groups ( $P > 0.05$ ). Similarly, there were no differences detected in telomere lengths between 'stable' and 'progressive' IPF PBMCs ( $P > 0.05$ ).

**Conclusion:** This study successfully identified 2 potentially relevant transcripts in circulation, found to be highly expressed in 'progressors' versus 'stable' IPF patients. Interestingly, no differences were observed in the transcriptome profiles and telomere lengths between PBMCs isolated from the two groups. This novel data has never been explored before, and likely indicates that PBMCs do not play a major role in the progression of IPF.

**Grant Support:** National Health Medical Research Council; Centre of Research Excellence in Pulmonary Fibrosis

**Declaration of Interest:** None of the authors have any conflicts of interest to declare.

TO 028

TO 029

### TEACHING FUTURE DOCTORS ABOUT EFFECTIVE PATIENT EDUCATION: LEARNING ABOUT INHALERS

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**Introduction:** 1 in 9 Australians have asthma and 1 in 7 adults over the age of 40 have COPD. Inhaled medications are used to control symptoms and improve quality of life however, studies have shown that up to 93% of patients are unable to use their inhaler devices correctly. Studies also report poor health care professional (HCP) knowledge of device use, with up to 89% of trained HCP unable to demonstrate correct technique. In order to improve this, Sydney University Westmead Clinical School invested in a novel teaching session for first year medical students.

**Aim:** To evaluate a hands-on training session for medical students.

**Methods:** As part of the Respiratory Sciences Block of the Sydney Medical Program, Stage One medical students were provided with their own inhaler devices kit and participated in an interactive workshop. The kit comprised of common placebo inhaler devices on the Australia market. Students (n = 49), actively participated in a one hour workshop. The structure of the workshop included relevant background information, a practical demonstration of correct use of devices, with students practicing teaching each other and simulating a patient education session using the devices. Following the session, students were asked to complete an online survey.

**Results:** 38 students (81%) responded to the survey. The gains reported by students were hands-on experience; practical application and importance of asking patients to demonstrate use. 89% of students reported that receiving their own placebo devices was 'extremely useful' with 91% stating they were 'very likely to use their placebos to teach patients in the future'.

**Conclusion:** A hands-on workshop using individual placebo devices kits is an effective way of teaching medical students about importance of patient education. The format of an interactive workshop is widely accepted, with students identifying the ongoing benefits of having their own kits.

**Grant Support:** Nil

### ASTHMA COPD OVERLAP VERSUS COPD ALONE IN AUSTRALIAN PRIMARY CARE

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**Introduction:** Many older adults with a history of smoking and asthma develop clinical features of both asthma and COPD, an entity now named Asthma-COPD Overlap (ACO) syndrome. People with ACO are at higher risk of poor health outcomes than patients with asthma or COPD alone. However understanding of ACO is limited, and more information is needed about its clinical and physiological characteristics to better inform patient management.

**Aim:** We aimed to compare the demographic characteristics, self-reported dyspnoea, quality of life and lung function between ACO and COPD, in adult long-term smokers or former smokers ( $\geq 10$  pack years) from Australian general practices participating in a trial of an interdisciplinary community-based model of care.

**Methods:** We used data from the RADICALS (Review of Airway Dysfunction and Interdisciplinary Community-based care of Adult Long-term Smokers) trial. Baseline characteristics, pre- and post-bronchodilator spirometry, dyspnoea scores and St. George's Respiratory Questionnaire scores were compared between 60 ACO patients and 212 with COPD alone. ACO was defined by bronchodilator reversibility.

**Results:** Pre-bronchodilator values of FEV<sub>1</sub> (mean  $\pm$  SD 58.4  $\pm$  14.3 vs 67.5  $\pm$  20.1 %predicted) and FVC (mean 82.1  $\pm$  16.9 vs 91.9  $\pm$  17.2 %predicted) were significantly lower in the ACO group ( $P < 0.001$ ), but no difference was found in post-bronchodilator spirometry. Demographic and clinical characteristics, dyspnoea, quality of life, comorbidities and treatment prescribed did not differ significantly between groups.

**Conclusion:** This study has described ACO in Australian general practices. Our finding of lower pre-bronchodilator lung function in ACO patients compared to COPD, provides further reinforcement to the importance of spirometry in primary care to inform the selection of pharmacotherapy/ management.

**Grant Support:** NHMRC

TO 030

TO 031

**SMOKING CESSATION BRIEF INTERVENTION-MADE EASY****MARSHALL T<sup>1</sup>**, SHAH S<sup>2,3</sup>, WICKS S<sup>1</sup>, LONGWORTH J<sup>1</sup>, COLLIMORE E<sup>1</sup>, TOWNS S<sup>1,2</sup><sup>1</sup>The Children's Hospital At Westmead, Sydney, Australia, <sup>2</sup>Faculty of Medicine and Health The University of Sydney, Sydney, Australia, <sup>3</sup>Westmead Hospital, Westmead, Australia**Introduction:** KidsQuit is an evidence based e-learning smoking cessation program for clinicians working with adolescents and families.**Aim:** To improve clinician knowledge and confidence around providing smoking cessation brief interventions.**Methods:** KidsQuit was developed by clinicians in a tertiary paediatric health care setting to provide smoking cessation brief intervention training to other clinicians. KidsQuit was piloted and assessed within The Children's Hospital at Westmead (CHW) then rolled out to clinicians within other local health districts across NSW. Participants completed pre/post knowledge and confidence questionnaires within this e-learning intervention. Only participant data of those individuals completing both the pre and post KidsQuit e-learning questionnaires were utilised for SPSS analysis to determine the statistical significance of the changes in the knowledge and clinical questionnaire scores using a Paired T test.**Results:** A total of 224 clinicians completed pre and post learning. There was a positive improvement in the mean knowledge scores from 64% to 93.4% ( $P < 0.001$ ). On completion of the clinical practice,  $n = 94$  reported an improvement in their clinical practice confidence comparing pre and post ( $P < 0.001$ ). Confidence in conducting smoking cessation brief interventions increased by 42% from pre learning to post learning. More health professionals reported utilising all components of the 5As of smoking cessation although there were still some challenges seen in arranging follow up due to for example time pressures.**Conclusion:** The overall results have demonstrated an increase in knowledge and confidence in clinicians providing smoking cessation brief interventions. The program is now accessible to clinicians and other professionals supporting adolescent smoking cessation and providing opportunistic brief interventions for parents, families and adolescents. [www.kidsquit.org.au](http://www.kidsquit.org.au)

learning clinical practice questionnaires. Out of the 224 completed pre and post learning knowledge questionnaires there was a positive improvement in the mean knowledge scores from 64.6% to 93.4%. Furthermore out of the 94 completed pre and post learning clinical practice questionnaires an improvement in reported clinical practice was established. Confidence in conducting smoking cessation brief interventions increased from around 30% pre learning to 55.8% post learning.

**Conclusion:** As part of the Respiratory Sciences Block of the Sydney Medical Program, Stage One medical students were provided with their own inhaler devices kit and participated in an interactive workshop. The kit comprised of common placebo inhaler devices on the Australia market. Students ( $n = 49$ ), actively participated in a one hour workshop. The structure of the workshop included relevant background information, a practical demonstration of correct use of devices, with students practicing teaching each other and simulating a patient education session using the devices. Following the session, students were asked to complete an online survey.**Results:** 38 students (81%) responded to the survey. The gains reported by students were hands-on experience; practical application and importance of asking patients to demonstrate use. 89% of students reported that receiving their own placebo devices was 'extremely useful' with 91% stating that they are 'very likely to use their placebos to teach patients in the future'.**Conclusion:** A hands-on workshop using individual placebo devices kits is an effective way of teaching medical students about importance of patient education. The format of an interactive workshop is widely accepted, with students identifying the ongoing benefits of having their own kits.**Grant Support:** Nil**NON-PHARMACOLOGICAL INTERVENTION TO IMPROVE BREATHLESSNESS MASTERY IN COPD: PILOT STUDY****SMITH T<sup>1,2</sup>**, ROBERTS M<sup>1,2,3</sup>, CHO J<sup>1,2,3</sup>, WHEATLEY J<sup>1,2,3</sup><sup>1</sup>Department of Respiratory and Sleep Medicine, Westmead Hospital, Westmead, Australia, <sup>2</sup>University of Sydney, School of Medicine, Westmead Clinical School, Sydney, Australia, <sup>3</sup>Ludwig Engel Centre for Respiratory Research, Westmead Institute for Medical Research, Westmead, Australia**Introduction:** Breathlessness is key symptom for patients with COPD, often persisting despite optimal pharmacological management.**Aim:** To pilot a complex, multidisciplinary, non-pharmacological intervention in Australian patients with COPD.**Methods:** We recruited patients with COPD (FEV1:FVC<70%; FEV1<60% predicted) and significant breathlessness(modified Medical Research Council(mMRC)≥2) to an 8-week non-pharmacological, complex intervention. Participants received individualised advice including hand-held fans, breathing techniques, exercise, energy conservation, relaxation and dietary advice from a multidisciplinary team (doctors, nurses, physiotherapist, occupational therapist and dietitian). We excluded patients with documented cognitive decline or those unwilling to participate in self-management. We assessed patients at baseline, Week-8 and 12-months using: Chronic Respiratory Questionnaire (CRQ; Range0-7au;higher scores = better) with our primary outcome being the CRQ mastery subscale; EQ-5D-5L; breathlessness intensity, unpleasantness and confidence managing breathlessness (0-10 numerical rating scale). All-cause hospitalisations for 12 months before and after clinic completion were collected from local hospital records. We used paired t-tests to compare data for baseline to 8 weeks and unpaired t-tests for baseline to 12 months.**Results:** Eleven patients (7 women) aged  $67.9 \pm 5.4$  years (mean  $\pm$  SD) with FEV1  $28 \pm 6\%$  predicted were recruited. CRQ mastery tended to increase (4.1 to 5.1 over 8 weeks;  $P = 0.07$ ). At 8 weeks, improvements were seen in: mMRC (-0.6;  $P = 0.01$ ), CRQ dyspnoea and fatigue (+1.02,  $P = 0.02$ ; +0.95,  $P = 0.01$ , respectively), EQ-5D-5L overall health (+12;  $P = 0.03$ ), and confidence managing breathlessness (+4;  $P = 0.01$ ). Eight patients contributed 12 month data (1 lost to follow up, 2 died) and no statistically significant changes were detected. Hospitalisations, predominantly due to reductions in respiratory admissions, were significantly reduced over 12 months (admissions/year:  $4.4 \pm 2.2$  at baseline vs  $2.5 \pm 1.8$  at 12 months;  $P = 0.045$ ).**Conclusions:** An 8-week multidisciplinary intervention reduced breathlessness and fatigue, improved overall health, increased confidence managing breathlessness and reduced hospitalisations over 12 months. These pilot data support undertaking a randomised controlled trial to evaluate the intervention.

TO 032

TO 033

**PATIENTS' PERCEPTIONS OF OPIOIDS PRE-PRESCRIPTION FOR BREATHLESSNESS IN CARDIORESPIRATORY DISEASE**

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**Introduction:** A series of studies suggest that low-dose, oral opioids may safely improve severe, chronic breathlessness in advanced cardiorespiratory disease. However, prescription of opioids for breathlessness management remains an off-label indication and occurs infrequently, with little known regarding patients' attitudes to using opioids for breathlessness.

**Aim:** To explore perceptions regarding opioids for the management of severe chronic breathlessness in patients with advanced cardiorespiratory disease.

**Method:** Cross-sectional, qualitative, in-depth interviews analysed using both a descriptive and exploratory thematic analysis framework.

**Setting/Participants:** Purposively-sampled, English-speaking outpatients with advanced COPD (n=7) and Chronic Heart Failure (n=7), not previously prescribed opioids for severe chronic breathlessness, recruited from cardiology or an integrative respiratory and palliative care service at a tertiary metropolitan hospital.

**Results:** Opioid naïve COPD and CHF participants held opinions which naturally aligned into two groups: being either extremely unwilling to use opioids for breathlessness, or reluctantly willing to accept them if the treating doctor considered they were required. Themes observed in participants unwilling to use opioids included: fear and avoidance, fatalistic beliefs, and limited knowledge. Participants who would reluctantly accept opioids had similar concerns, but also described facilitators, which included: a strong trusting relationship with health professionals and desperation to manage distressing breathlessness. Participants did not feel that written supporting information would help them in accepting opioids.

**Conclusion:** Lack of knowledge regarding the role of opioids in managing severe chronic breathlessness, misinformation regarding opioids generally and social stigmas are major barriers to patients accepting opioid therapy.

**Key Words:** *Breathlessness, chronic heart failure, chronic obstructive pulmonary disease, opioids, perceptions.*

**Nomination for New Investigator Award**

**Grant Support:** n/a

**PATIENTS' PERCEPTIONS OF OPIOIDS POST-PRESCRIPTION FOR BREATHLESSNESS IN ADVANCED COPD**

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**Introduction:** A series of studies suggest that low-dose, oral opioids may safely improve severe, chronic breathlessness in advanced cardiorespiratory disease. However, prescription of opioids for breathlessness management remains an off-label indication and occurs infrequently, with little known regarding patients' attitudes to using opioids for breathlessness.

**Aim:** To explore perceptions regarding opioids for the management of severe chronic breathlessness in patients with advanced cardiorespiratory disease.

**Method Design:** Cross-sectional, qualitative, in-depth interviews analysed using both a descriptive and exploratory thematic analysis framework.

**Setting/Participants:** Purposively-sampled, English-speaking outpatients (n = 10) with advanced COPD, currently or previously prescribed opioids for severe chronic breathlessness, recruited from an integrative respiratory and palliative care service at a tertiary metropolitan hospital.

**Results:** Participants described barriers related to their initial fear of using opioids, concerns regarding side effects, difficulty accessing opioids, social stigmas and generalized aversive tendencies. Fatalistic perspectives and risk of addiction however were not reported as barriers in this group. Key facilitators included improvement in quality of life after commencing opioids, a strong trusting relationship with the health professional who recommended opioids, and having realistic expectations regarding symptom improvement. Participants did not feel that written supporting information helped them in accepting opioids, choosing instead face to face communication with trusted healthcare professionals.

**Conclusion:** Many barriers to accepting opioid therapy for refractory breathlessness persist even amongst patients with active and previous prescriptions. Services focused on building strong relationships, continuity, and coordinated care through a multi-professional patient-centred approach are important facilitators to enable safe and effective prescribing.

**Key Words:** *Breathlessness, chronic obstructive pulmonary disease, opioids, perceptions.*

**Nomination for New Investigator Award**

**Grant Support:** n/a

TO 034

TO 035

### BURDEN, AETIOLOGY AND CHARACTERISTICS OF RESPIRATORY PATHOGENS IN PRETERM INFANTS

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**Background:** There is little understanding of the aetiology and burden of acute respiratory illnesses (ARI) in preterm infants.

**Aim:** To describe the epidemiology, clinical characteristics and burden of respiratory pathogens in preterm infants living in the community.

**Methods:** Very preterm infants (<32 w gestation) were followed prospectively for 12 months after neonatal discharge. ARI were identified using symptom diaries, phone calls and monthly respiratory questionnaires. ARI were classified into upper respiratory tract infections (URTI) or lower (LRTI), with and without wheeze. Nasal swabs were collected by parents each month and during ARI. Real-time PCR was used to detect 16 respiratory viruses, 7 bacterial species and a fungus. Frequencies were compared using Chi-square test.

**Results:** 543 swabs were analysed from 84 infants who completed the one-year follow-up. Respiratory viruses were detected in 234/380 (61.6%) ARI and 36/163 (22.1%) asymptomatic swabs. Virus and viral-bacterial codetections were more common in ARI compared to asymptomatic swabs (32 (8.4%) vs. 2 (1.2%);  $P = 0.002$ ) and (161 (42.4%) vs 26 (15.9%);  $P < 0.001$ ), respectively. Rhinoviruses were the most frequently identified virus during ARI (52.2% URTI, 23.9% non-wheezy LRTI and 43.1% wheezy LRTI). *Haemophilus influenzae* and viral-bacterial codetection were more commonly identified during wheezy compared to non-wheezy LRTI (31.9% vs. 18.3%;  $P = 0.025$ ) and (51.9% vs. 24.4%;  $P < 0.001$ ), respectively. RSV was only identified in 4.21% of ARI. However, RSV was more frequent in infants who had LRTI versus URTI (6.2% vs. 0.7%;  $P = 0.011$ ) and in those who presented to a hospital emergency department or were hospitalized compared to those managed at home (20.6% or 17.4% vs. 1.0%;  $P = 0.011$  and 0.002, respectively).

**Conclusion:** Preterm infants experience a significant burden of respiratory pathogens in early life. Given the limited knowledge of the long-term implications on respiratory health and the lack of effective preventative measures available, more research in this field is warranted.

**Grant Support:** National Health and Medical Research Council (NHMRC) Fellowship [APP1073301], NHMRC Preterm Infants Centre of Research Excellence [APP1057514], NHMRC [APP1047689], Wesfarmers Centre of Vaccine and Infectious Diseases (Seed funding) and The Custodian of The Two Holy Mosques' Overseas Scholarship Program, Ministry of Education, Saudi Arabia.

### PERFORMANCE OF GENEXPERT PCR ON POOLED SPUTUM VERSUS SMEAR MICROSCOPY IN TUBERCULOSIS.

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**Introduction/Aim:** The diagnostic performance of GeneXpert MTB/RIF<sup>®</sup> on combined sputum samples has not been systematically assessed in patients hospitalised with presumptive mycobacterium tuberculosis (TB). We aim to assess the diagnostic accuracy of a single GeneXpert MTB/RIF<sup>®</sup> test performed on two combined sputa versus smear microscopy performed on three separate sputum samples, using sputum culture as the reference standard.

**Methods:** We assessed all adult patients admitted to Blacktown Hospital between July 2017 and January 2018 with presumptive pulmonary TB. The presence of acid fast bacilli (AFB) in expectorated sputum samples, collected on three separate days, was assessed using auramine staining and microscopy. For GeneXpert MTB/RIF<sup>®</sup> testing we combined 0.5mL from each of the first two sputa. The same Sputa were also cultured in liquid medium (MGIT; Becton-Dickinson) for 8 weeks. The diagnostic accuracy, time in isolation, duration of hospital admission and final diagnosis were recorded.

**Results:** Forty patients met the inclusion criteria and 37 (92.5%) consented to study participation; 7 were excluded due to insufficient samples. Of 30 eligible patients, 4 (13.3%) had culture-confirmed pulmonary TB. Of the non-tuberculosis patients; 13 had pneumonia, 3 had non-tuberculous mycobacterium, 4 had TB in other sites and 6 had other pathology. GeneXpert MTB/RIF<sup>®</sup> detected 3 of 4 (75%) cases with 100% specificity, while smear microscopy was positive in only 2 of 4 cases (50%) with 95.5% specificity. The average time in respiratory isolation was 10.9 days and the average length of hospital stay was 12.5 days.

**Conclusion:** A single GeneXpert MTB/RIF<sup>®</sup> test on pooled sputum had negative predictive value (NPV) and positive predictive value (PPV) of 96% and 100% respectively. This reflects improved diagnostic yield and accuracy compared to standard smear microscopy with NPV of 93% and PPV of 67%. We postulate this could translate into cost savings for the health system.

**16S RRNA GENE-SEQUENCING IMPROVES MICROBIAL DIAGNOSIS OF INFECTIVE PLEURAL EFFUSIONS**

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**Introduction/Aim:** Pleural-space infections are treated with long-term antibiotics; however pleural fluid cultures often do not identify a causative organism. We assessed the utility of 16S rRNA gene sequencing of pleural fluid specimens for increasing the diagnostic yield of a causative pathogen.

**Methods:** A case-control study design was conducted at two tertiary hospitals between June 2017 and September 2018. We identified cases (16S requested) and controls (no 16S) at random from inpatients that required thoracentesis to investigate para-pneumonic pleural effusion with possible empyema. The decision to perform 16S rRNA gene sequencing was clinician-dependent. All patients had pleural fluid sent for culture. We compared the rate of microbial diagnosis between the two groups using Fisher's exact test with *P* < 0.05 considered significant.

**Results:** Of 18 patients in total, the 16S group had a significantly higher yield of pathogen detection at 89% (8/9) compared to the group without 16S testing 18% (2/9) with *P* = 0.015. The 16S group identified 7 bacterial organisms that were not cultured from the pleural specimens but are known to cause empyema. There were only 2 potentially pathogenic bacteria isolated using culture-based techniques. The mean hospital length of stay was lower in the 16S group, however it is unclear if this was related the positive identification of a causative pathogenic organism.

Table 1. No 16S group (culture only) vs. 16S group comparison data

	16S requested	No 16S requested	Microbes isolated
Exudate	9/9	9/9	16S group:
pH < 7.2	5/9	3/9	1-Prevotella spp
Mean LOS (days)	16.5	21.7	1-porphyrromonas gingivalis
Microbial isolation	8/9 (89%)	2/9 (18%)	1-mycobacterium morioakaense
True-positive	7/9 (unclear clinical significance of 1 result)	0/9 (based on suspected contamination)	1-fusobacterium spp
Final diagnoses	1/9 culture/ PCR-negative TB 1/9 lymphoma with unclear significance of mycobacterium morioakaense 7/9 16S+ parapneumonic effusions/ empyema	2/9 MTB with pleural disease 2/9 likely malignant effusions with pneumonia 5/9 culture-negative parapneumonic effusions/ empyema	1-streptococcus pneumoniae 1-streptococcus intermedius 2-mixed species (no further processing done) Culture group: 1-coagulase negative staphylococcus 1-propionobacterium acnes

**Conclusion:** The use of 16S rRNA sequencing significantly increased the diagnostic yield of para-pneumonic effusions with possible empyema compared to culture only techniques. Many of the organisms identified by 16S were anaerobic bacteria, which are difficult to grow in culture medium. The administration of antibiotics prior to pleural fluid sampling may also reduce the yield of pleural cultures. 16S rRNA testing on pleural fluid specimens may assist with the management of patients with suspected empyema.

**Grant Support:** Nil

**Conflicts of interest:** nil

**FIVE-YEAR IMPACT OF A TARGETED SCREENING PROGRAM FOR LATENT TUBERCULOSIS INFECTION IN A HIGH-RISK POPULATION**

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**Introduction/Aim:** A majority of tuberculosis cases in Australia are generated from the progression of latent tuberculosis infection (LTBI) acquired prior to migration in overseas-born individuals. Studies that have assessed the impact of school-based screening programs for LTBI in low-prevalence settings have generally screened children and young adults irrespective of individual risk profile. The objective of this study was to evaluate a targeted school-based screening program for LTBI amongst recently arrived migrants from high prevalence countries, identify factors predicting treatment uptake and completion, and perform a cost effectiveness analysis.

**Methods:** A retrospective review of prospectively collected data was performed. Screening is offered to newly arrived students from high-risk countries at participating South Australian schools. Individuals with tuberculin skin test (TST) ≥ 10 mm are automatically referred for CXR, medical review, and consideration of Isoniazid preventative therapy (IPT). Screening records from January 2013 to December 2017 were analysed. Treatment outcomes were extracted from electronic records and case notes. Cost data was collated from multiple administrative sources.

**Results:** 4736 students received a TST, of which 846 tests were positive (17.9%). 2 cases of active pulmonary tuberculosis were identified. 135 (16%) of the students referred for medical assessment completed a course of preventative therapy. A further 91 students (10.7%) commenced IPT but completed only partial courses or were transferred to another jurisdiction. Based on a 10% lifetime risk of reactivation, we estimate 13.5 notifications were avoided over a 5 year screening period, facilitating an estimated cost avoidance of \$155,736 AUD. Estimated expenditure on the program over the same period was \$102,276 AUD.

**Conclusion:** This targeted screening program facilitates access to screening for LTBI in a population at high risk of reactivation, and appears to be cost effective. Factors limiting adherence to preventative treatment, and refusal of screening participation require further investigation, and represent an opportunity to strengthen such programs.

**Grant Support:** Nil



TO 038

**MANAGEMENT OF ISONIAZID MONO-RESISTANT TUBERCULOSIS IN QUEENSLAND, AUSTRALIA: A RETROSPECTIVE CASE SERIES**

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**Introduction/Aim:** Amongst newly diagnosed cases worldwide, isoniazid-resistant/rifampicin-susceptible tuberculosis (HR-TB) is twice as common as multidrug- or rifampicin-resistant disease (MDR/RR-TB). HR-TB is associated with poorer outcomes with little high-quality evidence to guide consensus regarding treatment. The World Health Organisation (WHO) recently updated their guidelines – now recommending treatment with levofloxacin, rifampicin, ethambutol and pyrazinamide for six months. Data on resistance to second-line agents such as levofloxacin, however, are less well defined. Population studies suggest rates may be as high as 12.4% in countries where fluoroquinolones are prescribed more freely for pulmonary infection. We sought to define the frequency and treatment outcomes for HR-TB in Queensland with respect to patient and regimen factors in order to determine whether the new WHO guidelines should alter treatment in settings with well-resourced programmatic management with first-line agents.

**Methods:** Retrospective case series of all HR-TB cases notified in Queensland between 1 January 2000 and 31 December 2017. Basic demographic information, phenotypic and genotypic drug susceptibility as well as treatment regimen, duration and outcome were all recorded.

**Results:** demographic and outcome data are summarised in the table below.

Parameter	Overall (n=198)	OR (95% CI)	P-value
Age (years ± SD)	40.8 ± 19.2	1.02 (0.97-1.07)	0.43
Male gender (n, %)	103 (52.0)		
High-burden country of birth (n, %)	141 (71.2)		NS
<b>Site of disease</b>			
• Pulmonary (n, %)	136 (68.7)		NS
• Extra-pulmonary (n, %)	65 (32.8)		NS
• Disseminated/Miliary (n, %)	13 (6.6)	5.8 (0.72-35)	0.063
Sputum smear positive (n, %)	73 (41.2)		NS
HIV co-infection (n, %)	8 (4.0)	5.7 (0.26-49)	0.15
<b>Case type</b>			
• New (n, %)	181 (91.4)		NS
• Previously treated (n, %)	17 (8.6)	16.22 (2.68-29.76)	0.0017
High-level isoniazid resistance (n, %)	91 (46.0)		NS
Duration of treatment (weeks ± SD)	46.0 ± 17.5	1.16 (1.08-1.24)	0.0003
<b>Drug regimen</b>			
• First-line agents only (n, %)	148 (78.7)		NS
• Containing ≥6mths fluoroquinolone (n, %)	19 (10.1)		NS

**Frequency of treatment**

• Daily (n, %)	167 (88.8)	NS
• Intermittent (n, %)	21 (11.2)	NS

**Outcomes**

• Favourable (n, %)	155 (96.3)	
• Unfavourable (n, %)	6 (3.7)	

**Conclusion:** HR-TB affected 7.2% (198/2766) of all tuberculosis notifications in Queensland. Where assessable, favourable treatment outcomes were achieved in 96% (155/161) of cases. A favourable outcome was more likely with increased treatment duration. Previous treatment was associated with an unfavourable outcome. Importantly, there was no significant difference in treatment outcomes between drug regimens containing a fluoroquinolone or first-line agents only. We therefore conclude that the new WHO guidelines may not be expected to improve HR-TB treatment outcomes in a well-resourced setting such as Queensland. In this regard, avoidance of fluoroquinolone exposure may in fact help protect these agents for use in more extensively resistant disease.

**Grant Support:** none.

TO 039

TO 040

### POTABLE WATER AS A POSSIBLE SOURCE OF MYCOBACTERIUM ABSCESSUS INFECTION IN PEOPLE WITH CHRONIC LUNG CONDITIONS

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**Introduction/Aim:** *Mycobacterium abscessus* group (MABS) are emerging respiratory pathogens in people with underlying lung conditions. The acquisition and transmission of MABS infection is poorly understood. MABS has been detected in drinking water distribution systems (Thomson *et al*, BMC Infect Dis, 2013; Morimoto *et al*, ERJ Open Res, 2018). We aimed to determine the role of potable water in the acquisition and transmission of MABS respiratory infection.

**Methods:** A total of 241 MABS respiratory isolates from 90 participants with chronic lung conditions (including cystic fibrosis and bronchiectasis) stored at Queensland Mycobacterium Reference Laboratory from 2000-2017 were compared with MABS isolates recovered from potable water sampling (n=52). The whole genome sequences of the clinical and environmental isolates were compared to determine their relatedness using published definitions (Bryant *et al*, Science, 2016).

**Results:** Certain clinical and environmental isolates were closely related. Respiratory MABS isolates from unrelated people with chronic lung conditions were closely related to potable water MABS isolates suggesting a possible point source outbreak in the local water supply. Probable transmission events (<20 SNP) were observed in two people with CF and active MABS respiratory infection (<2 years since positive sputum culture) whose homes had MABS detected in the water. The home water MABS isolates when compared to the home occupier's respiratory isolate(s) were separated by a maximum of 1 SNP and 17 SNPs, respectively. The direction of infection, patient-to-environment or environment-to-patient, could not be inferred.

**Conclusion:** The environment is a likely source of MABS. Wider environmental sampling, combined with extended sequencing comparisons with clinical (including extra-pulmonary) MABS isolates, is required to determine the role of the environment (particularly direction of transmission) in the spread of MABS pulmonary and extra-pulmonary infection.

**Grant Support:** CF Foundation Therapeutics (US), The Prince Charles Hospital Foundation, Advance Queensland, NHMRC (APP1102494).

### CLINICAL RESPONSE TO MEPOLIZUMAB IN PATIENTS WITH SEVERE EOSINOPHILIC ASTHMA

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**Aim:** To describe the patient characteristics and response to mepolizumab, a monoclonal anti-interleukin 5 antibody for the treatment of severe eosinophilic asthma.

**Methods:** The AMR, a multi-centre post-marketing surveillance registry was established. Patients prescribed PBS-subsidised mepolizumab were characterised at baseline and after treatment. Asthma control (ACQ5) and quality of life (Juniper AQLQ) were assessed. Responders had a reduction in ACQ5 score of at least 0.5 or reduction in maintenance oral corticosteroid (OCS) dose.

**Results:** Between January 2017 and June 2018, 212 registered patients commenced mepolizumab. Patients were a median(Q1,Q3) age of 60(49,68) years and 54% were female. 62% were never-smokers, 46% were obese and 63% were atopic. Asthma duration was median (Q1,Q3) 26(13,43) years and 48% of patients were taking maintenance OCS. During the 12 months prior, they had required a median (Q1,Q3) of 3(2,6) OCS courses and 28% had been hospitalised for exacerbations.

After 3-5 months of mepolizumab treatment, median(Q1,Q3) peripheral blood eosinophils (PBE) reduced from 0.6(0.4,0.8) to 0.1(0.02,0.1) x10<sup>9</sup>/L, mean post-bronchodilator FEV1% predicted improved from 60.8 ± 19.4 (SD) to 65.7 ± 22.7, quality of life improved from median(Q1,Q3) AQLQ score 3.7(2.9,4.7) to 5.1(4.3,6.1) and mean ACQ5 score reduced from 3.54 ± 0.90V (SD) to 1.79 ± 1.13 (all *P* < 0.0001).

At 6-8 months post-commencement (n = 120 assessable), 106 patients were classified as responders, 14 had ceased mepolizumab [adverse drug reaction (n = 3), failed ACQ response (n = 7), other reason (n = 4)], and 92 were awaiting assessment. However, 53% of patients still had an ACQ5 score of at least 1.5 at this time-point.

Compared to the MENSA trial patients (1), the AMR group were older, with worse asthma control, higher PBE, and greater ACQ response to mepolizumab treatment.

**Conclusions:** Patients with severe eosinophilic asthma in Australia have a very significant and long-standing disease burden. Targeted anti-IL-5 treatment effectively reduced disease burden in these patients. Despite improvement, more than half remain uncontrolled, highlighting the need for further intervention in these patients.

#### References

- Ortega *et al*, NEJM, 371, 2014, 1198-1207.

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### LATE DISCONTINUATION OF OMALIZUMAB IN SEVERE ASTHMA

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**Introduction:** Anecdotal observation suggests there is a group of patients with severe asthma who, despite an adequate initial response to omalizumab, later stop responding and whose symptoms relapse (late treatment failure).

**Aim:** Identify and characterise patients who initially received approval from the Pharmaceutical Benefits Scheme (PBS) for continuation of omalizumab treatment at 6 months, but who subsequently discontinued omalizumab treatment, who may have been discontinued due to late treatment failure.

**Method:** Patients prescribed omalizumab were identified in the Severe Asthma Web-based Database (SAWD). These were characterised as patients who either discontinued treatment after an initial continuation at six months or those whose treatment was ongoing. The reasons for discontinuation were not recorded in the database.

**Results:** A total of 98 patients were included. Twelve patients (12.2%) were identified discontinuing after being initially continued. The absolute change in FEV1 following administration of bronchodilator was significantly higher in the late discontinuation group (520 mL  $\pm$  194.9 mL vs 333 mL  $\pm$  181.8,  $P = 0.024$ ). However, the difference in pre-bronchodilator FEV1 and percentage change post bronchodilator was not statistically significant. Age, weight, BMI, spirometry, bronchodilator response, IgE, blood eosinophils, asthma control (as assessed by the six item asthma control questionnaire score - ACQ6), age of asthma diagnosis, smoking history, atopic disease, asthma triggers and exacerbation history were not significantly different between the groups.

**Conclusion:** In our cohort of patients, there was a significant minority of patients where omalizumab was discontinued after an apparent initial clinical improvement. Aside from showing a greater degree of bronchodilator responsiveness, this group of late treatment failures were indistinguishable from the wider group of persistent treatment responders. The larger magnitude of bronchodilator response may be a marker of poor asthma control not captured by the ACQ. Further studies are required to define the incidence and possible contributors to the late treatment failure in omalizumab-treated patients.

### SERUM PREDNISOLONE LEVELS AS A MARKER OF ADHERENCE IN SEVERE ASTHMA

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**Introduction/Aim:** Precision medicine and treatable traits are promising tools to improve care for patients with severe asthma. Corticosteroid refractory (CR) eosinophilic asthma is an indication for monoclonal antibody therapy against IL-5. Non-adherence (NA) to prednisolone treatment, however, is likely to account for a proportion of this population. Thus, the ability to distinguish CR from NA has important treatment implications. In this project, we sought to determine if serum prednisolone levels could be used as a marker to help distinguish these two groups of participants.

**Methods:** Participants with severe asthma on a stable regular daily dose of prednisolone were surveyed about their adherence to their medications, the time of their last known dose, and a blood sample and induced sputum sample were taken. The blood sample was analysed for prednisolone and cortisol levels, and a cell count and differential was performed on the sputum.

**Results:** We surveyed 16 participants on a median of 7.5 mg prednisolone daily. Two participants were excluded because they either intentionally did not take their prednisolone in the last 24 hours prior to assessment or were on hydrocortisone. In the remaining 14, three had low serum prednisolone measurements. One of these participants reported non-adherence, with demonstrated ongoing sputum eosinophilia >3%. The other two had no evidence of sputum eosinophilia. Six likely adherent participants with sputum eosinophilia >3% had measurable levels of serum prednisolone ranging from 70-147 g/L. This cohort comprising 45% of the participants with severe asthma assessed are likely truly CR.

**Conclusion:** The use of serum prednisolone levels differentiates patients into those with CR asthma and those that are non-adherent. This will allow an objective means of identifying those with CR disease. It may be utilised to assess eligibility for more expensive add on therapies and allow counselling for those non-adherent with treatment.

Table 1: Number of participants with low vs measurable levels of prednisolone in serum compared to their sputum eosinophil counts.

	Low prednisolone	Measurable prednisolone	Total
Sputum eos $\leq$ 3%	2	5	7
Sputum eos >3%	1	6 (SR)	7
Total	3	11	14

**EFFICACY OF AZITHROMYCIN IN SEVERE ASTHMA**

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**Introduction/Aim:** Low dose azithromycin (AZM) is effective therapy for persistent asthma, however its benefit in severe asthma is not defined. Our objective was to describe the effect of azithromycin on asthma exacerbations and quality of life in severe asthmatics who were defined using various criteria.

**Methods:** Participants with severe asthma were identified from the AMAZES randomized placebo-controlled trial of long-term (48 weeks) low dose azithromycin. Participants who met one of the following severe asthma definitions: 1) GINA step 4 treatment with poor asthma control (ACQ score  $\geq 0.75$ ),  $n = 344$ ; 2) International Severe Asthma Registry (ISAR) definition,  $n=357$ ; 3) ATS/ERS severe asthma criteria ( $n = 211$ ) were included. The rate of total exacerbations was calculated for each subgroup and the efficacy of azithromycin compared to placebo. Asthma-related quality of life was assessed by validated questionnaire before and after treatment and adverse effects assessed.

**Results:** Azithromycin significantly reduced asthma exacerbations in each of the severe asthma groups. In ATS/ERS-defined severe asthma, the rate of asthma exacerbations with azithromycin treatment was 1.2/person-year, which was significantly less than for placebo (2.01/person-year), giving an incidence rate ratio (95% confidence interval) of 0.63 (0.41, 0.96). The proportion of participants experiencing at least one asthma exacerbation during treatment was reduced by azithromycin from 64% to 49% ( $P = 0.021$ ). A similar beneficial treatment effect was seen in participants who were poorly controlled with GINA step 4 treatment and those with ISAR-defined severe asthma. AZM also significantly improved quality of life in severe asthma ( $P < 0.05$ ). The treatment was well tolerated, with gastrointestinal symptoms the main adverse effect.

**Conclusion:** Long term low dose azithromycin reduced asthma exacerbations and improved quality of life in patients with severe asthma, regardless of how this was defined. These data support the addition of AZM as a treatment option for patients with severe asthma.

**Grant Support:** Work was supported by the NHMRC. PGG holds an NHMRC practitioner fellowship.

**WHAT SEVERE ASTHMA TREATMENT OUTCOMES MATTER TO PATIENTS?**

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**Introduction/Aim:** There is an increasing number of new therapies for severe asthma. The factors that determine medication choice are not known. This study sought to gain an understanding of what features are important to patients in their choice of asthma treatment.

**Methods:** Difficult-to-treat and treatment-refractory severe asthma participants ( $n=24$ ) from a severe asthma clinic completed a cross-sectional questionnaire involving hypothetical scenarios relating to medication choices for four add-on asthma treatments. Participants were asked to rank factors of importance against each other, as well as identify and rank asthma treatment outcomes of importance a seven-point Likert scale (0-6).

**Results:** Participants were predominately male (58.3%), with a mean (SD) age of 62.4 (13.2) years. They experienced 4.1 (2.4) exacerbations in the past year. Of the factors (asthma outcomes; cost; side-effects; mode-of-delivery) that informed choice of new treatments, the highest ranked factor was asthma outcomes (improved control, reduced steroids, fewer attacks, better quality-of-life) at 91.7%, followed by the side-effect profile (8.3%). Cost and mode-of-delivery (injection versus puffer) were not considered to be primary choice-drivers. From 17 possible treatment outcomes, participants ranked those that were most important to them. The top five treatment outcomes were: "to improve quality-of-life" 5.8 (0.5), "to be more physically active" 5.7 (0.7), "to reduce oral corticosteroid" 5.7 (1.1), "to reduce number and severity of asthma attacks", 5.6 (1.3) and "to be less breathless", 5.4 (1.2). When asked to rank these outcomes against each other, 63% of participants nominated "improve quality-of-life", 50% nominated "reduce number and severity of asthma attacks", and 37.5% nominated "reduce oral corticosteroids" in their top two priorities.

**Conclusion:** People with severe asthma value improved quality-of-life, increasing physical activity, reducing attacks and reducing oral corticosteroids as the most important outcomes they want from new treatments. These data can inform patient-centred care in the use of new asthma treatments.

**Grant Support:** N/A

TO 045

TO 046

### BENRALIZUMAB IMPROVES SMALL AIRWAY FUNCTION RAPIDLY IN PATIENTS WITH SEVERE EOSINOPHILIC ASTHMA

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**Introduction/Aim:** Benralizumab, an anti-interleukin 5 receptor  $\alpha$  monoclonal antibody, was recently approved in Australia for the treatment of severe eosinophilic asthma (SEA). Small airway function is abnormal in severe asthma contributing to the symptom burden. The effect of benralizumab on small airway function has not been described. We sought to describe changes in ventilation heterogeneity, a marker of small airway function, in patients commencing benralizumab.

**Method:** All patients with SEA despite high-dose inhaled corticosteroids/long-acting  $\beta$ 2-agonists had the following measurements at baseline (week0) and one month after commencing benralizumab (week4): 5-item Asthma Control Questionnaire (ACQ-5), spirometry, and multiple breath nitrogen washout to derive measures of ventilation heterogeneity in the conducting airways ( $S_{\text{cond}}$ ) and more distal acinar airways ( $S_{\text{acin}}$ ). All other asthma treatment was unchanged. Paired t-test and Pearson's correlations were performed.

**Results:** To date, 10 patients (6 males), mean  $\pm$  SD age  $53 \pm 23$  yrs, BMI  $27 \pm 5.2$  kg/m<sup>2</sup>, eosinophil count  $0.9 \pm 0.4 \times 10^9/L$ , FEV<sub>1</sub>  $51 \pm 15$  %predicted, FEV<sub>1</sub>/FVC ratio  $50 \pm 12$ %. At week 4, eosinophil count was undetectable and ACQ-5 improved significantly ( $2.4 \pm 0.76$  to  $1.16 \pm 0.76$ ,  $P = 0.001$ ). There was a significant improvement in  $S_{\text{cond}}$  ( $0.065 \pm 0.024$  to  $0.053 \pm 0.022$ ,  $P = 0.002$ ) and a trend for improvement in  $S_{\text{acin}}$  ( $0.312 \pm 0.184$  to  $0.240 \pm 0.163$ ,  $P = 0.06$ ) and FEV<sub>1</sub> ( $1.85 \pm 0.65$  to  $2.15 \pm 0.76L/s$ ,  $P = 0.08$ ). The change in ACQ-5 correlated only with the change in  $S_{\text{acin}}$  ( $r = 0.66$   $P = 0.04$ ).

**Conclusion:** In this preliminary analysis, benralizumab significantly and rapidly improved symptom control after 4 weeks. The improvement in small airway function correlated with improved symptoms.

**Key Words:** MBNW, ACQ, benralizumab, eosinophilic Asthma, ventilation heterogeneity

**Grant Support:** N/A

### HOST DEFENCE PEPTIDE AS AN INNOVATIVE NOVEL THERAPY FOR PSEUDOMONAS AERUGINOSA BIOFILM INFECTIONS IN THE CYSTIC FIBROSIS LUNG

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**Introduction/Aim:** *Pseudomonas aeruginosa* biofilm colonization is associated with declining lung function in cystic fibrosis (CF) patients. Biofilm formation is typically resistant to antibiotics and no effective therapy has been developed yet for their treatment. Interest in host defence peptides (HDPs) has grown due to their potential therapeutic applications and their possible use against biofilm. Here, novel short, synthetic cationic peptides were tested for their anti-biofilm effectiveness as well as their ability to inhibit and disperse *P. aeruginosa* biofilms.

**Method:** Clinical isolates ( $n=30$ ) of *P. aeruginosa* from CF patients were used to screen and evaluate a 17 novel anti-biofilm peptide candidate's activity (MIC/MBEC) in a high-throughput plate-based procedure, followed by confocal microscopy using live/dead bacteria staining. Their ability to inhibit and disperse the bacterial biofilms in human primary airway epithelial cell cultures derived from the CF children were assessed using an air-liquid interface (ALI) cell culture biofilm model and GFP tag bacteria.

**Results:** Six (HDP- 25,26,43,101,102,103) candidates were found to exhibit anti-microbial, anti-attachment and anti-biofilm activity at 8-16  $\mu\text{g/mL}$  compared with current conventional antibiotics (Amikacin 128-512  $\mu\text{g/mL}$ / Tobramycin 128-1024  $\mu\text{g/mL}$ / Ciprofloxacin 128-512  $\mu\text{g/mL}$ ). Of these, HDP 25, 26 and 102 were the most potent, resulting in >97% bio-volume reduction followed by induced disruption of the mature biofilms (ALI cultures), significant colony death (88-94%), 71% reduction in the production of the key chronic virulent factor pyocyanin, and 74% reduction of bacterial attachment to airway epithelial cells.

**Conclusion:** These findings highlight the potential of novel peptides as a new group of antimicrobial weapons for target and breaking down the biofilms associated with airway epithelium.

TO 047

TO 048

**E-CIGARETTES MAY PLAY A ROLE IN GLUCOCORTICOID RESISTANCE IN ASTHMATICS AS WELL AS DECREASING FLAVOUR AND COIL TEMPERATURE DEPENDENT PHAGOCYTOSIS OF BACTERIA**

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**Introduction/Aim:** A wealth of data now shows that E-cigarettes are likely to cause harm to the lungs of healthy non-smokers. However, little is known about the risks of E-cig use in groups with lung diseases such as asthma. Cigarette smoke has been shown to reduce alveolar macrophage phagocytic ability and cause glucocorticoid resistance via reduction of HDAC-2. We previously published that vapour extract (EVE) of 2<sup>nd</sup> generation E-cig caused a reduction in the phagocytic capacity of THP-1 macrophages. We investigated whether HDAC-2 was decreased in macrophages exposed to EVE and whether asthmatic alveolar macrophages (AM) had reduced phagocytic function after exposure to EVE. As 3<sup>rd</sup> generation devices allow for selection of temperature of the coil, we investigated whether these effects were flavour or coil temperature dependent.

**Methods:** THP-1 macrophages and AM from healthy or asthmatic volunteers were exposed to EVE from flavoured E-liquids (up to 10), nicotine, or E-liquid bases VG or PG. Phagocytosis of pHrodo-labelled NTHi and HDAC-2 expression were measured by flow cytometry and/or western blot.

**Results:** Healthy AM showed a flavour-dependent decrease in phagocytosis (as low as 2.9% vs 20.3% for control) as well as HDAC-2 (as low as 6.4% vs 41.2% for control). Preliminary data from asthmatic patients showed a decrease in phagocytosis and HDAC-2 in response to EVE. When EVE from the 3<sup>rd</sup> gen E-cig was assessed on THP-1 cells, we observed a decrease in phagocytosis enhanced by higher coil temperature for flavoured EVE, but not for nicotine.

**Conclusion:** E-cigarette vapour can reduce the phagocytic function of healthy and asthmatic AM and may affect glucocorticoid sensitivity by causing a reduction in HDAC-2. Furthermore, newer generations of E-cigs with a temperature mod may be more harmful to the lungs when higher temperatures are used.

**Grant Support:** Supported by NAC, the RAHRF, and the Rebecca Cooper Foundation.

**ASSESSING CF AIRWAY EPITHELIAL ANTIVIRAL RESPONSES FOLLOWING RHINOVIRAL INFECTION**

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**Introduction/Aim:** There remains conflicting data whether CF airway epithelial cells (AEC) can produce the appropriate IFN response to viral infection. This study investigated transcriptomic innate immune changes, specifically focusing on interferon signalling, in CF AEC infected with rhinovirus (RV).

**Methods:** Primary AECs cultured from 5 healthy (age 3.5 ± 1.4 years; 2 males) and 7 CF (age 2.4 ± 2.3 years; 4 males) children were infected with RV1B (multiplicity of infection: 12). RNA was extracted 24 hours later and sequenced (RNA-seq) by Illumina Hi-Seq2500. Sequence reads were mapped to human reference genome using 'HISAT2' and gene-level quantification (counts) was performed using SummarizeOverlaps. Polymerase chain reaction (PCR) and enzyme-linked immunosorbent assay (ELISA) was performed to corroborate transcriptomic data.

**Results:** Prior to infection, interferon stimulated genes (ISGs) including *BST2*, *GBP2*, *IFI6*, *IFITM1*, *ISG15*, *Mx1*, *AIM2* and *IFI127* were significantly lower (1.5-20 fold; *P* < 0.05) in CF AEC compared to their healthy counterparts. In response to RV, ISGs were significantly induced (7.5-340 fold; *P* < 0.05) in CF AEC compared to (4-119 fold; *P* < 0.05) healthy controls. However, type I and III interferon (*IFNB1*, *IFNL1*, *IFNL2*, *IFNL3*) genes were still lower in CF (34-67 fold; *P* < 0.05) than their healthy counterparts (97-190 fold; *P* < 0.05). Pathway analysis on post-infection samples confirmed type I, II interferon signalling in CF AEC. Network analysis also identified unique key hub genes *HSPA5*, *STAT3* and *TRAF2* regulating CF AEC interferon signalling. Finally, ELISA confirmed lower type I and III interferons including IFNbeta were lower in CF.

**Conclusion:** This data suggests baseline phenotypic differences between CF and healthy AEC in interferon pathways. CF AEC were able to induce type I, II interferon genes in response to RV infection, but this was lower compared to healthy AEC. The identified unique key hub genes that regulate interferon signalling in CF AEC could be of therapeutic interest.

**Grant Support:** NHMRC

TO 049

TO 050

### ELECTRONIC-CIGARETTE VAPING IN COMBINATION WITH A HIGH FAT DIET AUGMENTS LUNG FUNCTION AND INFLAMMATION

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**Introduction/Aim:** The separate effects of electronic-cigarette (eCig) vaping and high fat diet (HFD) on respiratory health has been investigated, however the combination of these two lifestyle choices has yet to be studied. In this study, we used a mouse model to test the hypothesis that e-Cig vaping alongside a high fat diet further induces inflammation and worsens lung function.

**Methods:** Female BALB/c mice on either a regular chow diet or a supplemented high fat diet for 10 weeks were vaped for 6 weeks with eCig ( $\pm$  18mg nicotine) or unexposed at room air (control group). At 16 weeks, lung function measurements were performed 24h after the last eCig exposure using a small animal ventilator (Scireq, Canada) in response to increasing concentration of methacholine (MCh). Airway inflammation was assessed in the bronchoalveolar lavage (BAL) fluid by counting total and differential immune cell influx. Lungs were fixed in formalin (for histological staining) or glutaraldehyde (for electron microscopy). Serum and BAL supernatant were analysed to measure cytokine expression by multiplex analysis.

**Results:** Mice on HFD alone showed no airway hyperresponsiveness (AHR) to MCh; while HFD+eCig (18mg nicotine) exposure lead to increased AHR when compared to chow+eCig(18mg nicotine), HFD+eCig (0mg nicotine) or HFD alone mice. Total immune cell influx in BAL was elevated in both groups exposed to eCig-vapour containing nicotine, with the HFD+eCig18mg group having a significantly greater number of macrophages, neutrophils and lymphocytes ( $P < 0.05$ ). BAL multiplex analysis revealed increased expression of Th2 cytokines IL4 and IL5 and proinflammatory cytokine IFN $\gamma$  in the HFD+eCig 18mg group when compared with other groups.

**Conclusion:** Our study suggests that eCig vaping in conjunction with a high fat diet results in worsened lung function and an altered airway inflammatory profile suggesting caution in people who are overweight and vape.

**Grant Support:** KM is supported by a UTS PhD scholarship, BO is supported by NHMRC funding, PS is supported by Rebecca Cooper Foundation funding.

### MODELLING A BACTERIAL-VIRAL POLYMICROBIAL INFECTION OF THE AIRWAY EPITHELIUM

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**Introduction:** Aetiology involving polymicrobial bacterial-viral pathogens in lower respiratory tract infections are significant but largely ignored. Additionally, their combined pathogenic mechanisms are poorly understood. Using primary airway epithelial cells (AEC) derived from children which were then differentiated by growing at the Air-Liquid Interface (ALI), we infected/inoculated Respiratory Syncytial Virus (RSV) and non-typeable *Haemophilus influenzae* (NTHi) to assess the interaction between viral infection, NTHi biofilm and AEC. We characterised this complex interaction through various functional, immunological, bacterial and viral endpoints. We hypothesised that an interaction occurs between RSV and NTHi manifested by enhanced formation of biofilms following viral infection, and release of planktonic NTHi from established biofilms following introduction of RSV.

**Methods:** Red fluorescent-tagged RSV (A2 strain, rrRSV-BN1,  $1 \times 10^6$  pfu) and green fluorescent-tagged NTHi (86-028 NP,  $2.5 \times 10^7$  CFU) were either inoculated individually, concurrently or sequentially onto fully differentiated AEC grown on Transwell inserts (Corning). Cultures were incubated for 7 days. Insert surfaces were fixed, excised, mounted and overlaid with coverslips. Five confocal microscopy field-of-views at 200x magnification were obtained (Nikon C2+ system). 3-dimensional images of the epithelium were reconstructed using NIS-Elements Imaging Software (Nikon). Biophysical properties of NTHi biofilms established on AEC apical surfaces were characterised by its thickness, surface area, biomass and surface area to biomass ratio, determined using the COMSTAT program.

**Results:** No red fluorescence arising from RSV infection and replication were detected in epithelial cells pre-colonised by NTHi. However, when infected earlier with RSV, NTHi were able to colonise and form biofilms on epithelial cells. Multiplex immunoassay of apical washes and basal media of inserts revealed a Th1 cytokine response by the AECs.

**Conclusion:** Prior NTHi colonisation of respiratory epithelium appears to shield against a secondary RSV infection, but not *vice versa*.

**Grant Support:** Wesfarmers Centre of Vaccines and Infectious Diseases PhD Top-Up Scholarship.

TO 051

TO 052

### EFFECT OF CONSECUTIVE RHINOVIRUS INFECTION ON BARRIER INTEGRITY AND FUNCTION

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**Introduction/Aim:** Tight junctions (TJ) provide a physical barrier against respiratory viral insults. Human rhinovirus (RV) has been shown to disrupt barrier integrity in airway epithelial cells (AECs). Despite TJs being extensively assessed, few studies have directly addressed the consequence on barrier integrity following TJ disassembly post consecutive RV infection. Furthermore, both phosphatase-tensin homolog (PTEN) and epidermal growth factor receptor (EGFR) have been associated with the regulation of AEC antiviral responses and have been previously demonstrated to be implicated with barrier integrity during RV infection (Looi *et al* 2016). Hence, this study aimed to assess barrier integrity post three consecutive RV infection in healthy and asthmatic AEC cultures.

**Methods:** Healthy and asthmatic AECs, obtained and cultured as previously described (Martinovich *et al* 2017) were differentiated into air-liquid interface (ALI) cultures before infection with RV-1B. Consecutive RV-1B infection every 24h at a multiplicity of infection (MOI) of 1 was performed on submerged and differentiated cultures. Barrier integrity was measured by in-cell western (ICW) protein expression of the TJ proteins claudin-1, occludin and zonula occluden-1 (ZO-1). Cytosolic expression of PTEN and membrane expression of EGFR was similarly assessed. Epithelial function was assessed via transepithelial electrical resistance (R<sub>T</sub>) measurement and a permeability assay.

**Results:** Healthy AECs showed a decrease in TJ protein expression of claudin-1 compared to uninfected controls after the first infection. Further decreases in expression were observed after the second infection, however, after the third infection, there was a significant increase in TJ expression ( $P < 0.05$ ). Increases in occludin, ZO-1, PTEN and EGFR protein expression was observed with each consecutive RV-1B infection. Preliminary data demonstrated concomitant decrease in R<sub>T</sub> and increase in permeability with consecutive infection.

**Conclusion:** Consecutive infections with RV-1B induces increasing changes to epithelial junctional proteins and altering barrier integrity. Indicates the possible role of PTEN and EGFR in epithelial barrier integrity.

**Grant Support:** TSANZ AstraZeneca Respiratory Research Fellowship

### ASSOCIATION BETWEEN INHALED CORTICOSTEROID THERAPY FOR COPD AND DIABETES ONSET AND PROGRESSION

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**Introduction:** Prior evidence suggests inhaled corticosteroid (ICS) therapy for COPD increases risk of type 2 diabetes (T2D). Currently, ICS is recommended only for patients with frequent COPD exacerbations despite optimal bronchodilator therapy. This study aimed to evaluate whether maintenance ICS therapy is associated with increased diabetes onset or progression.

**Methods:** This matched cohort study used de-identified data between 1990–2016 from two large UK general practice databases for patients aged  $\geq 40$  years initiating ICS or long-acting bronchodilators for COPD with  $\geq 1$ -year baseline and  $\geq 1.5$ -year outcome data. Patients had no prior diabetes (onset cohort; N=17,970) or already had T2D (progression cohort; N=804). After mixed matching (1:1–3:1 ratios) using direct matching and a propensity score, treatment groups were compared using stratified proportional hazards regression, adjusting for residual confounding.

**Results:** The onset cohort had median follow-up of 5 and 4 years in ICS and non-ICS groups, respectively. The progression cohort had median follow-up of 3 years in both groups. Risk of diabetes onset (diagnosis/therapy initiation) significantly increased with ICS therapy and showed a dose response (Table). Risk of diabetes progression (added or higher dose anti-diabetic medication) significantly increased at ICS doses  $\geq 500$   $\mu\text{g}/\text{day}$ .

**Conclusion:** Long-term, high-dose ICS therapy for COPD is associated with an increased risk of diabetes onset and progression.

**Grant Support:** This study was funded by Novartis Pharma AG, Basel, Switzerland

**Disclosure:** Dr. Konstantinos Kostikas was an employee of Novartis at the time of submission of the abstract.

Table: Risk of type 2 diabetes onset and progression in ICS-treated patients

Cohort	ICS, n	Non-ICS, n	Adjusted HR (95% CI)
Diabetes onset:	11,430	6540	
All patients			
Events per 100 patient-years	1.25 (1.16 to 1.35)	1.05 (0.90 to 1.20)	–
Proportional hazard regression			1.27 (1.07 to 1.50) <sup>†</sup>
Mean daily ICS dose*			Reference
<250 $\mu\text{g}/\text{day}$	3465		
250–499 $\mu\text{g}/\text{day}$	2768	–	1.17 (0.94 to 1.46)
500–999 $\mu\text{g}/\text{day}$	3203		1.27 (1.02 to 1.59)
$\geq 1000$ $\mu\text{g}/\text{day}$	1994		1.50 (1.18 to 1.90)
Diabetes progression:	480	324	
All patients			
Events per 100 patient-years	33.26 (30.19 to 36.33)	37.20 (32.96 to 41.44)	–



Proportional hazard regression			1.04 (0.87 to 1.25) <sup>†</sup>
Mean daily ICS dose*			
<250 µg/day	91	Reference	
250–499 µg/day	92	–	1.38 (0.91 to 2.11)
500–999 µg/day	103		1.69 (1.12 to 2.56)
≥1000 µg/day	194		2.54 (1.74 to 3.71)

\*Fluticasone propionate-equivalent dose; <sup>†</sup>Compared with the non-ICS group, number of patients; HR, hazard ratio; ICS, inhaled corticosteroid; CI, confidence interval

TO 053

### ICS WITHDRAWAL AND EXACERBATION RISK BY GOLD 2017 REPORT: POST HOC ANALYSIS OF THE WISDOM TRIAL

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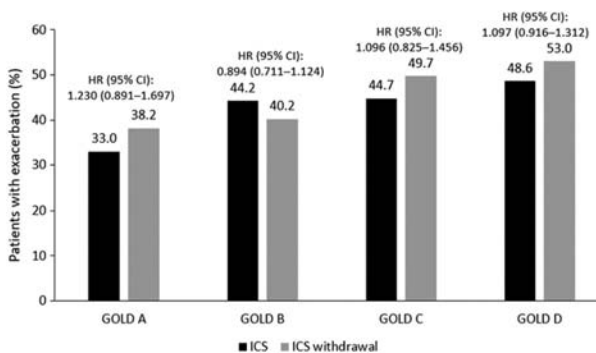
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**Introduction/Aim:** The 2017 GOLD\* A–D grouping scheme is solely based on exacerbation history and symptoms, and no longer considers lung function. We aimed to examine the effect of ICS withdrawal in the WISDOM trial within the new GOLD 2017 groups A–D.

**Methods:** In WISDOM – a 12-month, double-blind, parallel-group study – patients with COPD who had ≥1 exacerbation in the preceding 12 months and FEV<sub>1</sub> <50% predicted (GOLD 2013 C/D) received tiotropium, salmeterol and fluticasone propionate for 6 weeks, before randomisation to continue all three treatments or to stepwise withdrawal of fluticasone propionate. This is a *post hoc* analysis by GOLD 2017 stage.

**Results:** The proportion of the total population of patients experiencing exacerbations was lowest in the GOLD A group (35.8%) and highest in the GOLD D group (51.7%). There was no significant difference in exacerbations between ICS and ICS withdrawal in any group (Figure).

**Figure:** Patients with moderate-to-severe exacerbations by GOLD 2017 grouping.



**Conclusion:** The GOLD 2017 classification was a good predictor of exacerbation in WISDOM, with far fewer exacerbations in the GOLD A and B groups than in the C and D groups. Consistent with GOLD 2017 treatment recommendations and with the conclusions of the WISDOM trial, there was no significant increased risk of exacerbation with ICS withdrawal versus continuing ICS in any group.

\*Global Initiative for Chronic Obstructive Lung Disease 2017. Available from: <http://goldcopd.org>.

**Grant Support:** The study was funded by Boehringer Ingelheim.

**Conflicts of interest:** PF received travel support and/or honoraria from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, GOLD, Lung Foundation Australia, Menarini, Mundipharma and Novartis. KT, MH and AM are employees of Boehringer Ingelheim.

**INDACATEROL/GLYCOPYRROLIUM VS SINGLE LONG-ACTING MUSCARINIC ANTAGONIST IN LONG-ACTING BRONCHODILATOR-NAIVE COPD PATIENTS: POOLED ANALYSIS**

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**Introduction/Aim:** Data on the initial treatment with dual bronchodilation like indacaterol/glycopyrronium (IND/GLY) vs. single long-acting muscarinic antagonists (LAMAs) in COPD patients who were not previously on maintenance treatment with long-acting bronchodilators (LABD) are limited.

**Methods:** A pooled analysis of the ARISE<sup>1</sup>, SHINE<sup>2</sup> and SPARK<sup>3</sup> trials was conducted to evaluate the efficacy of once-daily (o.d.) IND/GLY 110/50 µg compared with open-label (OL) tiotropium (TIO) 18 µg o.d. and glycopyrronium (GLY) 50 µg o.d. in COPD patients (moderate to very severe) who were not on maintenance treatment with a LABD at study entry (LABD-naive). Efficacy variables were assessed at 24/26 weeks after the start of therapy.

**Results:** In total, 998 LABD-naive patients (IND/GLY, 353; OL TIO, 328; GLY, 317) were included. Patients treated with IND/GLY experienced greater improvements in trough FEV<sub>1</sub>, eDiary symptom score and rescue medication vs. OL TIO and GLY (**Table**). A greater proportion of patients achieved MCID with IND/GLY for trough FEV<sub>1</sub> vs. OL TIO and GLY (data not shown).

**Conclusion:** LABD-naive COPD patients treated with IND/GLY achieved improvements in lung function (FEV<sub>1</sub>), symptoms and rescue medication compared with those who received single LAMA.

**Grant Support:** This study was funded by Novartis Pharma AG, Basel, Switzerland

**Disclosure:** Dr. Konstantinos Kostikas was an employee and shareholder of Novartis at the time of submission of the abstract.

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Table: Efficacy of once-daily IND/GLY 110/50 µg o.d. vs. OL TIO 18 µg o.d. and GLY 50 µg o.d. after 24/26 weeks of treatment

	IND/GLY vs. TIO	IND/GLY vs. GLY
Trough FEV <sub>1</sub> , L	0.086 ± 0.016 (P < 0.0001)	0.080 ± 0.017 (P < 0.0001)
eDiary symptom score	-0.629 ± 0.148 (P < 0.0001)	-0.363 ± 0.149 (P = 0.0149)
Rescue medication use (number of puffs per day)	-0.531 ± 0.172 (P = 0.0022)	-0.499 ± 0.178 (P = 0.0052)

Data are presented as LS Mean treatment difference change from baseline ± SE

eDiary, electronic diary; GLY, glycopyrronium; IND/GLY, indacaterol/glycopyrronium; TIO, tiotropium

**ANTIBODY RESPONSE TO INFLUENZA VACCINE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)**

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**Introduction/Aim:** Emerging evidence indicates anti-viral host response declines with age, and that this may be more prominent in those with COPD, although the mechanisms are not well understood. Our aim was to determine the main predictors of antibody response to the seasonal influenza vaccine in people with COPD and healthy older people.

**Methods:** 165 participants were recruited: 89 COPD and 76 age-matched healthy participants, over 3 vaccine years (2015-2017), across two sites (Brisbane and Melbourne, Australia). Participants were inoculated with seasonal, quadrivalent, influenza vaccine just prior to "flu" season. Seroprotection rates (SPR) and seroconversion rates (SCR) were evaluated by measuring strain-specific serum haemagglutination inhibition (HAI) assay titres pre- and 28 days post inoculation (p.i.). Blood leukocyte numbers and systemic inflammation biomarkers were also measured pre- and 28 days p.i.

**Results:** Multivariate analyses indicate year and vaccine strain to be the strongest independent predictors of SPR 28 days post vaccination. In some years, very poor antibody responses were observed, notably when pre-vaccination antibody titres were high, i.e. in 2015 B/Brisbane/60/2008 strain had a SCR of 0% for both healthy and COPD groups. This correlation was significant in healthy groups for most influenza A strains (A/HongKong/4801/2014, P = 0.016; A/California/07/2009, P = 0.01; A/Michigan/45/2015, P = 0.006, Spearman rank correlation), however, for B/Brisbane/60/2008, both healthy (P = 0.004) and COPD (P = 0.002) groups were significant. Contrary to our expectations, the SCR, SPR and geometric mean HAI titres for each strain did not differ between COPD and healthy populations. There was no association between blood leukocyte numbers and post vaccine antibody titres.

**Conclusion:** Within individuals, antibody responses vary considerably by strain and from year to year. Because antibody responses can be poor in the context of pre-existing strain-specific antibodies, there may be a need to personalise influenza vaccination. Antibody responses to seasonal influenza vaccine appeared similar between healthy and COPD populations in this study.

**Grant Support:** NHMRC# APP1081433

**PERSISTENT BLOOD EOSINOPHILIA AND COPD EXACERBATION RISK AFTER ICS WITHDRAWAL FROM TRIPLE THERAPY IN THE SUNSET STUDY**

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**Introduction/Aim:** The role of blood eosinophilia as biomarker for the evaluation of exacerbation risk after direct inhaled corticosteroid (ICS) withdrawal from triple therapy has not been evaluated in non-frequently exacerbating COPD patients.

**Methods:** SUNSET, a 26-week randomised trial, assessed ICS withdrawal from long-term triple therapy to indacaterol/glycopyrronium (IND/GLY) 110/50 µg once daily (o.d.) or continuation of triple therapy (tiotropium [Tio] 18 µg o.d. + salmeterol/fluticasone propionate [SFC] 50/500 µg twice daily [b.i.d.]) in 1053 non-frequently exacerbating patients with moderate to severe COPD.<sup>1</sup> Moderate/severe exacerbations were predefined secondary endpoints and blood eosinophils were measured at screening and baseline (randomisation) 4 weeks apart.

**Results:** Annualised rates of moderate/severe COPD exacerbations did not differ between treatments in the overall population (rate ratio [RR] 1.08; 95% CI, 0.83 to 1.40). Only the minority of patients (16%) with consistently high blood eosinophils (≥300 cells/µL) at screening and randomisation had a strong trend for higher annualised rates of exacerbations (RR 1.85; 95% CI, 0.87 to 3.95) and decreased time-to-first exacerbation (hazard ratio [HR] 1.90; 95% CI, 0.92 to 3.89) with IND/GLY compared with TIO + SFC. Patients with eosinophil levels <300 cells/µL had a similar exacerbation risk (RR 1.06; 95% CI, 0.77 to 1.47) and time-to-first exacerbation (HR 0.96; 95% CI, 0.70 to 1.33) with IND/GLY vs. TIO + SFC. Furthermore, patients with inconsistent eosinophilia (both <300 cells/µL and ≥300 cells/µL at screening vs. baseline) also had similar exacerbation risk (RR 0.96; 95% CI, 0.45 to 2.04) and time-to-first exacerbation (HR 1.09; 95% CI, 0.50 to 2.36) with IND/GLY vs. TIO + SFC.

**Conclusion:** The direct ICS withdrawal from triple therapy may lead to increased risk of moderate/severe exacerbations in patients with consistently high blood eosinophils 4 weeks apart. Patients without eosinophilia or with intermittent eosinophilia did not present increased exacerbation risk.

**Grant Support:** The study was funded by Novartis Pharma AG, Basel, Switzerland.

**Reference**

- KR Chapman et al, Am J Respir Crit Care Med, 2018, 198, 329–339.

**Disclosure:** Dr. Konstantinos Kostikas was an employee and shareholder of Novartis at the time of submission of the abstract.

**CAREFUL USE OF PROPHYLACTIC INTERMITTENT AND CONTINUOUS MACROLIDES REDUCES EXACERBATION RATES IN COPD: SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Introduction/Aim:** There has been renewal of interest in the use of prophylactic antibiotics in chronic obstructive pulmonary disease (COPD). We aim to assess exacerbation rates and Quality of life (QOL) and assess the most beneficial antibiotic types, frequency of usage and adverse events.

**Methods:** Cochrane Airways Group Trials Register and bibliographies were searched for RCTs that compared prophylactic antibiotics vs. placebo in COPD until mid 2018. Two independent reviewers selected studies, with discrepancies being addressed involving a third review author. The co-primary outcomes for this systematic review were the number of exacerbations and quality of life.<sup>1</sup>

**Results:** 14 studies (2001 - 2015) involving 3932 participants were included. Nine were of continuous macrolide antibiotics, two on intermittent antibiotic prophylaxis (three times per week) and two were of pulsed antibiotic regimens (e.g. five days every eight weeks), with a study duration three to 36 months. The mean age was 65 and had at least moderate severity COPD. With use of prophylactic antibiotics, the number of patients experiencing one or more exacerbations was reduced (odds ratio (OR) 0.57, 95% CI 0.42 to 0.78; participants = 2716; studies = 8; moderate quality evidence). (NNTB) was 8 (95% CI 5 to 17). (Graph 1).

There was a statistically but not clinically significant improvement in QOL as measured by the St George's Respiratory Questionnaire (mean difference (MD) -1.93, 95% CI -3.02 to -0.84; participants = 2237; studies = 7, high quality evidence).

Adverse events recording varied depending on the antibiotics used. Concerning development of antibiotic resistance was measured in six studies

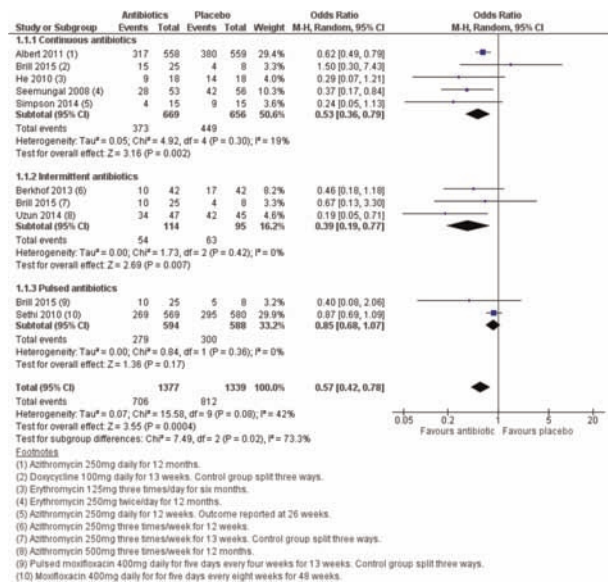
**Conclusion:** Use of continuous and intermittent prophylactic antibiotics, (all macrolides), results in a clinically significant reduction in exacerbations in COPD patients who were frequent exacerbators with at least moderate severity COPD. Use should be a mindful balance between benefits and harms to individual patients and the to the society.

- Herath SC, Normansell R, Maisey S, Poole P. Prophylactic antibiotic therapy for chronic obstructive pulmonary disease (COPD). Cochrane Database of Systematic Reviews 2018 (in press)

**Grant Support:** None

Graph 1: Forest plot on number of people with one more exacerbation prophylactic antibiotic Vs placebo

TO 058



**USE OF VENTILATION-PERFUSION SINGLE-PHOTON EMISSION COMPUTED TOMOGRAPHY (VQ SPECT) TO SELECT THE TARGET LOBE FOR ENDOBRONCHIAL VALVES LUNG VOLUME REDUCTION (EBV-LVR)**

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**Introduction/Aim:** Choosing the target lobe for EBV-LVR in emphysema is usually based on quantitative computed tomography (CT) scans as the gold standard. We investigated a novel method of lung lobar quantitative segmentation using VQ SPECT with CT to generate a parameter called the Ventilation-Perfusion Differential Index (VQDI). The aim was to validate VQDI for target lobe selection by evaluating its concordance to CT and to evaluate the effect of EBV on VQDI.

**Methods:** Prospective, multi-centre, single blinded, observational study of EBV-LVR patients. Pre and 3 months post intervention VQ SPECT and CT were performed along with St George Respiratory Questionnaire (SGRQ), lung function test, and 6 minute walk distance. The target lobe was chosen by the proceduralist using the CT. Then, the nuclear physician selected the target lobe based on VQDI (VQDI<sub>TL</sub>). Inter-rater agreement between CT<sub>TL</sub> and nuclear physician VQDI<sub>TL</sub> was calculated by Kappa statistic. The EBV effect on VQDI and treatment outcomes were analysed with a linear mixed-effects model.

**Results:** A total of 18 patients have been enrolled. There was near perfect agreement between CT<sub>TL</sub> and VQDI<sub>TL</sub> (89%, Kappa statistic=0.85). After EBV-LVR, target lobe VQDI showed relative reduction of 81% from mean 0.59 ± 0.28 to 0.15 ± 0.32 (P < 0.001). There was no significant difference in the ipsilateral untreated lobe VQDI (mean difference (MD) 0.03, P = 0.79) and the contralateral lung VQDI (MD 0.01, P = 0.57) following EBV-LVR. Post treatment, statistically significant outcomes were noted for FEV1 (MD +160ml, P < 0.001), target lobe volume reduction (MD -983ml, P < 0.001), RV (MD -790 mL, P < 0.001) and SGRQ (MD -9.9, P = 0.003).

**Conclusion:** Our study validates VQDI as a test for EBV-LVR target lobe selection with high concordance to CT. Further characterisation of the target lobe by combining the CT and VQDI may improve clinical outcome, especially in homogenous emphysema.

**Grant Support:** Nil.

**Declaration of Interest Statement:** No conflict of interest

### TRANSTHORACIC PNEUMONOSTOMY TO TREAT PATIENTS WITH SEVERE EMPHYSEMA AND HYPERINFLATION – A SAFETY AND FEASIBILITY STUDY

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**Introduction:** Bronchoscopic lung volume reduction can improve dyspnoea, exercise capacity and quality of life in patients with severe hyperinflation however, it is not effective in the presence of collateral ventilation. A surgically created exit passage through the chest wall could potentially allow trapped air to bypass the lung parenchyma/airways and escape, and thereby improve hyperinflation and symptoms, even in the presence of collateral ventilation.

**Aim:** To describe the feasibility and safety of a novel transthoracic pneumonostomy technique for lung volume reduction in patients with severe emphysema and hyperinflation.

**Methods:** Between 2008-2012, 15 patients with severe emphysema underwent surgical implantation of a transthoracic 10mm diameter Portaero Access Tube (Portaero™, Cupertino, CA, USA) to allow formation of a pneumonostomy track. The pneumonostomy was initially maintained by the Portaero™ Catheter and substituted 3-5 weeks later by an 8mm Portaero Disposable Tube (3-8cm long) and changed daily.

**Results:** 15 patients underwent the pneumonostomy procedure. Mean pre-operative baseline FEV1 was 0.78L (29% predicted), DLCO 35%, TLC 127% and RV 204%. No serious adverse effect related to surgery was noted. Loss of patency of pneumonostomy tract and stoma site due to granulation tissue was frequently seen; Debridement using bronchoscope and argon plasma diathermy was usually effective however repeat procedures for recurrence were needed. The pneumonostomy remained patent in 6 patients at 12 months and for 48 months in one patient. Mild bleeding and tract infection were observed. No related patient death was reported.

**Conclusion:** In this pilot study, transthoracic pneumonostomy for lung volume reduction in patients with severe emphysema was feasible and safe. Further studies are needed to refine patient selection and improve device design to prevent tract occlusion and improve efficacy.

**Grant Support:** RT - NHMRC and Cancer Council WA Early Career Fellowship

This study was funded by Portaero™, Cupertino, CA, USA.

### CHANGES IN LOBAR VENTILATION AND PERFUSION FOLLOWING ELVR IN COPD

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**Introduction/Aim:** We have previously reported the contralateral diagonal redistribution of *planar* (regional) ventilation and perfusion (VQ) following ELVR in severe COPD with endobronchial valves. This was found irrespective of whether the target lobe was upper or lower. However, changes in *lobar* V and Q following ELVR have not been described.

**Methods:** 12 patients with severe COPD were prospectively recruited and underwent unilateral ELVR between April 2017 and Sep 2018 at Macquarie University Hospital. Complex full pulmonary function tests (PFT), 6-minute walk tests (6MWT), and *lobar* VQ scans (as defined with SPECT CT and Technegas, Cyclomedica) were performed at baseline and 3 months post-ELVR.

**Results:** Compared to baseline, the average targeted lobe volume loss was  $503.42 \pm 126.73$  mL. Significant improvements in preBD FEV1% ( $8.21 \pm 2.01\%$ ), postBD FEV1% ( $7.39 \pm 1.68\%$ ), FEV1/FVC% ( $8.14 \pm 3.57\%$ ), RV% ( $-31.73 \pm 7.86\%$ ) and RV/TLC% ( $-6.56 \pm 2.17\%$ ) were seen 3 months post ELVR (all  $P < 0.05$ ). Irrespective of whether the upper (n=8) or lower lobes were targeted, patients showed a significant decrease in V ( $-7.83 \pm 3.14\%$ ) and Q ( $-8.25 \pm 2.71\%$ ) of the targeted lobe (both  $P < 0.05$ ). There were corresponding significant improvements in the V ( $7.46 \pm 1.74\%$ ) and Q ( $4.92 \pm 1.43\%$ ) of the contralateral non-targeted upper lobe post ELVR (both  $P < 0.05$ ). The improvement in lobar Q of the contralateral upper lobe was significantly correlated with improvement postBD FEV1% ( $r=0.611$ ,  $P < 0.05$ ).

**Conclusion:** For ELVR targeting both upper and lower lobes, there was significant improvement in *lobar* V and Q to the contralateral lung, with preferential distribution to the contralateral upper lobe. This correlates to improvement in FEV1. Redistribution of *lobar* V and Q with improved V/Q matching in the contralateral lung is a likely mechanism of action in ELVR.

**Key Words:** endoscopic lung volume reduction, COPD, lobar, ventilation, perfusion

**Nomination for New Investigator Award**

**Grant Support:** NIL

TO 061

TO 062

### STAGED ENDOSCOPIC LUNG VOLUME REDUCTION (ELVR) IN PATIENTS WITH SEVERE COPD TO PREVENT PNEUMOTHORAX

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**Introduction:** Pneumothorax (PTX) following ELVR with endobronchial valves for severe COPD is a recognised complication in up to 25% of patients. The risk is increased in collateral ventilation (CV) negative patients and those with disproportionately high target lobe volume. The mechanism is due to rapid target lobe volume reduction and compensatory hyperinflation of the non-targeted ipsilateral lobe which is the usual site of PTX. Our aim was to determine if staged ELVR reduces the risk of PTX in high risk patients by slowing the development of targeted atelectasis.

**Methods:** We describe a series of staged ELVR procedures in patients with a high risk of PTX. In patient 1, lung function revealed FEV1 0.41L (16%), RV 4.81L (263%). VIDA CT analysis revealed the RLL was the appropriate target (61% destruction at -950HU; R Oblique fissure 100% integrity; 2.63L). However, the remaining combined RUL/RML volume was only 0.93L.

**Results:** Utilising Intra-bronchial Valves (IBV Olympus), we performed a staged ELVR of the RLL. During procedure 1, IBVs were inserted into RB7, RB8, RB9 and RB10. Volume loss was seen on CXR immediately, with no PTX. On day 4, we inserted a fifth IBV into RB6 to complete ELVR of RLL, with further volume loss evident. CXR also revealed significant ipsilateral mediastinal shift, but no PTX. Pre and post procedure HRCT, CT Spect V/Q lung scans and lung function will be shown.

**Conclusion:** Staged ELVR may help prevent PTX in high risk COPD patients undergoing ELVR. The potential mechanisms for this will be discussed.

**Grant Support:** Nil

### PLEURAL DRAINAGE AND OXYGENATION IN INTENSIVE CARE: REVIEW AND META-ANALYSIS

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**Introduction/Aim:** Critical illness is associated with pathophysiological derangements that commonly result in pleural fluid accumulation. The prevalence of ultrasound-detectable pleural effusion is up to 60% in patients admitted to the intensive care unit (ICU). Observational studies have shown that pleural effusion is associated with failure of oxygen therapy, and poorer indices of oxygenation. Thoracentesis is a potential therapy for hypoxic patients in the ICU, but the evidence for drainage is based on small observational studies with inconsistent results. A systematic review was undertaken to clarify the current knowledge regarding the impact of pleural fluid drainage on oxygenation in ICU patients.

**Methods:** A systematic review of MEDLINE, EMBASE, and CINAHL databases was performed for studies published before August 2018. Prospective studies of ICU patients >18 years old undergoing drainage of pleural effusion, in whom the PaO<sub>2</sub>:FiO<sub>2</sub> (P:F ratio) could be calculated from the reported data, were included in the meta-analysis.

**Results:** 3336 studies were identified, of which 14 studies (enrolling 396 participants in total) were eligible for inclusion. None of the included studies were randomised and participants were their own controls. Significant methodological variation was observed, particularly with respect to post-procedure outcome measurements. Pleural drainage improved PaO<sub>2</sub>:FiO<sub>2</sub> by 21.2% (12 studies, n=350, 95%CI 15.2-27.3%, I<sup>2</sup>=55.8%), corresponding to an increase in PaO<sub>2</sub>:FiO<sub>2</sub> of 45.4mmHg (12 studies, n=350, 95%CI 28.4-62.2mmHg, I<sup>2</sup>=56.4%). Neither the volume evacuated, nature of effusion, positive end expiratory pressure (PEEP), nor mode of ventilation reliably predicted improvement in P:F ratio.

**Conclusion:** Pleural drainage is effective in improving oxygenation, but the clinical benefits and predictors of successful outcomes remain unknown. A randomised controlled trial of pleural drainage in the ICU, with a focus on both physiological and clinical outcomes, is planned.

**Grant Support:** Dr Fysh receives Research Fellowship funding from the Raine Foundation, the Department of Health (WA) and the NHMRC.

**Declaration of interest:** No conflicts of interest are reported.

### MALIGNANT PLEURAL EFFUSION MANAGEMENT COMBINING CURRENT BEST PRACTICE: APPLYING THE EPITOME ALGORITHM

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**Introduction/Aim:** Indwelling pleural catheters (IPC) have revolutionised malignant pleural effusion (MPE) management. Daily drainage via IPC and instillation of talc slurry via IPC have been separately shown to enhance rates of pleurodesis with long-term fluid control(1, 2). Combining talc slurry instillation with daily drainage via IPC may optimise outcomes.

**Methods:** A single-centre pilot study was performed. All patients with symptomatic MPE were offered IPC. If adequate lung re-expansion occurred, in the absence of contraindications, talc slurry (4g) was instilled via the IPC and the patient was discharged on daily drainage via vacuum bottle for 14 days or until pleurodesis was achieved (<50ml output on three consecutive drainage attempts). Patients with contraindications to talc were discharged on symptom-guided bag-drainage.

**Results:** Consecutive patients with MPE (n = 100, 67% male, 49% mesothelioma) were included. Median length of stay was 2.5 [IQR: 2-4] days. Fifty-three patients had contraindications to talc (60% due to trapped lung). Forty-seven patients underwent talc pleurodesis, of whom 74% achieved pleurodesis at a median of 20 days. All patients in the talc arm were followed for a minimum of 90 days and median overall follow-up was 109.5 [IQR: 55.5-230] days. Complications included IPC-related infection (n = 7), symptomatic loculation (n = 10) and reversible tube blockage (n = 3). Eleven patients (11%) had a further ipsilateral procedure but only 2 patients required re-intervention post-IPC removal.

**Conclusion:** IPC combined with talc slurry instillation and daily drainage where appropriate, was associated with high pleurodesis rates with few complications or recurrences. IPC remains the optimal choice for patients with contraindications to talc. The EPIToME algorithm provides a pragmatic approach for all MPE patients.

**Grant Support:** NHMRC Fellowships (RT, YCGL), WA Cancer Council (RT, YCGL),

WACPCN Fellowship (SM, DBF), ERS Long-term Research Fellowship (DBF).

**Declaration:** Rocket Med Ltd has provided free IPC drainage kits and an unrestricted educational grant for previous trials led by YCGL. YCGL has served on advisory boards of Carefusion/BD and Sequana Med Ltd.

#### Grant Support

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### MECHANISMS BEHIND IN UTERO PARTICULATE MATTER INHALATION AND SOMATIC GROWTH DEFECTS

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**Introduction/ Aim:** Gestational exposure to a range of different chemical sources has been associated with long-term consequences for offspring. Epidemiological data suggest that air pollution, specifically particulate matter (PM) inhalation, is associated with low birth weight, premature birth and cognitive and metabolic dysfunction. While birth defects are established, there is limited knowledge on the mechanism for how particulate matter causes such effects. Hence, the aim of this study was to characterise somatic growth and lung deficits in embryonic mice.

**Methods:** Eight-week-old pregnant C57BL/6J mice were exposed intranasally to saline, diesel exhaust particles (DEP), iron oxide, silica or house dust mite (HDM) particles at gestational day (E)7.5, E12.5 and E17.5. Foetuses were weighed, and crown-rump length was quantified. Lung and placenta were collected for histology, RNA and protein quantification. Embryonic lung structure was assessed according to American Thoracic Society and European Respiratory Society guidelines. Real-time PCR was performed on placenta, quantifying cortisol stress markers HSD11 $\beta$  and TSC22.

**Results:** Foetus weight was different between males and females ( $P < 0.001$ ). In males, *in utero* exposure to silica, iron oxide or HDM showed a significant decrease in weight ( $P = 0.02$ ,  $P < 0.01$   $P = 0.04$  respectively). Similarly, crown-rump length was decreased in male embryos exposed to iron oxide ( $P = 0.03$ ). Real-time PCR showed no significant difference in expression levels of HSD11 $\beta$  and TSC22 between saline exposed mice and mice exposed to either DEP, iron oxide, HDM or silica ( $P < 0.05$  for all comparisons).

**Conclusion:** Exposure to particulate matter alters foetal somatic growth in males. Interestingly, all exposures caused decreased weight in males irrespective of the physical or chemical composition. As none of our mechanistic markers showed concurrent changes, the mechanism remains unknown. However, somatic growth was decreased regardless of chemical composition, this suggest that there is an indirect effect of particulate matter on foetal somatic growth.

#### Grant Support: •

TO 065

TO 066

### PREDICTING OLDER AUSTRALIANS' LIFE EXPECTANCY FROM RESPIRATORY SYMPTOMS AND SMOKING

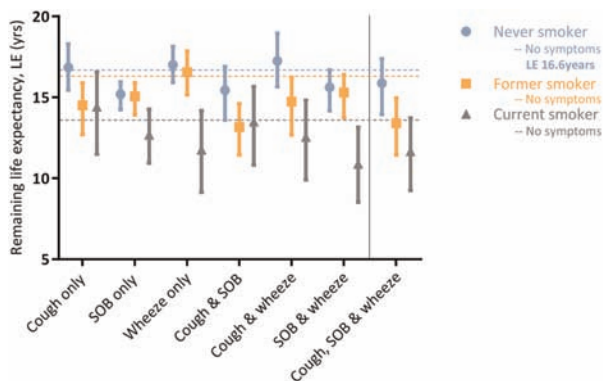
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**Introduction/Aim:** Respiratory symptoms are recognisable to patients and may be markers of chronic disease and mortality risk. This risk may be easier to conceptualise if presented as the impact on remaining life expectancy (LE) rather than hazard ratios. The study aimed to: a) evaluate respiratory symptoms as a predictor of mortality in an older population defined by smoking status, and b) predict the remaining life expectancy of those with respiratory symptoms.

**Methods:** This study used data from the Australian Longitudinal Study of Ageing (ALSA) (n=2,087), a prospective population-based longitudinal cohort study with 22years follow-up. Three respiratory symptoms were analysed: cough, shortness of breath (SOB) and wheeze. Primary outcome was all-cause mortality. The implied impact on LE was estimated using a parametric survival function.

**Results:** SOB predicted shorter LE irrespective of smoking status. Cough predicted shorter LE in former smokers and wheeze predicted shorter LE in current smokers after adjusting for co-variables (including age, gender, COPD, asthma, CVD). The estimated remaining LE of a 70 year old male never smoker with no respiratory symptoms was 16.6 (95%CI: 14.8 – 17.7) years. For a 70 year old male current smoker with cough, SOB and wheeze, the years of life lost compared to a never smoker with no symptoms was 4.93 (95%CI: 2.88 – 7.34) years (see Figure below).



**Conclusion:** Respiratory symptoms predict mortality in older people. Cough in former smokers, wheeze in current smokers and all those with SOB may benefit from further investigations and disease specific management.

**Grant Support:** KP and AJC were supported by an Australian Government Research Training Program Scholarship.

### CHILDHOOD MEASLES IS ASSOCIATED WITH LOWER RISK OF ADULT ATOPIC ASTHMA IN THE TAHS COHORT, BUT ONLY AMONG THOSE WHO HAD CHILDHOOD ECZEMA

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**Introduction/Aim:** The increase in allergic diseases in recent decades might be linked to fewer and less severe childhood respiratory infections. Measles infection has been associated with reduced atopy in later life but not allergic diseases per se. We had the unique opportunity to assess whether childhood measles infection modulated the relationship between childhood allergy and atopic asthma in a non-immunized middle-aged Australian cohort.

**Methods:** Data were from the population-based Tasmanian Longitudinal Health Study (TAHS) cohort born in 1961. Parental report of eczema-ever was recorded at the initial 1968 survey, and measles history was recorded by school health records. At the 2012-2015 follow-up, atopic asthma was defined by self-reported doctor-diagnosed asthma with skin prick test (SPT) positivity to at least one food and/or aeroallergen. Multivariable regression was used including an interaction term.

**Results:** Of 1,622 participants aged 51–55 years, 69.7% (n = 1,131) had measles in childhood. An interaction was seen between the effects of childhood measles and eczema on adult atopic asthma, regardless of allergen sensitization type ( $P$ -for-interaction=0.029). While there was no significant association with measles in the absence of childhood eczema [OR 1.23 (0.87–1.74),  $P = 0.24$ ], a protective association between childhood measles and adult atopic asthma was observed for those with childhood eczema [OR 0.48 (95%CI: 0.26–0.91),  $P = 0.023$ ]. This interaction was present with sensitization to HDM, cat and pollen ( $P$ -for-interaction = 0.028, 0.036 and 0.052 respectively), but not moulds or foods.

**Conclusion:** In this natural experiment prior to the introduction of measles immunization, for survivors, childhood measles predominantly attenuated the risk for atopic asthma in middle-aged Australian adults who also had childhood eczema, and this suggests a role for measles in modulating allergic diseases.

**Grant Support:** NHMRC; Asthma Foundations; Clifford Craig Medical Foundation; Helen McPherson Trust; Royal Hobart Hospital; University of Melbourne; GSK.



### IN-HOSPITAL MORTALITY FOLLOWING CARDIOVASCULAR EVENTS AND INTERVENTIONS IN PEOPLE WITH BRONCHIECTASIS: A USA POPULATION BASED STUDY

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**Introduction/Aim:** Epidemiological studies have suggested that people with bronchiectasis are at increased risk of cardiovascular co-morbidities. However, there are limited data on outcomes after acute myocardial infarction (AMI), coronary artery bypass graft (CABG) or percutaneous angioplasty (PCI) amongst people with bronchiectasis. The aims of our study were to determine in-hospital mortality following AMI, CABG and PCI in people with and without bronchiectasis.

**Methods:** We used data from the Nationwide Inpatient Sample, an anonymised stratified yearly sample of discharge records from community hospitals in the USA. People with a record of bronchiectasis from 2000 to 2011 were identified using ICD-9-CM codes. ICD-9-CM and procedure codes were also used to identify people with AMI, CABG and PCI. Multi-variable logistic regression was used to estimate odds ratios for in-hospital mortality following AMI, CABG and PCI in people with and without bronchiectasis, adjusting for age and sex.

**Results:** We identified 101,597 people with bronchiectasis. The mean age of the cohort was 57.2 years (SD 20.8) and 60.8% were female. 2195 (2.2%) individuals with bronchiectasis had an AMI, 366 (0.4%) underwent a CABG and 827 (0.8%) a PCI. Crude in-hospital mortality amongst people with bronchiectasis following AMI, CABG and PCI was 12.5%, 3.6% and 2.9% respectively. After adjusting for age and sex, we found no difference in in-hospital mortality following AMI, CABG or PCI in people with bronchiectasis compared to the general population (Table 1). There was some evidence that in-hospital death following AMI with modified by age ( $P = 0.052$ ), with people with bronchiectasis aged 55 or younger having the highest risk of death (OR 2.33, 95% CI 1.13-4.81).

**Conclusion:** Our findings suggest no difference in risk of death following AMI, CABG and PCI in people with or without bronchiectasis. This needs to be taken into account when considering patients for these procedures and counselling them on risks.

**Grant Support:** VN is funded by an NIHR Academic Clinical Lectureship

### LDCT LUNG CANCER SCREENING IN THE WA ASBESTOS REVIEW PROGRAM

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**Introduction:** Low-dose computed tomography (LDCT) screening for lung cancer reduces mortality in high-risk individuals. Asbestos exposure increases lung cancer risk; when combined with a tobacco exposure the risk is near multiplicative. We report the findings from LDCT screening of an asbestos-exposed cohort, the Western Australia Asbestos Review Program (ARP).

**Methods:** Between 2012-2017 annual LDCT chest scans were offered to ARP participants ( $\geq 3$  months cumulative asbestos exposure, regardless of tobacco exposure). An indeterminate nodule was defined as being  $>5\text{mm}$  and/or  $>50\text{mm}^3$ . All LDCT scans with nodules were reviewed by our ARP multidisciplinary team. The Brock model was used to calculate lung cancer risk in prevalent nodules.

**Results:** 1743 individuals (262 (15.0%) female) with a median (IQR) age of 69.8 (63.0 to 75.7) years underwent 5702 screening scans. 595 (34.1%) were never smokers, 131 (7.5%) were current smokers. Median pack year history was 17.1 (7.2 to 33.8). 610 (35%) had CT features of asbestosis and (62%) had pleural plaque on LDCT.

Prevalent nodules were detected in 150 (8.6%) individuals. 49 (2.8%) developed incident nodules. Over the 5 years, 167 (9.6%) underwent an additional follow-up scan for a nodule (usually 3 months interval) 23 of these required 2 or more interval scans. Lung cancer was confirmed in 18 (1.0%) and 7 mesotheliomas were diagnosed in the cohort. Of those with lung cancer only 3 would have been eligible for screening under current US guidelines. The majority of nodules had low Brock risk for lung cancer (Figure 1), 83% of the proven lung cancers had a risk  $>10\%$ . Median estimated radiation exposure per scan was 0.2 mSv.

**Conclusion:** The ARP cohort has a lung cancer rate comparable to other high-risk smoking cohorts, despite modest tobacco exposure. Current lung cancer screening selection criteria may not adequately account for the risk from asbestos exposure.

Table 1: In-hospital mortality and following AMI, CABG and PCI in people with and without bronchiectasis

	No of people with bronchiectasis (n=101,597) (%)	No of people without bronchiectasis (n=77,666,691) (%)	Crude in-hospital mortality in people with bronchiectasis (%)	Crude in-hospital mortality in people without bronchiectasis (%)	Adjusted Odds Ratio (95% CI) *
AMI	2195 (2.16)	2,423,961 (3.12)	12.5%	10.1%	0.97 (0.86-1.10)
CABG	366 (0.36)	732,373 (0.94)	3.6%	3.1%	0.90 (0.51-1.57)
PCI	827 (0.81)	1,791,318 (2.31)	2.9%	1.4%	1.40 (0.93-2.10)

\*Odds ratio adjusted for age and sex

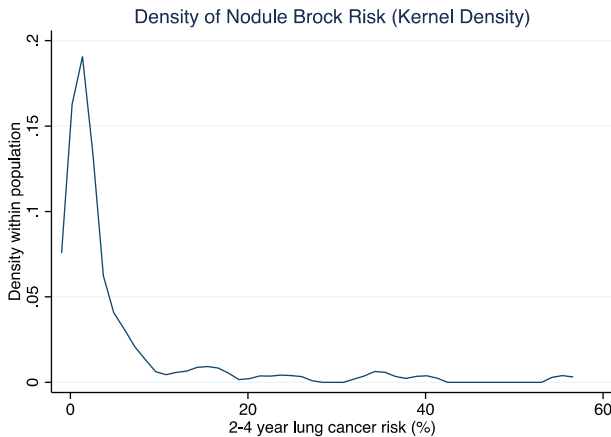


Figure 1 Density of Nodule risk for prevalent nodules based on Brock Model (Risk of nodule being diagnosed as lung cancer in next 2-4 years)

**Grant Support:** WA Department of Health

TO 069

**RADIOLOGICAL REVIEW OF QUEENSLAND MINERS WITH PNEUMOCONIOSIS FOLLOWING OCCUPATIONAL EXPOSURE TO COAL DUST WITH OR WITHOUT RESPIRABLE CRYSTALLINE SILICA.**

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**Introduction/Aim:** To identify whether occupational exposure to respirable crystalline silica (RCS) in Queensland miners with a diagnosis of pneumoconiosis is associated with higher radiological grades of disease.

**Method:** A retrospective radiological review of 36 male cases of pneumoconiosis diagnosed in Queensland miners. Disease severity and lung nodule type were reviewed using the International Labor Organisation (ILO) grading system by a B reader Chest Radiologist. The correlating computer tomography (CT) appearance was assessed as per the Hosoda-Shida Classification of CT for Pneumoconioses.

**Results:** Basic occupational history divided cases of pneumoconiosis in Queensland into three groups: workers with minimal occupational risk for silicosis diagnosed with Coal Worker's Pneumoconiosis (CWP) (n=17), workers with predominant exposure to RCS diagnosed with silicosis (n=9) and workers exposed to dust containing both coal and silica diagnosed with Mixed Dust Pneumoconiosis (MDP) (n=10). The ILO grades were higher in the cases of pneumoconiosis where workers had been exposed to RCS (silicosis and MDP). The association of higher radiological grades with occupational exposure to RCS was best reflected in the 18-point scale of the CT grading system with mean (and range) grades being 6.4 (3-12) for CWP, 7.6 (2-13) for MDP and 8.5 (3-13) for silicosis. Radiological features associated with a diagnosis of silicosis, such as the presence of larger pulmonary nodules, lymph node calcification, and subpleural nodularity or pseudoplaques, was more common in the workers with pneumoconiosis who reported occupational exposure to RCS. All cases of progressive massive fibrosis (n=4) occurred in workers with silicosis (n = 3) or MDP (n = 1).

**Conclusion:** The radiological pattern observed in cases of pneumoconiosis in Queensland miners suggests that workers with exposure to respirable crystalline silica have higher grades of disease.

**Key Words:** Coal worker's pneumoconiosis, silicosis, occupational lung disease

**Grant Support:** Australian Coal Association Research Program, Queensland Government.

TO 070

TO 071

### VARIATION IN THE CLINICAL MANAGEMENT OF PAEDIATRIC ASTHMA IN AUSTRALIA

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**Introduction/Aim:** There are national and international guidelines for the management of paediatric asthma, aimed at standardising clinical care across different healthcare providers and improving health outcomes. Despite the availability of guidelines, variation in care persists, highlighting the need for rigorous monitoring. We conducted a comprehensive assessment of guideline adherence in paediatric asthma care, including inpatient and ambulatory services, in Australia.

**Methods:** National and international Clinical Practice Guidelines (CPGs) relating to asthma in children were searched and 39 indicators were extracted. Retrospective medical record review was conducted across hospital inpatient admissions, Emergency Department (ED) presentations, and general practice (GP) and paediatrician consultations in three Australian states for children aged  $\leq 15$  years receiving care in 2012 and 2013. Adherence with indicators was assessed from medical records by nine experienced paediatric nurses (surveyors), who were trained to assess eligibility for indicator assessment and adherence to CPGs.

**Results:** Surveyors conducted 18,453 asthma indicator assessments across 1,600 visits for 881 children, in 129 locations. The average adherence for the 39 indicators assessed for asthma care provided was 54.4% at GPs (95% CI: 46.0-62.5), 77.7% by paediatricians (95% CI: 40.5-97.0), 79.9% at EDs (95% CI: 70.6-87.3) and 85.1% for inpatient care (95% CI: 76.7-91.5). For 14 acute asthma indicators, overall adherence was 56.3% (95% CI: 47.6-64.7). Adherence for recording of all four vital signs (conscious level, oxygen saturation, pulse rate and work of breathing) in children aged  $>2$  years presenting with asthma attack was 15.1% (95% CI: 8.7-23.7); and adherence for all three items to be reviewed prior to commencing a new drug therapy was 20.5% (95% CI: 10.1-34.8).

**Conclusion:** The study demonstrated a large gap between existing care and the CPGs for paediatric asthma care in Australia. Evidence-based interventions to improve adherence to CPGs may help to standardise quality of paediatric asthma care.

**Grant Support:** The research was funded as an Australian National Health and Medical Research partnership grant (APP1065898), with contributions by the National Health and Medical Research Council, Bupa Health Foundation, Sydney Children's Hospital Network, New South Wales Kids and Families, Children's Health Queensland, and the South Australian Department of Health (SA Health).

### SYSTEMATIC REVIEW AND META-ANALYSIS OF PREDICTORS OF FATAL PAEDIATRIC ASTHMA

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**Introduction/Aim:** Asthma is the most common chronic respiratory disease in children. Although the mortality rates are relatively low, the majority of deaths from asthma are preventable. We conducted a systematic review and a meta-analysis to identify the risk factors which predispose children to life-threatening asthma (LTA).

**Methods:** LTA was defined as an asthma exacerbation which required an intensive care unit (ICU) or paediatric intensive care unit (PICU) admission, intubation or mechanical ventilation, or resulted in a  $\text{PaCO}_2 \geq 45\text{mmHg}$ , or death. A systematic literature search was conducted using MEDLINE, EMBASE, CINAHL and Google Scholar to identify studies published in English during 1990 to 2018, that investigated risk factors for LTA in children aged  $<18$  years. Review Manager 5.3 software was used to apply a random effects model and the Mantel-Haenszel statistical method was used to estimate odds ratios with 95% confidence intervals.

**Results:** We identified 962 articles; 19 were included in the systematic review and 13 in the meta-analysis. The results from systematic review varied across studies. In the meta-analysis, severe asthma grade (OR=3.70, 95% CI 1.08–12.61), one or more hospitalisations in the prior year (OR=2.07, 95% CI 1.28–3.36), past ICU admission (OR=1.81, 95% CI 1.29–2.54), use of inhaled corticosteroids (OR=2.36, 95% CI 1.49–3.76), sensitisation to one or more allergens (OR=1.89, 95% CI 1.11–3.22), food allergy (OR=3.00, 95% CI 1.48-6.07) and exposure to second-hand smoke (OR=1.82, 95% CI 1.09-3.04) were associated with an increased risk of LTA.

**Conclusion:** To our knowledge this is the first comprehensive meta-analysis investigating risk factors for LTA in paediatric population. The data from the study can be used to develop a risk algorithm to identify and actively follow up children who are at risk of life-threatening outcomes.

**Grant Support:** Rotary Club of Sydney Cove and Sydney Children's Hospital Foundation.

### EVALUATING INHALED CORTICOSTEROID USE AMONG PREGNANT WOMEN WITH ASTHMA

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**Introduction:** Prescription database studies demonstrate that the rate of prescriptions for inhaled corticosteroids (ICS) drops in early pregnancy suggesting that some women cease their medication. However, this could also be related to non-adherence to prescribed asthma medication. ICS use during pregnancy has not previously been summarised. The aim of this systematic review and meta-analysis was to evaluate ICS use during pregnancy among women with asthma.

**Methods:** We performed a systematic search of literature using terms related to asthma, pregnancy and medication use. All English articles reporting asthma medication use among a (sub)-population of pregnant women with asthma were included (n=45). Prevalence and changes in ICS use during pregnancy were pooled.

**Results:** The proportion of pregnant women with asthma who used ICS during pregnancy ranged from 4% (Japan) to 78% (Saudi Arabia), with an overall pooled proportion of 42% (95%CI 37-48%). The prevalence of ICS use was highest in Europe (50%, 95%CI 38-62%) vs. other continents (40%), followed by North America (37%) and Australia (39%). In eight prescription databases, ICS prescription rates lowered in the first trimester of pregnancy, compared to pre-pregnancy, increased in the second trimester, and decreased in the third trimester. Five studies reported asthma medication adherence among pregnant women, using four differing measures of self-reported non-adherence. In two comparable studies with pooled ICS non-adherence of 40% (95%CI 36-44%).

**Conclusion:** The prevalence of ICS use among pregnant women with asthma is 42%. Prescription rates for ICS change throughout pregnancy. The early drop may be due to non-adherence while the mid-term increase may be a response to the increased prevalence of asthma exacerbations in the second trimester. ICS non-adherence among pregnant women with asthma is high and needs urgent attention.

**Grant Support:** Priority Research Centre Grow Up Well, University of Newcastle

### EXTRAPULMONARY DISEASE CHARACTERISTICS AND HEALTH-STATUS IN SEVERE ASTHMA AND BRONCHIECTASIS

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**Introduction/Aim:** Severe asthma and bronchiectasis are heterogeneous diseases that contribute to disability beyond the pulmonary system. The magnitude of the impact of these extrapulmonary features on health-related quality of life (HRQoL) is unknown.

**Methods:** We analysed the relationships between HRQoL (St. George Respiratory Questionnaire; SGRQ) and extrapulmonary characteristics, including physical activity (steps/day), anxiety and depression, isometric leg strength extension, systemic inflammation, and several comorbidities in adults with severe asthma (n = 70) and bronchiectasis (n = 61). Missing values were estimated using multiple imputation by chained equations.

**Results:** Participants with severe asthma and bronchiectasis (median [IQR] age: 55 [42, 68] and 68 [62, 73]; 54% and 87% female, respectively) had similar SGRQ scores and pulmonary and extrapulmonary characteristics ( $P > 0.05$ ). Greater anxiety and depression symptoms, fewer steps/day, lower isometric leg strength, greater systemic inflammation, presence of sarcopenia and greater Charlson Comorbidity Index were significantly associated with poorer HRQoL ( $P < 0.05$ ). In multivariable regression models, anxiety and depression, steps/day, systemic inflammation and leg strength remained independently associated with HRQoL. The full model explained 43.9% of the variance in SGRQ scores. Associations between extrapulmonary characteristics and SGRQ domains were stronger for activity and impact, than symptoms. Clear visual representations of dose-response relationships were illustrated in simple- and full-adjusted regression analyses using the extrapulmonary variables transformed into tertiles. These analyses showed, for instance, that the predicted mean SGRQ scores of participants doing  $\leq 4125$  steps/day versus those doing  $\geq 7048$  steps/day were 55.3 and 32.7 points, respectively ( $P < 0.001$ ). Similarly, leg strength values of  $\leq 54$  kg versus  $\geq 100$  kg were associated with worse predicted scores in the SGRQ that were twice the minimum clinical important difference (8.1 points).

**Conclusion:** Extrapulmonary features including physical activity, systemic inflammation and isometric leg strength, have a significant clinical impact on HRQoL in severe asthma and bronchiectasis, and may represent additional treatment targets to improve HRQoL.

TO 074

TO 075

### TREATABLE TRAITS PREDICT HEALTH STATUS AND TREATMENT RESPONSE IN AIRWAYS DISEASE

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**Introduction/Aim:** Treatable traits has been proposed as a new paradigm for airway disease management; traits are systemically assessed and treatment targeted accordingly. Given complex multi-morbidity of many patients and finite time and resources, identifying the treatments that provide “bang for buck” in terms of health impact is paramount. Our aim was to identify which treatments delivered during individualised management clinical trials most substantially influence health-related quality of life (HRQoL).

**Methods:** We pooled data from two parallel-group clinical trials of multidimensional assessment and individualised management versus usual care control for airway diseases (COPD[1] and severe asthma [2]) (intervention N=45; control N=46; 59% female; mean age 60yrs). Patients underwent multidimensional assessment to characterise up to 24 traits across pulmonary, extrapulmonary and behaviour/risk factor domains. The intervention group received treatments tailored to their expressed traits. We examined associations between traits and HRQoL (St George’s Respiratory Questionnaire) at baseline, and between each trait treatment and change in HRQoL post-intervention using Bayesian Model Averaging (BMA). BMA estimates models for all possible combinations of predictors then generates a weighted average.

**Results:** In both trials, intervention led to a large, significant improvement in HRQoL compared with usual care (Cohen’s  $d=1.19$ ,  $P < .001$ ). Treatable traits most substantially associated with poorer baseline HRQoL were dysfunctional breathing (mean standardised coefficient  $\pm$  SD  $0.35 \pm 0.10$ ), frequent chest infections ( $0.26 \pm 0.10$ ), depression ( $0.19 \pm 0.13$ ) and mucus hypersecretion ( $0.15 \pm 0.11$ ). Treatments for systemic inflammation ( $-0.39 \pm 0.20$ ), eosinophilic airway inflammation ( $-0.07 \pm 0.12$ ), exercise tolerance ( $-0.06 \pm 0.11$ ) and smoking ( $-0.05 \pm 0.10$ ) were associated with the largest HRQoL improvements.

**Conclusion:** Extrapulmonary traits featured prominently in predicting cross-sectional HRQoL impairment and treatment response. This study contributes to identifying treatable traits that matter. Traits associated with HRQoL impairment differed from those associated with the greatest improvements when treated, suggesting that these traits matter in different ways.

**Grant Support:** GlaxoSmithKline.

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### MACRONUTRIENT EFFECTS ON BRONCHODILATOR RESPONSIVENESS IN OBESE ASTHMA

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**Introduction/Aim:** Obesity in asthma is associated with worse symptoms despite increased use of asthma medications, including bronchodilators. We aimed to examine the effect of dietary macronutrient overload on response to the bronchodilator, salbutamol, in the airways of obese and non-obese asthmatics.

**Methods:** This was a randomised, crossover, acute feeding study in 23 asthmatic adults (n=12 non-obese, n=11 obese). Subjects fasted overnight, and asthma medications were withheld prior to the 3 study visits. Subjects completed a hypertonic challenge, concluding with the administration of 200mcg salbutamol. Subjects then consumed one of the 3 isocaloric meals enriched with either saturated fatty acids (SFA), n-6 polyunsaturated fatty acids (PUFA) or simple carbohydrates (CHO).

**Results:** Following salbutamol and each meal, FEV<sub>1</sub> (L) improved in non-obese subjects at 2, 3 and 4 hours. However, following the high SFA meal, obese subjects demonstrated no improvement in FEV<sub>1</sub> (L) and had an attenuated FVC (L) over the 4-hour period. In obese asthmatics only, the bronchodilator response was significantly lower following the SFA versus CHO meal ( $\Delta$ FEV<sub>1</sub> (L),  $P = 0.004$ ).

**Conclusion:** A high SFA meal suppressed salbutamol recovery in obese asthmatics. Saturated fatty acid modification in the airways of obese asthmatics may affect salbutamol medication action. The reduced efficacy of  $\beta$ -agonists is a major clinical problem as they are the key rescue medication used when asthmatics experience a life-threatening exacerbation.  $\beta$ -agonists are also used to relieve and prevent exercise-induced asthma, which is necessary to allow safe exercise in this population. Therefore, both obesity and saturated fat intake caused attenuation of salbutamol efficacy. Hence, restriction of dietary saturated fat intake may improve asthma pharmacotherapy action.

**Grant Support:** National Health and Medical Research Council of Australia Project Grant and a Hunter Medical Research Institute project grant sponsored by the Piggott family.

TO 076

TO 077

### TRANSCRIPTOMIC GENE SIGNATURES IN ADULTS WITH SEVERE ASTHMA: AN ANALYSIS OF U-BIOPRED STUDY AND PRC HEALTHY LUNGS MIAD STUDY

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**Introduction/Aim:** About 10% of the population with asthma suffer from severe asthma (SA). More than 60% of the asthma health care spending goes towards the management of SA patients mainly due to the lack of therapies that target the heterogeneity of asthma. A better understanding of mechanisms driving the severity of asthma is necessary. We aimed to identify mechanisms of pathogenesis involve in the wider population with SA by performing a comparison of differentially expressed genes and gene set pathway identification in endobronchial biopsies of subjects with SA and healthy controls (HC) from the European U-BIOPRED study and the MIAD study.

**Methods:** We performed microarray analysis in mRNA from endobronchial biopsies of adult subjects with SA according to ERS/ATSA guidelines. Gene Set Variation Analysis (GSVA) was performed and data analysed using R and Stata.

**Results:** We performed gene expression analysis in 53 UBIO adults and 49 MIAD adults with mean FEV<sup>1</sup> % pred of 72 and 73, respectively. All adults with SA were on high dose of ICS and OCS mean dose of 10um daily in both studies included. Comparison of differentially expressed genes identified 16 genes that overlap between the two populations with SA. When performing the GSVA analysis, the overlapping genes were enriched in SA vs. HC in both populations (UBIO  $P = <0.01$ ; MIAD:  $P = <0.01$ ).

We analysed the gene set enrichment for 105 published signatures. We identified four signatures associated with steroid response significantly enriched in subjects with SA vs. HC. We found significant enrichment for a CD4+Tcell signature (UBIO:  $P = 0.02$ ; MIAD:  $P = 0.03$ ) and a mast cell signature (UBIO:  $P = <0.01$ ; MIAD:  $P = <0.01$ ) in SA vs. HC.

**Conclusion:** Our results identified genes and underlying pathways involve in the pathogenesis of SA detectable in two geographically distinct populations with SA.

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### TRANSCRIPTOME-PROFILES ASSOCIATED WITH ATOPIC ASTHMA DETECTABLE IN UPPER/LOWER AIRWAY EPITHELIUM

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**Introduction/Aim:** The airway epithelium plays a critical role in respiratory health, and has been placed at the centre of asthma pathogenesis through both genetic and functional studies. The unified airway hypothesis postulates that vulnerability or dysfunction in the airway epithelium may be reflected throughout the airway. This concept is supported by clinical and experimental evidence, warranting study of upper airway epithelium in the context of lower airway diseases. We aimed to determine whether gene expression changes associated with atopy and or mild asthma were present in both upper and lower airway epithelium in children.

**Methods:** Matched upper and lower airway *ex vivo* epithelial brushings were collected from 63 children with and without atopy or mild asthma. Total RNA was extracted, and mRNA libraries were prepared and sequenced (Hi-Seq200 platform). Sequencing reads were aligned to the human genome, normalised and tested for differential expression between phenotypes in each tissue.

**Results:** Overall, disease associated changes were more prominent in the lower airway, particularly regarding the combined effect of atopy and mild asthma; 340 differentially expressed genes were identified (including several regulators of immune pathways). These disease related changes were partially reflected in nasal epithelium (overlap of 49 genes) including well-characterised asthma risk genes (IL1RL1, PTGS1, CCL26 and POSTN). Through network analysis we identified a cluster of co-expressed genes associated with atopic asthma in the lower airway, which importantly could equally distinguish atopic and non-atopic phenotypes in upper airway samples using unsupervised clustering.

**Conclusion:** Together, our findings demonstrate that disease-associated gene expression changes within epithelium are reflected throughout the airway, including several genes known to be important in asthma. Our findings support view of a unified airway, and the development of biomarker screening using nasal brushings.

**Grant Support:** This work was supported by a grant from Asthma Australia.

### UNDERSTANDING CORTICOSTEROID BIOLOGY USING TRANSCRIPTIONAL PROFILING OF BRONCHIAL BIOPSIES AND CRISPR-CAS9 KO MODELS

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**Introduction/Aim:** Corticosteroids are known for their anti-inflammatory effects in asthma and COPD. Severe asthma and COPD share common pathophysiologic traits such as airflow obstruction and corticosteroid insensitivity. We aimed to investigate genes upregulated by corticosteroid treatment and to determine their functional role in corticosteroid resistance.

**Methods:** A meta-analysis of 4 studies (Healthy (GSE83233 n = 11), Asthma (MAST n = 12, SAGE n = 20), COPD (GLUCOLD n = 26)) was conducted on bronchial biopsies matched for pre-and post-corticosteroid treatment. From this analysis, the top candidate gene was chosen to be knocked out in the lung epithelial cell line A549 using CRISPR-Cas9. To identify the functional role, glucocorticoid receptor (GR) and NFκB reporter assay and ELISA for the pro-inflammatory cytokine CXCL8 were performed on knock-out cells treated with Fluticasone Propionate (FP) 10-8 M (n = 6).

**Results:** The meta-analysis identified 93 genes increased and 170 genes decreased by corticosteroids (meta Bonferroni adjusted  $P < 0.05$ ). FKBP5, identified as the most significantly increased gene, was knocked out in A549 cells using CRISPR-Cas9. In the absence of FKBP5, the GR reporter activity increased ~6x further upon FP treatment ( $P < 0.05$ ) compared to wildtype, while the NFκB reporter assay was decreased at baseline. Additionally, the effectiveness of FP to suppress CXCL8 release upon TNFα stimulation was enhanced in the FKBP5 knockout compared to control A549 cells ( $P < 0.05$ ).

**Conclusion:** Based on our findings we propose that the expression of FKBP5 not only acts to suppress corticosteroid function but also aids in the activation of the NF-κB signalling leading to enhanced inflammation. This dual function of FKBP5 indicates that it plays an important role in regulating the function of inflammatory during corticosteroid treatment. Therefore, FKBP5 provides a novel therapeutic target to improve corticosteroid sensitivity.

**Grant Support:** •

### TRANSFORMING GROWTH FACTOR-BETA INCREASES AIRWAY FIBROSIS AND REACTIVITY TO METHACHOLINE

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**Introduction/Aim:** Transforming growth factor-beta (TGFβ) is a pleiotropic cytokine involved in a multitude of processes including wound healing and fibrosis. It is central to chronic lung diseases such as asthma and chronic obstructive pulmonary disease (COPD). Bronchoconstriction results in the release of TGFβ, but the potential autocrine effects of this increased TGFβ on airway contraction remains unknown. This study hypothesised that TGFβ leads to increased airway reactivity to methacholine (MCh).

**Methods:** We utilised a transgenic mouse model that over-expresses active TGFβ specifically in the lungs following doxycycline (Dox) administration. Dox was added to the drinking water for 8 weeks prior to experimentation, with normal water given to control mice. Lung plethysmography was used to measure airway resistance *in vivo*, before serum and BAL were collected for TGFβ ELISA. Formalin-fixed paraffin-embedded sections were also prepared, dewaxed and scanned using the Histoindex for analysis of collagen using Fibroindex. Separate control and Dox mice were used to prepare Precision Cut Lung Slice (PCLS) for *in vitro* methacholine challenge.

**Results:** Dox treatment to induce TGFβ over-expression increased TGFβ levels in BAL, but not serum. This was associated with ~25% higher lung collagen deposition, predominantly localised around the airways. TGFβ over-expression increased *in vitro* contraction of intrapulmonary airways to MCh (maximum %reduction in airway area: control 41 ± 5%; Dox 75 ± 9%; n = 5/group,  $P < 0.05$ ).

**Conclusion:** Elevated TGFβ levels in the lung results in greater airway contraction to MCh, despite increased airway fibrosis. This model can now be used to provide insights into the mechanisms underlying the potential contribution of TGFβ to airway hyperresponsiveness, and may identify novel therapeutic targets to oppose excessive airway contraction in chronic lung diseases.

**Grant Support:** nil

TO 080

TO 081

**HYPOXIA-INDUCED REDUCTION IN NO SIGNALLING AS WELL AS INCREASED OXIDATIVE STRESS AND INFLAMMATION ARE ASSOCIATED WITH DYSREGULATED ZINC HOMEOSTASIS IN ENDOTHELIAL CELLS**

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**Introduction/Aim:** Cardiovascular-related comorbidities are important contributors to morbidity and mortality in lung inflammatory diseases. Zinc homeostasis has vital physiological functions and we have shown its dysregulation in the epithelium and alveolar macrophages in COPD and in response to cigarette smoke. However, its role underlying vasculature dysfunction/inflammation are unknown. We hypothesised that hypoxia, a known pathologic factor in PAH, CF and COPD, induces oxidative stress, inflammation and downregulates NO signalling in airway microvasculature endothelia in association with dysregulated zinc homeostasis.

**Methods:** Expression and localization of zinc transporters (ZIPs), metallothioneins (MTs), eNOS and other markers were visualised by IF/confocal microscopy in microvasculature of human skin biopsies and in a human microvascular endothelial cell (HMVEC) line. Subcultures of HMVEC were exposed to hypoxia for 24h before secreted NO was measured by Griess assay, intracellular labile zinc by Zinpyr-1 dye and the mRNA expression of ZIPs, MTs and eNOS were also measured by RT-PCR. Unless particularly specified, changes are reported as averages from at least 3 independent experiments, for each of which  $P < 0.05$ .

**Results:** Differential expression and localization of ZIPs and MTs was shown in endothelia vs. smooth muscle of human microvasculature. In HMVEC, hypoxia significantly up-regulated protein markers of oxidative stress (MDA and PARP) and inflammation (NLRP3 and cleaved IL-1 $\beta$ ), down-regulated eNOS protein (57.3%) and mRNA (~2 fold in 2 experiments), eNOS phosphorylation at the Ser1117 residue (57.9%). Reduced protein expression of MT1/2 (31.2%), MT3 (48.5%), ZIP1 (25.1%), ZIP8 (28.6%) and ZIP12 (30.1%) was accompanied with ZIPs' disappearance from the plasma membrane, lamellipodia and filopodia.

**Conclusion:** We show for the first time that hypoxia-induced oxidative stress, inflammation and down-regulated NO signalling in endothelial cells is associated with zinc dyshomeostasis. Our findings support zinc signalling in vascular endothelium as a potential therapeutic target in hypoxia-related airway inflammatory diseases.

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**DOES PULMONARY REHABILITATION AGGRAVATE OR RELIEVE PAIN IN PEOPLE WITH COPD AND CHRONIC PAIN?**

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**Introduction/Aim:** Chronic pain can affect up to 88% of people with chronic obstructive pulmonary disease (COPD) and is an identified reason for not completing pulmonary rehabilitation. However, the effect of pulmonary rehabilitation on the pain intensity and pain coping ability in COPD is unknown. This study aimed to 1) determine the effect of pulmonary rehabilitation on pain qualities, pain coping behaviour and psychological symptoms in those with COPD and chronic pain and 2) compare the impact of pulmonary rehabilitation on exercise capacity and quality of life between individuals with COPD and chronic pain compared to those without pain.

**Methods:** Participants with moderate to severe COPD (with and without chronic pain at initial assessment) enrolled in a pulmonary rehabilitation program undertook measures of exercise capacity and quality of life before and after rehabilitation. Those with chronic pain also completed the Brief Pain Inventory, Coping Strategy questionnaire and the Hospital Anxiety and Depression scale before and after the program.

**Results:** Thirty-two participants with chronic pain and 33 participants without pain were included (mean  $\pm$  SD age 71  $\pm$  10 years; FEV<sub>1</sub> 46.6  $\pm$  18.4% predicted). In those with chronic pain, pulmonary rehabilitation did not affect pain intensity (median[IQR] 5[3-8] vs 5[3-7] points,  $P = 0.599$ ), coping ability (72[51-85] vs 61[51-82] points,  $P = 0.939$ ), anxiety (3[1-7.5] vs 5[3-9] points,  $P = 0.57$ ) or depression (5[3-7] vs 4[2-8] points,  $P = 0.32$ ). Both groups improved in exercise capacity (mean difference[95% CI] 44[-1.17-86] m), but those without pain had greater improvement in fatigue ( $P = 0.001$ ), emotional function ( $P = 0.005$ ) and mastery ( $P < 0.001$ ) compared to those with pain.

**Conclusion:** In individuals with COPD and chronic pain, pulmonary rehabilitation neither worsened nor improved pain intensity, and had no effect on pain coping ability or psychological symptoms. However, those with chronic pain had less improvement in quality of life compared to individuals without pain.

**Grant Support:** Ontario Respiratory Care Society



### FEASIBILITY AND REPRODUCIBILITY OF THE MODIFIED INCREMENTAL STEP TEST FOR PULMONARY REHABILITATION

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**Introduction/Aim:** Assessment of exercise capacity prior to pulmonary rehabilitation currently necessitates a visit to a healthcare centre, even for home-based programs. A modified incremental step test (MIST) that can be performed in the home setting may facilitate entirely home-based programs. However its utility has not been investigated. The aims of this study were to investigate: (1) the feasibility of the MIST as part of baseline pulmonary rehabilitation assessment, and (2) the reproducibility of the MIST in centre and home-based settings in people with stable chronic obstructive pulmonary disease (COPD).

**Methods:** Two MISTs (standardised protocol) were undertaken at the centre and home in random order prior to commencement of pulmonary rehabilitation. Feasibility was determined by the number of eligible patients who could undertake the test. Reproducibility was assessed using intraclass correlation coefficient (ICC)<sub>2,1</sub> and the Bland and Altman method.

**Results:** Twelve participants were recruited from 13 eligible patients (age mean 74 ± SD 8 years, FEV<sub>1</sub> 58 ± 19 %predicted, 8 male, 6MWD 395 ± 138 metres) out of 34 patients screened (36%). Reasons for exclusion were inability to perform the test due to use of gait aid (n=10), comorbidities precluding test performance (n = 7) and unsuitable home environment (n=4). Mean results for centre-based MIST were 40 (27) steps and home-based MIST 45 (34) steps (mean difference 5 [95%CI -2 to 12] steps). Excellent reproducibility was demonstrated (ICC<sub>2,1</sub> 0.93 [95%CI 0.78 to 0.98], *P* < 0.001) with limits of agreement -18 to 28 steps.

**Conclusion:** These preliminary results demonstrate reproducibility of the MIST as part of a home-based pulmonary rehabilitation assessment in people with COPD.

**Grant Support:** AB: NHMRC postgraduate scholarship, HITH Society Australasia Dr Nicholas Collins Fellowship. SDC: FAPESP SPRINT 17/50273-4.

### COMPARISON OF HEALTHCARE UTILISATION USING SELF-REPORT AND ADMINISTRATIVE DATA IN PEOPLE WITH COPD FOLLOWING PULMONARY REHABILITATION

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**Introduction/Aim:** The optimal method to collect accurate healthcare utilisation data in people with chronic obstructive pulmonary disease (COPD) is not well established. The aim of this study was to determine feasibility and accuracy of self-report methods compared to administrative records for healthcare utilisation in people with COPD for 12 months following pulmonary rehabilitation.

**Methods:** This is a secondary analysis of a randomised controlled equivalence trial comparing centre-based and home-based pulmonary rehabilitation. Healthcare utilisation data were collected for 12 months following pulmonary rehabilitation from administrative sources (Medicare Benefits Schedule, medical records) and self-report (monthly telephone questionnaires and diaries) for all health care contacts. Feasibility was assessed by the proportion of self-reports completed and accuracy was established using month-by-month and per participant comparison with administrative data.

**Results:** Data were available for 145 participants (age mean (standard deviation (SD)) 69(9) years, forced expiratory volume in one second 51(19) %predicted; n=83 male). For 1725 months where data collection was possible, 1160 (67%) telephone questionnaires and 331 (19%) diaries were completed. Accuracy of recall varied according to type of health care contact and self-report method, being higher for telephone questionnaire report of emergency department presentation (Kappa 0.656, *P* < 0.001; sensitivity 81%, specificity 96%) and hospital admission (Kappa 0.669, *P* < 0.001; sensitivity 72%, specificity 97%) and lower for general practitioner (Kappa 0.400, *P* < 0.001; sensitivity 77%, specificity 63%) and medical specialist appointments (Kappa 0.458, *P* < 0.001; sensitivity 72%, specificity 80%).

**Conclusion:** For self-reported methods of healthcare utilisation in people with COPD following pulmonary rehabilitation, monthly telephone questionnaires were more frequently completed and more accurate than diaries. Compared to administrative records, self-reports of emergency department presentations and inpatient admissions were more accurate than for general practitioner and medical specialist appointments.

**Grant Support:** Lung Foundation Australia / Boehringer Ingelheim COPD Research Fellowship, NHMRC APP1046353.

TO 084

TO 085

### CHARACTERISTICS OF SEDENTARY BEHAVIOUR IN PEOPLE WITH COPD

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**Introduction/Aim:** People with chronic obstructive pulmonary disease (COPD) are known to spend more time sitting and lying down than their healthy peers (Pitta et al, 2005). This study aimed to characterise sedentary behaviour in people with COPD living in metropolitan Sydney using subjective and objective methods.

**Methods:** This was a cross-sectional study of people with COPD recruited from the waiting lists of five pulmonary rehabilitation programs in metropolitan Sydney. Objective sedentary time was measured using a thigh-worn activPAL3 micro tri-axial accelerometer/inclinometer (PAL Technologies, Scotland) for seven days, 24 hours per day. If sedentary time was  $\geq 70\%$  of total waking wear time, participants were considered to be 'sedentary'. Self-reported sedentary time was measured using the Sedentary Behaviour Questionnaire (SBQ).

**Results:** 52 people with COPD (mean (SD) age 73 (10) years, mean FEV<sub>1</sub> 57 (19) % predicted, 48% male) had at least four days of valid activPAL monitor data. Average objective sedentary time was 10.5 (1.8) hours/day (71 (11) % of total waking wear time), of which 6.3 (2.4) hours/day were accumulated in prolonged bouts of  $\geq 30$  minutes. Thirty-one participants (60%) were regarded as being sedentary. The most commonly reported sedentary behaviour on the SBQ was television (TV) viewing, with an average TV viewing time of 3.5 (1.5) hours/day. Self-reported daily sedentary time was significantly lower than when measured objectively by the activPAL monitor (mean difference -2.0 hours, 95% CI -3.0 to -1.1).

**Conclusion:** Over half of the participants in this cohort were sedentary. Behaviour change strategies that target TV viewing is one potential intervention to reduce sedentary behaviour in people with COPD.

**Grant Support:** Nil. **Declaration of interest:** Nil. **Nomination for awards:** Physiotherapy.

### IS <5000 STEPS/DAY IS A GOOD INDICATOR OF SEDENTARY BEHAVIOUR IN COPD?

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**Introduction/Aim:** In adults, a step count of <5000 steps/day is a widely accepted indicator of a sedentary lifestyle. This study aimed to determine whether <5000 steps/day was an indicator of sedentary behaviour in people with chronic obstructive pulmonary disease (COPD) compared to objectively-measured sedentary time.

**Methods:** Cross-sectional study of people with COPD recruited from the waiting lists of five pulmonary rehabilitation programs in metropolitan Sydney. Daily step count and sedentary time were measured using a thigh-worn activPAL3 micro tri-axial accelerometer/inclinometer (PAL Technologies, Scotland) for seven days, 24 hours per day. The estimated measure of 'sedentary' was a step count of <5000 steps/day. The 'true' measure of 'sedentary' was a sedentary time of  $\geq 70\%$  of total waking wear time. The sensitivity, specificity and accuracy of the estimation of 'sedentary' was calculated by comparing the number of participants identified using the 'true' measure of sedentary. Exercise capacity was measured using the six-minute walk test.

**Results:** 52 people with COPD (mean (SD) age 73 (10) years, mean FEV<sub>1</sub> 57 (19) % predicted, 48% male) had at least four days of valid wear data. Average sedentary time was 10.5 (1.8) hours/day, which comprised 71 (11) % of total waking wear time; average step count was 4812 (2647) steps/day; and average six-minute walk distance was 363 (96) metres. A moderate association was found between step count and sedentary time ( $r = -0.64$ ,  $P < 0.01$ ). Of 32 participants with <5000 steps/day, 81% were correctly identified as sedentary, resulting in a sensitivity of 84%, a specificity of 65%, and an accuracy of 76%.

**Conclusion:** The majority of people with COPD in this cohort had a low step count and high sedentary time. In the absence of objectively measured sedentary time, a step count of <5000 steps/day may be a reasonable indicator of sedentary behaviour in people with COPD.

**Grant Support:** Nil. **Declaration of interest:** Nil. **Nomination for awards:** Physiotherapy.

### EXERCISE EFFECTS ON SALIVARY IGA DURING PULMONARY REHABILITATION IN PATIENTS WITH COPD

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**Introduction/Aim:** Chronic obstructive pulmonary disease (COPD) is characterised by exacerbations of respiratory disease. In healthy individuals, moderate intensity exercise training has been linked to improvement in mucosal immunity. The aim of this proof of concept trial was to determine the effect of 8-weeks supervised pulmonary rehabilitation on secretory immunoglobulin A (SIgA) in the saliva of people with COPD.

**Methods:** Saliva samples from individuals with COPD (FER<70) and smoking history  $\geq 10$  pack years were collected via passive drool pre- and post- an 8-week pulmonary rehabilitation program. SIgA was analysed using an enzyme-linked immunosorbent assay (ELISA). Blood contamination was determined by detection of haemoglobin in saliva on dipstix analysis. Functional capacity and symptoms were assessed using standard measures.

**Results:** 35 people with COPD (n = 13 male, n = 8 current smokers) were recruited with mean (SD) age 70 (10) yrs, FEV<sub>1</sub> 55 (18) %predicted and smoking history 45 (19) pack years. Twenty-three individuals (66%) completed pulmonary rehabilitation ( $\geq 11$  sessions) and achieved significant improvements in 6-minute walk distance (mean  $\Delta 23$ m,  $P = 0.04$ ), chronic respiratory disease questionnaire dyspnoea scale ( $\Delta 5.2$ ,  $P < 0.01$ ) and COPD Assessment Test ( $\Delta 4$ ,  $P = 0.007$ ). Of 58 saliva samples collected (n = 34 baseline) the vast majority (84%) were contaminated with blood and unable to be meaningfully analysed for SIgA. Therefore the effect of exercise training during pulmonary rehabilitation on SIgA was unable to be determined using the passive drool collection technique.

**Conclusions:** These preliminary data suggest that while pulmonary rehabilitation was effective, assessment of immune response to exercise in people with COPD using salivary IgA was not feasible. Common COPD comorbidities and medication use, as well as oral health, may contribute to the contamination of saliva samples. Further investigation of the impact of pulmonary rehabilitation on immune responses and exacerbation risk for individuals with COPD, using alternative biomarkers, should be considered.

**Grant Support:** LFA-Ludwig Engel Physiology Grant-in-Aid. NSC is the holder of an NHMRC early career fellowship.

### PHASE 2 SAFETY AND EFFICACY: CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR (CFTR) MODULATOR REGIMEN VX-445/TEZACAFTOR (TEZ)/IVACAFTOR (IVA)

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**Introduction/Aim:** CF patients with *F508del*/minimal function (*F/MF*) genotypes do not have approved CFTR modulator therapy. Adding a next-generation CFTR corrector to a corrector/potentiator regimen may substantially improve CFTR function in *F/MF* patients and enhance benefit over two-drug regimens in *F508del*/*F508del* (*F/F*) patients. Objective: evaluate *in vitro* efficacy and clinical safety and efficacy of VX-445, an investigational next-generation CFTR corrector, in triple combination (TC) with TEZ and IVA, or TEZ and VX-561 (deuterated IVA) in CF patients with *F/MF* or *F/F* genotypes.

**Methods:** Effects of TC on CFTR processing/trafficking/function were evaluated in bronchial epithelial cells from *F/MF* or *F/F* donors. TC regimens were evaluated in *F/MF* or *F/F* patients for up to 4 weeks, the latter after 4 weeks of TEZ/IVA run-in. Primary endpoints were safety and absolute change in ppFEV<sub>1</sub> from baseline (in *F/F* patients, after TEZ/IVA run-in). Sweat chloride and CF Questionnaire Revised (CFQR) respiratory domain score were secondary endpoints; reported *P* values are nominal for these endpoints as no multiplicity adjustment was performed. Data included are through last patient's last visit.

**Results:** VX-445/TEZ/IVA improved CFTR processing/trafficking and chloride transport more than TEZ/IVA *in vitro*. Both TC regimens were efficacious (Table), generally safe and well tolerated in *F/MF* and *F/F* cohorts; most adverse events (AEs) were mild/moderate. Of 95 TC-treated patients, four had AEs leading to discontinuation during the treatment period (rash, n=2; chest pain, n=1; increased bilirubin, n=1).

Absolute change (LS mean [SE]) in ppFEV <sub>1</sub> and sweat chloride through day 29 and CFQR respiratory domain at day 29					
		n	ppFEV <sub>1</sub>	Sweat chloride, mmol/L	CFQR respiratory domain <sup>b</sup>
<i>F508del</i> / <i>MF</i> , VX-445/TEZ/IVA	VX-445 50 mg qd + TEZ/IVA	10	11.1 (2.1)*	-38.2 (4.2)*	20.8 (5.4) <sup>†</sup>
	VX-445 100 mg qd + TEZ/IVA	22	7.9 (1.4)*	-33.2 (2.8)*	15.4 (3.7)*
	VX-445 200 mg qd + TEZ/IVA	21	13.8 (1.4)*	-39.1 (2.9)*	25.7 (3.7)*
	Placebo	12	0.0 (2.0)	-2.2 (3.9)	4.2 (4.9)
<i>F508del</i> / <i>MF</i> , VX-445/TEZ/VX-561	VX-445 200 mg qd + TEZ/VX-561	21	11.7 (1.6)*	-33.6 (2.8)*	20.2 (4.3)*
	Placebo	8	1.2 (2.6)	1.0 (4.6)	20.2 (6.9)
<i>F508del</i> / <i>F508del</i> <sup>a</sup> , VX-445/TEZ/IVA	VX-445 200 mg qd + TEZ/IVA	21	11.0 (1.5)*	-39.6 (2.8)*	20.7 (4.0)*
	Placebo + TEZ/IVA	7	0.4 (2.8)	0.8 (4.9)	5.2 (7.1)

\* $P < 0.0001$  within group; <sup>†</sup> $P = 0.0003$  within group

<sup>a</sup>*F/F* patients had a 4-week run-in with TEZ/IVA before treatment with VX-445 + TEZ/IVA or placebo + TEZ/IVA; <sup>b</sup>MMRM not adjusted for baseline CFQR respiratory domain. Doses for TEZ: 100 mg qd; IVA: 150 mg q12h; VX-561: 150 mg qd

**Conclusion:** VX-445 TC regimens demonstrated robust, consistent and clinically meaningful improvements in *F/MF* patients, in whom previous modulator regimens have not shown efficacy, and in *F/F* patients beyond those of TEZ/IVA alone. Further development of VX-445 TC in Phase 3 is ongoing.

**Grant Support:** Sponsored by Vertex Pharmaceuticals Incorporated.

**PHASE 2 SAFETY AND EFFICACY: CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR (CFTR) MODULATOR REGIMEN VX-659/TEZACAFTOR(TEZ)/IVACAFTOR(IVA)**

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**Introduction/Aim:** CF patients with *F508del*/minimal function (*F/MF*) genotypes lack approved CFTR modulator therapy. Adding a next-generation CFTR corrector to a corrector/potentiator regimen may substantially improve CFTR function in *F/MF* patients and enhance benefit over two-drug regimens in *F508del*/*F508del* (*F/F*) patients. Objective: evaluate *in vitro* efficacy and clinical safety and efficacy of VX-659, an investigational next-generation CFTR corrector, in triple combination (TC) with a corrector and potentiator, TEZ and IVA or TEZ and VX-561 (deuterated IVA).

**Methods:** Effects of VX-659/TEZ/IVA on CFTR processing/function were evaluated in bronchial epithelial cells from *F/MF* or *F/F* donors. VX-659/TEZ/IVA and VX-659/TEZ/VX-561 were evaluated in Phase 1/2 trials in *F/MF* or *F/F* patients for up to 4 weeks, after 4-week TEZ/IVA run-in in *F/F* patients. Primary endpoints were safety and absolute change in ppFEV<sub>1</sub> from baseline (in *F/F* patients, after TEZ/IVA run-in). Secondary endpoints were change in sweat chloride and CF Questionnaire Revised (CFQR) respiratory domain score; reported *P* values are nominal for these endpoints as no multiplicity adjustment was performed. Data included are through last patient's last visit.

**Results:** VX-659/TEZ/IVA improved CFTR processing/trafficking and chloride transport more than TEZ/IVA *in vitro*. Both TC regimens were efficacious (Table), generally safe and well tolerated; most adverse events (AEs) were mild/moderate. One patient on VX-659/TEZ/VX-561 discontinued due to an AE (drug hypersensitivity).

Absolute change (LS mean [SE]) in ppFEV <sub>1</sub> and sweat chloride through day 29 and CFQR respiratory domain at day 29					
		n	ppFEV <sub>1</sub>	Sweat chloride, mmol/L	CFQR respiratory domain <sup>a</sup>
<i>F508del</i> /MF, VX-659/TEZ/IVA	VX-659 80 mg qd + TEZ/IVA	11	10.2 (2.7) <sup>*</sup>	-45.7 (4.3) <sup>†</sup>	24.6 (5.8) <sup>‡</sup>
	VX-659 240 mg qd + TEZ/IVA	20	12.0 (2.0) <sup>†</sup>	-43.8 (3.4) <sup>†</sup>	19.8 (4.4) <sup>‡</sup>
	VX-659 400 mg qd + TEZ/IVA	22	13.3 (1.9) <sup>†</sup>	-51.4 (3.2) <sup>†</sup>	21.8 (4.1) <sup>‡</sup>
	Placebo	10	0.4 (2.8)	2.9 (4.6)	4.7 (6.1)
<i>F508del</i> /MF, VX-659/TEZ/VX-561	VX-659 400 mg qd + TEZ/VX-561	19	12.2 (1.9) <sup>†</sup>	-38.1 (3.0) <sup>†</sup>	14.7 (3.7) <sup>‡</sup>
	Placebo	6	-5.0 (3.4)	-1.3 (5.3)	-4.1 (6.6)
<i>F508del</i> / <i>F508del</i> <sup>a</sup> , VX-659/TEZ/IVA	VX-659 400 mg qd + TEZ/IVA	18	9.7 (1.5) <sup>†</sup>	-42.2 (2.2) <sup>†</sup>	19.5 (3.1) <sup>‡</sup>
	Placebo + TEZ/IVA	11	0.0 (1.9)	3.0 (2.8)	2.9 (4.0)

<sup>\*</sup>*P*≤0.0004 within group; <sup>†</sup>*P*≤0.0001 within group; <sup>‡</sup>*P*≤0.0006 within group  
<sup>a</sup>*F/F* patients had a 4-week run-in with TEZ/IVA before treatment with VX-659 + TEZ/IVA or placebo + TEZ/IVA; <sup>b</sup>MMRM not adjusted for baseline CFQR respiratory domain. Doses for TEZ: 100 mg qd; IVA: 150 mg q12h; VX-561: 200 mg qd

**Conclusion:** This proof-of-concept study demonstrated robust, consistent and clinically meaningful improvements with VX-659 TC regimens in *F/MF* patients, in whom previous modulator regimens have not shown efficacy, and in *F/F* patients beyond those of TEZ/IVA alone. Phase 3 studies are ongoing to support further development of VX-659 TC regimens.

**Grant Support:** Sponsored by Vertex Pharmaceuticals Incorporated.

**INFECTION CONTROL PRACTICES USED IN CYSTIC FIBROSIS CENTRES IN AUSTRALIA AND NEW ZEALAND**

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**Introduction/Aim:** The cystic fibrosis (CF) infection control guidelines have recently been updated (Saiman *et al*, Infect Control Hosp Epidemiol. 2014) and provide recommendations to prevent cross-infection. In this study, we investigated the current infection control practices used in CF centres in Australia and New Zealand.

**Methods:** Two online surveys were distributed to Australian and New Zealand CF centres: one survey for completion by the Medical Directors and CF Lead Nurse and the second survey for completion by the CF Lead Physiotherapists.

**Results:** The response rate was 60% (60/100) for medical/nursing and 58% (14/24) for physiotherapy.

The key findings were:

- **CF-specific infection control policies** were used in almost all CF centres (medical/nursing, 92%; physiotherapy, 100%).
- **Segregation strategies:** Inpatient accommodation provided for people with CF was predominantly single rooms with en-suites (47%). Segregation systems were in place for most (68%) outpatient clinics and all exercise sessions.
- **Mask policy:** 60% of CF centres had implemented a patient mask-wear policy. Centres providing care to children were more likely to have implemented a mask policy (67%). Surgical masks were the preferred interface (medical/nursing, 92%; physiotherapy, 91%).
- **Contact precautions:** The uptake of healthcare workers using personal protective equipment was variable when entering rooms of people with CF (regardless of infection status) (medical/nursing, 22%; physiotherapy, 43%) and during outpatient clinics (medical/nursing, 13%; physiotherapy, 36%).
- **Cleaning:** Inpatient rooms were cleaned daily in most (62%) CF centres. Most (72%) CF centres had implemented a cleaning procedure for outpatient clinics. The gym was always cleaned between patients.

**Conclusion:** The results of the survey highlight that variable infection control practices are used in CF centres in Australia and New Zealand. We anticipate that this survey will assist in standardising infection control practices used in CF centres.

**Grant Support:** CF Foundation Therapeutics (USA), The Prince Charles Hospital Foundation, Advance Queensland.

**AUSTRALIAN ADULTS WITH CYSTIC FIBROSIS COMMONLY USE EXERCISE AS AN ALTERNATIVE TO TRADITIONAL AIRWAY CLEARANCE TECHNIQUES: A NATIONAL SURVEY**

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**Introduction/Aim:** Some people with cystic fibrosis (CF) consider exercise as an alternative to traditional airway clearance techniques (ACTs). The type, frequency, duration and intensity of exercise that people with CF use instead of traditional ACTs has not been described. The aim of this study was to identify the beliefs and practices of adults with CF regarding the use of exercise as an alternative to traditional ACTs.

**Methods:** Adults with CF from all Australian CF centres were invited to complete a purpose-designed questionnaire examining their beliefs and practices regarding exercise as an alternative to traditional ACTs. Demographic data, including the participants' self-perceived severity of respiratory disease assessed by visual analogue scale were recorded. Data are presented as mean  $\pm$  SD, with significance  $P < 0.05$ .

**Results:** 758 eligible people were approached to participate, with 692 (91%) completing the survey (57% male,  $31.1 \pm 10.5$  years,  $FEV_{1\text{pred}} 63 \pm 23\%$ ). There were 43% who agreed/strongly agreed that exercise could be used as an alternative to traditional ACTs. Beliefs about the role of exercise for airway clearance were based on personal experience (85%), advice from an unspecified health professional (12%) and advice from a physiotherapist (7%). Exercise had been used as an alternative to traditional ACTs by 44% of participants in the last three months, with these participants having significantly better  $FEV_{1\text{pred}}$  ( $68 \pm 22\%$  vs  $60 \pm 24\%$ ,  $P < 0.001$ ) and lower perceived severity ( $3.4 \pm 2.3$  vs  $4.2 \pm 2.5$  cms,  $P < 0.001$ ) than those who had not.

**Conclusion:** Exercise was utilised by 44% of the participants as an alternative to traditional ACTs, particularly in those with milder disease. Further research is required to investigate the efficacy of exercise as an alternative to traditional ACTs.

**Grant Support:** This study was supported by an Australian Government Research Training Program Scholarship.

**AIRWAY CLEARANCE AND EXERCISE PRACTICES OF ADULTS WITH CYSTIC FIBROSIS: CURRENT AUSTRALIAN PRACTICE.**

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**Introduction/Aim:** While previous research has identified differences between countries in the airway clearance (ACT) and exercise routines performed by people with cystic fibrosis (CF), the routines of adults with CF across Australia have not been investigated. The aim of this study was to document the ACT and exercise routines of Australian adults with CF.

**Methods:** Recruitment was open for three months at all Australian adult CF centres, with participants completing a purpose-designed questionnaire examining their ACT and exercise routines over the preceding three months. Demographic data, including the participants' self-perceived respiratory disease severity and sputum quantity measured on visual analogue scales (0 = not severe at all/no sputum, 10 = extremely severe/extreme amount of sputum) were collected. Data are presented as means  $\pm$  SDs.

**Results:** 758 eligible people were approached, with 692 (91%) completing the survey (57% male,  $31.1 \pm 10.5$  years,  $FEV_{1\text{pred}} 63 \pm 23\%$ ). The three most common ACTs were: coughing (70%), huffing (59%) and positive expiratory pressure (PEP) (52%). All other ACTs were used by <20% of participants. Most participants performed an ACT on most days of the week (58%). Those not performing any ACT had significantly higher  $FEV_{1\text{pred}}$  (80% vs 62%,  $P < 0.001$ ) and lower perceived severity (1.8 vs 4.0,  $P < 0.001$ ) and sputum quantity (1.6 vs 3.6,  $P < 0.001$ ). Walking (76%), lifting weights (43%) and jogging (37%) were the most common types of exercise, with 72% of participants reporting exercising at least three days/week.

**Conclusion:** Coughing, huffing and PEP are the most commonly used ACTs in Australian adults with CF. Walking is the most common type of exercise. These self-reported data suggest 58% and 72% of participants achieve the recommended frequency for ACT and exercise respectively.

**Grant Support:** This study was supported by an Australian Government Research Training Program Scholarship.

TO 092

TO 093

**PEAK GLUCOSE LEVEL ON 30-MINUTELY OGTT IS ASSOCIATED WITH POORER LUNG FUNCTION AND NUTRITION IN CHILDREN WITH CF <10 YEARS OF AGE**

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**Introduction/Aim:** Cystic Fibrosis-related Diabetes (CFRD) causes more rapid clinical decline in patients with CF and decreases life expectancy. CFRD is usually diagnosed using the 2 hour glucose level during OGTT but increasing evidence suggests that clinical decline occurs prior to OGTT criteria for diabetes being met. The aim of this study was to determine if CF children <10 years of age demonstrated glucose abnormalities on OGTT and whether early elevations in glucose are associated with clinical status.

**Methods:** We analysed the results of 25 CF patients < 10 years undergoing 30minutely OGTT. We evaluated the association between peak glucose level and 120minute glucose level with lung function and nutritional parameters.

**Results:** The peak glucose level on OGTT was higher than the 2 hour level in 23/25 (92%) participants evaluated. There was a significant negative correlated between peak glucose and weight z-score ( $r_s = -0.54$ ,  $P = 0.006$ ) and peak glucose and FEV<sub>1</sub> ( $r_s = -0.65$ ,  $P = 0.003$ ) but no significant correlation with 2 hour blood glucose level was identified (weight  $r_s = -0.26$ ,  $P = 0.2$ ; FEV<sub>1</sub>  $r_s = -0.13$ ,  $P = 0.61$ ).

**Conclusion:** The 2 hour glucose level was not elevated in the majority of CF patients <10 years of age having OGTT. However, children did demonstrate high glucose levels at earlier time-points that correlated with clinical status. The OGTT may not be the appropriate test to use in this cohort to identify hyperglycaemia-related clinical decline.

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**IDENTIFYING CORRELATIONS BETWEEN DIETARY INTAKES AND MICROBIOTA IN CYSTIC FIBROSIS**

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**Introduction/Aim:** Respiratory and intestinal dysbiosis in cystic fibrosis (CF) is likely multifactorial and diet is an underexplored microbial modulator. This study aims to explore the 1) interplay between the gastrointestinal/respiratory microbiota and 2) relationship between the CF (high-calorie, high-fat) diet and microbiota.

**Methods:** This is a preliminary cross-sectional analysis of a prospective, longitudinal, observational cohort study at Sydney Children's Hospital Randwick. Children with CF and healthy controls (HC) completed a clinical survey, food frequency questionnaire (ACAES), and provided airway (sputum/oropharyngeal swab) and stool samples. Samples underwent 16s rRNA sequencing (V4 region) and faecal calprotectin was measured. Analyses were performed in RStudio (v3.4.4).

**Results:** 33 CF (16 female (48.5%); median age [IQR]=8.8 [4.6-12.0]) and 27 HC (17 female (63.0%); median age [IQR]=12.6 [10.1-15.1]) subjects were recruited. Respiratory beta diversity PERMANOVA revealed clustering between groups ( $P = 0.009$ ). Stool alpha diversity (Shannon Index) was significantly lower in CF compared with HC (mean (SD) = 2.39 (0.72) vs 3.67 (0.30) respectively;  $P < 0.001$ ). ANCOM stool analysis revealed that CF relative abundances of Enterococcus and Enterobacter were higher, while Akkermansia were lower (FDR < 0.05). Pearson analysis of CF respiratory (s) and stool (s) phyla revealed strong correlations between Candidate division SR1 (r) and Fusobacteria (s) ( $R = 0.92$ ,  $q < 0.001$ ); Deinococcus-Thermus (r) and Deinococcus-Thermus (s) ( $R = 0.85$ ,  $q < 0.01$ ); Euryarchaeota (r) and Proteobacteria (s) ( $R = 0.95$ ,  $q < 0.001$ ); and Tenericutes (r) and Fusobacteria (s) ( $R = 0.99$ ,  $q < 0.001$ ). CF faecal calprotectin was increased compared to HC (mean (SD) = 88.4 (4.8) vs 11.3 (4.8) respectively;  $P = 0.002$ ). CF dietary intake revealed: (i) meat positively correlated with intestinal Cyanobacteria ( $R = 1$ ,  $q < 0.001$ ), (ii) saturated fat positively correlated with calprotectin ( $R = 0.83$ ,  $P = 0.04$ ) and (iii) resistant starch negatively correlated with calprotectin ( $R = -0.83$ ,  $P = 0.04$ ).

**Conclusion:** These preliminary results demonstrate a robust study methodology, providing insight into the gut-lung axis in CF and associated microbial influences. Diet may be associated with alterations in the CF milieu.

**Grant Support:** •

TOL 001

TOL 002

### NECROPTOSIS IS ACTIVATED IN AND DRIVES PATHOGENESIS OF COPD

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**Introduction/Aim:** Necroptosis is a regulated, pro-inflammatory form of necrotic cell death which is executed by Receptor Interacting Protein Kinase 3 (RIPK3) and Mixed Lineage Kinase domain-Like protein (MLKL). COPD involves chronic inflammation of the airways and often features airway remodelling, emphysema and impaired lung function. We assessed the potential contribution of necroptosis-related signalling to COPD pathogenesis.

**Methods:** Wild-type (WT), RIPK3- and MLKL-deficient mice were exposed to cigarette smoke (CS) for 8 weeks. BALF was collected and total and differential leukocytes were enumerated. Histological and immunoblotting analysis of lung tissue was performed. Protein expression levels of RIPK3 and (phosphorylated) MLKL in lungs of never smokers, smokers without airflow obstruction and patients with COPD (GOLD II to IV) were evaluated by immunohistochemistry (IHC) and immunoblotting.

**Results:** RIPK3 and MLKL protein were increased in the lungs of CS-exposed mice. RIPK3- and MLKL-deficient mice had significantly reduced BALF cell counts and reduced airway remodelling and emphysema compared to WT mice. In clinical COPD samples, immunohistochemistry revealed positive staining for RIPK3 and MLKL primarily in airway epithelial cells. Quantification demonstrated significantly increased expression of MLKL but not RIPK3 in airway epithelium of patients with COPD, compared to smokers and never smokers. In addition, phosphorylation of MLKL was significantly increased in lung tissue of patients with severe COPD.

**Conclusion:** Genetic ablation of either RIPK3 or MLKL protected mice against chronic CS-induced airway inflammation, airway remodelling and emphysema, suggesting necroptosis plays an important role in the pathogenesis of experimental COPD. Our clinical data further support this hypothesis, with upregulation and activation of MLKL observed in the lungs and airways of patients with severe COPD. Pharmacological blockade of necroptosis-related signalling should be further investigated as a potential novel therapeutic strategy for COPD.

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### PULMONARY ADVERSE EFFECTS OF SMALL MOLECULE TYROSINE KINASE INHIBITORS: A META-ANALYSIS

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**Introduction/Aim:** Small molecule tyrosine kinase inhibitors (smTKI) are signaling molecules modulating the cytokine receptor-mediated intracellular signal cascade and have proven effective for the treatment of a number of autoimmune diseases and malignancies. As smTKI are novel, long-term safety is uncertain. Commonly reported side effects include infections, particularly of the respiratory tract. As published data mainly examines the molecule tofacitinib, the class effect of smTKI is unknown. We performed a meta-analysis of all published trial data on the pulmonary adverse effects of smTKIs.

**Methods:** EMBASE, MEDLINE, and CENTRAL databases were searched up to September 2018 for randomized controlled trials, observational studies, case reports, and post-marketing surveillance, comparing any smTKI with placebo or another therapy, or as monotherapy at different doses. Primary outcomes comprised of any respiratory complications including upper and lower respiratory tract infections, influenza, opportunistic respiratory infections, pneumonia, interstitial pneumonitis, pulmonary embolism, and lung neoplasm.

Meta-analysis of RCTs was performed using risk difference. Odds ratio could not be calculated in a number of trials, as there were many zero incidences. Observational studies and open label extension events were expressed as incidence per 100-patient years.

**Results:** We identified 2253 citations for screening, and selected 150 for full text review. Seventy-five studies were analyzed, including 49 RCTs, 16 observational studies, three case reports, and seven post-marketing surveillance, comprising 153,942 participants. Mean duration of RCTs was 26 weeks.

The overall risk of any pulmonary adverse event with smTKI is low across RCTs and observational studies. There was significantly increased risk of developing upper respiratory tract infections (RD 0.03, 95% CI 0.02 to 0.04, (P<0.00001), 36 studies, 16419 participants) after smTKI exposure. No significantly increased risk was found for other respiratory complications including thrombosis/pulmonary embolism.

**Conclusion:** SmTKI increases risk of URTI compared with placebo or conventional agents. The risk of any pulmonary adverse event with smTKI is low.

TOL 003

TOL 004

### BREATHING DIFFICULTY, CHEST AND BACK PAIN PREDICT BRONCHITIS AND EMPHYSEMA IN WOMEN

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**Introduction/Aim:** Progressive loss of respiratory function often attributed to normal ageing, may be delayed if the early signs of chronic respiratory disease can be identified. Apart from a history of smoking, the ability to predict the development of conditions such as chronic obstructive pulmonary disease has proven elusive. The aim of this study was to identify potential predictors of bronchitis or emphysema in women.

**Methods:** A retrospective analysis of data from the middle cohort (born 1946-51) of the Australian Longitudinal Study on Women's Health (ALSWH) was conducted to identify baseline (survey 1: year 1996) predictors of bronchitis or emphysema at survey 8 (year 2016) using logistic regression models. Predictors included difficulty breathing, chest pain, back pain and limitations in walking various distances.

**Results:** Of the 13,715 women enrolled in the 1946-51 cohort of ALSWH at baseline, 8,622 completed Survey 8. Results showed a dose-response relationship for breathing difficulty, implying those with greater difficulty early in life were more likely to be diagnosed with bronchitis or emphysema later in life compared to those without breathing difficulty (Rarely: Odds ratio (OR):2.534 95%CI:2.064, 3.100, p<0.001; Sometimes: OR:3.271, 95%CI:2.669, 3.997, p<0.001; Often: OR:6.271, 95%CI:4.617, 8.430, p<0.001 respectively). Similar results were seen for chest pain and back pain. Compared to those who were not limited in walking 1 kilometre, those who were limited a little or a lot were significantly more likely to be diagnosed with bronchitis or emphysema (p<0.001).

**Conclusion:** In women, breathing difficulty, chest and back pain at age 45-60 years are statistically significant predictors for a diagnosis of bronchitis or emphysema later in life. The presence of dose-response relationships suggests that earlier management of these symptoms may improve prognosis. Encouraging women to walk could also reduce their future risk of being diagnosed with bronchitis or emphysema.

**Grant Support:** ALSWH is funded by the Australian Department of Health. There was no specific funding associated with this project.

### CGAS IS A PIVOTAL MEDIATOR OF IPF LUNG FIBROBLAST SENESCENCE

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**Introduction/Aim:** Senescence contributes to the aberrant wound repair response that characterizes idiopathic pulmonary fibrosis (IPF). The DNA-sensing cyclic GMP-AMP synthase (cGAS) is thought to play a pivotal role in senescence by stimulating cytokine production. We propose that in IPF, cGAS reinforces and facilitates the spread of senescence (ie 'bystander effect') by binding DNA, including mitochondrial DNA (mtDNA), released into the cytoplasm and extracellular space of DNA-damaged-, mitochondrial-stressed senescent cells. This study specifically examines the contribution of (mt)DNA and cGAS to the senescent phenotype of lung fibroblasts (LFs) from IPF patients (IPF-LFs) *in vitro*.

**Methods:** cGAS was targeted in IPF-LFs with high baseline senescence, or LFs from age-matched controls (Ctrl-LFs) induced to become more senescent using etoposide (10µM). Senescence was assessed by increases in p21 expression, phosphorylated-histone 2AX nuclear foci, senescence-associated-β-galactosidase activity and IL-6 production: measured by PCR, immunofluorescence, cytochemical staining and ELISA respectively. Release of mitochondrial and nuclear DNA into culture supernatant and cytoplasm were assessed by PCR. Cytoplasmic cGAS was targeted using RU.521 (1 µM) or by silencing RNA (siRNA), whereas extracellular DNA in supernatants was degraded by addition of DNase I.

**Results:** Levels of mtDNA in supernatants and cytosol of IPF-LFs were higher than Ctrl-LFs by 198% and 112% respectively (P<0.05, n=5-7). Furthermore, etoposide increased mtDNA release by Ctrl-LFs in the supernatants and cytosol by 155% and 38% respectively (P<0.05, n=6). Incubation with DNase I or RU.521, or cGAS siRNA transfection decelerated senescence of IPF-LFs and attenuated pharmacological-induced senescence of Ctrl-LFs (P<0.05, n=5-7). Addition of DNA isolated from lung fibroblasts induced an increase in the senescence of naïve Ctrl-LFs.

**Conclusion:** We provide evidence that cGAS perpetuates senescence in LFs mediated by (mt)DNA. The targeting of cGAS to suppress senescent-like responses to both exogenous and endogenous DNA has potential important therapeutic implications in the treatment of IPF.



### LUNG ELASTIC RECOIL AND ACINAR VENTILATION HETEROGENEITY IN OLDER ASTHMATICS WITH FIXED AIRFLOW OBSTRUCTION.

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**Introduction/Aim:** Small airway function is abnormal in asthma and correlated with airway hyper-responsiveness and asthma control. Older asthmatics have worse small airway function. They are also more likely to develop fixed airflow obstruction (FAO), in turn associated with reduced elastic recoil. Thus, we hypothesise that worse small airway function in older asthmatics is due to loss of lung elastic recoil. We aimed to examine relationships between Sacin, a marker of small airway function, and lung elastic recoil and compliance.

**Methods:** Non-smoking asthmatics >40 years-old, treated with standardised high-dose inhaled corticosteroid/long-acting beta-agonist performed spirometry and multiple-breath nitrogen washout to derive acinar and conductive ventilation heterogeneity (Sacin, Scnd) and lung clearance index (LCI) during enrolment and after two months of treatment. At two months an oesophageal balloon measurement was used to construct the pressure-volume curve with an exponential fit to derive B/A% (lung elastic recoil) and K (lung compliance). Relationships were assessed using Spearman correlations.

**Results:** Eighteen subjects (11 male; mean  $\pm$  SD years: age  $64.1 \pm 8.0$ , asthma duration  $38.9 \pm 22.5$ ) demonstrated moderate FAO after one month (post-bronchodilator mean  $\pm$  SD z-score: FEV<sub>1</sub>- $2.2 \pm 0.5$ , FVC- $0.7 \pm 1.0$ , FEV<sub>1</sub>/FVC- $2.6 \pm 0.7$ ). After two months, spirometry did not change. MBNW indices were higher than normal and also did not change after two months: median(IQR) z-score: Sacin( $2.8$  ( $2.1$ - $3.8$ ))L<sup>-1</sup>, Scnd( $3.3$ ( $3.1$ - $4.2$ ))L<sup>-1</sup> and LCI( $4.6$ ( $2.3$ - $7.8$ )). Lung elastic recoil was reduced (B/A% z-score  $\leq -1.64$ ) in 5/18 subjects and compliance increased (K z-score  $\geq 1.64$ ) in 9/18 subjects. Increasing age was associated with reduced lung elastic recoil (B/A%,  $r_s = -0.52$ ,  $P = 0.02$ ) and increased lung compliance (K,  $r_s = 0.50$ ,  $P = 0.04$ ) but not with MBNW indices. Increased Sacin ( $r_s = -0.53$ ,  $P = 0.03$ ) and LCI ( $r_s = -0.52$ ,  $P = 0.03$ ) were associated with reduced lung elastic recoil (B/A%).

**Conclusion:** In older asthmatics with FAO, worse small airway function was associated with reduced lung elastic recoil but not increased compliance. This suggests that lung parenchymal mechanical properties are an important determinant of peripheral airway function in older asthmatics with FAO.

**Grant Support:** University of Sydney Bridging Grant.

### VENTILATION MEASUREMENTS FROM HYPERPOLARIZED <sup>3</sup>HE MAGNETIC RESONANCE IMAGING ARE A MARKER OF AIRWAY CLOSURE IN SUBJECTS WITH AIRFLOW OBSTRUCTION

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**Introduction/Aim:** Images from Hyperpolarised <sup>3</sup>He magnetic resonance imaging (<sup>3</sup>He MRI) provide exquisite detail of gas distribution across the lung. What is lacking is functional information from these images. In this study we examine the percentage of ventilated lung from <sup>3</sup>He MRI and compare these with measurements of ventilation heterogeneity and markers of airway closure.

**Methods:** Subjects with asthma (n = 10), fixed airflow obstruction (n = 9) and healthy controls (n = 10) attended two testing sessions. On visit one, full pulmonary function assessment (both pre and post methacholine challenge) was conducted. Measurements performed were: spirometry, plethysmography, multiple breath washout (MBW) and the forced oscillation technique (FOT). On visit two, <sup>3</sup>He MRI scans were conducted pre and post methacholine challenge. The percentage of voxels above 0.15 of the maximum voxel intensity was used to calculate the percentage of ventilation.

**Results:** Measurements of the percentage of ventilated lung from <sup>3</sup>He MRI scans were significantly reduced in subjects with asthma by  $-12.3 \pm 10.1$  (percent ventilation) ( $P < 0.001$ ) and in subjects with fixed airflow obstruction by  $-12.9 \pm 7.3$  (percent ventilation) ( $P = 0.015$ ), post methacholine. This reduction in percentage ventilation from <sup>3</sup>He MRI was positively correlated with a FOT marker of airway closure and a MBW marker of ventilation heterogeneity in the conducting region of the lung, in both asthma (Xrs 6Hz,  $r^2 = 0.54$ ,  $P < 0.01$  and Scnd,  $r^2 = 0.31$ ,  $P < 0.01$ ) and fixed airflow obstruction (Xrs 6Hz,  $r^2 = 0.28$ ,  $P < 0.01$  and Scnd,  $r^2 = 0.29$ ,  $P < 0.01$ ). Subjects with fixed airflow obstruction had a significantly higher pre methacholine value of Sacin ( $0.21 \pm 0.1$  L<sup>-1</sup> vs  $0.11 \pm 0.03$ ,  $P = 0.04$ ), which was also correlated ( $r^2 = 0.79$ ,  $P < 0.01$ ) with decreased percentage ventilation.

**Conclusion:** <sup>3</sup>He MRI scans enable remarkable visualisation of airway closure and ventilation heterogeneity. Measurements of percentage ventilation from <sup>3</sup>He MRI scans are associated with physiological markers of airway closure and ventilation heterogeneity in subjects with airflow obstruction.

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TO 096

TO 097

**COMPARISON OF ESTIMATING ELASTIC RECOIL FROM OESOPHAGEAL BALLOON AND THE FORCED OSCILLATION NILSEN K<sup>1,2,4</sup>, THOMPSON B<sup>1,2</sup>, CHAPMAN D<sup>4,6</sup>, THIEN F<sup>2,3</sup>, KING G<sup>4,5</sup>, TONGA K<sup>4,5</sup>, THAMRIN C<sup>4,5</sup>**

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**Introduction/Aim:** Loss of elastic recoil occurs with aging as well as in diseases such as emphysema and asthma. The gold standard method of measuring elastic recoil involves an oesophageal balloon to estimate transpulmonary pressure (Ptp); however, the test is invasive and thus of limited clinical use. This study aims to examine a new method of assessing elastic recoil using the forced oscillation technique (FOT), an easy-to-perform, emerging lung function test in the clinical setting.

**Methods:** Subjects with asthma (n = 16) and healthy controls (n = 17) completed spirometry and plethsmography before insertion of an oesophageal balloon. Subjects then performed inspiratory capacity manoeuvres during which Ptp and FOT were simultaneously obtained. The relationship between transrespiratory pressure, FOT reactance and lung volume was used to calculate a surrogate measure of Ptp. The Colebatch equation  $V = A \cdot Be^{-(kP)}$  was then used to model the relationship between volume (expressed as %predTLC) and Ptp derived from both methods, and the agreement between the two models compared in terms of k (compliance) and B/A ratio (measure of elastic recoil). We also examined differences between controls and asthma.

**Results:** There was no difference in k ( $0.026 \pm 0.022$  vs  $0.029 \pm 0.014$ ,  $P = 0.23$ ) between the two models, while bias was seen in B/A ( $61.4 \pm 18.6$  vs  $78.3 \pm 18.3$ ,  $P < 0.01$ ). There were no differences in k or B/A between controls and asthma, however change in FEV<sub>1</sub> post-bronchodilator was negatively correlated with B/A ( $r^2 = 0.57$ ,  $P < 0.001$ ) in asthma.

**Conclusion:** FOT provides a promising surrogate for elastic recoil that is easy to implement into clinical practice. Using this technique, we suggest that increase of elastic recoil may contribute to the loss of reversibility in asthma.

**BRONCHODILATOR RESPONSE IN ASTHMA USING THE FORCED OSCILLATION TECHNIQUE IS COMPARABLE TO SPIROMETRY AND RELATES TO ASTHMA CONTROL**

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**Introduction/Aim:** The presence of a significant bronchodilator response (BDR) contributes to diagnosis and management of asthma, and is associated with worse asthma control. The forced oscillation technique (FOT) measures respiratory system impedance and is more sensitive to changes in peripheral airways mechanics than spirometry. BDR cut-offs have been proposed for healthy subjects. We compared BDR in asthma measured using spirometry and FOT, and their relationship with asthma control.

**Methods:** Patients with asthma attending a tertiary adult Airways clinic completed FOT (Tremoflo C-100, Thorasys, Montreal) and spirometry (Masterlab, Jaeger, Hoechberg) before and after 400mcg salbutamol, in addition to the asthma control test (ACT). FOT parameters examined included resistance (Rrs) and reactance (Xrs) at 5Hz, and area under the reactance curve (AX; between 5Hz and resonant frequency). All patients withheld bronchodilator medication for at least 8 hours prior to testing. BDR for spirometry was based on ATS/ERS criteria and FOT according to Oostveen *et al*<sup>1</sup>.

**Results:** Data for 52 patients (18 male) were analysed (mean  $\pm$  SD: age  $53 \pm 18$  yrs, BMI  $28.6 \pm 6.8$  kg/m<sup>2</sup>, pre-BD %predictedFEV<sub>1</sub>  $70 \pm 19\%$  and %predictedFVC  $86 \pm 17\%$ , ACT  $17 \pm 6$ ). Absolute change Xrs ( $0.55$  cmH<sub>2</sub>O.s.L<sup>-1</sup>) or AX ( $-3.9$  cmH<sub>2</sub>O.L<sup>-1</sup>) most accurately detected a significant spirometric BDR (Xrs 84.6% sensitivity, 74.4% specificity; AX 92.3% sensitivity, 61.5% specificity). BDR on spirometry or FOT (Xrs, AX) were all associated with poor asthma control (ACT < 20; 92%, 85% and 85% of patients respectively; Chi-square tests all  $P < 0.01$ ). FOT BDR identified more patients with poor asthma control compared to spirometry BDR (Xrs 53%, AX 69%, FEV<sub>1</sub> 38%).

**Conclusion:** These preliminary results demonstrate FOT has good sensitivity to detect BDR in asthma. Whilst a significant BDR measured by either FOT or spirometry was associated with worse asthma control, FOT was able to identify additional patients with worse asthma control and may be a more sensitive measure of patient symptoms.

**Grant Support:** nil

**REFERENCE**

1. E. Oostveen *et al.*, ERJ, 2013, 6:1513-1523.

TO 098

TO 099

### HEALTHY AGEING ALTERS THE NEURAL CONTROL OF THE HUMAN DIAPHRAGM MUSCLE DURING EUPNOEA

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**Introduction/Aim:** There are changes in the skeletal, pulmonary and respiratory neuromuscular systems with healthy ageing. A study using a gastro-oesophageal catheter to record EMG reported higher diaphragm EMG during eupnoea in healthy subjects > 50 years, but these measures may be affected by the normalisation process used (1). The definitive method to assess neural drive is the single motor unit technique. Here, this technique was used to determine how healthy ageing affects the neural control of the diaphragm.

**Methods:** To assess age-related changes in neural drive to the diaphragm during eupnoea, EMG was recorded from the costal diaphragm using a monopolar needle electrode in participants from three age groups (n ≥ 7 each): older (65-80 years); middle-aged (43-55 years) and young (23-26 years). In each group, 154, 174, and 110 single motor units, respectively, were discriminated. Data were analysed with a mixed effects linear model.

**Results:** There were no significant differences between age groups for onset (group range 9.5-10.2 Hz) or peak (14.1-15.0 Hz) discharge frequencies during eupnoea. However, there was delayed onset (by ~10% of inspiratory time;  $P = 0.02$ ) and earlier offset (by ~20% of inspiratory time;  $P = 0.04$ ) of single motor unit activity in the older group. The respiratory parameters during the recordings were similar across groups. The area of motor unit potentials was ~40% larger in the middle-aged and older groups ( $P < 0.02$ ).

**Conclusion:** Although we found no age-related difference in firing frequencies during eupnoea, there were differences in the timing of motor unit activity in the older group. Changes in motor unit morphology indicate axonal sprouting and re-innervation of diaphragm muscle fibres is associated with ageing, even in middle-aged participants.

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### SYSTEMIC INFLAMMATION MODIFIES THE REGIONAL GENE RESPONSE TO MECHANICAL VENTILATION

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**Introduction/Aim:** Mechanical ventilation is known to injure the lung. We have previously shown in the naïve lung that lung stretch in response to mechanical ventilation varies regionally, resulting in regional variations in the gene response. The aim of this study was to assess the impact of pre-existing systemic inflammation on the regional response to mechanical ventilation.

**Methods:** 8 week old female BALB/c mice were injected intraperitoneally with 200 µg of lipopolysaccharide (LPS) in 200 µL of saline, or saline alone. Four hours later, mice were anaesthetised, tracheostomised and mechanically ventilated for 2 hours at 225 breaths/min with 12 cmH<sub>2</sub>O PIP and 2 cmH<sub>2</sub>O PEEP. Regional tidal volume and FRC was quantified at baseline, and after 2 hours of ventilation, using dynamic high-resolution (phase contrast) 4DCT lung images collected using a custom-built X-ray system. The regional expression of seven genes (*Tnf-α*, *IL-1β*, *IL-6*, *Ccl2*, *Cxcl2*, *MPO* and *Nfe2l2*) was assessed by qPCR.

**Results:** There was significant regional variation in FRC and tidal volume, however, these patterns were not altered by LPS (FRC,  $P > 0.13$  for all comparisons). LPS increased the expression of all genes ( $P < 0.001$ ). The expression of *IL-6* ( $P = 0.04$ ), *Ccl2* ( $P < 0.001$ ), *Tnf-α* ( $P = 0.02$ ) and *Cxcl2* ( $P < 0.01$ ) varied regionally. *IL-6* was negatively associated with FRC ( $P < 0.001$ ), while *TNF-α* ( $P < 0.01$ ) was positively associated with FRC.

**Conclusion:** Our previous studies in the naïve lung demonstrated a positive relationship between regional *IL-6* and *Ccl2* expression and tidal volume. The absence of this relationship in the context of pre-existing systemic inflammation suggests that the inflammatory state of the lung has a significant effect on the outcome. Our data suggest that low end-tidal lung volumes (atelectasis) may be problematic in endotoxemia.

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**THICKENING OF THE AIRWAY SMOOTH MUSCLE LAYER FROM LATE GESTATION TO CHILDHOOD IS FACILITATED BY INCREASED MEAN CELL VOLUME**

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**Introduction/Aim:** The volume of the airway smooth muscle (ASM) layer increases from birth until adulthood. It has yet to be established whether increased volume of the ASM layer is due to ASM cell hypertrophy, hyperplasia and/or an increase in the proportion of extracellular matrix (ECM). The aim of this study was to characterise the structural mechanisms producing growth of the ASM layer in early life.

**Methods:** Airways from post-mortem cases were available from 7 different age groups: <24 week GA (n=8), <31 week GA (n=8), term (n=8), <0.5 year (n=8), 0.5–1 year (n=8), 2–5 year (n=8) and 6–10 year (n=3). Peripheral airways were stained with haematoxylin or using Masson's trichrome technique. The ASM layer thickness was determined from cross-sectional area divided by the perimeter of basement membrane ( $P_{bm}$ ). Stereological techniques were used to estimate cells per volume of ASM layer ( $N_V$ ) and mean ASM cell volume ( $V_C$ ) after correcting for ECM. Number of cells per length of airway ( $N_L$ ) was also estimated. Point counting of ASM, ECM and 'OTHER' within the smooth muscle layer were performed to calculate the volume fractions of ASM ( $V_{VASM}$ ), ECM ( $V_{VECM}$ ) and OTHER ( $V_{VOTHER}$ ) respectively.

**Results:** Thickness of the ASM layer for a given airway size increased with age.  $V_C$  increased with age with a concomitant decrease in  $N_V$  (cell density of the ASM layer).  $N_L$  was similar across groups and was reduced with age when normalised for  $P_{bm}$ .  $V_{VASM}$  and  $V_{VECM}$  were not affected by age, however,  $V_{VOTHER}$  was reduced at 2-5 years of age compared with <24 week GA and 0.5–1 year old groups.

**Conclusion:** From late gestation to childhood, the increased thickness of the ASM layer is due to hypertrophy of ASM cells, rather than hyperplasia of ASM cells or increased deposition of ECM relative to ASM.

**Grant Support:** NHMRC (1090888, 1077791).

**Declaration of Interest Statement:** None.

**DIFFERENTIAL TNF $\alpha$ , TNFR1 AND TNFR2 EXPRESSION ON BLOOD- AND SPUTUM-DERIVED IMMUNE CELLS IN ASTHMA**

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**Introduction/Aim:** Tumour necrosis factor alpha (TNF $\alpha$ ) is a pro-inflammatory cytokine mediating cell communication, differentiation, survival and cell death. It signals principally via the two receptors TNFR1 and TNFR2. TNF $\alpha$  signalling pathway component expression is dysregulated in asthma and there is interest in therapeutically targeting this pathway, particularly in neutrophilic, corticosteroid refractory asthma. To identify the cell type(s) that may be sites of altered TNF ligand or receptor expression in asthma, we measured membrane-bound TNF $\alpha$ , TNFR1 and TNFR2 on blood and sputum immune cells derived from asthma patients with different airway inflammatory phenotypes and healthy controls.

**Method:** Whole blood and processed sputum cell suspension of 42 participants (36 adults with asthma and six healthy controls) were analysed using flow cytometry. The antibody panel identified neutrophils, eosinophils, monocytes, macrophages and lymphocytes and allowed the relative quantification of membrane-bound TNF $\alpha$ , TNFR1 and TNFR2. Comparisons were made between healthy vs. asthma, neutrophilic vs. non-neutrophilic asthma and eosinophilic vs. non-eosinophilic asthma.

**Results:** TNFR1 expression on blood monocytes and TNFR2 expression on neutrophils was significantly higher in asthma compared to healthy controls. Non-classical (CD14+CD16++) sputum monocytes and sputum eosinophils from those with asthma expressed significantly higher levels of TNFR2 than healthy controls. TNF $\alpha$  and TNFR2 were significantly increased on blood eosinophils in neutrophilic compared to non-neutrophilic asthma. TNF $\alpha$  and TNFR1 expression on sputum cells did not differ significantly between groups. Blood and sputum cells exhibited dissimilar expression patterns of the investigated proteins.

**Conclusion:** Expression levels of TNF $\alpha$  ligand and receptors were significantly different on specific cell types from adults with asthma compared with healthy controls. The results indicate potential TNF signalling alterations may occur in several important immune cell types in asthma. These data will inform the direction of further studies focusing on downstream signalling responses to TNF $\alpha$  ligation within a selected cell type.

**Grant Support:** Work supported by the NHMRC. NMN is an NHMRC-funded PhD student within the CRE in Severe Asthma. MF is an NHMRC- and TSANZ/AstraZeneca-funded post-doctoral fellow within the CRE in Severe Asthma. KJB holds a Lung Foundation Australia Boehringer Ingelheim COPD research fellowship. PGG holds an NHMRC practitioner fellowship.

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### INTERRELATIONSHIP BETWEEN MICRORNA-21, IL-1 $\beta$ AND SLC26A4 RESPONSES IN SEVERE ASTHMA

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**Introduction/Aim:** Mainstay treatments lack efficacy in patients with severe, steroid-resistant asthma (SSRA) and the development of effective therapies has been hampered by a poor understanding of the mechanisms that drive disease. There are several subsets of SSRA characterised by different immune/inflammatory phenotypes, which makes defining key processes difficult in humans. To identify new therapeutic targets we developed mouse models of respiratory infection- and ovalbumin-induced SSR allergic airways disease (SSRAAD) that are highly representative of human disease. Significantly, all our models have steroid-resistant airway hyper-responsiveness (AHR) suggesting that it may be driven by a universal or subset-specific mechanism(s). We recently showed that inhibition of miR-21 or NLRP3/IL-1 $\beta$  responses completely suppresses steroid-resistant AHR in SSRAAD. It is possible that miR-21 and NLRP3/IL-1 $\beta$  mediate distinct pathways that may, or may not, converge to drive steroid-resistant AHR.

**Methods:** Microarray analyses showed that the expression of *Slc26a4* is decreased in the lungs of mice with SSRAAD. Factor-focused bioinformatics analyses identified potential links between miR-21, IL-1 $\beta$  and *Slc26a4*-deficiency, in the pathogenesis of steroid-resistant AHR. We used our models to assess the role of *Slc26a4*-deficiency and the potential for miR-21:IL-1 $\beta$  cross-talk in mediating *Slc26a4*-deficiency, in SSRAAD, and validated our experimental findings in human SSRA.

**Results:** We show that *Chlamydia*, *Haemophilus*, and influenza respiratory infections suppress the induction of *Slc26a4* in the airways in AAD. Administration of *Slc26a4*-specific siRNA in steroid-sensitive AAD mimics the effects of *Slc26a4*-deficiency in SSRAAD by increasing lung IL-1 $\beta$  expression and inducing steroid-resistant airway inflammation and AHR. We demonstrate that lung miR-21, IL-1 $\beta$  and *Slc26a4* responses are linked in SSRAAD and show that miR-21 levels are increased, and *Slc26a4* mRNA decreased, in human SSRA.

**Conclusion:** We demonstrate that miR-21, IL-1 $\beta$  and *Slc26a4*-deficiency play important, interconnected roles in driving steroid-resistant AHR in SSRAAD and that findings from our mouse models directly translate to human SSRA.

**Grant Support:** NHMRC, TSANZ, Rebecca Cooper Foundation, HMRI

### RELATIONSHIP BETWEEN PULMONARY IRON REGULATION AND THE PATHOGENESIS OF ASTHMA

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**Introduction/Aim:** We conducted a complementary series of clinical and experimental studies to investigate the relationship between iron and asthma.

**Methods:** Iron levels and regulatory molecule expression were examined in airway tissue biopsy and bronchoalveolar lavage (BAL) samples from patients with asthma and healthy controls, and correlations between disease parameters and asthma severity were assessed. Murine models of asthma and iron overloading were also used to explore the functional relationship between iron and disease.

**Results:** Increased iron levels in the BAL supernatant of asthmatics and healthy controls positively correlate with FEV1% predicted, whilst an increase in iron-positive BAL cells correlate with reduced FEV1/FVC% predicted. Severe asthmatics have decreased levels of extracellular iron in BAL compared to mild asthmatics and healthy controls. Increased expression of the iron uptake molecules DMT1 and TFR1 in airways tissue correlate with a reduction in FEV1/FVC% predicted. Significantly, severe asthmatics have increased expression of these factors in the airway tissue compared to mild asthmatics and healthy controls. Iron levels in the lung significantly increase in a house dust mite (HDM)-induced model of experimental asthma. Importantly, systemic iron overloading in mice, which dramatically increases lung iron levels, increases type 2 cytokine responses, mucus secreting cell hyperplasia, airways hyper-responsiveness, small airway fibrosis and eosinophilic inflammation in HDM and/or ovalbumin (Ova)-induced experimental asthma. Importantly, iron overloading-induced severe, experimental asthma is resistant to steroids and treatment with the iron chelator, desferoxamine, decreases key features of HDM- and Ova-induced disease.

**Conclusion:** Together, these findings provide evidence that altered tissue/cellular iron is not only a feature of asthma but that increased iron levels in the lung may influence the severity of disease. These findings also highlight the therapeutic potential of correcting dysregulated iron homeostasis, and/or targeting increased iron levels with iron chelators, for the treatment of disease.

**Grant Support:** NHMRC & University of Newcastle

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### MITIGATING ER STRESS IS A POTENTIAL THERAPEUTIC INTERVENTION FOR ASTHMA

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**Introduction:** Airway remodelling characterised by goblet cell hyperplasia and mucus hypersecretion are characteristic features of asthma, poorly responsive to current treatments. Recent evidence implicates the endoplasmic reticulum-unfolded protein response (ER-UPR) in the pathogenesis of asthma. Persistent inflammation in the asthmatic airways has the ability to induce ER stress (ERS) and may contribute to airway remodelling. There is limited evidence that implicates this process in human asthmatic airways or that relates it to disease severity.

**Aims:** To demonstrate evidence of ERS in asthma based on severity and phenotypes and evaluate the efficacy of known FDA approved ERS inhibitors in particularly IL-13 induced mucus hypersecretion using differentiated primary human cell culture model.

**Methods:** Bronchial brushings, bronchial lavage (BL) (n = 10), endobronchial biopsies (n = 7) and induced sputum samples (n = 44) were collected from all types of asthma and categorised in to subgroups based on severity and inflammatory phenotypes. Control samples were collected from non-asthmatic controls. The expression of UPR related genes were analysed by qPCR and microarray. UPR related protein expressions were analysed by immunoblotting. Primary bronchial cells obtained from severe asthma (n = 5) were grown in air-liquid interface (ALI) cultures and treated with IL-13 with or without ERS inhibitors 4-PBA and TUDCA. Expression of epithelial mucin markers MUC5AC and MUC5B were assessed by qPCR and ELISA

**Results:** Upregulated ERS is a key feature of severe-moderate asthma but not mild asthma. In a cohort of severe-moderated asthma patient, key markers of UPR; CHOP, GADD34, EDEM1, ERO1L were significantly upregulated in eosinophilic and neutrophilic asthma. IL-13 treatment significantly induce MUC5AC and MUC5B gene expression (73 fold,  $P = 0.03$ ) in ALI cultures. Treating with TUDCA (42 fold,  $P = 0.09$ ) and 4-PBA (71 fold,  $P = 0.02$ ) significantly reduced IL-13 induced mucin expression both at mRNA and protein level.

**Conclusion:** Heightened UPR is a key feature of severe eosinophilic and neutrophilic asthma. Treating with ER stress inhibitors attenuate IL-13 induced mucus hypersecretion in asthmatic airway epithelial cells.

### IL-25 BLOCKADE AUGMENTS EPITHELIAL ANTIVIRAL IMMUNITY DURING RHINOVIRUS INFECTION

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**Introduction/Aim:** Rhinovirus (RV) infections are the foremost trigger of asthma exacerbations and are potentially driven by an imbalanced bronchial epithelial cell (BEC) response to RV infection defined by increased type-2 immune activation and deficient innate antiviral interferon. We have previously reported that IL-25, a type-2 immune activating cytokine is increased during experimental RV infection in individuals with asthma and this corresponded to increased nasal viral load. We hypothesised that IL-25 directly regulates airway epithelial anti-viral responses via suppression of interferon production.

**Methods:** BECs were collected from 11 donors with moderate to severe asthma and differentiated at air-liquid interface (ALI). Cells were pre-treated with an anti-IL-25 monoclonal antibody (mAb) or isotype control and infected 24 hour later with RV 1B. Apical culture media and cells were collected to measure anti-viral and pro-inflammatory mediator expression. Cellular RNA was harvested for analysis of immune mediator gene expression and viral load by qPCR. Proteins in cells and apical media assessed by ELISA and western blot.

**Results:** IL-25 gene and protein expression was increased in RV-infected BECs from asthmatic donors. Treatment with a therapeutic anti-IL-25 mAb (ABM125) significantly increased RV-induced interferon- $\beta$  and - $\lambda$  production by these cultures. In RV-infected BECs anti-IL-25 mAb treatment also reduced IL-25 receptor IL-17RB gene expression.

**Conclusions:** IL-25 is a well-known activator of type-2 inflammation. Using a therapeutic anti-IL-25 mAb (ABM125) we show for the first time that IL-25 also negatively regulates RV-induced epithelial interferon production by cells from asthmatic donors. Thus we have identified a new role for IL-25 in regulation of epithelial innate anti-viral immunity and provide further evidence to support the development of anti-IL-25 mAb for the treatment of viral asthma exacerbations. We are currently investigating the BEC immune transcriptome using the Nanostring platform to gain further insight into the mechanism of action.

**Grant Support:** Asthma Australia, University of Newcastle Research Scholarship (UNRSC)

Abeome Corp

**Conflict of Interest:** Researcher directed funding and anti-IL-25 mAb was provided by Abeome Corp

### SURVIVAL TRENDS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE REQUIRING INTENSIVE CARE ADMISSION

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**Introduction:** There is sparse epidemiological data describing outcomes from intensive care unit (ICU) admission in patients presenting with an exacerbation of chronic obstructive pulmonary disease (COPD).

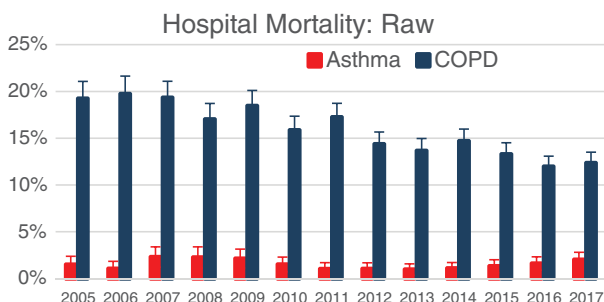
The objectives were to describe epidemiology and outcomes of patients admitted to ICU with COPD and to evaluate whether outcomes varied over time.

**Methods:** This bi-national observational study included all adult patients admitted to one of 184 ICUs across Australia and New Zealand between 2005 and 2017. Adult patients an index ICU admission diagnosis of COPD were eligible. To provide a comparator, a dataset of all patients presenting with a diagnosis of asthma was established. Changes in outcomes over time were determined using logistic regression, adjusting for illness severity (Australian New Zealand Risk of Death, ANZROD).

**Results:** Of 1,460,264 index ICU admissions, 31,991 patients (2.2%) had an admission diagnosis of COPD and 11,906 patients (0.8%) had an admission diagnosis of asthma. The mean age of patients with COPD was 68.3 (11.2) years and their ANZROD was 11.8% [6.4-21.4%] with 19.2% patients having a treatment limitation on admission to ICU. 35.4% of patients were mechanically ventilated, with 20.5% receiving invasive ventilation in the first 24 hours. Death in ICU and hospital occurred in 8.7% and 15.4% of patients, with 69.2% of patients discharged home.

A linear reduction in mortality over time for patients with COPD was observed that was not evident for patients with asthma (annual decline: COPD 0.94 [0.93-0.95] vs. asthma 1.01 [0.97-1.05];  $P < 0.01$ , Figure 1) and this was sustained when adjusting for illness severity (ANZROD). There was also a corresponding increase in those discharged home alive (annual increase: 1.04 [1.03-1.05] vs. 1.01 [0.99-1.03];  $P < 0.01$ ).

**Conclusions:** Figure 1



The mortality of patients with COPD who require ICU is reducing over time with the majority of survivors discharged home

**Key Words:** COPD, mechanical ventilation, respiratory failure

**Grant Support:** Not applicable

### INTERDISCIPLINARY MODEL OF CARE FOR COPD IN AUSTRALIAN PRIMARY CARE

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**Introduction:** Gaps exist between recommended guidelines and primary care management of COPD. The evidence for interdisciplinary, integrated disease management programs in COPD is still uncertain.

**Aim:** To evaluate the effectiveness of an interdisciplinary, primary care-based model of care on health-related quality of life, symptom severity, smoking cessation and lung function in patients with COPD.

**Methods:** A cluster randomised controlled trial (Review of Airways Dysfunction and Interdisciplinary Community-based care of Adult Long-term Smokers – RADICALS) was conducted across 43 general practice clinics in Melbourne, Australia. The model of care delivered in the intervention arm comprised smoking cessation support, home medicines review (HMR), and home-based pulmonary rehabilitation (HomeBase). Main outcomes measured at six and 12 months included changes in St George's Respiratory Questionnaire (SGRQ) score, COPD Assessment Test (CAT), modified Medical Research Council (mMRC) dyspnoea scale, smoking abstinence and lung function.

**Results:** A total of 272 participants with COPD were identified (157 intervention, 115 usual care). One-third of the intervention patients (50/157, 32%) completed both HMR and HomeBase. Intention-to-treat analysis showed no statistically significant difference in change in SGRQ score at six months (adjusted between group difference 2.45 favouring intervention, 95%CI -0.89 to 5.79). Per protocol analyses showed clinically and statistically significant improvements in SGRQ at six months in those receiving the full intervention compared to usual care (difference 5.41, 0.53 to 10.3). No significant differences were observed for change in CAT, mMRC, smoking abstinence or lung function.

**Conclusion:** No significant evidence was found for the effectiveness of an interdisciplinary model of care for COPD over usual care in primary care. Low intervention uptake from general practitioners and patients was a challenge. This model could potentially be more effective with strategies to improve adherence and intervention fidelity. A larger, well-powered trial in patients with more severe disease is warranted.

**Grant Support:** NHMRC, Boehringer Ingelheim, EMPHN, LFA

**REFERRALS TO PULMONARY REHABILITATION AFTER ACUTE EXACERBATIONS OF COPD: A MIXED-METHODS EVALUATION**

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**Introduction:** Australian guidelines recommend patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD) commence pulmonary rehabilitation (PR) within 2 weeks of discharge. Local adherence with this recommendation and factors that may facilitate improved future adherence for this patient group has not been explored.

**Methods:** Multi-site, Monash Health retrospective audit of electronic AECOPD patient records (DRG codes E65A/B) in 2016 and subsequent PR attendance (up to end 2017); qualitative survey of multidisciplinary acute healthcare staff.

**Results:** 739 patients presented with 1074 AECOPDs. Attendance at PR after AECOPD was low (n=41 [4 already in PR]; 5.5%), with mean (SD) time to commence PR 96 (73) days. Subgroup analysis (n=100) suggested ~25% of patients had evidence of PR discussion or referral from hospital, while 29% accepted referrals in hospital but did not commence PR. Survey data (n = 59) showed physiotherapists referred patients to PR more frequently than medical or nursing staff (P = 0.034), and referral rates were higher in staff who reported greater confidence in their ability to educate patients about PR (P = 0.013) and those with better awareness of the PR guidelines (P = 0.006). Factors proposed to improve PR referrals included clearer processes (63%), improved knowledge of eligibility criteria (53%) and better patient transport (51%).

**Conclusion:** Improvements are indicated to enhance adherence with national PR guidelines, whether aimed at staff or patient engagement after discharge.

**Grant Support** Lung Foundation Australia / Boehringer-Ingelheim COPD Research FellowshipGrant Support: •

**CARDIAC FUNCTION DURING EXACERBATIONS OF COPD ASSESSED USING CARDIAC MAGNETIC RESONANCE IMAGING**

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**Introduction/Aim:** Cardiac dysfunction is common in exacerbations of COPD and associated with poor outcomes. We assessed cardiac function using measurements of N-terminal pro-B-type-natriuretic peptide (NT-proBNP) and cardiac magnetic resonance imaging (CMR).

**Methods:** Patients admitted to hospital with exacerbations of COPD were recruited: 8 with high NT-proBNP (>220 pmol/L) and 15 with normal NT-proBNP. CMR was performed within 2 weeks of admission and at clinical stability (≥30 days later). This measured left and right ventricular ejection fraction (LVEF, RVEF), left and right end-systolic and end-diastolic volume indices (LVESVi, RVESVi, LVEDVi, RDEDVi), and left ventricular mass index (LVMI). 2 patients with high NT-proBNP died and one did not achieve clinical stability and did not have stable CMR scans.

**Results:** Most patients had impaired LVEF and RVEF in both acute and stable scans. There were no differences in LVEF and RVEF between high and normal NT-proBNP groups in the acute or stable CMRs. RVESVi was higher in acute than stable CMR in the normal NT-proBNP (P = 0.02) but not in the high NT-proBNP group. Patients with high NT-proBNP had higher LVMI than those with normal NT-proBNP in the acute and stable CMR. Patients with high NT-proBNP also had higher LVEDVi, RVEDVi and RVESVi than normal NT-proBNP in stable CMR.

**Conclusion:** Impaired biventricular ejection fractions are common in COPD exacerbations. The increased right ventricular systolic volume during exacerbations in the patients with normal NT-proBNP may reflect compensatory mechanisms but this was absent in people with high NT-proBNP. High NT-proBNP was associated with cardiac overload on CMR at clinical stability.

**Grant Support:** Department of Respiratory Medicine, Waikato Hospital.

**Declaration of Interest Statement:** The authors declare no conflict of interest.

	Acute CMR			Stable CMR		
	High (n = 8) median (IQR)	Normal (n = 15) median (IQR)	P	High (n = 5) median (IQR)	Normal (n=15) median (IQR)	P
LVEF	51 (35-54)	52 (38-54)	0.56	52 (43-53)	52 (44-58)	0.600
LVEDVi	67 (57-112)	67 (59-77)	0.561	93 (64-129)	61 (57-75)	<b>0.033</b>
LVESVi	38 (30-52)	34 (25-42)	0.333	53 (30-61)	32 (26-39)	0.074
LV mass i	55 (51-63)	42 (34-51)	<b>0.008</b>	55 (43-66)	40 (35-53)	<b>0.049</b>
RVEF	42 (27-53)	44 (41-49)	0.628	40 (36-44)	49 (45-53)	0.115
RVEDVi	83 (64-99)	66 (53-79)	0.093	85 (83-95)	62 (54-78)	<b>0.01</b>
RVESVi	46 (32.-81)	35 (30-42)	0.197	46 (43-76)	33 (29-39)	<b>0.005</b>



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### SMOKING CESSATION AND THE LUNG MICROBIOME IN HEALTHY CURRENT SMOKERS

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**Introduction/Aim:** Cigarette smoking is the major contributor to the development of chronic obstructive pulmonary disease (COPD) and lung cancer, and increases the risk of respiratory tract infections. Smoking cessation changes the human intestinal microbiome, but the effects on the lung microbiome are unknown. In this study, we investigated the impact of smoking reduction on the lung microbiome.

**Methods:** Twenty, healthy smokers (17 normal lung function, 3 sub-clinical COPD) underwent bronchoalveolar lavage (BAL) before smoking reduction and BAL was repeated at two time-points over an average of 14 months. Fourteen smokers completely ceased smoking, while six smokers substantially reduced their daily cigarette consumption. BAL samples were also collected from eleven, healthy age-matched non-smoker controls. DNA extracted from BAL cell pellets was analysed by 16S rDNA pyrosequencing.

**Results:** The lung microbiomes of smokers and non-smokers were different in terms of overall microbial community composition and the relative abundance of *Peptostreptococcus*, *Porphyromonas* and *Neisseria*. After 4 months of smoking reduction, the lung microbiota of the smokers was similar to that of non-smokers, but after 14 months smoking reduction, the lung microbiome community composition had changed further and was significantly different from baseline, but also still significantly different to that of non-smokers. Changes in body mass index on smoking reduction were correlated significantly with changes in diversity of the lung microbiome (Shannon index;  $P < 0.05$ ).

**Conclusion:** Current smokers without established COPD have a different lung microbiome to non-smokers. Smoking reduction results in significant changes to the lung microbiome, however it does not return to normal over a year or more. Changes in diversity of the lung microbiome appear related to weight gain on smoking reduction.

**Grant Support:** •

### MANAGING COPD EXACERBATIONS USING AN ELECTRONIC ORDERING SET

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**Introduction/Aim:** Adherence to guidelines in the hospital management of chronic obstructive pulmonary disease (COPD) exacerbations is variable. We evaluated whether a dedicated COPD care set in the electronic ordering system of a tertiary metropolitan hospital led to practice behaviour change and adherence rate to the COPD-X guidelines.

**Methods:** Data were retrospectively collected for all admissions for COPD exacerbations during May 1 to August 31 2016, prior to the implementation of the COPD careset. Concordance with COPD-X guidelines was assessed and compared with data from May 1 to August 31 2017.

**Results:** 134 patients (53% males,  $75.4 \pm 10.2$  [SD] years old, 40.3% respiratory, 30% general medicine, 18% Short Stay Unit [SSU]) and 227 patients (56% males,  $73.8 \pm 12.3$  years old, 33.5% respiratory, 30% general medicine, 19% SSU) were admitted in 2016 and 2017, respectively. Similar high concordance rates were demonstrated in both years in supplemental oxygen for oxygen saturation of  $<88\%$  (100% vs 95%), non-invasive ventilation for hypercapnic respiratory failure (100% vs 100%), prescription of inhaled bronchodilators (100% vs 100%) and systemic corticosteroids (88.8% vs 80.2%  $P = 0.03$ ). Venous blood gases (VBG) were preferred over arterial blood gases (ABG). Of those with VBG pH  $\leq 7.34$ , only a minority were further evaluated with ABG testing (36.1% vs 28%  $P = 0.11$ ). Oxygen therapy for those with  $SpO_2 \geq 88\%$  was overprescribed and guideline adherence worsened in 2017 (24.7% vs 13.8%  $P = 0.009$ ). Referrals to pulmonary rehabilitation were low in both years and unchanged (17.9% vs 12.8%  $P = 0.19$ ), with the majority of referrals made by the respiratory unit. Smoking cessation counselling in active smokers improved (13.4% vs 28.2%  $P = 0.001$ ), as did reviews of immunisation history (2.2% vs 10.1%  $P = 0.005$ ), though these were still unacceptably low overall.

**Conclusion:** The electronic COPD care set led to only minor improvements in the level of adherence to COPD-X guidelines, and further efforts are required to optimise awareness and usage.

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**Declaration of Interest:** the authors do not have any conflicts of interests to declare.

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**BLOCKADE OF TACE MITIGATES LUNG ADENOCARCINOMA**SAAD M<sup>1</sup>, ALHAYYANI S<sup>1</sup>, MCLEOD L<sup>1</sup>, YU L<sup>1</sup>, GARBERS C<sup>2</sup>, RUWANPURA S<sup>1</sup>, SAGI I<sup>3</sup>, ROSE-JOHN S<sup>2</sup>, JENKINS B<sup>1</sup><sup>1</sup>Monash University, Melbourne, Australia, <sup>2</sup>Christian-Albrechts-University, Germany, <sup>3</sup>Weizmann Institute of Science, Israel

**Introduction/Aim:** Oncogenic KRAS mutations are a hallmark of lung cancer, the most lethal among all cancers. Giving that the direct targeting of KRAS has proven challenging; the identification of “druggable” cooperating factors of KRAS provides an attractive approach to develop new therapies that indirectly block the oncogenic consequences of KRAS. Since the protease tumour necrosis factor- $\alpha$  (TNF- $\alpha$ )-converting enzyme (TACE) mediates shedding of bioactive protumourigenic growth factors, interleukins, and/or their receptors, including TNF $\alpha$ , soluble IL-6 receptor (sIL-6R), and EGFR ligands, we investigated the role of TACE in the pathogenesis of lung cancer.

**Methods:** Genetic (*Kras*<sup>LSL-G12D/+</sup>) and carcinogen (NNK)-induced mouse models of lung adenocarcinoma (LAC) were coupled with TACE<sup>ex/ex</sup> mice, which have low TACE expression. Oncogenic *Kras*<sup>G12D</sup> was activated using intranasal inhalation of Adenovirus Cre recombinase, while NNK (100mg/kg) was injected intraperitoneally into TACE<sup>ex/ex</sup> on the tumour-sensitive A/J background. CRISPR-Cas9-mediated deletion of TACE in human KRAS-mutant LAC cell lines was evaluated *in-vitro* and *in-vivo* (xenograft). Specific inhibition of TACE surface activity was also evaluated in LAC patient-derived xenograft (PDX).

**Results:** Genetic deficiency of TACE significantly reduced tumour burden in both *Kras*<sup>G12D</sup> and NNK-induced LAC models, which was accompanied by reduced cellular proliferation and inflammation. CRISPR-Cas9-driven TACE deletion in LAC cell lines similarly reduced cell proliferation and tumour growth *in-vitro* and *in-vivo*, respectively. Among TACE substrates, only sIL-6R - which drives IL-6 trans-signalling that promotes LAC - was preferentially reduced in LAC models upon the targeted blockade of TACE, which was associated with reduced downstream ERK1/2 MAPK activation. In the lungs of mouse models and LAC patients, when compared with their non-LAC counterparts, TACE phosphorylation was enhanced via a p38 MAPK-driven mechanism.

**Conclusion:** Our data suggest that TACE plays a crucial role in LAC development, paving the way for developing specific inhibitors of TACE that will be considered the next generation of anti-cancer therapies for KRAS-mutant LAC.

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**PATIENT EXPERIENCES OF HOME-BASED REHABILITATION IN INOPERABLE LUNG CANCER**EDBROOKE L<sup>1,2</sup>, DENEHY L<sup>1,2,3</sup>, GRANGER C<sup>1,3,4</sup>, KAPP S<sup>5</sup>, ARANDA S<sup>5,6</sup><sup>1</sup>University Of Melbourne, Melbourne, Australia, <sup>2</sup>Allied Health Service, Peter MacCallum Cancer Centre, Melbourne, Australia, <sup>3</sup>Institute for Breathing and Sleep, Melbourne, Australia, <sup>4</sup>Department of Physiotherapy, The Royal Melbourne Hospital, Melbourne, Australia, <sup>5</sup>Department of Nursing, The University of Melbourne, Melbourne, Australia, <sup>6</sup>Cancer Council Australia, Sydney, Australia

**Introduction/Aim:** Exercise is important in lung cancer, yet most people do not meet the physical activity guidelines. The aim of this study was to characterise the views and experiences of participants with inoperable lung cancer who completed a home-based rehabilitation program.

**Methods:** Individual semi-structured interviews were conducted with participants randomized to the intervention group (IG) of a trial of home-based exercise, behaviour change and symptom management. Data were independently coded by two researchers, cross-checked and analysed using content analysis with a summary of arising themes.

**Results:** 55% (25/45) of the IG were interviewed: mean (SD) age 67 (13) years; male 52%; disease stage n (%) III = 9 (36), IV=11 (44); radical treatment intent n (%) 13 (52). The majority of participants reported program benefits, both in the physical domain (reduced sedentary time and improved strength, fitness and function) and the mental domain (motivation to keep healthy, preventing boredom). Support to self-manage symptoms was well received and many participants reported increased confidence in managing their symptoms. Exercise enablers included: having expert health professional support; motivation to be stronger and better prepared for future challenges; and having an achievable and familiar program that was monitored. Treatment side-effects, pain from comorbidities and the weather were exercise barriers. The majority of participants found the use of a Fitbit™ activity tracker, SMS exercise reminders and an exercise diary helped promote adherence.

**Conclusion:** This home-based rehabilitation program was acceptable to most participants with multiple benefits reported including improved fitness, motivation and ability to manage symptoms.

**Grant Support:** This research was funded through a National Health and Medical Research Council project grant (APP1060484). Lara Edbrooke is the recipient of a Victorian Government Olivia Newton John Cancer Wellness and Research Centre Supportive Care PhD scholarship, through the Victorian Cancer Agency (ONJ16010).

### MULTIDISCIPLINARY REHABILITATION IN INOPERABLE LUNG CANCER: A RANDOMISED CONTROLLED TRIAL

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**Introduction/Aim:** Lung cancer is associated with poor health-related quality of life (HRQoL) and high symptom burden. This trial aimed to assess the efficacy of home-based rehabilitation versus usual care in inoperable lung cancer.

**Methods:** Parallel group, 1:1 randomized controlled (opaque envelope assigned by independent personnel) superiority trial, with stratification (treatment intent, recruitment site), and assessor-blinding. Eligible participants (inoperable lung cancer diagnosis, scheduled for active treatment) recruited from three tertiary-care Australian hospitals received usual care (UC) plus eight-weeks of aerobic and resistance exercise with behaviour change and symptom management support (intervention group [IG]) or UC alone. Assessments occurred at baseline, nine-weeks and six-months. The primary outcome was between-group six-minute walk distance (6MWD) change from baseline to nine-weeks (analysed for participants with baseline and at least one follow-up outcome measure in their original assigned groups). Secondary outcomes included physical activity levels, muscle strength, HRQoL, symptoms, exercise motivation, and survival. The trial is registered as active-not recruiting (Australian New Zealand Clinical Trials Registry: ACTRN12614001268639).

**Results:** Between December 5, 2014 and December 19, 2016, 92 participants were recruited (IG:45, UC:47; attrition: nine-weeks (15%), six-months (28%)). 78 participants were analysed at nine-weeks (UC:40, IG:38): mean (SD) age 63 (12) years; male 58%; disease stage n (%) III = 31 (40) and IV = 38 (49); radical treatment intent 50%. Median survival (days): IG:636, UC:406,  $P = 0.15$ . 6MWD between-group differences (IG minus UC) were non-significant (mean difference (95% CI): nine-weeks: -25.4m (-64.0, 13.3),  $P = 0.198$  and six-months: 41.3m (-26.7, 109.4),  $P = 0.232$ ). Significant six-month differences, favouring the IG, were found for HRQoL (FACT-L: 13.0 (3.9, 22.1),  $P = 0.005$ ), symptom severity (MDASI-LC: -2.2 (-3.6, -0.9),  $P = 0.001$ ) and exercise motivation (BREQ-2: -0.6 (-1.2, 0.0),  $P = 0.041$ ).

**Conclusion:** Home-based rehabilitation resulted in significant improvements in patient-reported outcomes at six-months without changing physical function significantly.

**Grant Support:** NHMRC project grant (APP1060484). Lara Edbrooke: Victorian Cancer Agency PhD scholarship (ONJ16010).

### POTENTIAL ONCOGENIC ROLE FOR 14-3-3 PROTEINS IN LUNG CANCER INITIATION

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**Introduction/Aim:** 14-3-3 proteins are a family of 7 ubiquitous cellular regulator molecules that are markedly increased in expression in up to 60% of Non-small cell lung cancer (NSCLC). Importantly, over-expression of 14-3-3 protein correlates with aggressive disease with poor prognosis. 14-3-3 proteins function by binding phospho-motif in proteins, thus resulting in altered function of the interacting protein. Oncogenic signalling through EGFR, FGFR and K-Ras in NSCLC are dependent on 14-3-3 protein function, highlighting their potential as therapeutic targets. The oncogenic role of 14-3-3 proteins has previously been studied by knock-down in cancer cells. Alternatively, in this study we over-expressed individual 14-3-3 protein isoforms in human airway epithelial cells to assess their potential contribution to initiation and progression of NSCLC.

**Methods:** Lentiviruses encoding individual 14-3-3 isoforms were used to transduce the immortalised human bronchial epithelial cell line BEAS-2B. Transduced cells were subjected to soft-agar colony formation assays to assess neoplastic transformation. The effect of 14-3-3 protein over-expression on cell proliferation and survival signalling was assessed by immunoblotting.

**Results:** Increased expression of individual 14-3-3 isoforms were confirmed using 14-3-3 isoform selective antibodies. Anchorage independent colonies of BEAS-2B cells in soft agar were observed after 3 weeks in culture with elevated numbers of colonies seen in 14-3-3 over-expressing populations compared to parental cells. Increased expression of the 14-3-3 isoforms resulted in varied expression of proliferation and survival proteins by immunoblot. Of note; forced expression of 14-3-3 epsilon isoform in BEAS-2B cells increased stability of survival associated proteins  $\beta$ -catenin and Mcl-1.

**Conclusion:** We have shown that increased expression of 14-3-3 isoforms in immortalised normal bronchial epithelial cells supported anchorage independent growth indicative of neoplastic transformation and enhanced cell proliferation signalling suggesting that increased 14-3-3 protein expression may play a direct role in lung cancer initiation and warrants further investigation as a potential therapeutic target.

**Grant Support:** RTP PhD scholarship, THRF postgraduate top-up scholarship.

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**EXHALED BREATH METHODS FOR ANALYSIS OF VOLATILE ORGANIC COMPOUNDS (VOCs) IN LUNG CANCER AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)**

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**Introduction/Aim:** Lung cancer and COPD are amongst the top five causes of death worldwide. If lung cancer, which is more common in people with COPD, can be diagnosed at an earlier, curable stage, survival rates could be improved for patients. The study of volatile organic compounds (VOCs) in exhaled breath using novel field asymmetric ion mobility spectrometry (FAIMS), could be a potential new, non-invasive method for diagnosing lung cancer and COPD.

**Methods:** Four groups were studied: healthy, never smoker controls (n = 10), subjects with COPD (n = 12), a healthy, ever-smoking control group (n = 10) and subjects with lung cancer (n = 15). A standard breath collection protocol was followed to collect exhaled VOCs. Samples were analysed using the FAIMS. Pulmonary function tests were conducted for all subjects. Random forest was performed to compare the subject groups.

**Results:** FAIMS determined VOC profiles successfully, distinguished healthy, never smoker controls from lung cancer subjects ( $P < 0.001$ , sens. 91%, spec. 90%), COPD subjects ( $P < 0.001$ , sens. 100%, spec. 100%) and ever-smoking controls ( $P = 0.025$ , sens. 75%, spec. 80%). Ever-smoking controls were also significantly different to both lung cancer subjects ( $P = 0.034$ , sens. 64%, spec. 92%) and COPD subjects ( $P < 0.001$ , sens. 89%, spec. 100%). FAIMS did not distinguish between lung cancer subjects and COPD subjects in this study.

**Conclusion:** The results from this study illustrate that FAIMS VOC profiles in subjects with lung cancer and/or COPD, are different to both healthy, never smokers and smoking controls. This data will contribute to our understanding of exhaled VOC collection as a potential diagnostic tool for different disease states.

**Grant Support:** There were no conflicting interests in the conduction of this study.

**RADIATION EXPOSURE REDUCTION IN THORACIC LOW-DOSE CT LUNG CANCER SCREENING**

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**Background:** Lung cancer screening with low-dose computed tomography (LDCT) in high-risk populations reduces mortality and screening programs are likely to be adopted internationally. Any radiation exposure from medical imaging should be as low as reasonably practicable. This study examined the role of a novel technique to reduce radiation exposure from LDCT.

**Methods:** Subjects: participants in the Asbestos Review Program (based in SCGH) with  $\geq 3$  months occupational asbestos exposure and/or presence of pleural plaques. Technique: Additional lateral scout image (to normal antero-posterior (AP) scout) as planning for CT chest in consecutive subjects undergoing annual screening. Radiation exposure from AP alone (1<sup>st</sup> scan) vs. lateral + AP scout (2<sup>nd</sup> scan) was compared in subjects using the dose length product (DLP) with conversion into millisieverts (mSv) using a factor of 0.014. All scans were performed using a Siemens Somatom Definition FORCE machine with Tin filter and automated exposure control.

**Results:** Between July 2016 and January 2018, 195 subjects underwent two annual scans, 179 (92%) were male, median age at the first scan was 72.8 years. There was no significant interval change in BMI over the study period. The median (IQR) DLP from the scout images increased from 0.8 (0.8-0.9; 1<sup>st</sup> scan) to 1.6 (1.5-1.7; 2<sup>nd</sup> scan:  $P < 0.001$ ), however, the total DLP reduced from 11.6 (9.3-14.5) to 6.8 (5.8-8.6),  $P < 0.001$ . This corresponds to an effective median radiation dose of 0.1 mSv with the new technique. No significant change in measured image quality between the paired scans was detected ( $P = 0.6$ ).

**Discussion:** This novel, simple technique reduces the effective radiation dose by 40% in an ultra LDCT screening program to that similar to a CXR, with no loss in image resolution. Wider adoption of this technique could reduce radiation exposure to high risk individuals undergoing CT screening with reduction in the risk of radiation induced malignancy.

### NEGATIVE MOOD WORSENS EXERTIONAL DYSPNOEA IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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**Introduction/Aim:** We have previously shown that inducing a negative mood state in healthy individuals, increased intensity of exertional dyspnoea (Sharma et al., 2016). For individuals with chronic obstructive pulmonary disease (COPD), exertional dyspnoea is a debilitating symptom that limits physical activity that and often associated with anxiety/depression affecting mood. The aim of this study was to examine the effect of a negative mood state on exertional dyspnoea/leg fatigue in individuals with COPD.

**Methods:** 18 individuals (11 females, 69 ± 6 yrs) with mild COPD (forced expiratory volume in one second = 65 ± 15%) and six-minute walk distance of 489 ± 83 m participated. On each day subjects viewed randomly assigned images designed to induce positive, negative, or neutral mood states (International Affective Picture System). Dyspnoea (intensity) and leg fatigue were recorded every minute using a 0 to 10 scale. Dyspnoea bother (0-10 scale) and mood (0, extremely unhappy to 10, extremely happy) were measured prior and immediately post each test.

**Results:** There was no significant difference in exercise heart rate or oxygen saturation between trials. Mood was significantly ( $P < 0.01$ ) reduced in the final minute of the negative (2.4 ± 1.3) compared to the neutral (6.4 ± 1.5) and positive (7.6 ± 1.3) trials. End-exercise dyspnoea intensity and bother were both significantly greater ( $P < 0.05$ ) during the negative trial (intensity: 5.6 ± 1.5; bother: 5.6 ± 1.9) compared to the neutral (intensity: 4.5 ± 1.5; bother: 4.0 ± 1.9) and positive trials (intensity: 4.7 ± 1.9; bother: 3.5 ± 2.2). However, there was no significant difference for leg fatigue between trials (end-exercise negative: 3.3 ± 2.2; neutral: 3.0 ± 2.4; positive: 3.4 ± 2.5)

**Conclusion:** Negative mood state is associated with greater intensity of exertional dyspnoea. Strategies to modify mood may impact on exertional breathlessness and in COPD. However, leg fatigue appears unchanged by mood state, suggesting that the sensory response to exercise (dyspnoea vs leg fatigue) are processed differently by the brain.

#### Reference

Sharma et al. J Appl Physiol. 120: 2016. 114-20

### PLEURAL EFFUSION AND SYMPTOM EVALUATION (PLEASE)-2 STUDY: QUANTIFYING DIAPHRAGMATIC FUNCTION USING ULTRASOUND

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**Introduction/Aim:** The findings from the PLEASE-1 study suggests that pleural effusion may cause breathlessness by impairing diaphragm function. The PLEASE-2 is a pilot study to refine the assessment of the diaphragm using advanced ultrasound techniques and symptom responses to pleural effusion drainage. Our aim was to determine whether bedside ultrasound measurements of diaphragm thickness and movement (excursion) predict improvements in breathlessness after pleural fluid drainage.

**Methods:** Patients with symptomatic pleural effusion undergoing therapeutic drainage were recruited. Pre- and Post-measurements included 1) Patient and effusion-related characteristics; 2) Degree of breathlessness using 100mm visual analogue scale; 3) Diaphragm morphology and motion using B-mode ultrasound; 4) Diaphragm excursion using M-mode during tidal and deep breathing and sniff; and 5) Diaphragm thickness using B-mode during end-inspiration and end-expiration (to calculate thickening fraction).

**Results:** The 26 patients (median age 65; 39% male) most commonly (85%) had malignant effusions. Most (88%) effusions were moderate- or large-sized (≥25% hemithorax on CXR) and had 1995 [median, IQR 1090–3120] mL drained. Breathlessness improved post-drainage by 34 ± 27mm (minimal clinical important difference = 14 mm); ( $P < 0.05$ ). Abnormal diaphragmatic morphology (flattened or inversion, 46%) and motion (paralysed or paradoxical, 42%) normalized in 100% and 84% of patients, respectively, post-drainage. Diaphragm excursion during sniffing improved (mean -0.14 ± 0.2;  $P < 0.05$ ) and a trend towards a significant improvement in diaphragmatic excursion during deep breathing (-0.08 ± 0.21;  $P = 0.057$ ) was observed on the contralateral side post-drainage. There was a moderate correlation between volume drained and contralateral diaphragm excursion during tidal and deep breathing ( $r = 0.46$  respectively;  $P < 0.05$ ). Diaphragm thickening did not change post-drainage. No significant correlation was seen between pre-drainage diaphragmatic excursion and thickness with baseline breathlessness score.

**Conclusion:** The pathophysiology of breathlessness in patients with pleural effusion is complex. This pilot study suggests that the contralateral diaphragm may have an important role in the mechanism breathlessness in patients with pleural effusion.

**Grant Support:** NHMRC Fellowships (SM, RT, YCGL, SJ, PE), WA Cancer Council (RT, YCGL), WACPCN Fellowship (SM, DF), ERS Long-term Research Fellowship (DF).

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**PHASIC INTERCOSTAL MUSCLE REDUCTION DURING RAPID EYE MOVEMENT SLEEP**

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**Introduction/Aim:** The excitatory and inhibitory processes in rapid eye movement (REM) sleep are hypothesized to be associated with diseases like sudden infant death syndrome (SIDS). We aim to characterize a phenomenon of decreased respiratory muscle activity in association with rapid eye movements (REMs) during REM sleep and to generate further hypotheses for neurophysiological mechanisms of central respiratory control and its role in disease and health.

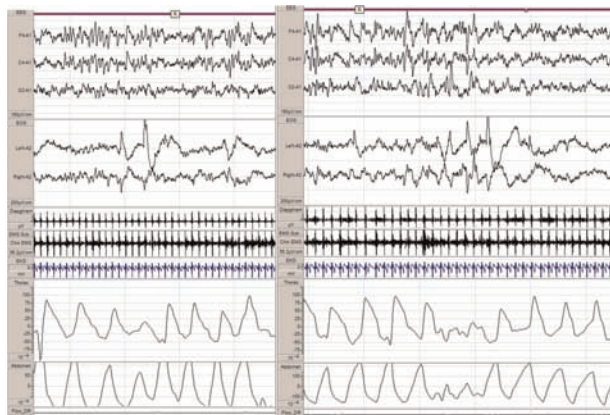
**Methods:** REMs and clusters of REMs from polysomnography (PSG) of children with Down syndrome (DS) and neurotypical children (TD) between ages two and five years old were retrospectively reviewed. Thoracic respiratory inductance plethysmography band (tRIP) signals were evaluated preceding and following REMs and REMs clusters. REMs or REMs clusters associated with a reduction in tRIP amplitude or central apnoea were counted as positive (dREMs or dREMs cluster). tRIP signals with no change in amplitude or associated with movement artefact were counted negative. Events were independently scored by MDW and SS.

**Results:** Five DS children vs. five TD children had a median increase in REMs (177 vs. 135), dREMs (86 vs. 59), REMs clusters (39 vs. 29), dREMs clusters (23 vs. 13) and REMs per minute of REM sleep (1.8 vs. 1.1). There were no significant differences in age, total sleep time, or sleep efficiency.

**Conclusion:** Children with low tone syndromes will exhibit greater phasic inhibition of respiratory muscle activity due to a disorder of central respiratory control and regulation and inhibitory/excitatory processes in sleep. Similar phenomena could contribute to gas exchange abnormalities noted in children with central dysrhythmic breathing.

**Key Words:** Rapid eye movement; REM sleep; Intercostal muscle; Phasic motor inhibition; Brainstem; Children

**Grant Support:**



**POLYSOMNOGRAPHY IN PAEDIATRIC SPINAL MUSCULAR ATROPHY**

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**Introduction:** Sleep disordered breathing (SDB) causing sleep disturbance and daytime symptoms occurs in spinal muscular atrophy (SMA). Although polysomnography (PSG) findings are well described in other neuromuscular disorders, PSG findings in the SMA group are less well described.

**Aim:** To characterise SDB in childhood SMA.

**Methods:** A cross-sectional cohort study of all children in Queensland with SMA was undertaken. Children had full diagnostic PSG, scored and reported by a single paediatric sleep physician in accordance with American Academy of Sleep Medicine Guidelines (2012).

**Results:** 27 children (15 males) were included (0.75-18.7years). Significant SDB (AHI >5) was seen in 14 (52%) and normal breathing (AHI <1) seen in only 2 children with type 2. SDB was seen in each type (See Table 1) with a predilection to REM sleep.

In SMA type 1, all patients exhibited SDB, 2 (50%) with central sleep apnoea (CSA) and 2 (50%) with mixed disease. In SMA type 2, 5 (36%) had CSA, 1 (7%) mixed disease, 6 (43%) had early SDB and 2 (14%) had normal sleep breathing. Lastly, for SMA type 3, 4 (44%) children had CSA and 5 had early SDB.

Table 1 Sleep Study Characteristics by SMA type

SMA Type	1	2	3
No. of patients (% of all SMA)	4 (15)	14 (52)	9 (33)
Age in years (median (range))	1.5 (0.75-6.25)	10.6 (2.8-18.7)	9.5 (4.2-15.4)
NIV use (No. (%))	3 (11)	8 (30)	1(4)
AHI (median (IQR, range))	12.3 (7.6, 6.6-31.4)	3.75 (4.25, 0.7-44)	2.1 (4.3, 1.1-18.2)
Obstructive Index (median (IQR, range))	3.5 (1.6,0-4.9)	0 (1.1,0-3.9)	0 (0.4,0-0.5)
Central Index (median (IQR, range))	9.9 (5.7, 3.5-17.8)	3.6 (4.3, 0.6-41.7)	2.1 (4, 1.1-17.7)
Min. Oxygen Saturation (IQR, median (range))	85 (77, 77-90)	89 (5.5, 81-93)	90 (3,86-94)
Max. Carbon Dioxide (median (IQR, range))	44.1 (2.3, 41-48.2)	46.5 (5.7, 38.8-63.2)	46.5(4.2, 44.2-49.8)

**Conclusion:** SDB is common in childhood SMA and was present in children with all types 1-3. Central sleep apnoea was the most common SDB present, although mixed SDB was also present in type 1 and 2 SMA.

**Grant Support:** None

**DOES COLLAPSE/CONSOLIDATION ON MEDICAL IMAGING OR OXYHAEMOGLOBIN DESATURATION ON ROOM AIR ACCURATELY PREDICT PULMONARY COMPLICATIONS AFTER ABDOMINAL SURGERY?**

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**Introduction:** Pulmonary complications are common and have serious consequences after major abdominal surgery. This study aimed to investigate the accuracy of collapse/consolidation on imaging and room air oxyhaemoglobin desaturation, to predict a postoperative pulmonary complication as diagnosed using a gold standard; the Melbourne Group Score.

**Methods:** Data from two prospective multicentre clinical trials were extracted. Participants were adults who had elective or emergency major abdominal surgery at five hospitals. All received standardised early ambulation and minimal chest physiotherapy. Blinded assessors screened participants for seven post-operative days for a pulmonary complication using the Melbourne Group Score. Oxyhaemoglobin saturation on room air was assessed daily and reports of lung collapse/consolidation on available medical imaging was collected. If no medical imaging was conducted participants were assumed to be clear of collapse/consolidation for that day. Sensitivity, specificity, and predictive values of these two assessments were calculated.

**Results:** Of 351 participants 25% (n=86) developed a pulmonary complication. The sensitivity and specificity of imaging to detect a pulmonary complication was 57% and 89% and oxyhaemoglobin desaturation was 80% and 84%. The positive and negative predictive value of imaging was 63% and 86% and oxyhaemoglobin desaturation was 62% and 93%.

	Post-operative pulmonary complication n = 86	No post-operative pulmonary complication n = 265
N = 351		
Collapse/consolidation on imaging	n = 49 (57%)	n = 29 (11%)
No collapse/consolidation on imaging or no results available	n = 37 (43%)	n = 236 (89%)
Oxyhaemoglobin saturation <90% on room air	n = 69 (80%)	n = 43 (16%)
Oxyhaemoglobin saturation ≥90% on room air	n = 17 (20%)	n = 222 (84%)

**Conclusion:** Both tests had low positive predictive values and shouldn't be used as stand-alone diagnostic criteria for a post-operative pulmonary complication. Further investigations are required to confirm a pulmonary complication. However, the serious consequences of a pulmonary complication would warrant additional physiotherapy in patients who desaturate on room air or with positive imaging as they could be early warning signs of deterioration. Compared to imaging, room air desaturation after abdominal surgery has a superior negative predictive value indicating that this simple bedside test of removing supplemental oxygen for two minutes daily may be a useful clinical assessment.

**Grant Support:** The authors have no interests to declare.

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**THE EFFECT OF MATERNAL HYPOXIA-INDUCED INTRAUTERINE GROWTH RESTRICTION ON DIAPHRAGM FUNCTION IN ADULT MICE**

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**Introduction/Aim:** The diaphragm develops *in utero* and any disturbance to the foetus may lead to dysfunction in the postnatal period. This study used a maternal hypoxia-induced mouse model of intrauterine growth restriction (IUGR) to investigate the impact of IUGR on diaphragm function and structure in male and female adult offspring.

**Methods:** Pregnant BALB/c mice were housed under hypoxic conditions (10.5% O<sub>2</sub>) from gestational day 11–17.5 (IUGR group; term = GD 21). Following hypoxic exposure, mice were returned to normoxic environment (21% O<sub>2</sub>). A second group of pregnant mice were housed under normoxic conditions throughout pregnancy (Control). Weights of offspring (Control male, n = 8; Control female, n = 10; IUGR male, n = 8; IUGR female, n = 8) were recorded until 8 weeks of age at which point diaphragm muscles were removed for organ bath experiments to measure maximum specific force, twitch responses (peak, time to peak, half relaxation time (½T<sub>R</sub>), maximum rate of force production (dF/dt) and fatigue index. A second strip of diaphragm muscle was snap frozen to determine myofibre cross-sectional area.

**Results:** The IUGR offspring were lighter at birth (Control, n = 35; IUGR, n = 33; P = 0.013) and remained lighter at 8 weeks of age compared with Controls (P < 0.001). The maximum specific force was not different between treatment (P = 0.478) or sex (P = 0.098). In terms of twitch responses, IUGR group had a longer ½T<sub>R</sub> compared with Control (P = 0.015) whereas other parameters were similar between groups. Females had lower maximum dF/dT (P = 0.049) and higher fatigue index (P = 0.001) compared with males, independent of IUGR. There was no difference in the myofibril cross-sectional area between groups or sexes.

**Conclusion:** Maternal hypoxia-induced IUGR reduces the rate of relaxation after a twitch contraction, suggesting that the diaphragm function in adults is affected by *in utero* insults. The mechanism behind sexual dimorphism in diaphragm contraction at the tissue level should be examined in future studies.

**Grant Support:** NHMRC (1090888, 1120128).

**Declaration of Interest Statement:** None.

**PROGRAMMED DEATH-1, CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND SUSCEPTIBILITY TO INFECTION**

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**Introduction/Aim:** Patients with chronic obstructive pulmonary disease (COPD) have an increased risk of contracting respiratory bacterial infections that cause serious exacerbations of their symptoms and often lead to pneumonia. This suggests that patients with COPD have defective anti-bacterial immune responses. Since several species of bacteria are associated with exacerbations and/or pneumonia in COPD, treatments that specifically target the dysregulated immune response(s) involved may be effective and potentially broadly applicable. Activation of the programmed death(PD)-1/PD-L pathway potentially suppresses immune responses in several cell types and COPD patients have increased proportion of PD-1<sup>+</sup> T-cells in their lungs. However, the role of this pathway in phagocytic cell-mediated bacterial clearing in COPD is yet to be investigated.

**Methods:** We induced respiratory *Streptococcus pneumoniae* infection in a clinically relevant mouse model of cigarette smoke-induced COPD (experimental COPD). We then profiled lung immune cell responses using flow cytometry to determine the cellular source(s) of PD-1/PD-L1 in experimental COPD. To assess the functional role of the PD-1/PD-L pathway on anti-bacterial defences, phagocytosis and killing capacity (of *S. pneumoniae*) were assessed in a macrophage cell line treated with cigarette smoke extract (CSE) and PD-1-neutralising antibody.

**Results:** Experimental COPD reduced *S. pneumoniae* clearance and, like clinical COPD, resulted in a dichotomy of increased influx and activation of inflammatory cells, such as macrophages and neutrophils, but increased the numbers of suppressive regulatory T-cells. Significantly, PD-1/PD-L1-expressing macrophages, dendritic cells and regulatory T-cells were elevated in experimental COPD. CSE exposure of macrophages resulted in increased PD-1/PD-L1 surface expression and reduced their capacity to kill *S. pneumoniae*. Importantly, blocking PD-1 signalling in CSE-exposed macrophages restored their capacity to kill *S. pneumoniae*.

**Conclusion:** We show a potential role for increased activation of the immunosuppressive PD-1/PD-L pathway in promoting susceptibility to *S. pneumoniae* infection in COPD, which may be therapeutically targeted with anti-PD1 treatment.

**Grant Support:** NHMRC & HMRI

**EXTRACELLULAR MATRIX SUBTYPES ARE ALTERED WITHIN THE AIRWAY SMOOTH MUSCLE LAYER IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE**

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**Introduction:** Chronic obstructive pulmonary disease (COPD) is characterised by chronic inflammation, airway remodelling and loss of lung function. We have previously observed an inverse relationship between FEV<sub>1</sub>% predicted and the volume fraction of total extracellular matrix (V<sub>V</sub> ECM) within the layer of airway smooth muscle (ASM) in obstructed smokers. There have been no quantitative studies of the volume fractions of specific ECM proteins within the ASM layer in relation to airflow obstruction.

**Aim:** To estimate the volume fractions of collagen-I, III, IV and V, biglycan, fibronectin and versican within the ASM layer in subjects with (n = 14) and without (n = 15) fixed airflow obstruction (defined as FEV<sub>1</sub>% predicted <80 and FEV<sub>1</sub>/FVC ratio < 0.7) who underwent lung resection for lung cancer.

**Methods:** Prior to surgery, post-bronchodilator FEV<sub>1</sub> was measured and smoking history recorded. From post-operative tissue, transverse airway sections were obtained and processed, and thin (0.5µm) sections cut and labelled using immunohistochemistry for ECM subtypes. Point counts were made within the ASM layer to estimate the volume fraction of positive staining within the ASM layer. The basement membrane perimeter was measured and used as an indication of airway size.

**Results:** FEV<sub>1</sub>% predicted (Mean ± SD) was 68 ± 11% for obstructed and 101 ± 15% for non-obstructed cases (P ≤ 0.001). FEV<sub>1</sub>/FVC% was 64 ± 8 for obstructed and 78 ± 7 for non-obstructed cases (P ≤ 0.001). A positive correlation was seen between V<sub>V</sub>Collagen-I and FEV<sub>1</sub>% predicted (r = 0.48, P = 0.04) and a negative correlation between V<sub>V</sub> Versican and FEV<sub>1</sub>% predicted (r = -0.58, P = 0.006). No other correlations were seen between ECM subtypes and FEV<sub>1</sub>% predicted.

**Conclusion:** The volume fraction of Collagen-I is decreased within the ASM layer while Versican is increased in patients with airflow obstruction. These data suggest that changes in the matrix composition within the ASM layer may contribute to fixed airflow obstruction.

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### DIFFERENT STRUCTURAL COMPONENTS OF THE AIRWAY SMOOTH MUSCLE LAYER DETERMINE POST-BRONCHODILATOR AND AIRWAY RESPONSIVENESS IN SMOKERS

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**Introduction/Aim:** The thickness and composition (increased extracellular matrix, ECM) of the layer of airway smooth muscle (ASM) is altered in subjects with fixed airflow limitation. This study assessed the relationship between airway wall structure and *in vivo* lung function and airway responsiveness.

**Methods:** Subjects (15M;7F, 37-78yrs) undergoing lobar resection were recruited prior to surgery and had pre- and post-bronchodilator FEV<sub>1</sub> and FVC measured. On a separate day a methacholine bronchial challenge was performed to determine airway responsiveness defined by PD<sub>20</sub> (provocative dose causing a 20% fall in FEV<sub>1</sub>) or dose-response slope (DRS). Post-operative lung tissue was collected and fixed to measure airway wall thickness ( $\sqrt{\text{area/perimeter}}$  of basement membrane -P<sub>bm</sub>) and airway size - small (P<sub>bm</sub><6mm) or large (P<sub>bm</sub>>6mm). Relative fractions of ASM (V<sub>VASM</sub>) and ECM (V<sub>VECM</sub>) within the ASM layer were measured by point counting.

**Results:** FEV<sub>1</sub>% predicted was inversely related to the thickness of the ASM layer ( $P = 0.01$ ), outer airway wall ( $P = 0.04$ ) and total airway wall ( $P = 0.03$ ) in large airways and positively to the thickness of the inner airway wall in small airways ( $P = 0.04$ ). No correlations were found between airway wall thickness and PD<sub>20</sub> or DRS. V<sub>VECM</sub> was inversely related to FEV<sub>1</sub>/FVC ( $r = -0.73$ ,  $P = 0.04$ ) in small airways. V<sub>VECM</sub> was not related to PD<sub>20</sub> or DRS. V<sub>VASM</sub> was inversely related to PD<sub>20</sub> ( $r = -0.57$ ,  $P = 0.04$ ), with a trend for a positive correlation with DRS ( $r = 0.47$ ,  $P = 0.06$ ), in the large airways but not the small airways.

**Conclusion:** Thickness of the airway wall (including the ASM layer) determines lung function but not airway responsiveness. Increased ECM fraction in the ASM layer is related to reduced airway function, whereas increased ASM fraction in the ASM layer is related to increased airway responsiveness. These findings suggest that the balance between ASM and tissue matrix within the ASM layer may determine the balance between fixed and reversible excessive airway narrowing.

**Grant Support:** NHMRC (1063068, 1045824)

### LC3-ASSOCIATED PHAGOCYTOSIS (LAP) IN COPD AND IN RESPONSE TO CIGARETTE SMOKE

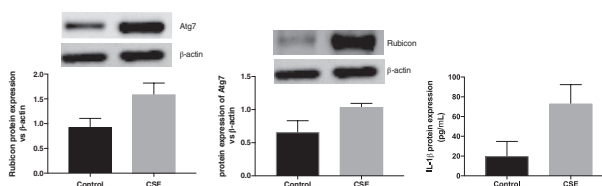
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**Introduction/Aim:** We have previously shown in COPD that defective efferocytosis of apoptotic cells leads to secondary necrosis of the uncleared cells and a resultant increase in lung inflammation. The precise mechanisms for these effects are unknown. A newly discovered pathway called LC3-associated phagocytosis (LAP) has been reported to be indispensable for effective phagocytosis and clearance of dead cells. We hypothesized that cigarette smoke would dysregulate LAP and increase inflammatory responses with the potential to induce lung injury and destruction of airways.

**Methods:** We examined the effects of 24h exposure with cigarette smoke extract (CSE) on the LAP pathway in THP-1 differentiated macrophage cells using Western blot, ELISA, Flow cytometry and Immunofluorescence.

**Results:** CSE exposure led to the activation of LAP and IL-1 $\beta$ . Proteins associated with LAP pathway including Rubicon and Atg7 were all activated by CSE exposure. We also observed increased levels of pro-inflammatory cytokines such as IL-1 $\beta$  in CSE exposed THP-1 macrophages.



**Conclusion:** LAP activation is required for effective efferocytosis and contributes to the regulation of inflammatory responses, and is dysregulated by cigarette exposure. Activation of LAP associated proteins after 24h of CSE exposure may be a defensive mechanism to protect against deleterious effects of CSE. Thus, targeting homeostatic restoration of LAP in smokers and COPD subjects may present a novel therapeutic strategy

### DIFFERENCES IN CONTRACTILITY OF HUMAN SMALL AIRWAY SMOOTH MUSCLE IN COPD AND ASTHMA

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**Introduction/Aim:** COPD and asthma are both characterised by airway hyperresponsiveness. Narrowing of the small airways in these diseases is thought to have a major contribution to total airway resistance. This study investigated contractility of small conducting airways from patients with and without airway disease with the aim to explore possible mechanisms for airway hyperresponsiveness.

**Methods:** Resected lung tissue from subjects (4M:7F, 47-83 years) was acquired. Seven with normal lung function, one asthmatic and three with COPD. Small airway rings (1 – 4 mm internal diameter; n = 41 tissues) were dissected free from the parenchyma and mounted into a wire myograph chamber. Length-tension curves were generated to KCl (60 mM) to establish optimum length ( $L_0$ ) for contraction. Dose-response curves to acetylcholine (ACh;  $10^{-8}$ M –  $3 \times 10^{-3}$ M) followed by histamine ( $10^{-9}$ M –  $3 \times 10^{-3}$ M) in the presence of atropine (1  $\mu$ M) were performed. Values are given as mean  $\pm$  SEM.

**Results:** In control tissues, maximal active wall tension ( $T_{Active}$ ) to ACh, histamine and KCl were  $33 \pm 16$ ,  $31 \pm 17$  and  $28 \pm 10$  cm-H<sub>2</sub>O, respectively (N = 25 tissues).  $T_{Active}$  for ACh, histamine and KCl for the asthmatic subject, were  $65 \pm 23$  and  $55 \pm 17$  and  $59 \pm 19$  cm-H<sub>2</sub>O, respectively (n = 4 tissues). For the COPD tissues,  $T_{Active}$  to ACh, histamine and KCl were  $33 \pm 20$ ,  $27 \pm 15$  and  $25 \pm 17$  cm-H<sub>2</sub>O, respectively (n = 12 tissues). For control tissues ACh responses were comparable with histamine (slope:  $0.96 \pm 0.02$ ), whereas responses to KCl underestimated tension generated to ACh and histamine ( $0.77 \pm 0.03$ ,  $0.79 \pm 0.04$ ; respectively). In contrast, for diseased tissues histamine and KCl responses both underestimated responses to ACh ( $0.77 \pm 0.05$ ,  $0.77 \pm 0.07$ ; respectively), however histamine and KCl were highly comparable ( $1.01 \pm 0.04$ ).

**Conclusion:** Preliminary data indicates apparent differences in the contractility of small airways to different stimuli between non-diseased and diseased patients. Although the mechanisms have not yet been elucidated, these results may indicate differences in calcium handling and therefore warrants further investigation.

**Grant Support:** NHMRC – 1063068

### STABILITY OF BLOOD EOSINOPHILS IN RECURRENT EXACERBATIONS OF COPD

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**Introduction/Aim:** In stable COPD, higher blood eosinophil counts (>0.15) identify COPD patients with favourable responses to corticosteroids and anti-IL5 therapy. Similarly, in acute exacerbations of COPD, higher blood eosinophil counts predict faster exacerbation recovery, possibly reflecting corticosteroid suppression of eosinophilic inflammation. Higher blood eosinophil counts may represent a clinical trait which drives exacerbation risk in a subset of COPD patients. The propensity for patients with previous eosinophilic exacerbations to have recurring eosinophilic exacerbations has not yet been reported.

**Methods:** Patients hospitalized for AECOPD (n = 155) were recruited to a prospective observational study with comprehensive assessment including blood eosinophil counts. AECOPD where no prehospital oral corticosteroid was administered were categorized as eosinophilic ( $\geq 0.15$ ) or non-eosinophilic (<0.15). We compared eosinophil counts in future exacerbations to that of the index exacerbation.

**Results:** The index admissions were non-eosinophilic in 94/155 (61%) and eosinophilic in 61/155 (39%). A total of 198 readmissions with no oral corticosteroid administered prior to hospitalisation occurred in 65/155 (42%) of the index patients. Patients with a baseline admission eosinophil count  $\geq 0.15$  had significantly higher blood eosinophil counts at readmission ( $0.23/0.24$  vs  $0.08/0.14$ ,  $P < 0.0001$ ). Amongst those with a non-eosinophilic exacerbation at baseline, future exacerbations remained non-eosinophilic in 99/117 (84.6%). Amongst those with eosinophilic exacerbations at baseline, 48/81 (59.3%) of subsequent exacerbations remained eosinophilic.

**Discussion:** Eosinophilia/non-eosinophilia may represent a clinical trait which recurs in serial exacerbators with potential therapeutic implications.

**Conclusion: Grant Support:**

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**MULTI CENTRE RANDOMISED CONTROLLED TRIAL WITH RADIAL EBUS (R-EBUS) COMPARING THIN VS THICK GUIDE SHEATH (GS) WITH THE ADDITION OF AN ASPIRATION NEEDLE BIOPSY, IN THE DIAGNOSIS OF PERIPHERAL LUNG LESIONS (REBUST 2)**

**HERATH S<sup>1,6</sup>, YAP E<sup>2</sup>, LOW I<sup>3</sup>, MAHJAN H<sup>4</sup>, ING A<sup>5,6</sup>**

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**Introduction/Aim:** R-EBUS of peripheral lung lesions has been increasingly used, but overall diagnostic yield remains suboptimal (1). The size of the biopsy instruments may impact the yield. We aim to compare the 2 available guide GS sizes (2mm and 2.6mm) to assess diagnostic yield and safety and the utility of an additional aspiration needle biopsy.

**Methods:** In a multi-centre randomised control trial, all patients referred for R-EBUS were randomised to thick or thin GS. All underwent conventional R-EBUS biopsies and sampling (forceps, brush, lavage). The thick GS arm had an additional aspiration needle biopsy in a pre-defined random order. All samples were assessed by blinded pathologists and adequacy of samples was agreed upon.

**Results:** 52 patients were recruited from March 2015 – June 2018. 20 were randomised to the thin GS and 32 to the thick. 4 patients with mediastinal LN positivity excluded. 48 patients were analysed. Mean age was 68.4 y (range 39-86; male 21 [44%]). Mean FEV1 was 1.54L (61%) (range 0.75 -3.45L). 72% of lesions were in the upper lobes.

The overall diagnostic of R-EBUS was 69% (79% for malignant lesions and 43% for benign).

The biopsy specimen with best yield was the aspiration needle in 13/33, followed by forceps 12/33, brush 6/33 and wash 2/33.

In thin GS arm (n = 19) the diagnostic yield was 47% (67 % for malignant lesions, 25% for benign).

In the thick GS arm (n = 29), the diagnostic yield was 82% (87% for malignant lesions, 66% for benign).

There was one pneumothorax (thin GS) and one minor bleed (thick GS).

**Conclusion:** Use of the thick GS resulted in statistically higher diagnostic yield for malignancy (87% vs 63%  $P < 0.05$ ). The use of an aspiration needle in the thick GS arm allowed an additional 17% patients to be diagnosed which would have been missed with conventional techniques. Adverse events were similar, and addition of a needle did not increase the pneumothorax rate.

**Grant Support:** None.

**Conflicts of interest:** None.

**REFERENCE:**

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**COMPARISON OF LINEAR ENDOBRONCHIAL ULTRASOUND – TRANSBRONCHIAL NEEDLE ASPIRATION (EBUS-TBNA) USING 22G PROCORE NEEDLE VS 22G OLYMPUS NEEDLE**  
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**Introduction/Aim:** EBUS-TBNA is the definitive investigation for mediastinal lymphadenopathy. Failure to obtain adequate tissue for diagnosis and ancillary tests results in repeat procedures. Both the 22G Olympus needle and the Echotip 22G ProCore needles have a bevelled tip, but the ProCore needle also has a reverse lateral bevel. This feature is designed to collect tissue during retrograde withdrawal of the needle. This study aims to determine if there is a difference between the needles in diagnostic rate or sample suitability for ancillary tests.

**Methods:** Patients undergoing linear EBUS were randomised to either the 22G Olympus needle or the 22G ProCore needle. The result of each TBNA pass was documented as sufficient or insufficient at rapid onsite examination (ROSE). Diagnosis and suitability of samples for ancillary tests were recorded. Fisher's exact test was used for statistical analysis.

**Results:** 80 patients were recruited. There were 34 benign cases, 34 malignant cases and 12 insufficient cases. Median number of passes was 5 for both needles. The diagnostic rate was higher for the Olympus needle (45/49 [92%]) than the Procure needle (23/31 [75%]) but this failed to reach statistical significance (Fisher exact statistic =0.0514 [ $P = < 0.5$ ]). For procedures with confirmed adequate sampling at ROSE, the average number of passes to reach adequacy was 0.9 for the Olympus needle and 1.7 for the Procure needle. Cell block yield for diagnosis was similar (Olympus 57%, Procure 51%). For malignant cases, there was no significant difference in obtaining sufficient samples for immunohistochemistry testing (Olympus 80%, Procure 79%). Due to the small number of malignant cases we were unable to assess for a difference in molecular testing.

**Conclusion:** While the difference between the 22G Procure needle and 22G Olympus needle was not statistically significant, there was a trend favouring diagnostic accuracy for the 22G Olympus needle.

**Grant Support:** Australian Postgraduate Award, University of Adelaide Dawe's Scholarship (top-up), Royal Adelaide Hospital.

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**RADIAL ENDOBRONCHIAL ULTRASOUND (EBUS) WITH TRANSBRONCHIAL CRYOBIOPSY VERSUS RADIAL EBUS ALONE FOR THE DIAGNOSIS OF PERIPHERAL PULMONARY LESIONS: A PROSPECTIVE RANDOMISED TRIAL**

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**Introduction/Aim:** Transbronchial lung biopsy (TBB) has long been utilised to sample pulmonary parenchyma for the investigation of peripheral pulmonary lesions (PPLs). However, even with guidance, diagnostic yield from meta-analyses is 70%. Cryobiopsy has emerged as another method for obtaining biopsies of greater size and quality. We aimed to assess the role of transbronchial cryobiopsy (TB-CB) with radial EBUS guide sheath (EBUS-GS) in the investigation of PPLs.

**Methods:** Patients were prospectively recruited and randomised to either EBUS-GS with conventional forceps TBB and one TB-CB, or conventional forceps alone (current standard of care). All CB were performed under general anaesthesia with intubation via endotracheal tube. Safety and complications were assessed. Patients were followed up to determine whether diagnosis was achieved, or if further investigations were required.

**Results:** 22 patients have been recruited; 11 were randomised to TB-CB. In the TB-CB group 2 cases were excluded from analysis due to presence of lymphadenopathy leading to linear EBUS and where the lesion resolved at the time of procedure. For the TB-CB group the probe was within the lesion for 7/9 cases and adjacent in 2/9 cases. In 2 cases CB was not possible where lesion was too proximal for safe biopsy and one case where the cryoprobe could not be manoeuvred in. Overall diagnostic yield for this group was 77.8% (7/9). Where CB was obtained, diagnosis was achieved in all cases except one where the biopsy was accidentally placed in saline (85.7% [6/7]). In the conventional TBB group, the probe was within the lesion in 9/11 cases, with overall diagnostic yield of 63.6% (7/11). 3 further procedures were subsequently required, compared to only 1 in the CB group. There were no pneumothoraces or serious bleeding complications in either group.

**Conclusion:** TB-CB is a non-inferior, alternative method for investigating PPLs.

**Grant Support Conclusion**

**TRANSESOPHAGEAL VS TRANSBRONCHIAL ULTRASOUND GUIDED SAMPLING OF MEDIASTINAL LYMPH NODES**

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**Introduction/Aim:** Sampling of mediastinal lymph nodes using endobronchial ultrasound guided fine needle aspiration (EBUS) is routine. Some centres also use EBUS endoscopes via the oesophageal route (EUS(B)), firstly to sample lesions not accessible via EBUS and secondly as subjectively EUS(B) appears quicker and easier in some circumstances for nodes accessible by either route. We compared diagnostic yield, procedure duration, sedation requirements and complication rate of EUS(B) and EBUS when used to sample lesions accessible by either procedure.

**Methods:** Data from 83 EUS(B) and 166 EBUS procedures were retrospectively analysed following matching for lymph node station and size.

**Results:** A definitive histological diagnosis was made in 75% of EUS(B) and 59% of EBUS procedures ( $P = 0.01$ ), whilst lymphoid tissue was present but no other diagnosis made in 13% of EUS(B) and 30% of EBUS procedures. Combining these categories, as is standard practice in EBUS studies, the overall sensitivity of EUS(B) and EBUS were similar at 88% and 89% respectively. EUS(B) was associated with less fentanyl use (mean EUS(B) 84mg, EBUS 95mg ( $P = 0.02$ )). Midazolam dose (3.7 mg vs 4.0 mg) and procedure duration (25 mins vs 24 mins) did not differ. Moderate bleeding occurred in one patient in each group.

**Conclusion:** In this single centre retrospective analysis, EUS(B) had a better definitive diagnostic yield compared to EBUS, which was unexpected. Overall diagnostic sensitivity was similar between procedures. There was a small reduction in sedation requirement with EUS(B) and no difference in procedure duration or complication rate. The increase in apparent diagnostic yield may have been due to procedural lists choosing to perform EUS(B) rather than EBUS in certain patients and the associated selection bias. A multicentre, randomised controlled trial using these data to power the study would be the next step in comparing EUS(B) and EBUS.

**Grant Support:** Nil

**USE OF INDWELLING PLEURAL CATHETER IN THE MANAGEMENT OF MALIGNANT ASCITES: A RETROSPECTIVE AUDIT OF 46 PATIENTS**

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**Introduction/Aim:** Patients suffering from malignant ascites often require repeated large volume paracentesis (LVP) for symptomatic relief. This typically requires hospital admission. The use of tunnelled indwelling pleural catheters for malignant pleural effusion is well established. Here we report the first Australian experience of placing indwelling pleural catheters peritoneally (IPeC) for management of recurrent malignant ascites.

**Methods:** A retrospective audit of IPeC use in patients with recurrent, symptomatic MA between 2010-2018 in three hospitals in Western Australia. Procedure data were collected from a database. Outcomes were procedure success rate and safety profile.

**Results:** Forty-six patients (median age 65; female 57%) underwent 48 catheter insertion procedures performed mostly by specialist pleural pulmonologists. The underlying cancers included gynaecological ones (33%), mesothelioma (25%) and gastrointestinal (20%) malignancies. The majority of patients (93%) had prior LVP (median 2.0 drainages) before IPeC insertion. All IPeC were inserted successfully under ultrasound guidance. Most patients (85%) were discharged within 3 days of the procedure. Adverse events were mild and most were self-limiting, including pain (27%), transient hypotension after initial fluid drainage (8%), bacterial peritonitis (8%), wound oozing (8%), fluid loculation (2%) and catheter dislodgement (2%). Most patients (98%) did not require further paracentesis after IPeC insertion. A total of five patients had IPeC removed because of dislodgement, suboptimal catheter tip position, peritonitis, fluid loculation and cessation of fluid production during chemotherapy. The former two patients had IPeC re-inserted shortly afterwards. Patients with bacterial peritonitis responded to antibiotics and only one required catheter removal.

**Conclusions:** Use of tunnelled IPeC can minimise further invasive drainage procedures and potentially reduce hospitalization in patients with symptomatic malignant ascites. Placement of IPeC was associated with a low rate of adverse events and most of them can be managed conservatively.

**Grant Support:** NHMRC Fellowships (RT, YCGL), WA Cancer Council (RT, YCGL), WACPCN Fellowship (SM, DF), ERS Long-term Research Fellowship (DF)

**Declaration of Interest Statement:** Rocket Med Ltd has provided free IPeC drainage kits and a unrestricted educational grant for previous trials led by YCGL. YCGL has served on the advisory boards of Carefusion/BD and Sequana Med Ltd.

**MULTICENTRE RANDOMIZED CONTROL TRIAL OF THE DIAGNOSTIC YIELD AND SAFETY OF RADIAL EBUS GUIDED CRYO-BIOPSY (CRYO-RADIAL) VERSUS CT GUIDED TRANSTHORACIC BIOPSY FOR LUNG MASSES DEMONSTRATE SIMILAR DIAGNOSTIC SUCCESS.**

(CT CROP)

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**Aim:** The addition of cryo-biopsy to R-EBUS procedures (Cryo-Radial) is increasingly utilised as a means of obtaining larger biopsy samples suitable for molecular and PDL-1 testing (1,2). We aimed to compare Cryo-Radial with the current gold standard CT guided transthoracic biopsy (CT-Bx) for diagnostic yield, adequacy for molecular and immune testing, and safety.

**Methods:** Multi-centre, non-blinded, Randomised Control Trial. In the Cryo-Radial arm, at least one conventional R-EBUS sample (brush+/- forceps) was performed. Two pathologists independently analysed the biopsy samples.

**Results:** 44 patients (61% male) in three centres were consented between March 2015 and Sept 2018. 19 were randomised to CT-Bx and 25 to Cryo-Radial. Mean age 70yrs (48-81). Mean FEV1 1.9L (69% [45%-105%]).

In the CT-Bx arm 4 patients did not undergo the procedure. 13/15 who underwent the CT-Bx had a successful biopsy (87%) with one pneumothorax (1/15) requiring intercostal catheter insertion (7%).

In the Cryo-Radial arm 3/25, the procedure was abandoned due to technical difficulty in reaching upper lobes. In 19/22 (86%) patients, the bronchoscopy procedure was successful. Further 3/25 did not progress to the cryo-radial biopsy as a positive diagnosis was obtained prior during the same bronchoscopy procedure. 16/25 had a successful cryo-biopsy (73%) of which 6/16 were benign with excellent diagnostic accuracy.

There was no significant bleeding or pneumothorax. The diagnostic success of CT-Bx compared with bronchoscopic Cryo-Radial for lung masses was not significantly different (87% Vs 86%). Patients with successful biopsies in both arms had adequate testing for molecular sampling.

**Conclusion:** The novel Cryo-Radial method appears to provide samples of sufficient size for a multitude of testing in peripheral lung masses. The two procedures have similar diagnostic accuracy compared with a possible superior safety profile for Cryo-Radial. Cryo-radial also has the advantage of being able to stage the mediastinum during the same procedure. A smaller cryoprobe will help navigate the technical difficulties faced during this study.

**Grant Support:** This study was supported by the below funding bodies:

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- 2. RACP Foundation grant 2: Arnott's Early career researcher in lung cancer. (RACP foundation)

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### BOS IS ASSOCIATED WITH DECREASED SIRT1 IN PERIPHERAL BLOOD PRO-INFLAMMATORY T AND NKT-LIKE LYMPHOCYTES FOLLOWING LUNG TRANSPLANT

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**Introduction/Aim:** Immunosuppression therapy following lung transplantation fails to prevent chronic rejection which is associated with lack of suppression of pro-inflammatory cytokines IFN $\gamma$  and TNF $\alpha$  in T and NKT-like cells. The class III NAD-dependent histone deacetylase (HDAC) Sirtuin 1 (SIRT1) is an important regulator of inflammation, however SIRT1 activity following lung transplant has not been studied. We hypothesized expression of SIRT1 would be decreased in pro-inflammatory lymphocytes following lung transplant and treatment with SIRT1 activators (resveratrol, curcumin) and agents preventing NAD depletion (theophylline) would upregulate SIRT1 and reduce pro-inflammatory cytokine expression in these cells.

**Methods:** Blood was collected from 5 patients with BOS, 15 stable lung transplant patients and 10 healthy aged-matched controls. Intracellular pro-inflammatory cytokines and expression of SIRT1 were determined in T and NKT-like cells cultured in the presence of  $\pm$  25 $\mu$ M resveratrol,  $\pm$ 1 $\mu$ M curcumin,  $\pm$ 5mg/L theophylline,  $\pm$ 1 $\mu$ M prednisolone,  $\pm$ 2.5ng/mL cyclosporine A using flow cytometry.

**Results:** There was a loss of SIRT1 in CD8+ and CD8-T and NKT-like cells in BOS patients compared with stable patients and controls (% CD8+SIRT1+T:  $17 \pm 10$ ;  $37 \pm 10$ ;  $30 \pm 10$  (mean  $\pm$  SD) BOS, stable, control respectively). Loss of SIRT1 was associated with increased T and NKT-like cells expressing IFN $\gamma$  and TNF $\alpha$ . There was a negative correlation between loss of SIRT1 expression by T cells with FEV1 ( $R = -.676$ ,  $P = .037$ ) and time post transplant ( $R = -.552$ ,  $P = .041$ ). All treatments upregulated SIRT1 and inhibited IFN $\gamma$  and TNF $\alpha$  production by T and NKT-like cells additively.

**Conclusion:** SIRT1 is decreased in T and NKT-like pro-inflammatory lymphocytes following lung transplant. Treatment options that increase SIRT1 may improve graft survival.

**Grant Support:** •

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### EXOSOME CHARACTERIZATION TO IDENTIFY PROTEINS UNIQUE TO PAH

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**Introduction/Aim:** Pulmonary arterial hypertension (PAH) is a fatal disease caused by intrinsic remodelling of the pulmonary small blood vessels that leads to increased arterial pressure and ultimately right side heart failure. There is incomplete knowledge surrounding the pathogenesis of the disease and a lack of treatment options. Exosomes are cellular vesicles that mediate cell-to-cell communication and could act as biomarkers of disease and have potential therapeutic benefits as they also contribute to pathogenesis. We hypothesized that the protein expression profile of exosomes from PAH patient blood outgrowth endothelial cells (OECs) would be different to that of controls.

**Methods:** OECs were isolated and cultured from 15mL of PAH ( $n = 4$ ) or control ( $n = 4$ ) peripheral blood. Exosomes were isolated from OEC cultured media via differential centrifugation, and characterised with a NanoSight, TEM and SEM. Mass spectrometry was used to generate exosome protein profiles.

**Results:** Exosomes were positively identified as 40-200nm via NanoSight, TEM and SEM. There were 500 proteins common to all controls, with 105 proteins that were distinct from PAH patients, and 85 proteins that were significantly upregulated in the PAH patients in comparison to the controls, including SPARC ( $P < 0.005$ ), a protein responsible for pathological responses of tissue after injury through regulation of cell growth. There were 440 common proteins across all PAH patients and out of these 45 were distinct from the controls, with 16 proteins significantly downregulated in the PAH patients in comparison to controls (Figure 1).

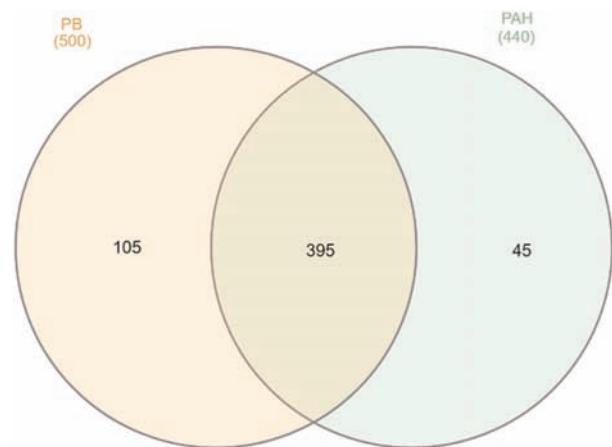


Figure 1. Cross over of exosome proteins derived from OECs identified by mass spectrometry in healthy controls (PB) and PAH patients, highlighting 105 proteins unique to healthy controls and 45 proteins unique to PAH patients

**Conclusion:** This work has enabled the identification of new proteins that could have potential as therapeutic targets, such as SPARC. Further investigation into these newly identified proteins will contribute to understanding of disease pathogenesis and further treatment options using cell therapies.

**Grant Support:** RAH Research Grant and NHMRC Grant.

**A PILOT RANDOMISED CONTROLLED TRIAL OF AMBULATORY OXYGEN VS AIR VIA PORTABLE CONCENTRATOR IN FIBROTIC INTERSTITIAL LUNG DISEASE**

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**Introduction/Aim:** Ambulatory oxygen therapy (AOT) is a common but costly treatment for patients with interstitial lung disease (ILD). The lack of evidence in this area leads to inconsistent clinical guideline recommendations and inequitable access to AOT in this population. This study aimed to examine the feasibility of conducting a randomised double-blinded sham-controlled trial of AOT in patients with ILD who experience dyspnoea and exertional desaturation.

**Methods:** Participants with normal resting oxyhaemoglobin saturation who desaturated to <90% on 6-minute walk test were randomised to 3-month supplemental oxygen or air delivered via portable concentrators, with assessments performed at baseline and weeks 4, 12 and 18. The feasibility of recruitment and blinding were evaluated. Potential efficacy outcomes assessed included exercise capacity, symptoms, health-related quality of life, physical activity and device utilisation.

**Results:** Of 194 patients invited to participate, 30 were randomised [mean age 72 (SD 8) years, FVC 71 (SD 14) % predicted, DLCO 42 (SD 12) % predicted, 11 idiopathic pulmonary fibrosis, 22 males] and 24 completed the study. The recruitment rate was 2.1/month, with the screening to randomisation ratio of 1.1:1. Blinding was successful [Bang's Blinding Index: Oxygen group = 0 (95% CI: -0.42, 0.42); sham group = 0 (-0.47, 0.47)]. Efficacy outcome completion rates were good at ≥80%, except for physical activity diary (53%). In comparison to the sham group, the oxygen group had a significantly smaller deterioration in the St George's Respiratory Questionnaire symptom domain score ( $P = 0.03$ ), and shorter duration of moderate and vigorous activities ( $P = 0.008$ ) at week 12.

**Conclusion:** This pilot trial confirmed feasibility and provided key information to inform the design of future trials. Changes in efficacy outcomes warrant further evaluation in a definitive randomised controlled trial, in order to clarify the therapeutic potential of AOT in patients with ILD.

**Grant Support:** NHMRC Postgraduate Scholarship, Austin Medical Research Foundation, Institute for Breathing and Sleep, Lung Foundation Australia, Air Liquide, Boehringer Ingelheim, Sir Edward Dunlop Medical Research Foundation

**QUADRICEPS STRENGTH IS A MODIFIABLE PREDICTOR OF FUNCTIONAL OUTCOME POST-TRANSPLANTATION**

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**Introduction/Aim:** Severely limited functional status with poor rehabilitation potential is considered an absolute contraindication to lung transplantation. However, defining a threshold of functional status or rehabilitation potential suitable for active listing is complex. Therefore, the study aim was to determine if candidates pre-transplant quadriceps strength along with demographics and respiratory function can predict six-minute walk distance (6MWD) at three months post-transplant.

**Methods:** This study used a prospective observational repeated measures design. All lung transplant recipients at a single institution between Dec 2006 and May 2018 were considered for inclusion. Candidates' demographics (age, sex, lung condition) and transplant hospital admission length of stay were recorded. 6MWD, and quadriceps strength corrected for body weight (QS%) were recorded pre- and three months post-transplant.

**Results:** 278 lung transplant recipients (142 male; mean age 45.7 ± 14.2 years; FEV<sub>1</sub> 33.6 ± 18.6%; 92 cystic fibrosis, 83 chronic obstructive pulmonary disease (COPD), 39 idiopathic pulmonary fibrosis) were studied. Pre-transplant 6MWD was 380.5 ± 138.6m and QS% was 98.8 ± 26.4%. Three months post-transplant 6MWD was 503.3 ± 116.2m. In a multivariate linear regression analysis, increased QS% pre-transplant ( $\beta = 0.81$ ,  $P = 0.001$ ), younger age ( $\beta = -1.59$ ,  $P = 0.011$ ), male recipients ( $\beta = 29.24$ ,  $P = 0.011$ ), and reduced length of stay post-transplant ( $\beta = -2.77$ ,  $P < 0.001$ ) were identified as independent predictors of increased 6MWD. In addition, a diagnosis of COPD ( $\beta = -64.47$ ,  $P = 0.001$ ) or idiopathic pulmonary fibrosis ( $\beta = -51.96$ ,  $P = 0.017$ ) independently predicted reduced 6MWD at three months post-transplant.

**Conclusion:** Pre-transplant quadriceps strength, age, sex, and diagnosis are independent predictors of post-transplant six-minute walk distance. Of these identified measures, only pre-transplant quadriceps strength is potentially modifiable. Quadriceps strength should be considered when assessing candidacy and should be a key outcome measure when assessing efficacy of interventions designed to improve post-transplant outcomes.

**Grant Support:** Nil.

### FUNCTIONAL DIFFERENCES IN OUTGROWTH ENDOTHELIAL CELLS FROM PULMONARY ARTERIAL HYPERTENSION PATIENTS UNDER HYPOXIA

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**Introduction/Aim:** Pulmonary arterial hypertension (PAH) is a devastating lung condition characterised by pulmonary vascular remodelling and over proliferation of vascular cells. Hypoxia is thought to play a significant role in disease pathogenesis and is used to induce PAH in animal models of disease. Outgrowth endothelial cells (OECs) play a role in vascular repair as well as angiogenic remodelling and have been found to be dysfunctional in PAH. This study aimed to characterise the differences in PAH and control OECs in hypoxic conditions.

**Methods:** OECs were isolated from PAH and control patient peripheral blood (15mL). Following characterisation and expansion, cells were exposed to either normoxia (5%CO<sub>2</sub>/atmosO<sub>2</sub>) or hypoxia (1%O<sub>2</sub>/5%CO<sub>2</sub>/94%N<sub>2</sub>) for five days. Proliferation and migration were assessed using MTT and scratch wound assays. Protein analysis was conducted via western blots and immunofluorescence.

**Results:** OECs originating from PAH patients proliferated at a similar rate to control OECs in normoxia (increases of 475% ± 231% and 490% ± 140% over five days respectively). However, under hypoxic conditions the number of control cells decreased to 75% ± 23% of the original population while the number of PAH cells increased by 162% ± 52%. PAH cells also demonstrated increased migratory capacity compared to control cells under hypoxic conditions, as well as altered fibronectin and VE cadherin expression and organisation.

**Conclusion:** PAH patient OECs are functionally different to those isolated from control subjects when placed under hypoxic stress. PAH OECs appear to possess a higher resistance to hypoxia and demonstrate changes in endothelial marker expression compared to control OECs. These findings suggest OECs could play a role in the pathogenesis of PAH as they can contribute to the aberrant proliferation and vascular remodelling seen in the condition.

**Grant Support:** NHMRC, RAH Research Fund.

### BALLOON PULMONARY ANGIOPLASTY IN PATIENTS WITH INOPERABLE CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

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**Introduction:** Chronic thromboembolic pulmonary hypertension (CTEPH) results from incomplete resolution of pulmonary thromboemboli that organise into fibrous obstructions within the arterial lumen. Pulmonary endarterectomy (PEA) surgery is the gold standard treatment, however fewer than 60% of patients with CTEPH are surgical candidates, and pulmonary hypertension persists or recurs in 17-31% of cases. Emerging evidence suggests significant haemodynamic and functional benefits in CTEPH patients can be obtained from percutaneous balloon pulmonary angioplasty (BPA).

**Aim:** To outline the safety, patient selection, efficacy and technical refinements of a state-wide BPA service.

**Methods Methods:** Single centre prospective evaluation from April 2017 to September 2018. CTEPH patients ineligible for surgery or with persistent or recurrent pulmonary hypertension following PEA were assessed for BPA candidacy. A staged approach involving 4-8 BPA sessions per patient over 6-9 months was undertaken in the angiography suite via femoral vein cannulation and with continuous pulmonary pressure measuring. Segmental and subsegmental pulmonary artery luminal defects were targeted using 0.014-inch guidewires and balloons ranging from 2mm – 5.5mm in diameter. Invasive and non-invasive haemodynamic and functional assessments were repeated after every 3-4 BPA sessions.

**Results:** Sixteen patients, 9 female, average age 63.2 ± 9.7 years (45-76) completed 60 BPA sessions (range 1-8, average 3.75). Pulmonary haemodynamics at baseline were systolic PAP 72.9 ± 21 mmHg, mean PAP 41 ± 10.4, pulmonary vascular resistance 682 ± 291 dynes.cm<sup>-5</sup> and cardiac index 2.35 ± 0.72 L/min/m<sup>2</sup>. Systolic PAP and mean PAP decreased to 51 ± 19.3 and 29 ± 10 mmHg respectively post BPA. 6 minute walk distance improved significantly from baseline. Reperfusion injury occurred in 2 patients, 1 contained vascular rupture and no puncture site complications. No patient deaths were recorded.

**Conclusion:** BPA is a safe and effective treatment for inoperable CTEPH.

**Grant Support:** Grant Support – Queensland Government New Technology Grant.

**Declaration of Interest:** Nil relevant conflicts of interest to declare



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## LUNG FUNCTION CHANGES WITH INITIATION OF NON-INVASIVE VENTILATION IN CHILDHOOD DUCHENNE MUSCULAR DYSTROPHY

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**Introduction/Aim:** The use of non-invasive ventilation (NIV) support in children has increased rapidly over the past decade. The aim of this study was to describe and analyse lung function (LF) changes with initiation of NIV in children with Duchenne Muscular Dystrophy (DMD), and assess for differences between Steroid Users and Steroid Naïve subjects.

**Method:** A retrospective clinical audit of children with DMD who were initiated on NIV in the past ten years was conducted. Serial LF data was collected for individuals throughout adolescence, including the period before and following NIV initiation.

**Results:** Twenty-nine males with DMD started NIV during the ten year study period. Nine subjects were using steroids, with a median age of commencement of 6 years (IQR 2.5, range 4-8). The median age that NIV was initiated was 14.66 years (IQR 2.35, 10.47-17.96) with no significant differences in initiation seen between Steroid Users vs. Steroid Naïve groups. Lung function is better (FVC z-score -3.26 vs -5.41,  $P < 0.02$ ) and the rate of decline is slower (FVC z-score -0.58 vs -0.68,  $P < 0.001$ ) in Steroid Users, compared to those who are Steroid Naïve. The median rate of decline in FVC z-score prior to NIV initiation was -0.72 z-score pa (95% CI -0.79, -0.64, SE 0.04,  $P < 0.01$ ) and following NIV initiation it was -0.46 z-scores pa (95% CI -0.54, -0.38, SE 0.04,  $P < 0.01$ ). This reduction in rate of decline following NIV initiation was significantly different,  $P < 0.001$ . The rate of decline in FVC is significantly reduced following NIV initiation in the steroid Naïve group, but increased in the Steroid User group and this reaches significance for z-scores ( $P < 0.001$ ) and % predicted values ( $P < 0.001$ )

**Conclusion:** The rates of decline in FVC are higher in boys with DMD prior to NIV than they are following NIV initiation. Long-term steroid use did not affect the age of NIV initiation in this cohort. However, Steroid Naïve patients have lower LF, and an increased rate of decline in LF prior to NIV initiation, which slows following NIV initiation.

**Grant Support:** None.

## AIRWAY MICROBIOLOGY IN TRACHEOSTOMISED CHILDREN

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**Introduction/Aim:** Children with tracheostomy frequently isolate pathogenic micro-organisms though there is limited published data to guide empirical therapy in the event of a respiratory exacerbation. Our aim was to describe the upper airway microbiology as found on endotracheal aspirate (ETA) in a cohort of children with tracheostomy and correlate it with lower airway microbiology through bronchoalveolar lavage fluid (BALF).

**Methods:** We retrospectively reviewed the records and airway microbiology of all children with tracheostomy currently attending the Queensland Children's Hospital. Sub-analysis was done based on ventilatory and multi-drug resistant organism (MRO) status. Sensitivity and specificity of ETA for *P. aeruginosa* was calculated using concomitant (within 6 months) BALF culture as gold standard, where available.

**Results:** 43 children (female, median age 68 months, 14 ventilated) were included from which different were isolated [mean(SD) 3.(2.2)]. *S. aureus* (n = 33,77%) and *P. aeruginosa* (n = 29,67%) were most frequently isolated. Ventilated children isolated significantly more types of [mean(SD) 4.(2.1) compared to non-ventilated children [mean(SD) 2.(2.)  $P = 0.011$ ]; with 93% of ventilated children isolating *S. aureus* and 86% *P. aeruginosa*. MROs were present in 12 (28%) children of which 8 (86%) were ventilated. MRSA was isolated in 9 (21%) children of which 6 (67%) were ventilated. 3 BALF samples with concurrent ETA were available for analysis. For *P. aeruginosa*, ETA had high sensitivity (95%) but low specificity (64.7%±3.3) when compared with concurrent BALF.

**Conclusion:** In children with tracheostomy, predominant respiratory bacterial are *S. aureus* and *P. aeruginosa*. Ventilated patients *P. aeruginosa*, a negative ETA potentially rules out lower airway isolation. Prospective studies with adequate power and quantitative bacterial cultures could enhance understanding and guide treatment in this cohort.

**Key Words:** endotracheal, BALF

**Grant Support:** None.

**Declaration of Interest:** No conflicts of interest.

**EXPLORING ASSOCIATIONS OF LOWER AIRWAY LYMPHOCYTOSIS AND MUCOSAL COBBLESTONE APPEARANCE IN CHILDREN UNDERGOING FLEXIBLE BRONCHOSCOPY**

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**Introduction/Aim:** Lower airway lymphocytosis and cobblestoning are common findings in children undergoing flexible bronchoscopy (FB). However, to date there are no paediatric studies that have explored possible associations with these findings. Thus, using our dataset of 242 children, we explored possible associations between lymphocytosis found in the bronchoalveolar lavage (BAL) and cobblestoning of mucosa seen at FB.

**Methods:** Our database consisted of 242 children with BAL data; 100 were consecutive FB recordings retrospectively screened and 142 children prospectively collected. We excluded FBs if: BAL data was unavailable, incomplete FB recording or FBs were on children who were immune-compromised or had endotracheal tube, tracheostomy or foreign body. Pearson's  $\chi^2$  test was used for the categorical variables and logistic regression was used to calculate odds ratio and 95% CI. Univariate and multivariate analysis were carried out of potential risk factors for BAL lymphocytosis (>15%) and for cobblestoning including whether viruses were present or not, whether bacteria ( $\geq 10E4$  cfu/ml BAL) were present or not, whether viruses and bacteria were present or not, age, gender and BAL eosinophilia. Here we report our preliminary findings.

**Results:** Lymphocytosis and mucosa cobblestoning were common, occurring in 66 (27%) and 61 (25%) children respectively. Univariate and multivariate analyses did not identify any significant associations for lymphocytosis (table 1). Specifically, the presence of any virus had OR of 0.69 95%CI 0.38-1.26). For mucosa cobblestoning, the sole significant association was age < 24-mo (compared to >24-mo) (Table 1)

**Conclusion:** Mucosal cobblestoning is more common in younger children aged <2 years. The importance of the common occurrence of lower airway lymphocytosis and mucosal cobblestoning requires further exploration.

**Grant Support:** KPE funded by an APSR Scholarship, ABC by NHMRC Practitioner Fellowship.

Table 1

		OR	95% CI	p	OR <sub>adj</sub>	95%CI	p
Lymphocyte >15%	Virus present	0.69	0.38-1.26	0.22			
	Pathogenic bacteria present	1.22	0.66-2.24	0.52			
	Virus and pathogenic bacteria present	0.87	0.44-1.73	0.70			
	Age < 24 months	1.45	0.82-2.56	<b>0.197</b>	1.38	0.77-2.45	0.28
	Gender male	0.91	0.51-1.64	0.76			
Cobblestoning	Cobblestoning present	1.6	0.85-2.97	<b>0.15</b>	1.51	0.8-2.84	0.21
	Virus present	0.81	0.44-1.5	0.50			
	Pathogenic bacteria present	1.42	0.75-2.68	0.28			
	Virus and pathogenic bacteria present	1.12	0.54-2.31	0.76			
	Age < 24 months	1.99	1.10-3.58	<b>0.02</b>	1.97	1.09-3.58	<b>0.03</b>
	Gender male	1.23	0.67-2.28	0.50			
	Eosinophils < 1%	2.19	0.97-4.96	<b>0.06</b>	2.16	0.95-4.94	0.65

**LIMITING RESPIRATORY HOSPITAL ADMISSIONS FOR CHILDREN WITH NEUROMUSCULAR DISEASE (NMD): HOME PHYSIOTHERAPY LED MODEL OF CARE**

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**Introduction/Aim:** Children with severe NMD often have frequent and lengthy hospital admissions for respiratory infections/compromise and require intensive physiotherapy intervention. The aim was to develop a post-acute care/hospital avoidance strategy to facilitate early discharge and keep children with NMD in their home environment safely.

**Method:** Brisbane based NMD infants and children were referred to CHQatHome prior to discharge or via clinician review from January 2017. A Respiratory Physiotherapy Home Action plan was established in collaboration with the family, indicating the parameters for escalating care and contact information, with a physiotherapy visit within 24hrs. A 7-day service was provided with 1-2 sessions per day as needed. Therapists were able to Facetime colleagues from the patient's home to ensure timely access to review and facilitate continuity of care.

**Results:** 8 children were referred, and data reviewed 12 months pre- and post- CHQatHome program engagement.

Pre: Mean LOS 13 days, average admissions 1.75 per year & average ED presentations 2.9 per year

Post: Mean LOS 8.67 days, average admissions 0.75 per year & average ED presentations 0.6 per year,

CHQatHome Physiotherapy sessions average 7.75 per child per year  
Since implementation, 6 of the 8 children have had no unplanned admissions. One child with a complex social situation has accounted for four of the admissions. Feedback from families has been overwhelmingly positive.

**Conclusion:** The risk of hospital acquired infections is significant in this patient group, as are as the costs associated with admissions. Using a proactive & individualised hospital avoidance strategy; LOS, DEM presentations and admissions for children with NMD reduced. Despite expected progression of disease, this cohort of children could be effectively managed at home. Due to the success of this model it has now been expanded to other patients with chronic complex respiratory conditions, with Action Plans utilised across Queensland to support and advise local services.

**Key Words:** Neuromuscular, Physiotherapy, Discharge, Hospital Avoidance

### THE MUCOPOLYSACCHARIDOSIS (MPS) IIIA MOUSE DEMONSTRATES INCREASED AIRWAYS RESISTANCE

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**Introduction/Aim:** Mucopolysaccharidosis type IIIA (MPS IIIA) is a lysosomal storage disorder caused by a deficiency in activity of the lysosomal hydrolase sulphamidase. MPS IIIA patients exhibit respiratory dysfunction and in severe cases respiratory infections may lead to death in children. We have shown that the MPS IIIA mouse demonstrates increased storage of heparan sulphate (HS) in lung tissue and concomitantly increased HS and decreased surfactant lipids in secreted alveolar surfactant. In addition, the surfactant exhibits a reduced ability to lower surface tension. Here we determine whether lung function is affected by alterations in surfactant composition and function.

**Methods:** Thoracic gas volume (TGV) was measured using plethysmography in age-matched (20-week) control (n = 29) and congenic C57BL/6 MPS IIIA mice (n = 15). Lung function parameters (airway resistance -  $R_{aw}$ , tissue damping - G and tissue elastance - H) were determined using the forced oscillation technique. Volume dependence of lung function was measured during slow inflation-deflation.

**Results:** TGV was greater in MPS IIIA ( $0.278 \pm 0.014$  mL,  $P < 0.001$ ) compared with control mice ( $0.222 \pm 0.008$  mL). As TGV was different between treatments, we calculated specific (s) lung function parameters.  $sR_{aw}$  was higher in MPS IIIA ( $0.101 \pm 0.006$  hPa.s<sup>-1</sup>,  $P = 0.013$ ) compared with control mice ( $0.085 \pm 0.003$  hPa.s<sup>-1</sup>). sG was higher in MPS IIIA ( $2.583 \pm 0.1234$  hPa,  $P = 0.007$ ) compared with control mice ( $2.193 \pm 0.075$  hPa). There was no significant difference in sH. During volume dependence measurements both G and H were lower for MPS IIIA mice at a given lung volume.

**Conclusion:** Increased airway resistance and tissue damping suggest that MPS IIIA mice demonstrate increased resistance to airflow in the main conducting airways and obstruction of the small conducting airways, respectively. Lack of change in sH and decreased G and H during deep inflation suggest that lung parenchyma is less resistant/more compliant in MPS IIIA mice. It is possible that subtle lung structural alterations in MPS IIIA mice compensate for detrimental changes in surfactant.

**Grant Support:** Lung Foundation Australia, Ludwig Engel Grant-in-Aid for Physiological Research Award.

### BURDEN OF PNEUMONIA AFTER IMPLEMENTATION OF 13-VALENT CONJUGATE PNEUMOCOCCAL VACCINE STRACHAN R<sup>1</sup>

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**Introduction/Aim:** *Streptococcus pneumoniae* (Sp) is the leading cause of bacterial pneumonia in children. The introduction of the 7-valent conjugate pneumococcal vaccine (7-vPCV) among Australian infants was associated with a reduction in bacterial pneumonia-associated hospitalisations, but a paradoxical contemporaneous increase in empyema linked to serotype replacement. We assessed the change in pneumonia and empyema among children <19 years following the introduction of 13-vPCV (covers types 1, 3 and 19A) in 2011.

**Methods:** National de-identified hospitalisation data were sourced from the Australian Institute of Health and Welfare National Hospital Morbidity Database between 1 January 2007 and 30 June 2017. International Statistical Classification of Disease and Related Health Problems (ICD-10-AM) diagnosis codes were used to identify all pneumonia (bacterial and viral) and empyema coded hospitalisations. The 7-vPCV and 13-vPCV periods extended between 1 June 2007- 31 May 2010 and 1 June 2011- 31 May 2017 respectively. Mid-year population estimates for Australia were obtained from Australian Bureau of Statistics 2016 census estimates. Incidence rates for the 7-vPCV and 13-vPCV periods were calculated as total number of hospitalisations divided by total child-years (aged <19 years) in the two time periods.

**Results:** In the 7-vPCV and 13-vPCV periods there were 43,190 pneumonia (32,458 bacterial), 290 empyema and 88,795 pneumonia (55,823 bacterial); 687 empyema coded hospitalisations respectively. The incidence rates/1000,000 (95% confidence intervals) child-years in the 7-vPCV and 13-vPCV periods were 2,567 (2,542-2,591) vs 2,520 (2,503-2,536) for all pneumonia, 1,929 (1,908-1,950) vs 1,584 (1,570-1,597) for bacterial pneumonia, and 17 (15-19) vs 19 (18-21) for empyema hospitalisations.

**Conclusion:** Replacement of 7-vPCV with 13-vPCV was associated with a reduction in bacterial pneumonia coded hospitalisations but a similar decline was not observed in empyema coded hospitalisations. Enhanced surveillance is needed to understand the influence of vaccine changes on pneumonia and empyema caused by specific pneumococcal serotypes.

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### THE LOWER AIRWAY MICROBIOME IN PATIENTS WITH PRIMARY CILIARY DYSKINESIA

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**Introduction/Aim:** Primary ciliary dyskinesia (PCD) is a rare inherited disease characterized by abnormal ciliary function, leading to compromised mucociliary clearance and persistent bacterial infection of the upper and lower airways. Consequently, patients develop chronic productive cough and bronchiectasis, though progression and disease severity varies considerably between individuals. Despite heterogeneity in disease characteristics, the potential to refine disease phenotypes based on airway microbiome composition, or to gain additional prognostic insight, is unexplored. We aim to apply metagenomic sequencing approaches to prospective longitudinal samples from an Australia-wide cohort, and to relate microbiota composition to patient genetics and clinical characteristics. We report a pilot amplicon-sequencing analysis from an initial patient cohort.

**Methods:** Spontaneous and induced sputum was collected from 10 PCD patients attending the Concord Hospital, Sydney, and 5 healthy controls, respectively. Amplicon sequencing was performed on sputum DNA extracts and bacterial taxonomy was assigned using QIIME2, according to the SILVA bacterial database.

**Results:** The microbiota composition of PCD was significantly different compared to healthy (Pseudo-F = 2.69,  $P = 0.049$ ) and characterised by lower bacterial diversity (Shannon Wiener's diversity  $P = 0.028$ ) and lower evenness of the microbiota composition (Pielou's evenness  $P = 0.040$ ). While the sputum microbiota composition of healthy controls exhibited a high degree of inter-subject similarity, with the uniform predominance of the genus *Streptococcus*, PCD patients displayed substantially greater heterogeneity. The predominant genus in PCD sputum microbiota was variously *Pseudomonas*, *Haemophilus*, *Streptococcus*, *Pasteurella*, and *Neisseria*, representing on average 74.5% of total airway bacterial biomass.

**Conclusion:** Significant differences exist between the lower airway microbiome in those with PCD and to healthy controls. Substantial inter-subject variance in airway microbiota composition in PCD suggests the potential for microbiome analysis to inform the identification of specific disease phenotypes.

**Grant Support:** Supported by SAHMRI.

### SPUTUM PROCALCITONIN LEVELS IN PATIENTS ADMITTED TO HOSPITAL WITH ACUTE EXACERBATIONS OF BRONCHIECTASIS

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**Introduction:** Serum procalcitonin is a biomarker of infection, used to facilitate diagnosis, initiation and cessation of antibiotic therapy and predict outcomes in sepsis and respiratory tract infections. Despite bronchiectasis being characterised by frequent infection-related exacerbations, serum procalcitonin levels are not usually elevated in these patients.

**Objectives:** To investigate the role of sputum procalcitonin as an alternative to serum procalcitonin in bronchiectasis exacerbations requiring hospitalisation.

**Methods:** Patients aged over 18 years, with radiologically confirmed bronchiectasis, admitted to hospital with an acute pulmonary exacerbation were enrolled. Measurements assessed included; sputum and serum procalcitonin concentration, peripheral blood white cell counts, serum C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), sputum bacterial culture, sputum viral panel and patient self-scored symptom scores. Blood samples were taken at hospital admission and sputum supernatant was obtained from spontaneous sputum samples.

**Results:** Fifteen patients were enrolled and the median procalcitonin level in sputum was 2.0 ng/mL (range 0.6–6.8 ng/mL) and <0.05 to 0.4 ng/mL in serum. There was a significant positive correlation between baseline sputum procalcitonin concentration and ESR (Spearman correlation coefficient: 0.56,  $P = 0.04$ ), positive but not statistically significant correlation with CRP (Spearman correlation coefficient 0.37,  $P = 0.18$ ) and no correlation with white cell count, serum procalcitonin or symptom scores.

**Conclusion:** This is the first study to investigate sputum procalcitonin. Procalcitonin levels during acute bronchiectasis exacerbations appear to be substantially higher in sputum compared with serum. Further studies investigating sputum procalcitonin in stable bronchiectasis are now warranted to determine its role guiding antibiotic therapy and diagnosing pulmonary exacerbations.

**Key Words:** procalcitonin, bronchiectasis, exacerbations, biomarkers

**Grant Support:** This research was undertaken with a grant from the Centre for Clinical Research and effective practice (CCRRep), now known as Middlemore Clinical Trials.

**MANAGEMENT: A HEALTH PROFESSIONAL PERSPECTIVE**

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**Introduction/Aim:** Bronchiectasis management influences both patient and health service outcomes. Audits globally have identified gaps in management in relation to guidelines, but little is known about what makes bronchiectasis management more effective. This study aims to identify what are the barriers and enablers to bronchiectasis management from a health professional perspective.

**Methods:** Qualitative one-on-one interviews were conducted with 14 health professionals about bronchiectasis management. Health professionals were respiratory specialist doctors (six), physiotherapists (five) and nurses (three) working with bronchiectasis patients in an outpatient setting (mean of 11.3 years  $\pm$  7.9 years). Transcripts were typed verbatim and coded under categories of the theoretical domains framework using NVIVO software.

**Results:** A lack of knowledge about bronchiectasis guidelines was identified amongst health professionals. Barriers identified to bronchiectasis management include availability of resources for sputum clearance, accessibility of antibiotics, a lack of consensus in antibiotic length of treatment, reduced confidence levels in managing and supporting opportunistic infections and clinic time, space and funding. Enablers to bronchiectasis management include working together with the multidisciplinary team (including respiratory physiotherapists and respiratory nurses), using a chronic disease approach to working with patients, and having patient engagement.

**Conclusion:** The value of guidelines is acknowledged by health professionals but lack of knowledge about specific bronchiectasis guidelines highlights the need for greater promotion when updates are released. Health professionals recognise the value of a multidisciplinary approach but referral to physiotherapists and respiratory nurses is often made late in the patient disease journey. A dedicated multidisciplinary clinic may ensure that all patients have more timely access to a range of health professionals to better management and support their bronchiectasis.

**Grant Support:** Nil.

**ORAL CLONIDINE IMPROVES QUALITY OF LIFE IN PATIENTS WITH BRONCHIECTASIS**

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**Introduction/Aim:** Bronchiectasis is a chronic disease characterised by airway inflammation, repeated respiratory infections, and impaired quality of life. Clonidine, a centrally acting  $\alpha$ 2-adrenergic receptor agonist, has been shown to have potent anti-inflammatory effects in both zebrafish and mammalian translation systems. We aimed to assess the anti-inflammatory effects of oral and transdermal clonidine in patients with bronchiectasis.

**Methods:** We undertook a single-arm, pre-post, open-label, dose-escalation study at three centres (Middlemore, Waikato, and Auckland City Hospitals) in New Zealand. Within this study a randomised sub-study of drug delivery formulations was conducted. We enrolled patients with bronchiectasis who were 18 to 90 years of age. Patients were randomly assigned to receive oral (maximum dose 150  $\mu$ g twice a day) or transdermal clonidine (maximum dose 300  $\mu$ g TTS-3 patch weekly) for 8 weeks. The primary endpoint was sputum IL-8.

**Results:** 19 patients received oral clonidine and 17 patients received transdermal clonidine. Sputum and plasma cytokines (IL-8, IL-1 $\beta$ , IL-6, GM-CSF, TNF $\alpha$ ), CRP, and lung function (FEV1, FVC) did not change significantly from baseline with clonidine treatment. All domains of the St Georges Respiratory Questionnaire (SGRQ - total score, symptoms, activity, impacts) improved significantly from baseline in the oral group but not in the transdermal group. Total SGRQ score improved from baseline by 9.6 units (95% CI 4.7 to 14.6;  $P = 0.001$ ) in the oral group. Respiratory Symptoms and Emotional Functioning scales of the Quality of life – Bronchiectasis questionnaire (QOL-B) improved from baseline in the oral group but not transdermal group. Adverse effects were common but were generally mild. 11 (60%) patients in the oral clonidine group and 8 (47%) of the transdermal group had treatment-related adverse effects.

**Conclusion:** In patients with bronchiectasis, treatment with oral clonidine improved respiratory symptoms and quality of life. Neither oral or transdermal clonidine impacted on sputum cytokine levels.

**Grant Support:** Funded by the Health Research Council of New Zealand (HRC 15/400).

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### HIGH DOSE ORAL NICOTINAMIDE REDUCES AIRWAY INFLAMMATION IN BRONCHIECTASIS

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**Introduction/Aim:** Bronchiectasis is characterised by recurrent respiratory infection, productive cough and deterioration in lung function. The importance of identifying novel, non-antibiotic treatments for bronchiectasis cannot be understated. Nicotinamide (a form of vitamin B3) demonstrates anti-inflammatory and antioxidant properties, inhibits pro-inflammatory cytokines and has antimicrobial activity at high doses in murine models. We aimed to assess anti-inflammatory effects of high-dose oral nicotinamide in patients with bronchiectasis.

**Methods:** In this exploratory single-centre, single-arm, open-label study, patients received 3g daily for 1 week, then 3.5g daily for 1 week, and subsequently 4g daily for 6 weeks. Individual, maximal-tolerated dose was used for the main phase of the study. Primary endpoint was sputum cytokines (TNF $\alpha$ , IL-1 $\beta$ , IL-6, IL-8, GM-CSF). Secondary endpoints included plasma cytokines, plasma nicotinamide level, sputum and plasma CRP, blood neutrophil count, lung function, and health-related quality of life. We also assessed the safety profile, tolerability of the treatment, and adherence.

**Results:** 30 patients received nicotinamide treatment; all patients completed the study. Sputum levels of IL-1 $\beta$ , IL-8 and GM-CSF all fell significantly after treatment. Non-significant reductions were seen in levels of TNF $\alpha$  and IL-6 in sputum. No effects were seen on plasma cytokines, CRP or lung function. Adverse effects were common; 29/30 patients reported an adverse effect, although in general these were mild at 3g daily or lower. 4 patients discontinued treatment due to nausea, which was the most common adverse effect. Other adverse effects included dizziness, headache, diarrhoea and stomach-ache; no serious adverse effects occurred.

**Conclusion:** Nicotinamide has anti-inflammatory effects in the airways of patients with bronchiectasis. However adverse effects are common, especially at doses of 3g daily or more; nausea is the most commonly reported adverse effect.

**Grant Support:** This study was funded by the Health Research Council of New Zealand.

**Declaration of Interest:** No conflicts of interest to declare.

### INFLUENZA A VIRUS INFECTION DURING PREGNANCY INDUCES SEVERE MATERNAL VASCULAR DYSFUNCTION AND FOETAL GROWTH RESTRICTION

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**Introduction/Aim:** Influenza A virus (IAV) infection during pregnancy can be life-threatening to both mother and child. IAV-infected pregnant women have a higher incidence of acute respiratory distress syndrome, pneumonia and heart failure. Although IAV is not vertically transmitted to the foetus, the risks to the offspring include preterm birth, congenital malformations, growth restriction, and long-term chronic immune and cognitive diseases later in life. How IAV infection in pregnancy causes these adverse foetal effects *in utero* is unknown.

**Methods:** Eight-to-twelve-week old time-mated pregnant (E12 gestation) and non-pregnant C57BL/6 female mice were intranasally infected with the H3N2 IAV strain (HKx31; 10<sup>4</sup> PFU) or PBS for tissue analysis 3 days post-infection. Maternal and pup weights were recorded. Inflammation and viral mRNA expression in lungs, aorta and placenta were determined by qPCR or flow cytometry. Thoracic aorta reactivity was assessed with myography and endothelium-dependent and independent smooth muscle relaxation determined using Ach and sodium nitropruside, respectively

**Results:** IAV infection during pregnancy resulted in exacerbated systemic inflammation characterised by a significant increase in blood neutrophils and circulating cell-free fetal DNA compared to non-pregnant IAV-infected mice. Pup and placental weights were significantly reduced with IAV-infection. IAV infection during pregnancy caused a significant ~70% impairment in maximal relaxation of the thoracic aorta. This was associated with significantly elevated levels of pro-inflammatory cytokines and influenza viral mRNA. No impairment in vascular function was observed in non-pregnant IAV-infected mice.

**Conclusion:** This study is the first to demonstrate that IAV infection disseminates into the maternal aorta causing severe impairment of vascular function that occurs only during pregnancy. This impairment in vascular function is likely to reduce the blood flow to the placenta and offspring resulting in fetal growth restriction. Therapies restoring vascular function are an exciting and novel strategy for the management of IAV infection during pregnancy.

**Grant Support**

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### EXPLORING THE POTENTIAL ROLE OF THE CALCIUM-SENSING RECEPTOR IN A HOUSE DUST MITE MODEL OF ALLERGIC AIRWAY DISEASE

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**Introduction/Aim:** The calcium sensing receptor's (CaSR) ability to detect changes in extracellular calcium ( $Ca^{2+}_o$ ) to maintain  $Ca^{2+}_o$  homeostasis is well characterized<sup>1</sup>. Recently the CaSR has emerged as a putative drug target in asthma since it is upregulated in asthmatic patients, and its agonists, polyamines induce bronchoconstriction via the CaSR<sup>2</sup>. Further, CaSR negative allosteric modulators can reduce airway contraction, airway inflammation, and airway smooth muscle thickness and fibrosis in a mixed allergen treated mouse model of asthma<sup>2,3</sup>. Therefore, we sought to examine the involvement of the CaSR in *in vitro* airway responsiveness to the polyamines, spermine, compared to methacholine (MCh) using precision cut lung slices (PCLS) from a short term house dust mite (HDM) mouse model of allergic airway disease.

**Methods:** Eight-week-old female Balb/C mice were sensitized and challenged with 100 ug HDM on Day 0 and Day 14. Lung sections were prepared on Day 15 for blinded scoring of peribronchial inflammation (0 - no inflammation; 4 - severe), and PCLS prepared to measure changes in area of intrapulmonary airways in response to spermine and MCh under phase contrast microscopy.

**Results:** Moderate cell aggregates were evident around the airways after HDM sensitization and challenge (inflammation score: saline  $0.5 \pm 0.5$ ; HDM  $2.9 \pm 0.2$ ; mean  $\pm$  SEM,  $n = 6$ /group,  $P < 0.05$ ). In airways matched for size, spermine caused concentration-dependent contraction with lower potency and maximum contraction compared with MCh in PCLS from saline mice (% reduction in area: 3 mM spermine  $31 \pm 5\%$ ; 3  $\mu$ M MCh  $60 \pm 8\%$ ;  $n = 3$ /group). Contraction to spermine and MCh was not increased by HDM.

**Conclusion:** Our short term HDM model induced airway inflammation, but did not increase spermine or MCh-induced contraction *in vitro*. A chronic HDM model that leads to significant airway remodelling and hyperresponsiveness may be required to determine the contribution of the CaSR to increased airway contraction in asthma.

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### THE MAN WHO'D NEVER SEEN A DOCTOR

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**Case Presentation:** We present a case of a 70yo man with 2 months of progressive exertional dyspnoea, orthostatic pre-syncope as well as painful swollen right calf. He described no infective symptoms, no cough or haemoptysis, no chest pain and no orthopnoea. He had travelled from the United States to Australia three months earlier. Initially he did not appear to be in respiratory distress and his vital signs were within normal limits. He was sent for a CTPA which demonstrated a saddle pulmonary embolus with partial occlusion of the left and right pulmonary arteries. After returning from CT he was noted to be in significant respiratory distress with stridor, as well as tongue and facial swelling. In addition, he had become hypotensive which failed to respond to fluids or vasopressors. A decision was made to administer full dose systemic thrombolysis. Several days later he developed chest pain associated with lateral ST-segment depression and troponin elevation. A coronary angiogram was planned, however given his possible contrast hypersensitivity reaction, he was started on a desensitisation protocol. During desensitisation he developed an urticarial reaction on his face and chest as well as severe chest pain. His mast cell tryptase was elevated. A resting MPS demonstrated widespread perfusion defect.

**Discussion:** This man's dramatic and sudden decompensation was likely a combination of his large thrombus burden combined with an allergic contrast reaction. He had a second allergic reaction during contrast desensitisation associated with an acute coronary syndrome. The combination of allergy with acute coronary syndrome has been described in case reports since the 1930s, but was not well described until 1991. It is now known as Kounis syndrome. The usual mechanism is histaminergic coronary artery vasospasm. When suspected, beta-blockers, adrenaline and opiates should all be used with caution.

TP 004

TP 005

**THE USE OF EUCAPNIC VOLUNTARY HYPERVENTILATION AS A BRONCHOPROVOCATION TECHNIQUE FOR EXERCISE INDUCED BRONCHOCONSTRICTION IN THE CLINICAL SETTING**

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**Introduction/Aim:** To evaluate the clinical use of eucapnic voluntary hyperventilation (EVH) as a bronchial provocation test (BPT) for exercise induced bronchoconstriction in the clinical setting.

**Methods:** A retrospective review of lung function database results for all patients who completed EVH at the Alfred Hospital was conducted, including outcomes, additional BPTs completed and timing of these.

**Results:** 132 patients completed EVH at the Alfred Hospital between 2004 and March 2018. Of these, 57 patients (43%) were positive for exercised induced bronchoconstriction, 59 (45%) were negative, and 16 (12%) were inconclusive (fall in FEV<sub>1</sub> less than 10% and target ventilation of 85% not achieved). 3 patients with inconclusive results went on to have other BPTs. 25 (19%) patients referred were high level athletes, and 2 of these had an inconclusive finding. A further 2 were for police or defence force recruitment, and 6 were for scuba diving medicals. 21 (16%) patients also underwent other types of BPT including: mannitol (15), hypertonic saline (6) and methacholine (1). The additional tests were all negative except for one mannitol challenge completed after a negative EVH test. 15 of the other BPTs were completed prior to EVH and 7 mannitol challenges were completed post EVH.

**Conclusion:** EVH is used clinically to assess for exercise induced bronchoconstriction with approximately 20% of referrals for individuals performing exercise at high levels. About 10% of EVH challenges were inconclusive, suggesting that the test is not suitable for assessing all patients. Additional BPT before or after positive or negative EVH is unlikely to change clinical position.

**Grant Support:**

**FEVIPRANT DEMONSTRATES NOVEL ANTI-INFLAMMATORY EFFECTS ON BLOOD AND AIRWAY GENE EXPRESSION IN PATIENTS WITH PERSISTENT EOSINOPHILIC ASTHMA**

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**Introduction/Aim:** Feviprant is a potent selective prostaglandin D<sub>2</sub> receptor 2 (DP2) antagonist, currently in Phase III development for treatment of uncontrolled asthma. In a study involving patients with eosinophilic asthma, feviprant reduced sputum eosinophils, improved lung function and asthma-related quality of life and was well tolerated<sup>1</sup>. In this exploratory analysis, RNA sequencing using mRNA from blood and bronchial epithelial brushings was used to further explore the biology of feviprant's mechanism of action on DP2 pathway.

**Methods:** DESeq2 was used to detect differentially expressed genes. As no single gene reached FDR<0.05, we used a combination of single gene, and pathway-based post-analysis for biological interpretation. Single gene analysis identified a number of genes differentially regulated in the same direction in both tissues. Among top enriched pathways, we considered only those containing genes identified by single gene analysis.

**Results:** Feviprant/placebo was administered to 30/31 asthma patients, respectively, for 12 weeks. In total, after QC, 57 placebo and 51 treatment samples from blood, 25 placebo and 22 treatment samples from airway brushings were analysed. We observed a reciprocal downregulation of humoral (Th2-related) genes, and upregulation of neutrophilic (Th1-related) genes post-treatment in the feviprant arm, and not in the placebo arm. In addition, genes in the immunoglobulin family, keratin, and Nociceptin family were downregulated. Genes linked to Th1/Th17 biology and several chemokine genes were upregulated.

**Conclusion:** Overall, the downregulation of keratin genes associated with cytoskeletal remodelling, cell migration and proliferation aligns with the reported reduction in airway smooth muscle mass. In addition, the downregulation of Nociceptin family and associated genes, immunoglobulin family genes, and the changes in Th1/Th17 genes indicate potential new mechanisms underlying the anti-inflammatory effects of feviprant arising from blockade of the DP2 pathway in asthma.

**Grant Support:** The study has been funded by Novartis Pharma AG, Basel, Switzerland.

**REFERENCE:**

S Gonen et al, *Lancet Respir Med*, 2016, 4, 699–707.



TP 006

TP 007

### FEVIPRANT INHIBITS PROSTAGLANDIN D2 MEDIATED ACTIVATION OF GROUP 2 INNATE LYMPHOID CELLS (ILC2S)

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**Introduction/Aim:** Fevipiprant is a potent selective prostaglandin D<sub>2</sub> receptor 2 (DP2) antagonist which reduces eosinophilic airway inflammation in patients with persistent asthma and raised sputum eosinophil counts. Increased number of group 2 innate lymphoid cells (ILC2s) are found in blood and sputum of severe eosinophilic asthmatics. They express the DP2 receptor that mediates various cellular functions. The aim of the study was to comprehensively characterise the inhibitory effects of fevipiprant on DP2 pathway-mediated cellular functions of ILC2s.

**Methods:** ILC2s were isolated from peripheral blood of healthy volunteers and cultured. Effects on migration, cytokine production, apoptosis and adhesion molecule expression in response to PGD<sub>2</sub> (200 nM) in the presence of increasing concentrations of fevipiprant were determined with chemotaxis-, apoptosis-, quantitative-PCR-, ELISA- and Luminex- assays. The specificity of DP2 pathway activation in ILC2s was confirmed by using DP1 agonist (BW245C) and antagonist (BW868C). The alternative DP2 antagonist (TM30089) was used as positive control. Half-maximal inhibitory concentrations (IC<sub>50</sub>) for fevipiprant were calculated.

**Results:** Fevipiprant specifically inhibited PGD<sub>2</sub> induced ILC2 migration (IC<sub>50</sub> = 6.3 nM), apoptosis suppression, cytokine and other pro-inflammatory molecule production (IC<sub>50</sub> for IL-4, IL-5, IL-8, IL-13, GM-CSF and CSF1 = 0.2 to 1.96 nM), and cell adhesion molecule expression (IC<sub>50</sub> for ICAM1 = 0.56 nM, for PECAM1 = 0.85 nM).

**Conclusion:** Fevipiprant is a potent inhibitor of DP2-mediated activation of ILC2s. Given the role of ILC2s in uncontrolled asthma, these data support further development of fevipiprant in this indication and its inhibitory effects on ILC2s in asthma patients.

**Grant Support:** The study was funded by Novartis AG, Basel, Switzerland.

### FEVIPRANT, A POTENT SELECTIVE ANTAGONIST OF THE PROSTAGLANDIN D2 RECEPTOR 2, MODULATES THE ALLERGIC EFFECTOR UNIT VIA INHIBITION OF EOSINOPHIL MIGRATION TOWARDS MAST CELLS

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**Introduction/Aim:** Prostaglandin D<sub>2</sub> receptor 2 (DP2; previously CRTh2), a receptor for prostaglandin D<sub>2</sub> (PGD<sub>2</sub>), is expressed on adaptive and innate immune cells and plays a major role in pathophysiology of asthma. PGD<sub>2</sub>, produced mainly by activated mast cells (MCs), is a chemoattractant for eosinophils and other immune cells. It is increased in asthmatic lungs after allergen challenge. Consequently, the PGD<sub>2</sub>-DP2 pathway is a promising target for new asthma therapies. Fevipiprant, a potent selective DP2 antagonist reduces eosinophilic airway inflammation and raised sputum eosinophil counts in patients with persistent asthma,<sup>1</sup> and is in Phase III development for treatment of uncontrolled asthma. Here, we report effects of fevipiprant on the crosstalk between two main effector cells of allergic inflammation that comprise the allergic effector unit, MCs and eosinophils.

**Methods:** Cord blood derived MC and peripheral blood eosinophils were purified from healthy or asymptomatic, mildly allergic or asthmatic subjects not on medication during sampling, and co-cultured in vitro with fevipiprant (0.001 μM to 10 μM). The effect of fevipiprant was examined in migration, degranulation and viability assays.

**Results:** Fevipiprant significantly inhibited eosinophil migration towards IgE-activated MCs in a dose-dependent manner, with 60% reduction observed (from 28% of eosinophils migrating with medium down to 12% with the highest drug concentration). No drug-related effect on DP2 receptor surface expression on eosinophils in the absence of PGD<sub>2</sub> was observed. Fevipiprant had no effect on eotaxin-mediated eosinophil migration. Other allergic effector unit activities, such as MC-induced eosinophil survival, or eosinophil-induced MC degranulation, previously described, were not modulated by fevipiprant, suggesting no involvement of PGD<sub>2</sub> signalling in these aspects of the co-culture system.

**Conclusion:** Fevipiprant specifically inhibits PGD<sub>2</sub>-mediated MC-induced eosinophil recruitment, one of the early steps of allergic inflammation mediated by the allergic effector unit. These results demonstrate a potential mechanism by which this drug ameliorates lung inflammation.

**Grant Support:** This study was funded by Novartis Pharma AG, Basel, Switzerland.

**Reference:**

S Gonen et al, Lancet Respir Med, 2016, 4, 699–707.

**FEVIPRANT, A POTENT SELECTIVE PROSTAGLANDIN D<sub>2</sub> RECEPTOR 2 (DP<sub>2</sub>) ANTAGONIST, DOSE-DEPENDENTLY INHIBITS PULMONARY INFLAMMATION IN A MOUSE MODEL OF ASTHMA**

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**Introduction/Aim:** Feviprant is a potent selective DP<sub>2</sub> receptor antagonist which is in Phase III development for treatment of uncontrolled asthma. The present study reports the pharmacological characterisation of feviprant *in vitro* and *in vivo* in mice.

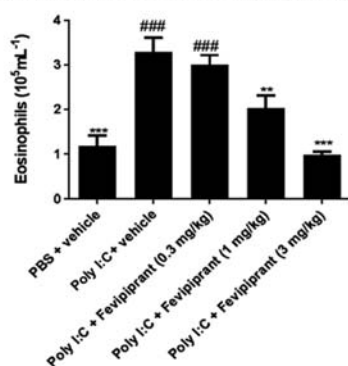
**Methods:** *In vitro* murine DP<sub>2</sub> receptor affinity was determined in a <sup>3</sup>H-PGD<sub>2</sub> scintillation proximity assay with the receptors stably transfected into Chinese Hamster Ovary (CHO) cell membranes, and functional antagonism confirmed by GTP-γS binding. Plasma exposures were measured after oral dosing to Balb/c mice, with the unbound fraction determined *in vitro* by equilibrium dialysis. Utilizing a DP<sub>2</sub> pathway dependent Balb/c mouse asthma model, featuring double-stranded RNA (polyinosine-polycytidylic acid; polyI:C) potentiated ovalbumin (OVA)-induced pulmonary eosinophilia, feviprant was administered once at doses of 0.3, 1 and 3 mg/kg p.o. DP<sub>2</sub>-thromboxane A<sub>2</sub> receptor antagonist ramatroban (30 mg/kg p.o.) was employed as positive control.

**Results:** Feviprant showed K<sub>i</sub> 5.2±0.7 nM at the murine DP<sub>2</sub> receptor and was a functional antagonist with IC<sub>50</sub> 25±0 nM. Following a 5 mg/kg p.o. dose, total plasma C<sub>max</sub> of feviprant was 15 μM, with a half-life of 5.7±1.3 hrs. The unbound fraction in plasma was 0.17. Feviprant exhibited significant dose-dependent inhibition of polyI:C potentiated OVA-induced pulmonary eosinophilia in bronchoalveolar lavage fluid (BAL) (Figure 1) with an approximate ED<sub>50</sub> at 1 mg/kg. Furthermore, a dose-dependent reduction in BAL neutrophils was observed.

**Conclusion:** Feviprant shows similar affinity for DP<sub>2</sub> receptors, functional antagonism and plasma protein binding in mice and humans, while plasma exposure after oral dosing in mice was high. The dose-dependent inhibition of pulmonary inflammation in the murine asthma model by feviprant is consistent with the reduction in sputum eosinophilia observed in asthma patients. The polyI:C challenge model mimics aspects of the enhanced asthmatic inflammatory response upon viral infection, supporting investigation of feviprant as a potential therapy for viral-induced exacerbations in asthma.

**Grant Support:** This study was funded by Novartis Pharma AG, Basel, Switzerland.

**Figure 1: Eosinophils in BAL fluid of OVA challenged sensitised mice**



Bar graph representing total number of eosinophils in BAL fluid from mice sensitized with OVA (15 μg s.c. in 25 μl Alum) and challenged with 0.5% w/v OVA (aerosol, days 21-24). Animals received phosphate buffered saline (PBS) or poly I:C (100 μg/animal, i.n., 16 h post final allergen challenge). BAL fluid was taken 24 hrs after the final OVA aerosol challenge. Data represents mean ± SEM, n=10 with groups compared to PBS + vehicle (#) and Poly I:C + vehicle (\*) using ANOVA followed by Dunnett's post hoc test. \*\*, ### P<0.01 and \*\*\*, #### P<0.001. BAL, bronchoalveolar lavage; OVA, ovalbumin; Poly I:C, polyinosine-polycytidylic acid

**FORCED EXPIRATORY FLOW AS AN ALTERNATIVE PAEDIATRIC LUNG FUNCTION MEASUREMENT**

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**Introduction/Aim:** FEV<sub>1</sub> may appear normal in children with asthma and may not correlate with asthma severity. Forced expiratory flow (FEF<sub>25-75%</sub>) could be a more sensitive parameter to assess changes in peripheral airway function in paediatric patients. We compared changes in FEF<sub>25-75%</sub> and FEV<sub>1</sub> following tiotropium add-on therapy or placebo in children with symptomatic asthma.

**Methods:** Four Phase III trials were analysed. Each age group included one 12-week trial in patients with symptomatic severe asthma (6-11 years, NCT01634152; 12-17 years, NCT01277523) and one 48-week trial in patients with symptomatic moderate asthma (6-11 years, NCT01634139; 12-17 years, NCT01257230). Patients received tiotropium (5μg or 2.5μg) or placebo once daily via Respimat<sup>®</sup> added onto inhaled corticosteroids (ICS) ± other controllers. Lung function endpoints (as % predicted) for individual trials are reported at 12 weeks for severe asthma trials and 24 weeks for moderate asthma trials, respectively. Association between trough FEV<sub>1</sub> and trough FEF<sub>25-75%</sub> responses for individual trials was determined using Pearson's correlation coefficient.

**Results:** Tiotropium add-on consistently improved trough FEF<sub>25-75%</sub> (% predicted normal; 6-11 years, tiotropium 10.6-17.6% vs placebo 4.3-5.2%; 12-17 years, tiotropium 11.2-15.7% vs placebo 8.5-9.6%), which were more pronounced improvements than in trough FEV<sub>1</sub> responses (% predicted normal; 6-11 years, tiotropium 7.6-10.5% vs placebo 5.3-5.5%; 12-17 years, tiotropium 7.6-10.7% vs placebo 6.8-7.5%). This was true when analysed by severity across ages. For all treatments, analysis demonstrated moderate-to-high association between changes in absolute trough FEF<sub>25-75%</sub> (L/s) and trough FEV<sub>1</sub> (L) in each trial (0.735-0.799).

**Conclusion:** Tiotropium Respimat<sup>®</sup> add-on therapy improved FEV<sub>1</sub> and FEF<sub>25-75%</sub> in paediatric patients with symptomatic asthma receiving ICS ± other controllers, with a strong association between the lung function measures demonstrated in these trials. This suggests that FEF<sub>25-75%</sub> should be evaluated as an alternative lung function measurement in paediatric patients, especially when assessing low-level changes in FEV<sub>1</sub>.

**Grant Support:** The study was funded by Boehringer Ingelheim.

**Conflict of Interest:** BVH, ME, PMZ, MS and RS are employees of Boehringer Ingelheim. SG, CV, EH and SS have nothing to declare.

TP 010

TP 011

### PERSISTENT AIRFLOW LIMITATION IN SEVERE ASTHMA: REMODELING OR UNCONTROLLED INFLAMMATION

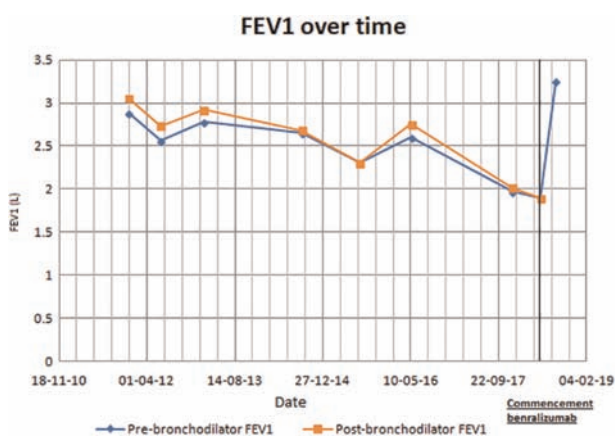
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**Introduction/Aim:** Asthmatics with persistent airflow limitation are typically viewed as less responsive to treatment, and this is often attributed to airway wall remodelling. We present a case of a 48year man with severe eosinophilic asthma complicated by severe airflow limitation and minimal evidence of bronchodilator responsiveness over ten years despite treatment with high dose inhaled steroids, continuous low dose oral steroids and long acting bronchodilators. On commencement of benralizumab (a new anti-IL5 receptor monoclonal antibody) there was a marked improvement in lung function.

**Methods:** Case report.

**Results:**



**Conclusion:** Persistent airflow limitation in asthma may be a consequence of uncontrolled airway inflammation rather than airway wall remodelling. Benralizumab may be effective for selected patients with severe asthma, despite a lack of bronchodilator reversibility. Further research is required to confirm this finding.

**Grant Support:** NA.

### IS ASTHMA LONGITUDINALLY RELATED TO PHYSICAL ACTIVITY IN EARLY CHILDHOOD?

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**Introduction/Aim:** Physical inactivity, with its numerous associated adverse health outcomes, continues to be an important public health problem globally. Previous research suggests that children who experience asthma and wheeze may lead less physically active lives. The aim of this study was to investigate whether the presence of asthma or wheeze at 4 years leads to lower objectively-measured physical activity levels at 6 years.

**Methods:** This analysis was conducted in 391 children who participated in the HealthNuts Study in Melbourne. Data on current asthma and current wheeze were collected via questionnaires at the 4-year follow up. Physical activity data were collected via accelerometers at the 6-year follow up and was defined as the average time in minutes spent doing moderate to vigorous physical activity over the course of 4 days. Relationships were investigated using linear regression models, adjusted for gender and the presence of older siblings.

**Results:** The mean [sd] time spent in physical activity at age 6 years was 98 [35] mins per day, and boys were more active than girls (111 [35] vs. 85 [30], respectively). There was no association between age 4 current asthma (8.1 mins, 95%Confidence Interval (CI) -4.1, 20.3,  $P = .189$ ) or age 4 current wheeze (7.0 mins 95%CI -7.2, 21.2,  $P = 0.318$ ) at age 4 and minutes spent in physical activity at age 6.

**Conclusion:** Children who experienced asthma or wheeze at 4 years were not significantly less active than their peers at 6 years. This suggests that physical activity is not restricted in these Melbourne children who experience asthma and wheeze in early life. It is important to educate and encourage children with asthma and their caregivers to maintain such physically active lifestyles.

**Grant Support:** The HealthNuts study was funded by the National Health and Medical Research Council of Australia. Research at the Murdoch Childrens Research Institute is supported by the Victorian Government's Operational Infrastructure Program.

TP 012

TP 013

### ASTHMA HOSPITAL MORTALITY: A 10-YEAR RETROSPECTIVE AUDIT

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**Introduction/Aim:** Asthma is a common cause for hospital presentation and accounted for 10 544 admissions in NSW in 2016/17.<sup>1</sup> This study describes those patients who were admitted to a metropolitan tertiary hospital for asthma and died of a potentially preventable and treatable disease.

**Methods:** A retrospective audit identified patients who died of asthma who were admitted to the Respiratory Department of St George Hospital in Sydney over a 10-year period from Jan 2008 to June 2018. Data was extracted from the electronic and paper medical records.

**Results:** A total of 6 out of 708 deaths recorded over this 10-year period were due to asthma or had significant contribution from asthma. Mean age was 56 years. 2 patients were female and 4 were male. All 6 patients had a previous diagnosis of asthma, but only 4 were known to a respiratory physician. All patients had been prescribed inhaled corticosteroid (ICS) containing medications but only 2 patients were compliant. One patient was a current heavy smoker, one was an ex-smoker and 4 were non-smokers. 2 patients had never been admitted to hospital for asthma. 1 patient had multiple Emergency Department presentations and 2 patients had multiple hospital admissions for asthma. 4 patients had significant co morbidities, including ischaemic heart disease, atrial fibrillation, diabetes mellitus, obesity, Kartagener's syndrome with bronchiectasis, mental health and substance misuse.

**Conclusion:** Mortality due to asthma is rare (<1%) in this study population. It is associated with failure to recognise its severity and poor compliance with prescribed therapy (including ICS therapy). Interventions including education, close follow up and increased vigilance in management of co-morbidities may improve outcomes.

**Grant Support:** Nil.

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### HOW DO PEOPLE LIVING WITH SEVERE ASTHMA EXPERIENCE AUTONOMY? AN EXPLORATORY STUDY

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**Introduction/Aim:** Severe asthma affects around 3-10% of the asthma population. People with severe asthma have ongoing symptoms and exacerbations. Guidelines emphasise patient centeredness, shared decision-making and self-management, at the heart of which concepts is autonomy, a term widely used and valued in the health care literature. This study aimed to explore the role of autonomy in patient's narratives about their experiences of living with and managing severe asthma.

**Methods:** Participants were included if they were ≥18 years old and diagnosed by a respiratory physician with severe asthma. Rigorous qualitative research methods were used to conduct in-depth semi-structured interviews. Interviews were video recorded, transcribed and analysed thematically using the constant comparative method.

**Results:** Face-to-face interviews, lasting 1.5 - 4 hours, were conducted with 36 participants. Findings revealed that living with severe asthma affects physical and mental well-being, relationships and quality of life. Participants reported their views about being actively involved in managing their condition and strategies they learned. Three broad categories were discerned from the analysis illustrating the ways in which autonomy was enacted, or challenged: 1) maintaining personal control in order to preserve valued activities, 2) re-gaining control and the role of healthcare providers 3) exercising volition when their autonomy was challenged.

**Conclusion:** Our findings show that autonomy was enacted and challenged in a range of situations, such as interactions with healthcare professionals, managing symptoms and medications, and maintaining valued roles. Our findings draw attention to the importance of identifying patient priorities and needs, sharing knowledge and supporting patient autonomy. Healthcare systems encourage patient self-management, however, our findings highlight that people living with severe asthma would like healthcare providers to take a more holistic approach to assessing and understanding their needs, and providing care, beyond that of symptom management and treatment.

**Grant Support:** Seed Grant from the NHMRC Centre for Research Excellence in Severe Asthma.

**Declaration of Interest:** None.

TP 014

TP 015

### GASP: INTEGRATED APPROACH TO MANAGING PATIENTS IN GENERAL PRACTICE

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**Introduction/Aim:** Asthma is a heterogenous disease, individual in its expression and complex in its treatment options; it's clear a personalised approach to providing care is most likely to produce positive results for patients. Currently, evidence suggests many people with asthma do not achieve optimal control of their condition. GASP – Giving Asthma Support to Patients - is Asthma Australia's flagship program aiming at addressing the burden of asthma by facilitating respiratory health expertise among dedicated primary healthcare nurses, enabling them to best coordinate care for their asthma patients.

**Methods:** We aim to assess the effectiveness of this program through quantitative and qualitative analyses. The quantitative analysis via a pre and post period of treatment design evaluates the number of asthma exacerbations requiring medical intervention - unplanned GP attendances and ED attendances, hospital admissions for asthma, and asthma control in the 12 months before and after patients join the GASP program. The qualitative component will involve telephone interviews with people with asthma, practice nurses and GPs to elicit program usefulness and acceptability, and explore the practice priority setting, infrastructure and business model against which the program is likely to succeed.

**Results:** GASP is running in 20 practices between the Illawarra region and greater Sydney in NSW. We have recorded 449 consultations from 259 patients so far. Between months 0, 6 and 12, we are seeing the following improvements:

Indicator	M0	M6	M12
% reporting no unscheduled (GP/ED) visits	45.9	65.9	53.3
% reporting no oral steroid courses	57.5	70.5	90
% reporting no SABA use	17	34.1	36.7
% with correct inhaler technique	64.5	88.6	90
% reporting high adherence	44.8	47.7	43.3

We haven't conducted any qualitative interviews to date.

**Conclusion:** Whilst the evaluation is ongoing, we are encouraged by early signs indicating practices are embracing best practice and evidence-based asthma care principles. Current trends indicate potential for significant improvement in primary and secondary outcome measures. If current trends continue, this evidence provides impetus for further uptake of this innovative program, increased investment in nurse-models of care and ultimately overall quality improvement for people with asthma in primary health.

**Grant Support:** •

### HAZARD REDUCTION BURNING AND ASTHMA; SURVEY OF EXPERIENCES AND ACTIONS

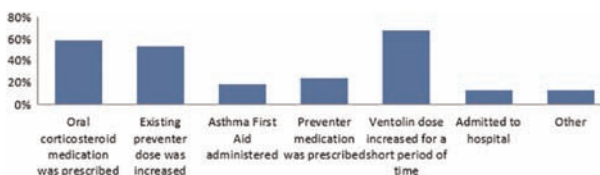
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**Introduction/Aim:** During May 2018 several hazard reduction burns were conducted around greater Sydney resulting in 17 'poor' or 'hazardous' air quality days due to smoke. Smoke can trigger asthma symptoms and lead to severe asthma flare-ups. Asthma Australia was contacted by consumers who reported significant impact on their asthma health. Asthma Australia conducted a survey to understand experiences and actions of affected consumers, to inform advocacy and communications strategies.

**Methods:** The survey used a mixed methods approach including sixteen multiple choice questions and one open ended response using online survey tool *Survey Monkey*. It was sent via email to a convenience sample of 25,888 consumers with Sydney postcodes, who had consented to being contacted by Asthma Australia. The survey was open for one week in August 2018.

**Results:** 682 people completed the survey; most respondents (74.5%) were people with asthma. 60% of respondents said they or someone they cared for experienced respiratory symptoms, of which 51% sought urgent medical attention, 24% at an emergency department. 68% of respondents reported needing reliever medication and 59% were prescribed oral corticosteroids.



Respondents first learnt of poor air quality when they saw smoke or smog in the area (78%). 28% of respondents provided qualitative feedback which was analysed for common themes. Responses mostly called for better communication of burning activity and detailed significant personal impact of smoke and poor air quality.

**Conclusion:** The survey demonstrated poor air quality events during May had widespread impact on people with asthma. The measures people employed to address asthma flare-ups included emergency departments visits and use of oral corticosteroids. People were also limited in their ability to take evasive action, highlighting need to consider overall bushfire risk management strategies which have a lesser impact on human health and opportunities to improve communication about burns.

**Grant Support:** Research was not funded by any external bodies.

TP 016

TP 017

**AN ONLINE PATIENT PORTAL TO ENHANCE CLINICAL COMMUNICATIONS FOR PATIENTS WITH CHRONIC ASTHMA**  
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**Introduction/Aim:** Despite being well received by parents of children with chronic conditions (Britto et al 2013, The Journal of Pediatrics), research into how online portals such as carer-facing apps can be integrated with face-to-face care is limited. This study explored the experiences of patients/families with chronic asthma using the My Health Memory (MHM) app, implemented in an Australian tertiary children's hospital. Its initial functions included, syncing appointments with the native phone calendar, rescheduling appointments, and messaging services to contact hospital staff.

**Method:** A 24-question online survey was disseminated 10 months post-MHM implementation. The survey asked parents about their experiences of the app, and demographics information. Responses to open-ended questions were thematically analysed, and descriptive statistics of the quantitative data are reported.

**Results:** Twenty-five parents of twenty nine children with asthma completed the survey. Most respondents who used the app, used it at least once a month (62.5%, N = 5). All respondents reported the app as being helpful, 63.6% (N = 7) or very helpful, (36.4% (N = 4). Appointment reminders, and communication with staff in the Asthma clinic, were reported as the most useful features of MHM (endorsed by 75% and 50% of participants, respectively). Respondents who had not used the app indicated it was because they were unaware it was available or they did not have frequent clinic visits. Despite this, all respondents saw value in the app for improving management of care and would like to use it. One respondent commented "I feel the app is really helpful. It's a good way of keeping track of my children's asthma episodes and all communication is recorded in one location both the hospital staff and myself can access."

**Conclusion:** Families and patients found the portal an effective means of managing aspects of their care more efficiently, including appointment scheduling and communication with staff.

**Key Words:** asthma, eHealth, patient portals, paediatrics

**Nomination for New Investigator Award:** No

**Grant Support:** No.

**DUPILUMAB IMPROVES ASTHMA OUTCOMES REGARDLESS OF BASELINE LUNG FUNCTION**

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**Introduction/Aim:** Dupilumab, a fully human VelocImmune<sup>®</sup>-derived anti-interleukin (IL)-4 receptor  $\alpha$  monoclonal antibody, inhibits IL-4 and IL-13, key drivers of type 2 inflammation, and is approved for treatment of adults with inadequately controlled moderate-to-severe atopic dermatitis. In the phase 3 LIBERTY ASTHMA QUEST study (NCT02414854), dupilumab 200 mg and 300 mg every 2 weeks vs matched placebo reduced annualized severe exacerbation rates and improved pre-bronchodilator FEV<sub>1</sub>, quality of life measures, and was generally well tolerated in patients with uncontrolled moderate-to-severe asthma. This analysis assessed the efficacy of dupilumab in subgroups by baseline percent predicted FEV<sub>1</sub> (high [60%–90%] or low [ $<$ 60%]).

**Methods:** Annualized severe exacerbation rates during the 52-week treatment period and change from baseline in pre-bronchodilator FEV<sub>1</sub> (L) at Week 12 were stratified and analyzed by baseline FEV<sub>1</sub> (60%–90%/ $<$ 60%).

**Results:** Dupilumab 200 mg and 300 mg vs matched placebo significantly reduced annualized severe exacerbation rates in high (43% and 49% reduction) and low (53% and 44% reduction) baseline FEV<sub>1</sub> subgroups (nominal  $P < 0.01$ ). Placebo groups with low FEV<sub>1</sub> experienced higher annualized rates of severe exacerbations (1.046/1.160) than those with high FEV<sub>1</sub> (0.734/0.814). Dupilumab 200 mg and 300 mg improved pre-bronchodilator FEV<sub>1</sub> at Week 12 (LS mean change from baseline in FEV<sub>1</sub> [L] vs placebo): high FEV<sub>1</sub>, 0.22 (0.02 SE) vs 0.13 (0.03), and 0.23 (0.02) vs 0.14 (0.03); low FEV<sub>1</sub>, 0.43 (0.03) vs 0.25 (0.04), and 0.45 (0.03) vs 0.28 (0.04), respectively (nominal  $P < 0.01$ ). The most frequent adverse event in the dupilumab-treated groups vs placebo was injection-site reactions (15%/18% vs 5%/10%).

**Conclusion:** Dupilumab significantly reduced severe exacerbation rates and improved FEV<sub>1</sub>, regardless of baseline percent predicted FEV<sub>1</sub>, in patients with uncontrolled moderate-to-severe asthma. Improvements in FEV<sub>1</sub> were greater in patients with low baseline FEV<sub>1</sub>. Treatment was generally well tolerated.

**Grant Support:** Research sponsored by Sanofi and Regeneron Pharmaceuticals, Inc.

TP 018

TP 019

**KNOWLEDGE AND CONFIDENCE OF HEALTH PROFESSIONALS IN PROVIDING ASTHMA MANAGEMENT IN PREGNANCY: RESULTS OF AN AUSTRALIAN NATIONWIDE SURVEY**

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**Introduction/Aim:** Asthma affects 12.7% of pregnant women in Australia. Uncontrolled asthma is associated with increased maternal and infant morbidity. Complications can be reduced by optimal antenatal asthma management. National and International guidelines provide recommendations for optimal asthma care in pregnancy, however, the use of these guidelines in antenatal asthma management by health care professionals (HCP's) in Australia is currently unknown. The aim of this study was to explore the current use of asthma in pregnancy guidelines by HCP's in Australia and their knowledge and confidence in providing optimal antenatal asthma management.

**Methods:** An online survey which asked about HCP's current knowledge and practice of antenatal asthma management was developed, piloted and opened for completion from March 2017 to July 2018, by health care professionals who provide care to pregnant women. The survey was distributed via professional organisations and social media platforms.

**Results:** In total 466 HCP's completed the survey. Participants included 393 (84%) maternity carers (midwives and obstetricians), 46 (10%) respiratory specialist physicians and nurses and 26 (6%) primary carers (GPs and practice nurses). All states and territories of Australia were represented. Data showed that 51% of maternity carers and 54% of primary carers, compared to 85% of respiratory specialists followed guidelines for the management of asthma during pregnancy. Of the maternity carers, 12% rated their knowledge as 'good' or 'very good', compared to 50% of primary carers and 65% of respiratory specialists. Confidence ratings of 'somewhat' or 'not at all' were recorded by 84% of maternity carers compared to 65% of primary carers and 28% of respiratory specialists.

**Conclusion:** Asthma in pregnancy guidelines are not used by 45% of HCP's who provide antenatal care in Australia. Maternity HCP's who care for the majority of pregnant women revealed a lack of knowledge and confidence in providing optimal antenatal asthma management.

**Grant Support:** NHMRC, University of Newcastle.

**A SYSTEMATIC REVIEW AND META-ANALYSIS OF ASTHMA MEDICATION USE IN OBESE ASTHMA**

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**Introduction/Aim:** Obesity is a common co-morbidity in asthma which is associated with poorer asthma control, more frequent and severe exacerbations, and reduced response to asthma pharmacotherapy. In Australia, over \$300 million per annum is spent on asthma pharmaceuticals, attributed mainly to inhaled corticosteroids, with a disproportionate amount being used by obese asthmatics. This review examines the differences in asthma medication use between obese and healthy weight asthmatics using meta-analyses.

**Methods:** Relevant studies up to April 2018 were identified with the use of online databases. Studies were considered eligible if they recorded asthma medication type and/or dosage in normal weight and obese asthmatic adults; and meta-analysis was performed where possible.

**Results:** Forty studies were included. Meta-analyses indicated that obese asthmatics are more likely to use most classes of asthma medications including: oral corticosteroids [odds ratio (OR): 1.76; 95% CI: 1.53-2.02;  $P < 0.001$ ]; long-acting  $\beta$ -agonists (OR: 1.66; 95% CI: 1.23-2.24;  $P < 0.001$ ); inhaled corticosteroids (OR: 1.35; 95% CI: 1.14-1.59;  $P < 0.001$ ), leukotriene receptor antagonists (OR: 1.36; 95% CI: 1.17-1.60;  $P < 0.001$ ), short-acting  $\beta$ -agonists (OR: 1.38; 95% CI: 1.10-1.73;  $P = 0.005$ ), and anticholinergics (OR: 1.62; 95% CI: 1.16-2.24;  $P = 0.004$ ) compared to healthy weight asthmatics. Inhaled corticosteroid dose in asthmatics was also significantly increased by obesity (mean difference (95% CI): 166.92 (86.06-247.77)  $\mu\text{g/day}$ ;  $P < 0.001$ ).

**Conclusion:** Our review and meta-analyses supports the hypothesis that obesity is associated with reduced response to asthma pharmacotherapies, by providing evidence that obese asthmatics have increased asthma medication use at increased doses. The association was stronger with certain medication types (particularly oral corticosteroids, long-acting  $\beta$ -agonists, and anticholinergic therapies). The reduced efficacy of asthma pharmacotherapies in the obese population is a major clinical problem considering their disease state and restoring efficacy may increase exercise capacity.

**Grant Support:** n/a.

## REVIEW OF CLINICAL TRIAL DESIGN IN PAEDIATRIC PATIENTS WITH ASTHMA

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**Introduction/Aim:** Asthma disease progression and treatment outcomes are similar between children and adults, meaning that extrapolation from adult efficacy data may be appropriate to predict clinical response in children. Here, we review endpoints used in the tiotropium development programme to help facilitate future trial design in children.

**Methods:** Recent clinical trials with tiotropium for asthma involving 5,066 patients were reviewed (patients aged 6-17 years [NCT01634152, NCT01277523, NCT01634139, NCT01257230] and adults [NCT00772538, NCT00776984, NCT01172808, NCT01172821, NCT01316380]).

**Results:** In the paediatric clinical trial programme, peak FEV<sub>1(0-3h)</sub> and trough FEV<sub>1</sub> % predicted normal improvements with 5 µg tiotropium add-on versus placebo were comparable with previous findings in adults (treatment difference in individual trials 1.64-6.52% and 0.83-4.44% [paediatric]; 3.63-5.80% and 3.01-4.63% [adult], respectively). Tiotropium also consistently improved trough forced expiratory flow (FEF<sub>25-75%</sub>) % predicted in pooled paediatric studies (treatment difference 7.1% for tiotropium 5 µg vs placebo at Week 12, P<0.0001). In sufficiently powered adult tiotropium trials, significant improvements in asthma control and exacerbations have been reported (odds ratio for improvement in Asthma Control Questionnaire [ACQ] responder rates 1.32; time to first exacerbation 0.69 [5 µg tiotropium vs placebo; individual trial data]). In paediatric patients, trends for improved asthma control and reduced exacerbation risk, assessed as exploratory endpoints, were noted versus placebo, comparable with findings in adults (odds ratio of 0.99-2.43 for improvement in ACQ responder rates; 0.60-0.82 for time to first exacerbation).

**Conclusion:** Results from the tiotropium clinical programme emphasise that clinical trials, providing meaningful data, in paediatric patients with asthma can be performed. To assess lung function, FEV<sub>1</sub> and FEF<sub>25-75%</sub> were shown to be reliable endpoints. The tiotropium programme also demonstrated a partial extrapolation concept may be applied from adult to paediatric trials for exacerbation and symptom endpoints, thereby keeping sample size and study duration in line with ethical considerations.

**Grant Support:** This study was supported by Boehringer Ingelheim.

**Conflict of Interest:** BVH, ME and MS are employees of Boehringer Ingelheim. EH, CV and SS have nothing to declare.

## INITIATING ANTI-IL-5 THERAPY IN SEVERE ASTHMA: BASELINE OBSERVATIONS AND SWITCHING OF BIOLOGICAL AGENTS

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**Introduction/Aim:** Biological anti-IL-5 treatments are effective to treat severe asthma based on blood eosinophils as a biomarker of response. Recently benralizumab was introduced in Australia after two other biological agents (omalizumab and mepolizumab) had been in regular use. We examined characteristics of patients newly treated with benralizumab as part of an early access severe asthma program.

**Methods:** Data was obtained from all patients initiated on benralizumab as part of auditing with Ethics approval a severe asthma programme at Monash Medical Centre, Melbourne. Baseline demographic and treatment data were obtained, pulmonary function, total IgE, and blood eosinophils measured and skin prick testing (SPT) done. ACQ-5 scores were obtained and reasons for switching from other biological agents noted. Descriptive analyses were done.

**Results:** A total of 24 patients were initiated on benralizumab, 16 were female. Mean (±SEM) age was 52.1±3.9 years, FEV<sub>1</sub> (% predicted) was 59±2.9% and patients had a median 2 exacerbations per year. All patients took dual ICS/LABA, 9 patients (38%) also used LAMA and 8/24 (33%) used regular OCS. Total IgE was raised (1475±619 IU/L, n=18), ACQ-5 scores were high (4.1±0.3) and blood eosinophils raised (800±100/uL). SPT was positive in 13/19 (68%) and significant comorbidities were noted in 22/24 patients (91%). Surprisingly, 14/24 patients (58%) had been intentionally switched from treatment with omalizumab (7/24, 29%) and mepolizumab (7/24, 29%). All switches were made for lack of efficacy except in four patients formerly on mepolizumab for reasons of convenience (2-monthly rather than monthly injections).

**Conclusion:** Our findings confirm appropriate use of benralizumab in an early access severe asthma program. Patients had poor asthma control, numerous comorbidities and frequent oral steroid use. Corroboration of and explanations for high levels of changing to this alternative biologic need to be examined in a larger group of patients.

**Grant Support:** AstraZeneca.



TPL 002

TP 021

**COMPARING DIFFERENT ROUTES OF IPSC- AND MESENCHYMOANGIOBLAST-DERIVED MESENCHYMAL STEM CELLS IN EXPERIMENTAL CHRONIC ALLERGIC AIRWAYS DISEASE**

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**Introduction/Aim:** There are currently no effective cures for the airway remodelling (AWR) associated with chronic allergic airways disease (AAD)/asthma, which contributes to irreversible airway obstruction. Using a therapeutic stem cell platform technology, CymerusTM, Cynata Therapeutics developed specialised mesenchymal stem cells that were derived from induced-pluripotent stem cells (iPSCs) and mesenchymoangioblasts (MCA-MSCs); which can be acquired from a single healthy donor. As a recent study had demonstrated the anti-remodelling and anti-fibrotic effects of intranasal (i.n)-administration of these MCA-MSCs in an ovalbumin (OVA)-induced model of chronic AAD1, in this study we determined if (clinically-feasible) intravenous (i.v) or endotracheal (e.t) delivery of cells achieved similar efficacy.

**Methods:** 7-8 week old female Balb/c mice were subjected to 11 weeks of OVA-induced chronic AAD. Sub-groups of mice then received once-weekly i.n-, i.v-, or e.t-delivery of 1x10<sup>6</sup> MCA-MSCs at the beginning of weeks 9 and 10; or no treatment at all. Changes in airway inflammation (AI), airway remodelling (AWR) and fibrosis, and airway hyperresponsiveness (AHR) were then measured at week 11. Saline sensitised/ challenged mice were used as controls.

**Results:** Mice with chronic AAD had significant AI, goblet cell metaplasia, epithelial thickening and aberrant TGF- $\beta$ 1 levels, subepithelial myofibroblast accumulation, airway/lung fibrosis and AHR (all p<0.001 vs saline controls). While all three routes of MCA-MSC administration did not affect ongoing OVA-induced AI or goblet cell metaplasia, these cells strikingly decreased subepithelial collagen deposition and total lung collagen concentration (measures of fibrosis), irrespective of delivery mode, to levels that were no longer different to that measured from saline controls (all p<0.01 vs OVA alone). Furthermore, i.n- and i.v-delivery of MCA-MSCs decreased AHR (both p<0.01 vs OVA alone) back to levels measured from saline controls.

**Conclusion:** MCA-MSCs demonstrate striking anti-fibrotic effects, even in the presence of ongoing AAD, and may complement anti-inflammatory corticosteroids as an effective treatment for asthma.

**Reference:**

1. Royce et al., FASEB J 2017 31:4168-78.

**Key Words:** Asthma, airway remodelling, fibrosis, stem cell therapy

**Nomination for New Investigator Award**

**Grant Support:** Cynata Therapeutics Ltd funding.

**MICRORNA-17~92 CLUSTER REGULATES PRO-INFLAMMATORY RESPONSES IN THE TH1/17-BIASED CYTOKINE ENVIRONMENT OF COPD**

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**Introduction/Aim:** COPD is a chronic inflammatory disease of the airways characterised by a Th1/Th17-biased inflammatory environment. Airway epithelial cells (AECs) play a key role in the pathogenesis and progression of COPD via the production of pro-inflammatory cytokines. The production of AEC-derived cytokines may be regulated by miRNAs. This study aims to identify miRNAs that may contribute to the regulation of pro-inflammatory responses in COPD and identify potential pathways involved.

**Method:** Differentially expressed miRNAs in AECs from patients with COPD were identified using high-throughput microRNA assays. Validated miRNA targets and relevant pathways were identified via bioinformatic analysis. Changes in expression for selected miRNAs (miRNA-17, miRNA-1290, miRNA-27b and miRNA-130b) were confirmed using the Taqman miRNA assays. The effect of the Th1/17-biased environment on selected miRNAs were also evaluated in Calu-3 AECs grown in a Th1/17-biased environment. The effect of miRNA-17 on *TNF*, *TLR7* and *TGFBR2* (targets for the miRNA-17~92 cluster) was assessed following overexpressing and silencing of miRNA-17. These effects were also confirmed in the Th1/17-biased environment.

**Results:** 40 differentially expressed miRNAs were identified in AEC from patients with COPD. The targets for these miRNAs are commonly engaged in pathways regulating immune responses, cell growth and apoptosis, and cancer development. Four members of the miRNA-17~92 cluster, including miR-17, were increased in COPD AECs, compared to control cells. This change was also observed in Calu-3 cells grown in a Th1/17-biased environment. *TNF* and *TLR7* were elevated by miRNA-17, while *TGFBR2* was inhibited. Same pattern in expression for these genes were also observed in Th1/17-cytokine treated cells.

**Conclusion:** miRNAs may regulate the inflammatory responses in COPD, and their expression may be altered by the local Th1/17-biased environment. The miRNA-17~92 cluster may enhance pro-inflammatory responses by targeting *TNF*, *TLR7* and *TGFBR2*.

**Key Words:** miRNA-17~92 cluster, inflammatory response, COPD, Th1/17-biased environment

**Nomination for New Investigator Award**

**Grant Support:** Nil

TP 022

**A WINDOW TO TOLERANCE: HUMAN LUNG ALLOGRAFTS ARE ENRICHED FOR CD39+FOXP3+ REGULATORY T CELLS**

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**Introduction/Aim:** Regulatory T cells (Tregs) play a vital role in the induction and maintenance of transplant tolerance. Though suppressive pathways of Tregs are well defined, identifying Treg phenotypes with respect to local tissue environment is of importance to understand their role in solid organ transplant. Adenosine triphosphate (ATP) is released from apoptotic and necrotic cells and can be released from inflammatory cells and platelets during inflammation, infection, ischemia and hypoxia. The ecto-enzyme CD39 hydrolyses ATP to immunosuppressive adenosine which functions to limit effector T cell proliferation and enhance suppressive function of Tregs. Since inflammation is associated with poor outcome in transplant recipients, we compared the proportion of blood and lung CD39<sup>+</sup>Treg in T cells with the aim of determining if immunosuppressive CD39<sup>+</sup>Tregs are present in the lung post-transplant.

**Methods:** Blood and bronchoalveolar lavage (BAL) cells isolated from 15 transplant patients (median 12 (1-140) months post-transplant; 9 female; 6 male; 6 CF; 2 IPF; 6 COPD; 1 ILD). These cells were analysed by a newly developed multicolour flow cytometry panel comprising 14 fluorescent antibody markers to identify Treg subsets.

**Results:** CD39<sup>+</sup> FoxP3<sup>+</sup> Treg were more prevalent in BAL than in blood (5.0 ± 1.3% (SEM) vs 0.6 ± 0.20% (SEM) of total CD4<sup>+</sup> T cells, *P*<0.01(Figure 1)). There was no correlation between BAL and blood CD39<sup>+</sup> FoxP3<sup>+</sup> Treg (*r* = -0.1547, *P* = 0.5819 (Figure 2)).

**Conclusion:** The lung allograft is enriched with a specialized sub-population of FOXP3<sup>+</sup>CD39<sup>+</sup> Tregs with capability of metabolising pro-inflammatory ATP to enrich the lung microenvironment with immunosuppressive adenosine. Future work will examine the frequency and functional capacity of these cells and relationship to transplant outcome.

**Grant Support:** The Prince Charles Hospital Foundation for PhD Scholarship.

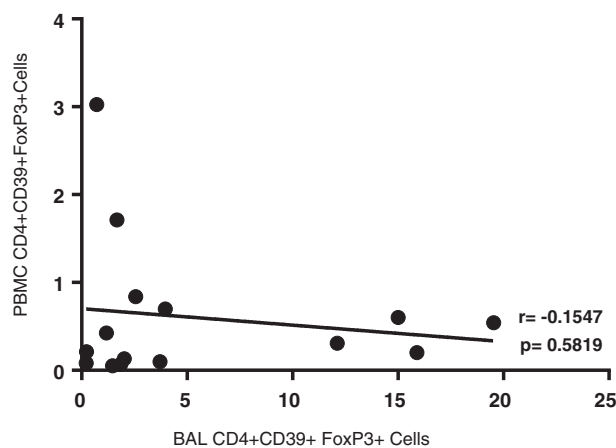


Figure 1. Proportion of CD39+ FoxP3+ Tregs in BAL and PBMC

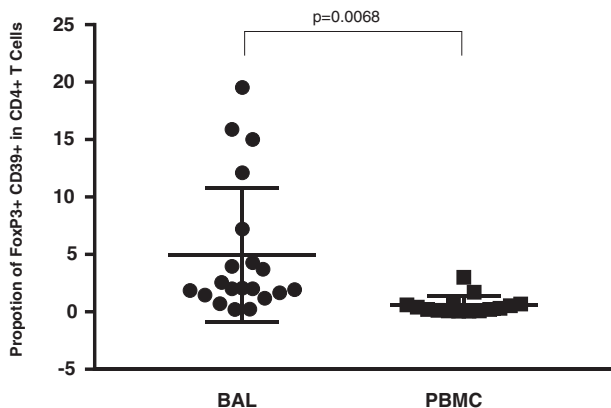


Figure 2. Correlation between CD4+CD39+FOXP3+ Cells in Blood and BAL

TP 023

TP 024

### COMPARISON OF TWO DIFFERENT CYTOLOGY BRUSHES FOR COLLECTION OF NASAL MUCOSAL CELLS

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**Introduction/Aim:** Nasal epithelial cell brushing is an established diagnostic procedure. Primary nasal epithelial cell culture models have been established as an appropriate and non-invasive surrogate for bronchial epithelial cells in cystic fibrosis (CF) research. Various instruments have been used for collection of nasal cells. It remains unclear if a particular brush type provides a more uniform mucosal sample without compromising cell viability. Our aims were to evaluate and compare the total cell count, viability and success rate in establishing cell cultures using the two different instruments.

**Methods:** Phase 1. The inferior turbinate of anaesthetised patients was brushed once with one small bronchial cytology brush. The opposite inferior turbinate was brushed once with one larger cervical cytology brush. Cell count and viability from the 2 different brushes were compared.

In phase 2 we examined the data for cells collected using the cervical cytology brush over a 16 month period. We compared data from CF patients brushed awake, CF patients under GA and Non CF patients under GA.

**Results:** Phase 1: Two brushes were tested in 7 patients. Median age 2.9 (1.33-4.5) years, 4 CF, 3 non CF. The cervical brush collected significantly more total cells (and live cells) than the bronchial brush (table 1). Phase 2: The cervical brush was used to brush 155 patients (Table 2). Lower cell counts were collected from awake patients than anaesthetised. Success rate in establishing primary cell cultures (seeded with identical initial cell count) was similar between groups. The epithelial phenotype of cultures was confirmed by immunofluorescence staining for E-cadherin and p63 markers.

Table 1.

	Small (bronchial)	Large (cervical)	P
Total cell count $\times 10^5$	14.1 [4.16-38.3]	22.0 [10.4-81.2]	0.03
Live cell count $\times 10^5$	2.17 [1.11-7.66]	9.15 [5.48-18.5]	0.02
%Viable cells	23 [8-48]	56 [44-61]	0.10

n = 7 median [IQR range]

Table 2.

	GA CF (n = 53)	Awake CF (n = 78)	GA Non CF (n = 25)	P
Total Cell count $\times 10^5$ median [IQR range]	55.1 [30.4-82.4]	12.0 [5.8-21.3]	33.7 [17.4-64.1]	<0.0001
Live cell count $\times 10^5$ median [IQR range]	18.0 [11.5-34.5]	4.11 [1.76-7.86]	17.4 [6.20-24.1]	<0.0001
Successful culture (%)	82	80	96	

**Conclusion:** Both instruments allow collection and growth of human nasal epithelial cells. The cervical cytology brush is a more efficient collection tool than the smaller brush. The larger brush can be used successfully in both awake and anaesthetised paediatric patients.

**Grant Support:** SCHN Foundation.

### NEONATAL PREDICTORS OF ABERRANT WOUND REPAIR IN VERY PRETERM INFANTS

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**Introduction/Aim:** More than 2 million babies are born <32 weeks gestation annually and these infants are at significant risk of severe respiratory infections in early life and poor lung function throughout life. Our pilot study (Hillas et al., 2018) identified an innate functional repair defect in the airway epithelial cells of preterm infants. The current study aimed to validate initial findings in a larger cohort, and correlate the severity of this functional defect with neonatal factors.

**Methods:** Upper airway nasal epithelial cells (NECs) were obtained from 35 children born preterm (24-31.7 wks gestational age (GA)) at 1.07-1.22 yrs corrected age (17 males; 8 Bronchopulmonary dysplasia (BPD)) and 6 full-term children born after 42wks GA (2.4-6.5yr; 4 males). NECs were cultured, mechanically wounded (IncuCyte ZOOM<sup>®</sup>, Essen Bioscience), and wound closure assessed over a 72h period. Wound closure was then correlated with neonatal factors including gestation, birth-weight, duration of respiratory support, and antenatal/postnatal steroids.

**Results:** Primary cell cultures were established in 22 preterm infants NEC, with cells exhibiting a cobblestone morphology. Epithelial lineage was validated using immunofluorescence. Full-term NECs were found to fully repair wounds by 60h. In contrast, preterm infants wound closure was significantly altered. Repair was observed to fall into three groups; delayed but complete repair (>80% n = 5), significant but incomplete closure (50-80% n = 6) and incomplete wound closure (20-50% n = 10). Neonatal factors, did not predict altered wound repair, except that infants born to mothers completing a course of antenatal steroids (n = 13) exhibited significantly worse NEC repair (P = 0.017, 47.30% vs 74.02%).

**Conclusion:** Data confirm that preterm infants have an innate functional defect in their airway reparative capacity which we show may be further impaired after exposure to antenatal steroids. The long-term impact of antenatal steroid exposure should be examined.

#### Reference:

Hillas et al. 2018. *Respirology*, 2018; 23(S1):TP018.

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**Declaration:** No conflict of interest.

### EXOSOME-RELATED MEDIATORS IN SERUM AND EXHALED BREATH CONDENSATE IN SARCOIDOSIS

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**Introduction/Aim:** Exosomes are cell-derived intercellular vesicles that can transfer biological mediators. In sarcoidosis, interferons (IFN), interleukins, tumour necrosis factor (TNF) and microRNAs (miRNA) have been implicated in disease activity. This study aimed to isolate and characterise exosomes from serum and exhaled breath condensate (EBC), and to assess potential biomarkers miR-155-5p, miR-29a, IL-18 mRNA, IL-12-p40 mRNA, TNF- $\alpha$  mRNA and IFN- $\gamma$  mRNA in exosomes from patients with sarcoidosis. The capacity of exosomes from patients with sarcoidosis to promote TNF- $\alpha$  secretion by monocytes was assessed ex-vivo.

**Methods:** Serum, peripheral blood mononuclear cells (PBMCs) and EBC were collected from patients with sarcoidosis and healthy controls. Exosomes were isolated using Size Exclusion Chromatography (SEC) by qEV columns, characterised by electron microscopy, mass spectrometry, and nanoparticle tracking analysis. The presence of potential exosome biomarkers was measured using qRT-PCR. The level of TNF- $\alpha$  secretion by autologous exosome-stimulated monocytes ex-vivo was measured using ELISA.

**Results:** Sarcoidosis patients (n = 24, 12 males; 53.13  $\pm$  15.5 (SD) years old) and healthy controls (n = 25, 18 males; 43.7  $\pm$  13.89 years old) were recruited. Exosomes were identified in serum and EBC. However, there was no significant difference in the concentration of serum exosomes between the patients and controls. The presence of mRNA for IL-18 in serum exosomes was significantly higher in the patient group ( $P = 0.0213$ ). The production of TNF- $\alpha$  by autologous monocytes was significantly greater in response to stimulation with exosomes from patients with sarcoidosis compared to exosomes from healthy controls ( $P = 0.03$ ,  $r = 0.68$ ).

**Conclusion:** Exosomes are present in the serum and EBC and have the potential to transport biologically active mediators which may contribute to the pathogenesis of sarcoidosis. Serum and EBC exosome mediators could be potential biomarkers in this disease.

**Key Words:** Exosomes, sarcoidosis, EBC, serum, TNF- $\alpha$ , IL-18

**Grant Support:** Nil.

### DEFECTIVE AIRWAY EPITHELIAL CELL REPAIR IN THE UPPER AND LOWER AIRWAYS OF ASTHMATICS: FURTHER EVIDENCE FOR THE UNIFIED AIRWAY HYPOTHESIS

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**Introduction/Aim:** Lower airway epithelium from asthmatics elicits a dysregulated response to injury. Emerging evidence suggests significant overlap exists between upper and lower airways, which may translate to disease abnormalities being expressed throughout the airways, typically known as the "unified airway hypothesis". Here, it was hypothesised that dysregulated epithelial repair is consistently observed in upper and lower airways of asthmatics.

**Methods:** Initially, published transcriptomic datasets (n = 3) using airway epithelial cells (AEC) from upper or lower airways of asthmatics were assessed for repair signatures common with one established by our laboratory. Matched upper and lower airway brushings of non-asthmatic (n = 7; age range: 2.1-3.1year; 4 males) and asthmatic (n = 6; 3.2-12.7year; 4 males) children were then utilised for AEC isolation and culture. Wounding assays were performed to assess repair and cell migration trajectories (IncuCyte ZOOM<sup>®</sup>, Essen Bioscience).

**Results:** Interrogation of transcriptomic datasets corroborated pathways associated with unresolved wound repair, at baseline in asthmatics and following virus-induced exacerbations. Matched upper and lower AEC from asthmatic children displayed significant reduction ( $P < 0.05$ ) in wound repair at 48h (upper and lower AEC (median(IQR))); 34.3% (21.1-43.8%) and 39.5% (14.3-53.7%) compared to their non-asthmatic counterparts (98.3% (91.7-100.0%) and 96.1% (81.5-99.3%)). Furthermore, aberrant cell migration was observed in upper and lower AEC from asthmatics. Specifically, significantly lower distance (upper and lower AEC (median(IQR))); 98.7  $\mu$ m (52.9-166.0 $\mu$ m) and 119.0  $\mu$ m (67.9-200.4  $\mu$ m)), velocity (0.16  $\mu$ m/min (0.09-0.28  $\mu$ m/min) and 0.16  $\mu$ m/min (0.09-0.31  $\mu$ m/min)), directionality (0.56AU (0.35-0.75AU) and 0.64AU (0.42-0.80AU)) and forward migration index (0.92AU (0.72-0.98AU) and 0.79AU (0.48-0.93AU)) was observed in AEC from asthmatic children compared to their non-asthmatic counterparts, distance (363.5  $\mu$ m (222.4-451.6  $\mu$ m) and 239.5  $\mu$ m (163.9-328.4  $\mu$ m)), velocity (0.61  $\mu$ m/min (0.37-0.75  $\mu$ m/min) and 0.38  $\mu$ m/min (0.27-0.55  $\mu$ m/min)), directionality (0.83AU (0.73-0.88AU) and 0.94AU (0.89-0.97AU)) and forward migration index (0.99AU (0.96-1.00AU) and 0.98AU (0.94-1.00AU)) ( $P < 0.05$ ).

**Conclusion:** Unresolved wound repair processes were present in datasets from upper and lower airways of asthmatics and were associated with viral-induced exacerbations. Response to *in vitro* wounding was consistently abnormal in AEC from upper and lower asthmatic airways further corroborating the "unified airway hypothesis".

**Grant Support:** This work was supported by a grant from Asthma Australia.

**COMPARATIVE TOXICITY OF VARIOUS BIODIESEL EXHAUSTS COMPARED WITH COMMERCIAL MINERAL DIESEL IN AN IN VITRO HUMAN AIRWAY EPITHELIAL CELL MODEL**

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**Introduction/Aim:** Biodiesel is promoted as a sustainable replacement for commercial mineral diesel. As global production increases and usage becomes more widespread, concerns have been raised about health effects of biodiesel exhaust exposure. As biodiesel fuel properties, and thus exhaust components, change depending on the source oil, the aim of this project was to compare the effects of exposure to exhaust generated by the combustion of diesel and biodiesel made from different source oils.

**Methods:** Human airway epithelial cells obtained from healthy volunteers were exposed for 1 hour to diluted exhaust generated by a diesel engine running on diesel or biodiesel created from various oils including soy, canola, tallow, palm and eucalypt. Exhaust was characterised for toxic gases and the physico-chemical properties of the particulate matter. Cells were incubated for 24 hours after exposure before health outcomes including cellular viability and inflammatory mediator production were assessed.

**Results:** Exhaust gas composition varied significantly between fuels. All biodiesel exhausts contained higher concentrations of known respiratory irritants including nitrogen oxides and carbon dioxide. Exact concentrations varied between biodiesel types. Particle size spectra also differed between exhaust types with all biodiesels displaying peaks of varying intensity in the ultrafine particle size (<100 nm) which were not observed in diesel. Mean particle size was also smaller for all biodiesel exhausts. Exposure to all biodiesel exhausts resulted in cell death and the release of inflammatory mediators compared with unexposed controls. Some biodiesel exhausts were also significantly more toxic than diesel and resulted in significant inflammatory responses.

**Conclusion:** When combusted in a diesel engine, most biodiesels produced smaller particles and more toxic exhaust compared with diesel. Certain biodiesel exhaust exposures were significantly more harmful to human airway epithelial cells *in vitro* compared with both diesel exhaust and controls, and caused a greater release of inflammatory cytokines.

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**MINIATURISATION OF AN IN VITRO TRANSMIGRATION MODEL OF NEUTROPHIL RECRUITMENT TO CYSTIC FIBROSIS AIRWAYS**

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**Introduction/Aim:** Upon recruitment to cystic fibrosis (CF) airways, polymorphonuclear neutrophils (PMN) undergo proinflammatory reprogramming that reduces phagocytic ability and induces hyperexocytosis via increased CD63<sup>1,2,3</sup>. An *in vitro* transmigration model of PMN recruitment to the airways can successfully recreate the PMN phenotypes observed in CF *ex vivo* samples<sup>2</sup>. However, low volumes of BALF retrieved from young children with CF limits the translation of the migration model for studying paediatric CF lung disease. To address this, we sought to miniaturise the migration model.

**Methods:** A small airway epithelial cell line H441 was seeded onto collagen coated 12 well Alvetex 3D scaffolds as described<sup>2</sup>. Cultures were grown at air-liquid interface (ALI) for 2 weeks, after which the scaffold was inverted and naive human PMN were added to the upper chamber (basal side). A sterilised, acrylic plastic plug (4.7mm thick, 22mm diameter) was inserted into the bottom chamber (apical side) and chemoattractants (IL-8, LTB4, or fMPL) diluted in RPMI-1640 were added. Migration was permitted for 18 hours then PMN were harvested for flow cytometry and the epithelial scaffold cultures assessed by histology.

**Results:** Miniaturisation reduced the volume of dilute stimulant necessary to induce migration by 8 fold (2 mL to 0.25 mL). Flow cytometry determined that addition of the plastic plug did not significantly affect the number of migrated PMNs retrieved (CD45: 12106 ± 3930 with plug, 20694 ± 11095 no plug, *P* = 0.10) or the mean fluorescence intensity of PMN markers of interest (CD63 MFI: 615 ± 208 with plug, 728 ± 162 no plug, *P* = 0.32). Histology of post-PMN transmigration scaffolds indicated the reduced volume did not affect the integrity of the H441 epithelial layer.

**Conclusion:** This study successfully established a miniaturised version of the PMN transmigration model. Future studies will utilise this model to test the effects of paediatric CF BALF on PMN recruitment and reprogramming.

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**Declaration of Interest:** The authors declare no conflict of interest.

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TP 029

TP 030

### PHOSPHOLIPASE D-DEPENDENT INHIBITION OF THE NUCLEAR HORMONE RECEPTOR GR BY (LYSO) PHOSPHATIDIC ACID

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**Introduction/Aim:** Our previous work has provided strong evidence for a role of phospho-cofilin1 in glucocorticoid (GC) insensitivity induced by TGF- $\beta$ 1 in airway epithelia. Phospho-cofilin1 has been well-documented as an activator of phospholipase D (PLD) [1, 2], raising the possibility that PLD activation may contribute to GC insensitivity.

**Aims:** To investigate the potential link between PLD activation and GC insensitivity; and to further investigate the underlying mechanism of PLD activation-impaired GC activity

**Methods:** Phospho-cofilin1 and PLD expression was assessed by immunohistochemistry (IHC) in human asthmatic cohort. *In vitro* GC activity in BEAS-2B cells was assessed by RT-qPCR and GRE-SEAP assays. The potential involvement of PLD in these settings was ascertained using pharmacological (VU0155069/FIPI) and genetic (siRNA) inhibition, as well as by the addition of exogenous PLD products ((lyso)phosphatidic acid). Data are presented as the mean  $\pm$ SEM for *n* independent experiments.

**Results:** Severe, steroid-resistant asthmatic airway epithelium showed increased levels of immunoreactive phospho-cofilin1 and PLD1/2. Phospho-cofilin1 was implicated in the activation of phospholipase D (PLD). The PLD products (lyso)phosphatidic acid mimicked the TGF- $\beta$ 1-induced GC insensitivity in airway epithelia. TGF- $\beta$ 1 induction of the nuclear hormone receptor corepressor, SMRT (NCOR2), was dependent on cofilin1 and PLD activity. siRNA-mediated depletion of SMRT prevented GC insensitivity induced by TGF- $\beta$ 1.

**Conclusion:** We show here for the first time that the products of PLD-mediated membrane phospholipid remodelling, lyso-phosphatidic acid and phosphatidic acid, induce GC insensitivity. This pathway for GC insensitivity offers several promising drug targets that potentially enable safer modulation of TGF- $\beta$ 1 in chronic inflammatory diseases than is afforded by global TGF- $\beta$ 1 inhibition.

[1] Han, L., *et al.* (2007). *EMBO J* 26, 4189-4202.

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### DYSREGULATED S1P SIGNALLING IN MOUSE MODEL OF CYSTIC FIBROSIS-LIKE LUNG DISEASE PRODUCED BY $\beta$ ENAC OVEREXPRESSION

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**Introduction/Aim:** Recent studies suggest that mechanisms of cystic fibrosis (CF) may include dysregulated sphingolipid signalling. We hypothesized that altered expression/localization of sphingosine kinases (SPHK1/2, for synthesis of sphingosine-1-phosphate, S1P) and Spinster 2 homologue (Spns2, for export of S1P) may contribute to mucostasis and inflammation in CF. A mouse model of CF-like lung disease – elicited by overexpression of the beta subunit of the epithelial Na<sup>+</sup> channel ( $\beta$ ENaC) was utilized to test the hypothesis.

**Methods:** Lung paraffin sections from  $\beta$ ENaC overexpressed mice and their littermate controls were examined by immunofluorescence/confocal microscopy. Investigators were blinded to the mouse genotypes. Morphometric analysis using ImageJ software was performed to generate quantitative readouts for SPHK, Spns2, NLRP3, IL-1 $\beta$ , IgG, myeloperoxidase (MPO), neutrophil elastase (NE), apoptosis (cleaved caspase-3/pyknosis) and for correlation analyses.

**Results:** SPHK1/2 and Spns2 were abundantly expressed in the bronchial epithelium. Bright Spns2 at the apex and its positive correlation with SPHK1 levels ( $R^2 = 0.4903$ ;  $P < 0.001$ ) supported the bronchial epithelium as an active generator of extracellular S1P. Spns2 showed sharp downregulation (38%,  $P < 0.001$ ) and loss of apical localization in association with mucostasis and/or plugging in  $\beta$ ENaC mice. MPO/NE-positive neutrophils were infiltrated into mucus plugs where they became strongly degranulated and apoptotic. Mucus plugs also revealed bright immunofluorescence for NLRP3, IL-1 $\beta$ , and IgG.

**Conclusion:** Our findings suggest that mucostasis and inflammation in lungs displaying CF-like disease is associated with dysregulated S1P signalling; in particular the inside-out S1P signalling, and could offer a potential therapeutic target in CF.

TP 031

TP 032

### INCREASED HEPARAN SULPHATE AND DECREASED LIPIDS IN ALVEOLAR SURFACTANT OF THE MUCOPOLYSACCHARIDOSIS (MPS) IIIA MOUSE.

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**Introduction/Aim:** Mucopolysaccharidosis type IIIA (MPS IIIA) is a lysosomal storage disorder caused by a deficiency in the activity of the lysosomal hydrolase sulphamidase. This results in primary storage of heparan sulphate (HS) and secondary storage of gangliosides GM2 & GM3 and cholesterol in brain and liver. MPS IIIA patients exhibit airway obstruction, restrictive lung disease and in severe cases respiratory infections may lead to death in children. We have previously shown increased HS, bis-(monoacylglycerol) phosphate (BMP) and cholesterol storage in MPS IIIA mouse lung tissue. The aim of this study was to characterise HS and lipid changes in secreted alveolar pulmonary surfactant.

**Methods:** Bronchoalveolar lavage fluid (BALF) was obtained from age-matched (20-week) control (n = 16) and congenic C57BL/6 MPS IIIA mice (n = 13). Changes in BALF concentrations of heparan sulphate (ng/mL) and lipids (pmol/mL) were measured by liquid chromatography electrospray ionisation tandem mass spectrometry and presented as mean ± SE.

**Results:** BALF components.

BALF components	Control	MPS	p value
Heparan sulphate	37.1 ± 3.5	899.2 ± 61.3	<0.0001
BMP 18:1_18:1	90.2 ± 4.0	77.1 ± 4.8	=0.0430
BMP 18:1_20:4	16.9 ± 1.3	12.8 ± 1.2	=0.0300
BMP 18:1_22:6	38.9 ± 3.0	29.8 ± 2.5	=0.0325
Total cholesterol (free and esters(CE))	5533 ± 211	4416 ± 269	=0.0026
CE 18:3	27.2 ± 2.3	12.5 ± 1.4	<0.0001
CE 18:2	644.8 ± 55.0	290.4 ± 32.6	<0.0001
CE 20:4	533.7 ± 58.9	210.3 ± 24.2	<0.0001
CE 22:6	102.9 ± 10.5	44.6 ± 5.3	<0.0001

**Conclusion:** We have demonstrated changes in HS, BMP and CE in MPS IIIA mouse lung BALF when compared to control BALF. These results suggest that lamellar body biosynthesis may be altered in MPS IIIA which may have implications for the functionality of surfactant and therefore lung function, potentially contributing to the observed respiratory pathology in MPS IIIA.

**Grant Support:** Sansom Institute for Health Research Grant

### MECHANISMS OF IMPAIRED ANTI-BACTERIAL RESPONSES IN PATIENTS WITH COPD

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**Introduction/Aim:** COPD is a chronic respiratory inflammatory disease. COPD patients may experience acute exacerbations of COPD (AECOPD) which are associated with accelerated disease progression and pulmonary bacterial infections. This suggests an impaired host immune system (e.g. impaired phagocytic function) but little is known about the mechanisms causing increased susceptibility in COPD. Thus, we aimed to determine:

1. The level of phagocytosis and TLR2/4 expression by monocytes.
2. The level of CTLA-4 and PD-1 on T cell subsets.
3. If phagocytosis can be improved by CTLA-4 or PD-1 blockade.

**Methods:** Cryopreserved cells isolated from excised lung samples from COPD patients (n = 10) and non-COPD controls (n = 10) were cultured with NTHi pre-labelled with pHrodo™ with or without PD-1 or CTLA-4 blockade for two hours and phagocytosis were assessed by flow cytometry. Cells were also immunophenotyped for the expression of TLR-2/4 and inhibitory receptors (PD-1 and CTLA-4) on CD4+ T cells and regulatory T cells.

**Results:** Phagocytosis of pHrodo™-NTHi by monocytes was lower in COPD than non-COPD ( $P = 0.01$ ). TLR-4 expression on monocytes was significantly reduced in COPD than non-COPD ( $P = 0.001$ ). Additionally, TLR-2 and TLR-4 expression on monocytes was positively correlated with phagocytosis by monocytes. Although the frequencies of CD4+ T cells and Tregs expressing intracellular CTLA-4 and PD-1 did not differ in COPD compared to non-COPD, CTLA-4 levels on CD4+ T cell and Tregs were negatively correlated with phagocytosis by monocytes ( $r = -0.89$ ,  $P = 0.001$  and  $r = -0.64$ ,  $P = 0.04$ ). Increased phagocytosis by monocyte after PD-1 and CTLA-4 blockade were seen only in a proportion of COPD and non-COPD subjects.

**Conclusion:** Increased expression of CTLA-4 could account for the impaired phagocytic response and hence increased risk of infections in COPD patients. Blocking multiple anti-inflammatory signals could improve anti-bacterial responses to prevent AECOPD.

**Grant Support:** Royal Perth Hospital Medical Research Foundation/Ada Bartholomew Medical Research Trust Grant.

TP 033

TP 034

### CELLULAR SENEESCENCE IN DIFFERENTIATED HUMAN PRIMARY NASAL EPITHELIAL CELLS

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**Introduction/Aim:** An appropriate cellular stress response is critical for maintaining tissue integrity and function. Cells can respond to stress by senescence and cellular senescence is linked to aging and promoting chronic inflammation which may result in disease, including lung disease. The aim of this study was to characterize the stress response in differentiated human primary nasal epithelial cells (HNECs) culture at the air-liquid interface (ALI) and establish a model of stress response, inflammation and cellular senescence. ALI culture is thought to be a physiological relevant model of the human upper airways.

**Methods:** The ex vivo nasal epithelia samples were collected from healthy adults aged between 25 and 40. HNECs were differentiated in ALI culture and classified into 3 stage groups, 4, 8, 16 weeks after differentiation. Then they were exposed to various concentrations of hydrogen peroxide for 1 hour as an acute exposure to observe the responses in different stages of cells by TEER measurement, permeability assay and LDH assay.

**Results:** We observed that in the older cultures, the tight junction was loosened, which was thus more permeable than the early cultures. Hydrogen peroxide exposures caused different responses in different stage groups of cells. Compared with the early stage cultures group, after exposing to 25mM H<sub>2</sub>O<sub>2</sub> the permeability was increased by 5.4-fold in older cultures group ( $P < 0.001$ ). Also, we observed 3 times more cell death in the older group ( $P < 0.001$ ).

**Conclusion:** This model presents similar morphology and functions of the upper airway epithelium in human. Our results demonstrate that oxidative stress response in these cells is influenced by the time in culture.

### IL-1 IS ASSOCIATED WITH NECROSIS AND STRUCTURAL LUNG DISEASE IN CHILDREN WITH CYSTIC FIBROSIS

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**Introduction/Aim:** Necrosis of airway epithelial cells (AEC) resulting in airway inflammation driven by interleukin (IL)-1 is a characteristic finding in cystic fibrosis (CF), driven by mucus obstruction of the airway and previously suggested as a potential response to respiratory viral infection. Since little is known about the role of IL-1 and AEC in the pathogenesis of CF lung disease, and our previous research discovered associations between IL-1 in the CF airway and inflammation and structural lung changes, this study aimed to assess cellular and inflammatory responses of AEC exposed to anoxia and human rhinovirus (RV).

**Methods:** AECs (n = 10/CF, 9/non-CF) exposed to anoxia and RV infection were assessed via flow cytometry for viability, necrosis and apoptosis using Annexin V and TO-PRO-3 (percentage of control, mean ± SD). IL-1 $\alpha$  and IL-1 $\beta$  was measured in supernatants via AlphaLISA, IL-1Ra and IL-8 via ELISA. Wilcoxon signed-rank test and Pearson correlations were used to assess significance ( $P < 0.05$ ).

**Results:** Anoxia did not affect non-CF and CF AEC viability however increased non-CF and CF AEC necrosis (131.1% ± 17.04,  $P < 0.01$  & 112.3% ± 12.96,  $P < 0.05$  respectively) but not apoptosis (99.03% ± 15.07 & 105.4% ± 12.44 respectively). RV infection resulted in decreased viability in non-CF AEC (63.89% ± 6.77,  $P < 0.05$ ), increased necrosis in non-CF and CF AEC (156% ± 27.56,  $P < 0.05$  & 139.4% ± 22.93,  $P < 0.05$  respectively) and increased apoptosis in non-CF AEC (140.5% ± 35.48). Anoxia did not affect IL-1 $\alpha$  from non-CF and CF AEC, however RV infection significantly increased IL-1 $\alpha$  protein in non-CF (877% ± 625,  $P < 0.05$ ) and CF (726% ± 448,  $P < 0.05$ ) supernatant. IL-1 $\alpha$  in supernatant positively correlates with necrosis in CF AEC but not non-CF AEC after rhinovirus infection ( $r = 0.80$ ,  $P < 0.0001$  and  $r = 0.12$ ,  $P = 0.4$  respectively).

**Conclusion:** Exposure of CF and non-CF AEC to anoxia and RV infection resulted in increased necrosis, associated with IL-1 $\alpha$  after RV infection in CF AEC only, suggesting this pathway as a novel anti-inflammatory target.

**Grant Support:** Cystic Fibrosis Australia, Cystic Fibrosis Western Australia.



TPL 003

TPL 004

#### APOCYNIN PREVENTS OXIDATIVE STRESS-INDUCED ATROPHY IN C2C12 SKELETAL MUSCLE MYOTUBES

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**Introduction/Aim:** Comorbidities are major drivers of morbidity and mortality associated with COPD and are thought to be caused by increased oxidative stress. Patients with COPD have elevated levels of the oxidant hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) in their EBC and this is further increased during AECOPD. Skeletal muscle wasting (SMW) is seen in ~40% of individuals with COPD and there are currently no effective pharmacological therapies to treat SMW in COPD. Thus, our aim was to determine whether oxidative stress induces skeletal muscle atrophy, and whether prophylactic treatment with the antioxidant apocynin reduces skeletal muscle atrophy.

**Methods:** Murine C2C12 myoblasts were exposed to oxidative insults (H<sub>2</sub>O<sub>2</sub> and cigarette smoke extract [CSE]) for 24 hours, in the presence or absence of apocynin (500 nM). ELISA, qPCR, immunostaining and Western blotting were used to assess muscle atrophy.

**Results:** Oxidative stress significantly reduced myotube diameter (~36% reduction, P<0.001), which was prevented by apocynin treatment. H<sub>2</sub>O<sub>2</sub> significantly increased pro-inflammatory IL-6 gene (4 fold) and protein (3 fold) expression, NOX2 (oxidative stress enzyme) gene expression (6 fold), and atrogin-1 and myostatin (atrophic factor) gene expression (2 fold, all P<0.05). Both H<sub>2</sub>O<sub>2</sub> and CSE blunted IGF-1 (hypertrophic factor) gene and protein expression (50% reduction, P<0.05). Prophylactic treatment with apocynin inhibited H<sub>2</sub>O<sub>2</sub>- and CSE-induced increases in NOX2 gene expression and prevented the reduction in IGF1 gene and protein expression.

**Conclusion:** Oxidative stress may trigger the onset of SMW and dysfunction by reducing the expression of IGF-1. Apocynin may protect against SMW and dysfunction by preserving IGF-1 expression. Targeting oxidant/antioxidant balance may be a plausible strategy to treat SMW in COPD.

**Grant Support:** NHMRC Australia (Project Grant ID 1138915)

#### MODELLING P. AERUGINOSA INFECTION/INFLAMMATION ON A CO-CULTURE OF CYSTIC FIBROSIS HUMAN BRONCHIAL EPITHELIAL AND MACROPHAGES: PERSPECTIVES FOR DRUG AND NANOPARTICLE DELIVERY

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**Introduction/Aim:** *Pseudomonas aeruginosa* is a most relevant pathogen in cystic fibrosis (CF) that contributes to lung tissue impairment. Its transition from planktonic stage to biofilm formation is considered as critical issue in antibiotic resistance. During the infection, tissue macrophages play an essential role in the inflammatory host response, in which they are recruited to the site of infection, and transmigrate across the bronchial epithelium to clean the bacteria. Our aim is to establish a new cell culture model for investigating the role of macrophages during infection of cystic fibrosis epithelia.

**Methods:** The human cystic fibrosis cell-line CFBE410- was grown under air-liquid interface (ALI) conditions on Transwell® filters, allowing to form a tight epithelial barrier (i.e., transepithelial resistance (TEER) > 300 Ω.cm<sup>2</sup>). Afterwards, adherent THP-1 macrophages were applied on the basolateral side of the filter and the co-culture was apically infected with *P. aeruginosa*.

**Results:** Macrophage transmigration was detected 3 to 6 hours after infection; 6 hours after infection, we observed bacteria aggregation indicative for biofilm formation. The inflammatory response to *P. aeruginosa* infection also led to an increased release of IL-8, IL1β, and IL-6, detectable 4 to 6h post infection. This increase was mostly caused by the macrophages, as it did not change in macrophage-epithelial co-cultures.

**Conclusion:** ALI grown human CF bronchial epithelial cells in co-culture with macrophages allows studying host-pathogen responses towards *P. aeruginosa* infection in terms of macrophage transmigration and cytokines release. As an alternative to animal testing, such human-based cell culture model allows investigation of cellular and immune responses upon infection by biofilm forming bacteria and thus appears valuable for investigating anti-infective drugs and delivery systems.

**Grant Support:** GradUS University of Saarland, Germany

### MARKERS OF NEUTROPHIL EXTRACELLULAR TRAPS (NETS) ARE HIGHER IN EMPYEMA THAN IN MALIGNANT AND TRANSUDATIVE EFFUSIONS

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**Introduction/Aim:** Neutrophil Extracellular Traps (NETs) are implicated in acute and chronic inflammatory conditions. They are known to be present in asthma, COPD, CF and pneumonia but controversy remains regarding their benefit or harm. There are no data regarding NETs in pleural effusions. We investigated markers of NETs in pleural effusions of different aetiologies.

**Methods:** Pleural fluid specimens were collected from 83 patients with undiagnosed pleural effusion. They were allocated to three clinical groups: Empyema/ parapneumonic, malignant and transudative, based on accepted clinical and biochemical criteria. Markers for NETs were extracellular DNA (eDNA) and  $\alpha$ -defensin 1-3 concentrations and were measured in cell free pleural fluid, using PicoGreen dsDNA assay and ELISA.

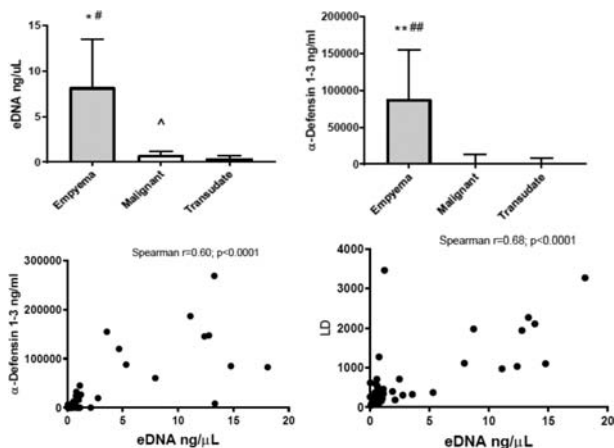
**Results:** There were 13 participants classified as empyema/parapneumonic, 29 participants with malignant effusion and 19 with transudative effusion.

Nineteen participants were excluded from analysis based on aetiology outside one of the defined clinical groups and a further 3 were excluded due to incomplete data.

As expected, pH was lower and protein higher in the empyema group ( $P < 0.05$  for both). Participants with empyema had 10-fold higher pleural fluid eDNA and  $\alpha$ -defensin 1-3 concentrations compared with both malignant ( $P < 0.01$  for eDNA and  $P < 0.001$  for  $\alpha$ -defensin 1-3) and transudative effusions ( $P < 0.001$  for eDNA and  $P \leq 0.001$  for  $\alpha$ -defensin 1-3). Lactate dehydrogenase (LD) levels were higher in empyema compared with transudative effusion ( $P \leq 0.001$ ). The concentrations of eDNA and LD were also significantly higher in the malignant vs the transudative group ( $P < 0.05$  for both). There was a correlation between  $\alpha$ -defensins and eDNA (Spearman,  $r=0.60$ ,  $P < 0.001$ ) as well as LD and eDNA ( $r=0.68$ ,  $P < 0.001$ ).

**Conclusion:** NETs concentrations are higher in empyema and parapneumonic effusions than in malignant and transudative effusions and may be implicated in empyema formation.

**Grant Support:** John Hunter Hospital Charitable Trust Project Grant.



### DOUBLE DIFFUSION METHOD FOR EVALUATING DLCO AND DLNO IN HEALTH AND COPD

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**Introduction/Aim:**  $D_{LCO}$  measures the gas transfer capacity of the lung and is used to evaluate and follow progression of lung diseases including chronic obstructive pulmonary disease (COPD). Measurement of the nitric oxide diffusing capacity ( $D_{LNO}$ ) can help disentangle the effects of alveolar membrane function vs pulmonary vasculature on gas transfer. The relationship between  $D_{LCO}$  and  $D_{LNO}$  has been established in health<sup>1</sup>, but is relatively unknown in COPD. We sought to examine the relationship in both health and COPD. We also investigated the equivalence of gas transfer indices using 5-s and standard 10-s breathholds.

**Methods:** Healthy volunteers and patients with COPD performed two sets of two manoeuvres in randomised order on each of the Medisoft systems (Leeds, United Kingdom): standard  $D_{LCO}$  protocol with 10-s breathhold using a BodyBox and a 5-s breathhold using a HypAir double diffusion, which simultaneously measures  $D_{LCO}$  and  $D_{LNO}$ . Trials were accepted according to international guidelines.

**Results:** 15 healthy subjects (6 males, age  $33.3 \pm 10.1$  yrs (SD), BMI  $25 \pm 3$ ) and 3 COPD patients (2 males, age  $62.3 \pm 8.5$  yrs, BMI  $26 \pm 4$ ) were analysed. Among the healthy subjects, there was a strong correlation between  $D_{LNO}$  and  $D_{LCO}$  ( $r = 0.93$ ,  $P < 0.01$ ). The  $D_{LNO}/D_{LCO}$  ratios in health were  $4.8 \pm 0.34$  and COPD  $5.5 \pm 0.47$ . There were no significant differences between the 5-s and 10-s protocols in  $D_{LCO}$ ,  $K_{CO}$  and  $V_A$  (paired t-test  $P = 0.13$ ,  $0.20$ , and  $0.28$  respectively). Intra-session repeatability and test-to-test measurement error were 1.3 and 3.5 for  $D_{LCO}$  and 5.0 and  $13.8 \text{ mL}\cdot\text{min}^{-1}\cdot\text{mmHg}^{-1}$  for  $D_{LNO}$ .

**Conclusion:** In this preliminary analysis, the  $D_{LNO}$  and  $D_{LCO}$  relationship and repeatability of both measures in healthy subjects were consistent with previous studies. No differences were apparent in  $D_{LCO}$ ,  $K_{CO}$  and  $V_A$  between the breathhold protocols. These results will help towards determining the potential utility of  $D_{LNO}$ .

**Key Words:**  $D_{LCO}$ ,  $D_{LNO}$

#### REFERENCE:

<sup>1</sup>Zavorsky et al., *Eur Respir J* 2017; 49.

**Grant Support:** N/A

### DIETARY FIBRE ELEVATES SCFAS AND PROTECTS AGAINST EXPERIMENTAL COPD.

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**Introduction/Aim:** Short chain fatty acids (SCFAs) are derived from fermentation of dietary fibre by gastrointestinal bacteria, and have potent anti-inflammatory effects in both the gut and the lungs. Fibre intake is associated with reduced risk of chronic obstructive pulmonary disease (COPD), and cigarette smoke (CS) reduces caecum SCFA concentration in rodents. Exploring the protective effects of dietary fibre and SCFAs may provide novel therapeutic strategies for COPD.

**Methods:** Female c57BL/6 mice received a diet supplemented with fermentable fibre (high amylose maize starch) or drinking water supplemented with SCFA (sodium propionate; 200 mM) and exposed to CS for 12 weeks to develop hallmark features of COPD. Controls received conventional chow/water and were exposed to room air. Caecum and plasma SCFAs were quantified by gas chromatography, and disease severity was quantified by assessing lung inflammation (bronchoalveolar lavage fluid (BALF), parenchymal inflammation), histopathology (alveolar destruction, collagen deposition) and lung function (Flexivent; Scireq, CAN). Cytokine responses were assessed by ELISA/qPCR.

**Results:** Cigarette smoke exposure reduced caecal SCFAs (181 ± 67 mg/L vs. 3293 ± 231 mg/L in controls), which were restored by fibre supplementation (3153 ± 683 mg/mL). Fibre supplementation alleviated inflammatory cells in BALF (5.9 ± 1.0 × 10<sup>4</sup> cells/mL vs. 9.6 ± 1.4 × 10<sup>4</sup> cells/mL in CS-exposed), lung pathology, central airway resistance (0.18 ± 0.01 cmH<sub>2</sub>O.s/mL vs. 0.20 ± 0.02 cmH<sub>2</sub>O s/mL in CS-exposed) and transpulmonary resistance (0.47 ± 0.03 cmH<sub>2</sub>O.s/mL vs. 0.55 ± 0.06 cmH<sub>2</sub>O.s/mL in CS-exposed). The effects of sodium propionate were similar to that of fibre supplementation. n = 6-9; data presented as mean ± SEM; P < 0.05.

**Conclusion:** Dietary fibre is protective against features CS-induced COPD in mice, mediated in part by facilitating the production of SCFA by the gastrointestinal microbiota.

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Lungs and Australian Gastrointestinal Research Alliance. We especially thank Anne Greaves, Michael and Felicity Thompson and The Rainbow Foundation for their support.

### PROVIDING PULMONARY REHABILITATION TO INDIVIDUALS FROM CALD BACKGROUNDS

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**Introduction/Aim:** Pulmonary rehabilitation (PR) is effective in improving health outcomes in individuals with Chronic Obstructive Pulmonary Disease (COPD), as well as many other chronic respiratory diseases (Spruit 2013). Despite growing cultural diversity within the Australian population (ABS 2017), the impact of this diversity on participation in PR has not been investigated. The aim of this study was to investigate referral and participation rates of individuals from culturally and linguistically diverse (CALD) backgrounds in PR programs in Sydney, Australia, as well as potential barriers and facilitators to providing PR to these individuals.

**Methods:** This was a mixed methods study, using a sequential, qualitative dominant, participant-selection variant of explanatory design. Participants were coordinators of PR programs in Sydney. Stage one involved a primarily quantitative web-based survey, stage two used semi-structured interviews to gain qualitative information, and stage three involved the integration of quantitative and qualitative data to provide analysis of the key outcomes.

**Results:** All participants reported receiving referrals of individuals from CALD backgrounds, including a diverse range of cultural backgrounds, although the numbers of referrals varied between programs. Interpreters were often used for initial assessments of individuals with limited English proficiency, however were not often used for exercise classes or final assessments. Barriers included cultural factors that programs were unable to accommodate, communication difficulties, challenges using interpreters, and resource limitations. Potential facilitators included using alternate methods of communication, engaging family support, and optimising utilisation of interpreters.

**Conclusion:** This study identified that whilst many individuals from CALD backgrounds are referred to PR there are a number of potential barriers to providing PR to these individuals. A greater understanding of these barriers, and the harnessing of potential facilitators, may help to improve the participation of individuals from CALD backgrounds in PR.

**Grant Support:** Nicole Turney Memorial Grant from Australian Physiotherapy Association Cardiorespiratory Group.

### EVALUATION OF INPATIENT OXYGEN THERAPY IN HYPERCAPNIC CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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**Introduction/Aim:** High concentration oxygen therapy in patients with hypercapnic chronic obstructive pulmonary disease (COPD) is associated with increased mortality. In COPD patients at risk of hypercapnia, guidelines recommend oxygen therapy titrated to achieve oxygen saturation 88-92%. We investigated the association between adherence to guidelines and in-hospital adverse events.

**Methods:** An audit of hypercapnic (PaCO<sub>2</sub> 45 mmHg) COPD patients admitted to a tertiary teaching hospital from June 2016 to June 2017 was performed. Comorbidities, lung function, blood gases, oxygen prescription and ward observations were abstracted from medical records. Over-oxygenation was estimated using the proportion of oxygen saturation observations >92% and the duration of exposure and categorised (<24 hours, 1-3 days and ≥4 days). A composite adverse outcome was defined as in-hospital new respiratory acidosis, medical emergency team (MET) call, intensive care unit admission or death. The association between over-oxygenation and an adverse outcome was assessed using logistic regression modelling.

**Results:** The study population comprised 117 patients (56% male, mean age 75 years) who experienced 161 admissions. Adverse events occurred in 39 (25%) of 157 admissions with data, comprising 12 deaths (6 had new acidosis), 16 new-onset acidosis episodes and 11 respiratory-related MET responses. Over-oxygenation occurred in 86% of admissions. The oxygen target was specified for 82% of admissions. Without oxygen target specification, 11/29 (38%) had adverse outcomes compared to 22% when specified. Duration of exposure to over-oxygenation was associated with adverse outcomes ( $P = 0.001$ ). Compared to the reference category (<24hours), exposure for ≥4 days markedly increased odds of an adverse outcome (OR: 8.9; 95%CI: 2.6-30.5) after adjusting for age and Charlson comorbidity index.

**Conclusion:** Adherence to guideline oxygen therapy in COPD inpatients is suboptimal. Over-oxygenation is common and is independently associated with in-hospital adverse events. This study reinforces the critical importance of accurate titrated oxygen delivery in hypercapnic COPD inpatients.

**Grant Support:** Nil

### UNDERSTANDING MAORI PREFERENCES FOR HEALTHCARE SERVICES

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**Introduction/Aim:** Maori with chronic airways disease experience worse health outcomes than non-Maori and non-Pacific peoples. Reasons for this include access to (obtaining entry into and through) health services, and relationships between the patient and healthcare professionals. The purpose of this study is to generate knowledge from interviews with Maori patients and their whanau (family).

**Methods:** A qualitative research approach has been taken, using a kaupapa Maori methodology, which involved semi-structured interviews with 17 patients and whanau.

**Results:** Within the context of colonisation and in the setting of chronic disease management, participants prioritised 'what matters' to them, within the constraints of their lives. Engaging with health services, and making decisions on whether to adopt health-promoting behaviours were subject to a cost-benefit analysis which was positively influenced by relationships with healthcare providers based on trust. Our current western health model is underpinned by ideologies and assumptions which result in health services not reaching Maori, contributing to health inequity.

**Conclusion:** There is a mismatch between Maori preferences, expectations and practices and healthcare structures and practices which leads to health inequity.

**Grant Support:** Clinical Research Training Fellowship (Health Research Council, Asthma and Respiratory Foundation), Asser Trust.

TP 040

### CHARACTERISTICS AND TREATMENT OF PATIENTS WITH COMORBID COPD AND HEART FAILURE

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**Introduction:** Comorbid heart failure (HF) is common in patients with COPD (2.6 times greater odds vs. non-COPD) and may result in different disease management. The objective of this study was to examine associations between COPD and HF with regard to disease burden and factors affecting treatment adequacy.

**Methods:** This multiphase study used anonymised, longitudinal data from two large UK healthcare databases to identify patients aged  $\geq 40$  years old with COPD, HF, or both COPD and HF. Patients with other chronic respiratory diagnoses were excluded. Cohorts were matched using direct matching methods.

**Results:** In matched cohorts of 4831 patients, the modified medical research council dyspnoea score in COPD+HF vs. COPD cohorts was 3 or 4 for 19% vs. 11% of patients, respectively ( $P < 0.001$ ). Patients with HF and new COPD were as likely to receive adequate COPD therapy (long-acting bronchodilators) as those with only COPD (adjusted hazard ratio 1.04; 95% CI, 0.98 to 1.11). Patients with COPD and new HF (matched cohorts,  $n = 5877$ ) were less likely to receive adequate HF therapy ( $\beta$ -blockers) than those with only HF (36% vs. 58%;  $P < 0.001$ ). Of those with pre-existing HF, women, current smokers, non-obese patients, and those with poor recording of disease severity were less likely to be adequately treated for new COPD (Table).

**Conclusion:** Patients with COPD+HF are more breathless than those with only COPD, and patients with comorbid COPD and HF often receive suboptimal COPD or HF treatment.

**Grant Support:** This study was funded by Novartis Pharma AG, Basel, Switzerland

**Disclosure:** Dr. Konstantinos Kostikas was an employee of Novartis at the time of submission of the abstract.

Body mass index<sup>†</sup>

<30 kg/m<sup>2</sup> (n=997) 411 (41.2) 586 (58.8) 0.016\*

$\geq 30$  kg/m<sup>2</sup> (n=658) 307 (46.7) 351 (53.3)

FEV<sub>1</sub> available 416 (57.3) 358 (34.7)

FEV<sub>1</sub> % predicted, median (IQR) 56 (43–68) 60 (48–70) <0.001\*\*

Data are presented as n (%), unless otherwise specified. \* $\chi^2$  test; \*\*Mann-Whitney U test. <sup>†</sup>Gender, smoking status and body mass index are presented as row percentages; the other variables are calculated using column percentages.

Adequate treatment for COPD was defined as having long-acting bronchodilator prescription(s), and inadequate treatment as having only short-acting bronchodilators, within 3 months of COPD diagnosis

HF, heart failure; IQR, interquartile range

Table: Adequacy of COPD therapy for patients with comorbid COPD and HF

Variable	Adequate treatment (N=726)	Inadequate treatment (N=1031)	P value
Gender <sup>†</sup>			
Women (n=689)	242 (35.1)	447 (64.9)	<0.001*
Men (n=1068)	484 (45.3)	584 (54.7)	
Smoking status <sup>†</sup>			
Current smokers (n=506)	181 (35.8)	325 (64.2)	0.001*
Ex-smokers (n=986)	449 (45.5)	537 (54.5)	
Non-smokers (n=206)	89 (43.2)	117 (56.8)	

TP 041

TP 042

### WEANING FROM NIV AFTER ACUTE HYPERCAPNIC RESPIRATORY FAILURE: A RETROSPECTIVE AUDIT OF CURRENT STRATEGIES

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**Introduction/Aim:** There is a paucity of evidence guiding clinicians when weaning patients from non-invasive ventilation (NIV) after resolution of acute respiratory acidosis due to exacerbation of COPD. Techniques that are currently advocated include stepwise or immediate withdrawal of support or gradual reduction in pressure support. Our aim was to determine current NIV weaning practices and compare outcomes according to weaning strategy.

**Methods:** Retrospective audit of all adult patients admitted between January 2017 and September 2018, with respiratory acidosis due to exacerbation of COPD who required >24 hours of ward-based NIV.

**Results:** 72 NIV episodes were included in the analysis. After 24 hours of continual ventilation, group 1 (n = 12) underwent stepwise withdrawal of diurnal and nocturnal support, group 2 (n = 40) received nocturnal NIV with PRN usage during daytime, and group 3 (n = 20) had abrupt withdrawal of NIV. Baseline characteristics across all groups were similar, however patients in the immediate withdrawal group had a significantly lower BMI (34.1 vs 31.6 vs 26.0,  $P = 0.04$ ). Weaning was successful in 62 (86%) which was similar across all groups ( $P = 0.42$ ). Group 3 had a significantly shorter total NIV duration (77.33h vs 62.83h vs 40.54h,  $P = 0.002$ ), however hospital LOS was similar between groups (9 vs 8 vs 12 days,  $P = 0.38$ ). Factors associated with successful weaning were lack of focal CXR opacification (50.0% vs 11.3%,  $P = 0.048$ ) and  $a_pH$  after 24 hours of NIV ( $7.35 \pm 0.03$  vs  $7.37 \pm 0.05$ ,  $P = 0.05$ ).

**Conclusion:** In our hospital population, there is significant variation in weaning practices. Although abrupt cessation of NIV is associated with reduced NIV duration, weaning success and hospital LOS is similar regardless of weaning strategy. Patients with a higher pH after 24 hours on NIV, and those without radiological evidence of pneumonia, have a higher chance of successful weaning from NIV.

**Grant Support:** Nil

### EVALUATION AND IMPACT OF FRAILTY IN PATIENTS WITH ACUTE EXACERBATIONS OF COPD

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**Introduction:** Frailty is a clinically important, treatable trait that rarely features in Australian respiratory care models for patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD). This study evaluated the prevalence of frailty in patients with AECOPD and its clinical relevance.

**Methods:** 74 patients with AECOPD (mean FEV<sub>1</sub> 47.5%, age 72years, BMI 27) were assessed within 48 hours of admission according to the Fried phenotype and Short Performance Physical Battery (SPPB), and a status of 'frail' or 'not frail' determined. Frailty prevalence was compared between instruments and associations between frailty and clinical outcomes explored via t tests, univariate logistic regression and Kaplan-Meier survival curves.

**Results:** Frailty was detected in 48% (Fried) and 18% (SPPB) of patients. Compared to those who were not frail, frailty associated with increased age and falls history, decreased muscle force, gait speed and 6-minute walk distance ( $P < 0.01$  for all) and an approx. 3-fold increased risk of 90-day re-admission / mortality ( $P = 0.051$ ).

**Conclusion:** Frailty is common amongst patients with AECOPD and associates with poor clinical outcomes. This subgroup may require additional supportive care strategies after hospital discharge.

**Grant Support:** Lung Foundation Australia/Boehringer-Ingelheim COPD Research Fellowship.

TP 043

TP 044

### SWIMMING BETWEEN THE FLAGS: OXYGEN PRESCRIPTION IN A TERTIARY HOSPITAL

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**Introduction/Aim:** In 2015 the TSANZ published clinical practice guidelines: "Swimming Between the Flags" to guide acute oxygen therapy in the inpatient setting. These guidelines encourage recognition of patients who are at elevated risk of hypercapnoea, due to chronic lung disease, and safe oxygen administration. We created an oxygen prescription program for all adult patients admitted to the Royal Hobart Hospital.

**Methods:** Oxygen prescription stickers were created for the National Inpatient Medication Chart (NIMC) and included: target oxygen saturations, indication for oxygen therapy and device for oxygen delivery. A pre-implementation audit of patients located two wards to establish current hospital practice was piloted. A hospital-wide education program, particularly directed towards junior medical officers and nursing staff was conducted. Three- and twelve-month post-implementation audits were completed to assess the long-term adherence to prescription.

**Results:** 101, 102 and 110 patients were included in each of the audit phases. 33.4% of medical patients in the pre-implementation audit were receiving appropriate oxygen according to the TSANZ guideline. At 3 and 12 months post-implementation 72.5% and 82.7% of patients respectively were receiving appropriate oxygen. An oxygen prescription was completed for 63.7% and 55.4% at 3 and 12 months respectively. Appropriate modifications to rapid response team criteria were completed for 70.2% of patients pre-implementation, and 94.1% and 97.3% at 3 and 12 months respectively.

**Conclusion:** The use of an oxygen prescription sticker and education program was successful in reducing inappropriate oxygen use in admitted patients. We encourage the introduction of oxygen prescription to the NIMC, just as DVT prophylaxis and warfarin dosing sections are included.

**Grant Support:** Nil.

### SYMPTOM BURDEN FOR INPATIENTS WITH ACUTE EXACERBATIONS OF COPD

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**Introduction:** Understanding symptom burden is important to deliver effective patient care.

**Aims:** i) Describe symptom burden for inpatients with acute exacerbations of COPD(AECOPD) within 72hours of hospitalisation. ii) Assess feasibility for a larger study.

**Methods:** English-speaking patients admitted under Respiratory Medicine at Westmead Hospital with AECOPD were recruited between June and August 2018. Patients with cognitive impairment, admitted to ICU or unable to converse were excluded. Patients were assessed within 72hours using the Condensed Memorial Symptom Assessment Scale (CMSAS). The CMSAS assesses bothersomeness of 11 physical and frequency of 3 psychological symptoms. Total score, physical and psychological subscales were calculated (higher scores = worse symptoms; score 0-4au). Cough, sputum and anxiety are not included in the CMSAS and were assessed using the same methodology. Detailed pain assessment (site, intensity [0-10score] and cause) was performed. Feasibility was assessed by patient survey. Data presented as mean (SD) or median(IQR).

**Results:** Of thirty-five patients approached, 32 were recruited, aged 69.8(9) years, 43.8% female, FEV1 37.0(13) %predicted. Mean total CMSAS score was 1.5(0.7). Mean physical score was 1.5(0.7) and mean psychological score was 1.5(1.3). Breathlessness, cough and dry mouth were the most prevalent physical symptoms (91%, 84%, 81%). Worry was the most prevalent psychological symptom (72%). Breathlessness (3.2[1.6-4.0]), cough (2.8[1.6-4.0]) and lack of energy(2.8[1.4-4]) were rated the most bothersome of the physical symptoms. Eighteen patients reported pain in 31 locations with a pain score of 4.8(2.7). The most common pain locations were chest (23%), back(23%) and shoulders(13%) with pain most commonly caused by cough or arthritis. Feasibility was supported by most patients (81%) reporting no difficulties with study completion.

**Conclusion:** Symptom burden in inpatients with AECOPD was moderate. Although breathlessness and cough were expected, the prevalence of dry mouth, worry and pain were likely under-appreciated clinically suggesting specific assessment may be warranted. A larger study appeared feasible.

**Grant Support:** Nil. Declaration of Interest Statement: Nil.

TP 045

TP 046

### LUNG DIFFUSION OF CARBON MONOXIDE IS A PREDICTOR OF DESATURATION DURING HIGH ALTITUDE SIMULATION TESTING

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**Introduction/Aim:** High altitude simulation testing (HAST) is the most common method by which respiratory physicians inform the decision of whether patients are safe to fly at without supplemental oxygen; predicting who should be referred for testing remains a difficult task. We sought to determine whether diffusion of carbon monoxide (DCO) was a sensitive marker for hypoxia.

**Methods:** Retrospective analysis of all subjects who had undergone both DCO testing and HAST in our laboratory in the last 10 years (n = 96). HAST was conducted under normobaric pressures with subjects breathing 15% FiO<sub>2</sub> for 20 minutes. Desaturation below SpO<sub>2</sub> 88% was deemed significant. Patients were analysed as a whole and within diagnostic subcategories. Receiver operator curves (ROC) were constructed to determine the utility of DCO against other measures of .

**Results:** Significant desaturation during HAST that would lead to a recommendation for supplemental oxygen at altitude. For these; DCO below 51% had a sensitivity of 0.81 and a specificity of 0.8; with an AUC for the ROC of 0.84 (SE 0.04; 95% CI 0.76-0.92). Baseline SpO<sub>2</sub> below 96% had a sensitivity of 0.87 and a specificity of 0.73. patients with chronic obstructive pulmonary disease had a significant desaturation; for these a DCO below % had a sensitivity of and a specificity of 0.; with an AUC for the ROC of 0.98 (SE 0.19; 95% CI 0.94-1.00).

**Conclusion:** DCO represents a good predictor of desaturation during HAST; particularly in patients with COPD. We would recommend performing HAST on all patients with a DCO below % who are considering flying.

### ASSESSING THE RATE OF ELIGIBILITY OF LUNG VOLUME REDUCTION WITH ENDOBRONCHIAL VALVE TREATMENT FOR PATIENTS PRESCRIBED LONG TERM OXYGEN THERAPY

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**Introduction/Aim:** Lung Volume Reduction with Endobronchial Valve (EBV) insertion is a bronchoscopic treatment that can improve exercise tolerance and quality of life in a select group of patients with Emphysema treated with maximal therapy. We aimed to assess the rate of eligibility by baseline characteristics of Lung Volume Reduction with EBV Treatment for the cohort of patients prescribed long term oxygen therapy at out institution.

**Methods:** We identified all patients prescribed long term oxygen therapy through the Northern Adelaide Local Health Network (NALHN) through our local database. All patients were prescribed Domiciliary Oxygen as per the Thoracic Society of Australia and New Zealand Position Statement Adult Domiciliary Oxygen Therapy January 2014. Case note audit was undertaken for these patients to review baseline clinical characteristics.

EBV inclusion/exclusion criteria was the basis of the audit as per the International Consensus, based on the European Respiratory Journal 2012. 73% patients were excluded from the EBV Treatment. This was due to the respiratory diagnosis, age, uncontrolled pulmonary artery hypertension, cardiac disease, 6MW distance and other reasons including patients already had Endobronchial Valve Treatment and patients already excluded. Further audit for inclusion/exclusion criteria for Lung Volume Reduction with EBV Treatment is required for the remaining 27% of patients.

**Results:** 219 patients were identified. Of these 73% demonstrated clinical characteristics consistent with ineligibility for Lung Volume Reduction with EBV Treatment. Further auditing required for the remaining 27% of patients to assess the rate of eligibility of Lung Volume Reduction with EBV Treatment.

**Conclusion:** 27% of patients prescribed long term oxygen therapy demonstrate the requisite baseline clinical characteristics that would allow consideration of Lung Volume Reduction with EBV Treatment. Active case finding should be considered within this population to maximise potential improvements in dyspnoea and quality of life.



TP 047

TP 048

### A RETROSPECTIVE REVIEW OF COPD EXACERBATIONS REQUIRING ADMISSION TO THE INTENSIVE CARE UNIT

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**Introduction/Aim:** Acute exacerbations of chronic obstructive pulmonary disease can vary in severity and the degree of ventilatory support that is required, and there remain a significant cohort of patients that require admission to the intensive care unit for this indication. The aim of this study is to define the characteristics of patients admitted to the intensive care unit with exacerbations of COPD, with a focus on their comorbidities, and their mortality.

**Methods:** Retrospective review of patient admitted to the ICU at Logan Hospital with the primary diagnosis of an exacerbation of COPD, between 2014 and 2017.

**Results:** A total of 117 patients with an average age of 68 were admitted to the ICU for the management of an exacerbation of COPD. The prevalence of comorbidities was high, including obesity (45%), hypertension (43%), and obstructive sleep apnoea (31%). The main reason for admission was hypercapnic respiratory failure, though this wasn't the exclusive cause, and 36% of patients were not acidaemic at the time of ICU admission. The predicted risk of death in hospital using APACHE2 ICU scoring system was 26.5% compared with the observed mortality of 22%. One year mortality was 47%. Only 45% of the admitted patients were known to the local respiratory team prior to admission to ICU.

**Conclusion:** Patients who required ICU admission due to an exacerbation of COPD were defined by multiple comorbidities and these admissions were associated with high mortality at 30 days and one year. Optimal monitoring and follow-up can potentially be aided by acknowledging these findings.

**Grant Support:**

### INVESTIGATING ASTHMA-COPD OVERLAP USING MOUSE MODELS

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**Introduction/Aim:** Up to 20% of patients with obstructive airway disease exhibit features of both asthma and chronic obstructive pulmonary disease (COPD), which is commonly referred to as asthma-COPD overlap (ACO). These patients have eosinophilic airway inflammation (characteristic of asthma) as well as neutrophilic inflammation and non-reversible airflow limitation (characteristic of COPD). Patients have increased exacerbations and hospitalisations, and current treatment options are limited in this cohort. Importantly, ACO likely encompasses several heterogeneous phenotypes that are yet to be characterised and complicate the identification of novel therapeutic targets in humans. We sought to establish a mouse model of ACO that mimics hallmark features of human disease to elucidate the mechanisms driving pathology.

**Methods:** Mice were exposed to house dust mite (HDM; 25µg/dose) or PBS (5 days/week; weeks 0-11), and cigarette smoke (CS; 12 cigarettes/day, 5 days/week; weeks 4-11). Inflammation (bronchoalveolar lavage/blood), airway remodelling (collagen deposition), diffusing capacity of the lung for carbon monoxide (DLCO), and baseline lung function and airway hyperresponsiveness (AHR) were assessed.

**Results:** Airway inflammation was increased following treatment with HDM alone, CS alone, and HDM+CS, compared to PBS controls. HDM alone induced a predominantly eosinophilic airway inflammation whereas combined HDM+CS exposure promoted a mixed airway inflammatory phenotype (eosinophils and neutrophils) reminiscent of ACO in humans. HDM+CS, compared to HDM alone, also increased neutrophil numbers in the blood, small airway-associated collagen deposition, and enhanced the HDM-induced increase in baseline tissue damping and elastance, baseline transpulmonary resistance (fixed airflow obstruction) and AHR to methacholine. HDM+CS-treated mice also had 85±4% predicted DLCO.

**Conclusion:** Our model of asthma-COPD overlap exhibits many hallmark features of ACO in humans, including increased mixed eosinophilic/neutrophilic inflammation, increased collagen and impaired lung function. Therefore, this model is an ideal platform to elucidate the mechanisms that drive these disease features and identify novel therapeutic targets.

**Grant Support:** NHMRC.

### INTERVENTIONS TO INCREASE NRT PRESCRIPTION IN ACTIVE SMOKERS ADMITTED WITH AN EXACERBATION OF COPD

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**Introduction/Aim:** Smoking cessation is the only proven way of modifying the natural course of COPD, and hospitalisation is a time when patients are more receptive to smoking cessation interventions. A clinical audit was undertaken to assess the effectiveness of interventions to improve the prescription of nicotine replacement therapy (NRT) for active smokers admitted to a regional hospital with an acute exacerbation of COPD (AECOPD).

**Methods:** A retrospective audit of NRT prescription was undertaken on all active smokers admitted with AECOPD over a three month period based on DRG coding. Data was gathered from discharge summaries, progress notes and medication charts.

The following interventions were then undertaken for all active smokers admitted with AECOPD:

1. An education session for JMOs regarding assessment of nicotine dependence and NRT prescription utilising NSW health NRT tools.
2. NSW health NRT tools placed in bedside notes
3. 'No smoking' sticker placed on medication charts by hospital pharmacists when undertaking medication management reviews.

A retrospective audit was then repeated for the subsequent 3 months to assess the effect of the above interventions.

**Results:** Rates of active smoking in AECOPD admissions were similar in both groups (26/57 (46%) pre-intervention vs. 37/90 (41%) post-intervention). NRT was prescribed for 9/26 (35%) and 30/37 (81%) of patients in the pre-intervention and post-intervention groups respectively. Documentation of nicotine dependence as an issue in the discharge summary occurred in 3/26 (12%) and 21/37 (57%) of patients in the pre-intervention and post-intervention groups respectively.

**Conclusion:** Education of JMO's on the assessment and prescription of NRT as well as visual prompts in the form of NRT tools and 'no smoking' stickers increased the prescription of NRT in active smokers admitted with AECOPD and improved documentation of nicotine dependence in patient discharge summaries.

### EXPLORING HEALTH PROFESSIONAL EXPERIENCES AND PERSPECTIVES OF BEST PRACTICE CARE FOR PEOPLE WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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**Aim:** To identify perceived and actual barriers and facilitators to the provision of guideline-concordant care for people with COPD.

**Method:** Semi-structured interviews were conducted with medical officers, including respiratory specialists, general medical physicians and junior medical officers who routinely manage COPD patients across multiple hospitals in South Australia. Purposive and snowball sampling were used to recruit participants until data saturation was achieved. Interviews followed a standardised moderator guide and were transcribed verbatim, then validated by participants. A questionnaire that included demographic questions and nine, seven-point Likert scales was completed to facilitate data triangulation. Deductive thematic analysis was performed by multiple coders under guiding principles of the Theoretical Domains Framework using QSR NVivo version 10.

**Results:** Data saturation was reached with recruitment of n = 11 medical officers across two large teaching hospitals. Medical officers had a mean age of 41.45 ± 6.50 years with a mean 15.22 ± 6.20 years' experience treating people with COPD. Participants indicated an awareness of current guidelines that did not translate to actual use in practice. Main barriers identified were layout, accessibility and time. However, technology was viewed positively as a potential facilitator to overcome this; especially smartphone functionality. General medical physicians expressed a greater lack of engagement and knowledge of COPD guidelines compared to respiratory specialists. This was confirmed by the Likert scale data, which showed respiratory specialists were significantly more likely to actively seek information relating to COPD care than general medical physicians (6.4 ± 0.21 vs 4.74 ± 0.2; P = 0.002).

**Conclusion:** This qualitative research suggests that a multi-faceted intervention is required to address poor guideline adherence in practice for management of people with COPD. Such an intervention must improve awareness of the guidelines themselves as well as address organisation-level barriers. Incorporation of facilitators including smartphones and specialist nurses are likely to enhance motivation and positive responses from health professionals.

### CHARACTERISATION OF UK AND US COPD POPULATIONS IN REFERENCE TO EXACERBATION FREQUENCY AND BLOOD EOSINOPHILS LEVEL

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**Introduction/Aim:** Analysis of the WISDOM study suggested that inhaled corticosteroid (ICS) is of value on top of long-acting  $\beta_2$  agonist plus long-acting muscarinic antagonist (LABA + LAMA) in COPD patients with high blood eosinophils (EOS) and frequent exacerbations. As long-term ICS use may be associated with significant adverse events, one should limit use to those likely to benefit.

**Methods:** We examined the number and profile of COPD patients in 2014 with reference to exacerbation frequency (0, 1, and  $\geq 2$  exacerbations) and blood EOS distribution ( $<150$ ,  $150$ – $299$ ,  $300$ – $399$ ,  $\geq 400$  cells/ $\mu\text{L}$ ), using UK Clinical Practice Research Datalink (CPRD), a database of primary care records and US Optum Clinformatics™ Data Mart (CDM), a claims database of a commercially insured population.

**Results:** There were 15,771 and 139,465 COPD patients in CPRD and CDM. The percentages of patients with 0 (47.2%, 36.0%), 1 (22.1%, 26.0%), and  $\geq 2$  (30.7%, 38.1%) exacerbations are slightly different in CPRD and CDM. Among patients with  $\geq 2$  exacerbations, 31.5% (UK) vs. 27.2% (US) had EOS count  $\geq 300$  cells/ $\mu\text{L}$ , and 17.1% (UK) vs. 13.3% (US)  $\geq 400$  cells/ $\mu\text{L}$ . Among those who had  $\geq 2$  exacerbations in 2014, 82.8% (UK) vs. 80.6% (US) exacerbated at least once in 2015. Among those who had EOS  $\geq 400$  cells/ $\mu\text{L}$  in 2014, 76.5% (UK) and 76.5% (US) continued having elevated EOS  $\geq 300$  cells/ $\mu\text{L}$  in 2015. The EOS variability was higher for patients with EOS count of 300–400 cells/ $\mu\text{L}$ . Patients with both  $\geq 2$  exacerbations and high EOS count were 10.4% and 10.6% (EOS  $\geq 300$  cells/ $\mu\text{L}$ ), or 5.6% and 5.2% (EOS  $\geq 400$  cells/ $\mu\text{L}$ ) of the COPD population in CPRD and CDM respectively.

**Conclusion:** Only a small percentage of COPD patients had  $\geq 2$  exacerbations and blood EOS  $\geq 300$  or 400 cells/ $\mu\text{L}$  suggesting that ICS is overprescribed in the UK and US.

**Grant Support:** The study was funded by Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States.

**Disclosure:** Dr. Konstantinos Kostikas was an employee and shareholder of Novartis at the time of submission of the abstract.

### SELF-REPORTED SEDENTARY BEHAVIOUR IN PEOPLE WITH COPD AND BRONCHIECTASIS

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**Introduction/Aim:** Few studies have examined sedentary behaviour in chronic respiratory disease (CRD), yet the limited evidence suggests that higher levels of sedentary behaviour are associated with increased risk of mortality. This study aimed to compare self-reported total sedentary time between people with chronic obstructive pulmonary disease (COPD) and bronchiectasis, as well as identify associations between both total sedentary time and pulmonary function with functional performance measures and quality of life (QoL).

**Methods:** This observational study was conducted within the pulmonary rehabilitation programs of two metropolitan hospitals in Sydney. Participants were invited if they had doctor-diagnosed COPD or bronchiectasis of any severity. Participants completed the Sedentary Behaviour Questionnaire (SBQ) from which average total sedentary time (hours/day) during waking hours was determined from nine common sedentary behaviours. Functional performance was measured using the six-minute walk test, the four-metre gait speed test and the five sit-to-stand test. QoL was measured using the St George's Respiratory Questionnaire (SGRQ). Univariate analysis explored relationships amongst variables.

**Results:** The sample consisted of 103 people with COPD (52% male; mean age (SD) = 73 (9) years, FEV<sub>1</sub> = 56 (23) % predicted) and 33 people with bronchiectasis (52% male; mean age (SD) = 74 (8) years, FEV<sub>1</sub> = 60 (25) % predicted). Average total sedentary time was 7.6 (2.7) hours/day in COPD and 8.0 (4.1) hours/day in bronchiectasis, with no between group difference (-0.4, 95% CI -1.7, 0.8). No associations were found with total sedentary time and any functional performance outcome or with QoL. Weak associations were found between FEV<sub>1</sub> % predicted and 6-minute walk distance ( $r = 0.22$ ,  $P = 0.01$ ).

**Conclusion:** There was no difference in total sedentary time between people with COPD and bronchiectasis based on the SBQ. Sedentary behaviour was not associated with functional performance or disease-related QoL in people with CRD.

**Grant Support:** Nil

**Declaration of Interest:** Nil.

**Nomination for awards:** Physiotherapy.

TP 053

TP 054

### DECREASED MACROPHAGE SIRT-1 IN RESPONSE TO CIGARETTE SMOKE

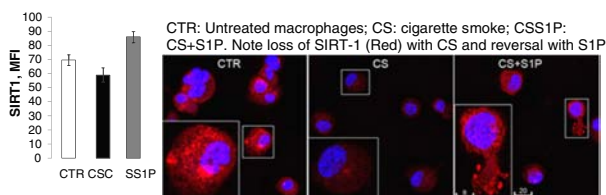
RAM A<sup>1</sup>, WEEN M<sup>1,2</sup>, TRAN H<sup>1,2</sup>, LIU H<sup>2</sup>, HODGE S<sup>1,2</sup>

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**Introduction/Aim:** In COPD, defective efferocytosis can lead to secondary necrosis of the uncleared apoptotic cells, a defect that has been linked to increased lung inflammation, cigarette smoke (CS) and hypoxia. The class III NAD-dependent HDAC, Sirtuin 1 (SIRT1), is an important regulator of inflammation. We hypothesized that there is decreased SIRT1 in COPD airways and in macrophages exposed to CS, oxidative stress or hypoxia that can contribute to macrophage phagocytic dysfunction, and that the mechanism may involve the sphingosine-1 phosphate (S1P) pathway.

**Methods:** Differentiated THP-1 macrophages were exposed for 24h to CS extract (CSE, 10%), oxidative stress (2,2'-azobis(2-methylpropionamide) dihydrochloride, AAPH) and hypoxia. SIRT-1, PARP, pADPr were assessed using immunofluorescence and Western blot. Phosphorylated (Thr530-P, Biorbit orb186148) and non-phosphorylated SIRT-1 (Abcam ab7343) was assessed. ELISA and open array qPCR were applied to assess SIRT1 in BAL from COPD patients and healthy controls. The potential effects of S1P on CS-treated macrophages were investigated.

**Results:** CS decreased the expression of SIRT1 and increased pADPr in THP-1 macrophages. Immunofluorescence staining showed heterogeneous expression of phosphorylated and non-phosphorylated SIRT1 in vesicles near the surface, and Golgi-like domains that was decreased with CS exposure (Fig. below). SIRT-1 levels were below the limits of detection of the ELISA. Open array qPCR analysis is underway. Treatment of CS-exposed cells with sphingosine-1 phosphate improved SIRT-1 expression (Fig. below).



**Conclusion:** SIRT1 expression is decreased in macrophages by exposure to CS, oxidative stress and hypoxia. Treatment options including S1P that increase SIRT1 may improve macrophage phagocytic function and reduce inflammation in COPD.

### EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) REQUIRE FREQUENT AMBULANCE AND EMERGENCY DEPARTMENT MANAGEMENT IN QUEENSLAND

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**Introduction/Aim:** Exacerbations of COPD are serious complications that frequently require management by ambulance services, emergency departments (ED), and hospitals. The pattern of emergency COPD presentations in Queensland, including mode of presentation and admission rate, has not yet been comprehensively described.

**Methods:** A retrospective observational analysis was undertaken of patients older than 40 who presented to an ED in Queensland with a Principal Diagnosis of COPD in 2015-2016. Patient data from the Queensland Ambulance Service (QAS), emergency departments and hospitals were linked and analysed to provide a comprehensive picture of emergency COPD presentations in Queensland.

**Results:** 11,403 patients (51% male, 49% female) were identified who required 20,087 presentations to the ED for COPD. Of these patients, 31% presented to the ED more than once in the two year period, and 5% presented five or more times. 37% of patients were triaged as either TC1 resus or TC2 emergency, requiring medical attention within one or ten minutes respectively. 80% of ED visits for COPD resulted in admission to a short stay, observation, or hospital ward, or were transferred to another hospital. 71% of COPD patients were transported to the ED by ambulance services and, of these, 86% were admitted or transferred.

**Conclusion:** COPD exacerbations are a frequent cause of QAS presentations, ED visits and hospital admissions in Queensland. Many patients with COPD exacerbations require multiple presentations to the ED, and the majority are transported by ambulance services. Patients with COPD often present to the ED acutely unwell, requiring urgent medical attention and admission for further management. Those who are transported by ambulance services have an even higher admission rate, indicating they are more significantly unwell. Further investigation of critical factors determining ED presentation, admission and mortality of COPD exacerbations in Queensland is warranted.

**Key Words:** COPD, exacerbation, ambulance, emergency department  
**Nomination for New Investigator Award:** N/A  
**Grant Support:** Nil

TP 055

TP 056

### ACUTE EXACERBATIONS OF COPD: 'DECAF' VALIDATION AND QUALITY-CARE ASSESSMENT

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**Introduction/Aim:** Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) are an important clinical entity, contributing to significant morbidity and mortality. Despite this, data describing hospitalised populations are limited. This study details the epidemiology and clinical management of patients admitted with AECOPD, and validates the use of the 'DECAF' AECOPD severity score in an Australian population.

**Methods:** Consecutive patients admitted with AECOPD in a 12-month period at the Royal Hobart Hospital were identified retrospectively through clinical coding. Data, including DECAF components, were collected from the medical records and analysed. Results were compared to best-practice care, and validation of the DECAF severity score was assessed using area under the receiver operating characteristic (AUROC) curve.

**Results:** 368 patients were admitted with AECOPD across the study period. The median age was 77 years (IQR 64-75), 53.5% were female, mean FEV<sub>1</sub> of 47.1% predicted (SD (+/- 20.1), median length of stay 3 days (IQR 1.75-4), and in-patient mortality 3.8%. While high adherence to best practice care was demonstrated across many domains – acquisition of chest XR (99.7%), appropriate NIV use (90.5%), appropriate in-patient oxygenation (82.7%) – worrying deficiencies were demonstrated in appropriate pre-hospital oxygenation (45.5%) and provision of smoking-cessation support (46.1%). The DECAF score demonstrated an excellent ability to detect patients at low-risk of in-patient mortality with AUROC of 0.91 (0.86-0.96).

**Conclusion:** Despite the low mortality rate and quality care provision across a number of domains, weaknesses in pre-hospital oxygenation and smoking cessation provision were identified. Given the low cost and proven mortality benefit of these therapies, this represents an important area for future intervention. Within an Australian centre, the DECAF score was demonstrated to be highly effective at identifying those at low in-patient mortality risk. Further exploration of utilising the score in identifying patients for expedited discharge and hospital-in-the-home programs is warranted.

**Grant Support:** Nil

**Declaration of Interest:** Nil

### PREVALENCE AND CLINICAL ASSOCIATIONS OF PSEUDOMONAS AERUGINOSA IN AECOPD

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**Introduction/Aim:** *Pseudomonas aeruginosa* (PsA) is recognised as a relevant pathogen in AECOPD. The primary aim was to define the prevalence of chronic PsA infection and compare the clinical outcomes and baseline characteristics of patients admitted to hospital with AECOPD with PsA-positive and PsA-negative sputum cultures. The secondary aim was to describe the antibiotic resistance profile of PsA isolates.

**Methods:** A retrospective review was performed at the Lyell McEwin Hospital, including all admissions with a diagnosis of AECOPD (J44.0 and J44.1) between January 2016 and December 2016. Baseline characteristics and clinical outcomes (complexity of admission, length of stay (LOS), length of ICU stay, readmissions) were analysed. Resistance patterns for gentamicin, piperacillin-tazobactam, ciprofloxacin and ceftazidime were analysed between January 2014 and December 2017 for PsA isolated from the entire cohort.

**Results:** 609 patients (70.7 ± 11.7 years) with 863 encounters were included. Sputum culture and susceptibility testing were performed during 46.6% (402/863) of these encounters. PsA was isolated in 10.9% (44/402) of the cultures. Patients with PsA positive cultures were older (75.1 vs. 69.8 years old,  $P = 0.007$ ), had more complex admission (75.0% versus 53.1%,  $P < 0.001$ ) and longer LOS (158.4 vs. 121.3 hours,  $P = 0.02$ ). 6.1% of the patients (37/609) had chronic PsA infection. Chronic PsA infection had longer LOS (142.3 vs. 101 hours,  $P = 0.01$ ) and higher 1-year readmission rates (1.8 vs. 1.4 visits,  $P < 0.01$ ). There was no difference in mean FEV<sub>1</sub> between patients who had chronic PsA infection and non-chronic PsA carriers. Across the cohort, rates of resistance of ciprofloxacin has increased over a four-year period of surveillance.

**Conclusion:** The prevalence of chronic PsA infection in patients admitted to for an AECOPD was 6.1%. PsA infection is associated with worse outcomes for patients admitted with an AECOPD. PsA resistance patterns are concerning, and evidence based guidelines for antimicrobial strategies are urgently required.

TP 057

TP 058

### PORTABLE SPIROMETRY IN THE DIAGNOSIS AND RATIONALISATION OF INHALED CORTICOSTEROID THERAPY IN COPD INPATIENTS

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**Introduction/Aim:** Spirometry is key for the accurate diagnosis, severity re-assessment and initiation of inhaled corticosteroid (ICS) therapy in Chronic Obstructive Pulmonary Disease (COPD). At our institution, inpatients with presumed or previously proven COPD usually undergo outpatient laboratory-based spirometry (LS) approximately 4 weeks following discharge. However, patients' difficulty with attending LS appointments delays diagnosis and severity re-assessment. Portable spirometry (PS), a proven, easy to perform, surrogate device provides a convenient method to overcome this issue. The purpose of this study was to compare PS values, obtained prior to hospital discharge, with LS results undertaken 4 weeks later and assess their relationship to ICS prescription.

**Methods:** Inclusion criteria included adults with clinically suspected or previously known COPD and smoking history >10 pack-years. PS was performed prior to discharge, and LS 4 weeks later. Inhaler therapy use was recorded. Reliability between spirometry results were assessed with the Intraclass Correlation Coefficient. PS results were not available to the treating team.

**Results:** 33 eligible patients participated. Mean age 69.3±6.8 (SD) years and 19 were male. Patients' severity were similar at both time points. All patients, without evidence of previous spirometry, were diagnosed with airflow limitation on PS and LS. 29 (88%) patients were discharged on ICS; including 7 without a clear indication for this therapy and with an FEV<sub>1</sub> over >50% predicted at both visits.

Spirometry variable	Intraclass correlation coefficient (95% confidence interval)
Pre-Bronchodilator FEV <sub>1</sub>	0.96 (0.90-0.98)
Post-Bronchodilator FEV <sub>1</sub>	0.94 (0.86-0.98)
Post-Bronchodilator FEV <sub>1</sub> /FVC	0.95 (0.90-0.98)

**Conclusion:** The reliability of PS undertaken before discharge compared with outpatient LS is excellent. Additionally, as patients' severity were stable between visits, it indicates that PS and LS may be used interchangeably. Providing spirometry results to the treating team before discharge, allows timely diagnosis and institution of targeted guideline-based inhaler therapy with rationalisation of ICS use.

**Key Words:** COPD, portable spirometry, inhaled corticosteroids.

**Grant Support:** Nil.

### METABOLOMIC RESPONSE OF HEALTHY AND CYSTIC FIBROSIS EPITHELIUM TO RHINOVIRUS

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**Introduction/Aim:** Acute exacerbation episodes in Cystic Fibrosis (CF) are typically associated with rhinovirus (RV) infection. Responses by CF lung tissue to RV are aberrant. To gain insight into the host-rhinovirus interaction signature after infection, we used both a metatranscriptomic strategy to determine the viral load along with a metabolic approach to profile the metabolites associated with the viral infection of primary bronchial epithelial cells obtained from healthy children (H) and those with CF.

**Methods:** Whole transcriptome shotgun sequencing and hydrophilic interaction liquid chromatography (HILIC) coupled to mass spectrometry were used to identify the differences between RV coverage and metabolites produced by H (3.9 ± 1.5 years; n = 8) and CF (2.6 ± 1.8 years; n = 8; all p.Phe508del/p.Phe508del) primary epithelial cells at 24 hours post infection with human rhinovirus 1B. Multivariate analysis was performed to identify differentially abundant metabolites that could discriminate between infected and non-infected cells as well as disease phenotype.

**Results:** Viral genome coverage was performed to confirm the viral infection and assess viral load. The RV coverage in uninfected cells (Mock) was less than 0.5X. Infected cells of H and CF children presented 44.4X and 101.6X of RV, respectively. RV infection was associated with an increase in the levels of Nicotinamide (Vitamin B3 pathway), Pyridoxal (Vitamin B6 pathway) and Uracil independently of host genetics. A strong positive correlation between these metabolites was observed (Pearson correlation <0.7, P < 0.01), suggesting a co-regulation in the production of these compounds.

**Conclusion:** We have identified three host-derived metabolites associated with RV infection independent of the host's genetic background. Although functional analysis are required to understand the biological meaning underlying these metabolic changes, these compounds may be used as biomarkers of RV infection. Future analysis will help to understand whether their production can be targeted for antiviral purposes.

**Grant Support:** NHMRC, Telethon Perth Children's Hospital Grant.

TP 059

TP 060

**'IS TELEHEALTH AS EFFECTIVE AS FACE TO FACE THERAPY FOR DELIVERY OF WHOLE BODY VIBRATION TRAINING (WBVT) AS AN ADJUNCT TO PHYSIOTHERAPY IN CHILDREN AND YOUNG PEOPLE WITH CYSTIC FIBROSIS (CF)?'**

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**Introduction/Aim:** An increased life expectancy of individuals with cystic fibrosis (CF), now recognises bone mineral deficits and reduced muscle mass (sarcopenia), as long term health concerns. Importantly, muscle mass has been shown as an independent predictor of bone accrual in individuals with CF.

Whole body vibration training (WBVT) has shown a therapeutic impact on bone and muscle response in adults, and some paediatric cohorts, with CF. Our project aimed to demonstrate the utility of telehealth-supported home treatments with WBVT via a model of service delivery which reduces travel time, costs, and negative impacts on quality of life (QOL), while providing an efficacious clinical intervention.

**Methods:** 15 pre-pubertal outpatients with CF, mean age 7.94 ± 1.35 years, were randomised to WBVT (n = 9) or usual care (n = 6, control). Individuals in WBVT cohort performed a 12 week standardised WBVT program (20 minutes, 5 times per week), combined with normal physiotherapy airway clearance. Reviews either face-to-face (n = 3) or via telehealth (n = 6) were provided over the 12 weeks. The control cohort continued normal physiotherapy airway clearance. Anthropometric data and primary outcome measures of total body lean body mass (LBM) via dual-energy X-ray absorptiometry (DXA) were taken at baseline and 12 weeks. Secondary outcome measures include Cystic Fibrosis Quality of Life Questionnaire-Revised (CFQ-R), spirometry and bone parameters (DXA) were collected at these time points.

**Results:** Baseline data were not different between groups, and while both groups showed increases in height and weight, they were not different between groups. Compared to usual care, over 12 weeks of intervention, the WBVT group showed: increased bone mineral content adjusted for height ( $P = 0.046$ ) and bone mineral content for the amount of LBM ( $P = 0.041$ ). Interestingly, upward trends in bone mineral content considered for LBM, fat mass, height and age seen in the WBVT group were not observed in the control group. There were no significant changes in QoL measures for either group.

**Conclusions:** WBVT showed increased lean mass and bone mineral content for the individual's size that may imply a positive functional change in muscle and bone response. Further, the WBVT did not add a burden of care, as indicated by unchanged QoL scores. Our pilot study, with a small sample size, implies physiological changes that warrants further investigation.

**Grant Support:** HREC new researcher grant-project number HREC/16QRCH103; Hypervibe<sup>®</sup> (Loan of 6 plates) <https://www.hypervibe.com/au/>

**'RECOVERY TO BASELINE PULMONARY FUNCTION AFTER EXACERBATION IN CYSTIC FIBROSIS PATIENTS AT THE PRINCE CHARLES HOSPITAL**

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**Introduction/Aim:** Pulmonary exacerbations (PEXs) occur intermittently in patients with cystic fibrosis (CF). Up to 25% fail to recover their baseline lung function following treatment. The aim of this study was to determine what proportion of patients recover their baseline lung function.

**Methods:** Retrospective chart audit of every CF PEX admission to The Prince Charles Hospital in 2017. Recovery to baseline lung function was deemed to have occurred if the patient's best FEV1 in the 3 months post discharge equalled or was greater than 90% of the patients best FEV1 in the 6 months prior to admission.

**Results:** A total of 133 patients experienced 304 admissions for PEX during 2017. Admissions were excluded from analysis if patients received a lung transplant or died in the three months following PEX. Twenty-two admissions had insufficient data to determine recovery.

A total of 268 admissions from 118 patients were included in analyses. The study population were 58.5% males, mean age 31 years. The median number of admissions for each patient was two.

For their first admission in the study period 105 patients (89%) recovered lung function (95% CI: 82-94%). Patients who failed to recover had higher length of stay (15 versus 13 days), initial CRP (33 versus 9) and lower initial FEV1 (1.26L versus 1.93L) (Figure 1). Overall, lung function recovered in 222 of 268 (83%) admissions (95% CI: 77-88%). The most common combination of antibiotics used was Tobramycin and Ceftazidime (48.5%).

Recovery was less likely if Fosfomycin or Aztreonam were used or if Aspergillus or Achromobacter species were present in sputum. A diagnosis of pancreatic insufficiency, CF related diabetes or CF related liver disease did not differ between recovered and non-recovered patients.

**Conclusion:** Overall, lung function recovered in 83% of admissions. This recovery rate is greater than that reported in the literature.

**Grant Support:** None.

### UPDATE ON THE AUSTRALIAN CYSTIC FIBROSIS RAT COLONY

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**Introduction/Aim:** We have established a cystic fibrosis (CF) rat colony in Adelaide via CRISPR-Cas9 gene editing. The two CF rat genotypes we created are i) the Phe508del Class II *CFTR* mutation, and ii) a Class I nonsense mutation designated a *CFTR* knockout (KO). Here we provide an update on the phenotype characteristics of these two models, and present the differences in severity of disease pathology.

**Methods:** KO rats were maintained by breeding heterozygous pairs, while Phe508del rats were bred using female homozygous Phe508del CF rats and heterozygous males. Due to their propensity to gastrointestinal obstructions, all CF rats received ColonLyte in the drinking water, as well as a high fat diet. Nasal potential difference (PD) measures were performed on anaesthetised, intratracheally-cannulated rats. Nasal airways were perfused with a range of buffer solutions using our standard methods. Histology tissues were formalin-fixed, sectioned and stained for assessment by a veterinary pathologist.

**Results:** KO rats demonstrate a higher mortality rate compared to Phe508del rats both pre- (68% vs 10%) and post-weaning (21% vs 14%), lower than average body weights and abnormal dentition. Male rats of both genotypes had poorly developed vas deferens, seminal vesicles and epididymides consistent with a CF human phenotype. When compared to wild-type rats, KO rats demonstrate a classic CF electrophysiological phenotype in the nasal epithelium, with Phe508del producing a milder phenotype. To date few significant CF histopathologies have been detected in lung, trachea, liver or pancreas compared to wild-type.

**Conclusion:** The main cause of mortality and morbidity in these rats is severe gut obstruction, abnormal dentition and failure to thrive. Characterisation to date indicates Phe508del and KO rats exhibit mild features of the human CF phenotype in some organs. Whether CF rats are more susceptible to bacterial-induced lung disease pathogenesis are underway.

**Grant Support:** The Fay Fuller Foundation, NHMRC GNT1098127, and Cure4CF Foundation.

### THE EFFECT OF CFTR MODULATORS ON STRUCTURAL LUNG DISEASE IN CYSTIC FIBROSIS

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**Introduction/Aim:** There is a lack of sensitive clinical trial outcome measures to assess disease progression and treatment efficacy of novel therapies in early life cystic fibrosis (CF). This study assessed the effect of Ivacaftor on CF lung disease progression using chest computed tomography (CT) analysis methods suitable for early disease.

**Methods:** Patients with CF contributed clinical data and chest CT scans performed before and after initiation of Ivacaftor. This multi-site retrospective case-control study assessed CT image biomarkers derived from the Perth Rotterdam Annotated Grid Morphometric Analysis for CF (PRAGMA-CF), CF-CT and mean airway-artery dimensions from segmental generations 3,4,5 combined. Analysis of covariance (ANCOVA) was used to compare lung disease progression in treatment and control groups. Subgroup analyses were performed on 1) paediatrics subjects and 2) data excluding Phe508del homozygous Ivacaftor subjects.

**Results:** The dataset comprised 16 Ivacaftor and 25 control subjects with CF. Phe508del homozygous Ivacaftor subjects ( $n = 5$  adults) received Lumacaftor/Ivacaftor. Median (range) age of Ivacaftor subjects was 12.55 (4.25-36.49) years at CT<sub>1</sub> and 14.88 (5.83-40.83) years at CT<sub>2</sub>. For controls, 8.34 (3.47-38.29) at CT<sub>1</sub> and 12.40 (5.16-42.26) at CT<sub>2</sub>. Ivacaftor subjects improved in PRAGMA-CF total lung disease [-2.88(-4.45,-1.30),  $P = 0.001$ ] and bronchiectasis [-2.07(-3.13,-1.02),  $P < 0.001$ ] extent compared to controls. Differences in airway wall thickening, bronchiectasis and tapering measured using airway-artery dimensions were not statistically significant between treatment groups. Significant differences were not detected for CF-CT total lung disease, bronchiectasis and mucous plugging. Subgroup analysis of paediatric data showed that Ivacaftor subjects improved in PRAGMA-CF bronchiectasis [-0.88(-1.70,-0.07),  $P = 0.035$ ] and intra-branch tapering [1.61(0.05,3.17),  $P = 0.044$ ]. When Phe508del homozygotes were excluded, Ivacaftor subjects improved in PRAGMA-CF total lung disease [-2.32(-4.04,-0.60),  $P = 0.010$ ] and bronchiectasis [-1.70(-2.80,-0.61),  $P = 0.004$ ] compared to controls.

**Conclusion:** Quantitative CT image biomarkers provide more sensitive assessments of novel therapies like Ivacaftor than standard clinical trial outcome measures. However, a larger study population is needed to assess changes in airway-artery dimensions between treatment groups.

**Supported by:** Vertex Independent Medical Grant for Investigator Initiated Study, AREST CF Ad Hoc Scholarship, Cystic fibrosis WA PhD Top-Up Scholarship.

**Prize Eligibility:** Ann Woolcock New Investigator Award, Janet Elder International Travel Award, oral prize

**Conflicts of interest:** None.



TP 063

TP 064

### KINETIC EXPRESSION OF GENES AND RECEPTORS DURING MONOCYTE TO MACROPHAGE DIFFERENTIATION IN CYSTIC FIBROSIS

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**Introduction/Aim:** Previous studies reported cystic fibrosis transmembrane conductance regulator (CFTR)-dependent defective alternative polarization (M2) of macrophages in patients with cystic fibrosis (CF). Later it was shown that defects also reside in the CF monocytes, the precursor cells of macrophages. This study aimed to identify differences in expression of genes, receptors and other regulators associated with monocyte-to-macrophage differentiation between CF and controls.

**Methods:** Kinetic expression of M1 and M2 genes and miR-155 were analysed by real-time PCR during monocyte to macrophage differentiation. Surface expression of receptors IL-4R $\alpha$  and IL-13R $\alpha$ 1 were analysed by flow cytometry.

**Results:** Expression of Cox-2 and IRF4 were minimal during monocyte to macrophage differentiation in both groups. Surface expression of IL-4R $\alpha$  and IL-13R $\alpha$ 1 increased progressively in control cells during macrophage differentiation but not in CF cells. Expression of miR-155 was consistently higher during macrophage differentiation in CF compared to control cells.

**Conclusion:** The failure to upregulate surface expression of IL-4R $\alpha$  and IL-13R $\alpha$ 1 in CF monocytes as they differentiate into macrophages may be explained, in part, by the higher expression of miR-155 during this process. The link between miR-155 expression and lack of CFTR function remains to be explored.

**Grant Support:** The project is funded by Cystic Fibrosis Foundation Therapeutics (CFFT), US, the Ann Maree Bosch Fellowship from the Cystic Fibrosis Australia (CFA) and University of Queensland Research Training Scholarship.

**Declaration of Interest:** None

### OPTIMISATION OF BRONCHOSCOPIC LENTIVIRAL VECTOR DELIVERY FOR DIRECT LOBE TARGETING IN RAT LUNGS

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**Introduction/Aim:** Current gene therapy delivery methods produce variable distribution within the lungs. Covering the entire lung has proven difficult with large quantities of lentiviral (LV) vector required. Recently, we developed a bronchoscope method to target specific rat lung lobes, improving LV transduction. However, shear stresses imposed on the LV vector during bronchoscopic delivery can reduce vector efficiency. The aim of this study was to determine the effects of a range of factors including the draw up method, efficacy of protectants, and the delivery speed.

**Methods:** NIH-3T3 cells were transduced with a lentiviral vector (GFP reporter gene) delivered through a bronchoscope. Vector was delivered through the working channel using a standard syringe, no-dead volume syringe, or a glass syringe with metal and non-metal needles. Vector was also drawn directly up into the working channel or delivered by standard bolus. A range of delivery rates were tested. Utilising the best delivery method, heat inactivated mouse serum was used to stabilise the vector during delivery. LV vector recovery was analysed by flow cytometric analysis.

**Results:** Delivery using syringes resulted in significantly decreased recovery compared to bolus, with no-dead volume syringes resulting in the best recovery. However, drawing up directly into the bronchoscope was the most efficient method, resulting in an ~85% recovery. The addition of heat inactivated serum resulted in a decrease in recovery.

**Conclusion:** The most efficient LV delivery method we tested was directly drawing up into the bronchoscope. Unfortunately, the addition of serum to stabilise the vector reduced vector recovery, possibly due to the viscosity causing some LV to remain trapped within the bronchoscope. We now plan to assess the effects of LV titre on recovery, other protectants, and evaluate whether these modifications improve in vivo transduction.

**Grant Support:** •

### ADULTS WITH CYSTIC FIBROSIS DISPLAY SIMILAR CARDIORESPIRATORY AND SYMPTOMATIC RESPONSES DURING MAXIMAL RAMP AND CONSTANT WORK RATE CYCLE-ERGOMETRY TESTS

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**Introduction:** Maximal incremental cardiopulmonary exercise tests are the gold standard method to assess exercise capacity in people with cystic fibrosis (CF). In non-CF populations, constant work-rate exercise tests may be preferred due their responsiveness. It is unclear whether constant work-rate exercise tests elicit near maximal cardiorespiratory and symptom responses in adults with CF.

**Methods:** Ten adults with CF (31 ± 6 year, FEV<sub>1</sub> 55 ± 12% predicted) undertook an incremental-ramp and a constant work-rate cycle ergometry test (80% maximum work rate [W<sub>max</sub>]) on non-consecutive days. Both tests comprised 1-minute of rest, 1-minute of unloaded cycling, a work phase and a 5-minute recovery.

#### Results:

	Incremental-ramp	Constant	p-value
	Mean ± SD (unless stated)		
VO <sub>2</sub> (final 30s)(L/min)	2.0 ± 0.5	1.9 ± 0.6	0.82
VO <sub>2</sub> (final 30s)(% predicted)	79 ± 22	77 ± 25	0.89
VCO <sub>2</sub> (L/min)	2.5 ± 0.7	2.3 ± 0.7	0.58
Respiratory exchange ratio (RER)	1.2 ± 0.1	1.2 ± 0.2	0.69
VE <sub>peak</sub> (L/min)	69.1 ± 19.5	66.5 ± 20.2	0.78
Peak heart rate (HR)(bpm)	166 ± 11	159 ± 12	0.19
HR 5-min post-test (bpm)	122 ± 9	112 ± 8	0.01*
Change from peak HR (% drop)	27 ± 6	30 ± 4	0.39
Peak dyspnoea (Borg 0–10)(median [IQR])	7 [5,8]	5 [5,7]	0.72
Peak leg fatigue (Borg 0–10)(median [IQR])	9 [8,9]	6 [6,7]	0.49
Nadir SpO <sub>2</sub> (%)	93 ± 1	92 ± 3	0.33
Duration (min:sec)	8:59 ± 1:14	4:27 ± 0:49	0.001*

**Conclusion:** In adults with CF, constant work-rate test elicited similar cardiorespiratory responses to the incremental-ramp test. The incremental-ramp test elicited greater symptoms. While this difference was not statistically significant, it is likely to be perceived as clinically important. As constant work-rate tests are terminated by the investigator at 20 min, a test duration of 4:27min suggests that performing this test at 80% W<sub>max</sub> offers ample opportunity for improvement following an intervention.

**Grant Support:** Curtin University and Sir Charles Gairdner Hospital (Physiotherapy Department and the Research Advisory Committee). Institute for Respiratory Health (Conquer Cystic Fibrosis Research Program), Australian Government Research Training Program Scholarship and Cystic Fibrosis Australia (Australian Cystic Fibrosis Research Trust Top-Up Scholarship). VC is funded by a Cancer Council Western Australia Post-doctoral Research Fellowship.

### HEART RATE RECOVERY IS SIMILAR FOLLOWING INCREMENTAL-RAMP AND CONSTANT WORK-RATE EXERCISE AND RELATED TO VO<sub>2</sub>PEAK IN ADULTS WITH CYSTIC FIBROSIS

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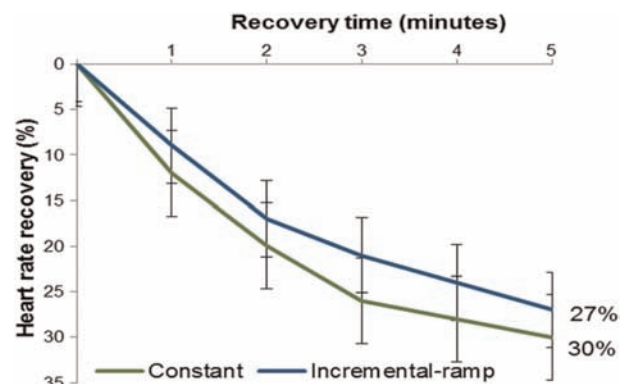
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**Introduction:** Exercise capacity (i.e. peak rate of oxygen uptake [VO<sub>2peak</sub>]) is associated with survival in people with cystic fibrosis (CF). In other populations, heart rate (HR) recovery following maximal exercise is also related to survival. Little is known about HR recovery in adults with CF. Our research questions were, in adults with CF: (i) is the magnitude of change in HR recovery different following incremental-ramp and constant work-rate exercise, and (ii) is the magnitude of change in HR recovery at 5-minutes post exercise associated with VO<sub>2peak</sub>, age, or lung function?

**Methods:** Ten adults with CF (31±6 yr, FEV<sub>1</sub> 55±12% predicted) undertook an incremental-ramp and a constant work-rate cycle ergometry test (80% maximum work rate [W<sub>max</sub>]) on non-consecutive days. Tests comprised 1-minute of rest, 1-minute of unloaded cycling, a work phase (incremental-ramp or constant work-rate) and a 5-minute 'recovery'.

#### Results:

	Incremental-ramp	Constant	P value
	Mean ± SD		
End-test VO <sub>2</sub> (mL/kg/min)	27.9 ± 7.7	27.0 ± 9.1	0.80
Resting HR (bpm)	86 ± 12	85 ± 12	0.85
Peak HR (bpm)	166 ± 11	159 ± 12	0.19
% predicted HR	88 ± 6	84 ± 7	0.19
Heart rate 5-minutes post-test (bpm)	122 ± 9	112 ± 8	0.01*
% change from peak HR	27 ± 6	30 ± 4	0.39



The magnitude of HR recovery following both exercise tests was comparable ( $P = 0.39$ ). For both tests, the magnitude of HR recovery at

5-minutes was associated with  $VO_{2peak}$  ( $r^2 = 0.74$  [incremental-ramp];  $r^2 = 0.78$  [constant work-rate]). Age and  $FEV_1$  were not associated with HR recovery.

**Conclusion:** In adults with CF, HR recovery following incremental-ramp and constant work-rate exercise was similar suggesting that either test could be used in future studies to assess relationships between HR recovery and survival in this group. People with greater aerobic capacity demonstrate faster HR recovery after exercise.

**Grant Support:** Sir Charles Gairdner Hospital (Physiotherapy Department and the Research Advisory Committee). Institute for Respiratory Health (Conquer Cystic Fibrosis Research Program), Australian Government Research Training Program Scholarship and Cystic Fibrosis Australia (Australian Cystic Fibrosis Research Trust Top-Up Scholarship). VC is funded by a Cancer Council Western Australia. Postdoctoral Research Fellowship.

#### MODULATION OF MACROPHAGE POLARIZATION AND FUNCTION IN PATIENTS WITH CYSTIC FIBROSIS BY MUTATION-INDEPENDENT IMMUNOMODULATORY COMPOUNDS

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**Introduction/Aim:** Progressive lung disease is the major killer of patients with cystic fibrosis (CF). Macrophages with their pro-inflammatory M1 and anti-inflammatory M2 phenotypes play key roles in initiation and resolution of pulmonary inflammation. We previously reported CFTR-dependent fundamental defect in M2 macrophage polarization from patients with CF that may underlie the exaggerated lung inflammation in CF. Inhibition of CFTR in healthy macrophages mimics CF phenotype. Azithromycin (AZM), a macrolide antibiotic, is used in CF to modulate pulmonary inflammation, but the mechanism is unknown. We aimed to restore anti-inflammatory M2 macrophage polarization using mutation-independent biologic compounds.

**Methods:** Monocytes were sorted from the blood from healthy donors (n = 5) and differentiated to macrophages and polarized into M1 and M2 macrophages by LPS and IL-13 respectively, in presence or absence of CFTR inhibitor (C-172) and azithromycin (AZM). Frequency of CD80+ M1 macrophages and CD209+ M2 macrophages were analysed by flow cytometry and function of these polarized macrophages assessed.

**Results:** AZM has no effect on macrophage differentiation and polarization. Incubation with C-172 reduced the percentage of CD209+ M2 macrophages. Interestingly, the addition of AZM restored CD209+ M2 macrophages when C-172 was treated compared to C-172 treated cells only. Macrophages conditioned in AZM plus C-172 medium showed enhanced endocytic ability compared those conditioned in C-172 only. AZM+C-172 reduced the percent of CD80+ M1 macrophages, reduced TNF- $\alpha$  secretion compared to C-172 alone. While, C-172 reduced phagocytic function of M1 macrophages, AZM did not restore phagocytosis of C-172 treated M1 macrophages.

**Conclusion:** Our preliminary data showed restoration of anti-inflammatory M2 macrophage polarization and reduced frequencies of M1 macrophages in CFTR-inhibited macrophages following AZM treatment. These modulations of macrophage polarization and functions is mutation-independent and show a scope of treating patients with CF with non-antibiotic macrolides, which will reduce the chance of antibiotic resistance.

**Grant Support:** Cystic Fibrosis Foundation Therapeutic (CFFT), US.

TPL 006

TPL 007

### NON-TUBERCULOUS MYCOBACTERIA INFECTION IN PEOPLE WITH CYSTIC FIBROSIS ATTENDING CF TREATMENT CLINICS IN AUSTRALIA

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**Introduction/Aim:** Chronic nontuberculous mycobacterial (NTM) infections have rapidly emerged in people with CF and pose a significant threat to their survival. This prospective study aims to determine the prevalence and incidence of NTM in Australia as part of the ongoing National NTM in CF study.

**Methods:** A risk based cohort study is underway in 19 CF centres in Australia. Recruits are consenting adult or paediatric individuals with CF who produce a respiratory sample as part of a routine clinical visit (sputum, bronchoalveolar lavage or induced sputum). Samples are collected at baseline, six and 12 months and sent for mycobacterial culture. Nationally 508 adult and 304 paediatric recruits have provided up to 3 sputum samples for mycobacterial culture (September 2016 – December 2018).

**Results:** Preliminary findings indicate that NTM infection is higher in paediatric recruits (9.9%) compared to adult recruits (6.5%) nationally. Mycobacterium abscessus group (MABS) infections (51.0%) are the predominant NTM infection in paediatric patients followed by *M. avium* complex (MAC) infections (39.2%). In contrast, MAC species are the most commonly isolated NTM species (49.0%) in adults, followed by MABS (36.7%). Preliminary data indicates that this pattern of infection varies from state to state within Australia. In the National cohort, NTM positive recruits are significantly younger than the NTM-negative recruits ( $p < 0.05$ ). Recruits infected with MABS have a significant reduction in mean FEV1% pred ( $62.3\% \pm 17.8$  SD) when compared to age matched NTM negative recruits ( $79.3\% \pm 20.0$  SD).

**Conclusion:** Younger people with CF are more likely to acquire MABS. Participants with MABS infections have reduced lung function compared to age matched peers without NTM infections or those infected by slow growing mycobacterial species. It is not known if poor lung function is a marker for acquisition of MABS or a result of MABS infection.

**Grant Support:** NHMRC Project Grant (APP1102494).

### ADULT CYSTIC FIBROSIS (CF) PATIENTS PREFER TO PERFORM IMPULSE OSCILLOMETRY (IOS) IN COMPARISON TO SPIROMETRY

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**Introduction/Aim:** Spirometry is the gold standard method for monitoring lung function in CF. Spirometry is a forceful manoeuvre and has been reported to cause patient discomfort. IOS is an alternative diagnostic tool that has been recently introduced to monitor lung function. IOS is less forceful and is simple to perform but studies have been limited to the paediatric population. The aim of this study is to compare patient preference and assess patient discomfort among adult CF patients in using IOS and spirometry.

**Methods:** Two prospective studies are being conducted simultaneously to compare the sensitivity of IOS and spirometry in detecting lung function improvements in CF patients. One group is being monitored before and after the commencement of ORKAMBI and the second group is being monitored before and after intravenous antibiotic therapy for pulmonary exacerbations. Patients were given questionnaires after lung function measurements to assess for patient preferences between the two diagnostic methods. The patients were also asked to rate their level of discomfort for each test on a scale between 0 (very comfortable) and 10 (extreme discomfort). The same questionnaires were used in both patient groups.

**Results:** A total of 28 patients ( $n=28$ ) were recruited; 12 patients from CF exacerbation study and 16 from ORKAMBI study. The mean  $\pm$  SD age was  $31.2 \pm 8.6$  years; 22 patients were males (79%). The majority of patients (75%,  $n=21$ ) preferred performing IOS. Six (21%) patients preferred performing spirometry, while one patient (4%) had no preference.

Five patients (18%) reported experiencing discomfort while performing spirometry compared to one patient (4%) using IOS. Spirometry had an overall mean discomfort score of  $1.9 \pm 2.2$  compared to mean discomfort score of  $0.6 \pm 1.0$  for IOS, this difference was not statistically different ( $p=0.11$ ).

**Conclusion:** Adult CF patients prefer to perform IOS in comparison to spirometry. More patients experienced discomfort when performing spirometry in comparison to IOS.

**Grant Support:** None.

TPL 008

TPL 009

**INHALED DRY POWDER ALGINATE OLIGOSACCHARIDE (OLIGO) IN CYSTIC FIBROSIS: SUB-GROUP ANALYSES OF A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED, EFFICACY AND SAFETY TRIAL**

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**Introduction/Aim:** The objective was to demonstrate efficacy of inhaled OligoG in adults with Cystic Fibrosis (CF) as determined by FEV1, Mucociliary and Cough Clearance, Lung Clearance Index, Rheology, Microbiology and Quality-of-Life. OligoG is a low molecular weight alginate oligosaccharide that has been shown in pre-clinical studies to restore the normal viscoelastic properties of mucus, potentiate the activity of antibiotics and antifungal agents and disrupt biofilm formation.

**Methods:** A randomized placebo-controlled cross-over study design was used to demonstrate efficacy and safety of inhaled alginate oligosaccharide for 28 days in subjects with CF. Patients were randomly allocated to receive OligoG 1050 mg per day or matching placebo for 28 days in the first treatment period, followed by a 4 week washout period, then a second treatment period of 28 days with the alternate treatment (placebo or OligoG), followed by a 4 week washout and follow-up.

**Results:** A total of 90 patients were screened and 65 randomized. For the primary efficacy variable, change in FEV1, no significant improvement was seen in the ITT population. However, post-hoc analyses (without correcting for multiple testing) indicated improvement in FEV1 with OligoG treatment compared to placebo in selected subgroups: concomitant tobramycin (9.7% improvement at 28 days,  $p=0.0010$  and 15.8% at 56 days,  $p=0.0095$ ); continuous inhaled antibiotics and <100% adherence (8.7% improvement at 28 days,  $p=0.0190$ , and 12.8% at 56 days,  $p=0.0204$ ); <100% adherence (5.5% improvement in FEV1 at 28 days,  $p=0.0738$ , and 8.5% improvement at 56 days,  $p=0.0690$ ); and younger patients (4.4% improvement at 28 days,  $p=0.35$ , and 9.5% at 56 days,  $p=0.21$ ).

**Conclusion:** Repeated inhalation of OligoG DPI was safe in adult CF patients. Although the primary objective was not met in the ITT population, subgroup analyses indicate possible efficacy of OligoG in CF patients through mucus mobilization, improved lung function, and antibiotic potentiation.

**Grant Support:** Supported by Cystic Fibrosis Foundation, Eurostars Programme (No.: EI6628) and AlgiPharma AS.

**TRANSFORMATIVE THERAPIES FOR ULTRA-RARE CFTR MUTATIONS IN PRIMARY PRE-CLINICAL MODELS**

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**Introduction/Aim:** Genotype-directed therapies that target the underlying defect of Cystic Fibrosis (CF), abnormal CFTR protein is now available for over half the CF population with some common CFTR mutations. Some individuals with rare CFTR mutations may benefit from the available modulator treatments. A way forward to improve the clinical outcome for CF patients with rare mutations, was achieved by testing of the therapies ex-vivo on patient derived cell material. We have developed a novel organoid screening platform (miCF AVATAR platform), using cells derived from patient's respiratory and intestinal biopsies. We present this platform using an example of therotyping an ultra-rare CF causing variant.

**Methods:** We performed *in silico* docking simulations of compounds on CFTR structure models to predict that this mutation could be corrected and potentiated. Patient derived materials I: Bronchial epithelial cells (HBE), II: rectal biopsies and III: intestinal organoids were generated from an individual with I37R/F508del CFTR genotype. I37R mutation was characterized by RT-PCR, Immunofluorescence and Western blot. The efficacy of CFTR modulators was tested using Intestinal current measurements (ICM) on rectal biopsies and short circuit measurements (Isc) for HBEs and by forskolin-induced swelling (FIS) assay in intestinal organoids.

**Results:** Data from ICM, FIS assay and Isc indicate I37R has residual CFTR-mediated Cl<sup>-</sup> secretion. The residual activity was further enhanced by potentiators (Genestine, GLPG1837 and VX-770) whereas, correctors (VX-809 and VX-661) alone failed to induce any significant increase in intestinal organoid swelling or alter Isc in HBE. Next we assessed the synergy among potentiators, with and without correctors at optimal concentration of forskolin. Results indicated that all possible combinations of tested potentiators synergistically repaired CFTR-dependent FIS of organoids with I37R./F508del genotype.

**Conclusion:** We propose that this multi-disciplinary approach, combining electrophysiology and organoid swelling assay to profile modulators using primary tissue, will facilitate therapy development for patients with rare CF mutations.

**Grant Support:** SCHN Foundation, Paediatric, Rebecca L Cooper Foundation, UNSW Triple I SPHERE and CF Australia Innovation Grant

TPL 010

TP 068

### CYSTIC FIBROSIS BONE DISEASE IN THE WA CF ADULT POPULATION

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**Introduction/Aim:** Bone disease is a common problem in people with cystic fibrosis, with a multifactorial aetiology. There is newer evidence to suggest that CFTR mutations have a direct effect on BMD and that CFTR modulator therapy can improve BMD. This study aims to assess the prevalence of CF related osteopenia and osteoporosis in the adult CF cohort, assess the proportion of patients receiving appropriate therapies and to identify the prevalence of potentially modifiable risk factors of patients, particularly looking at the effect of CFTR modulator therapy on BMD.

**Methods:** BMD and T Scores of the lumbar spine and hip were recorded in 94 individuals with CF using DEXA scanning from the last 15 years. Variables including presence of CFTR modulator treatment, presence of bisphosphonate therapy and serum calcium and vitamin D were also recorded. Patients also filled out a questionnaire about their fracture history.

**Results:** A total of 94 patients were included in the preliminary analysis, with 35 patients on lumacaftor/ivacaftor, 17 on ivacaftor and 42 on no CFTR modulator therapy. 12/94 (12.8%) patients had osteoporosis, and 28/94 (29.8%) had osteopenia. Patients on lumacaftor/ivacaftor were overrepresented in regards to osteoporosis with 7/35 (16.7%), while 1/17 (5.9%) patients on ivacaftor had osteoporosis and 4/42 (9.5%) patients on no CFTR treatment had osteoporosis. 28/58 (48.2%) of patients had had a previous fracture.

CFTR treatment...

**Conclusion:**

**Grant Support:**

### ADHERENCE TO COPD-X GUIDELINES AND TREATMENT ADHERENCE IN REGIONAL VICTORIA

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**Introduction/Aim:** Adherence to clinical guidelines and treatments is imperative to good health outcomes. To assess adherence to COPD-X guidelines and patient adherence to treatment in a regional setting.

**Method:** A prospective study (May–July 2018) of patients admitted for a COPD exacerbation through the emergency department of a regional teaching hospital was conducted. Data were obtained through structured patient interviews including the Tool for Adherence Behaviour Screening (TABS), a review of medical notes and medication reconciliation forms, and a follow-up phone call 2 weeks after hospital discharge.

**Results:** Sixty-six patients (mean [SD] age 69.91 [10.47]; 29 [43.9%] males; 19 [28.8%] current smokers mean 15 cigarettes/day) were included in the study. The mean FEV<sub>1</sub>% predicted (n = 38) was 50.16 (16.23); the COPD was classified as mild 13 (20%); moderate 15 (23%); and severe 10 (15%). Asthma (23; 34.8%) was the most common comorbidity.

On admission, only 2 (3%) patients were fully managed according to the COPD-X. 21 (32%) had completed pulmonary rehabilitation; vaccination rates were: pneumococcal 31 (47%) and influenza 49 (74%). Within the last 12 months, 25 (38%) participants had their inhaler/spacer technique reviewed; 22 (33%) had a pharmacist home medicines review. Non-adherence was identified (using TABS) in 56 (84.8%) patients; 11/40 (27.5%) had poor inhaler technique.

Antibiotics initiated included doxycycline (46; 83.6%), ceftriaxone (27; 49.1%), benzylpenicillin (25; 45.5%); amoxicillin (23; 41.8%); and azithromycin (15; 27.3%). Systemic corticosteroids (mean duration 3.5 days) were given for the correct duration in only 4/53 (7.5%) patients. COPD-X adherence increased to 4/48 (8.3%) after hospital discharge, while self-reported nonadherence decreased to 30/48 (62.5%) post-discharge.

**Conclusion:** Gaps exist between guidelines and management of COPD in both primary and secondary care in the regional setting. Health professional education focusing on COPD-X and consumer education targeting treatment adherence are needed.

**Key Words:** COPD, COPD-X, management.

**Grant Support:** None.

TP 069

TP 070

**A COMPREHENSIVE ANALYSIS OF PULMONARY EMBOLUS (CAPE) STUDY: THROMBOPHILIA SCREENING APPROPRIATENESS AND OUTCOMES**

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**Introduction/Aim:** Pulmonary embolus can be a life threatening presentation and investigations for such include markers of cardiac insult (troponin and brain natriuretic peptide) but and potentially assessment for hereditary and acquired thrombophilias. Anecdotally thrombophilia testing is performed indiscriminately despite clear guidelines from the Haematology Society of Australia and New Zealand (HSANZ). In this arm of the CAPE (Comprehensive Assessment of Pulmonary Embolus) study we performed a retrospective analysis on all patients under 50 years presenting with pulmonary embolus to the emergency department of a tertiary centre over a 10 year period to assess the frequency with which thrombophilia screens are performed at presentation and assess the appropriateness, yield and cost of this test sequence.

**Methods:** Retrospective case analysis of all unique presentations to the emergency department with ICD 10 code I26.x between July 2008 and June 2017. All data was derived from electronic sources including The Viewer (a statewide hospital record program which includes blood and imaging results as well as discharge summaries), Auslab (pathology) and EUnity (imaging). This research was approved by the TPCH HREC.

**Results:** 689 cases met the initial criteria, of which approximately 50% were included in the final analysis. The primary reasons for non-inclusion was incorrect coding or insufficient data available. Thrombophilia screens were performed in 65% of included patients, of which almost 40% would be deemed inappropriate by HSANZ. The most commonly identified thrombophilia was Factor V Leiden heterozygosity. Of the screens performed not meeting HSANZ criteria over 10% returned a positive result. Of those patients who did not undergo a thrombophilia screen a significant proportion met criteria for the test.

**Conclusion:** This analysis demonstrates a significant lack of concordance with current HSANZ guidelines, with consequences extending across patient outcome and health economic domains. It provides a solid evidence base with which to provide further education to our clinicians.

**Grant Support:** Nil

**A COMPARATIVE STUDY OF THE ACUTE PRESENTATION OF THE RESPIRATORY PROBLEMS AMONG INDIGENOUS AND NON INDIGENOUS AUSTRALIANS IN THE TOP END.**

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**Introduction/Aim:** Respiratory disorders are second most common cause of acute hospitalisation. They contribute to the high rates of hospitalisation and mortality among indigenous Australians. 30% of northern territory population are aboriginals who live in remote communities making healthcare delivery challenging.

**Methods:** It is retrospective study of the patients who presented to the emergency department of Royal Darwin Hospital. It was ethically approved by Menzies school of health Research. The data were collected from the patients' medical records.

**Results:** A total of 220 patients above the age of 18 years presented to emergency department in a month. 46% of patients and 59% of the female patients were of aboriginal descent. 45% of patients were active smoker. 65% of smokers were of aboriginal background of which 60% were female. Eight percent of patients were referred by health professionals from other institutes. 54% of patients were discharged from emergency department after assessment. Infections (54%), exacerbation of obstructive airway disease (39%) and pulmonary embolism (4%) were the most common causes of hospital presentation so were the most common causes of admission to ward.

Most of the patients received a blood test (84%) and Chest x-ray (88%). However, only 36% of patients had their sputum tested, of which 23% grew at least one organism in culture. 75% of the patients received at least one dose of antibiotics via intravenous or oral route. Overall 12% of the patient had readmission within 30 days for respiratory related issues and this rate was higher among aboriginal patients (19%) contributing to the majority (73%) of readmissions. Six months mortality among these patients was nine percent and 50 % of these patients were those who had exacerbation of their obstructive airway disease.

**Conclusion:** Aboriginal Australian have higher rate of smoking, presentation with acute respiratory illness and readmission.

**Grant Support:** None.

TP 071

TP 072

### DIAGNOSTIC TRENDS OF MALIGNANT EFFUSIONS IN A NEW PLEURAL UNIT

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**Introduction/Aim:** Malignant Pleural Effusion (MPE) is a common medical problem. This audit aimed to study the yield of diagnosis with first pleural procedure for MPE in a newly established pleural medicine unit. Secondary objectives were to determine varying rate of diagnosis with different tumour type and to correlate trends of mortality from the initial time of diagnosis.

**Methods:** Retrospective data of all patients who had a confirmed diagnosis of MPE between January 2015 to January 2018 were pooled and analysed. Data from the initial procedure to the point of confirmation of MPE were traced to obtain number of diagnostic procedure undertaken to confirm MPE. Data on subtypes of MPE were collected to deduce variable yields of diagnosis according to subtype of malignancy. Patients were also followed through at 3, 6, and 12 months from confirmed diagnosis to collect mortality data on these intervals.

**Results:** We identified total of 178 confirmed samples of MPE in the study period. The cohort had a mean age of 67 years with 52.2% of patients being Male. Subtype of MPE included Non small-cell lung adenocarcinoma (68), breast cancer (35), malignant mesothelioma (28) and other adenocarcinomas (11). Of the 178 malignant pleural effusions, 153 patients were newly diagnosed. Of these, 88.9%(136) were diagnosed at first procedure. Of the majority requiring 2 or more procedures (11.1% of all patients), 70.6% (12) of these patients were diagnosed with malignant mesothelioma. Cumulative 12-month mortality rate for this cohort was 55.6%.

**Conclusion:** In line with established guidelines for MPE, our audit supports good diagnostic yield for MPE with first procedure. Variable cytological diagnosis of malignant mesothelioma is quite prevalent and hence these patients usually required 2 or more procedures to confirm diagnosis. MPE upstages the cancer staging and hence is indicative of poor overall survival in most malignancies.

**Grant Support:** Nil

### CLINICAL FEATURES AND LONG-TERM OUTCOME OF PATIENTS WITH SADDLE PULMONARY EMBOLISM: EXPERIENCE FROM TWO TERTIARY CENTRES

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**Introduction/Aim:** Saddle pulmonary embolus (SPE) is characterised by a straddling thromboembolus spanning the bifurcation of the main pulmonary artery trunk. SPE can cause an unstable, large clot burden and haemodynamic instability. Its frequency has been reported to be 2-9%, with a mortality rate of 5-29%. Despite the current available data on SPE, there is still limited data on its short- and long-term outcome. In this study, we aim to determine the frequency, clinical presentation, and outcome of SPE patients.

**Methods:** Patients with pulmonary embolus (PE) diagnosed between 1-August-2015 and 31-July-2017 at Sir Charles Gairdner Hospital and Fiona Stanley Hospital were identified by medical records. Of the 769 patients identified, 681 patients (89%) were diagnosed with CT pulmonary angiogram and included in the analysis, 88 (11%) were diagnosed by either ventilation-perfusion scan or clinical diagnosis. Cases of SPE were identified by examining patients' CT scan, with clinicopathological data collected from medical records (demographics, clinical findings, radiological features, and treatment). Each case was followed up for a maximum of 12 months.

**Results:** A total of 55 SPE cases were identified out of all PE patients (8%). Most of the patients were male (61%), with a mean age of 62 years-old. Most common treatment modality was anti-coagulation (intravenous heparin infusion or subcutaneous low-molecular-weight-heparin) in 80% of patients, followed by surgical embolectomy (11%) and systemic thrombolysis (9%). Previous venous thromboembolisms (27%) and malignancy (25%) are the most common identified risk factors. Sixty-one percent of patients had echocardiogram at the initial assessment – out-of-which, 37% of patients exhibited elevated pulmonary artery systolic pressure. There were 3 (7%) deaths identified as directly resulting from SPE.

**Conclusion:** This study showed that the frequency and mortality rates of saddle PE in our centres are comparable to other studies. As far as authors aware, this is the largest study describing SPE in Australia.

**Grant Support:** Nil.



TP 073

TP 074

### RECURRENCE RATE AND SPREAD OF SARCOIDOSIS ARE ASSOCIATED WITH BMI

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**Introduction/Aim:** According to various studies, subjects with obesity have a higher risk of developing sarcoidosis. However, the influence of BMI on the features of sarcoidosis is unknown. Our aim was to investigate how BMI is related to the recurrence rate and number of affected organs in patients with sarcoidosis.

**Methods:** We identified 82 patients with biopsy-proven pulmonary sarcoidosis who were observed in our clinic within the period of 2 years (from Sep 2016 to Sep 2018). All patients underwent 12-lead electrocardiogram, daily monitoring of electrocardiogram, echocardiography, ophthalmology examination, endocrinology and neurology examination, gastroscopy, spirometry, and high resolution computed tomography. Also, examination of skin and ultrasound examination of peripheral lymph nodes were conducted. BMI, the rate of recurrences and the number of localizations were evaluated.

**Results:** except of pulmonary sarcoidosis, involvement of skin and peripheral lymph nodes was found in 18.3% of patients and was confirmed by biopsy. Other localizations were not found. BMI significantly correlated with the recurrence rate ( $P = 0.005$ ) and number of involved organs ( $P = 0.001$ ). Also in multivariate regression analysis which included sex, age, smoking and BMI the factor associated with the recurrence rate and number of localizations was BMI ( $P < 0.05$ ).

**Conclusion:** BMI is associated with the recurrence rate and number of affected organs among patients with sarcoidosis.

**Grant Support:** No.

### PSYCHOMETRIC PROPERTIES OF THE QUALITY OF LIFE-BRONCHIECTASIS QUESTIONNAIRE IN AUSTRALIA.

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**Introduction/Aim:** Valid and reliable patient-reported outcome measures are cardinal in assessing treatment effects from a patient's perspective. Psychometric properties of the QoL-B have been established in North America and Europe, yet no bronchiectasis-specific questionnaire has been evaluated in Australia. This study aimed to confirm the reliability and validity of the QoL-B within the Australian population.

**Methods:** Pre-intervention data were extracted from a multi-centre phase III trial in stable Australian bronchiectasis patients, recruited from six sites in NSW and Queensland (ACTRN12611001199909). Internal consistency, construct validity, and criterion validity of the QoL-B were evaluated, including comparisons to other subjective respiratory questionnaires and objective measures of lung function and exercise capacity. Participant demographics were compared to 776 patients in the Australian Bronchiectasis Registry (ABR).

**Results:** 131 participants provided data for this study (mean  $\pm$  SD) ( $62 \pm 13$  years, 74% female), with mild to severe lung disease (FEV<sub>1</sub>% predicted  $68 \pm 21$ , range 28% ~ 118%; FEV<sub>1</sub>/FVC  $0.65 \pm 0.13$ ). The participants had similar age and lung function compared to the ABR population. Internal consistency was high in all domains (Cronbach's alpha  $> 0.64$ ). All items demonstrated the strongest association with their designated domain ( $r_s = 0.21-0.90$ ,  $n = 102-131$ ,  $P < 0.01$ ). Strong correlations were found between *Respiratory* QoL-B and St George Respiratory Questionnaire Symptoms scale ( $r = -0.704$ ,  $n = 131$ ,  $P < 0.01$ ) and *Physical* QoL-B and Modified Shuttle Test distance ( $r_s = 0.713$ ,  $n = 127$ ,  $P < 0.01$ ). The *Physical*, *Health* and *Respiratory* domains differentiated disease severities according to FEV<sub>1</sub>% predicted ( $P < 0.05$ ). There was no statistical difference in QoL-B scores between people with additional significant respiratory comorbidities and those without.

**Conclusion:** The excellent reliability, internal and external validity of the QoL-B were confirmed in the Australian population. QoL-B scores were not confounded by non-bronchiectasis respiratory comorbidities. It can be applied with confidence in Australian clinical and research settings in addition to the objective and generic respiratory subjective outcome measures currently undertaken.

**Grant Support:** The primary trial was funded by the National Health and Medical Research Council. No funding was required for this study. There is was conflict of interest to declare.

#### THE FEASIBILITY OF 24-HOUR EXACERBATION SUPPORT: COPD AT HOME

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**Introduction:** Central Adelaide Local Health Network annually receives around 1000 emergency department (ED) presentations due to Chronic Obstructive Pulmonary Disease (COPD). A proportion of ED presentations, and subsequent hospital are avoidable, result from poor self-management misinterpretation or severity.

**Aim:** To assess if the implementation of a 24-hour exacerbation support service using respiratory nurses (RespRNs) and the South Australian Ambulance Service (SAAS) Extended Care Paramedics (ECPs) was feasible; the factors affecting implementation and use by patients and determine local data on key outcomes to inform a future trial

**Methods:** Fifteen participants were block randomised to control or intervention. All participants received self-management education (i.e. a written COPD Action Plan and/or emergency pack) with the intervention group receiving the additional exacerbation support service. Inclusion criteria were: a confirmed diagnosis of COPD by pulmonary function testing, minimum 2 ED presentations and/or hospital admissions for COPD in the preceding 12 months and possession of ambulance cover.

**Results:** For the intervention group, ECPs responded to 9 calls with 3 (33.3%) resulting in ED avoidance. RespRNs received 12 calls; 6 related to exacerbations with 2 requiring ED presentation (66.6% avoided); 6 calls were for other reasons including anxiety management. The control group presented to ED on 7 occasions for COPD related illness. Average baseline data indicates moderate levels of depression and anxiety, and low quality of life. RCT feasibility issues included the influence of education in the control group, loss of and forgetting to use dedicated contact number by participants, communication difficulties between SAAS and the project team.

**Conclusion:** The results have highlighted several areas of improvement for the next phase of the project, where improved communication protocols and adjusted patient education tools, will allow full assessment of the viability of this intervention to reduce ED burden of COPD.

**Grant Support:** •

#### THE AUSTRALIAN BRONCHIECTASIS REGISTRY: LEARNINGS FROM ESTABLISHING AND OPERATING THE LARGEST RESPIRATORY DISEASE REGISTRY IN AUSTRALIA

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**Introduction/Aim:** The paucity of longitudinal, national data pertaining to bronchiectasis, a resurgent disease, has prompted the development of the Australian Bronchiectasis Registry (ABR). The aim was to apply a staged rollout, with data quality and improvement of patient outcomes featuring prominently on the agenda.

**Method:** A data collection platform was developed in partnership with the European Bronchiectasis Registry (EMBARC). Multisite ethics approvals were obtained and linkage to healthcare and pharmaceutical utilisation data was included as part of the project design. However, unlike our US and European counterparts, the ABR collects both paediatric and adult data. Assessment of collected data was conducted at 18 months post commencement, identifying a need to improve both data quality and completeness. A number of strategic approaches were applied in an attempt to optimise data collection.

**Results:** Progress at 18 months post commencement:

5. 20 sites across Australia and nearly 900 patients (original targets: 15 and 300 respectively)

- 59% consent rate or Medicare and Pharmaceutical data access
- high interest resulted in a negative impact on resources and insufficient capacity for sustainability

Impact of quality improvement intervention:

- audit and feedback reports deemed as most effective strategy by ABR users

- increase from 28% to 96% in clinical data capture

Key challenges:

- inadequate local resources for data entry
- limited data completeness pre-intervention
- ethics and research governance requirements

**Conclusion:** Interest in the ABR from patients and clinicians remains high with registration far exceeding projected expectations. Despite high demand, our ability to increase the number of actively participating health services is currently limited by the lack of continued funding for the Registry. We believe that the significant improvement in data quality and completeness is related to a structured quality assessment process, which was underpinned by individualised site engagement.

**Key Words:** bronchiectasis, clinical registry, quality improvement,

**Grant Support:** The establishment of Australian Bronchiectasis Registry was made possible through the generous support from Aradigm, Bayer Healthcare, Insmid, Novartis and Pfizer.

TP 077

TP 078

### LUNG IMAGING AT MEDICAL EMERGENCY TEAM CALLS FOR INPATIENTS: LIMIT CTPA

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**Introduction/Aim:** Computed tomography pulmonary angiography (CTPA) is the gold standard test for pulmonary embolism (PE), but accumulating evidence points to its overuse. This has not been well studied in the Australian inpatient setting. We aimed to evaluate CTPA use following inpatient medical emergency team (MET) calls for clinical deterioration at an Australian hospital. Specifically, we studied diagnostic yield, presence of alternative diagnoses on CTPA, and adherence to current guidelines.

**Methods:** We performed a retrospective audit of all patients who underwent CTPA for suspected PE within 24 hours of a MET call at The Alfred Hospital, Melbourne between 1 January 2017 and 31 December 2017. Demographic details, clinical history and imaging results were analysed.

**Results:** 155 patients underwent CTPA during the study period. PE was diagnosed in 19 patients (12.3%). 94.7% of detected PEs were segmental or larger. CTPA revealed clinically relevant alternative diagnoses in 91 patients (58.7%), most commonly consolidation or pleural effusion. These were not visible on initial chest X-ray in 40 cases, and had therapeutic consequences in 19 cases (12.3%). Validated clinical decision-making tools were used infrequently. Only 2 patients had a documented Wells' score and only 9 had a d-dimer tested. Chest X-ray was used as an initial test in 79.3% of patients. Normal chest x-ray predicted a higher rate of PE on CTPA (22.2% vs 9.2%,  $P = 0.037$ ). Other predictors of PE were recent orthopaedic or spinal surgery.

**Conclusion:** CTPAs performed at our centre in acutely deteriorating inpatients had a higher yield than predicted, revealing a diagnosis of significant PE or other clinically relevant pathology in 70% of patients, and influencing management in 25%. More stringent application of validated tools such as Wells' score and d-dimer, and use of chest x-ray prior to CTPA imaging, could serve to further reduce unnecessary resource utilisation and radiation exposure in this patient group.

**Grant Support:** None.

**No conflicts of interest to declare.**

### ROLE OF VATS IN RESPIRATORY DISEASES: EXPERIENCE AT A TERTIARY CARE CENTRE IN WESTERN INDIA

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**Aim:** Video-assisted thoracoscopic surgery (VATS) has led to improved patient outcomes in patients suffering from respiratory diseases, mainly pleural disorders. There is scarcity of such data from India due to lack of expertise in VATS. As an experienced centre in VATS surgery, we aimed to evaluate the results of VATS in patients with empyema thoracis at a tertiary care hospital in Western India.

**Method:** We retrospectively analysed the results of VATS on twenty five patients of respiratory diseases with respect to post-operative pain, lung function improvement, cosmesis and time to return to normal daily activity.

**Results:** Majority of patients who underwent VATS showed good post-operative outcomes. Patients who underwent conversion to open thoracic procedures had more prolonged history of presentation with thick pleural adhesions making VATS impossible to be performed.

**Conclusion:** Surgical intervention with VATS showed early recovery and improved overall clinical outcomes.

**Key Words:** VATS, empyema thoracis

**AUDIT OF RIGID BRONCHOSCOPIC INTERVENTIONS FOR CENTRAL AIRWAY OBSTRUCTION (CAO)**

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**Introduction/Aim:** CAO is a relatively rare but critical medical problem, with outcome of therapeutic interventions influenced by patient-, disease-, operative- and anaesthetic factors. We aim to examine the outcomes of CAO in our centre and to assess the predictors of outcome.

**Methods:** This is a retrospective review of all rigid bronchoscopic procedures by a single operator conducted at Westmead Public and Private hospitals for CAO. Data were collected on patients' demographics, anaesthetic requirements, pathology, interventions performed, complications and mortality. Data was analysed using SPSS.

**Results:** 50 patients (26 males; median age 65 years with IQR 56.1-72.6 years) had 65 rigid bronchoscopic procedures between 2010 and 2018. Most had an ASA of 3 or 4. Median FEV1 was 1.22L (IQR 1.01L-1.84L) and Median FEV1% was 53 (IQR 41-68)). All procedures were performed under general anaesthesia. Median length of hospital stay was 2 days following procedure. Only 1 of 8 patients with benign pathology has passed away with a complication unrelated to the procedure. Of the 42 patients (84%) with malignancy, 30-day mortality was 11.9%, with overall median survival of 5 months. There were no procedure-related deaths. However 1 patient died from respiratory failure 10 days following incorrect stent placement that failed to achieve complete airway patency. Smoking history, presence of disease in the right main bronchus or multiple-sites, and placement of multiple stents were all related to higher mortality rates on univariate analysis.

Table 1 Complications and follow-up after rigid bronchoscopy

Immediate complications	Follow-up data till-date
Haemoptysis: 12/65 (18%), all minor	Stent migration/ replacement: 10/50 (20%)
Respiratory failure: 17/65 (26%) (8 transient, 2 NIV, 1 intubation, 4 failed extubation)	Recurrent lumen obstruction: 16/50 (32%)
Pneumothorax: 1/65 (1.5%) (bilateral, requiring ICCs)	Repeat procedures: 19/50 patients (38%)
	Repeat admission related to airway pathology or bronchoscopic procedure: 25/50 (50%) (pneumonia as most common reason)

**Conclusion:** CAO carries a significant morbidity in a generally unwell cohort. Those with malignancy had limited survival, with their post-operative phase frequently involving repeat hospital admissions, repeat bronchoscopies and ongoing complications related to their stents and disease progression. Prospective data on quality of life scores will be useful. Our complication and 30-day mortality rates appeared to be similar to the American AQuiRE registry data.

**Grant Support:** Nil.

**USE OF RADIAL-EBUS TO AID DIAGNOSES OF PERIPHERAL PULMONARY LESIONS**

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**Introduction/Aim:** This study aims to examine the diagnostic yield and complication rates of the use of radial endobronchial ultrasound (rEBUS) in our patient population.

**Methods:** All rEBUS procedures conducted at our tertiary centre were evaluated for this retrospective audit. Data was collected on patients' demographics, lung function, radiology, and procedures. Patients' notes were followed till September 2018. Primary outcomes included diagnostic yield and complication rates. Secondary outcomes included documentation of patient and pathology characteristics.

**Results:** 50 patients (26 Male [52%]) had rEBUS procedures performed between July 2016 and September 2018 by a single operator.

Overall 28 patients had malignancies, of which 19 (68%) were diagnosed during the bronchoscopic procedure. This increased to 76% for lesions visualised on rEBUS. 17/50 were diagnosed to be benign including organising pneumonia and benign inflammatory nodules. 5 diagnoses remain unclear. 9/22 non-malignant diagnoses were made on rEBUS. Procedural complications included hypercapnic respiratory failure in 1 patient with OSA and pneumothorax in 2 patients who required observation only. Lesion size ranged from 5mm to 63mm with median size 24mm. 70% of the procedures were done under sedation. 9/50 (18%) patients had sub-optimal procedure due to sedation limitation and 5 of these required repeat procedures for diagnostics. Patients had multimodal biopsies via rEBUS including forceps, brush, FNA, cryobiopsy and GenCut core biopsy (see table). 34% of patients also had linear EBUS performed concurrently.

Table 1 Demographics, mass characteristics, anaesthetic data

Demographics	Mass characteristics	Drug doses for sedation procedures (36/50: 70%)	Bronchoscopy characteristics
Median age 68 years (range 29-88 years, IQR 59-76 years)	Median size: 24mm (IQR 15-33mm)	Midazolam: 4.5mg	Lesion seen on rEBUS: 42/50
Males: 26/50 (52%)	Air bronchograms present: 41/50 (82%)	Fentanyl 100micrograms	Seen of rEBUS if air bronchogram present: 38/41
Median ASA: 3	Location in thirds: 14 inner, 19 middle, 17 outer	Propofol 35 mg	Seen on rEBUS if no air bronchogram present: 4/9
Median FEV1: 1.85L (IQR 1.45-2.28L)		Anaesthetic complications: 1 hypercapnia (known OSA, requiring overnight admission)	Procedures performed: Washings: 19/50, BAL: 15/50, Brushings: 47/50, Forceps biopsy: 24/50, FNA: 23/50, GenCut Core biopsy: 5/50, Cryobiopsy: 2/50, Linear EBUS: 17/50

**Conclusion:** Radial EBUS provides a useful and safe diagnostic modality for suspected lung malignancies.

Our unit had success rates comparable to other published papers however our lesion size was significantly smaller (24 mm) in comparison and the patients had much worse lung function and higher co morbidities. Sedation resistance proved to be a barrier in achieving diagnostic success. The lower lung function or high ASA was not associated with adverse events.

**Grant Support:** Nil.

**Conflicts of interest:** Nil

### COSTS OF ESTABLISHING AND RUNNING A RADIAL-ENDOBRONCHIAL ULTRASOUND (REBUS) SERVICE

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**Introduction/Aim:** Radial EBUS is a relatively new advent that allows bronchoscopic investigation of peripheral pulmonary lesions. There is little data published on costs of establishing and running a rEBUS service. This audit addresses costs of initiating and performing rEBUS procedures at our centre since establishment of the service in 2016.

**Methods:** We documented administrative and staff training costs, equipment purchase costs, consumables usage and equipment maintenance costs for all patients who have had a rEBUS procedure. Staff education costs were calculated based on person-hours spent on in-service and by staff hourly wages. Equipment costs were obtained from our centre's H-TRAK software and cross-referenced with bronchoscopy reports.

**Results:** A total of 63 rEBUS-guided procedures have been performed (Table 1). A total of 4 in-services of 2-hours duration have been performed with mean attendance of 3 nurses, 1 specialist and 1 Olympus representative per session, giving a total cost of A\$795. During this period two rEBUS probes were replaced (A\$9,000). Currently there are two functioning rEBUS probes in use (A\$9,000). The rEBUS probe driver cost was A\$30,000 with the total cost of A\$48,795. This does not include the purchase of an EBUS processor.

A total of A\$26,873 has been spent on 63 rEBUS procedures for consumables with median cost of A\$333.74 per procedure (range A\$111.90 – A\$874.25; IQR A\$285.33 - A\$536.05). Our service has access to a cryobiopsy machine and lung point navigation under grant funding. These are not included in the cost analysis.

Table 1. rEBUS procedure breakdown and costs

rEBUS procedures performed	Item	Cost (\$AUD), range included	Items used	Total costs (\$AUD)
Washings: 27	Trap	6.48	51	330.48
Lavage: 24	Guide Sheath Kit	132.40-156.50	60	8615.70
Brushings: 56	FNA/core needles	95-500	57	10238.10
Forceps biopsy: 33	Biopsy Forceps	40	4	160
Cryotherapy: 3	Cytology Brush	35	5	175
Radial FNA: 30	Arndt Blocker	225-250	8	1950
Radial Core (GenCut): 5	Miscellaneous equipment, inc suction and biopsy valves			903.68
Linear EBUS-TBNA: 22	Equipment Cleaning	50	90	4500

**Conclusion:** To our knowledge, no prior studies assess costs of establishing and maintaining a rEBUS service in this manner. Initial setup and replacement costs can be significant. Once established, running cost for consumables is accessible given the low side effect profile is acceptable. Increase staff training is required for longevity of the probes with at least 3-monthly in-service suggested.

**New innovator aware nominee**

**Grant Support:** Nil.

### TECHNICAL SUCCESS AND COMPLICATION RATES OF CT-GUIDED TRANSTHORACIC LUNG BIOPSY (CT-TLB)

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**Introduction/Aim:** CT-TLB is a minimally invasive diagnostic procedure for tissue diagnosis of pulmonary lesions. We evaluated the technical success and complication rate of a CT-TLB service at an outer metropolitan centre. Subsequently, we analysed factors that are correlated with the occurrence of procedural success and complications.

**Methods:** The medical records of 47 patients who underwent 50 CT-TLBs between Jan 2017 and April 2018 at Ipswich Hospital were retrospectively analysed. Technical success of CT-TLB was defined as an adequate sample for pathological diagnosis. SPSS IBM Version 25 was used for data analysis.

**Results:** The patient cohort had a mean age of 69 ± 9(SD) years, 89% had a smoking history and 64% had emphysema. Of the pulmonary lesions biopsied, 15/50(30%) were small (<2 cm) and 40/50(80%) peripherally located. Core biopsy was performed in 98% with a large biopsy size (>8 mm) in 34%.

The technical success rate was 86%. Biopsy sample size was associated with technical success, although did not reach statistical significance ( $P$  0.08). Technical success was not associated with emphysema, nodule size, nodule location or PET assistance.

Pneumothorax on immediate CT occurred in 26 (52%). Only 4/26(8%) were large, requiring chest drain insertion. Of these 4/4(100%) had a smoking history, 3/4(75%) had emphysema/COPD and 4/4(100%) were upper lobe location. On univariate analysis a history of prior malignancy was associated with lower pneumothorax risk ( $P$  0.044).

Minor pulmonary haemorrhage occurred in 16/50(32%) and small-volume haemoptysis in 5/50(10%). None required intervention. Central ( $P$  < 0.001) and upper lobe ( $P$  0.008) nodule locations were correlated with pulmonary haemorrhage. Haemoptysis was correlated with biopsy size >8 mm ( $P$  0.003).

**Conclusion:** The technical success and complication rates are comparable to that reported in literature. Major complications were uncommon and overall CT-TLB is a safe procedure. The study revealed several variables that can be used to identify patients at risk of complications.

**Key Words:** transthoracic lung biopsy, pulmonary nodule

**Grant Support:** Nil to acknowledge.

TP 083

TP 084

### CORRELATION BETWEEN FUNGAL CYTOLOGY AND CULTURE RESULTS ON BRONCHOALVEOLAR LAVAGE

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**Introduction/Aim:** Fungal respiratory infection can cause potentially life-threatening angioinvasive disease, particularly amongst immuno-compromised patients. At bronchoscopy, fungal cytological testing and culture are performed on all patients. With no established correlation between these tests, if either returns positive, treatment remains physician opinion-based. This study examines their correlation, positive/negative predictive values between tests and examines predictive factors in immuno-competent/compromised populations.

**Methods:** Bronchoscopy fungal cytology and culture results were retrospectively analysed for 300 patients undergoing bronchoscopy between 31/07/17-31/07/18 at a single centre. Patients were identified via the hospital bronchoscopy register and medical records accessed to obtain background information including medical history, anti-fungal treatment and imaging reports.

**Results:** 300 patients were analysed, 43 were immuno-competent and 257 were immuno-compromised. 94 patients (31.3%) had positive fungal cytology or culture, of which 11 were immuno-competent (11.7%) and 83 were immuno-compromised (88.3%). Of the 94 positive results, 74 had positive cytology, 45 positive culture and 25 had both. Fungal cytology had 33.78% PPV (CI26.2-42.31) and 91.15% NPV (CI88.08-93.49%) and fungal culture had a PPV of 55.56% (CI42.48-67.9) and NPV of 80.78% (CI78.05-83.25). Of 29 patients with radiologist-reported radiographic features of fungal infection, 16 patients had had a positive culture or cytology result, giving an odds ratio of 3.05 (CI1.39-6.62,  $P = 0.005$ )

129 patients were on anti-fungals at time of bronchoscopy, 47 had a positive fungal result of which 25 were sub-therapeutic at the time, with a non-significant trend toward increased risk of positive fungal results if sub-therapeutic (OR 1.78, CI0.86-3.66,  $P = 0.12$ )

**Conclusion:** There is poor correlation between fungal cytology and culture results on bronchoalveolar lavage, however fungal culture has a slightly higher PPV. These results continue to require interpretation in the clinical context. Positive radiographic features of fungal infection predicted positive fungal results at bronchoscopy however sub-therapeutic anti-fungal levels didn't significantly increase the risk of fungal infection amongst immuno-compromised patients.

**Grant Support:** Nil.

### A SINGLE 45-MINUTE UNSTRUCTURED BRONCHOSCOPY SIMULATION SESSION IMPROVES BRONCHOSCOPIC DEXTERITY, THOUGH MAINTENANCE OF LEARNING GAIN IS LIMITED.

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**Introduction/Aim:** Simulation is increasingly being recognized as an invaluable tool in bronchoscopy training. Studies reporting improved procedure time, dexterity/technique, and trainee satisfaction have generally utilized highly structured teaching programs supported by low- or high-fidelity simulators.

We sought to determine

1. What learning gain in bronchoscopic dexterity may be achieved through a single 45 minute unstructured trainee exposure to a low-fidelity simulator.
2. The maintenance of acquired skills over an 8 week period in which trainees received no interim exposure to either simulated or clinical bronchoscopy.

**Methods:** Using a 3D-printed low-fidelity model<sup>1</sup>, medical students were assessed on bronchoscopic dexterity before and after an unstructured self-directed 45-minute simulation session.

Bronchoscopic dexterity was assessed according to:

1. Time taken to enter a target bronchus
2. The modified Bronchoscopy Skills and Tasks Assessment Tool (mBSTAT)<sup>2</sup>.

Scores were compared at baseline, post-simulation, and 8 weeks post simulation. Changes in individual domains of the mBSTAT were also compared to identify any specific skill demonstrating more significant deterioration.

**Results:** 28 medical students completed the initial simulation session. 15 returned at 8 weeks. Significant improvement in bronchoscopic skills were observed immediately following the simulation session (mBSTAT scores  $3.7 \pm 1.2$  pre vs  $7.0 \pm 0.9$  post-test,  $P < 0.001$ ). mBSTAT scores had deteriorated significantly at 8 weeks ( $5.7 \pm 1.8$ ,  $P = 0.03$ ) but remained superior to baseline mBSTAT scores ( $P = 0.002$ ). Of the four domains assessed, Precision did not demonstrate any change between post-test and review assessments ( $P = 0.14$ ). Anatomic Recognition ( $P = 0.07$ ), Economy of movement ( $P = 0.06$ ), and posture ( $P = 0.06$ ) all demonstrated trends towards significant deterioration between post-training score and 8-week review scores.

**Conclusion:** A single 45-minute unstructured bronchoscopy simulation session resulted in significant improvement in bronchoscopic dexterity. Significant decay in bronchoscopic dexterity is observed, suggesting repeat simulation may be valuable following periods without bronchoscopy exposure. Review of bronchial anatomy and correct posture/hand position may be valuable following a period without bronchoscopic practice.

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TP 085

TP 086

### PLEURAL EFFUSION MANAGEMENT AT AUSTIN HEALTH: A SINGLE-CENTRE AUDIT

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**Introduction:** Pleural effusions are common presentations with a wide range of differential diagnoses. A structured approach for thoracentesis is essential for timely diagnosis and appropriate management. To maximise procedural safety and diagnostic yield, current guidelines recommend the use of bedside ultrasound guidance in addition to appropriate sample collection and testing.

**Aim:** To assess the standard of care provided for patients presenting with pleural effusions at Austin Health between 2015 and 2016. In particular, to evaluate the timing and method of thoracentesis and appropriateness of pleural fluid testing.

**Methods:** A retrospective audit was performed of all patients who presented to Austin Health with pleural effusions between 2015 and 2016. Data was extracted from scanned medical records relating to patient demographics; aetiology of pleural effusions; timing and method of thoracentesis; and pleural fluid testing.

**Results:** Over 700 patients were included in the audit, with median age of 69 and a slight male predominance. These patients were admitted under a range of medical and surgical specialty units. The majority of patients presented with simple unilateral effusions and underwent thoracentesis within 24 hours of admission. In most cases, the procedure was performed by the admitting unit after remote sonographic localisation. Most episodes of thoracentesis resulted in appropriate pleural fluid testing. However, surgical teams performed less biochemical analysis of the pleural fluid and the median volume of fluid sent for cytological analysis was less than 10 mL.

**Conclusion:** Most patients presenting with pleural effusions underwent timely thoracentesis with appropriate pleural fluid analysis. However, the majority of procedures were performed with remote ultrasound localisation without consistent biochemical testing. This highlights areas of improvement for the inpatient management of pleural effusions, and forms the basis of a prospective study into the use of bedside ultrasound for thoracentesis by dedicated respiratory proceduralists.

**Grant Support:** Nil.

### SAFE AND EFFECTIVE USE OF CRYOBIOPSY WITH RADIAL EBUS FOR LUNG MASSES WITH A HIGH BLEEDING RISK: CASE SERIES AND DESCRIPTION OF TECHNIQUE

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**Introduction/Aim:** Cryo-biopsy is an emerging tool in the diagnostic armory for suspected lung cancer (1,2). We describe our experience in using cryo-biopsy with radial EBUS (R-EBUS) in tumours of high bleeding risk and describe the technique we adopted.

Case series: (Table 1)

**Case 1:** 54 years, Female, non-smoker with incidentally detected spiculated opacity in Right upper lobe. Cryo-radial biopsy (CR-BX): Organising pneumonia.

**Case 2:** 57 years, male, current smoker with Right lower lobe mass. CR-BX: malignant melanoma.

**Case 3:** 77 years, male, lifetime non-smoker presented with a diagnosis of atypical cells suggestive of small cell lung cancer on a trans-bronchial biopsy of a Right middle-lobe.

CR-BX: typical carcinoid tumour.

**Case 4:** 60 years, Male, heavy smoker presented with Right upper-lobe mass. CR-BX: vasculitis. He had high C-ANCA levels. Mass resolved with high dose immunosuppression. All cases required Radial EBUS for visualisation of the lesion. Mean of two CR-BX were done per patient. The sample size of 7 mm were noted without significant bleeding or pneumothorax.

**Description of technique:** All cases were done under general anaesthesia using a 12 mm storz rigid bronchoscopy. A 5F fogarty catheter was placed prophylactically adjacent to the lesion and inflated post biopsy. The radial EBUS with Guide sheath(GS) (Olympus 203) was used to locate lesion and the cryoprobe was inserted through the GS. Once in place cryo-probe was activated for 4 seconds. Cold saline, adrenaline and tranexamic acid was drawn and kept but was not required.

**Discussion:** All patients underwent CR BX for lung cancer but ended up with diagnosis of tumours that are usually categorised as higher bleeding risk.

Correct use of cryo-radial can give excellent diagnosis in benign as well as malignant tumours and can be used safely even in tumours carrying a higher risk of bleeding with the use of correct technique in units with adequate resuscitation facilities.

**Grant Support:** None

**Conflicts of Interests:** None


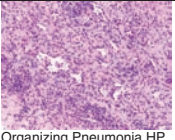
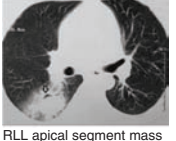
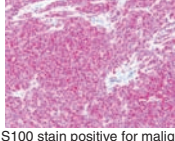

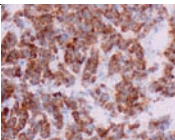
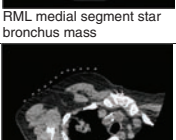
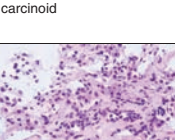
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#### Key words:

Lung cancer, cryo-radial biopsy, safety, large samples, bleeding risk

Table 1: comparing the Radiological appearances to the Histological appearances from cryobiopsy showing well preserved large samples.

Tumour type	CT appearance	Cryobiopsy
Case 1 Pneumonia	 RUL anterior segment mass	 Organizing Pneumonia HP
Case 2 Malignant melanoma	 RLL apical segment mass	 S100 stain positive for malignant melanoma
Case 3 Carcinoid Tumour	 RML medial segment star bronchus mass	 Chromogranin Stain positive for carcinoid
Case 4 Vasculitis (Wagener's granulomatosis)	 RUL apical segment mass	 Acute capillaritis on biopsy: Vasculitis

**THERAPEUTIC USE OF RADIAL EBUS WITH ASPIRATION NEEDLE VIA THE GUIDE SHEATH. CASE REPORT AND DESCRIPTION OF TECHNIQUE.**

**HERATH S<sup>1</sup>**

<sup>1</sup>Westmead Hospital, Sydney, Australia

**Introduction/Aim:** Radial Endobronchial USS guided biopsy (R-EBUS) is becoming popular diagnostic tool (1). Therapeutic use of R-EBUS is not reported. We report a case of a cystic lung mass that was drained using a 21G aspiration needle via the R-EBUS GS.

**Case report:** A 67-year-old, non-smoking female was referred for Respiratory opinion for a Left upper lobe (LUL) mass with a background history of a recently diagnosed locally advanced cervical squamous cell cancer as a malignancy was suspected.

Patient was asymptomatic and afebrile with normal biomarkers. She had no other co-morbidities. She had history of fully-sensitive tuberculosis treated in the Philippines in 2002.

A R-EBUS procedure was planned under sedation using BF TH190 rotatable bronchoscope and large GS (Olympus 203). The lesion was concentrically visualised. Initial biopsy with the forceps and brush met with wall like resistance and did not yield diagnostic material.

Additional 21G Medtronic aspiration needle (21G, 8mm length 1.9mm diameter) was used via the GS and the thick wall of the cyst was pierced. Initial aim was only to obtain a diagnostic sample, however, despite stopping the suction, continuous oozing of brown thick fluid occurred under pressure through the needle sheath. A 150ml of turbid fluid was drained. GS was removed without any complications of bleeding or pneumothorax.

A post procedure CT chest demonstrated complete drainage of the cyst.

12-month post follow-up, the cyst remained dry and stable and deemed to be a previous tuberculous cavity.

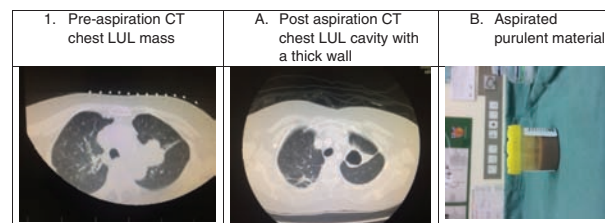
**Conclusion:** R-EBUS with a GS and aspiration needle was used safely to completely drain this large cyst without any adverse events under sedation, highlighting not only the diagnostic but also the therapeutic utility of using an aspiration needle via the GS.

Further studies will be required to explore the use in bronchoscopic aspiration of cavities and even introduction of medications to the cavity.

**Grant Support:** None.

**Conflicts of interest:** None.

**Table 1 A:** Pre-aspiration CT chest LUL mass B: Post aspiration CT chest LUL cavity with a thick wall C: Aspirated purulent material



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TP 088

TP 089

**AUTOLOGOUS BLOOD FOR PERSISTENT AIR LEAK FOLLOWING ENDOBRONCHIAL VALVE-INDUCED PNEUMOTHORAX****HERSCH N<sup>1</sup>**, MOOLAN J<sup>1</sup>, ING A<sup>1</sup>, SAGHAIE T<sup>1</sup>, WILLIAMSON J<sup>1</sup><sup>1</sup>*MQ Respiratory and Sleep, Macquarie University Hospital, Sydney, Australia*

**Introduction:** Intrapleural instillation of autologous blood (blood patch) has been used to manage persistent air leaks from primary and secondary pneumothorax (PTx) and in the postsurgical setting. Evidence supporting its use and standardised protocols are lacking. We report a case where a blood patch successfully treated a prolonged air leak following endoscopic lung volume reduction (ELVR).

**Methods:** A 68yo man developed a large PTx requiring intercostal catheter (ICC) insertion hours following left upper lobe ELVR. Leak persisted despite -20cmH<sub>2</sub>O suction and removal of 2/3 valves on day 7. On day 28, under sterile conditions, 100mLs of venous blood was withdrawn via a cubital fossa cannula and injected through the ICC followed by a 20mL saline flush. The ICC tubing was elevated 1m above the insertion site and the patient kept on bed rest.

**Results:** Within 15 minutes the air leak resolved. Prophylactic intravenous antibiotics were administered for 24 hours. The following day, the tube was clamped for 4 hours, a subsequent chest X-ray showed no PTx, and the ICC was removed. Oral antibiotics were continued on discharge.

**Conclusion:** In this case, a blood patch proved to be a painless, inexpensive and efficacious method to treat persistent air leak following ELVR-induced PTx. Early use could reduce deconditioning and avoid the requirement for valve removal at 7 days. Risk of pleural infection may be mitigated by prophylactic antibiotics.

**Grant Support:** Nil.

**ENDOBRONCHIAL VALVE INSERTION FOR BRONCHOPLEURAL FISTULAS: AN AUSTRALIAN CASE SERIES****LAU H<sup>1</sup>**, BASHIRZADEH F<sup>1</sup><sup>1</sup>*Royal Brisbane And Women's Hospital, Brisbane, Australia*

**Introduction/Aim:** Bronchopleural fistula (BPF) is an abnormal communication between the bronchial tree and pleural space which manifests as a prolonged air leak with persistent pneumothorax. The insertion of one-way endobronchial valves (EBV) represents an emerging, minimally invasive technique for the treatment of BPF. They are particularly attractive in the management of patients with multiple co-morbidities who are deemed at high risk for surgical complications. We aim to present the first case series on the use of EBV insertion for BPF in an Australian setting.

**Methods:** All patients who were treated with EBV insertion for BPF at the Royal Brisbane and Women's Hospital between 2013 and 2016 were included in the case series. Treatment failure was defined as death, surgery, or the use of a long-term, indwelling pleural catheter, while success was defined as diminution or cessation of air leak allowing removal of external pleural drainage.

**Results:** 9 patients received 35 valves (range 2–9 valves) over 10 procedures for the treatment of BPF. Pneumothorax was the most common cause for BPF (7), followed by empyema (1) and as a complication of intercostal catheter insertion (1). All patients had significant underlying lung or pleural disease. Treatment was successful in over two-thirds of cases. Median time between initial ICC insertion and EBV placement was 19 days (range 8–47 days). Median length of inpatient stay was 34 days (range 13–83 days) for those treated successfully with EBV. Two patients had complications arising from valve insertion including an expectorated valve and mild bleeding on elective valve removal.

**Conclusion:** Even in patients with multiple co-morbidities, EBV insertion appears to be an effective and safe treatment for BPF. Increasing awareness of EBV as a treatment modality for BPF may help to reduce inpatient length of stay in the future.

**Grant Support:** Nil

TP 090

TP 091

#### USE OF 19G NEEDLE IN ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL NEEDLE ASPIRATION (EBUS-TBNA) FOR THE EVALUATION OF SUSPECTED LYMPHOMA

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**Introduction/Aim:** Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) represents a minimally-invasive approach in the evaluation of mediastinal and/or hilar lymphadenopathy. Diagnostic performance of EBUS-TBNA in lymphoma with standard 22-gauge (22G) needles is limited by sample volumes that are often inadequate for histopathologic assessment. This study examines the diagnostic utility of 19-gauge EBUS-TBNA needles in the evaluation of lymphoma.

**Methods:** We prospectively collected clinical and procedural information for patients undergoing EBUS-TBNA with 19G needle at Royal Melbourne Hospital for suspected lymphoma. Procedural diagnoses were recorded, and where EBUS did not achieve a definitive diagnosis, final diagnosis was determined through subsequent investigation, or a minimum of 6 months radiologic surveillance.

**Results:** Over a two-year period, 28 patients underwent EBUS-TBNA with 19G needle for evaluation of suspected lymphoma. Seven patients had a prior diagnosis of lymphoma. EBUS-TBNA achieved definitive diagnosis in 18 patients. Lymphoma was ultimately diagnosed in 14 of 28 patients (50%). Of these, five had a prior diagnosis of lymphoma. EBUS-TBNA demonstrated lymphoma in 11 patients, with two patients requiring surgical biopsy to definitively characterise lymphoma sub-type. Sensitivity and specificity for detection of lymphoma using 19G EBUS-TBNA were 79% and 100% respectively. Sensitivity for definitive diagnosis of lymphoma using 19G EBUS-TBNA was 64%. In patients with a prior history of lymphoma, sensitivity and specificity for definitive diagnosis of lymphoma were 80% and 100% respectively.

**Conclusion:** EBUS-TBNA remains a viable modality for evaluation of mediastinal and/or hilar lymphadenopathy. Diagnostic performance with 19G needle appears consistent with that reported for 22G needle. Further invasive testing is required following non-diagnostic EBUS-TBNA procedures.

**Grant Support:** N/A

#### A RETROSPECTIVE AUDIT: EVALUATION OF THE AETIOLOGY, MANAGEMENT PATHWAY AND CLINICAL OUTCOMES OF PATIENTS PRESENTING WITH HAEMOPTYSIS AT A TERTIARY REFERRAL PUBLIC HOSPITAL IN SYDNEY, AUSTRALIA

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**Introduction/Aim:** Haemoptysis is expectoration of blood that originates from the lower respiratory tract. Pulmonary infections are reported to be the main cause of haemoptysis. The aim of this audit is to examine the causes, management pathway and the outcomes of patients who presented with haemoptysis to a tertiary referral public hospital.

**Method:** Retrospective data were collected from the electronic medical records of all patients presenting with haemoptysis to the emergency department and /or were admitted under the care of the respiratory team over a 2 year period.

**Results:** 61 patients (32 females and 29 males) had 78 presentations with haemoptysis to the emergency department at a tertiary referral public hospital from January 2016 to January 2018. Pulmonary Infections were the most common cause of haemoptysis presentations (61%) accounting for 48 of 78 cases. No cause was found in 22 presentations (28%). Over anticoagulation with warfarin was the reported cause of haemoptysis in one patient. The remaining causes were found to be due to Neoplasm (7%) and pulmonary embolism (3%). Representation with haemoptysis occurred in 12 out of 61 patients (19.6 %). COPD was the most common respiratory comorbidity in this cohort (16%). Bronchoscopy was performed in less than half of the presentations (29/78). In the majority of cases (68/78), haemoptysis was self-limited with conservative management (with or without antibiotics). Three patients were referred to cardiothoracic services for procedures including lobectomy and embolectomy. Radiologically guided bronchial artery embolisation was performed in 7 cases. Death was reported in three inpatients (4.9%), all of whom were in the group conservatively managed.

**Conclusion:** Pulmonary infections remain the most common cause of haemoptysis in this cohort. In the majority of the presentations, conservative treatment is sufficient to control the haemoptysis. Further interventions including bronchial artery embolisation and surgical procedures are occasionally needed. There were no documented adverse outcomes as a result of intervention.

**Key Words:** Haemoptysis, infection, lobectomy, embolisation

**Nomination for New Investigator Award**

**Grant Support:** Nil

### LONG-TERM SAFETY AND EFFICACY OF INTRAPLEURAL TPA/DNASE FOR PLEURAL INFECTION

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**Introduction/Aim:** Intrapleural tPA/DNase therapy significantly reduces hospital length-of-stay and need for surgery in pleural infection, however long-term safety data following tPA/DNase treatment is lacking.

**Methods:** Patients treated with tPA/DNase >12 months previously for pleural infection were recruited from four centers in Australia and NZ. Chest radiographs, full lung function or spirometry, a safety questionnaire and a 36-item short form health survey (SF-36v2) were conducted.

**Results:** All participants (n = 62; mean age 57 ± 16) had returned to baseline employment status; one reduced work hours at follow-up (median 617 days). No participants had recurrence of pleural infection or required hospitalisation for its complications. Eight patients had further hospitalisations for respiratory tract infections and twenty participants for non-respiratory illnesses. No systemic bleeding was reported within the initial 3-months post-discharge.

Ten participants reported intermittent pleuritic chest pain at follow-up. The mMRC Breathlessness scale was 0 in 28, 1 in 27 and 2 in 5 participants. Many (69%) participants had smoked and 50% had known chronic respiratory disease. Most (82%) of the participants who had airflow obstruction (mean FEV1/FVC = 69.9%) had >10 pack-years of smoking history or asthma. Restrictive lung functions were evident in 19% (n = 11). Three had mixed restrictive/obstructive lung functions. QoL in all 8 domains fell within 1 SD of the general population.

Radiographic pleural thickening progressively reduced in all participants from discharge. Most participants had no (n = 38) or minimal (1-5 mm) (n = 23) pleural thickening on CXR at the study visit. Thirty-six participants had no radiographic evidence of residual effusion; 20 had costophrenic blunting or trace effusion (n = 5).

**Conclusion:** No major adverse consequences were found in this long-term follow-up study of patients treated with tPA/DNase therapy.

**Grant Support:** Sir Charles Gairdner Hospital Research Advisory Council Grant

### BRONCHOSCOPIC TREATMENT OF SUBGLOTTIC STENOSIS: A TEN-YEAR REVIEW OF EPIDEMIOLOGY AND OUTCOME

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<sup>1</sup>Sir Charles Gairdner Hospital, Perth, Australia, <sup>2</sup>University of Western Australia, Perth, Australia, <sup>3</sup>Institute of Respiratory Health, Perth, Australia

**Introduction:** Sub-glottic stenosis in adults is a poorly understood disease that can cause dyspnoea and stridor. It may be secondary to previous endotracheal intubation, granulomatosis with polyangiitis (GPA), etc, or idiopathic where the primary aetiology is unknown. Symptomatic patients are treated with surgery or bronchoscopy, however there is little published Australian data on bronchoscopy treatment outcomes.

**Aim:** To describe the epidemiology of adult symptomatic sub-glottic stenosis and outcomes following bronchoscopic treatment.

**Methods:** A retrospective review was performed of all adult patients with symptomatic sub-glottic stenosis who underwent bronchoscopic treatment at Sir Charles Gairdner hospital, Perth during a ten-year period (2006-2016). Demographics, aetiology, symptoms, spirometry, number and type of bronchoscopy, systemic therapy, outcomes, and need for repeat procedures were recorded.

**Results:** Fifteen patients (13 female, age 25-80 years) with symptomatic sub-glottic stenosis who required interventional bronchoscopy were identified from the bronchoscopy database. The underlying aetiology was GPA (3 cases, 20%), gastro-oesophageal reflux (3, 20%), post-intubation (1, 7%), inflammatory myofibroblastic tumour (1, 7%) and idiopathic (7, 47%). Auto-immune antibody testing was performed in all patients; three patients had positive ANCA and ten had non-specific and variably elevated ANA. Exertional dyspnoea and noisy breathing/stridor were the predominant symptoms. In all cases, the stenosis was noted on bronchoscopic examination to start 1-1.5cm below the vocal cords. Tracheal dilatation using a balloon, rigid bronchoscope or bougie; diathermy, electrocautery or laser ablation; and local injection of methylprednisolone or mitomycin were the main bronchoscopic techniques used. All patients reported significant but transient improvement in dyspnoea and stridor. No major complication or death related to the procedure were observed.

**Conclusion:** Sub-glottic stenosis mainly affects females and is commonly idiopathic. Bronchoscopic interventions can safely and effectively improve stenosis and symptoms, however there was high rate of recurrence.

**Grant Support:** RT - NHMRC and Cancer Council WA Early Career Fellowship

TP 094

TP 095

### ENDOVASCULAR EMBOLISATION OF ANEURYSMIC SYSTEMIC BRONCHIAL ARTERY TO PULMONARY ARTERY FISTULA: A CASE REPORT AND PICTORIAL REVIEW.

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**Introduction/Aim:** Bronchial artery aneurysms (BAA) as well as bronchial artery to pulmonary artery fistulas are a rare vascular phenomenon [1,2]. They can be congenital in nature or secondary to infection and can lead to serious complications if they rupture [1].

A 58-year-old female was found to have an incidental right BAA associated with bronchial artery to pulmonary artery fistula on a computed tomography (CT) scan of her abdomen for investigation of suspected appendicitis.

**Methods:** Retrospective case and image review.

**Results:** CT arch aortogram and selective bronchial artery angiography revealed a tortuous bronchial artery arising from the medial and proximal aspect of the left subclavian artery and an aneurysmal segment distally with outflow to the descending pulmonary artery on the right. Subsequent spiral CT pulmonary angiography with delayed arterial phase contrast enhancement was completed to further delineate the vascular abnormality. It confirmed the 2.4cm aneurysm anterior to the right hilum, filling via a bronchial artery with outflow to the descending pulmonary artery through a stenosed communication at the inferomedial aspect of the aneurysm. There was also a direct communication from the bronchial artery to the medial inferior pulmonary artery on the right in keeping with a sequestration.

Management options of any pulmonary vascular malformations include: transcatheter embolisation with detachable coils, AMPLATZER™ vascular plug (St Jude Medical, Minnesota, USA) or Micro Vascular Plug System (Medtronic, Dublin, Ireland) or surgical resection [1,3].

**Conclusion:** Our patient underwent endovascular embolisation of the distal bronchial artery with detachable coils under direct visualisation using pulmonary angiogram. Follow up annual CT chest with contrast over the next 2 years illustrated a marked decrease in aneurysm size (now 1.4cm) and was no longer observed to fill with contrast.

#### Grant Support

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### COMPLIANCE OF A MAJOR TERTIARY CENTRE WITH THE BROCK MODEL AND FLEISCHNER SOCIETY GUIDELINES FOR THE INITIAL SURVEILLANCE OF INCIDENTAL PULMONARY NODULES: A RETROSPECTIVE STUDY OVER 5 YEARS

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**Introduction/Aim:** Several major guidelines currently exist for the initial surveillance of incidental pulmonary nodules. We aimed to review our centre's initial follow up and surveillance of such nodules compared to the Brock Model and Fleischner Society Guidelines.

**Methods:** Patients were identified from an internal pulmonary nodule surveillance database from January 2013 to April 2018 inclusive. Exclusion criteria were: Previous/concurrent cancer, nodule size > 30mm, mediastinal/nodal masses, and incomplete data-sets to satisfy the Brock Model. Age, sex, smoking status, history of emphysema and family history were obtained from outpatient letters. Where available, emphysema history was supported with pulmonary function tests. Lung nodule size, location and characteristics were obtained from radiological imaging. Results were analysed against the Brock Model and Fleischner Society Guideline to obtain respective recommended initial surveillance and management plans. These were then compared with actual plans from the Respiratory specialists at our centre.

**Results:** A total of 278 patients with newly identified pulmonary nodules were found. Of these, 181 (65.1%) satisfied inclusion criteria. Compared to Fleischner Society Guidelines, appropriate nodule surveillance recommendations occurred in 134/181 cases (74.0%), over investigated in 45/181 cases (24.9%) and under investigated in 2/181 cases (1.1%). Based on the Brock Model appropriate surveillance recommendations occurred in 120/181 cases (66.3%), over investigated in 42/181 cases (23.2%) and under investigated in 19/181 cases (10.5%). Using at least 1 model, appropriate surveillance plans occurred in 153/181 cases (84.5%), over investigated in 26/181 cases (14.4%) and under investigated in 2/181 cases (1.1%).

**Conclusion:** Overall, appropriate initial lung nodule surveillance was provided by respiratory physicians at our centre for the majority of patients, but a large proportion (almost a quarter) are over investigated according to current guidelines Future analysis will include percentage of cancers eventually identified in this group during long term follow up.

#### Grant Support: •

TP 096

TP 097

### ENDOVASCULAR SMALL CELL LUNG CANCER WITH ANTI-HU ANTIBODY: CASE REPORT

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**Introduction/Aim:** We present an unusual case of an entirely pulmonary artery-based malignancy with Hu-antibody associated progressive peripheral neuropathy. We discuss our difficulties in investigating and treating an entirely vascular-based tumour.

**Case report:** Ms. SS is a 59-year-old heavy ex-smoker who initially presented with a 6-month history of progressive lower limb paraesthesiae and weakness associated falls. Auto-immune screen, MRI Brain and whole spine and lumbar puncture showed no abnormalities. A sural nerve biopsy demonstrated chronic active axonal neuropathy. 15 months following onset of symptoms, serum Anti-Hu antibody returned as positive. Subsequent staging CT and PET scan demonstrated a highly FDG avid (SUVmax 18.9) mass (30 × 6 mm) at the right hilum that appeared to be minimally invading the proximal pulmonary artery.

An urgent linear EBUS was remarkable for an entirely endovascular 30x30mm mass at the distal pulmonary trunk. On EBUS it was pendulous, moving with the blood flow and nearly completely occluding the arterial lumen (Image 1, Video 1). EBUS-guided biopsy and endovascular biopsy or resection through right heart catheterisation were deemed unsafe with tear in the pulmonary artery, tumour dislodgement as well as pulmonary arterial thrombus formation all being life-threatening complications to consider. Pneumonectomy and resection under ECMO were discussed. Ms. SS underwent an attempted resection under ECMO however complete resection was not feasible. Biopsy specimens resulted in a diagnosis of SCLC. She was commenced on urgent chemotherapy 17 months from her initial symptoms.

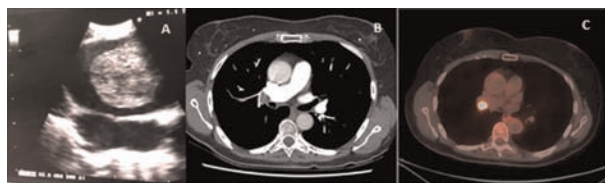


Image 1: Right pulmonary artery mass on EBUS (A), CT Pulmonary Angiogram (B), PET scan (C)

**Discussion:** To our knowledge, this is the first case report of an entirely endovascular proximal pulmonary arterial small cell lung cancer that presented with peripheral neuropathy and Hu antibody. A biopsy was a significant challenge. Utilising ECMO and performing an endovascular biopsy was safer and prevented an unnecessary pneumonectomy. This is also the first reported case of using ECMO to successfully obtain a biopsy for an endovascular SCLC.

**Grant Support:** None.

**Conflicts of Interests:** None.

Attachment Image 1: EBUS, CT- and PET images of endovascular tumour

Attachment Video 1: EBUS video of endovascular tumour

### THE TIMELINESS OF LUNG CANCER DIAGNOSIS AND TREATMENT

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**Introduction/Aim:** Delays in the diagnosis and treatment of lung cancer may lead to progression to more advanced disease and reduce the capacity for cure. We aimed to evaluate the timeliness of lung cancer management in a Queensland outer metropolitan hospital.

**Method:** We retrospectively analysed the medical records of 69 patients who presented to the respiratory service of Ipswich Hospital between April 2017 and April 2018 with a new clinical or pathological diagnosis of lung cancer as identified by the International Classification of Diseases. Time intervals between referral, first outpatient (OPD) review and initial treatment were assessed.

**Results:** There were 69 new diagnoses of lung cancer identified. Of these, 9 were from the pulmonary nodule surveillance pool and were excluded from the timeframe analysis. Twenty patients (30%) were inpatients at the time of initial referral. The patient cohort had a mean age of 69.3 ± 10.8(SD) years. A history of cigarette smoking was present in 91%, lung disease in 57% and prior malignancy in 22%.

The median time from referral to first OPD was 6 days (IQR, 0-13) and from referral to initial treatment 42 days (IQR, 21-72). Overall, 77% and 53% of patients met the Australian Cancer Council recommendations of 2 weeks (14 days) from referral to OPD and 6 weeks (42 days) from referral to treatment, respectively. Of the patients who waited longer than these recommendations, patient-related delays were identified in 30% and institutional delays in 41%. Overall, diagnostic procedures were performed at an alternate health facility in 32% of patients and treatment in 52% of patients.

**Conclusion:** Overall, lung cancer care timeliness in this study meets current Australian Cancer Council recommendations, however significant delays have been identified at various stages. Greater understanding of these delays will assist in the development of strategies to expedite lung cancer care in the future.

**Key Words:** Lung cancer, diagnosis, treatment delays

**Grant Support:** Nil to acknowledge.

TP 099

TP 100

### RESULTS OF INITIAL AUDIT PROGRAMME FOR A SINGLE INSTITUTIONAL LUNG CANCER MULTIDISCIPLINARY TEAM (MDT)

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**Introduction/Aim:** Quality assurance is of emerging interest in MDT lung cancer care. Our institution introduced quarterly audit presentations in 2018 with transition to a new data platform. This study aims to present the pooled findings with particular focus on tumour characteristics, treatment intent and modality and timeliness data.

**Method:** All new cases presented to the MDT were reviewed. Variables of interest included demographics (gender, age, ECOG status, smoking pack-year history), tumour characteristics (histopathology, stage), treatment intent and timeliness data including time to diagnosis and time to treatment start.

**Results:** From 1 Jan to 30 June 2018 there were 109 case presentations at the MDT comprising 78 new patients and 31 repeat presentations. Of 78 new patients, 59% were male with average age 69 years, 72% ECOG 0. Smoking history recorded that 35% were non-smokers, 15.3% had 0-19 pack-years (py), 16.7% 20-39py and 25.6% 40+py, 7.8% unknown. Of total smokers, 12% were current. Of 78 new patients there were 55 primary lung cancers: 48 NSCLC, 3 SCLC, 4 Carcinoid, and 23 other lesions including 3 metastatic non-lung cancers and 4 pulmonary nodules for ongoing imaging surveillance. Of 48 NSCLC stage distribution showed 25.6% stage I, 9.3% Stage II, 25.6% Stage III and 39.5% Stage IV. For new cases treatment intent was curative (41%), palliative (37%), surveillance (8%) and investigational (14%). For newly diagnosed primary lung cancer, mean time to diagnosis (first scan to biopsy) was 28.5 days (SD 20.4), and mean time to treatment (diagnosis to treatment initiation) was 30.7 days (SD 21.6).

**Conclusion:** Regular audits of MDT data can provide pivotal information to direct quality assurance initiatives.

**Grant Support:** Nil.

### ACQUIRED HYPERTRICHOSIS LANUGINOSA: A CASE OF PARANEOPLASTIC EXCESSIVE HAIR GROWTH IN LUNG CANCER

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**Introduction/Aim:** We describe a case of acquired hypertrichosis lanuginosa (AHL), a rare paraneoplastic dermatologic phenomenon characterised by abnormal and excessive growth of unpigmented, lanugo-type hair typically near the eyebrows, forehead, ear or nose or less commonly, the extremities.

**Methods:** A 63-year-old tobacco and marijuana smoker presented with an incidentally-detected right upper lobe pulmonary mass on CT thorax performed during investigation following a perforated peptic ulcer. He had also suffered from weight loss of 20kg over 6 months. Clinical examination revealed cachexic man with noticeably widespread and excessive long, fine hair over his face, trunk, back and extremities, consistent with AHL (figures below). Further questioning confirmed that the hair growth was a recent development.



He underwent fine needle aspiration of a palpable supraclavicular lymph node that confirmed squamous cell carcinoma of lung (T3N3M0, stage IIIB). The patient underwent only curative-intent radiotherapy; combined treatment with chemotherapy was omitted given his frailty, malnutrition and intractable diarrhoea. Post-treatment imaging five months after therapy showed cancer progression with metastases to the liver and bone. There was no significant improvement in severity or extent of the hypertrichosis. He was managed with palliative intent and died nine months after the initial diagnosis.

**Result:** We present a case of paraneoplastic AHL in a patient with rapidly progressive squamous cell carcinoma of lung. AHL is a rare paraneoplastic syndrome with an estimated prevalence of <1 in 1,000,000. It is most commonly associated with colorectal, lung and breast cancers and usually denotes advanced disease with poor prognosis. It may be associated with malnutrition and chronic diarrhoea.

**Conclusion:** A new development of lanugo-type hypertrichosis is highly indicative of internal malignancy and should raise a high index of suspicion.

**Grant Support:** RT - NHMRC and Cancer Council WA Early Career Fellowship.

TP 101

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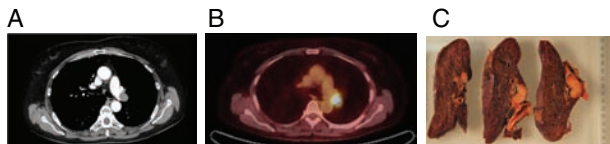
### A RARE CASE OF INTRALUMINAL PULMONARY ARTERY SMALL CELL LUNG CARCINOMA MIMICKING AN INTRAVASCULAR THROMBUS

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**Introduction:** Malignant neoplasms arising from the pulmonary artery are rare, and usually arising from sarcoma of various subtypes. Herein we present a case of a pulmonary small cell carcinoma presented as intravascular pulmonary artery lesion.

**Methods:** A 64-year old female smoker was admitted with progressive lower limb weakness and falls. Neurological evaluation and electromyography confirmed a diagnosis of Lambert-Eaton myasthenic syndrome. Screening computed tomography of the chest identified a polypoid intraluminal lesion in the left main pulmonary artery extending into the upper lobe branch, suggestive of pulmonary thromboembolism or intravascular malignancy (Figure A). Positron emission tomography (PET) confirmed an isolated 18-fluorodeoxyglucose (FDG) uptake in the lesion to support a diagnosis of malignancy (Figure B). She proceeded to have a surgical excision of the lesion based on the high likelihood of pulmonary artery sarcoma given the imaging characteristics. Video-assisted thoracoscopic pneumonectomy and mediastinal lymph node dissection were successfully performed. Histopathological examination of the lesion revealed small cell lung carcinoma immediately next to the pulmonary artery with direct extension through the wall to form an intraluminal mass (Figure C). She was treated with adjuvant chemotherapy and prophylactic whole brain radiotherapy. Four years later, surveillance 18-FDG-PET has shown no evidence of cancer recurrence.



**Results:** An intraluminal pulmonary artery malignancy is rare; when present, they are usually sarcomas and rarely are they of carcinomatous origin. Definitive diagnosis is often difficult as imaging mimics a thrombus leading to misdiagnosis as pulmonary thrombo-embolic disease. Usually surgical excision is necessary to make a definitive diagnosis. The development of a paraneoplastic syndrome like Lambert-Eaton myasthenic syndrome as seen in this case should raise a high index of suspicion for malignancies such as small cell lung carcinoma.

**Conclusion:** Intraluminal pulmonary artery tumour including both sarcoma and carcinoma could mimic thrombus and should be considered in the differential diagnosis.

**Grant Support:** RT - NHMRC and Cancer Council WA Early Career Fellowship

### EXAMINING IMPACT OF TIMELINESS OF ENDOBRONCHIAL ULTRASOUND UTILISATION ON LUNG CANCER DIAGNOSIS AND TREATMENT DELAY. A RETROSPECTIVE OBSERVATIONAL STUDY

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**Introduction/Aim:** EBUS is routinely engaged to confirm lung cancer diagnosis and staging. The availability of EBUS and waiting time to EBUS may negatively impact the timeliness of lung cancer diagnosis and treatment. We examined the impact of EBUS wait interval on diagnosis and treatment delay in newly diagnosed lung cancer.

**Methods:** We conducted a retrospective chart review of all newly diagnosed lung cancer patients undergoing EBUS (linear and radial) at the Alfred Hospital between August 2013 and September 2018. We recorded waiting interval between EBUS referral and procedure and examined impact on lung cancer management timeliness from lung cancer referral to lung cancer diagnosis and first treatment.

**Results:** 104 EBUS procedures were completed on 97 patients aged 37-88 years old. Lung cancer referral to diagnosis interval had mean 23.2 days(30.5 SD), diagnosis to treatment interval had mean 24.1 days (21.2 SD), and referral to treatment interval had mean 47.4 days(35.9 SD). EBUS referral to EBUS interval had mean 5 days(3.9 SD, range 0-19 days). EBUS waiting time was compared for lung cancer referral to diagnosis interval (within vs delay of greater than 28 days), and diagnosis to treatment interval (within vs delay of more than 14 days). EBUS wait time was greater for delayed referral to treatment interval (more than 42 days), than within 42 days ( $P = 0.012$ ).

	Referral to diagnosis	Diagnosis to treatment	Referral to treatment
n	89	76	76
Mann-Whitney U	0.052	0.093	0.012
Mean (SD)	4.8 (3.7)	5.1(3.8)	5.1(3.8)
Range	0-16	1-16	1-16
IQR	2-7	2-7	2-7

**Conclusion:** Delay in investigation has the potential to delay key management issues including lung cancer diagnosis and treatment. Prolonged wait for EBUS lead to a trend towards diagnosis delay and significant delay in referral to treatment interval in this cohort and warrants further investigation.

**Grant Support:** None. No conflicts to declare.

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### ADHERENCE TO LUNG CANCER MULTIDISCIPLINARY TEAM (MDT) RECOMMENDATIONS: SINGLE CENTRE REVIEW

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**Introduction/Aim:** Lung cancer MDT care is widely accepted. Literature shows improvements in treatment receipt and survival with MDT management. However MDTs are "resource-intense", with multiple attendees and technological requirements. Regular audit provides insights into patient and disease characteristics, recommendations and subsequent treatment. This study aims to evaluate adherence to recommendations for new cases presented in 2018.

**Methods:** All new cases presented to the institutional MDT were reviewed. Data entered weekly into the OMIS (Oncology Management Information System - MOSAIQ) were analysed for demographics, tumour characteristics, stage, treatment intent and recommendations. Subsequent actual treatment received was derived from hospital-based data sources including MOSAIQ, the electronic health record and institutional databases.

**Results:** Audit data were presented for quarterly periods. A total of 78 new cases were presented for Q1 and Q2 2018. Of these, 59% were male, 72% ECOG 0 and average age 69 years. Smoking history recorded that 35% were non-smokers, 15.3% had 0-19 pack-years (py), 16.7% 20-39py and 25.6% 40+py, 7.8% unknown. Of total smokers, 12% were current. There were 55 confirmed primary lung cancers: 48 NSCLC, 3 SCLC, 4 carcinoids and 23 other lesions. Of NSCLC, 37 were adenocarcinoma, 3 Large cell carcinoma and 7 SCC. Stage distribution for NSCLC showed 25.6% Stage I, 9.3% Stage II, 25.6% stage III and 39.5% stage IV. Treatment intent was curative (41%), palliative (37%), surveillance (8%) and investigational (14%). Treatment recommendations included surgery in 18%, radiotherapy in 31% and systemic therapy in 50% with some cases recommended for dual or triple therapy.

Initial adherence analysis found that 83% adhered to recommendations, 3% did not and 14% were unknown. Further review of adherence details is underway.

**Conclusion:** Analysis of prospectively collected data for new cases presented to a single-centre lung cancer MDT allows for regular audit of treatment recommendations and subsequent adherence to recommendations.

**Grant Support:** Nil.

### MODALITY OF TISSUE BIOPSY AND MUTATIONAL ANALYSIS IN NON-SQUAMOUS NON-SMALL CELL LUNG CANCER: A SINGLE CENTRE AUDIT

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**Introduction/Aim:** Several mutations, including EGFR, EM4-ALK and ROS1, have been identified as oncogenic drivers of non-squamous non-small cell lung cancer (NSCLC-NS). Molecular testing for these mutations has become standard practice with the development of targeted therapies. Acquisition of sufficient tissue for analysis has subsequently increased in importance. The aims of this study were to assess i) the appropriateness of molecular testing, ii) the incidence and type of mutations identified, iii) the likelihood of obtaining sufficient tissue for mutational analysis with different modalities of tissue acquisition, and iv) the requirement, type and success rate of repeat procedures.

**Methods:** Data prospectively collected in the Princess Alexandra Hospital Lung Cancer Multi-Disciplinary Meeting database formed a cohort of 200 new case NSCLC-NS diagnosed in 2017. The rates, sampling modality and outcomes of molecular testing were analysed.

**Results:** Molecular testing was successful from initial biopsy in 148 cases (77% of 192 tested), with an identified mutation incidence of EGFR (12%), EM4-ALK (2.8%), BRAF (8%) and KRAS (35.5%). 8 patients were deemed not to require molecular testing. Only 3.6% of cases did not undergo appropriate mutational testing. Tissue was acquired via CT-guided lung biopsy (35.5%), convex EBUS (cEBUS) nodal biopsy (18%), bronchoscopy (10.5%) and other (36%). Sufficient tissue was obtained in 70% of cEBUS cases compared with 64% for CT-guided lung biopsy. Repeat procedures for initial insufficient tissue was successfully undertaken in 20 out of 24 cases, largely through cEBUS.

**Conclusion:** This real-world study of molecular testing in NSCLC-NS, demonstrated a high rate of appropriate testing, mutational profiles consistent with international literature and a higher rate of successful molecular analysis with cEBUS than CT-guided lung biopsy. However, a significant proportion of patients required repeat intervention to yield a final molecular profile. Therefore, a review of sample handling is the next step, aimed at limiting repeat invasive procedures.

**Grant Support:** Nil.

**Conflict of Interest:** Nil.



TP 105

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### NEGATIVE PREDICTIVE VALUE OF A PET-CT SCAN FOR OCCULT MEDIASTINAL NODAL METASTASES IN EARLY STAGE LUNG CANCER

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**Introduction/Aim:** Increasing evidence indicates that accuracy of PET-CT alone is insufficient to assess mediastinal nodal involvement in early stage NSCLC. This study aims to determine the rate of occult nodal metastases in patients with N0 and N1 disease by PET-CT scans who underwent surgical resection over a three-year period.

**Methods:** All patients who underwent surgical resection of early stage NSCLC from January 2015 to December 2018 were identified. Pre-surgical staging was determined by a multidisciplinary team. Agreement between the clinical staging and true pathological staging following surgery was determined. Main outcomes are the rate of occult hilar and mediastinal nodal metastasis in patients with N0 or N1 disease respectively by PET-CT and the negative predictive value (NPV) of a PET-CT in this patient population.

**Results:** Total of 69 patients (median age 66 years (range 39 to 81) were included in the study. Median time from PET-CT scan to surgery was 36 days, with 94% (n = 65) undergoing a lobectomy. Two patients had pneumonectomies and others had bilobectomies. Thirteen patients (18.9% (95% CI 11.6-29.6) had upstaging of lymph node status after surgery (N0 to N1 in 8 patients, N0 to N2 in 2 patients, N1 to N2 in 3 patients). There was no difference in the average time from PET-CT to surgery in patients who had upstaging of nodal status compared to others. The NPV of a PET-CT was 92.5% for mediastinal disease, 85.1% for N1 disease and 80.6% for overall nodal status.

**Conclusion:** Although the NPV of a PET-CT is satisfactory, overall underestimation of nodal disease status is not uncommon. The role for complete staging of mediastinal lymph nodes with EBUS-TBNA in patients without evidence of mediastinal nodal metastases on PET-CT requires further investigations.

**Grant Support:** •

### ACCURACY OF QUANTITATIVE CT AND L1 HOUNSFIELD UNIT METHOD IN DETECTING LOW BONE MINERAL DENSITY IN A LUNG CANCER SCREENING COHORT

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**Introduction/Aim:** Screening CT scans gather incidental information, such as detail of the spine, which is currently not systematically assessed but could add value to screening. As demonstrated in the 2018 Nelson trial, lung cancer screening reduces mortality. The importance of osteoporosis could be prevalent in lung cancer screening participants due to shared risk factors. We hypothesized that measuring the density of the L1 vertebra in Hounsfield Units (L1HU) is a simple and accurate way to screen for low bone mineral density (BMD) compared to Quantitative BMD measurement (QCT). We aimed to retrospectively compare accuracy of the L1HU method against QCT in CT chest scans undertaken in the Queensland Lung Cancer Screening Study.

**Methods:** QLCSS recruited 256 volunteers at risk of lung cancer. Participants were screened using a low-dose protocol. L1 vertebrae were analysed at baseline (T0) and second incidence screen (T2) using Mindways QCT software (American College of Radiology QCT guidelines were used to classify density) and the L1HU method (single ROI placed in the anterior, upper portion of the vertebral body; HU density threshold <110HU defined low BMD). Accuracy was determined by calculating sensitivity, specificity, and area under receiver operating characteristic curve.

**Results:** 444 scans were assessed by both methods (256 T0 and 188 T2). Prevalence of low BMD at T0 and T2 time-points was 78% and 70% (QCT) and 67% and 59% L1HU respectively ( $P = 0.05$ ). Compared to QCT, L1HU method had sensitivity 73%, specificity 86% and AUROC 0.66. The L1HU method had true positive rate = 57%, true negative rate = 19%, false negative rate = 21% and false positive rate = 3%.

**Conclusion:** Low BMD was highly prevalent in our cohort. L1 HU method appears simple and rapid and may have utility in screening for low BMD in CT scans performed for lung cancer screening, avoiding extra radiation/time for the patient.

**Grant Support:**

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### RADICAL RESECTION AND RADIOTHERAPY PREVENTS THORACIC ADENOID CYSTIC CARCINOMA RECURRENCE

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**Introduction:** Adenoid cystic carcinoma (ACC) is a rare cause of thoracic malignancy and the prognosis may depend on extent of surgical resection and adjuvant radiotherapy. Complete resection has low rates of local recurrence but is complicated by the involvement of central airways. Adjuvant radiotherapy is frequently recommended, but unproven.

**Aims:** We describe the technicalities of radical resection and adjuvant radiotherapy, using the endpoints of locoregional recurrence and distant metastasis.

**Results:** 12 patients (8 male) diagnosed between 1999 and 2016, at an average of 44±12 years. Six of these were operable (operative group), and six had non resectable lesions (radiotherapy group). Resections were classed as microscopically and macroscopically clear (R0) or only macroscopically clear (R1).

In the operative group (average follow-up was 6.1 ± 4.3 years), three had tracheal disease and three had bronchial disease. Tracheal lesions underwent excision with tracheal anastomosis (all R1 resections). Main bronchial lesions underwent complete excision via pneumonectomy (Two R0 and one R1 resection). All these patients received 50-60 Gy of adjuvant radiotherapy. At 1, 5 and 10 years, survival free from locoregional recurrence was 100% (n = 6/6), 60% (n = 3/5) and 33% (n = 1/3) and survival free from metastasis was 100% (n = 6/6), 80% (n = 4/5) and 33% (n = 1/3) respectively. All patients who had metastasis had locoregional recurrence. In the radiotherapy group, the average follow-up was 5.4 ± 4.2 years (Range 1-11 years). All had invasive locoregional disease at diagnosis, and three had metastasis. Of the non-metastatic patients (n = 3), survival free from metastasis was 33% (n = 1/3) at 1 year, and 0% (n = 0/2) at 5 years.

**Conclusion:** Our case series consolidates evidence that early radical resection and radiotherapy is associated with a low risk of local recurrence in patients with thoracic ACC.

**Grant Support:** Nil

### INCIDENCE, OUTCOMES AND TOLERANCE IN EGFRM AND ALK-REARRANGEMENT POSITIVE NSCLC

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**Introduction:** Non-small-cell lung cancer (NSCLC) is comprised of histological, genetic and molecular subtypes. Patients with mutation-positive epidermal growth factor receptor (EGFRm) and anaplastic lymphoma kinase (ALK) gene rearrangement have been shown to have a favourable response to treatment with tyrosine kinase inhibitors (TKI), with improved survival outcomes compared to convention chemotherapy.

**Aim:** To describe the incidence of EGFRm/ALK positive NSCLC in the selected population, assess survival and performance status, and tolerance of treatment with tyrosine kinase inhibitors.

**Methods:** A retrospective audit including all patients who presented to the Gold Coast Health Service from January 2015 to December 2017 with NSCLC.

**Results:** A total of 543 patients were included, with 49 found to have EGFR mutation (7.7%) or ALK rearrangement (1.2%) positive cancer. Complete clinical data was available for review in 46 patients. The mean age of the 46 patients was 67 (±2) years and 29 (63%) were female. At the time of initial diagnosis, 31 (67%) had stage IV disease and performance status was ECOG 0 in 12, I in 19, II in 7 and III in 2 patients (4 patients had missing data). Molecular analysis identified an EGFR mutation in 38 patients and ALK was positive in 7 patients. 28 patients received a tyrosine kinase inhibitors, 7 patients immunotherapy and 22 patients received conventional chemotherapy. 84% of patients with metastatic disease were treated with TKIs; many patients received chemotherapy prior to confirmation of mutation status or after progression while on TKI treatment. Adverse effects were common and was reported in 26 patients (GI in 10 patients, dermatological in 14 patients and haematological in 2 patients).

**Conclusion:** The incidence of mutations to EGFR/ALK were lower than the national average. Side effects were common with intolerance leading to reduced dose/duration of treatment in some patients.

**Grant Support:** Nil

### PULMONARY FUNCTION CHANGES IN A COHORT OF WESTERN AUSTRALIAN MINERS

HARRIS E<sup>2,5</sup>, FRANKLIN P<sup>1</sup>, KAMIYA H<sup>1</sup>, SODHI-BERRY N<sup>1</sup>, KAISTHA P<sup>1</sup>, MUSK B<sup>1,2</sup>, REID A<sup>3</sup>, DE KLERK N<sup>4</sup>, BRIMS F<sup>2,5</sup>, PETERS S<sup>6</sup>

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**Introduction/Aim:** Mining has been associated with an increased rate of lung function decline. However, mining practices and exposure standards have improved over time. Our aim was to estimate annual change in lung function in a modern-day mining cohort and its determinants.

**Methods:** Lung function change was assessed in miners who worked in Western Australia (WA) between 1996 and 2013 and had at least two assessments that complied with ATS/ERS spirometry guidelines. Z-scores for spirometric values were calculated based on Global Lung Function Initiative predicted values. Linear mixed effects models were used to examine the effect of time and various factors on the change in FEV<sub>1</sub>, FVC and FEV<sub>1</sub>/FVC between the first and last assessments. Variables included in the models were time between assessments (years), age started in mining, sex, ever-smoking status, ever-asthma status, ever-underground mining and employment duration ( $\geq 10$  years or  $<10$  years). Results are expressed as annual change in z-scores.

**Results:** Data from 30,780 miners were included. Compared to the reference population, miners experienced small but significantly greater annual declines in FEV<sub>1</sub>, ( $\beta = -0.011$ , 95% CI = -0.012 to -0.010) and FEV<sub>1</sub>/FVC ( $\beta = -0.034$ , -0.035 to -0.032). Males, ever-asthmatics and ever-smokers had significantly greater annual declines in FEV<sub>1</sub>. For FEV<sub>1</sub>/FVC, the annual decline was greater for females, ever-asthmatics, ever-smokers and miners with employment length  $<10$  years. There was, on average, a significantly slower decline in annual FVC ( $\beta = 0.007$ , 0.005 to 0.008), compared to the reference population with the annual change being greater for females, never-asthmatics, never-smokers, ever-underground miners and miners with employment length  $\geq 10$  years.

**Conclusion:** Annual changes in lung function are small and the clinical implications are uncertain. However, the changes are consistent with the development of an obstructive lung function pattern, which has been observed in other studies of miners.

**Grant Support:** Maurice Blackburn Grant-In-Aid for Occupational Lung Disease

### METFORMIN MAY REDUCE MESOTHELIOMA AND LUNG CANCER INCIDENCE AMONG ASBESTOS-EXPOSED

HARRIS E<sup>1,2</sup>, FRANKLIN P<sup>3</sup>, SODHI-BERRY N<sup>3</sup>, OLSEN N<sup>3</sup>, MUSK A<sup>3</sup>, REID A<sup>4</sup>, DE KLERK N<sup>5</sup>, BRIMS F<sup>1,2</sup>

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**Introduction/Aim:** While use of metformin has been shown to slow or stop onset of diabetes in people at risk of diabetes mellitus, it has come under increasing interest as a possible cancer prevention agent, causing inhibition of a variety of tumour cells. We aimed to estimate any effect of metformin use on onset of asbestos-related thoracic cancers.

**Methods:** The Western Australia (WA) Asbestos Review Program (ARP) is a surveillance program for asbestos-exposed individuals that was established in 1990. As part of the annual visit protocol, dates of use of all medications are recorded, based on self-report. Linkage to the WA Death, Cancer and Mesothelioma Registers provides information on cancer incidence and causes of death. Participants were considered exposed to metformin from their date of first recorded prescription until 6 months after their last recorded prescription date. Otherwise they were considered unexposed. Rates of mesothelioma, adjusted for sex, asbestos exposure and age, and lung cancer, adjusted for smoking, sex and age were compared between periods with and without exposure to metformin using Cox regression with time-dependent covariates.

**Results:** Data from 4585 participants were included with 207 cases of mesothelioma and 191 with lung cancer occurring from 1990 to 2015. At entry to the program 129 participants were already taking metformin and a further 280 participants commenced over the period of follow up. After adjustment for age and sex the hazard ratio (HR) for mesothelioma and metformin use was 0.67 (95% CI 0.34-1.31,  $P = 0.2$ ), which increased to 0.74 after adjustment for asbestos exposure. Similar effects were found with lung cancer (HR 0.68, 95% CI 0.36-1.29, after adjustment).

**Conclusion:** Use of metformin may affect the incidence of mesothelioma and lung cancer in asbestos-exposed populations, but results here are far from conclusive.

**Grant Support:** Dust Diseases Board NSW; NHMRC; Cancer Council WA

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### RECORDING OF SPIROMETRY AMONGST PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS IN PRIMARY CARE: A UK GENERAL POPULATION BASED STUDY

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**Introduction/Aim:** We have previously shown that the incidence of idiopathic pulmonary fibrosis (IPF) in the UK is on the rise and that some individuals with IPF may be symptomatic up to five years prior to diagnosis. The aim of our study was to investigate recording of spirometry, in particular, Forced Vital Capacity (FVC) amongst incident cases of IPF in primary care.

**Methods:** Using data from The Health Improvement Network (THIN), an electronic longitudinal UK primary care database, we ascertained what proportion of incident cases of IPF had at least one recorded FVC prior to diagnosis. We used previously published Read Codes to identify incident cases of IPF and extracted information on FVC recorded prior to date of diagnosis. Logistic regression was used to generate odds ratios for the probability of having at least one recorded FVC amongst incident cases of IPF stratified by age, sex and calendar period of diagnosis.

**Results:** Our cohort consisted of 2,070 incident cases of IPF, of which 1,305 (63.0%) were male and the mean age at diagnosis was 74.6 years (Standard Deviation [SD] 9.6). 488 cases (23.6%) had at least one FVC recorded prior to date of diagnosis. The median time between spirometry recording and diagnosis was 5.7 months (interquartile range [IQR]: 2.1 to 14.5). Mean recorded FVC was 1.96 L (SD 0.73). There was no association between gender and a record of FVC, after adjusting for age and calendar period of diagnosis. (Odds Ratio [OR] 0.97, 95% confidence interval [CI] 0.76 to 1.23). We also found that people with IPF over the age of 85 years were 63% less likely to have a recorded FVC compared to individuals with IPF under the age of 65 (OR 0.37, 95% CI 0.24 to 0.58) and individuals diagnosed from 2010 onwards were almost 19 times more likely to have a recorded FVC compared to individuals diagnosed prior to 2005 (OR 18.99, 95% CI 13.07 to 27.58)

**Conclusion:** At present, spirometry amongst patients with IPF in primary care is poorly recorded, especially in the elderly.

**Grant Support:** VN is funded by an NIHR Academic Clinical Lectureship

### FEW ASSOCIATIONS BETWEEN FIREFIGHTING EXPOSURES AND CHANGES IN LUNG FUNCTION

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**Introduction/Aim:** We have previously observed a normal rate of change FEV<sub>1</sub> and FVC in a contemporary cohort of professional South Australian Metropolitan Fire Service (SAMFS) firefighters. In this analysis we examined the effect of self-reported occupational exposures on the long-term rate of change in lung function.

**Methods:** Spirometry was conducted in five stages (2007-2016) on all available and consenting full-time firefighting staff. We used linear mixed effects modelling to examine the effect of self-reported occupational exposure (years of service at baseline, involvement in firefighting tasks, and exposure to dust, smoke or fire and use of respiratory protection during the 12 months prior to each assessment) on FEV<sub>1</sub> and FVC trajectories.

**Results:** 854 individual firefighters (98.4% male; mean age (SD): 42.6 (9.1) years) contributed a median of 2.6 (IQR 1-4) measurements over a median follow-up period of 4.9 (0-8.4) years. Of those, 51.5% had been employed for more than six years and 10% were smokers. FEV<sub>1</sub> and FVC were normal, with average z-scores of 0.38 (0.98) and 0.86 (0.90), respectively. Longitudinally, FEV<sub>1</sub> (adjusted for baseline age and height) declined by 32 (95% CI, 30 to 35) mL/yr while FVC declined by 26 (95% CI, 23 to 29) mL/yr. Preliminary analyses did not show any consistent pattern of associations between occupational exposures and longitudinal changes in lung function. Relative to never smokers, participants who smoked at baseline had an additional 11 mL/yr decline in FEV<sub>1</sub>, but no differences were observed with FVC.

**Conclusion:** Based on self-reported data, cigarette smoking may be the most important exposure affecting longitudinal firefighter lung function. However, more robust methods of measuring occupational exposures in firefighters may be required in order to detect any deleterious effects that may be present.

**Grant Support:** This research was supported by the SAMFS and an Australian Government Research Training Program Scholarship (FS).

**INFLAMMATORY EFFECTS OF IRON OXIDE AND SILICA PARTICLES ON MACROPHAGES****WILLIAMS L<sup>1</sup>**, TRISTRAM S<sup>1</sup>, ZOSKY G<sup>1</sup><sup>1</sup>University Of Tasmania, Hobart, Australia

**Introduction:** Understanding of the respiratory health consequences of geogenic (earth-derived) particulate matter (PM) is limited. Geogenic PM typically contains large concentrations of silica and iron oxide. Whilst silica particles induce chronic, irreversible lung damage, recent evidence suggests that iron may augment this response. Additionally, inhalation of these particles is ubiquitous with the presence of bacteria. These bacteria often produce the potent endotoxin, lipopolysaccharide (LPS). We investigated the inflammatory and cytotoxic potential of silica and iron oxide particles alone, and in combination, on macrophage cells in the presence of LPS.

**Methods:** THP-1 monocyte derived macrophages were incubated with either LPS, or LPS free media for 4 hours before being exposed to 0-100 µg/mL silica or iron oxide for 24 hours. Further experiments exposed macrophages to combinations of silica and iron oxide to assess the effect of combined exposure to the particles. Cytotoxicity and cytokine production (IL-6, IL-8, IL-1β and TNF-α) were analysed by LDH assay and ELISA respectively for all experiments.

**Results:** Silica induced cytotoxicity and secretion of IL-1β, IL-6, IL-8 and TNF-α depending on the presence of LPS. Iron oxide induced increased levels of cytotoxicity and secretion of IL-1β and IL-8 with the addition of increased IL-6 secretion after LPS incubation. The addition of either of the iron oxides to silica did not augment the response of silica in the macrophage cells.

**Conclusions:** While previous studies have suggested that iron may augment silica-induced inflammation, we saw no evidence of this in human monocyte-derived macrophages. Macrophages responded strongly to the presence of iron oxide, which is generally thought to be biologically inert, exerting a cytotoxic and pro-inflammatory response. This response was significantly increased in the presence of LPS.

**Grant Support:** This work was supported by an Australian Respiratory Council Harry Windsor Research Grant.

**BMI AS A CORRELATE OF SPIROMETRY FINDINGS IN THE MORBIDLY OBESE****WILLIAMS K<sup>1</sup>**, DUONG N<sup>1</sup>, LEE H<sup>1</sup>, EATHER G<sup>1</sup>, MATIGIAN N<sup>1</sup><sup>1</sup>Queensland Health, Brisbane, Australia, <sup>2</sup>QFAB Bioinformatics, Institute for Molecular Bioscience, University of Queensland, Brisbane, Australia

**Introduction/Aim:** This retrospective cohort study looks at the relationship between BMI and spirometry results in a cohort of 1456 patients who were evaluated for sleep-disordered breathing at a tertiary teaching hospital in Queensland Australia, between March 2015 and March 2018. 1104 (76%) of this cohort were classified as obese, with 443 (30%) classified as morbidly obese with a BMI >39. 1219 (84%) of the total cohort and 76% of the obese cohort were subsequently diagnosed with sleep-disordered breathing.

**Methods:** Spirometry results including FEV1, FVC and FEV1/FVC were obtained from the cohort above at the time of their review in the sleep clinic. These measurements were correlated with BMI using linear regression analysis and multi linear regression analysis, and adjusted for smoking history and documented history of chronic lung disease. Smoking history had been obtained on presentation to the Sleep Clinic. Contribution of covariate factors influencing FEV1, FVC and FEV1/FVC were explored using multivariate regression analysis.

**Results:** 1456 patients were evaluated. 42 (12.7%) of non-obese patients had an FEV1 less than the lower limit of normal (using the Global Lung Initiative reference range), compared to 211 (19.1%) in the obese cohort ( $P = 0.01$ ), and 113 (25.5%) of the morbidly obese cohort ( $P < 0.001$ ). 18 (5%) of non-obese had an FVC less than the lower limit of normal compared with 81 (18%) of the morbidly obese cohort, and 254 (22%) of the super obese (BMI >45). 50 (13%) of the non-obese cohort had an FEV1/FVC ratio less than the lower limit of normal compared to 44 (9%) of the morbidly obese cohort.

**Conclusion:** In this cohort of mostly obese individuals when adjusted for smoking history and chronic lung disease, the spirometric values of FVC and FEV1 are shown to be inversely proportionate with increasing BMI. There is no statistically significant linear correlation between BMI and FEV1/FVC ratio.

**Acronyms:** GLI (Global Lung Initiative), BMI (BODY MASS INDEX).

**Grant Support:** Nil.

**Declaration of Interests:** Nil.

### INCREASING CHILDHOOD AND ADOLESCENT ADIPOSITY IMPAIRS PEAK ADULT LUNG FUNCTION

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Obesity is associated with impaired lung function in adulthood. Longitudinal studies show that increases in Body Mass Index (BMI) in adulthood are associated with reductions in lung function, but the impact of increasing adiposity during childhood and adolescence on lung function growth is unknown. This study investigated associations between changes in BMI during childhood and adolescence and peak lung function in early adulthood.

**Methods:** Participants were members of the Dunedin Multidisciplinary Health and Development Study – a longitudinal population-based birth cohort of 1,037 individuals born in 1972/1973. Spirometry was performed at age 9 and 21 years. Height and weight were measured at each age to calculate BMI. Multiple linear regression was used to assess the longitudinal associations between changes in BMI between ages 9 and 21 and lung function at age 21. Analyses were conducted for men and women separately and adjusted for height and lung function at age 9 and changes in height. Participants with asthma at age 9, smokers, and pregnant women were excluded from the analyses.

**Results:** 407 participants (55% male) were included. The mean  $\pm$  SD BMI was  $16.3 \pm 1.6$  at age 9 and  $24.2 \pm 3.6$  at age 21. Greater increases in BMI between ages 9 and 21 were associated with lower FEV<sub>1</sub> values at age 21 in men and lower FEV<sub>1</sub>/FVC ratios at age 21 in women. No associations were observed between changes in BMI and FVC at age 21.

	Men (n = 222)			Women (n = 185)		
	Coeff (per kg/m <sup>2</sup> )	95% CI	p	Coeff (per kg/m <sup>2</sup> )	95% CI	P
FEV <sub>1</sub> (L)	-0.021	-0.038, -0.003	<b>0.019</b>	-0.004	-0.016, 0.007	0.475
FVC (L)	-0.010	-0.032, 0.012	0.378	0.008	-0.005, 0.021	0.217
FEV <sub>1</sub> /FVC (%)	-0.231	-0.495, 0.034	0.087	-0.277	-0.469, -0.085	<b>0.005</b>

**Conclusion:** Increasing adiposity during childhood and adolescence may impair peak lung function in early adulthood. These effects may be different in men and women. Even though the effect sizes are small at age 21 (a five kg/m<sup>2</sup> increase in BMI would reduce mean FEV<sub>1</sub> by 0.105L in men, and mean FEV<sub>1</sub>/FVC by 1.4% in women), these findings suggest that increasing adiposity in adolescence may increase the risk for COPD later in adulthood.

**Grant Support:** Health Research Council of New Zealand.

### PULMONARY LYMPHANGITIS CARCINOMATOSA SECONDARY TO MALIGNANT PERITONEAL MESOTHELIOMA

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**Introduction/Aim:** Peritoneal mesothelioma is the second most common type of mesothelioma and usually confines to abdominal cavity with uncommon haematogenous or lymphatic spread to extra-abdominal organs. We report a case of parenchymal pulmonary involvement secondary to malignant peritoneal mesothelioma.

**Case Report:** 59 year-old female presented with abdominal discomfort and abdominal lump for 2 months associated with significant weight loss. She denied history of asbestos exposure. The abdominal CT scan showed a diffuse omental mass with abdominal wall infiltration. Ultrasound-guided biopsy of the mass revealed a high-grade tumor with immunohistochemistry positive for calretinin, CK5/6, D 2-40, AE 1/3, WT 1, CK 7, p53, p16, results of which favored a diagnosis of malignant peritoneal mesothelioma. Three weeks later, the patient developed cough and breathlessness. A contrast CT scan of the chest confirmed the right sided pleural effusion, bilateral hilar lymphadenopathy with bilateral diffuse pulmonary infiltrate. Pleural fluid analysis was exudative and inconclusive cytology. Bronchoscopic trans-bronchial lung biopsy (TBLB) confirmed pulmonary malignant mesothelioma, with positive WT1 and calretinin stains.

**Discussion:** Unlike pleural origin, only 33-50% of the patients with peritoneal mesothelioma reported asbestos exposure. There is no randomized control trial for optimal management. Median survival without treatment is 12 months. Retrospective studies showed cyto-reduction surgery and heated intra-abdominal chemotherapy improve median survival to 53 months. The patho-physiology of pulmonary involvement is thought to be related to haematogenous metastasis or by diffuse retrograde permeation and embolization of the lymphatic system. Bronchoscopic TBLB can be considered for diagnosis.

**Conclusion:** Malignant peritoneal mesothelioma is a still rare malignancy in Australia. The association with asbestos exposure is weaker in this tumor with only 33-50% reported prior exposure. Distant metastasis to extra-abdominal organs is uncommon however can rarely present with diffuse pulmonary infiltrate.

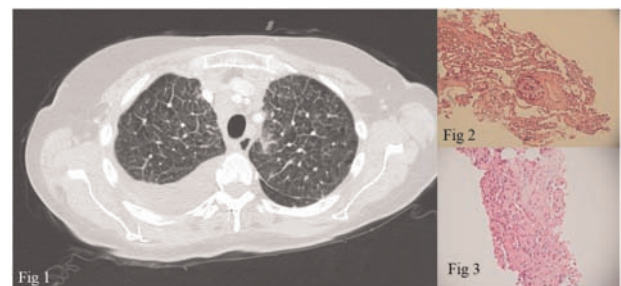


Fig 1: CT Chest showing pulmonary lymphangitis and right sided pleural effusion

Fig 2: Peritoneal biopsy showing malignant mesothelioma

Fig 3: Trans-bronchial lung biopsy showing malignant mesothelioma

### PREDICTING FITNESS TO FLY IN INTERSTITIAL LUNG DISEASE

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**Introduction/Aim:** High altitude simulation testing (HAST) is an effective method to assess risk of adverse effects during air travel in patients with respiratory disease. To date, studies have mainly focused on COPD patients, leaving a need for more detailed air travel guidelines for patients with interstitial lung disease (ILD). The aim of this project was to identify clinical factors predictive of positive HAST testing in ILD patients.

**Methods:** Data from patients attending the RPAH ILD clinic undergoing HAST between 2011 and 2017 were analysed. An arterial blood gas showing PaO<sub>2</sub> ≤ 50 mmHg or SpO<sub>2</sub> < 85% whilst breathing FiO<sub>2</sub> 15% was considered indicative of the need for in-flight oxygen, following international guidelines. The relationship between clinical parameters and a positive HAST result was explored.

**Results:** 83 ILD patients underwent HAST (53 males; mean age 64.9 ± 10.6 years; BMI 29.1 ± 6.5; 48 current or former smokers; 20.2 ± 16.6 pack-year history). Baseline clinical data showed moderate physiologic impairment [resting room air (RA) SpO<sub>2</sub> 95.6 ± 1.7%; FVC 71.1 ± 21.0%; DLCO 52.3 ± 16.7%]. A positive HAST was observed in 48/83 (57.8%) patients. These patients had significantly lower RA SpO<sub>2</sub> (94.9 ± 1.4 versus 96.2 ± 1.8, *P* = 0.02) and nadir 6MWT SpO<sub>2</sub> (86.4 ± 7.7 vs 91.7 ± 6.1%, *P* = 0.01). There were no significant differences in other markers of disease severity. PaO<sub>2</sub> at HAST correlated with degree of 6MWT desaturation (*r* = 0.50, *P* < 0.001) and with DLCO %predicted (*r* = 0.32, *P* < 0.01). 6MWT nadir SpO<sub>2</sub> was predictive of positive HAST on multivariate regression analysis, independent of RA SpO<sub>2</sub> and other markers of disease severity (OR 0.82, 95% CI 0.69 – 0.98, *P* = 0.03).

**Conclusion:** Exercise desaturation in ILD patients is predictive of the need for oxygen at altitude.

### BASELINE INFLAMMATORY MARKERS AND SURVIVAL IN PATIENTS WITH INTERSTITIAL LUNG DISEASE

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**Introduction/Aim:** The interstitial lung disease (ILD) constitutes a broad array of rare lung diseases of varying prognoses. As part of the initial assessment of patients with ILD, serum C-reactive protein (CRP) and albumin levels are collected as part of a prospective protocol. We aimed to determine the association between these levels and survival in our patients.

**Method:** We undertook a retrospective audit of patients seen in the ILD clinic at Austin Health over two years. Data collected included patient demographic and diagnosis, baseline albumin and CRP levels, respiratory function tests, and six-minute walk tests. Patients were excluded if they did not have blood tests at diagnosis or if their blood tests were performed during hospitalisation.

**Results:** 161 patients were identified (male *n* = 78 (65%); mean age = 65.9 (±13.6); deceased = 34 (21%). The median follow up was 25 months (range = 1 to 107). One patient received lung transplantation, and was included in the deceased group. The survivor group was younger and had better lung function and exercise capacity compared to the deceased group (Table). A range of diagnoses were present within both groups, with idiopathic pulmonary fibrosis and connective tissue disease-related ILD being the common ones. Compared to the survivor group, the proportion of patients with low albumin levels (*P* = 0.03), combined low albumin and elevated CRP levels (*P* < 0.0005) were significantly higher than the deceased group.

Table. Serum CRP and albumin levels in the survivor and deceased groups\* Results expressed as mean ± standard deviation

	Survivor Group [ <i>n</i> = 127]	Deceased Group [ <i>n</i> = 34]	<i>P</i> value
Elevated CRP	55 (43%)	21 (62%)	0.08
Low Albumin	21 (17%)	12 (35%)	0.29
Dual Abnormalities	12 (9%)	10 (29%)	0.0002
Dual normal	64 (50%)	11 (32%)	
Age (years)*	64.5 ± 14.2	71.2 ± 9.8	0.01
FVC (% predicted)*	82.2 ± 18.1	64.4 ± 17.0	< 0.0001
DLCO (% predicted)*	57.9 ± 19.5	37.2 ± 12.0	< 0.0001

**Conclusion:** In a cohort of ILD patients of varying diagnoses, our preliminary analyses suggest that abnormal baseline albumin and CRP levels appear to be associated with poorer survival.

**Key Words:**

**Nomination for New Investigator Award**

**Grant Support:** •

**ILD MDM IN CLINICAL PRACTICE: AN AUDIT****HO K<sup>2</sup>**, KEAT K<sup>1,2</sup>, KATELARIS C<sup>1,2</sup><sup>1</sup>*Immunology Unit, Department of Medicine, Campbelltown Hospital, Campbelltown, Australia,* <sup>2</sup>*School of Medicine, Western Sydney University, Campbelltown, Australia*

**Introduction/Aim:** Interstitial Lung Diseases (ILD) is a group of heterogeneous disorders involving the lung parenchyma. The correct diagnosis is paramount because the different subtypes of ILDs have distinct treatment, management strategies and prognoses. Multidisciplinary discussion is the gold standard for diagnosis of ILD. There have been recent advancements in the treatment of Idiopathic Pulmonary Fibrosis (IPF), a subset of ILD, with two new anti-fibrotic therapies, pirfenidone and nintedanib. The study aimed to audit the compliance of ILD diagnosis in Campbelltown Hospital and to ascertain the diagnostic value of multidisciplinary discussion in ILD.

**Methods:** This is a retrospective audit of patients with ILD who were discussed at the Macarthur Multidisciplinary Meeting (MDM) for ILD. The data was analysed to identify cohort demographics and determine compliance rates. The effect of MDM was evaluated by noting the diagnoses before and after MDM to see if it resulted in changed diagnosis.

**Results:** 101 patients were discussed in the Macarthur MDM from March 2015 to September 2017. This audit showed that MDM resulted in a change in diagnosis in 51% of the cases. Compliance with recommended tests for all patients with ILD was mostly satisfactory and included FBC (98%), EUC (96%), LFT (95%), pulmonary function testing (91%) and HRCT (89%). Tests with unsatisfactory compliance rates were urinalysis (39%), ANA (86%), RF (61%) and anti-CCP (35%). Access to pulmonary rehabilitation should be available to all patients with ILD but this audit revealed low rates (23%).

**Conclusion:** Campbelltown Hospital was mostly compliant with the diagnostic workup of patients with ILD with the exception of urinalysis, autoimmune serology and access to pulmonary rehabilitation. This audit demonstrated the importance of multidisciplinary discussion for achieving or clarifying diagnosis in ILD. Further studies should assess the diagnostic accuracy of MDM and compare performance between MDM in other regions.

**Grant Support:** Nil.

**PORTABLE OXYGEN CONCENTRATOR FOR DELIVERY OF AMBULATORY OXYGEN IN INTERSTITIAL LUNG DISEASE: A CROSSOVER TRIAL****HOFFMAN M<sup>1</sup>**, COX S<sup>1,2</sup>, BURGE A<sup>1,3</sup>, MCDONALD C<sup>2,4,6</sup>, CORTE<sup>6,11</sup>, CHAMBERS<sup>7,11</sup>, EKSTROM<sup>8</sup>, GLASPOLE<sup>9,11</sup>, GOH<sup>2,4</sup>, HOLLAND<sup>1,2,3,11</sup><sup>1</sup>*La Trobe University, Melbourne, Australia,* <sup>2</sup>*Institute for Breathing and Sleep, Melbourne, Australia,* <sup>3</sup>*Physiotherapy, Alfred Health, Melbourne, Australia,* <sup>4</sup>*Respiratory and Sleep Medicine Austin Health, Melbourne, Australia,* <sup>5</sup>*University of Melbourne, Melbourne, Australia,* <sup>6</sup>*Royal Prince Alfred Hospital, Sydney, Australia,* <sup>7</sup>*The Prince Charles Hospital and University of Queensland, Brisbane, Australia,* <sup>8</sup>*Lund University, Faculty of Medicine, Department of Clinical Sciences Lund, Respiratory Medicine and Allergology, Lund, Sweden,* <sup>9</sup>*Respiratory Medicine, Alfred Health, Melbourne, Australia,* <sup>10</sup>*Monash University, Melbourne, Australia,* <sup>11</sup>*National Health and Medical Research Council Centre of Research Excellence in Pulmonary Fibrosis, Australia*

**Introduction/Aim:** Portable oxygen concentrators (POC) are lighter and easier to manoeuvre than portable oxygen cylinders, however their ability to meet the oxygen requirements of people with interstitial lung disease (ILD) during exercise has not been extensively evaluated. This study aimed to compare the effects of ambulatory oxygen delivered during exercise using POC (Inogen One G3 HF) to ambulatory oxygen delivered with a standard portable cylinder in individuals with ILD.

**Methods:** Individuals with a confirmed diagnosis of fibrotic ILD who exhibited oxygenhaemoglobin saturation (SpO<sub>2</sub>) <90% during routine 6-minute walk test (6MWT) were eligible for inclusion. Potential participants were excluded if they were currently using continuous oxygen therapy, had SpO<sub>2</sub><90% on room air, were unable to perform a 6MWT or had comorbidities that limited walking. Two 6MWTs were performed on the same day using the POC (setting 5) or portable cylinder at flow rate of 4l/minute, in random order.

**Results:** Ten individuals with fibrotic ILD (n = 7 men), mean (standard deviation) age 72(7) years, carbon monoxide transfer factor 46(13)% predicted, and FVC 70(17)% predicted were recruited. There was no difference in nadir SpO<sub>2</sub> between 6MWTs with POC or portable cylinder 82(3)% vs. 81(6)% respectively (P = 0.43). 6MWT distance was statistically significantly greater with POC than portable cylinder 519(98) vs. 503 (88) metres (P = 0.023), although difference was not clinically significant. There was no difference in breathlessness or leg fatigue at the end of either test (P > 0.05). Eight participants preferred POC over portable cylinder during exercise, due to greater manoeuvrability (n = 6) and less perceived stigma (n = 2).

**Conclusion:** Oxygen desaturation during exercise testing in people with ILD is similar when using POC or a portable oxygen cylinder. Future research should examine the ability of POC to deliver ambulatory oxygen during physical activity in daily life in people with fibrotic ILD.

**Grant Support:** NHMRC Project grant (APP1139953).



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### NINTEDANIB: EFFECTS ON EXTRACELLULAR MATRIX TURNOVER BIOMARKERS IN IDIOPATHIC PULMONARY FIBROSIS

JO H<sup>1</sup>, MAHER T<sup>2</sup>, STOWASSER S<sup>3</sup>, NISHIOKA Y<sup>4</sup>, WHITE E<sup>5</sup>, COTTIN V<sup>6</sup>, NOTH I<sup>7</sup>, SELMAN M<sup>8</sup>, WACHTLIN D<sup>9</sup>, DIEFENBACH C<sup>10</sup>, JENKINS R<sup>11</sup>, ON BEHALF OF THE INMARK TRIAL INVESTIGATORS

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**Introduction:** A hallmark of idiopathic pulmonary fibrosis (IPF) is the excess accumulation of extracellular matrix (ECM) in the lungs. When ECM is degraded by metalloproteinases (MMPs), free-circulating protein fragments (neoepitopes) are generated. INMARK (NCT02788474) is an ongoing trial assessing the effects of nintedanib on changes in biomarkers of ECM turnover and on the association between changes in such biomarkers and disease progression in patients with IPF and limited FVC impairment (FVC  $\geq$ 80% predicted).

**Aim:** To summarize the baseline characteristics of patients participating in INMARK.

**Methods:** Patients were randomized 1:2 to receive nintedanib 150 mg bid or placebo for 12 weeks followed by open-label nintedanib for 40 weeks. The primary endpoint is the rate of change in serum c-reactive protein degraded by MMP-1/8 (CRPM) from baseline to week 12. The proportion of patients with disease progression (defined as absolute decline in FVC  $\geq$ 10% predicted or death) over 52 weeks is a key secondary endpoint.

**Results:** Recruitment for the INMARK trial is complete. A total of 346 patients have been treated. At baseline, mean (SD) age was 70.3  $\pm$  7.4 years; the majority of patients were white (61.8%), male (75.7%), and former or current smokers (72.8%). Mean (SD) FVC was 3241.4  $\pm$  812.2 mL and 97.5  $\pm$  13.5% predicted; mean (SD) diffusing capacity of the lungs for carbon monoxide was 63.8  $\pm$  19.5% predicted. Mean (SD) FEV1/FVC ratio was 79.5  $\pm$  6.3 and mean (SD) blood oxygen saturation was 96.4  $\pm$  1.9%.

**Conclusion:** The INMARK trial will provide insights into the association between changes in biomarkers of ECM turnover and disease progression, and whether treatment with nintedanib affects the rate of change in such biomarkers, in patients with IPF and limited FVC impairment. Results will be presented in 2019.

**Grant Support:** The INMARK trial is funded by Boehringer Ingelheim.

### THE CLINICAL IMPACT OF SELF-REPORTED SYMPTOMS OF CHRONIC RHINOSINUSITIS ON QUALITY OF LIFE IN ADULTS WITH BRONCHIECTASIS

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**Introduction/Aim:** Chronic rhinosinusitis (CRS) affects 59% of adults with bronchiectasis and has been linked to greater disease severity. However, the impact of self-reported symptoms of CRS on health-related quality of life (HRQOL) is unknown. This study aimed to 1) establish the relationship between symptoms of CRS, HRQOL and health status and 2) identify predictors of HRQOL in adults with bronchiectasis and symptoms of CRS.

**Methods:** Individuals with a diagnosis of bronchiectasis and symptoms of CRS completed measures of HRQOL including the Quality of Life–Bronchiectasis (QOL-B) Questionnaire, Leicester Cough Questionnaire (LCQ) and Bronchiectasis Health Questionnaire (BHQ). Symptoms of CRS were evaluated by the Sinonasal Outcome Test-22 (SNOT-22) and the Total Nasal Symptom scores for 12 and 24 hours (TNSS<sub>12</sub> and TNSS<sub>24</sub>). Bronchiectasis severity was assessed using the Bronchiectasis Severity Index (BSI) and high-resolution computed tomography (HRCT) scoring.

**Results:** Sixty participants (male n = 21) with bronchiectasis (mean  $\pm$  SD age 59 $\pm$ 18 years; FEV<sub>1</sub> 73.2  $\pm$  25.5% predicted) were included. More severe CRS symptoms (based on SNOT-22 total score, TNSS<sub>12</sub> and TNSS<sub>24</sub>) were associated with poorer cough-related QOL (all  $r >$  -0.60) and reduced health status ( $r >$  -0.400). There was no difference in the severity of CRS symptoms according to gender. A higher SNOT-22 total score was moderately associated with poorer physical function ( $r = -0.518$ ), less vitality ( $r = -0.631$ ), reduced social function ( $r = -0.546$ ), greater treatment burden ( $r = -0.411$ ) and increased severity of respiratory symptoms ( $r = -0.534$ ). More severe symptoms of CRS were weakly related to a higher BSI ( $r = 0.29$ ). CRS symptoms were unrelated to HRCT scoring. The BSI, SNOT-22 and LCQ total scores were predictors of each of the domains of the QOL-B.

**Conclusion:** CRS symptoms have a negative impact on disease-specific and cough-related QOL, are weakly related to disease severity, and predict QOL in adults with bronchiectasis.

**Grant Support:**

**CURRENT AUSTRALIAN AND NEW ZEALAND PHYSIOTHERAPY PRACTICES IN THE USE OF AIRWAY CLEARANCE TECHNIQUES IN THE MANAGEMENT OF INDIVIDUALS EXPERIENCING AN ACUTE EXACERBATION OF BRONCHIECTASIS**

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**Introduction/Aim:** Airway clearance techniques (ACTs) are recommended for people with bronchiectasis both in stable state and during an acute exacerbation. The current use of ACTs by physiotherapists in the management of individuals during an acute exacerbation of bronchiectasis is unclear. The aim of this study was to establish what current physiotherapy practices in the use of ACTs in clinical practice in Australia and New Zealand comprise for people experiencing an acute exacerbation of bronchiectasis.

**Methods:** A cross sectional online survey was employed, disseminated by the peak professional bodies in both Australia and New Zealand between August 2016 and April 2017. Participants were physiotherapists who had treated adults or children diagnosed with an acute exacerbation of non-cystic fibrosis bronchiectasis in the last 12 months.

**Results:** The survey was accessed by 130 physiotherapists and 121 of those deemed themselves eligible and consented to participate. Most participants (89%) reported prescribing ACTs for up to 81-100% of individuals during an acute exacerbation of bronchiectasis. The most commonly used ACTs with adults were directed huffing (92%), exercise (89%) and the active cycle of breathing technique (89%). The most commonly used ACTs for paediatric patients were: new born-3 years - percussion (85%) and positioning (77%); 4-10 years - directed huffing (100%) and exercise (85%); 11-18 years - directed huffing (92%) and exercise (77%), active cycle of breathing technique (77%) and positive expiratory pressure therapy (77%). The majority (97%) of participants felt that further research was required regarding the use of ACTs with individuals with an acute exacerbation of bronchiectasis.

**Conclusions:** This survey demonstrates that ACTs are routinely used as part of physiotherapy management of adults and children experiencing an acute exacerbation of bronchiectasis, with the most common techniques in adults being components of ACBT and physical exercise. In children, technique choice was dependent on age.

**Declaration of Interest:** None.

**DIFFERENTIATING BETWEEN DEPRESSION, ANXIETY AND A GRIEF REACTION. TRICKY TIMES FOR MOST IPF PATIENTS, THEIR CAREGIVERS AND THEIR CARE TEAM.**

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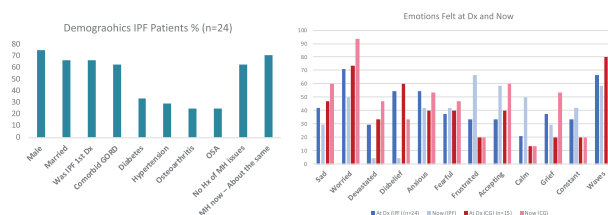
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**Introduction/Aim:** This study comprehensively investigates the psychological impact of idiopathic pulmonary fibrosis (IPF) for patients and their caregivers.

Very little is currently known about the patient's experience, the burden the disease places on family members and caregivers and the needs of both during the disease course. Our study aims to change that!

**Methods:** We used specifically designed semi-structured clinical interview plus validated scales. In the IPF patient cohort we investigated the prevalence of preparatory grief, anxiety, depression, stress and their personality sub-type. In the caregiver cohort we investigated grief, caregiver well-being, stress, anxiety and depression.

**Results:** Preliminary results from the grief scales used indicate that preparatory grief is experienced by IPF patients 45% moderate, 30% high (n = 24) and their caregivers 60% moderate (n = 15) regardless of time since diagnosis.



**Conclusion:** Results indicate that grief reactions are experienced by IPF patients and caregivers. Only 38% of IPF participants at diagnosis identified they felt 'grief', yet 68% said their distressing emotions came in waves. Indicating that many patients and caregivers identify distress but may not recognise it as grief. Similarly, results from the Grief Inventory (PGDS), indicated that the levels of grief measured were inconsistent with IPF participants perceptions of the 'felt' grief emotion.

Differentiating between depression, anxiety and a grief reaction can be difficult. A simple measure is to ascertain if the distressing emotions are there 'constantly' indicating a depressive or anxiety response. Whereas, a grief reaction presents in 'waves' of emotion. Whilst this is not a failsafe measure it quickly indicates the type of distress and possible treatment pathway to be considered.

Grief is an emotion that aids adjustment to life-changing events and responds to supportive psychological input. Depression scales may give false positive results. Treating grief as depression or anxiety with pharmacotherapy may be unwarranted.

**Grant Support:** Royal Adelaide Hospital Research Grant

**FROM BENCH TO BEDSIDE: NINTEDANIB FOR PROGRESSIVE FIBROSING INTERSTITIAL LUNG DISEASES**  
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**Introduction/Aim:** Some patients with interstitial lung diseases (ILDs) develop fibrosis that becomes progressive and self-sustaining, independent of the underlying aetiology. No drugs are licensed for the treatment of ILDs other than idiopathic pulmonary fibrosis (IPF). Nintedanib is an approved treatment for IPF that slows disease progression by reducing decline in FVC by about 50%.

**Methods:** Human cellular systems representing mechanistic aspects of progressive fibrosing ILDs, including lung fibroblasts, cells of the immune system and the vasculature, were used to explore the *in vitro* activity of nintedanib. The *in vivo* activity of nintedanib was explored in diverse animal models reflecting mechanisms involved in different ILDs such as silicosis, hypersensitivity pneumonitis (HP), rheumatoid arthritis-associated ILD (RA-ILD), and systemic sclerosis-associated ILD (SSc-ILD).

**Results:** Nintedanib attenuated the release of immune-stimulating and pro-fibrotic mediators; the migration and differentiation of fibrocytes; the proliferation, migration and contraction of fibroblasts and their transformation into myofibroblasts; and functions of endothelial cells, vascular smooth muscle cells and pericytes. In two mouse models nintedanib reduced (bleomycin- and silica-induced) lung fibrosis. In a model resembling the fibrotic and vascular manifestations of systemic sclerosis, nintedanib reduced the number of myofibroblasts, hydroxyproline levels, and the fibrotic area of the lung evident on histology, as well as the extent of skin and heart fibrosis. In a model of RA-ILD, nintedanib reduced hydroxyproline levels and lung collagen measured by histology. In a model of chronic allergic remodelling resembling features of chronic HP, nintedanib reduced hydroxyproline levels in the lung.

**Conclusion:** Nintedanib attenuates fundamental processes in the pathobiology of progressive fibrosing ILDs, with anti-fibrotic activity that is independent of the initiating trigger. Ongoing clinical trials are exploring the efficacy and safety of nintedanib in patients with SSc-ILD (SENSCIS<sup>®</sup> trial; NCT02597933) and patients with progressive fibrosing ILDs of various clinical diagnoses (INBUILD<sup>®</sup> trial; NCT02999178).

**Grant Support:** Boehringer Ingelheim.

**INTERSTITIAL LUNG DISEASE MULTIDISCIPLINARY MEETINGS CHANGE DIAGNOSIS AND TREATMENT**

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**Introduction/Aim:** Accurate diagnosis of Interstitial Lung Disease (ILD) is a challenge faced by treating physicians. Multidisciplinary meetings (MDM) increase diagnostic confidence, change diagnosis and treatment of ILD and are recommended by international guidelines. We hypothesized that the introduction of MDM would alter diagnosis for ILD patients in New Zealand. We aim to describe the first cohort of New Zealand patients to undergo a dedicated ILD MDM discussion and to determine its effect on change in diagnosis and treatment.

**Methods:** This is a single centre retrospective review of patients discussed at the Waikato Hospital ILD MDM between July 2016 and November 2018. Demographics, clinical features, lung function, radiology and pathology results were assessed. Pre and post MDM diagnoses and treatments were compared.

**Results:** 211 patients were included. Māori made up 6% of ILD cases compared with 22% of the local population. The most common post MDM diagnoses were idiopathic pulmonary fibrosis (n=43, 20%), connective tissue disease associated ILD (n=37, 18%) and unclassifiable ILD (n=40, 19%). Eighty-three (40%) patients had their diagnosis changed by MDM. MDM significantly altered diagnosis for all major diagnostic categories. Treatment of 69 (32%) patients was modified following MDM discussion.

**Figure:** Treatment modification based on suspected ILD diagnosis. IS = immunosuppression, Ob = observation, Smoking cess = smoking cessation, Treat UL = treat underlying disease, IS+cess = immunosuppression + cessation of aggravating drug, AF = anti-fibrotics.

**Conclusion:** MDM discussion significantly alters diagnosis and treatment of patients with ILD.

**Grant Support:** SMF is supported by a University of Auckland Summer Student grant.

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### PERILS OF PULMONARY ARTERIAL HYPERTENSION; AN UNUSUAL PRESENTATION

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**Introduction/Aim:** Pulmonary arterial hypertension leads most commonly to right heart failure, however other complications, such as sudden cardiac death can occur in up to 25% of patients without evidence of prior deterioration. We describe a rare presentation of pulmonary artery dissection diagnosed ante-mortem and discuss an approach to patients with primary pulmonary artery pathology beyond pulmonary arterial hypertension.

**Case report:** 48 year old Indian male, functional WHO Class II, presented with large volume haemoptysis 8 years following initial diagnosis of pulmonary hypertension on transthoracic echocardiogram in India. CTPA demonstrated a dilated right main pulmonary artery with a 3.5cm intramural thrombus confirmed on echocardiogram. Mean pulmonary artery pressure on right heart catheterisation was 57 mmHg with a mean pulmonary capillary wedge pressure of 2mmHg and a peripheral vascular resistance of 13.4 units.

**Discussion:** There have been limited case reports of chronic pulmonary artery dissection described ante-mortem. Given our patient's clinical presentation, we performed a Medline search of published pulmonary artery pathologies and summarise the broad differential diagnoses for an unusual pathology.

**Conclusion:** Pulmonary artery dissection is a very rare complication of pulmonary arterial hypertension, and typically leads to sudden cardiac death, pericarditis or chronic dissection. Our patient is currently stable on dual agent therapy for pulmonary arterial hypertension with no further episodes of haemoptysis.

**Grant Support:** N/A.

### AUDIT OF DIAGNOSTIC WORKUP OF PATIENTS WITH SUSPECTED ILD AT THE GOLD COAST UNIVERSITY HOSPITAL

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**Introduction/Aim:** Interstitial lung diseases (ILD) encompass a heterogeneous group of lung disorders and consensus diagnosis via a multidisciplinary meeting (MDM) is well established. As a large tertiary referral centre, we described our diagnostic approach to ILD, including submissions to the regional MDM, and characterised the ILD patient population.

**Methods:** We analysed the year of 2017. Patients were identified via a search through the lung function laboratory patient database. Search terms included, 'interstitial', 'fibrosis', 'ILD', 'IPF', and 'idiopathic'. Key information including demographics, diagnosis, lung function, MDM discussion, and follow up were recorded.

**Results:** During the study period, we identified 151 patients who were referred to our service for diagnostic evaluation and management of suspected ILD. Mean ( $\pm$ SD) age of the cohort was 72 ( $\pm$ 12) years, 97 (64%) were males and 81 (54%) were current smokers. Mean ( $\pm$ SD) FVC and DLCO were 84 ( $\pm$  22)% predicted and 50 ( $\pm$ 16)% predicted respectively. A majority (131, 87%) of patients underwent a HRCT ILD protocol. There were 25 lung biopsies (17%) and bronchoalveolar lavage was completed in 27 (18%) patients. Patients had 63% of the recommended serological investigations completed. 12% had the full serological work up. 34 patients (23%) were presented to the regional MDM. In our cohort, a final diagnosis was reached in 72% of patients. IPF was the diagnosis in 42 (28%) patients. The remaining diagnoses were unclassifiable (28%), CT-ILD, NSIP, chronic HP, drug induced ILD, smoking related ILD, COP and sarcoidosis.

**Conclusion:** Our cohort had similar demographic and physiological parameters to the general Australian IPF population. A robust work up facilitated a diagnosis in the majority of patients, focussing presentations to the MDM for diagnostic dilemmas and IPF for rapid access to anti-fibrotic therapy. Future research may explore the benefits and pitfalls of using a protocolised approach to investigating patients with suspected ILD.

**Grant Support:** None

**Declaration of interests**

None relevant to this study

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**THE EXPERIENCE OF PRIMARY PULMONARY AMYLOIDOSIS AT A TERTIARY HOSPITAL ON THE GOLD COAST, AUSTRALIA – A CASE SERIES**

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**Introduction/Aim:** Primary pulmonary amyloidosis is an uncommon presentation of a rare disease. There are four major clinico-radiological presentations making diagnosis and management challenging. We present five cases of primary pulmonary amyloidosis at a major tertiary referral centre in a bid to improve the knowledge and understanding of this important disease.

**Methods:** Cases were collected consecutively from 2012 to 2018. Demographic and clinical data was recorded, including age, sex, diagnosis, biopsy type, protein subtype and radiology.

**Results:** Over a six year period, five cases of primary pulmonary amyloidosis were encountered at our centre. The age of the cohort ranged from 41 to 82 years old, four male and one female patient. Nodular amyloidosis was the predominant subtype, with tracheobronchial second most common. The diagnosis was confirmed histologically in all cases, with the majority of biopsies achieved via CT guided approach. All cases were AL amyloid, with AP protein most common. All our patients had mild positivity to  $\lambda$  light chains, not  $\kappa$ , the significance of which is uncertain. There were a variety of clinical presentations, highlighting the heterogeneity of the cohort and this condition. Both nodular cases were managed conservatively without proceeding to surgical resection. One of the tracheobronchial cases required laser therapy, the other is under observation. At time of writing, none of the patients had an underlying mucosal associated lymphoid tissue (MALT) lymphoma or lymphoproliferative neoplasm (LPN) diagnosed.

**Conclusion:** Primary pulmonary amyloidosis is uncommon and represents an important differential in patients presenting with respiratory symptoms or a pulmonary nodule. Its diagnosis should prompt thorough investigations in search of an underlying cause, namely plasma cell disorders, LPN, autoimmune disease and chronic inflammation. Management is largely dependent on the anatomical deposition of the amyloid protein, and of any underlying disorder.

**Grant Support:** None

**Declaration of Interest:** None relevant.

**CHARACTERISTICS, MANAGEMENT AND OUTCOMES OF AN AUSTRALIAN SARCOIDOSIS PATIENT COHORT**

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**Introduction/Aim:** Sarcoidosis is a multisystem granulomatous disorder with large heterogeneity in its incidence, manifestations and outcomes. Recent advances have resulted in a shift in the diagnostic pathways, treatments used and outcomes observed. This study aimed to evaluate these parameters in a cohort of Australian sarcoidosis patients.

**Method:** A retrospective review of the medical records of 105 patients was performed. Patients included were those aged  $\geq 18$  years with a diagnosis of pulmonary sarcoidosis based on the International Classification of Diseases (4B20) and were treated at a tertiary metropolitan hospital between January 2016 and January 2018.

**Results:** Patients had a mean age at diagnosis of  $48 \pm 13$ (SD) years, 48% were female and 80% were of Caucasian ethnicity. Pulmonary stage at diagnosis was 0,1,2,3,4 and unknown in 3%, 50%, 36%, 6%, 2% and 3% respectively.

Extra-pulmonary sarcoidosis was present in 40 (38%) patients. Systems involved included eye (16%), skin (8%), joint (5%), renal (5%), central nervous system (4%), gastrointestinal tract (4%), cardiac (3%) and other (11%).

Histological confirmation was obtained in 79% of patients. Serum angiotensin-converting enzyme levels were above the upper limit of normal in 61% of patients.

Fifty-seven patients (54%) required active treatment; of these 26 patients (46%) were treated with oral corticosteroid monotherapy, while 31 patients (54%) required combination therapy. Additional treatments included methotrexate (42%), mycophenolate (16%), azathioprine (5%), hydroxychloroquine (5%), infliximab (4%) and cyclophosphamide (2%). Treatment related side effects occurred in 44%. Relapse was documented in 15% of patients.

**Conclusion:** Sarcoidosis in Australia is a multisystem disorder with significant heterogeneity. In this study extra-pulmonary involvement was common with eye and skin most frequently involved. The need for treatment and treatment type was highly variable. These findings are consistent with prior studies from Australia and other countries with predominant Caucasian populations. Larger multi-centre investigation is needed to further define the Australian Sarcoidosis cohort and advance management.

**Key Words:** Sarcoid, granulomatous, Australia

**Grant Support:** Nil to acknowledge.

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**SEEING (CONGO) RED****GERHARDY B<sup>1</sup>**, ALDONS P<sup>1</sup><sup>1</sup>*The Prince Charles Hospital, Brisbane, Australia*

**Introduction/Aim:** We demonstrate a case of a 78 year old Caucasian male with a 50 pack year tobacco history presenting subacute dyspnoea and diffuse bibasal predominant infiltrates with satellite lesions and mediastinal plus hilar lymphadenopathy. Radiologically highly suggestive of malignancy, he underwent bronchoscopy with transbronchial nodal aspirate which showed no malignancy but did demonstrate extracellular material staining for Congo red and crystal violet, with subsequent immunohistochemistry positive amyloid P protein, confirming a diagnosis of pulmonary amyloidosis. Serum protein electrophoresis taken on admission reveal a positive monoclonal band (Kappa IgG) with a normal K/L ratio and no Bence Jones protein on urine. Full blood count and serum calcium was normal. There was no other classic symptoms of myeloma. At time of writing he is awaiting review by our haematological service.

**Conclusion:** Pulmonary amyloidosis has three forms: nodular pulmonary amyloidosis, trachea-bronchial amyloidosis and diffuse alveolar septal amyloidosis. We present a brief overview of these three disease manifestations and outline the rarity with which pulmonary amyloidosis is diagnosed ante-mortem. Treatment options for each subtype are also discussed.

**Grant Support:** Nil.

**IN VIVO LPS EXPOSURE DIFFERENTIALLY ALTERS  
INTRAPULMONARY ARTERY AND AIRWAY REACTIVITY IN  
MOUSE PRECISION CUT LUNG SLICES**

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**Introduction:** Acute respiratory distress syndrome (ARDS) can result in decreased long-term quality of life, including increased risk of pulmonary hypertension. In animal models, ARDS can be induced by *in vivo* lipopolysaccharide (LPS) exposure which disrupts the pulmonary endothelial barrier and increases the release of pro-inflammatory cytokines. Small intrapulmonary arteries play an integral role in the pathogenesis of pulmonary hypertension, but are relatively understudied *in vitro* due to their inaccessibility compared to large pulmonary arteries. With the development of the precision cut lung slice (PCLS) technique, the effect of LPS on reactivity of mouse intrapulmonary arteries as well as airways can be assessed.

**Aims:** To assess whether *in vivo* treatment of mice with LPS induces dysfunction of contractile responses of pulmonary arteries and airways measured in PCLS.

**Methods:** 8-week old male C57BL6 mice were briefly anaesthetised for intranasal administration of LPS (10µg/50µl) or 50µl saline daily for 4 days. Mice were culled the following day for preparation of PCLS. Contraction of intrapulmonary arteries (80-200 µm) and airways (150-400 µm) in response to the thromboxane mimetic U46619, endothelin-1 (ET-1) and 5HT were assessed *in situ* under phase contrast microscopy.

**Results:** LPS increased pulmonary artery contraction to U46619 (maximum % reduction in lumen area (mean ± SEM): saline 16±2% n = 5; +LPS 41±11% n = 4; *P* < 0.05). A trend to increased vasoconstriction to ET-1 was also observed (mean ± SEM: saline 27 ± 5% n = 5; +LPS 44 ± 13% n = 6), but reactivity to 5HT was unchanged. *In vivo* LPS exposure did not alter airway responses to the same constrictors.

**Conclusions:** This study demonstrates differential effects of *in vivo* LPS exposure on artery and airway contraction in PCLS. The specific increase in vascular contraction to U46619 was not evident in the airways. The application of this technique has the potential to provide insights into mediators contributing to elevated pulmonary arterial pressure and mechanisms underlying increased reactivity in disease context.

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### DISEASE CHARACTERISTICS OF CHRONIC HYPERSENSITIVITY PNEUMONITIS

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**Introduction:** Hypersensitivity pneumonitis (HP) is a granulomatous interstitial lung disease (ILD) caused by prior sensitisation and repeated exposure to inhaled antigens. It can be difficult to accurately distinguish from other fibrotic ILD including idiopathic pulmonary fibrosis (IPF) and often responds poorly to immunosuppressive therapy.

**Aim:** To assess baseline disease features and survival in patients with HP compared to patients with IPF.

**Methods:** Data from patients attending the RPAH ILD clinic with a consensus multidisciplinary meeting diagnosis of HP or IPF between 2013 and 2017 were analysed. The relationship between clinical parameters and prognosis in these two disease groups were explored.

**Results:** 40 HP and 116 IPF patients were included in the study. HP patients gender 70% female, mean age 66.3 ± 10.6, BMI 31.5 ± 9.5, FVC 71.5 ± 20.9%, DLCO 55.0 ± 17.0%. Features associated with reduced survival included male sex (HR 6.71,  $P = 0.008$ ), and low baseline FVC (HR 0.96,  $P = 0.04$ ) and DLCO (HR 0.95,  $P = 0.03$ ). There were no significant differences in survival between fibrotic and non-fibrotic HP ( $P = 0.075$ ). HP patients had significantly greater survival compared to IPF subset who were not on anti-fibrotic therapy (HR 3.1,  $P = 0.01$ ). Overall, there was no significant difference in survival between HP and IPF patients.

**Conclusion:** In this cohort of patients, baseline disease severity and long term survival between HP and IPF patients were similar despite differences in aetiology and demographics.

### THE AUSTRALASIAN INTERSTITIAL LUNG DISEASE: ANALYSIS OF PHASE ONE

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**Introduction/Aim:** Interstitial Lung Diseases (ILD) are a group of complex lung conditions inflammation and/or fibrosis of the interstitium difficult to study. The Australasian Interstitial Lung Disease Registry (AILDR) aims to provide a uniform platform for collaboration and ultimately lead to better care of our ILD patients.

**Methods:** The AILDR is a secure database for the prospective collection of clinical and demographic information of ILD patients. During the initial pilot phase (2016–8), four Australian specialist ILD referral centres have entered data. Each site has a regular multi-disciplinary team meeting for ILD diagnosis.

**Results:** 869 patients were entered into the AILDR. Of these, 732 (84%) had complete data entry and are included in this study [R, 400 (55%); J, 200(27%), F, 71(10%). The Alfred, 57(8%)]. Mean age was 68.1yrs 356 (48%) were male mean FVC%pred was 83%20% mean DLco%pred 56.17%ean 6MWT distance was 457m120m with mean nadir SpO2 92.29%.

ILD diagnosis was made at ILD in the majority (84%) of patients. Diagnoses included: IPF (n = 209, 33%), CTD-ILD (n = 136, 21%), HP (n = 60, 10%), other IIP (n = 41, 7%), and other ILD (n = 174, 28%). Baseline demographics, physiology and diagnosis were not significantly different across the 4 centres.

**Conclusion:** The AILDR provides a useful tool, both as a repository of data used to guide clinical decisions at a local level and as a means to facilitate collaborative research. The AILDR is now entering its second phase as thirteen additional sites from Australia and New Zealand will begin entering data

**Grant Support:** Lung Foundation Australia the NHMRC Centre of Research Excellence in Pulmonary Fibrosis.

**PERCEPTIONS ON DIAGNOSIS AND MANAGEMENT OF IDIOPATHIC PULMONARY FIBROSIS: EARLY ANALYSIS FROM THE AUSTRALIAN IPF REGISTRY**

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**Introduction/Aim:** Idiopathic pulmonary fibrosis (IPF) is characterised by its insidious and heterogenous disease progression, often delaying diagnosis. In the current era of antifibrotic therapy, we sought to describe the challenges and perception of both IPF patients and their physicians, regarding the management of their disease.

**Methods:** Patients with newly-diagnosed IPF through a multidisciplinary meeting were recruited onto the Australian IPF Registry. Patients were requested to complete a questionnaire capturing information about their individual experiences in the diagnostic process and the management options discussed with their physicians. Physicians involved were also required to complete a questionnaire detailing their experiences on the management of their patients. Statistical analysis was performed using Stata/SE 15.1.

**Results:** To date, we included 58 initial questionnaires completed by patients and their treating physicians. The mean age of patients is 73.7 ± 8.2 years. Most patients were symptomatic with dyspnoea (82%) and cough (78%), although a majority of patients were mild with a WHO functional class I (48.5%) and II (45.5%). Interestingly, there were equal prescription numbers of Pirfenidone (53%) and Nintedanib (47%). 43.5% of patients and 53.5% of physicians believed they had equal input into the choice of antifibrotic prescription. Patients regarded the impact of potential side effects being important in the choice of antifibrotics (80%), followed by their medical comorbidities (40.5%). Similarly, physicians rated both the impact of potential side effects (89%) and other medical comorbidities (53%) to be important factors in the choice of antifibrotic agents prescribed. Overall, 92.5% of patients were satisfied with the care received.

**Conclusion:** In conclusion, this preliminary analysis describes the experiences of both IPF patients and respiratory physicians in an early period of antifibrotic agents and highlights ongoing areas of improvement in the diagnostic and management journey of IPF patients.

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**IDENTIFICATION OF DIFFERENTIALLY EXPRESSED GENES IN LUNG APICES COMPARED TO BASES OF PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS BY RNA SEQ**

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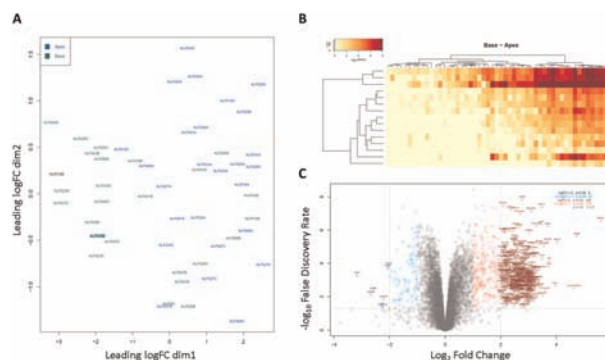
**Introduction/Aim:** Idiopathic pulmonary fibrosis (IPF) is a lethal fibrotic lung condition with an unpredictable disease course. The pathology of IPF starts in the lung bases such that a patient's lung apices are comparatively less fibrotic at the time of transplantation. RNA sequencing of the lung apices and bases may identify novel genes involved in IPF pathogenesis and lead to better therapeutic targets.

**Methods:** High-quality mRNA was collected from resected lung apex and base tissue from 17 patients with IPF. RNA Seq analysis was performed on a total of 52 samples. The expression of known biomarkers relevant to IPF, such as matrix metalloproteinase-7 (MMP7), MUC5B, ACTA2 ( $\alpha$ -smooth muscle actin), CXCL12, and fibulin-1 was assessed. A gene with a Log<sub>2</sub> fold change of greater than 2 was considered differentially expressed (DE).

**Results:** Multidimensional scaling plot analysis showed that samples from lung apices and lung bases clustered separately and 738 genes were DE in lung apices compared to lung bases of patients with IPF (Figure 1). Of these, 693 were upregulated and 95 genes were downregulated. The epithelial genes MMP7 and MUC5B were upregulated in lung bases compared to lung apices. ACTA2, CXCL12 and fibulin-1 were not DE. Expression of markers of epithelial progenitor cells (KRT5, KRT14) and alveolar type I cells (AQP5, AQP3) previously linked to IPF were also upregulated.

**Conclusion:** Gene expression heterogeneity is expected due to the diverse fibrotic processes simultaneously at play in a patient with IPF. Our results demonstrate that the expression profile in lung bases is vastly different to that in regions of the lung apices within the same patient. Genes important in regulating epithelial cell regeneration may provide clues to halting fibrosis. The results of our study suggest that personalised therapeutics may be designed based on the genetic endotypes we describe here.

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**Figure 1. Differentially expressed (DE) genes in lung bases vs lung apices of patients with idiopathic pulmonary fibrosis (IPF)**

RNA Seq was performed on high quality mRNA isolated from explanted lung tissue. (A) Multidimensional scaling plot of samples from lung apices and bases. Principal component analysis was performed on 52 matched samples isolated from explanted lung of 17 patients with IPF. Samples



derived from lung apices (blue) clustered separately from samples derived from lung bases (green). (B) Heat maps show significant upregulation (more red) of genes in lung bases compared to lung apices. (C) Volcano plots indicate more genes were upregulated compared to down-regulated in lung bases compared to lung apices.

#### RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED DOSE-ESCALATION PHASE 1 STUDY OF AEROSOLIZED PIRFENIDONE

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**Introduction/Aim:** This clinical trial evaluated the pharmacokinetics and safety/tolerability of inhaledpirfenidone solution in volunteers and patients with idiopathic pulmonary fibrosis.

**Methods:** Forty-four adults in 6 cohorts consented to receive single doses of a 12.5 mg/mL pirfenidone solution or placebo to assess tolerability and pharmacokinetics. Cohorts 1, 2, and 3 (normal healthy volunteers (NHV)) (n=6 active; n=2 placebo in each cohort) received 25, 50, and 100 mg pirfenidone, respectively. Cohort 4 (NHV) (n=6 all active) received 100 mg of pirfenidone and underwent bronchoalveolar lavage (BAL) to measure epithelial lining fluid pirfenidone concentrations. Cohort 5 (prior or current smokers with greater than 20 pack year use) (n=6 active; n=2 placebo), and Cohort 6 (IPF patients) (n=6 all active), received 100 mg of pirfenidone. All treatments were administered with an Investigational eFlow<sup>®</sup> Nebulizer System; PARI Pharma GmbH. Serial measures of urine and plasma pirfenidone were collected during the 24-hour post dose in all subjects.

**Results:** Administration time ranged from 1.4 to 2 min/ml. No clinically relevant adverse effects on respiratory rate, spirometry, or oxygenation were observed. Drug-related adverse events were predominantly cough, n=8/44 (1 in IPF cohort), all mild, transient and not dose-limiting. Mean plasma pirfenidone C<sub>max</sub> levels in the 25, 50, 100 mg NHV, 100 mg smoker, and IPF cohorts were 202, 292, 802, 1370,1016 and 1026 ng/ml, respectively. BAL cohort estimated ELF C<sub>max</sub> was 135.9±54.5 µg/ml. In the BAL and IPF cohorts, 24-hour urine excretion of pirfenidone and metabolites data suggests similar alveolar deposition.

**Conclusion:** Aerosol pirfenidone was well tolerated in normal volunteers, smokers and IPF patients. High epithelial lining fluid concentrations were achieved in normal healthy volunteers with a 100 mg nebulizer dose. The 100 mg nebulizer dose averaged a 15-fold lower systemic pirfenidone exposure than reported with oral administration of the licensed oral dose.

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### CONTROLLED INHALATION IMPROVES TOTAL AND PERIPHERAL LUNG DEPOSITION IN CF

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**Introduction/Aim:** Inhaled therapies are used extensively in the treatment of patients with cystic fibrosis (CF). With progressive impairment of lung function, aerosol deposition of inhaled drug occurs more centrally in the lung. The aim of this study was to determine whether slow, prolonged inhalations with a dosimetric nebuliser might improve penetration of drug aerosol into the peripheral lung areas.

**Methods:** A comparison of two inhalation modes was undertaken in 5 subjects with moderately severe CF lung disease (aged 12-18 years; FEV<sub>1</sub> 63-80%) in a crossover study. The pattern of aerosol distribution was compared using a) long (6-8 seconds) slow inhalations with the dosimetric AKITA delivery system with Pari LC Sprint nebuliser, and b) tidal breathing with a standard Pari LC Sprint nebuliser and compressor. Distribution and total aerosol dose deposited corrected for attenuation was obtained using gamma scintigraphy.

**Results:** Slow, prolonged inhalation with the AKITA was associated with a higher proportion of the delivered dose depositing in the lungs (74.5%), when compared to tidal breathing (32.1%) with significantly less upper airway deposition with the AKITA. The mean peripheral to central deposition ratios for the 5 subjects were long slow breath 2.16 vs tidal breathing 2.13 ( $P = 0.90$ ).

**Conclusion:** Given that the increased lung dose achieved with long slow inhalation is likely to contain a disproportionate amount of larger droplets that are likely to be deposited centrally, particularly in the presence of significant lung disease, the data supports the suggestion that a greater proportion of the finer droplets reach the periphery of the lungs. Hence total lung dose and peripheral dose are increased by controlling the inspiratory profile.

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### RISK SCORE TO PREDICT LIFE THREATENING ASTHMA IN CHILDREN

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**Introduction/Aim:** Despite advances in asthma management, children still die from asthma attacks. Preventing asthma-specific severe morbidity and mortality depends on early and proper identification, follow up and management of high-risk patients. The aim of this study was to develop and validate a risk prediction algorithm for identifying children at risk of developing life-threatening asthma (LTA).

**Methods:** LTA was defined as an asthma attack requiring intensive care unit (ICU) admission. We conducted a retrospective record review of all children 2-17 years old, who were admitted to the ICU (cases) and general ward (comparison group) at Sydney Children's Hospital between 2011-2016 with a primary diagnosis of asthma. All eligible children were randomly divided into a development and validation cohort. The regression coefficient of each independent predictor variable associated with LTA derived from the development cohort was used to estimate each child's risk of developing LTA in the validation cohort. Predictive performance of the risk score was evaluated by the area under the receiver operating characteristic curve (AUROC) and Hosmer-Lemeshow goodness-of-fit test.

**Results:** 1171 children were included: 586 and 585 in the development and validation cohort respectively. Regression coefficients from significant predictor variables derived from development, including age (OR = 1.1, 95%CI 1.0-1.2,  $\beta = 0.1$ ), socioeconomic status (lowest SES OR = 6.4, 95%CI 1.9-21.7,  $\beta = 1.9$ ; highest SES OR = 1.6, 95%CI 0.8-3.0,  $\beta = 0.4$ ), a family history of asthma/atopy (OR = 2.3, 95%CI 1.3-4.4,  $\beta = 0.9$ ), and previous asthma hospitalisations (1-3 hospitalisations OR = 2.1, 95%CI 1.1-3.9,  $\beta = 0.7$ ;  $\geq 4$  hospitalisations OR = 16.1, 95%CI 7.2-36.1,  $\beta = 2.8$ ), were used to develop a risk score for the validation cohort. Internal validation gave an AUROC of 0.759 (sensitivity = 55.7%; specificity = 89.5%).

**Conclusion:** The risk algorithm generated from our study can be used to develop a user-friendly risk tool which may help in early identification of children at risk of developing LTA and improve clinical decision making.

**Grant Support:** This work was funded by Rotary Club of Sydney Cove.

**Declaration of Interest:** No conflict of interest was identified.

### COMPARISON OF IN-HOSPITAL AND HITH-BASED TREATMENT OF RESPIRATORY EXACERBATIONS IN CHILDREN WITH BRONCHIECTASIS

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**Introduction/Aim:** Children with bronchiectasis have recurrent exacerbations and many require hospitalisation. 'Hospital in the home (HITH)' is used as an alternative to hospitalisation for children with Cystic-Fibrosis (CF) but to date, there is little data in those without CF. Thus, we describe our experience of HITH in a cohort of children with bronchiectasis comparing outcomes between hospital- and HITH-based pathways.

**Methods:** Medical records were retrospectively reviewed in children with bronchiectasis without CF who were hospitalised at our centre from January-2017 to June-2018. Children spending more than half of their total IV antibiotic course duration on HITH were categorized as the **HITH** group. We assessed duration of treatment, symptom resolution, use of oral antibiotics after intravenous therapy, adverse events and time to next exacerbation.

**Results:** We analyzed 54 exacerbations (HITH n = 38, 70%) in 46 children [median age = 4.5 (IQR 2-10.25) years; females = 26, Indigenous = 6, *Pseudomonas aeruginosa* infection = 8]. Mean (SD) IV antibiotic therapy was for 14.9 (2.7) days. There was no difference in duration of treatment between the HITH [median = 14 (IQR 14-16.25) days] vs. hospital groups [14 (14-14); *P* = 0.65]. 21/38 (55.2%) children in the HITH group had symptom resolution at end of IV treatment compared to 10/16 (62.5%) in the hospital group; *P* = 0.62 with 26% children in the HITH group discharged on oral antibiotics compared to 47% of the hospital group; *P* = 0.13. There was no difference in time to next exacerbation between groups [HITH median = 12 (7-15.75) weeks, hospital = 9 (6-24)]. No differences in any adverse events were seen between the two groups. Over the same study period, HITH was used in a small minority in those with CF (<20% of total admissions).

**Conclusions:** A high proportion of pulmonary exacerbations in children with bronchiectasis requiring IV antibiotics are being managed by HITH. The equivalence of HITH to in-hospital based therapy would remain conjectural until prospective studies are undertaken. The disparity between children with and without CF requires further attention.

**Grant Support:** None.

**Declaration of Interest:** No conflicts of interest.

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This abstract has been withdrawn.

### CARDIORESPIRATORY RESPONSES TO EXERCISE IN CHILDREN WITH AIRWAY OBSTRUCTION

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**Introduction:** Although widely used, peak aerobic capacity (VO<sub>2</sub>) poorly discriminates between respiratory diseases in childhood. Other cardiorespiratory measures during exercise may discriminate between obstructive diseases. The aim of this study is to evaluate and compare cardiorespiratory responses to exercise in healthy children with obstructive respiratory disease.

**Methods:** A retrospective descriptive analysis of cardiorespiratory measures during incremental exercise tests in healthy children (n = 36), untreated exercise induced asthma (EIA) (n = 18), persistent asthma controlled with ICS (n = 42), persistent asthma controlled with LABA/ ICS (n = 34) and exercise induced laryngeal obstruction (EILO) (n = 14) was performed.

**Results:** Mean age of children- 13.4 (2.4) years

	Healthy (n = 36)	EILO (n = 14)	EIA (n = 18)	ICS (n = 42)	ICS/LABA (n = 34)
VO <sub>2</sub> (mL/kg/min)	38.4 (6.0)	36.7 (9.0)	34.1 (10.3)	37.5 (7.3)	38.1 (7.8)
FEV1 (z score rest)	-0.2 (0.1)	-0.2 (0.1)	-0.1 (0.1)	-0.3 (0.1)	-0.2 (0.1)
Ti/Ttot peak	0.52 (0.07)	0.64 (0.11)*	0.36 (0.08)*	0.47 (0.09)	0.51(0.10)
FV loop	N	Abn Inspiration	Abn Expiration	N	N
Vtpeak/ Vt rest	2.2	0.7*	1.6	1.8	2.3
VE/MVV peak	67 (4)	69 (3)	89 (6)*	68 (4)	71 (7)
Ve/VO2 slope	33.2 (4.1)	34.1 (4.9)	39.4 (6.1)*	33.8 (5.3)	37.9 (5.6)*
HR25%	120 (8)	127 (10)	122 (6)	118 (5)	136 (6)*
HR100%	194 (7)	184 (8)	188 (7)	191 (6)	194 (8)
VO2/HR peak	15.2 (2.7)	14.6 (3.5)	11.1 (5.5)*	14.8 (4.3)	14.9 (4.5)
OUEP	43 (4)	41 (5)	24 (6)*	40 (4)	31(5)*

\**P* < 0.05 Student *t* test

**Conclusion:** Cardiorespiratory measures during exercise may be useful in discriminating between obstructive respiratory diseases in childhood and may be better outcome measures to assess clinical response to therapy than peak VO<sub>2</sub>.

**Grant Support:** •

### COMPLIANCE TO RESPIRATORY CARE GUIDELINES FOR CHILDREN WITH NEUROMUSCULAR DISEASE AT SYDNEY CHILDREN'S HOSPITAL

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**Introduction:** The British Thoracic Society (BTS) published a guideline for the respiratory management of children with neuromuscular weakness in 2012. Our aim was to determine whether the respiratory care provided by the Sydney Children's Hospital (SCH) multidisciplinary neuromuscular clinic is compliant with BTS recommendations.

**Methods:** A retrospective electronic and paper medical chart review of patients seen by the neuromuscular clinic at SCH from January 2016 to December 2017 was conducted. The primary outcome measure was compliance to adapted BTS guideline criteria over 2 calendar years.

**Results:** A total of 190 patients were reviewed, median age 11.5 years (IQR: 6.50–15.5). Compliance to the adapted BTS criteria for our cohort varied from 36% to 87.5%. Less than half (40.5%) of the cohort was seen by a respiratory specialist at least once over the 2 years, and only 51.6% of patients aged  $\geq 5$  years had lung function testing. 87.5% of patients with  $\geq 3$  lower respiratory tract infections (LRTI) per year were prescribed airway clearance, and 87.5% of patients with FVC  $< 60\%$  predicted underwent at least one sleep study. Significantly higher proportions of patients with spinal muscular atrophy (SMA, 60%) and Duchenne muscular dystrophy (DMD, 65.9%), were reviewed by a respiratory specialist ( $P < 0.0001$ ). Patients who were reviewed by a respiratory specialist were more likely to be non-ambulatory, have  $\geq 3$  LRTI per year, have airway clearance therapy prescribed, have lower vital capacity, and on positive airway pressure support.

**Conclusion:** Compliance to the BTS respiratory management guideline was suboptimal.

**Key Words:** Neuromuscular disease, clinical guideline, respiratory care

**Declaration of Interest Statement:** Nil.

**Table 1:** Summary of compliance to the BTS respiratory management guideline at SCH.

Care component	Proportion of patients meeting guideline recommendation		
	Total (n = 190)	SMA (n = 20)	DMD (n = 44)
Assessment by a respiratory physician	77/190 (40.5)	12/20 (60.0)	29/44 (65.9)
Assessment of lung function			
• Vital capacity in children aged $\geq 5$ years	82/159 (51.6)	8/10 (80.0)	33/39 (84.6)
• Cough peak flow aged $\geq 12$ years	40/90 (44.4)	2/4 (50.0)	15/22 (68.2)
Airway clearance education for patients with:			
• Cough peak flow $< 270$ litres/min	10/18 (55.6)	1/1 (100)	7/9 (77.8)
• $\geq 3$ episodes of LRTI per year	7/8 (87.5)	2/2 (100)	1/1 (100)
At least one sleep study in the following groups of patients:			
• FVC $< 60\%$ predicted	14/16 (87.5)	2/2 (100)	5/7 (71.4)
• Non-ambulatory due to progressive muscle weakness or never attain the ability to walk	37/84 (44.0)	7/19 (36.8)	17/38 (44.7)
• Have symptoms of OSA or hypoventilation	19/40 (47.5)	2/6 (33.3)	7/15 (46.7)
• $\geq 3$ episodes of LRTI per year	5/8 (62.5)	1/2 (50.0)	0/1 (0)
Titration study no less than annually in:			
• Patients established on non-invasive ventilation	9/25 (36.0)	2/4 (50.0)	3/7 (42.9)

### DAY-TO-DAY VARIABILITY IN HOME-BASED FORCED OSCILLATION TECHNIQUE PARAMETERS CORRELATES WITH ASTHMA CONTROL AND EXACERBATION BURDEN IN PAEDIATRIC ASTHMA SUBJECTS

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**Introduction:** Forced Oscillation Technique (FOT) offers exciting potential as a monitoring tool in asthma, given its effort-independent nature as a tidal breathing measure of lung mechanics assessing airway calibre and lung stiffness (respiratory system resistance, Rrs, and reactance, Xrs). In pilot data (Robinson et al., Chest 2014) day-to-day variability in FOT parameters, measured in school children in an asthma camp setting over one week, differentiated asthma severity and levels of asthma control. This study explores home-based utility over an extended period.

**Aims:** To determine whether extended home-based, parent-supervised FOT monitoring (day-to-day variability in Rrs and Xrs) reflects asthma control and exacerbation burden in paediatric subjects.

**Methods:** Persistent asthmatics (8-18 years,  $\geq 2$  asthma exacerbations in last 12 months) were recruited from CHW asthma clinic (n = 25). After training, FOT (tremoFlo™, Thorasys Ltd) was collected daily with parent supervision for 4 months, supplemented by asthma questionnaires (daily symptom, weekly ACQ and monthly ACT and AQLQ) and medication adherence (SmartInhalers™, Adherium). Linear regression analysis examined correlation of Rrs and Xrs day-to-day variability (CoV across monitoring period) and asthma control (mean ACQ, ACT and AQLQ score) and exacerbations (%exacerbation days, total n).

**Results:** 25 subjects (mean  $\pm$  SD age 13.3  $\pm$  2.5 years, baseline FEV<sub>1</sub> 92.5  $\pm$  16.7% predicted) with 20 completed monitoring periods to date (mean  $\pm$  SD 116.8  $\pm$  21.4 days, 81.5  $\pm$  13.1% days acceptable FOT data). Rrs CoV significantly correlated with ACQ ( $r^2 = 0.25$ ,  $P = 0.024$ ) and trended toward significance with ACT ( $r^2 = 0.17$ ,  $P = 0.077$ ). A trend toward significance was observed between Xrs CoV and ACQ ( $r^2 = 0.17$ ,  $P = 0.071$ ). Total exacerbations (3.1  $\pm$  2.3) correlated with Rrs CoV ( $r^2 = 0.35$ ,  $P = 0.006$ ) and Xrs CoV ( $r^2 = 0.25$ ,  $P = 0.024$ ). %Exacerbation days (23.0  $\pm$  17.7%) correlated with Rrs CoV ( $r^2 = 0.20$ ,  $P = 0.049$ ).

**Conclusion:** Home-based paediatric day-to-day FOT parameter variability correlated with asthma control and exacerbation. These findings support future studies to define clinical utility of this monitoring strategy.

**Grant Support:** Sydney Medical School Foundation and Asthma Foundation (Ross Trust)

### LONGITUDINAL UTILITY OF PERIPHERAL AIRWAY FUNCTION TESTS IN PULMONARY GRAFT VS. HOST DISEASE IN PAEDIATRIC BONE MARROW TRANSPLANT PATIENTS

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**Introduction:** Pulmonary graft versus host disease is a pathological process arising in peripheral airways causing significant morbidity and mortality post-Bone Marrow Transplantation (BMT). Current screening and diagnosis focuses on spirometry change from baseline to identify Bronchiolitis Obliterans Syndrome (BOS), and an at-risk pre-BOS stage BOS0p ( $\geq 10\%$  fall FEV<sub>1</sub>). Sensitive peripheral airway function tools exist but remain under-utilised and utility is unclear.

**Aim:** To investigate longitudinal peripheral airway function change, detected by Multiple Breath Washout (MBW) and Forced Oscillation Technique (FOT), in paediatric BMT subjects with/without BOS and BOS0p.

**Methods:** Children aged  $\geq 3$  years were recruited. Testing occurred at baseline, monthly during 1<sup>st</sup> year and 6-monthly to 3yrs: MBW (LCI, S<sub>cond</sub> and S<sub>acin</sub>, Exhalys<sup>®</sup>, Ecomedics), FOT (R<sub>rs</sub> and X<sub>rs</sub> at 5Hz, AX, F<sub>res</sub>, tremoFlo<sup>®</sup>, Thorasys) and, if feasible, spirometry, plethysmography and DLCO. Groups (BOS, BOS0p, unaffected) compared at baseline, 12, 24 and 36 months.

**Results:** Of 24 recruited subjects (mean  $\pm$  SD (range) age 10.2  $\pm$  4.2 (3.3-18.1) years at BMT, 54% AML/ALL diagnosis, 71% male), 1 withdrew and 6 died (5 within 12 months). BOS and BOS0p alone were detected in 3 (12.5%) and 8 (33.3%), respectively. BOS was associated with pattern of marked abnormality, significant increases from baseline were observed in LCI, S<sub>cond</sub>, S<sub>acin</sub>, X<sub>rs</sub>, AX and F<sub>res</sub>. One subject developed BOS3 at 105 days (1<sup>st</sup> feasible post-BMT test). MBW/FOT abnormality was detected 26 and 207 days prior to BOS $\geq 1$  in other cases. LCI trajectory increased with increasing BOS severity. At 3 years, statistically significant differences between BOS0p vs unaffected were observed for LCI ( $P = 0.009$ ), S<sub>acin</sub> ( $P = 0.03$ ), X<sub>rs</sub> ( $P = 0.004$ ) and approached significance for AX ( $P = 0.09$ ) and F<sub>res</sub> ( $P = 0.09$ ).

**Conclusion:** BOS and its earlier at-risk stage BOS0p were associated with significant peripheral airway abnormality detectable on MBW and FOT. MBW and FOT abnormality predated BOS $\geq 1$  in 2/3 BOS cases.

**Grant Support:** Robert Maple Brown Research establishment fellowship (RACP).

### MANAGING AND WEANING HOME OXYGEN IN CHRONIC NEONATAL LUNG DISEASE

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**Introduction/Aim:** In 2005, Australia and Queensland had 20127 and 7670 patients respectively on home oxygen with chronic neonatal lung disease (CNLD) being the most common paediatric indication. No consensus guidelines exist for weaning home oxygen in CNLD including overnight oximetry interpretation. We aim to describe our approach and outcomes to managing home oxygen in CNLD.

**Methods:** A retrospective review of all overnight oximetries for infants under 2 years old with primary diagnosis of CNLD received by the Paediatric Respiratory and Sleep Department over a 12 month period.

**Results:** 191 overnight oximetry studies from 79 infants were identified within a 12 month period. 47 infants were weaned off oxygen at a median 24 weeks (IQR 18) post-menstrual age. Median PaCO<sub>2</sub> at term corrected age was 52 (IQR 9). Specific follow-up findings are outline in table 1.

**Conclusion:** Overnight oximetry is used extensively to guide home oxygen weaning despite the limited evidence for interpretation of oximetry studies in this population. Most studies were undertaken at home suggesting that this is a valid method of monitoring infants. There was a highly varied follow-up frequency and oximetry evaluation post-hospital discharge. Preliminary analyses have not shown any specific patient or oximetry parameters that can reliably predict timing of successful home oxygen wean. Further data analysis is underway and key findings to be presented.

Table 1. Preliminary overnight oximetry follow-up data

Corrected gestational age (weeks)	0-6	7-16	17-32
Hospital oximetry	45	10	9
Home oximetry	8	51	46
*Mean SpO <sub>2</sub>	99.15% (0.8)	98.2% (1.3)	97.8% (1.7)
*Mean HR	147 (17)	124 (11)	116 (12)
*Time < 90%	0.85% (1.4)	0.6% (1)	0.35% (0.8)
*Time $\geq 94\%$	98.4% (2.23)	98.1% (2.3)	98.6% (2.8)
*Oxygen (mL/min)	162.5 (250)	0 (200)	0 (0)
*Weight (kg)	3.54 (1)	5.57 (1)	6.99 (1)
*Length (cm)	50 (4)	58.1 (5)	64.7 (4)

\*Values expressed as median (interquartile range)

HR = heart rate; PMA = post-menstrual age; SpO<sub>2</sub> = oxygen saturation

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**CASE STUDY: USE OF THE HIGH FREQUENCY CHEST WALL OSCILLATION (HFCWO) TO SUPPORT AIRWAY CLEARANCE IN A CHILD WITH SMA 1 (SPINAL MUSCULAR ATROPHY)**

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**Introduction/Aim:** SMA 1 is a neuromuscular disease(NMD) that leads to significant respiratory failure in infancy. A 5yr old girl with SMA 1 was admitted to PICU with probable aspiration having progressed from overnight nasal non-invasive ventilation 16/4 to continuous via full face-mask 18/4. She had right middle/lower lobe collapse/consolidation, an oxygen requirement and showed minimal improvement despite antibiotics and intensive physiotherapy 6 x day.

The aim of physiotherapy was to find a child and family centred intervention that was safe, effective yet sustainable.

**Method:** Physiotherapy included manual techniques, assisted cough with cough assist device (Nippy Clearway) and suction. Day 5 she rapidly declined and oxygen demand escalated from FiO<sub>2</sub> 0.5 to 1.0, heart rate(HR) 160, respiratory rate(RR) 60, SpO<sub>2</sub> >88%, P<sub>c</sub>CO<sub>2</sub> 34mmHg.

A decision was made to trial HFCWO (The Vest<sup>®</sup>) in an attempt to avoid intubation. HFCWO uses an inflatable jacket that compresses the chest wall producing oscillations to facilitate secretion movement proximally. It was also postulated it could improve expiratory flow rates by mimicking chest wall strapping. To prevent airway collapse during HFCWO, IPAP was increased during treatment and combined with cough assist device and suction.

**Results:** The treatment with HFCWO was well tolerated with a reduction in reported treatment associated pain, significant sputum clearance demonstrated, including a large mucus plug. Following treatment FiO<sub>2</sub> reduced to 0.4, HR 140 and RR 28. Over the following days and right sided CXR changes resolved and NIV weaned to home setting in air prior to discharge to Post Acute Care Physiotherapy service.

**Conclusion:** Due to the successful outcomes with The Vest<sup>®</sup> the family have continued to use it as part of her physiotherapy management at home. The patient has had no unplanned admissions to hospital in the year since discharge home with a Respiratory Physio Action plan including HFCWO.

**Key Words:** Neuromuscular, SMA, HFCWO, non-invasive ventilation, Physiotherapy, Discharge, Hospital Avoidance

**"POWERFUL MESSAGE": HEALTHCARE PROFESSIONALS' RESPONSES UPON VIEWING PATIENTS' ASTHMA DRAWINGS**

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**Introduction/Aim:** Patient drawings of their illness have provided rich understandings of their personal experiences. It is not uncommon for patients and healthcare professionals (HCPs) to have contrasting views about health and illness. These differences can influence communication, rapport, treatment and health outcomes. Our study explored this alignment of perspectives by asking HCPs to view and respond to patients' drawings and accounts of their experience of asthma.

**Methods:** HCPs were shown drawings made by adult patients about their personal experiences of asthma. They were invited to share their views and impressions of the drawings. A thematic inductive approach was used to analyse the data.

**Results:** Twenty-three HCPs from a range of professions participated in the study. The patients' previously drawn expressions served as a prompt in engaging the HCPs in perceptive contemplation regarding their expectations of the general illness experience of asthma and the associated clinical implications. Three themes emerged from the analysis: (1) revisiting expectations, (2) acknowledgment and empathy, and (3) clinical reflexivity. Upon seeing the patients' drawings, most of the HCPs' immediate reaction was one of *surprise*. They did not expect portrayals of the psychological and social burden asthma placed on patients. Although they recognised that fear of asthma could be a logical feeling for patients, they thought patients' expression of this fear was something often overlooked in consultations. The drawings, the HCPs felt, had allowed them a deeper understanding of patients' concerns.

**Conclusion:** Our findings provide support for the use of patients' drawings in bringing HCPs closer to the patient lived experience. The drawings fostered deeper insight on patient perspectives of asthma and stimulated critical reflection on current healthcare practices. As such, patients' drawings have potential applications in continuing professional development and university education in health.

**Grant Support:** Australian Government Research Training Program stipend, Asthma Australia Mickie Hardy PhD scholarship

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### MATERNAL CIGARETTE SMOKE-EXPOSURE AFFECTS LUNG FUNCTION OF OFFSPRING AND GRAND-OFFSPRING

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**Introduction/Aim:** Cigarette smoking (CS) results in a range of lung diseases including cancer, COPD, asthmatic exacerbations and susceptibility to respiratory infections. Smoking is highly prevalent amongst pregnant women in Australia (12%) with a high proportion (36.7%) of pregnant smokers being teenagers. CS during pregnancy leads to numerous detrimental effects on the offspring, including low birth weight, and impaired lung development. We aim to investigate how maternal smoking affects the first, second and third generation's lung function outcomes.

**Methods:** We use a murine nose-only CS-exposure model to recapitulate the effects of maternal CS during pregnancy. Control animals were exposed to air. We evaluated the early-life and adult offspring's, and grand-offspring's baseline spirometry. Lung pathology was assessed by histological analysis, and whole lung gene expression of lung development quantified by RT-qPCR.

**Results:** Neonatal inspiratory capacities are severely reduced in pups born to mothers who had smoked ( $0.065 \pm 0.003$ ,  $n = 13$  smoke vs  $0.083 \pm 0.006$ ,  $n = 14$  air;  $P < 0.05$ ; mean  $\pm$  SEM). Altered lung function is also observed in adult mice born to mothers who were smoked during pregnancy; with reduced inspiratory capacity ( $0.405 \pm 0.023$  smoke vs  $0.525 \pm 0.007$  air;  $P < 0.01$ ) and total lung capacity ( $0.405 \pm 0.023$  smoke vs  $0.525 \pm 0.007$  air;  $P < 0.01$ ). Increased transpulmonary resistance ( $0.622 \pm 0.042$  smoke vs  $0.482 \pm 0.015$  air;  $P < 0.05$ ) and alveolar diameter ( $27.61 \pm 0.367$  smoke vs  $25.62 \pm 1.4$  air;  $P < 0.05$ ) was also observed in these mice. These effects were also observed in the second generation of offspring. However, at the third generation these affects were abated.

**Conclusion:** These results highlight that smoking during pregnancy affects the lung development of offspring, and grand-offspring. We can use this model as a platform to study the immunological/physiological mechanisms responsible for causing changes in lung function throughout the generations. This model can also be used to investigate the mechanisms that lead to increased susceptibility to respiratory virus infections and asthma in offspring of mothers who smoke.

**Grant Support:** NHMRC

### PATIENTS' PERSPECTIVES ON THE USE OF A PULSE OXIMETER AT HOME

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**Introduction/Aim:** Home pulse oximetry is commonly used by patients with respiratory disorders. We explored patients' experiences with these devices.

**Methods:** Participants using a pulse oximeter at home were recruited. They completed a structured survey exploring: knowledge about their device; usage patterns; and how results impacted on self-management.

**Results:** Thirty participants (mean age 71 years; 16 females) were recruited. Diagnoses included airways disease (60%), interstitial lung disease (10%), pulmonary hypertension (10%), lung cancer (6.7%) and mixed disease (13.3%). Eighty-three percent of participants used home oxygen therapy. Pulse oximeters were purchased online (46.7%), from a pharmacist (40%), medical equipment store (6.67%), clinic/hospital (3.3%), or an oxygen supplier (3.3%). Use was self-initiated in 56.7%, or recommended by family (13.4%), respiratory nurse (6.7%), doctor (6.7%), exercise physiologist (3.3%), another patient (3.3%), hospital/clinic (3.3%), respiratory laboratory (3.3%), or pulmonary rehabilitation (3.3%). Sixty percent of participants used the oximeter daily. Ninety percent of participants were confident in interpreting the oximeter reading, although 20% felt they needed further education. Participants learnt how to interpret a pulse oximeter reading from medical professionals, pulmonary rehabilitation, the internet and through inpatient experiences. Participants (90%) often adjusted their activity levels or management, including through titrating oxygen flow rates, according to their oximetry reading. When readings were low, some participants reduced their activity levels, while others used different pharmacologic or non-pharmacologic strategies, including increased oxygen flow rates, opiates and deep breathing exercises. The majority of participants reported that using a pulse oximeter at home was helpful in judging their physical limitations, and provided reassurance and confidence in their disease management.

**Conclusions:** These patients appeared confident in their home use of pulse oximeters. Health professionals should identify patients who use a pulse oximeter at home, and ensure that they are able to interpret the readings and, if appropriate, adjust management safely.

**Grant Support:** We hereby declare that we have no pecuniary or other personal interest, direct or indirect, in any matter that raises or may raise a conflict with our role in conducting this research project. This research project was funded by IBAS (Institute for Breathing & Sleep)

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### NON-INVASIVE POSITIVE PRESSURE VENTILATION DURING EXERCISE IN EXCESSIVE DYNAMIC AIRWAY COLLAPSE AND VOCAL CORD DYSFUNCTION: TWO CASE STUDIES

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**Introduction/Aim:** Non-invasive positive pressure ventilation (NIPPV) has been shown to reduce work of breathing and dyspnoea in chronic respiratory disease populations which in turn can increase their exercise tolerance. In the pulmonary rehabilitation context, we utilized NIPPV with two clients whose breathlessness could be largely attributed to a physiological airway obstruction.

**Methods:** Two retrospective case studies. Mr M, a 46-year-old male with severe excessive dynamic airway collapse (EDAC) completed exercise during pulmonary rehabilitation on CPAP 20cmH<sub>2</sub>O initially and then BiPAP. Case study 2, Mrs P an 86-year-old female with left vocal cord paralysis exercised on CPAP 9cmH<sub>2</sub>O.

**Results:** Mr M's initial six-minute walk test (6MWT) unaided on room air resulted in unremitting shortness of breath (>20min recovery required). His repeat six-minute walk test on CPAP 20cmH<sub>2</sub>O although less in distance, resulted in less breathlessness as reported on the Borg scale and required only five minutes of recovery. Post completing pulmonary rehabilitation on NIPPV, Mr M 6MWT distance on room air was 632m (+121 meters). His St George Quality of Life Score improved by 7.1 points.

Mrs P's initial 6MWT distance: 87 m on room air and was limited by dyspnoea (Borg 5). Initial 6MWT distance on CPAP 9 cmH<sub>2</sub>O: 113m (Borg 3). Mrs P completed centre based exercise 1x week and home-based exercises both on CPAP 9 cmH<sub>2</sub>O for 10 weeks. Mrs P. post exercise 6MWT distance on CPAP 9 cmH<sub>2</sub>O: 214 m (+22 m). Her St George Quality of Life score improved by 12.3 points.

**Conclusion:** For EDAC and vocal cord palsy, NIPPV was an effective adjunct tool to manage dyspnoea and assisted these clients to exercise sufficiently that after 8-10 weeks, improvements were observed in both their endurance capacity (walk distance) and quality of life.

**Grant Support:** Nil.

### LIMITED IMPACTS OF LONG-TERM, MILD EXPOSURE TO E-CIGARETTE AEROSOLS IN ADULT MICE

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**Introduction/Aim:** Electronic nicotine delivery systems (ENDS) heat and aerosolise a liquid for inhalation. Due to their relatively recent introduction into widespread use, the health effects of ENDS have not been extensively studied. We have previously shown that ENDS aerosols from glycerin-based excipients cause functional impairments in juvenile mice akin to cigarette smoking. The aim of this study was to investigate the effects of long-term ENDS aerosol exposure in adult mice. Secondary aims were to compare the effects of ENDS aerosols with/without nicotine and with/without flavouring.

**Methods:** Adult (8week old) male and female BALB/c mice (n = 24/treatment) were exposed to ENDS aerosols for 1hour/day, 5days/week for 8 weeks. Aerosols varied based on excipient (propylene glycol vs glycerin), nicotine content (0 mg/mL vs 18 mg/mL) and flavour presence/absence. "Control" groups were exposed to medical air or cigarette smoke for the same duration. Lung volume, function and responsiveness to methacholine were measured using plethysmography and the forced oscillation technique. Bronchoalveolar lavage was assessed for cellular inflammation via microscopy.

**Results:** ENDS aerosols did not increase BAL inflammation, although cigarette smoke exposure increased total cells in BAL by ~45% compared with Air controls. ENDS aerosol exposure had limited effects on lung volume, function or responsiveness to methacholine regardless of nicotine content or flavour. Responses were similar to Air controls. Cigarette smoke exposure for the same period had greater impacts on these parameters.

**Conclusion:** Mild exposure to ENDS aerosols over a period of 8 weeks did not elicit significant changes in lung volume, function or inflammation in adult mice. At this dosing regime, only cigarette smoke exposure resulted in any negative health impacts, and even these were relatively minor. Our results suggest that the adult lung may be more resilient to the effects of ENDS aerosols, compared with the developing lung.

**Grant Support:** NHMRC Project Grant 1128231.



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#### AUDIT OF LONG TERM OXYGEN THERAPY RELATED SEVERE ADVERSE OUTCOMES

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**Introduction/Aim:** Long term oxygen therapy (LTOT) has mortality and morbidity benefits in patients with chronic hypoxemia including but not limited to chronic obstructive lung disease (COPD) and heart failure. However, there is a paucity of data on the potential harms that may be associated with LTOT. Previous overseas case series have reported instances of burns to LTOT users and their co-inhabitants, falls, nasal irritation and epistaxis, contact dermatitis as well as psychological burden. The aim of this study was to evaluate the incidence of LTOT related adverse outcomes especially burns for patients in our health service.

**Methods:** Patients prescribed LTOT through the Gold Coast Hospital and Health Service between 1<sup>st</sup> January 2014 and 31<sup>st</sup> December 2017 were considered for this study. Their progress during the period of 1<sup>st</sup> January 2014 to 30<sup>th</sup> June 2018 was retrospectively reviewed using electronic medical records to assess for any need for inpatient admission. Inpatient admission notes were screened for the following outcomes: burns and physical injuries attributable to LTOT, any falls requiring admission, any inpatient psychiatric admissions.

**Results:** 291 patients (136 male, 155 female) had been prescribed LTOT during the study period. The predominant indications for LTOT were COPD (167 patients), ILD (52 patients), lung cancer (20 patients) and heart failure (5 patients). 31 LTOT users admitted to smoke cigarettes while concurrently on LTOT. 4 patients required admission due to LTOT related adverse events. 3 admissions were related to falls, with one admission being complicated by calcaneal fracture. One admission was a result of a patient's power outage at home.

**Conclusion:** Inpatient admission was an infrequent complication of LTOT use. Despite ongoing smoking by some users, no patients had sustained burns. 3 out of 4 hospitalisations were for falls and its related complications.

**Grant Support:** •

#### GENERAL PRACTITIONER AND NEXT OF KIN DETAILS: A SINGLE DAY AUDIT

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**Introduction/Aim:** Communicating with patients' general practitioners (GP) and next of kin (NOK) is important for comprehensive care. We aimed to document the accuracy of GP/NOK details.

**Methods:** All patients admitted to a respiratory ward on 9<sup>th</sup> March 2018 under Respiratory Medicine were asked to nominate their GP and NOK. We cross-referenced the patient's nominated GP, GP practice, address, phone and fax numbers with records on Powerchart and Isofit patient manager (iPM).

If practice name, address and contact number were available, this was recorded as complete. When details were incomplete, we undertook a simple internet search using available data. If missing information was found, this was recorded as complete. NOK name and contact number were judged as correct if they were concordant with iPM. Discordant or missing details were recorded as incomplete. Post hoc, we compared accuracy of GP details to admission method (via emergency or direct admission).

**Results:** 22 patients were recruited. iPM performed better with GP details available for 13 patients (59.1%) and GP phone number available for 5 patients (22.7%). Only one patient (4.5%) had a recorded GP fax number. Powerchart had GP details available for 5 patients (22.7%) and GP phone number available for 2 patients (9.1%). No GP fax numbers were recorded. NOK contact number was only available in iPM and was generally accurate (19 patients, 86.4%). Direct admissions had 100% of GP details recorded compared to 50% for ED admissions.

**Conclusion:** Correct, complete GP details were frequently unavailable. Despite combining available details with simple internet searching, GP details were unavailable for 40.9% of patients. NOK details were usually accurate. Recent changes linking iPM to Powerchart should improve data availability. Systems changes are needed to ensure GP details are accurately recorded regardless of route of admission.

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**EMPHYEMA THORACIS IN FAR NORTH QUEENSLAND****BASHFORD J<sup>1</sup>**, SIMPSON G<sup>2</sup><sup>1</sup>Cairns Hospital, Cairns, Australia, <sup>2</sup>Cairns Hospital, Cairns, Australia

**Introduction/Aim:** To audit the epidemiology, patient characteristics, treatment and outcomes of adult patients treated for pleural emphyema at Cairns Base Hospital between July 2015 to July 2018.

**Methods:** Patients were identified by clinical coding for admissions during the stated period. A retrospective case note review was performed.

**Results:** 50 cases were identified, giving an incidence of per 6 per 100,000. 34 patients were male; 14 female. Median Age was 50 years (20-95 years) with a bimodal distribution consistent with previous studies. 20 percent of patients were of indigenous or Torres Strait Islander heritage. All patients included had diagnostic pleural fluid findings. Clinical features were variable, with the most consistent features being pleurisy and raised serum inflammatory markers. Causative organism was identified in 28% of patients with the commonest organism being Streptococci. 20 of the patients had originally been seen at peripheral hospitals, and 19 by non-thoracic medical teams at Cairns Hospital and these patients had later identification of their emphyemas. 39 patients received intrapleural alteplase and DNAase.

There were three deaths. Eight patients required surgical intervention, with the majority of these patients being treated in the earlier period of the study.

**Conclusion:** The incidence of emphyema in Far North Queensland is higher than previous studies elsewhere. A disproportionate number of patients were treated in non-specialist respiratory units, perhaps reflecting late recognition of parapneumonic effusions. Adverse outcomes such as death or need for surgery are uncommon with the adoption of dual intrapleural enzyme therapy.

**Grant Support:** •

**CHARACTERISING THE OUTCOME AND TOXICITY OF TREATMENT FOR DRUG RESISTANT TUBERCULOSIS IN NSW****CHANG V<sup>1</sup>**, LING R<sup>1</sup>, CHIAM D<sup>1</sup>, BRITTON W<sup>2,3</sup>, FOX G<sup>1,2</sup><sup>1</sup>The Sutherland Hospital, Sydney, Australia

**Introduction/Aim:** Management of Multidrug-resistant tuberculosis (MDR-TB) is a major challenge for clinicians including the need for prolonged treatment, worse treatment outcomes, risk of treatment-related toxicity and increased cost of treatment for individuals and public health systems. A recent study identified discordance between current International standards of care and clinical practices in four countries of Europe. This highlighted the importance and need to evaluate practice and ensure the translation of policies into practice in order to optimise MDR-TB case management, prevention and control.

**Methods:** 43 patients were identified with bacteriologically confirmed MDR-TB diagnosed between 2000 and 2016 from 5 hospitals in NSW. We reviewed the demographics, duration of treatment, outcomes of the patients and the infection control facilities of the treating facility are presented. We also describe the prevalence of LTBI and management of the contacts.

**Results:** Mean age for the study population was 35 years old. 55% of patients were male and the mean weight was 62kg. 72.1% (31 patients) were diagnosed with pulmonary TB and 15 patients were smear positive on sputum culture with 29% of patients presented with normal CXR at diagnosis. The mean duration of treatment for inpatient and outpatient were 29 days and 613 days respectively. 88% of the patients received injectables treatment during intensive phase of the MTB-TB regimen with 22 patients received Capreomycin and 16 patients received Amikacin. Ototoxicity (60%) and hepatic toxicity (53%) were the most common side effects recorded for the patients. 81% of the patients completed the MDR-TB treatment according to the Laserson Criteria.

**Conclusion:** This study highlighted the high rate of toxicity using injectable antibiotics for MDR-TB treatment. This supports the transition to the new guidelines to resolve the morbidity for MDR-TB patients in Australia.

**Grant Support:** Nil.

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**NITROFURANTOIN ASSOCIATED ORGANISING PNEUMONIA**CHEAH R<sup>1</sup>, DESHPANDE S<sup>2</sup>, JOOSTEN S<sup>2,3,4</sup>, SUM R<sup>2</sup><sup>1</sup>Pharmacy Department, Monash Health, Clayton, Australia, <sup>2</sup>Monash Lung and Sleep, Clayton, Australia, <sup>3</sup>School of Clinical Sciences, Monash University, Clayton, Australia, <sup>4</sup>Epworth Partners, Richmond, Australia**Introduction:** To describe a case of nitrofurantoin associated organising pneumonia.**Background:** Nitrofurantoin is an antibacterial agent indicated for treatment of uncomplicated urinary tract infection (UTI) or for prophylaxis in those patients with recurrent UTIs. It is rarely used as a first line agent owing to its potential for adverse reactions such as pulmonary toxicity.<sup>1</sup> Organising pneumonia is a pathological syndrome associated with dyspnoea, non-productive cough, bilateral crackles on chest examination and hypoxaemia at rest.<sup>2</sup> We report a case of nitrofurantoin associated organising pneumonia responsive to drug withdrawal and corticosteroid initiation, this is a rare occurrence, with only a few reported cases worldwide.**Interventions, Case Progress and Outcomes:** A 73-year-old female ex-smoker with a history of multiple allergies, Graves' disease, and recurrent UTIs who was treated with long-term nitrofurantoin presented with an 8-week history of worsening dyspnoea on exertion, pleuritic chest pain when coughing, nausea, decreasing appetite, weight loss and increasing lethargy. Computed Tomography (CT) of the chest revealed widespread bilateral airspace and peribronchovascular ground glass opacities indicative of organising pneumonia. Following diagnosis of organising pneumonia, nitrofurantoin was ceased and high dose prednisolone commenced. After rapid clinical response to treatment, the patient was discharged long-term on high dose prednisolone. On routine 4-week follow up, the patient's symptoms had improved significantly. A repeat CT chest demonstrated dramatic reduction in ground glass changes.**Conclusion:** Nitrofurantoin associated organising pneumonia is a rarely reported adverse reaction and is often associated with poor outcomes.<sup>3</sup> This case report highlights that nitrofurantoin associated organising pneumonia can improve dramatically with prompt withdrawal of the causative agent and commencement of corticosteroids. It also reinforces the importance of thorough medication history reconciliation and careful discretion in prescribing prophylactic antibiotics.**REFERENCES**

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**Key Words:**

Cryptogenic organising pneumonia, Corticosteroids, Bronchiolitis Obliterans Organising Pneumonia, Anti-infectives, Adverse Drug Reactions

**DOES THE BRONCHOSCOPE OR CLEANING PROCESS PROPAGATE PULMONARY INFECTION?**JOSHI E<sup>1</sup>, JO H<sup>1</sup>, AL-HINDAWI Y<sup>1</sup>, KAJBAFZADEH M<sup>1</sup>, MORGAN L<sup>1</sup>, VEITCH E<sup>1</sup>, PETERS M<sup>1</sup><sup>1</sup>Concord Repatriation General Hospital, Sydney, Australia**Introduction/Aim:** A quality assurance project to review the indications, adverse events of bronchoscopy and incidence of patient to patient transmission of infection from interventional bronchoscopic and pleuroscopic procedures.**Methods:** A retrospective review of all bronchoscopies and pleuroscopies performed from 1<sup>st</sup> August 2017 to 1<sup>st</sup> August 2018. Indications and complication rates were reviewed. Microbiology of bronchoscopy washings, BAL or pleuroscopy specimens was reviewed from the Electronic Medical Records. For organisms of interest, a search for similar isolates was conducted 3 days either side of the procedure. The specific endoscope used was identified for each procedure.**Results:** 199 interventions were performed- 188 bronchoscopies and 11 pleuroscopies. Indications for bronchoscopy were mainly to investigate for infection (36%) and malignancy (15%). Bronchoscopy procedures included 170 washings or BAL, 21 endobronchial or transbronchial biopsies, 10 brushings. 2 washings were cultured from pleuroscopy. The table below shows the clinically significant organisms cultured from more than one patient. The endoscope used was able to be identified in 198 cases.

Organism	Isolates	Close proximity	Same scope
<i>Mycobacterium tuberculosis</i>	8	1	No
Non-tuberculous mycobacteria	6		
<i>Aspergillus fumigatus</i>	18	3	No(2) Uncertain(1)
<i>Aspergillus niger</i>	7	1	No
<i>Pseudomonas aeruginosa</i>	6		
<i>Haemophilus influenzae</i>	13	1	No
CMV DNA	3		
PJP DNA	3		
<i>Pneumocystis jirovecii</i>	2		
<i>Klebsiella pneumoniae</i>	2		
<i>Staphylococcus aureus</i>	4		
Nocardia species	2		

*Mycobacterium tuberculosis* was the expected and proven diagnosis for the second MTb patient. 12% of patients had bronchoscopic complications; bleeding was most common (4%) which either self-resolved or after cold saline and none were life-threatening.**Conclusion:** Record keeping was very good and facilitated this audit. We found no evidence of cross-infection or cross-contamination via bronchoscopy or pleuroscopy. Bronchoscopic serious complication rate was low.**Grant Support:** Investigator-initiated study, no funding required.

We hereby declare that we have no pecuniary or other personal interest, direct or indirect, in any matter that raises or may raise a conflict with our role in conducting this research project.

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### COST EFFECTIVENESS AND CLINICAL UTILITY OF URINARY ANTIGENS IN PNEUMONIA

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**Introduction/Aim:** Pneumonia is a significant contributor to morbidity and mortality. Current Australian treatment guidelines on community-acquired pneumonia recommend performing blood cultures on all hospitalised patients and urinary antigen testing in severe disease, based on the SMART-COP or CORB severity scores. However, diagnostic yield for aetiology remains low. The availability of urinary antigen testing for *S. pneumoniae* and *Legionella pneumophila* has enabled rapid aetiological diagnosis and directed antibiotic therapy. There is conflicting data on the clinical utility of pneumococcal and legionella urinary antigen testing and its impact on antibiotic prescribing in community-acquired pneumonia. The aim of this study was to evaluate the clinical utility of pneumococcal and legionella urinary antigen testing and its cost effectiveness within Western Health, a tertiary public hospital servicing the west of Melbourne.

**Methods:** A retrospective audit of medical records was performed. All adult patients admitted under the Respiratory Unit at Western Health between 1<sup>st</sup> April and 30<sup>th</sup> September with a diagnosis of community-acquired pneumonia were included. Medical records were reviewed to evaluate the proportion of cases where urinary antigen testing was performed and antibiotic treatment was de-escalated in the setting of a positive urinary antigen result. Observance of local guidelines for diagnostic testing and evaluation of cost-benefit analysis of urinary antigens were also assessed.

**Results:** 156 patients were included. Pneumococcal and Legionella urinary antigen was performed in 58% of patients. *Streptococcal pneumoniae* was detected on urinary antigen in 19% of tested patients. No patients were identified to have a positive Legionella urinary antigen. Antibiotics were de-escalated in only 41% of pneumococcal urinary antigen positive patients.

**Conclusion:** The diagnostic and clinical utility of pneumococcal and legionella urinary antigens is low in community-acquired pneumonia. Due to the low prevalence of positive urinary antigen results and limited impact on antibiotic treatment, routine testing in hospitalised patients is not cost-effective.

**Grant Support:** None

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### ALTEPLASE DOSE ASSESSMENT FOR PLEURAL INFECTION THERAPY (ADAPT)-2

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**Introduction/Aim:** Intraleural tPA/DNase therapy has revolutionised management of pleural infection by reducing hospital length-of-stay and surgery. The initial randomised trial employed an empirical dose of 10mg tPA. Bleeding risks and costs remain key deterring factors in the uptake of tPA/DNase. The ADAPT project is a series of dose de-escalation studies to establish the lowest effective dosing regimen for tPA/DNase.

**Methods:** Consecutive patients with pleural infection treated with open-label tPA 2.5 mg (and DNase 5 mg) were included from two centres in Australia and UK. Dose-escalation to 10 mg tPA was permitted as judged by attending physician. Data relating to treatment success, radiological changes, C-reactive protein, pleural fluid volume drained, length-of-stay and complications were extracted retrospectively.

**Results:** 55 patients (63.6% male, 59[18.7] years) were prescribed tPA 2.5 mg (with DNase) for pleural infection. In total, 90.9% of patients were treated successfully using an endpoint of discharge from hospital and avoidance of surgery within 30-days. Fourteen patients had dose-escalation; in nine this was an attempt to break a non-communicating locule. One patient required surgery and four patients died from sepsis.

Treatment success was corroborated by significant clearance of pleural opacities on chest radiography, increase in pleural fluid drainage (from 200mL before treatment to 1700 mL [IQR 1188-2699] at 72 hours,  $P < 0.05$ ) and a reduction in CRP (48.7% from baseline at day 5,  $P < 0.05$ ). The median length-of-stay was 8.5 (IQR 6-13) days from the first dose of tPA.

The median number of doses administered was 5 (IQR 3-6), with 9 (16.3%) patients receiving >6 doses. One patient experienced a thoracic bleed (1.8%) 24-hrs following the sixth dose of 2.5mg tPA but was haemodynamically stable. Pain needing escalation of analgesia affected 40% of patients.

**Conclusion:** Using a starting dose of tPA (2.5 mg) combined with DNase (5 mg) is effective in a majority of patients with pleural infection; its use should be further explored.

**Grant Support:** Institute for Respiratory Health and Sir Charles Gairdner and Osborne Park Hospital Research Advisory Council Grant

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### AETIOLOGY OF HOSPITAL MANAGED COMMUNITY-ACQUIRED PNEUMONIA IN WESTERN AUSTRALIAN PRIVATE HOSPITALS

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**Introduction/Aim:** Community-acquired pneumonia (CAP) is a leading cause of hospitalisation and death worldwide. Knowledge of local pathogens guides antimicrobial treatment; however the aetiology of CAP in Western Australia has not been well studied, especially in the private hospital system. We hypothesised that *Streptococcus pneumoniae*, *Chlamydia pneumoniae*, *Mycoplasma pneumoniae* and respiratory viruses would be common pathogens detected in patients hospitalised with CAP. We further hypothesised that the pneumococcal vaccination would impact upon rates of *Streptococcus pneumoniae* detection.

**Methods:** A retrospective analysis of two private hospital medical record databases identified all patients 18 years or older admitted with CAP in 2015. Patients with recent hospitalisation, significant immunosuppression, chronic respiratory disease or active cancer were excluded. All investigations ordered during admission were reviewed.

**Results:** 184 patients met the necessary criteria with radiographic evidence and clinical features of CAP. Mean age was 66 years (range, 20-96), 19 patients required admission to intensive care and 3 patients died. There were 75 pathogens detected in 55 patients (30%). The most common pathogens detected were influenza virus (7%), *Streptococcus pneumoniae* (7%) and *Haemophilus influenzae* (7%). Only one of seven 'high-risk' patients with isolated *Streptococcus pneumoniae* was appropriately vaccinated.

**Conclusion:** Causative agents were not detected in the majority of patients. Bacteria were most frequently detected, however influenza virus was the most common single pathogen detected. There were missed opportunities in administering pneumococcal vaccinations in the community. We believe a prospective study ensuring consistent and updated diagnostic protocols is overdue.

**Grant Support:** N/A

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This abstract has been withdrawn.

### VIRAL LOWER RESPIRATORY TRACT INFECTIONS REQUIRING HOSPITALISATION AMONG JORDANIAN ADULTS

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**Introduction/Aim:** Acute lower respiratory tract infection (LRTI) is the most common condition treated in primary care, and it was considered the third leading cause of death worldwide in 2017. The objective of this study is to demonstrate the spectrum of the etiological agents that cause viral LRTI at a tertiary hospital in Jordan.

**Methods:** We conducted a retrospective study on patients who were admitted to Jordan University Hospital with the diagnosis of LRTI between January, 2011 and January, 2016. We used Fast-track Diagnostics<sup>®</sup> Respiratory 21 Kit (Fast-track Diagnostics, Luxembourg) real-time PCR and we investigated pandemic H1N1 2009 swine flu virus using rapid test PCR.

**Results:** This study involved 495 patients with a mean age of 57.79 ± 18.43 years. The rate of ICU admission was 16.8%, and the mortality rate of LRTI was as low as 3.64%. The causative agents were identified in 157 patients out of 495 patients (31.7%). The percent of cases who were positive for H1N1 in patients who were investigated by PCR and rapid test for pandemic H1N1 2009 swine flu virus was 4.2%. Fast-track Diagnostics (FTD) real-time PCR was done for 170 patients, and the test was positive for seasonal Influenza A virus in 7.1% of patients, influenza B in 4.1%, RSV in 4.7%, metapneumovirus in 4.1%, adenovirus in 4.1%, corona 229E/NL63 in 4.1%, parainfluenza virus in 7.6%, and rhinovirus in 3.5%.

**Conclusion:** The Lower respiratory tract infection's causative agents vary throughout the year. Viral LRTI is more common in winter season, especially in January. Remarkably, Influenza A and Parainfluenza viruses were the main viral causative agents for LRTI in our study. This highlights the importance of the administration of seasonal influenza vaccines, especially in elderly patients, as well as patients with comorbidities

**Grant Support:** Nil.

The authors have no conflict of interest to declare.

**THE AETIOLOGY OF PAEDIATRIC PNEUMONIA AND EMPYEMA AT MONASH CHILDREN'S HOSPITAL AND FACTORS ASSOCIATED WITH COMPLICATED DISEASE, IN THE PNEUMOCOCCAL CONJUGATE VACCINE-13 ERA.282**  
**CHAN Q<sup>1,2</sup>**, HORNE R<sup>1,2</sup>, MCCULLAGH A<sup>3</sup>

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**Introduction:** Bacterial pneumonia is most commonly caused by *Streptococcus pneumoniae*. Following the introduction of the first pneumococcal conjugate vaccine, PCV7, a fall in the rate of paediatric pneumonia was observed however empyema rates increased with the emergence of non-vaccine serotypes. To address this, PCV13 was introduced in 2011. This study aims to identify the bacterial aetiology of pneumonia and empyema at Monash Children's Hospital and the prevalence of PCV13 serotypes. Furthermore, factors associated with the development of empyema were identified.

**Methods:** 63 pneumonia and 44 empyema patients were prospectively recruited between November 2015 – July 2018, as part of the TESTOV-Pneumo study.

Nasopharyngeal swabs, blood and pleural fluid were tested for bacterial aetiologies using Polymerase Chain Reaction and cultures. *S. pneumoniae* positive samples were serotyped. Separate nasal swabs were analysed for viruses. Demographic and clinical factors were compared between the groups.

**Results:** *Streptococcus pneumoniae* was the most commonly identified pathogen in both the pneumonia (22.2%) and empyema (68.2%) groups. *S. aureus* was identified in both pneumonia (20.0%) and empyema (15.9%) and *S. pyogenes* was found in 22.7% of empyema cases.

The prevalence of PCV13 serotypes were: 1(0%), 19A(2.3%) and 3(41.9%).

Viral co-infection was more common in empyema (36.4% vs 17.5%;  $P = 0.047$ ). C-reactive Protein (CRP) on admission over 120mg/L (OR 8.45; 95% CI 2.1- 33.4) and use of ibuprofen during hospital stay (OR 9.81; 95% CI 1.2-76.7) were associated with development of empyema.

**Conclusions:** In the PCV13 era, the rate of pneumonia and empyema caused by serotype 3 remains high and *S. pyogenes* was identified as a cause of complicated disease. Elevated CRP >120 mg/L on admission and use of ibuprofen during hospital stay were associated with the development of empyema.

**Keywords:** pneumonia, empyema, paediatrics, pneumococcal conjugate vaccine, PCV13

**ORAL CARE INTERVENTION TO REDUCE INCIDENCE OF VENTILATOR ASSOCIATED PNEUMONIA IN INTENSIVE CARE UNIT, HOSPITAL USM279**

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**Introduction/Aim:** VAP is a common nosocomial infection that increase mortality rate and length of hospital stay. Oral care may not only improve patient's oral health, but also reduced the incidence of VAP. We aimed to investigate the incidence of VAP following two different oral care to reduce the incidence of VAP in ICU, Hospital USM.

**Methods:** A randomized controlled trial conducted between May,20016 to April 2017.A total of 63 patients were randomized in chlorhexidine (CHG) group and CHG with toothbrushing (CHG with TB) group. Oral care was addons with VAP prevention bundle. Baseline data of oral hygiene index (OHI-S) and CPIS scores of the patients was obtained until day 11 unless extubated. Oral care intervention was done thrice daily.

**Results:** The mean age of the patients were 44.4 years (SD 19.59). Of 63 patients, 31 were enrolled into the CHG with TB group and 32 were into CHG alone group. The application of 0.2% CHG with TB established a lower incidence of VAP during the intervention period (6 VAP cases – 0.2% CHG group, 3 VAP cases – 0.2% CHG with TB group) with a significant decrease in the mean OHI-S and CPIS score ( $P = 0.001$ ), which supports the tendency toward improved clinical outcome for the CHG with TB group. Bacteria inhabit in plaque in the oropharynx, are transferred to the lungs via micro-aspiration. Dental plaque can be eliminated only by toothbrushing, so the present study demonstrated that toothbrushing is a more effective way to reduce VAP because it eradicates the plaque that harbours bacteria.

**Conclusion:** Chlorhexidine with tooth brushing oral care is more effective to reduce the incidence of VAP in ICU settings.

**Grant Support:** N/A.

### NOSOCOMIAL TRANSMISSION OF TUBERCULOSIS TO A SURGEON FOLLOWING WASHOUT OF A TUBERCULOSIS SEPTIC ARTHRITIC ELBOW

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Nosocomial transmission of *Mycobacterium tuberculosis* from patients with pulmonary disease is well described, particularly in cases where the disease is not suspected. Nosocomial transmission of extrapulmonary tuberculosis is rare with the limited reported cases linked to the inadvertent aerosolisation of bacilli following the irrigation of tuberculosis skin or soft tissue abscesses. We report a case of nosocomial *M. tuberculosis* transmission to a surgeon resulting from intra-operative irrigation of a tuberculosis septic elbow.

The source patient presented with florid septic arthritis of the elbow and underwent two early washouts in the operating theatres, using the InterPulse high-pressure pulsed Lavage system (Stryker, USA). The operating room staff employed standard precautions and did not use N95 respirators. The diagnosis of smear-positive tuberculous septic arthritis was made on day 3 of the patient's admission, after which ward tuberculosis precautions were implemented. The patient had no respiratory symptoms, and contact tracing procedures were not initially followed.

Six months later the previously well surgeon presented with fevers, night sweats, persistent cough and shortness of breath. The surgeon was found to have a large left-sided pleural effusion which drained a large volume exudate which was acid fast bacilli smear and culture negative. Sputum samples isolated fully susceptible *M. tuberculosis* after which standard short course of first-line treatment commenced with subsequent cure.

The isolates from the source patient and surgeon were compared by Whole Genome Sequencing using Nextera XT library kit and sequenced on NextSeq500 (Illumina, USA). The isolates were found to be genetically identical, without single nucleotide polymorphism variation, consistent with recent transmission from the source patient to the surgeon. No other transmission events following this incident were identified.

To our knowledge, this is the first case of transmission of *M. tuberculosis* following septic arthritis irrigation. Healthcare workers need to be aware of the risks of extrapulmonary tuberculosis transmission when performing procedures that aerosolise bacilli, including in cases of undiagnosed septic arthritis. Contact tracing procedures should be implemented in cases of extrapulmonary tuberculosis where there has been aerosolisation.

### SHORT COURSE TREATMENT FOR MDR TB: THE AUSTRALIAN EXPERIENCE

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**Introduction/Aim:** Treatment for MDR-TB is resource intense, requires prolonged administration of second-line agents, and is associated with greater toxicity. In 2015, the WHO updated treatment guidelines to endorse the use of a shorter 9-12 month regimen in selected patients with pulmonary MDR-TB. The aim of the study was to determine the uptake of use of the standardised shorter regimen by TB specialists in Australia, and review rates of completion, medication side effects, and adherence to WHO-approved treatment guidelines.

**Methods:** This retrospective case series reviewed use of the shorter course regimen in Australia by approaching specialist TB services in each state via the National Tuberculosis Advisory Committee. Case details were provided by treating clinicians from medical and laboratory records at their respective centres. Demographic, clinical, treatment and outcome data were collected.

**Results:** Five patients in four states have received the shorter course regimen to date. In two additional cases, short course treatment was terminated due to the results of drug susceptibility testing. All patients were born overseas and arrived in Australia as adults, and primary transmission was suspected in three of five cases. All patients experienced side effects and in one case treatment interruption occurred due to adverse effects. Treatment success has been recorded in all patients. Treatment occurred in accordance with WHO recommendations, except for use in one case of MDR-TB lymphadenitis.

**Conclusion:** Uptake of the short course treatment regimen for MDR-TB has been gradual in Australia. Outcomes in this small group have been favourable, though the period of follow-up is still limited. Short course treatment may be advantageous in carefully selected patients as Australia is affected by the increasing regional burden of MDR-TB.

**Grant Support:** Nil

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### NON-VENTILATOR-ASSOCIATED HOSPITAL-ACQUIRED PNEUMONIA: CLINICAL AND PROJECTED FINANCIAL IMPACTS IN AUSTRALIA.

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**Introduction/Aim:** NV-HAP constitutes majority of Hospital acquired pneumonia (HAP). Federal funding models that penalise health care institutions for HAP are planned. We aimed to study the risk factors for NV-HAP, and quantify its clinical and financial impacts on our patients and health-care organisation respectively.

**Methods:** We performed a retrospective audit of a selection of cases of HAP identified through a database populated by the Quality Innovative Program, a nationally endorsed company which collects hospital case mix data for the National Safety and Quality Health Service (NSQHS) Standards accreditation. Chart review was undertaken for each of the identified cases. We aimed to establish the veracity of the diagnosis and study the prevalence of risk factors. We calculated mortality, ICU admission length of stay, and projected financial burden based on planned changes to federal funding of public hospitals.

**Results:** 79 cases of HAP were identified between July 2016 and June 2017 at the Lyell McEwin Hospital. 39 cases were due to incorrect diagnoses or incorrect coding of hospital data. There were 6 cases of Ventilator-associated pneumonia. There were 34 cases of NV-HAP. NV-HAP was associated with a mortality rate of 26%, ICU admission rate of 47%, average length of stay (16.2 days). 79% of patients with NV-HAP had  $\geq 3$  risk factors based on existing evidence on HAP. Most patients acquired NV-HAP despite being positioned adequately (71%) and/or had modified diet (65%). Incorrect diagnoses and coding resulted in projected final burden of AUD 157,888 (43% of total projected financial burden of AUD 388,863).

**Conclusion:** NV-HAP was associated with significant mortality, ICU admission and costs. These patients typically have multiple risk factors for NV-HAP. Opportunities for reduction in the burden of disease appeared relatively limited. Accurate diagnoses and coding of hospital data will minimise the financial impact of the disease in view of impending changes to federal funding.

**Grant Support:** Nil.

### MORTALITY IN HOSPITAL ACQUIRED PNEUMONIA AND VENTILATOR ASSOCIATED PNEUMONIA: A COMPARISON BETWEEN CULTURE POSITIVE AND CULTURE NEGATIVE PATIENTS

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**Introduction/Aim:** Hospital Acquired Pneumonia (HAP) and Ventilator Associated Pneumonia (VAP) are the second most common cause of nosocomial infection, and the leading cause of death from nosocomial infection in the critically ill. Despite this, there are few studies examining risk factors for morbidity or mortality. We aimed to explore this; in particular looking at the effect of culture positivity (sputum or blood) on mortality.

**Method:** A retrospective observational study looking at patients coded as having HAP or VAP, and confirmed to meet diagnostic criteria, over a 1 year period (2015/2016). We recorded comorbidities, demographic and microbiological data. The primary outcome was mortality, with discharge destination and length of stay (LOS) as secondary outcomes.

**Results:** 235 patients with confirmed HAP/VAP were identified with 134 excluded. 55 patients (23%) were found to have culture positive HAP or VAP (HAP n = 33; VAP n = 22), with 180 (77%) found to be culture negative (HAP n = 163; VAP n = 17). Culture negative patients were subdivided into sputum negative (n = 62), and sputum not sent (n = 118). Culture positive patients had significantly higher mortality compared to culture negative (33% vs 14%;  $P = 0.002$ ). This was also true when comparing culture positive and sputum negative patients (33% vs 15%  $P = 0.02$ ). Culture negative patients were more likely to be discharged home than require hospital transfer, rehabilitation, nursing home placement, or die on discharge (48% vs 33%;  $P = 0.04$ ). This was also true when comparing sputum negative and culture positive patients (53% vs 33%,  $P = 0.03$ ). There was no significant difference in LOS between culture positive and culture negative. There was no significant difference in mortality, LOS or discharge destination between HAP and VAP.

**Conclusion:** This study demonstrates that culture positive patients have increased rates of mortality. This suggests that obtaining sputum cultures may have important implications not just for management but also prognostication.

**Key Words:** HAP, VAP, Mortality.

**Grant Support:** None.



**MICROORGANISMS AND RESISTANCE IN CULTURE  
POSITIVE HOSPITAL ACQUIRED PNEUMONIA AND  
VENTILATOR ASSOCIATED PNEUMONIA****WELLS S<sup>1</sup>**, INMAN D<sup>2</sup>, DAVESON K<sup>1</sup>, SCHEMBRI S<sup>1</sup><sup>1</sup>The Canberra Hospital, Canberra, Australia, <sup>2</sup>Calvary Hospital, Canberra, Australia

**Introduction/Aim:** Hospital Acquired Pneumonia (HAP) and Ventilator Associated Pneumonia (VAP) is a leading cause of mortality in hospitalised patients. Empiric treatment is often guided by local microbial data and risk factors for microbial resistance. We aimed to explore risk factors for microbial resistance and mortality.

**Method:** A retrospective observational study looking at patients coded as having HAP or VAP, confirmed to meet diagnostic criteria, and found to be culture positive, over a 1 year period (2015/2016). We recorded comorbidities, demographic and microbiological data, including microbial resistance (defined as resistance to empiric agents Ceftriaxone and Piperacillin/Tazobactam). The primary outcome was mortality, with discharge destination and length of stay (LOS) as secondary outcomes.

**Results:** 55 patients were found to have culture positive HAP or VAP (HAP n = 33; VAP n = 22) with 314 excluded. *Staphylococcus aureus* was the most common microorganism in the VAP group (36%), with *Pseudomonas aeruginosa* the most common in the HAP group (33%). There was a significantly higher number of Gram positive organisms in the VAP group compared to HAP (36% vs 12%  $P = 0.04$ ). There were significantly more resistant microorganisms in the HAP group compared to VAP (27% vs 5%,  $P = 0.03$ ). We also found that resistant microorganisms were more likely in patients with known IV antimicrobial use in the last 90 days (30% vs 7%  $P = 0.03$ ). No other factors were significantly associated with microbial resistance. There was no significant difference in mortality, LOS or discharge destination between HAP and VAP. Within the whole group, CCF was found to be a risk factor for increased mortality ( $P = 0.03$ ).

**Conclusion:** This study suggests that IV antibiotic within 90 days is a risk factor for infection with resistant microorganisms. The predominance of *Staphylococcus aureus* and *Pseudomonas aeruginosa* in VAP and HAP patients respectively may help guide empiric therapy in these sub-groups.

**Key Words:** HAP, VAP, *Staphylococcus aureus*, *Pseudomonas aeruginosa*.

**Grant Support:** None.

**REDUCING HOSPITAL ADMISSIONS FOR LRTI IN AN AGING  
POPULATION****YU C<sup>1</sup>**, PALFREYMAN S<sup>1</sup><sup>1</sup>Alfred Hospital, Melbourne, Australia

**Introduction/Aim:** Older people living in nursing homes are frequently admitted to hospital for lower respiratory tract infections (LRTI). These account for a significant number of bed days and resource allocation in hospital. The rate of increase in the aging population in Australia is not matched by the medical workforce. This has led many hospitals to develop residential in-reach services that provide hospital type care to residents at their residential aged care facilities (RACF) to avoid hospital presentations. We examine the role of the nurse practitioner in preventing hospital admissions by providing mobile assessment and treatment to RACF residents with LRTI.

**Methods:** Patients at risk of admission to hospital were identified via primary care or hospital service referral and randomly assigned to either NP or medical review. We retrospectively studied 629 patients over a 19 month period reviewed by a NP.

**Results:** We report over a 16 month period, 24% (149) of the reviews in nursing homes were attributable to LRTI. Of these 149 patients, the most frequent presenting complaint was a cough and 1 month admission rate to hospital following initial review was significantly low.

**Conclusion:** The role of the nurse practitioner in a mobile assessment service for the management of LRTI in patients in nursing homes is a replicable model that has the potential to reduce the rates of hospital admission.

**Grant Support:** Nil.

**DO PATIENTS WITH SEVERE REM RELATED OSA REQUIRE MORE OR LESS PRESSURE DURING PRESSURE DETERMINATION STUDIES THAN PATIENTS WITH SEVERE NON-STAGE SPECIFIC OSA?**

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**Introduction/Aim:** Rapid eye movement (REM) related obstructive sleep apnoea (OSA) is a phenotype of OSA where events occur more often or exclusively in REM sleep. We hypothesise that the anatomical pathophysiology may relate to collapsible airways susceptible to muscle paralysis in REM, possibly explaining why few events occur outside REM. Our aim was to evaluate whether difference in the recommended pressure in severe REM related OSA compared to severe non-stage related OSA existed. Secondary aims to describe demographics of severe REM-related OSA and whether correlation between REM AHI and pressure existed.

**Methods:** A retrospective ethics approved observational study. Patients identified from a Concord Hospital inpatient diagnostic polysomnography datasheet (2012 to 2018, n = 2166). REM-related OSA = REM AHI > 30, NREM <5. Severe OSA = overall AHI >30. Patients excluded if no adequate pressure determination (PD) study, REM % total sleep time (TST) <15 or TST < 300 minutes. Statistical analysis using Graphpad. Two-tailed unpaired t-test was used comparing recommended pressure, Pearson's R-test to analyse correlations between pressure and AHI.

**Results:** Of 57 patients with severe REM-related OSA, 21 had a CPAP PD. Of 215 with severe non-stage related OSA, 145 had CPAP PD. There was a statistically significant difference in recommended pressure, mean REM-OSA = 10.9 vs. non-stage severe OSA = 12.9 ( $P = 0.019$ , 95% CI 0.31-3.52). There was a female predominance in the severe REM OSA group; mean age was the same. No significant correlation between REM AHI and pressure or overall AHI and pressure in either group.

**Conclusion:** There was a statistically significant difference in recommended pressure between patients with severe REM related OSA versus severe non-stage related OSA. Further pathophysiological studies into airway collapsibility and pressure required for airway patency in this group compared to non-stage related OSA would be helpful in tailoring treatment.

**Grant Support:** Nil.

**THE SOURCE OF INFECTION AFFECTS SEPSIS-ASSOCIATED AKI PATIENTS' OUTCOME**

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**Introduction/Aim:** Patients with sepsis-associated AKI show independently higher hospital mortality, and the pathogenesis and pathophysiologic mechanism remain unclear. We hypothesized the site of the infection, as the most primary cause, did matter in the development of this deadly disease.

**Methods:** We identified patients admitted to our Emergency Center with the diagnosis of sepsis-associated AKI from Jan. 2013 to Jan. 2018, then divided all the 113 patients into two groups according to the infection sites. And the data from their admission till the death or hospital discharge had been collected, we also collected the outcomes of the discharged patients in the 90 days from admission.

**Results:** In all 113 patients, the most common site of infection among sepsis-associated AKI patients was the lung (52 in 113, 46%), followed by gastrointestinal (25 in 113, 22.1%) and urinary (22 in 113, 19.5%) source.

It was found that the lung infected source SA-AKI patients had worse outcome that they were more likely to dead in the 90 days ( $P < 0.001$ ), whose kidney recovery was also worse than that in non-pulmonary patients by judging through the creatinine and urea changes ( $P = 0.015$ ). Otherwise, the non-pulmonary infection patients were more tend to shock ( $P = 0.037$ ).

**Conclusion:** The study, as one of a few focusing on the infection anatomy sites, demonstrated that the source of infection independently influences the outcome of the SA-AKI patients, and the pulmonary infected patients are more likely to have a worse outcome. What's more, we indicated that the lung injury may also affect the renal function in some unknown ways and at that point it affects the recovery of kidney function in the SA-AKI patients group.

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### ADVERSE EVENTS AFTER PULMONARY FUNCTION TESTING WITH RECENT MYOCARDIAL INFARCTION

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**Introduction/Aim:** Current ATS/ERS guidelines, based on expert opinion and exercise testing studies, list myocardial infarction (MI) within one month as a contraindication to Pulmonary Function Testing (PFT). Since chronic obstructive pulmonary disease is associated with poor post-coronary artery bypass graft (CABG) surgery outcomes, PFTs are important pre-operatively. However, often these patients have suffered recent MIs. We aimed to review post-PFT and post-operative outcomes for CABG patients who had PFTs within one month of MI at our institution.

**Methods:** A retrospective review of CABG patients for calendar year 2017 was performed. Subgroups analysed were: (1) MI<1-month pre-PFTs; (2) MI>1-month pre-PFTs; (3) MI/no PFTs; (4) no MI+PFTs. Primary outcome was rate of post-PFT MI or serious cardiac arrhythmia in the MI<1-month pre-PFT group. Post-operative outcomes analysed were: Intensive Care Unit length of stay (LOS), days on ventilator, pneumonia rates, readmission rates, total LOS, and mortality. Data were analysed using unpaired *t*-tests.

**Results:** 119 patients were identified. Breakdown of group numbers were: 21/119 (17.6%) MI<1-month pre-PFTs; 10/119 (8.4%) MI>1-month pre-PFTs; 25/119 (21.0%) MI/no PFTs; 63/119 (52.9%) no MI+PFTs. Primary outcome of the MI<1-month pre-PFTs group showed zero incidence of MI or arrhythmia post PFTs. This group showed a significantly longer total LOS compared to the MI>1-month pre-PFTs group ( $P = 0.02$ ) and the no MI group ( $P = 0.0001$ ), but no difference with the MI/no PFTs group ( $P = 0.20$ ). Patients who did not have a MI had significantly shorter LOS compared to those that did, regardless of whether or not PFTs were performed ( $P = 0.002$ ).

**Conclusion:** 119 patients were identified. Breakdown of group numbers were: 21/119 (17.6%) MI<1-month pre-PFTs; 10/119 (8.4%) MI>1-month pre-PFTs; 25/119 (21.0%) MI/no PFTs; 63/119 (52.9%) no MI+PFTs. Primary outcome of the MI<1-month pre-PFTs group showed zero incidence of MI or arrhythmia post PFTs. This group showed a significantly longer total LOS compared to the MI>1-month pre-PFTs group ( $P = 0.02$ ) and the no MI group ( $P = 0.0001$ ), but no difference with the MI/no PFTs group ( $P = 0.20$ ). Patients who did not have a MI had significantly shorter LOS compared to those that did, regardless of whether or not PFTs were performed ( $P = 0.002$ ).

**Grant Support:** None of the authors received any grant support for this project.

### IGLON5 DISEASE: CASE REPORT OF A NOVEL NEUROIMMUNE SLEEP DISORDER

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**Introduction/Aim:** Anti-IgLON5 disease is a complex neurodegenerative condition first described in 2014. Most patients develop sleep disordered breathing or REM and Non-REM parasomnia, which may be preceded or accompanied by bulbar symptoms, gait abnormalities, oculomotor problems or cognitive decline. The condition is associated with specific autoantibodies to the neuronal cell adhesion molecule IgLON5 and neuropathologically with an atypical tauopathy of the brainstem tegmentum and hypothalamus. There is also a strong association with the HLA-DRB1\*10:01 and HLA-DQB1\*05:01 alleles. Current treatment is immunotherapy, with poor clinical response and high mortality.

**Method/Case report:** A 70-year old retired mechanic of Italian origin was admitted to intensive care following a presentation with acute hypercapnoeic respiratory failure requiring intubation. He had no pre-existing respiratory or neuromuscular disease. Further history revealed 6 months of progressive dysphagia, noisy breathing, abnormal sleep vocalisation and periodic limb movements. There was no history of gait disturbance, cognitive dysfunction or peripheral neuromuscular weakness. He demonstrated progressive bulbar dysfunction, intermittent severe central hypoventilation, parasomnia and dysautonomia. Episodic prolonged respiratory arrest necessitated reintubation twice then tracheostomy placement. On one such occasion he failed to trigger the ventilator for more than 36 hours before recovering respiratory drive.

**Results:** After extensive investigation, serum anti-IgLon5 antibodies returned positive. Subsequent tissue typing confirmed positive HLA-DRB1\*10:01 and HLA-DQB1\*05:01 status. CSF anti-IgLON5 antibodies are pending. Diagnostic polysomnography with tracheostomy demonstrated mild obstructive sleep apnoea with most events at sleep-wake transition, severe sleep fragmentation and frequent periodic limb movements. REM was not observed and the tracheostomy challenged hypopnoea assessment. Treatment with intravenous immunoglobulin was commenced empirically, followed by methylprednisolone and rituximab upon diagnosis, ongoing at present on an inpatient basis.

**Conclusion:** With fewer than 30 cases described, this disease forms part of an increasingly recognised spectrum of neuroimmune sleep disorders that we believe are important for clinicians to be aware of.

**Grant Support:** Nil

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### THE FORCED OSCILLATION TECHNIQUE HAS MODERATE LONGITUDINAL CONCORDANCE WITH SPIROMETRY AND ASTHMA CONTROL

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**Introduction/Aim:** Longitudinal assessment of spirometry and symptoms in asthma are used to evaluate treatment response and guide management. The forced oscillation technique (FOT) measures respiratory system impedance and is increasingly used in clinical practice. The longitudinal concordance between spirometry, FOT and symptoms has not been described. We examined the agreement between spirometry, FOT and symptoms in patients with asthma who had attended multiple clinic visits.

**Methods:** Patients with asthma attending a tertiary adult Airways clinic completed spirometry (Masterlab, Jaeger, Hoechberg), FOT (Tremoflo C-100, Thorasys, Montreal) and the asthma control test (ACT) before and after a period of clinical management. FOT parameters examined included resistance (Rrs) and reactance (Xrs) at 5Hz. A significant improvement between visits was defined as:  $\geq 8\%$  or 150mL for FEV<sub>1</sub> or FVC<sup>1</sup>;  $\geq 17.4\%$  or  $\geq 0.94\text{hPa.s.L}^{-1}$  for Rrs and  $\geq 36.7\%$  or  $\geq 0.49\text{hPa.s.L}^{-1}$  for Xrs<sup>2</sup>; and  $\geq 3$  for ACT. Agreement between measures was assessed using Cohen's Kappa ( $\kappa$ ).

**Results:** Data for 50 patients (24 male) were analysed (mean $\pm$ SD: age 57 $\pm$ 15yrs, BMI 28.7 $\pm$ 6.9kg/m<sup>2</sup>, %predictedFEV<sub>1</sub> 70 $\pm$ 19%, %predictedFVC 89 $\pm$ 15%, ACT score 17 $\pm$ 6, time between visits 394 $\pm$ 284days). Rrs had stronger agreement than Xrs with spirometric parameters. There was moderate agreement between absolute Rrs improvement and both absolute FEV<sub>1</sub> improvement ( $\kappa = 0.423$ ,  $P = 0.001$ , sensitivity 44%, specificity 94%) and FVC improvement ( $\kappa = 0.457$ ,  $P = 0.001$ , sensitivity 50%, specificity 92%). Absolute Rrs had stronger agreement with ACT than absolute FEV<sub>1</sub> ( $\kappa = 0.455$ ,  $P = 0.001$  vs  $\kappa = 0.341$ ,  $P = 0.016$ ).

**Conclusion:** Rrs is highly specific but moderately sensitive in detecting longitudinal improvement in lung function as determined by spirometry. Rrs has a closer relationship with symptomatic improvement than FEV<sub>1</sub>, suggesting FOT is a sensitive measure of patient symptoms and useful in longitudinal asthma management.

**Grant Support:** nil

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### A CASE OF CORONARY SINUS/LEFT CORONARY CIRCUMFLEX ARTERY FISTULA ASSOCIATED WITH PULMONARY HYPERTENSION AND PULMONARY EMBOLI

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**Introduction/Aim:** Coronary Artery Fistulae are a rare, diverse and heterogeneous group of congenital coronary AVM both in anatomy, presentation and clinical course.

We present the case of a Coronary Sinus/Left Circumflex Artery fistula associated with pulmonary hypertension and pulmonary emboli, who presented with shortness of breath.

**Methods:** A cardiac-MRI revealed a dilated left-circumflex artery with distal drainage into the distal coronary sinus. A full heart study demonstrated a PCWP mean of 15, a PAP of 44 and a PVR of 5.6 woods units. A V/Q scan was suggestive of multiple segmental pulmonary emboli.

**Results:** The patient was commenced on therapeutic anticoagulation with warfarin, with subsequent resolution of both pulmonary emboli and pulmonary hypertension. A decision was to continue anticoagulation until percutaneous correction of the shunt was performed.

**Grant Support:** None

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### CONTROLLED VS UNCONTROLLED BREATHING PROTOCOL IN ADULTS USING MULTIPLE BREATH NITROGEN WASHOUT (MBNW) TO MEASURE VENTILATION HETEROGENEITY

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**Introduction/Aim:** Multiple Breath Nitrogen Washout (MBNW) provides indices of ventilation heterogeneity, which may help detect and quantify early onset of small airway dysfunction. Two protocols are commonly used: uncontrolled tidal breathing vs 1-L controlled tidal volume breathing. We aimed to determine if the two protocols provided equivalent MBNW indices in healthy adults, and compared FRC obtained from both protocols against plethysmographic FRC. We also examined factors contributing to any observed differences.

**Method:** Healthy individuals with a smoking history <5pk yrs, performed both the 1-L controlled breathing and uncontrolled tidal breathing protocols, in randomised order, on the Eco Medics Exhalyzer<sup>®</sup> D system, according to ATS/ERS criteria. Indices from each protocol were extracted from the pooled results 3 trials per session: FRC, LCI (lung clearance index), Scond and Sacin (ventilation heterogeneity primarily in the conductive and acinar airways, respectively). For the uncontrolled protocol, Scond and Sacin were corrected for tidal volume. The two protocols were compared using paired-t tests, correlations, and Bland-Altman plots.

**Results:** Data from 13 (8 males) individuals (age range 19-51yrs, mean  $\pm$  SD BMI  $23 \pm 2.56$ , FEV<sub>1</sub>%pred  $102.15 \pm 15.7$  FEV<sub>1</sub>/FVC  $84.4 \pm 6.92$ ) are presented. FRC measurements between the two methods were highly correlated ( $r = 0.98$ ,  $P < 0.0001$ ). There were no significant differences between the two methods for FRC, Scond and LCI, while Sacin was higher using the 1-L controlled protocol (paired t-test,  $P = 0.009$ ). However, Bland-Altman plots revealed significant proportional bias, i.e. the differences in FRC and Sacin between the two protocols depended on their magnitudes ( $P = 0.0158$  and  $P < 0.0001$ , respectively). Furthermore, the 1-L controlled protocol increasingly overestimated FRCpleth in individuals with larger FRCpleth ( $P = 0.030$ ).

**Conclusion:** Lung volume and ventilation heterogeneity assessed using the two protocols may not be comparable in taller individuals. These preliminary results will aid in the ongoing standardisation efforts for MBNW, which are critical for its clinical application, and form a basis for future comparisons in patients with lung disease.

**Key Words:** Multi-Breath Nitrogen Washout (MBNW), FRC, Protocols

**Grant Support:** No.

### AN AUDIT OF WARD-BASED NON-INVASIVE VENTILATION PRACTICES AT THE GOLD COAST UNIVERSITY HOSPITAL MACKINTOSH D<sup>1</sup>, SRIRAM B<sup>1,2</sup>

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**Introduction/Aim:** Non-invasive ventilation (NIV) is becoming a more frequent intervention on general respiratory wards. Although it is an established evidence-based practice for patients with respiratory acidosis in the setting of COPD, or acute respiratory failure due to acute pulmonary oedema (APO), a paucity of evidence exists to support use of ward NIV in other domains. Thus, we sought to examine the current trends of ward-based NIV in order to determine clinical outcomes and adherence to evidence-based guidelines.

**Methods:** A retrospective audit of all episodes of acute NIV that occurred on our 24-bed general respiratory ward between January 2017 and July 2018. In-hospital complications and 3-month readmission and mortality data was collected.

**Results:** 88 patients had a total of 128 NIV admissions during the study period. Median age (IQR) was 70 (63-78) years, and 48 (55%) were female. NIV was initiated in ED in 62.5% and outside of business hours in 62.5% of cases. The primary diagnosis was COPD in 94 (71%); NIV was initiated in the absence of respiratory acidosis or APO in 28 cases (22%). Initial ABG was performed in 44 (34%) cases and there was a lack of NIV failure contingency plan documented in 38 (30%). NIV was considered successful in 103 (80.5%) patients, with 102 (79.7%) surviving to hospital discharge and 89 (69.5%) alive at 3 months. Variables associated with NIV failure were neuromuscular disorder ( $P < 0.001$ ), respiratory ward initiation of NIV ( $P < 0.001$ ), focal CXR opacification ( $P < 0.01$ ), and lower BMI ( $P < 0.01$ ) and malnutrition screening test score ( $P = 0.011$ ).

**Conclusion:** Our audit identified that a substantial portion of patients receive NIV for non-standard indications, a lack of initial ABG to guide therapy and poor documentation of NIV failure contingency plan. These results will be used to guide a pilot GCUH staff NIV education program.

**Grant Support:** Nil.

### SLEEP-STUDY PATTERNS AND POSITIVE-AIRWAY PRESSURE REQUIREMENTS IN MOTOR NEURON DISEASE

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**Introduction:** In Motor neurone disease (MND), progressive loss of upper and lower motor neurons leads to respiratory failure, often with diaphragm dysfunction. Diaphragm being active inspiratory muscle during rapid eye movement (REM) sleep, there is theoretically a higher risk of sleep disorders especially in REM sleep. This precedes chronic respiratory failure and impacts quality of life and survival. However, there is insufficient data on the sleep disordered breathing (SDB) and positive pressure requirements in MND. The purpose of study was to give insight towards the same.

**Methods:** In a retrospective analysis, the sleep studies, records, letters of patients identified to have MND were assessed. The information about main diagnosis, comorbidities, sleep study results, trends in pressure requirements were collected and analysed.

**Results:** Twenty-six patients were identified to have MND. Sleep-study records were available for 16 patients. 4 did not have sleep apnoea, seven had mild to moderate SDB while 5 had severe SDB. Of those with severe disease, 1 had CCF, 1 had COPD. Nine had REM hypoventilation. Out of Fourteen patients who had pressure titration study, only one needed Continuous positive airway pressure (CPAP) and rest needed bilevel ventilation. Spontaneous mode Bilevel-PAP helped achieve control in three while rest needed timed mode. Inspiratory Positive Airway Pressure (IPAP) ranged between 14-18 cm H<sub>2</sub>O and Expiratory Positive Airway Pressure (EPAP) ranged from 5-12 cm H<sub>2</sub>O.

**Conclusion:** Most MND patients have mild-moderate SDB with REM hypoventilation. Bilevel Ventilation with IPAP 14-18 cm H<sub>2</sub>O and EPAP 5-12 cmH<sub>2</sub>O is needed in most cases.

### A NEW TOOL TO MONITOR DISEASE IN IPF

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**Introduction/Aim:** Idiopathic pulmonary fibrosis (IPF) is a chronic progressive fibrotic lung disease characterised by a restrictive ventilatory deficit. The changes in lung mechanics include increased elastic recoil. The current gold standard method of measuring elastic recoil requires oesophageal balloon measurements. This method is not used in standard clinical practice, as it is labour intensive and invasive for the patient. Recently we have developed a surrogate measure of elastic recoil from the forced oscillation technique (FOT). We hypothesise that FOT derived elastic recoil will be higher in subjects with IPF compared to health.

**Methods:** Subjects with IPF (n = 15) and healthy controls (n = 15) completed FOT measurements followed by spirometry, gas transfer (DLCO) and plethysmography. FOT reactance and lung volume was used to calculate a surrogate measure of transpulmonary pressure. The relationship between volume and transpulmonary pressure was used to estimate elastic recoil. Differences between controls and IPF were compared. Correlations between elastic recoil and other lung function parameters and composite physiologic index (CPI) were also compared.

**Results:** Subjects with IPF had higher elastic recoil derived from FOT ( $2.2 \pm 0.70$  vs  $0.95 \pm 0.79$ ,  $P = 0.001$ ) compared to control subjects. Measurements of DLCO ( $r^2 = 0.43$ ,  $P < 0.01$ ) and CPI ( $r^2 = 0.35$ ,  $P < 0.01$ ) were positively correlated with elastic recoil in subjects with IPF.

**Conclusion:** FOT provides a promising surrogate for elastic recoil that is easy to implement into clinical practice. Here, we show that elastic recoil is increased in subjects with IPF. This may have potential clinical applications for screening, monitoring and prognosis in IPF.

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### EFFECT OF MISREGISTRATION ON MR IMAGED SPECIFIC VENTILATION

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**Introduction/Aim:** Specific Ventilation Imaging (SVI) utilizes a time series of MRI lung images, acquired near FRC, during multiple breath washin and washout of oxygen. Inevitably, some images are acquired with the subject not at FRC, introducing misregistration errors. In-silico modelling has predicted that such errors result in only modest errors in the calculated outcome of heterogeneity. We aimed to compare these predictions with observed errors seen in data sets collected on naïve subjects.

**Methods:** SVI data sets of 220 images collected on successive breaths during alternating 20-breath blocks of inspired room air and oxygen were collected in 4 subjects who were naïve to the protocol. Images were acquired using a 1.5T Magnetom Avanto Fit Siemens scanner using an Inversion Recovery HASTE sequence providing T<sub>1</sub> sensitivity to the effects of O<sub>2</sub> dissolved in lung tissue. Subjects were instructed to be at FRC for each image and to inspire and expire between images. Data sets were automatically registered to an operator chosen reference image acquired at FRC using a deformable image registration algorithm and analysed with the same custom software to yield the heterogeneity of SV (width of distribution at FWHM).

**Results:** Registration altered the observed heterogeneity of SV by only 1.2% (unreg: 0.28±0.08, reg: 0.29±0.11,  $P = 0.89$ ). The SD of the change in the area of the lung ROI, taken as a measure of the amount of registration required, did not correlate with the change in heterogeneity ( $R^2 = 0.05$ ).

**Conclusion:** The effect of misregistration was less than that predicted by in silico modelling suggesting that realistic degrees of misregistration are not detrimental to the outcome SV maps. This suggests that in the future, data sets acquired during free-breathing can be utilized, obviating the need for patient control of breathing.

**Grant Support:** NIH R01-HL119263, Maurice and Phyllis Paykel Trust Grant.

### MELATONIN IN THE MANAGEMENT OF DELIRIUM IN THE ELDERLY: DOUBLE-BLIND RANDOMISED CONTROLLED PILOT TRIAL (MINTED)

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**Introduction/Aim:** Delirium is a frequent complication of hospitalised elderly patients and successful treatment options remain limited. Circadian rhythm disturbance leading to abnormal sleep-wake cycles is a hallmark clinical feature, and likely contributor to ongoing delirium. This double-blind, randomised controlled pilot study aimed to assess the feasibility of studying melatonin's effects on delirium severity and sleep-wake patterns in patients admitted to a subacute ward following an acute illness.

**Methods:** All patients admitted into the Geriatric Medicine unit of a Melbourne tertiary hospital were screened for delirium with the Confusion Assessment Method and 4-AT rapid delirium screening tool. Participants were randomised to receive slow-release melatonin 4mg or placebo daily for five days. Delirium severity was assessed daily using the Memorial Delirium Assessment Scale (MDAS). Each participant wore an actigraph device for monitoring of sleep-wake patterns.

**Results:** Ten (melatonin n = 5, placebo n = 5) patients were included in the study. MDAS score on day 5 was similar between the two groups (10.3 ± 8.3 vs 8.5 ± 1.9  $P = 0.6$ ). The melatonin group had a longer total sleep time (292 ± 41mins vs 211±80mins  $P = 0.075$ ) and shorter sleep latency (113 ± 46 mins vs 151 ± 32mins  $P = 0.17$ ), but the difference did not reach statistical significance.

**Conclusion:** This trial confirmed the feasibility of conducting a randomised controlled study in an elderly delirious population. Although no statistically significant impact on delirium severity was demonstrated, the trend seen in improved sleep architecture in the melatonin group warrants further exploration in a larger study.

**Grant Support:** None.

**Declaration of Interest:** The authors do not have any conflicts of interests to declare.

**DESCRIPTIVE ANALYSIS OF MAINTENANCE OF WAKEFULNESS TEST (MWT) IN A TERTIARY HOSPITAL AND CORRELATION OF POLYSOMNOGRAPHIC DATA WITH MWT**

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**Introduction:** Excessive daytime sleepiness and fatigue are common complaints in the sleep clinic. MWT is a polysomnographic (PSG) procedure for the evaluation of the ability to remain awake during soporific circumstances and assesses the ability to remain awake while resisting the pressure to fall asleep.

**Aim:** Descriptive analysis of the patients having MWT test and to assess the relationship between MWT results and PSG data.

**Methods:** Retrospective chart review of previous 34 months who underwent a PSG followed by MWT were analyzed. Patients demographics, polysomnographic data, urine drug screen, comorbidities and medications were analyzed. Variable data were analyzed with SPSS (Version 22) and ANOVA.

**Results:** Total of 53 MWT studies were identified for 47 patients. 36 (76%) were males. 32 (60.3%) of the patients had a MWT followed by a diagnostic sleep study and 21 patients (39.6%) had MWT followed by a CPAP Pressure determination study. MWT was positive in 21 patients (39.6%) and 61.9% (n = 13) were not on any CPAP treatment. Urine drug screen was positive only in 4 patients for sedatives out of 2 had positive MWT test. Depression was the commonest co-morbidity identified (n = 11, 20.7%). Efficacy of wake promoting agents were tested in 8 (15%) of cases. There was a weak but statistically significant co-relation with body weight and positive MWT ( $P < 0.05$ ) although there was no co-relation with the Epworth sleepiness scale (ESS), Arousal index, Severity of sleep apnoea, total duration of sleep, duration of REM and Non REM sleep periodic leg movement index.

**Conclusion:** Correlation between MWT and perceived sleepiness, and polysomnographic data were poor. Results show impaired wakefulness and mechanisms of alertness and sleep propensity does not correlate well.

**Intended outcome:** Further analysis of the cohort with effect of wake promoting agents and analysis of a larger cohort.

**Keywords:** Excessive sleepiness, MWT

**Grant Support:** Nil.

**ESTABLISHMENT OF A MOTOR NEURONE DISEASE SERVICE: PITFALLS, PROTOCOLS AND SUCCESS FACTORS**  
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**Introduction/Aim:** Motor neurone disease (MND) is a progressive, fatal neurodegenerative disease. The Princess Alexandra (PA) hospital in Brisbane runs Queensland's only multidisciplinary motor neurone disease service. This research aims to explore its strengths and weaknesses thus helping other centres hoping to establish a similar service to avoid some of the pitfalls experienced and potentially incorporate some of its strengths.

**Methods:** This research involved 2 components. Firstly, an audit on how the current service compares to international standards. Secondly, a qualitative questionnaire for members of the multidisciplinary team exploring the strengths and areas of improvement for the existing service.

**Results:** This service fulfils most of the international guidelines for the management of motor neurone disease. Specifically, patients are seen rapidly post referrals being made, they are seen frequently (on average every 3 months). Although on average patients are seen within 4 weeks of referral, the NICE guidelines recommend review within 4 weeks of *diagnosis* which is limited by timeliness of referrals. Non-invasive ventilation is typically discussed early (within first 12 months as per guidelines) and sleep studies are performed in a timely manner. Advanced health directives and the need for an enduring power of attorney are discussed early. Where appropriate, spirometry and testing of respiratory muscle function (i.e. SNIP/MIP/MEP) are performed at each clinic appointment. An area for potential improvement includes timely referral for insertion of PEG tubes whilst FVC remains above 50% which is essential in reducing surgical risks. Similarly, it was noted that it would have been helpful when the service was initially established to have a dedicated psychology service and palliative care team involved.

**Conclusion:** The PA hospital's motor neurone disease service endeavours to provide timely, individualised and patient-centred care that fulfils most of the recommended

**Grant Support:** NA.



TPL 015

TPL 016

### PULMONARY FUNCTION TESTING FOR EARLY DETECTION OF DRUG-INDUCED LUNG DISEASE

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**Introduction/Aim:** Pulmonary function tests (PFT) are sometimes monitored during treatment with known pulmonary toxic drugs such as Bleomycin to detect asymptomatic drug induced lung disease (DILD). We conducted a systematic review to assess the accuracy of PFTs, including the diffusing capacity for carbon monoxide (DLCO), for early detection of DILD in a range of drugs.

**Methods:** We used a pre-specified, registered review protocol and searched OvidMEDLINE and EMBASE from 1946 to February 2018. Two reviewers independently screened abstracts and reviewed full text articles for inclusion. Primary outcome data was extracted and entered into RevMan5 to estimate sensitivity and specificity (and 95% CIs).

**Results:** We identified 4065 citations and included 42 studies. The most commonly studied drugs were Bleomycin and Amiodarone. Due to clinical heterogeneity between studies, a pooled analysis was not performed. Sensitivity of monitoring with DLCO (for a threshold of >15% or 20% decline from baseline) varied between 0% and 100%, with the majority of studies finding a sensitivity of <80%. Confidence intervals were wide for the majority of studies. Specificity was less than 90% in all studies. Risk of bias was high for the majority of studies for the quality domain of reference standard.

**Conclusion:** Our findings do not support routine PFTs for early detection of DILD. Due to methodological limitations, the relatively small number of participants and the low prevalence of DILD in the included studies, there remains significant uncertainty about the sensitivity of PFTs to screen for DILD.

**Grant Support:** None.

**Declaration of interest:** The authors have no conflicts of interest to declare.

### EARLY AGE AT NATURAL MENOPAUSE IS ASSOCIATED WITH REDUCED LUNG FUNCTION IN THE TASMANIAN LONGITUDINAL HEALTH STUDY

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**Introduction/Aim:** Lower lung function, a significant predictor of mortality, has been observed in post-menopausal women when compared to those still menstruating. While the timing of this transition (menopausal age) is a known risk factor for several adverse health outcomes, little evidence was available on the relationship between menopausal age and lung function impairments, particularly for post-bronchodilator lung function measures. We aimed to fill this gap in knowledge and determine the association between early age at natural menopause and lung function.

**Methods:** The Tasmanian Longitudinal Health Study (TAHS) is a population-based cohort. Lung function was measured at age 7 and again at 53 years. Additional data on relevant confounders were collected in childhood and during follow-up at age 45 years, and at 53 years, information was also collected on most recent menstrual period and menopausal status (n = 795). Multiple linear regression was performed to determine the association between menopausal age and pre- and post-bronchodilator spirometry while controlling for potential early and adult life confounders.

**Results:** Post-menopausal women reporting an early age at natural menopause (<45 years) had lower post-bronchodilator FEV1 (-173mL; 95%Confidence Interval [CI] -273, -73) and FVC (-196 mL; 95%CI -305, -86) compared with post-menopausal women reporting menopause at a later age (≥45 years). Adjustment for early life confounders, particularly childhood social class and lung function, strengthened these associations. FEV1/FVC% was not affected by timing of menopause (-0.64; 95%CI -2.22, 0.95), suggesting a restrictive rather than obstructive defect.

**Conclusion:** Early menopausal age is associated with reduced lung function. This new evidence from data on post-bronchodilator measurements and early life confounders should raise clinical awareness on the potential for women with early menopause to be at risk of biologically relevant lung function impairment.

**Grant Support:** National Health and Medical Research Council, Cliff-ford Craig Foundation, and Asthma Foundations of Tasmania, Victoria and Queensland.

TPL 017

TPL 018

**NON-INVASIVE VENTILATION ACCORDING TO BEST PRACTICE RECOMMENDATIONS: A SINGLE SITE PROSPECTIVE AUDIT**

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**Introduction/Aim:** The British Thoracic Society has recently published guidelines of best practice non-invasive ventilation (NIV) service delivery to address key areas of concern regarding patient safety. The aim of this study was to conduct a prospective audit based on these guidelines with the goal of identifying areas for improvement.

**Methods:** All patients admitted to the ward-based respiratory failure unit and treated with acute bi-level NIV from January to December 2018 were included. Data were collected prospectively using electronic medical records.

**Results:** 164 patients were admitted and 85 were included in the study. The median age was 67 and 46% were men. Oxygen saturation was maintained between 88-92% in 46%. Initial prescription was made by staff with an appropriate level of competency in 98%. Advanced care plans prior to treatment were made in 54%. Treatment was commenced within one hour of a blood gas in 39%. Ventilator settings documented on a standard form in 71%. When NIV was used in patients with pneumonia, it was considered appropriate in 92% of cases. A plan for future admission was made in 64%. Arterial blood gasses were used exclusively to guide treatment in 64%. High flow nasal prongs were used in 38%. The patient was intolerant of NIV in 9%. The most common diagnoses were COPD (85%) and pulmonary oedema (15%). 49% of patients were referred for consideration of home NIV. Mortality was 13% at 3 months and 26% at 6 months.

**Conclusion:** This study has highlighted a number of areas for service delivery improvement including safe administration of supplemental oxygen, delays in treatment, and defining appropriate levels of care. Mortality data and the level of senior doctor supervision was reassuring. This study will be extended following the introduction of a modified unit admission checklist.

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**UTILISATION OF SPIROMETRY IN PATIENTS WITH A CLINICAL DIAGNOSIS OF COPD**

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**Introduction/Aim:** The diagnosis of COPD relies on demonstrating persistent airflow obstruction on spirometry. Previous studies suggested that spirometry is underutilised in the diagnosis of COPD which may lead to misdiagnosis and inappropriate prescribing. Our aim was to determine the utilisation of spirometry in patients that were hospitalised and had a clinical diagnosis of COPD. Prescribing patterns of COPD medicines were also examined.

**Methods:** All inpatients admitted to a metropolitan health service in Victoria between October 2016 and March 2018 with a primary or secondary diagnosis of COPD were included. Medical records were reviewed to determine if spirometry had been performed prior to the index admission, and if it was consistent with a clinical diagnosis of COPD. Where available, pharmacy records were extracted for this population in order to evaluate the use of inhaled COPD medicines at discharge.

**Results:** During the study period, 1460 patients were admitted with a discharge diagnosis of COPD. The majority were male (55%) with a mean age of 72 at admission. There were no spirometry results for 649 (44.4%) of these patients. Of the 811 who had previously undergone spirometry, 542 (37.1%) had results consistent with a diagnosis of COPD. Prescribing data at discharge was available for 834 of the overall cohort. COPD medicines were frequently prescribed for both patients that had not previously undergone spirometry or who had spirometry results inconsistent with a clinical diagnosis of COPD.

**Conclusion:** These results from a single centre confirm underutilisation of spirometry in hospitalised patients with a clinical diagnosis of COPD. COPD medicines were often prescribed in the absence of spirometry or in those who had not demonstrated persistent airflow obstruction when tested. Strategies to improve access to spirometry and its clinical interpretation may help to reduce the apparently high rate of inappropriate prescribing of COPD medicines.

**A PILOT STUDY OF THE ROLE OF IMPULSE OSCILLOMETRY (IOS) IN COMPARISON TO SPIROMETRY IN DETECTING IMPROVEMENTS AFTER TREATMENT FOR ADULT CYSTIC FIBROSIS (CF) PULMONARY EXACERBATIONS**

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**Introduction/Aim:** Spirometry is the current gold standard method for monitoring patients with CF and is a primary tool for detecting lung function decline such as that seen during an exacerbation. Spirometry is routinely measured to detect lung function improvements with intravenous antibiotic treatment. IOS is a diagnostic tool that detects airway resistance and requires significantly less patient effort than spirometry. IOS has been shown to be a useful diagnostic test in the paediatric CF population but there are limited studies in the adult population. The aim of this study is to determine if IOS is a more sensitive diagnostic tool in determining the effectiveness of intravenous antibiotic treatment in adult patients with CF exacerbation than spirometry.

**Methods:** CF patients commencing intravenous antibiotic treatment for pulmonary exacerbations were prospectively recruited into the study. CF patients who were colonised with *Mycobacterium abscessus*, *Burkholderia cepacia* and *Pandorea sp.* were excluded from the study. IOS and spirometry were performed prior to and at the cessation of antibiotic treatment.

**Results:** Seven patients (n = 7), 31 ± 7.1 years (mean±SD) have completed the study to date. Six (86%) were males. Two patients (29%) required more than two weeks of antibiotic treatment. Mean pre-exacerbation FEV<sub>1</sub> and FVC were 3.0±1.0L (74.1 ± 20.3% predicted) and 4.4±1.4L (87.9 ± 20.1% predicted). Paired t-tests were used to determine statistical significance between pre and post antibiotic treatment, the results are shown in table 1 below. Spirometry and airway resistance values showed a significant change (P < 0.05), which correlated with a decrease in inflammatory markers. There was no significant change in reactance variables (P > 0.05).

**Conclusion:** Spirometry still remains the gold standard tool for monitoring CF exacerbations in this patient group. Airway resistance measurements utilising IOS may be a helpful additional monitoring tool but the results were limited due to the study size. Recruitment to this study is ongoing.

**Grant Support:** None

**RETROSPECTIVE REVIEW OF SAFETY AND EFFICACY OF INDWELLING PLEURAL CATHETERS FOR THE MANAGEMENT OF MALIGNANT PLEURAL EFFUSION**

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**Introduction/Aim:** Malignant pleural effusion (MPE) is a common complication of many cancers (e.g. lung, breast, ovarian), resulting in breathlessness, exercise limitation and reduced quality of life. Treatment options for MPE are customised for each individual based on underlying malignancy, estimated prognosis, degree of lung involvement and patient preference. MPE where the lung does not re-expand and fluid accumulates, a permanent drain can be placed to palliate dyspnoea, known as Indwelling Pleural Catheters (IPCs). This study aimed to assess the rate of complications of IPC in patients with malignant pleural effusion and the clinical course, in a retrospective cohort of patients with malignant pleural effusion.

**Methods:** A retrospective cohort of patients treated between January 2014 - January 2018 with IPC for MPE was reviewed from a log-book has been prospectively kept from January 2014. De-identified demographic, cancer specific and IPC safety data (infections, product failure, admission requirements) were collected.

**Results:** From 2014 – 2018, forty nine IPCs were inserted. The majority (15, 31%) were inserted for mesothelioma and adenocarcinoma lung (14, 29%). The average IPC duration was 4.5 months (SD ± 5 months), average survival overall was 13.7 months (SD ± 15months). 91% of IPCs had no complications encountered. 5% (n = 2) of IPCs were reported to have early complications with drainage issues and 2% (n = 1) had late drainage troubles. Only 1 significant pleural space infection occurred and 2 IPC wound site infections (*Staphylococcus spp.*). One blood stream infection with *Escherichia coli* was detected, but probably unrelated to the IPC. The infection rate was 6%. 4 cases of cap locking mechanism failure were detected.

**Conclusion:** IPCs are a widely used treatment option for MPE, and the experience at the PA hospital demonstrates infection rates well within the internationally reported literature. This study did not account for whether patient were or were not receiving chemotherapy which may have contributed to infection rates. Survival remains poor for patient requiring management for MPE. Cap locking mechanisms has been notified to the manufacture and is part of an Australia wide product review.

**Grant Support:**

**Table 1** Spirometry and IOS values before and after antibiotic treatment in adult patients with cf exacerbation

Parameter	Pre-antibiotics treatment	Post-antibiotics treatment	Mean percentage change (%)	p-value
FEV <sub>1</sub> , L	2.51±0.76	2.81±0.79	13.73±10.78	0.01*
FVC, L	3.84±1.28	4.26±1.25	12.57±12.02	0.03*
FEV <sub>1</sub> /FVC, L	65.57±8.66	66.43±8.73	13.55±3.57	0.41
R5, kPa/L/s	0.48±0.13	0.41±0.11	-13.60±14.62	0.03*
R20, kPa/L/s	0.40±0.09	0.36±0.08	-11.12±11.05	0.02*
AX, Hz	0.72±0.58	0.48±0.28	-20.14±42.52	0.14
Fres, Hz	16.29±4.43	14.50±3.42	-9.57±15.24	0.15
CRP	42.85±83.58	5.83±6.19	-39.51±74.78	0.31

FEF25-75: forced expiratory flow between 25-75% of FVC; R5: Resistance at 5 Hz; R20: Resistance at 20 Hz; X5: Reactance at 5Hz; X20: Reactance at 20Hz; AX: area under the reactance curve; Fres: resonance frequency \*p<0.05 statistically significant. Results are presented as mean±standard deviation

**EVALUATING THE PROCESS OF TRANSITIONING PATIENTS CARE FROM THE HOSPITAL TO GENERAL PRACTICE**

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**Introduction:** Mepolizumab is a monoclonal antibody for the treatment of severe eosinophilic asthma. We administer the first three injections in the hospital clinic setting with patients required to remain for 1 hour of observation. After the first 3 months, the patient treatment is transitioned to their general practitioner (GP) for ongoing care and mepolizumab administration with six monthly specialist reviews.

**Aim**

1. To evaluate the proficiency and outcome of the referral process, including GP satisfaction with the handover, and communication of information in regard to the requirements of administration of this medication.
2. To assess whether the current method of communication is sufficient to empower the GP to be clinically comfortable managing the administration of the drug.
3. To evaluate the transition of treatment management from the clinic setting to G.P. setting from a patient perspective.

**Methods:** Questionnaires were administered to 26 patients by telephone or face to face in clinic and 27 GPs by telephone.

**Results Patient Response:** 96% reported that they had received sufficient information; 100% found hospital visit valuable; 19% had some difficulties with transition.

**GP Response:** 1 GP failed to receive any information; 2 GP's refused to administer treatment. In other cases transition was successful with no patient returning to receive routine injections in the clinic.

**Conclusion:** Information received by both patients and GP was sufficient. All patients found the hospital visits were valuable giving reassurance and confidence with the treatment. Difficulties of transition of care for patients were overcome by effective communication and increased knowledge.

**Grant Support:** Nil.

**ARE INPATIENT SMOKERS CONSISTENTLY IDENTIFIED AND OFFERED SMOKING CESSATION INTERVENTIONS: A QUALITY IMPROVEMENT PROJECT WITH FOLLOW UP AUDIT.**

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**Introduction/Aim:** We previously audited documentation of smoking status during the transition from paper to electronic records. We found that smoking status could be more consistently recorded and documented, provision and/or documentation of smoking cessation interventions was poor, and transition to EMR may be a risk for poorer health service provision. Since our initial audit, an education program has been implemented for all clinical staff in the respiratory ward along with two mandatory smoking cessation modules from 'my health learning' site. The intervention of smoking cessation advice is a mandatory competency on the respiratory ward.

**Methods:** Electronic medical records (EMR) of Respiratory Medicine inpatients were analysed for documentation of smoking status on admission to hospital, and the offering of brief advice and pharmacotherapy or referral to specialist support services for current smokers. Chi<sup>2</sup> tests were used to assess statistical significance.

**Results:** 122 EMR were analysed here. 61 paper/61 EMR were in the previous audit.

Performance parameter	Audit 1		Audit 2
	Paper	EMR	
Smoking status	92%	67%	79%
Smoking cessation advice	54%	14%	40%

Data for smoking status and advice are not significantly different from paper or EMR in audit 1.

**Conclusion:** Smoking status determination/documentation has improved with the intervention and is no longer significantly lower than paper statistically but has not reached numerical equivalence. EMR may be a risk for poorer health service provision or documentation. There is a need for improvement in documentation by health professionals if smoking interventions as per NSW government guidelines are to be achieved

There is no conflict of interest

**Grant Support:** Nil.

TP 187

TP 188

### IMPACT OF A CASE-MANAGEMENT PROGRAM FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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**Introduction/Aim:** Background: Chronic Obstructive Pulmonary Disease (COPD) is classed as the second leading potential 'avoidable' hospital admission diagnosis in Australia. COPD is an ever increasing detriment on health and the wellbeing of people who have smoked, been exposed to smoke or in some cases have the disease through genetics. It is not curable and the decline in lung function will progressively continue. Frequent exacerbations of COPD are shown to have considerable effects on health-related quality of life (QoL). In addition to this, hospital admissions and re-admissions are increasingly impacting on the government health expenditure. The aim was to demonstrate if a comprehensive community-based tailored case-management approach to managing COPD would affect admission and re-admission rates within the Northern Adelaide Local Health Network.

**Methods:** Using a cross-sectional study design, data was retrieved from case-mix; reviewing the number of admissions 6 months pre case-management intervention and 6 months post case-management intervention. This was then compared to the same time period in the previous year. Inclusion criteria for case-management as follows; >18 years, 2 or more COPD admissions in 6 months, and/or 3 or more COPD presentations in 12 months.

**Results:** Overall the study showed a 72% reduction in admission rates in patients included in the case management program. This 72% is inclusive of patients who did not have an admission within the 6months pre and 6months post intervention.

**Conclusion:** To assist in the management of the number of potentially avoidable hospital admissions a comprehensive community-based case-management program for COPD within the Northern Local Health Network is favourable.

**Grant Support:**

### STAFF KNOWLEDGE AND ADHERENCE TO SUPPLEMENTAL OXYGEN THERAPY GUIDELINES WITHIN AN ACUTE AGED CARE INPATIENT SETTING.

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**Introduction:** Supplemental oxygen therapy is a commonly used therapeutic to treat hypoxaemia. In the healthcare setting, oxygen is considered to be *like a drug*. Like any drug, when used inappropriately, it can cause harm. National respiratory guidelines (Thoracic Society of Australia and New Zealand oxygen guidelines for acute oxygen use in adults: 'Swimming between the flags'<sup>1</sup>) state supplemental oxygen should be prescribed on the medication chart with target oxygen saturation ranges based on patient risk. Supplemental oxygen therapy used throughout the hospital, not just in respiratory wards.

**Aim:** To assess current adherence to supplemental oxygen therapy guidelines in an Acute Aged Care inpatient setting. To assess the knowledge of staff working in an Acute Aged Care inpatient setting regarding supplemental oxygen therapy administration.

**Methods:** Prospective ward audits to identify adherence to oxygen guidelines and administration of questionnaires to staff to assess level of knowledge.

**Results:** Three initial ward audits revealed 0% oxygen prescription and 50% inappropriate supplemental oxygen administration. 69 subjects (58% registered nurses, 17% medical officers, 14% allied health staff & 10% enrolled nurses) were enrolled in part two of the study. Knowledge regarding oxygen therapy was variable (scores 17 – 89%). Following a targeted education intervention, three repeat ward audits revealed a massive improvement of adherence to guidelines with 100% oxygen prescription and 0% inappropriate administration of oxygen. Reassessment of staff knowledge is currently underway.

**Conclusion:** It is important to ensure all inpatient settings are following national guidelines regarding supplemental oxygen. Following a targeted educational intervention in an Acute Aged Care setting, adherence to national oxygen guidelines are improved.

**Grant Support:** NA.

TP 189

**EVALUATION OF THE HEALTH RELATED QUALITY OF LIFE (HRQOL) AND HAEMODYNAMICS OF PULMONARY HYPERTENSION (PH) PATIENTS TREATED WITHIN THE PRINCESS ALEXANDRA HOSPITAL MULTIDISCIPLINARY CLINIC**

**ROSS J<sup>1</sup>**, ELLENDER C<sup>1</sup>, KEIR G<sup>1</sup>, WAHI S<sup>1</sup>, KORCZYK D<sup>1</sup>

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**Introduction/Aim:** Our aim was to evaluate the HRQoL in PH patients using the Emphasis 10 questionnaire and haemodynamics of patients at the Princess Alexandra Hospital from 1 January 2018 to 5th July 2018. Generic HRQoL surveys have mostly been used in clinical trials pre and post medications on average for 12 weeks, showing slight improvement with medical treatment. The Emphasis 10 was recently validated as a PH specific QoL survey. Emphasis 10 consists of 10 questions. Higher scores indicate a poorer health status.

**Methods:** Routine data collected as standard of care including echocardiogram, six minute walk distance (6MWD), New York Heart Association Functional class (NYHA FC) and +/- right heart catheter (RHC) was reviewed. All patients on PH treatment who completed the Emphasis 10 questionnaire were audited to compare with FC, 6MWD, Mean Pulmonary Artery Pressure (mPAP) and Pulmonary Vascular Pressure (PVR), and Right Ventricular Systolic Pressure (RVSP).

**Results:** 66 patients were included for review. 54 (80%) female. Ages ranging from 23 yrs to 83 yrs, the most predominant age group being 60-70 yrs. The predominant aetiology was group Group 1 (52, 78%), followed by Group 4 (9, 14%). Of the 66 patients on treatment 32, (47%) were Functional Class 2 and 3.

**Conclusion:** Little relationship was found between HRQoL and routinely collected invasive and non-invasive measures of physiological fitness. Patients with the same level of function measured by NYHA FC had vastly different HR QoL. This data adds to the literature that whilst PH patients on therapy may have improved physiologically, there is still considerable impairment and suffering from this chronic condition. Further review of changes over time with combination pharmacotherapy is needed to ensure that medications are not just helping patients live longer, but live with better quality of life.

**Grant Support:**

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