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ANZSRS ORAL PRESENTATIONS

WINDS OF CHANGE: BRONCHODILATOR RESPONSIVENESS FROM MORE THAN ONE DIRECTION

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Introduction: Positive bronchodilator responsiveness (BR) using current American Thoracic Society and European Respiratory Society (ATS/ERS) criteria, purportedly ensures spirometric variability is significantly exceeded. The ATS/ERS guidelines acknowledge there is no clear consensus about what constitutes bronchodilator responsiveness in subjects with airflow obstruction.

Aim: This study investigated the individual variability in multiple spirometric parameters in patients having reversibility tests. We address how spirometric variability can inform current guidelines for identifying a clinically significant bronchodilator response.

Method: 102 consenting participants performed slow vital capacity (SVC) and flow volume loops (FVL) before and after Salbutamol administration. Measurement of symptom control used the clinical chronic obstructive pulmonary disease questionnaire and dyspnoea and wheeze used the visual analogue scale. Two determinants of BR: ATS/ERS criteria and a t-score calculation were compared by correlation with the subjective measurements of respiratory impairment.

Results: 63 participants had positive bronchodilator responses by t-score calculation compared with 16 by current ATS/ERS guidelines. T-scores showed a weaker correlation with subjective measures of respiratory impairment than per cent and absolute change. Inspiratory vital capacity (IVC), SVC, and inspiratory capacity (IC) correlated more strongly with symptom control, wheeze and dyspnoea than FEV_1 or FVC. The mean individual variability and standard deviation (SD) for each parameter is shown in the table.

	n	**Mean, SD (L)** Pre-bronchodilator	*CV, SD (%)	**Mean, SD (L)** Post bronchodilator	*CV, SD (%)
FEV_1	101	2.58 (0.98)	1.89 (1.46)	2.74 (1.00)	1.67 (1.45)
FVC	101	3.60 (1.09)	1.64 (1.27)	3.71 (1.06)	1.35 (1.45)
FIVC	97	3.57 (1.06)	2.29 (2.06)	3.63 (1.07)	1.89 (1.61)
SVC	100	3.56 (1.08)	1.91 (1.22)	3.74 (1.03)	1.45 (1.04)
IC	100	2.83 (0.80)	2.95 (2.56)	3.03 (0.82)	2.33 (1.50)

*CV = Coefficient of Variation;

Conclusion: The low individual variability may explain the poorer discriminatory ability of BR by t-score because a smaller change is required to be considered significant. T-scores may overestimate bronchodilator responsiveness, particularly in patients with normal spirometry at baseline. Spirometry values that are less influenced by dynamic compression have potential utility in bronchodilator response testing. Ongoing recruitment will allow further investigation into the utility of t-scores and alternative spirometry values for participants with airway obstruction.

Key Words: Spirometry, variability, bronchodilator response
Nomination for New Investigator Award
Grant Support: Nil

ASSESSING THE SUITABILITY OF FRACTIONAL EXHALED NITRIC OXIDE (FENO) CUT-OFF RANGES FOR ABORIGINAL AND/OR TORRES STRAIT ISLANDER CHILDREN AND YOUNG ADULTS

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Introduction/Aim: Fractional exhaled nitric oxide (FeNO) is used as a non-invasive measure of eosinophilic airway inflammation. It is unknown how appropriate the recommended FeNO cut-off ranges are for Aboriginal and/or Torres Strait Islander patients. Our aim was to assess the distribution of healthy Aboriginal and/or Torres Strait Islander FeNO results according to current American Thoracic Society cut-off guidelines.

Methods: We measured FeNO (using Aerocrine NioxMINO) in 991 Indigenous children and young adults (aged 3 to 25 years) from seven Queensland communities. Questionnaires and medical charts were reviewed to identify healthy participants (no respiratory and/or atopic illness ever).

Results: Acceptable FeNO measurements were achieved by 553 children (≤12 years) and 288 adults (>12 years). Participants with a history of respiratory and/or atopy conditions were excluded resulting in a healthy cohort of children (n=401, 72.5%) and adults (n=193, 67%). The geometric mean FeNO results for children and adults were 11.1ppb and 12.5ppb respectively. Table 1 summarises the distribution of healthy FeNO results for each ethnic group according to current cut-off ranges.

	Child ≤12 years (ppb)				**Adult >12 years (ppb)**		
	Normal ≤20	Inter 21-34	Inflam ≥35		Normal ≤25	Inter 26-49	Inflam ≥50
Aboriginal (n=112)	88%	7%	5%	(n=51)	90%	6%	4%
Torres Strait Is (n=134)	83%	6%	11%	(n=87)	83%	10%	7%
Both (n=155)	85%	8%	7%	(n=55)	87%	9%	4%

Is=Islander, Both=Aboriginal and Torres Strait Islander
Int=Intermediate, Inflam=Inflammation

Conclusion: Although the majority of participants had FeNO results within the age-respective normal ranges, we found a proportion of healthy participants with elevated FeNO results in all groups. The greatest proportion of elevated results was seen in Torres Strait Islander children and adults, and Aboriginal/Torres Strait Islander children. This suggests that the recommended cut-off ranges may not be appropriate for these groups. Further investigation is still needed.

Key Words: FeNO, Aboriginal and/or Torres Strait Islander, cut-off ranges
Nomination for New Investigator Award: Yes

COMPARISON OF METHODS FOR POOLING MULTIPLE BREATH NITROGEN WASHOUT DATA

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Introduction/Aim: The multiple breath nitrogen washout (MBNW) test measures ventilation heterogeneity in the small airways. Analysis of how the concentration-normalised phase III slope (SnIII) of the expirogram progresses through the washout can provide further insight. This partitions ventilation heterogeneity into a convection-dependent component, primarily reflecting conductive airways (Scond), versus a diffusion-convection-dependent component, primarily reflecting acinar airways (Sacin). Current ERS/ATS consensus[1] recommends SnIII values from three technically acceptable washouts be pooled for reliable estimation of Scond and Sacin. We aimed to compare current methods for pooling MBNW data, to provide evidence to guide ongoing standardisation efforts.

Methods: Three methods were examined: (i) AllBreaths: using all breaths from all three washouts[2], (ii) AvgSlopes: analysing each washout separately and averaging the three Scond and Sacin values [unpublished, default method in commercial MBNW software], (iii) AvgBreaths: averaging each corresponding breath of the 3 tests to produce an average breath 1, 2, etc[3]. Data were collected using an Exhalyzer D system (Eco Medics AG, Duernten, Switzerland).

Results: Data from 10 healthy subjects (3 males, mean±SD age 25±3 years, height 171±7 cm, weight 72.2±13.8 kg) were analysed. AvgBreaths tended to yield lower Scond (mean±SD shown in Table), but this was not statistically significant (one-way repeated measures ANOVA, p=0.17). There were no differences seen in Sacin across all methods (p=0.12).

	AllBreaths	AvgSlopes	AvgBreaths
Scond, L^{-1}	0.017±0.009	0.017±0.009	0.015±0.008
Sacin, L^{-1}	0.061±0.020	0.061±0.020	0.062±0.020

Conclusion: In this preliminary analysis, no differences were apparent between the three methods of pooling MBNW data. Further work will examine a wider range of Scond and Sacin values in health and disease. These results help identify any potential sources of differences between laboratories performing MBNW.

[1] Robinson et al, ERJ 2013;41:507-52
[2] Verbanck et al, Thorax 2012;67:789-795
[3] Kjellberg et al, Respir Med 2016;117:92-102

Key Words: Multiple breath nitrogen washout, SnIII analysis, ventilation heterogeneity

IS THE DESATURATION PROFILE APPARENT DURING A 6 MINUTE WALK TEST CONSISTENT WITH THE PROFILE ESTABLISHED DURING A MAXIMAL EXERCISE TEST?

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Introduction/Aim: To corroborate previous findings that patients desaturate more during six minute walk tests (6MWT) than incremental cardiopulmonary exercise tests (CPET). Secondary aim was to explore predictive characteristics for exercise desaturation.

Method: Retrospective data analysis of patients completing pulmonary rehabilitation (PR) between 2014 and 2016. Inclusion criteria: primary diagnosis of respiratory disease, completed both CPET and 6MWT. Significant exercise desaturation defined as ≥4% change in SpO_2 from rest. Chi-squared analysis was undertaken to investigate whether DLCO, $EqCO_2$, $P(A-a)O_2$, or the VE/VCO_2 slope were predictive for exercise desaturation. Wilcoxon signed rank test was used to establish differences between resting and minimum saturation levels on pre and post PR 6MWTs.

Results: A total of 35 patients (of 387) met the inclusion criteria. Mean age 60.1 (±SD 11.57) years and FEV1% predicted of 63% (±SD 17.14). Eight patients did not desaturate during either test, 12 desaturated during both tests, 14 desaturated during the 6MWT only and one desaturated during the CPET only. Detailed results are presented in Table 1. CPET achieved a higher peak HR than 6MWT (p-value 0.000). Only DLCO less than 55% predicted desaturation during CPET alone. Markers of gas exchange were not able to predict significant desaturation. Resting and minimum 6MWT SpO_2 measurements obtained before and after PR were not significantly different (p-value 0.760 and 0.577 respectively).

Table 1 Predictors of significant desaturation

Parameter	p-value
A-a gradient above ULN (*n*=30)	0.654
VE/VCO2 slope above 34 (*n*:34)	1.00
$EqCO_2$ (*n*=34)	0.508
DLCO 55% predicted or less CPET (*n*=29)	0.010 *
DLCO 55% predicted or less 6MWT (*n*=29)	0.227

*p-value significant.

Conclusion: Consistent with other reports, more patients demonstrated significant desaturation during 6MWT than CPET. Gas exchange parameters failed to predict exercise desaturation during CPET. In agreement with other studies, low DLCO was predictive of desaturation during CPET.

Key Words: Desaturation, Cardiopulmonary exercise test (CPET), Six minute walk test (6MWT).

Nomination for New Investigator Award: Yes

DO EXERCISE PROTOCOLS INFLUENCE CLINICAL DECISIONS?

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Introduction/Aim: Cardiopulmonary exercise testing (CPET) is an important component of patients' work up for lung resection surgery for lung cancer. A peak V'O$_2$ (V'O$_{2Pk}$) <15 mL.min^{-1}.kg^{-1} is classified as high risk [1], thus a patient is required to exceed this threshold to be eligible for lung resection surgery.

In 2007 the Auckland District Health Board Adult Respiratory Laboratory changed its CPET exercise protocol from an in-house developed treadmill based ramp protocol (Whitlock-Harris (WH)) to a standardised exponential exercise protocol (STEEP) [2]. Our study aimed to compare the V'O$_{2Pk}$ outcomes from these two different protocols to determine if there was a difference in the number of patients achieving >15 mL.min^{-1}.kg^{-1} threshold, and thus determine if the protocol used influenced the measure of V'O$_{2Pk}$ used for assessing fitness for surgery.

Method: A retrospective analysis was performed on 159 patients who had been referred for CPET testing for fitness for lung resection surgery between 2004-2010 excluding 2007. Comparisons between the mean V'O$_{2Pk}$ and proportion of those achieving > 15 mL.min^{-1}.kg^{-1} were made for those tested with the WH and STEEP protocol.

Results: Those tested with the WH (n=86) achieved and mean V'O$_{2Pk}$ of 17.5 mL.min^{-1}.kg^{-1} whilst those tested with the STEEP (n=73) achieved and mean V'O$_{2Pk}$ of 20 mL.min^{-1}.kg^{-1}. (p=0.002). There were no significant differences in age, weight or BMI between groups. For those tested with the WH protocol 30% achieved V'O$_{2Pk}$ < 15 mL.min^{-1}.kg^{-1} compared to 18% of those tested with STEEP.

Conclusion: Our findings suggest that the exercise protocol used significantly affects the V'O$_{2Pk}$ attained during testing, and can therefore ultimately influence the decision for lung resection surgery.

Key Words: CPET, V'O$_2$, lung cancer, oxygen consumption, lung resection

Nomination for New Investigator Award

I would like to be considered for the new investigator award.

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2. Northridge, David B., Stanley Grant, I. Ford, J. Christie, J. McLenachan, D. Connelly, J. McMurray, S. Ray, E. Henderson, and H. J. Dargie. "Novel exercise protocol suitable for use on a treadmill or a bicycle ergometer." *Heart* 64, no. 5 (1990): 313-316.

LUNG VOLUME PLETHYSMOGRAPHY OCCLUSION TECHNIQUES: PANTING TO TIDAL BREATHING COMPARISON

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Introduction/Aim: Lung volumes plethysmography (LVpleth) requires a panting manoeuvre of around 0.5-1.0 Hz (~± 10 cmH2O)during a 2-3 second occlusion obtaining a pressure at functional residual volume (FRC), with a vital capacity manoeuvre to calculate total lung capacity (TLC).

The aim was to determine if there was a difference in test method; and whether there was a preferred technique by patients.

Method: Stratified recruitment occurred for patients already attending a full lung function test at The Queen Elizabeth Pulmonary Function Laboratory. Each patient performed spirometry (pre- and post-bronchodilator), gas transfer, LVpleth (panting, followed by the tidal breathing method). Patients were asked which technique was preferable to perform, and which test instructions were easier to follow.

Data was analysed to determine whether tidal TLC & FRC data fell within ±5% of the GOLD standard panting technique. Paired sample t-tests were used to determine significanceMicrosoft Excel 2010 was used for analyses.

Results: 27 patients were tested (55.6% new patients, 51.9% male, mean age 59yrs, mean BMI of 31.67). Based on clinical diagnosis (by a respiratory consultant following American Thoracic Society guidelines), 37% were normal, 33.3% obstructive, 26% restrictive, 3.7% mixed.

Of 15 patients asked (40% new patients), 40% preferred performing tidal breathing, 26.7% 'panting', 33.3% indifferent. Tidal breathing was identified by 53% as easier to follow. FRC loops were of similar quality, correlating with tidal TLC and FRC analysis and within 5% agreement of the panting technique with no significant difference.

Conclusion: Tidal breathing was identified as easier to follow by patients and had a higher preference. However this may have been bias as the panting was performed first and the ease may be a result of a learned effect. For patients that become overwhelmed with the panting technique, tidal breathing may be a good alternative to obtain FRC values.

Key Words: FRC, TLC, lung volumes plethysmography

AO 007

ASSESSING THE 2017 ERS/ATS SINGLE-BREATH DIFFUSING CAPACITY ACCEPTABILITY AND REPEATABILITY CRITERIA

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Introduction/Aim: The 2017 European Respiratory Society/American Thoracic Society standards for single-breath carbon monoxide uptake in the lung propose several changes to acceptability and repeatability criteria.

The aim of this study was to assess current patient results against three of the new criteria – an inspired volume of test gas (VI) greater than 90% of the largest VC, VI >85% and alveolar volumes (VA) within 200mLs or 5%, and DLCO measurements within 2ml/min/mmHg of each other.

Method: The results of 965 consecutive single-breath diffusion measurements (490 male; (mean±SD) age 65±14 years; DLCO 16.88±6.61 ml/min/mmHg) from July-September 2017 were analysed, all of which were acceptable and repeatable per the 2005 standards.

Results: 97% of tests met the new repeatability criteria for DLCO, while 79% of tests had both inspiratory efforts meeting the new VI acceptability criteria. When taking into account the 200 tests with at least one VI ≥85% and <90% of the largest VC, only 37 did not meet the criteria for a repeatable VA.

Conclusion: The 2017 ERS/ATS DLCO acceptability and repeatability criteria should be easily achievable by the majority of patients.

Key Words: Single breath diffusing capacity, DLCO, technical standards

Grant Support: N/A

AO 008

PREVALENCE OF ABNORMAL HAEMOGLOBIN LEVELS IN A LUNG FUNCTION LABORATORY POPULATION: IMPACT ON TLCO INTERPRETATION

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Introduction/Aim: The effect of abnormal haemoglobin (Hb) concentration, and anaemia in particular, on TLCO is well understood. The ERS/ATS 2017 standard recommends Hb correction as optional, leaving open the question of when to apply it. We determined the prevalence of abnormal Hb concentrations in patients attending a public hospital laboratory. We also evaluated the frequency with which correcting for Hb changed TLCO interpretation from normal to reduced (from above to below the lower limit of normal) and from reduced to normal.

Method: 4390 consecutive TLCO measurements performed since January 2016 were analysed. Hb was measured in all patients. TLCO was corrected for Hb using the ERS/ATS recommended equations (to 14.6 for males>14 years and 13.4 gm/dL for females and children<15 years).

Results: The prevalence of Hb<12, <10 and >18 gm/dL was 26.3, 4.8 and 0.6%. Table 1 shows the distribution of Hb's and change in TLCO after corrected for Hb. Table 2 illustrates the impact of Hb correction on TLCO interpretation.

Table 1

	median	5th-95th perc.	range
Hb (gm/dL)	13.2	10.1 to 15.8	6.1 to 22.1
ΔTLCO (ml/min/mmHg)	+0.4	-0.8 to +2.6	-2.7 to +8.4
ΔTLCO (% pred)	+1.5	-2.8 to +9.4	-8.6 to +37.4

Table 2

	n	n (%)
Unchanged	4160	95%
Normal → reduced	40	1%
Reduced → normal	190	4%

Conclusion: A small but significant proportion of patients referred for TLCO measurements have levels of Hb that require correction in order to avoid misdiagnosis of abnormality. These results suggest a role for routinely correcting for Hb when TLCO is measured.

Key Words: TLCO, haemoglobin correction, CO transfer factor

SMALL AIRWAY FUNCTION IMPROVEMENT WITH MEPOLIZUMAB IN SEVERE EOSINOPHILIC ASTHMA

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Introduction/Aim: Mepolizumab is a monoclonal antibody against interleukin-5 that was recently approved in Australia for severe eosinophilic asthma. In clinical trials, monthly treatment with mepolizumab results in clinically significant reductions in exacerbation rates, coupled with modest improvements in symptom control scores and FEV1. The acute effects of this biologic treatment on small airway function have not been previously described. The aim of this study is to describe changes in ventilation inhomogeneity as a marker of small airway function after the commencement of mepolizumab in adult with severe eosinophilic asthma.

Methods: This is a prospective case series of 5 patients (3 males) commencing mepolizumab for severe eosinophilic asthma according to the Pharmaceutical Benefit Scheme pre-specified criteria. At each monthly visit, patients underwent lung function testing including exhaled nitric oxide (eNO), spirometry and the multiple breath nitrogen washout test to measure functional residual capacity (FRC) and global (Lung Clearance Index, LCI) and regional indices of ventilation inhomogeneity attributed to the acinar (Sacin) and conducting (Scond) airways. Results at baseline and four weeks after the first injection are reported.

Results: Mean (range) age of patients was 61 (41-76) years, BMI 23.6 (23-25) kg/m^2, post bronchodilator FEV1 50 (36-61) %predicted, FEV1/FVC ratio 50 (31-68) % and median (IQR) eNO 42 (32-75) ppb. One month after the first injection, post bronchodilator FEV1 improved only by 56 (27-151) mL. However, mean FRC improved by 800mL, falling from 3.87 to 3.07 L. Measures of ventilation inhomogeneity were abnormal in all 5 patients and all improved at one month: LCI 17.6 (13.5-21.6) down to 12.0 (8.96-19.43), Sacin 0.380 (0.247-0.600) /L down to 0.256 (0.140-0.399) /L, Scond 0.075 (0.053-0.100) /L down to 0.061 (0.036-0.105) /L.

Conclusion: Our initial observation suggests an improvement in small airway function as early as four weeks after the first injection of mepolizumab in patients with severe eosinophilic asthma. Measures of ventilation inhomogeneity appear to have greater sensitivity to these improvements than traditional forced manoeuvres.

Key Words: severe asthma, nitrogen washout, small airways, ventilation heterogeneity

POOR LUNG FUNCTION TRACKS FROM CHILDHOOD TO YOUNG ADULTHOOD, AND IS ASSOCIATED WITH PERSISTENT ASTHMA IN 22 YEAR OLD PARTICIPANTS OF THE WESTERN AUSTRALIAN PREGNANCY (RAINE STUDY) COHORT

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Introduction: Impaired lung function in childhood is recognised as a risk factor for impaired lung function and asthma in adulthood.

Aim: This study aimed to explore how lung function tracks through childhood and into young adulthood and identify whether poor lung function in childhood is associated with asthma at age 22 years in a community cohort.

Methods: Participants performed spirometry at 6, 14 and 22 years of age. Quartiles for FEV_1 and FEV_1/FVC z scores were calculated at age 6 years and lung function at each follow-up was tracked within each quartile group. Associations between childhood low lung function and bronchial hyper-responsiveness, wheezing, asthma medication use, hay fever and asthma outcomes of persistence, remittance and later-onset at age 22 years were investigated.

Results: Participants with FEV_1 and FEV_1/FVC in the lowest quartile at age 6 years demonstrated persistently reduced lung function at all ages compared to those with lung function in the highest quartile (p<0.00). Low lung function at age 6 years was significantly associated with persistent asthma (p=0.021), current wheeze (p=0.031) and use of asthma medications at age 22 years (p=0.049).

Conclusions: We found that poor childhood lung function was significantly associated with persistent asthma and asthma symptoms in early adulthood. We also found evidence of lung function tracking from childhood into early adulthood. These results suggest that poor lung function, and an increased risk of asthma in adulthood may be established in early life.

AO 011

REPEATABILITY OF PULSE OXIMETRY MEASUREMENTS RECORDED ON PATIENTS PERFORMING THE SIX MINUTE WALK TEST AFTER PULMONARY REHABILITATION

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Introduction/Aim: The aim of this study was to assess repeatability of pulse oximetry measurements obtained from repeat 6 minute walk tests (6MWTs). This evaluation would validate if changes in SpO_2 reflect variations in physiological factors rather than methodological artefact.

Method: Retrospective analysis of 6MWT oximetry data from pulmonary rehabilitation (PR) program patients (2014 - 2016). Inclusion criteria were: two post PR 6MWTs (ATS/ERS standards), 30 minutes rest between tests, not on supplemental oxygen, reliable oximetry as reported by supervising scientist and no rest periods during test. Differences between SpO_2 on repeat walks were tested using Wilcoxon signed rank test. Differences between resting heart rate (HR), peak HR and walk distance between walks were measured by paired t-test.

Results: A total of 103 patients met the inclusion criteria, mean age 70 years ($\pm$SD 9.03) with mean FEV1 % predicted 64.87 % ($\pm$SD 21.05). Minimum SpO_2 was not different between walks. Although statistical difference for distance, resting SpO_2, HR and end test HR were found, the absolute differences were not clinically important.

Table 1 Summary results of clinical assessments

Clinical measure	Walk 1	Walk 2	P-value
Distance (m)*	424 (97)	431 (99)	0.000
Resting SpO_2 **%** [#]	97 (96-98)	97 (96-98)	0.045
Minimum SpO_2 **%** [#]	94 (90-96)	94 (91-95)	0.141
Resting HR BPM *	83 (14)	85 (14)	0.006
Maximum HR[#]	113 (101-130)	115 (102-131)	0.003

*data displayed as mean ($\pm$sd)
[#]data displayed as median (lower quartile - upper quartile). Median reported as data not uniformly distributed

Conclusion: Despite there being a statistical difference between walks for resting SpO_2 values, minimum SpO_2 did not differ. The repeatability of minimum SpO_2 suggests observed desaturation is likely due to physiological factors and not a result of measurement artefact. This is reinforced by the repeatability of HR results and small changes in walk distance between tests.

Key Words: Saturation, Six minute walk test (6MWT), oximetry
Grant Support: Nil

AO 012

VENTILATORY LIMITATION DURING EXERCISE IN PHYSICALLY ACTIVE ADOLESCENT FEMALES

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Introduction/Aim: This study aimed to determine to what extent ventilatory limitation exists in a population of physically active adolescent females and to correlate this with exertion induced dyspnoea (EID).

Method: Females (n=24) aged 12 to 18 who were participating in regular organised physical activity (> 4h/week) were recruited. Participants underwent pulmonary function assessment and, if prescribed short acting β-agonist, a post-bronchodilator response. A cardiopulmonary exercise test was then carried out during which inspiratory capacity manoeuvres were performed and dynamic flow-volume loops were recorded. At the end of the exercise test Borg score was recorded to assess EID. Flow-volume loops were analysed, using a novel technique to quantify remaining flow reserve, to determine the presence of expiratory flow limitation (EFL), whilst the IRV/FVC ratio calculated to determine presence of an inspiratory limitation (i.e. IRV/FVC <0.1).

Results: Demographic data and peak oxygen consumption data are described in table below.

n=24	Mean	SD	Range
Age (y)	14.3	2.1	12-18
BMI (kg/m2)	20.4	2.5	17-24.2
Peak V'O_2 (mL/min/kg)	46.5	5.3	35.6-59.2

Five participants were prescribed with β-agonists, however none demonstrated post-bronchodilator effect. 12 of the 24 participants demonstrated EFL during exercise, when combining this group with those whose IRV/FVC were <0.1, 16/24 participants demonstrated some form of ventilatory limitation during exercise. Ventilatory limitation was not correlated with peak V'O_2. Only subjects who demonstrated ventilatory limitation during exercise reported a post exercise Borg score >4 (p<0.05).

Conclusion: A significant majority of participants (67%) demonstrated ventilatory limitation during exercise, and this was highly correlated with their sensation of breathlessness. Whilst EID was observed this did not appear to effect peak performance. This study demonstrates that ventilatory limitation in active adolescent females is common and is highly correlated with EID.

Key Words: Exercise, Flow Limitation, Peak V'O_2
Nomination for New Investigator Award: NA
Grant Support: Auckland District Health Board A+ Trust, Greenlane Research and Education Fund
Declaration: Authors have no conflicts to declare.

ANZSRS POSTER PRESENTATIONS

SURVEILLANCE OF HIGH ALTITUDE SIMULATION TEST PROTOCOLS IN AUSTRALIA AND NEW ZEALAND

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Introduction: Popularity of air travel and an ageing population with respiratory disease has led to an increased need for High Altitude Simulation Tests (HAST). This test is routinely performed across major hospitals in Australia and New Zealand. Despite the abundance of testing, there is a lack of consensus on the method of testing. The British Thoracic Society guidelines do not require exercise during testing[1].

Aim & Hypothesis: To determine the most common HAST protocol in respiratory function laboratories in Australia and New Zealand. We hypothesised that the most common protocol included use of a 15% oxygen(O_2) mixture, assessment at rest and during exercise, and use of O_2 supplementation at rates of 2 and 4L/min.

Method: SurveyMonkey® was used to survey respiratory function laboratories on HAST protocols. Questions included mask type, fraction of inspired oxygen (FiO_2), hypoxic gas mixture flow, delivery method, supplemental O_2 flow and whether the test involved patient exercise.

Results: Responses were received from 45 respiratory function laboratories and 36 (80%) performed HAST. Among these 36 laboratories, a gas mixture with FiO_2=15.0-15.1% was used at 34 (94.4%) laboratories; a protocol using a mask/reservoir bag was used at 12 (33%) laboratories; supplemental O_2 was used at 25 (69.4%) laboratories mostly (22, 88%) by nasal prongs; O_2 flow rates of both 2 and 4L/min were used at 10 (27.8%) and flow rates of only 2L/min at 9 (25%) laboratories; and patients were exercised during testing at 11 (30.6%) laboratories and this exercise consisted of stepping at 5 (45.5%) of these laboratories.

Conclusion: Various HAST methods are used in respiratory function laboratories in Australia and New Zealand. The commonest protocol used a 15% O_2 mixture with supplemental O_2 at 2 and 4L/min and did not require the patient to exercise. Increasing HAST protocol consistency between laboratories should be considered in the future.

Key Words: HAST, Survey Monkey®, oxygen, supplemental, mask, titration

REFERENCE

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MAGNETIC VERSUS ELECTRICAL PHRENIC NERVE STIMULATION: COMPARISON OF RELIABILITY, SUBJECT DISCOMFORT AND NERVE/MUSCLE LATENCY

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Introduction: In patients with diaphragm weakness, unilateral phrenic nerve stimulation can be used to determine the integrity and conduction properties of each phrenic nerve. Phrenic nerve latency is typically 6-8 milliseconds in adults and may be delayed in demyelinating polyneuropathies e.g. Guillain-Barre syndrome and chronic inflammatory demyelinating polyneuropathy. The phrenic nerve can be stimulated either electrically or magnetically.

Aim & Hypothesis: To compare the reliability, subject discomfort and phrenic nerve/diaphragm latency of the magnetic versus electrical phrenic nerve stimulation. We hypothesised that compared to electrical stimulation, magnetic stimulation was more reliable, less distressing to the subject, and produced identical nerve/diaphragm latencies.

Method: In 8 healthy male subjects, each phrenic nerve was stimulated at the neck electrically (150 V, duration 0.1 ms., delay 0.01 ms., rate 0.5 Hz) and magnetically (MagStim) at 30, 50, 70 and 90% maximum output. Compound muscle action potentials (CMAP) were detected using surface electrodes placed in the mid-axillary line at the 8th and 9th rib interspaces, and displayed on a digital chart recorder (PowerLab). We measured the number of stimulations required to elicit an analysable CMAP, the degree of discomfort (using a Borg CR-10 questionnaire), and nerve/muscle latencies. Data are expressed as mean $\pm$ SD and were compared using paired t-tests. Significance was defined as $p<0.05$.

Results: Subjects were aged 36.1$\pm$15.3 years and had BMI 25.2$\pm$2.8 kg/m^2.

	Electrical	Magnetic			
Output		30%	50%	70%	90%
Number of stimuli to elicit CMAP	23$\pm$14	-	1$\pm$0*	1$\pm$0*	1$\pm$0*
Discomfort score (units)	3.0$\pm$1.4	0.4$\pm$0.4*	1.0$\pm$0.9*	1.8$\pm$0.9*	2.4$\pm$1.2
Phrenic nerve/ diaphragm latency (ms)	5.7$\pm$1.9	5.8$\pm$1.0	5.0$\pm$0.6	4.8$\pm$0.7	4.5$\pm$0.4*

*$p<0.05$ difference from electrical stimulation

Conclusions: Compared to electrical phrenic nerve stimulation, magnetic stimulation was more reliable and, except at high output, caused less discomfort and obtained similar latencies.

Key Words: phrenic nerve stimulation, electrical, magnetic, latency, discomfort, Borg score

COUGH SENSITIVITY TO MANNITOL INHALATION CHALLENGE IDENTIFIES SUBJECTS WITH COUGH

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Introduction/Aim: It is unknown whether cough sensitivity to mannitol identifies subjects with cough and whether it correlates with subjective cough severity.

Method: Subjects with cough as the primary symptom (n=17), with other airway symptoms (n=52) and healthy subjects (n=15) performed mannitol challenge and completed the Leicester Cough Questionnaire (LCQ).

Results: The mean (95%CI) number of provoked coughs divided by the cumulative dose of mannitol (CDR) was 21.1 (12.6 – 35.4) in subjects with cough, 6.25 (4.15 – 9.40) in those with other symptoms and 2.80 (1.3 – 6.10) coughs/100 mg in the healthy subjects (p<0.001). Area under the receiver-operating characteristic curve comparing cough subjects against healthy subjects was 0.95 and when comparing cough subjects against healthy controls and subjects with other symptoms it was 0.80. There was a significant correlation between CDR and LCQ total score (r_s= -0.50, p=0.04) within the cough group, as well as when combining both subjects with cough and other airway symptoms (r_s= -0.43, p<0.001).

Conclusion: Cough sensitivity to mannitol identifies subjects with cough and correlates with subjective cough severity. Since mannitol challenge can be performed without complicated equipment or trained personnel in a standardised fashion, it is a promising diagnostic test for cough hypersensitivity syndrome.

Key Words: cough hypersensitivity, mannitol

Grant Support: Nil

GASTRIC-OESOPHAGEAL (GOR) REFLUX DURING SPIROMETRY. PREVALENCE AND EFFECTS

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Introduction: Variability during spirometry can persist despite control of technical and personal factors. We hypothesised that spirometry may induce GOR which may influence upper airway variability leading to variability of spirometry.

Aim: Pilot study assessing prevalence of GOR during spirometry and its effects on spirometry variability in subjects having outpatient GOR assessment.

Method: At the end of oesophageal manometry and 24hr pH monitoring, 56 subjects performed 2 sets of spirometry separated by 10-minutes. The De-Meester score quantified 24hr GOR ($\geq$14.72 in significant GOR). Assessment for GOR during spirometry started with 1st spirometry and ends with 2nd spirometry manouvres. Variability of spirometry was assessed between those with GOR and no GOR.

Results: In 26 subjects (44%) had GOR during spirometry assessment: 18 during the 10-minute break with 3 persisting into the 2nd spirometry, 5 throughout assessment, and 3 during spirometry only. They tended to have higher De-Meester scores (mean 39.8 vs 26.8, t-test p=0.13) and were more likely have a GOR event preceding the 1st spirometry (median time interval [min] 8.5 [IQR 5–12] vs 25 [IQR 10–70]), compared to 30 subjects without GOR during spirometry assessment. In the GOR group both FEV_1 and PEF were reduced in the second spirometry set; FEV_1 by 84mL (p<0.05), PEFR by 0.5L/s (p<0.001). FVC is not changed. Mean variability of spirometry (%) $\pm$ SD was similar between GOR and non-GOR groups as described in Table below.

Spirometry	GOR Present (n=25)		No GOR (n=30)	
	1st	2nd	1st	2nd
FVC variability	6.8 $\pm$ 7.3	5.1 $\pm$ 4.3	5.5 $\pm$ 4.7	5.8 $\pm$ 5.9
FEV1 variability	9.7 $\pm$ 11.3	10.1 $\pm$ 13.3	7.9 $\pm$ 7.7	7.1 $\pm$ 7.2

Conclusion: GOR occurs during and following spirometry in subjects having outpatient GOR assessment, but does not significantly impact spirometry variability over 10-minutes in this patient population.

Key Words: spirometry, gastric oesophageal reflux

BETTER INCREMENTAL WORKLOAD EQUATIONS ARE NEEDED TO PREDICT MAXIMAL WORKLOAD FOR CARDIOPULMONARY EXERCISE TESTS (CPET) PERFORMED IN AN OPTIMAL TEST TIME

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Introduction/Aim: Cardiopulmonary Exercise Tests provide a global assessment of multi-organ system function. In order to obtain optimal results and ensure accurate interpretation, it is advantageous to perform the CPET with an appropriate workload protocol and incremental phase lasting 8-12 minutes. This study aimed to determine which of 6 progressive workload equations best predict the maximal workload during an ideal test time of 10 minutes.

Method: 50 patients aged 23-82 (M= 23, F=27) were referred to the Laboratory for cardiopulmonary assessment. The maximal CPET included Spirometry in all, Maximal Voluntary Ventilation (MVV) in 15 patients, and used an incremental ramp protocol. Paired T tests compared the achieved workload of each subject to six progressive workload equations. Bland-Altman analysis was applied to this comparison to determine the average bias. For equations 4-6 which predict a ramp increment, a multiplier of 10 was applied to achieve a predicted maximum workload (wmax) at 10 minutes.

Equation Number	Sample size	Mean wmax achieved $\pm$ SD (watts)	Mean wmax predicted $\pm$ SD (watts)	T-test (achieved wmax vs. predicted wmax)	Mean Differences $\pm$ SD (watts)
1	n=50	141$\pm$77	128 $\pm$ 59	NS	13 $\pm$ 51
2	n=19	152 $\pm$ 91	270 $\pm$ 100	p= 5.015E-06	-118 $\pm$ 78
3	n=15	162 $\pm$ 90	234 $\pm$ 107	p= 0.001	-72 $\pm$ 66
4	n=50	141 $\pm$ 77	109 $\pm$ 47[#]	p= 3.67E-05	32 $\pm$ 49
5	n=21	131 $\pm$ 59	112 $\pm$ 46[#]	p=0.03	19 $\pm$ 37
6	n=50	141 $\pm$ 77	131 $\pm$ 56[#]	NS	10 $\pm$ 51

ramp*10 to predict wmax at 10 minutes.

Results:

Conclusion: This study demonstrated that wmax predicted by Equations 1 and 6 best correspond to the achieved workload in this patient group due to minimal bias. These equations utilise age, height and either ideal or measured weight. Inclusion of FEV1 to predict MVV (2), actual measured MVV (3), FEV1 coupled with anthropometric data (4), and diffusion capacity (5) all measures of the individual's respiratory health, did not further improve the prediction of wmax.

Reference Equations: 1. Wasserman-Hansen-Bruce (1984), **2.**Estimated max load from V'Emax based on FEV1 (2016), **3.**Estimated max load from V'Emax based on MVV (2016)

4.Pretto without DLCO (2001), **5.**Pretto with DLCO (2001), **6.**Wasserman-Hansen-Sue (1987)

Key Words: Cardiopulmonary Exercise Test, Workload, Ramp
Nomination for New Investigator Award: No
Grant Support: No

AP 006

A COMPARISON OF MEDGRAPHICS AND JAEGER LUNG FUNCTION EQUIPMENT WITH SPIROMETRY, DIFFUSING CAPACITY AND BODYPLETHYSMOGRAHPY PARAMETERS BY LUNG FUNCTION BIOCONTROL MEASUREMENTS

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Introduction/Aim: There may be inherent variability in the measurement of respiratory manoeuvres between different lung function equipment. Therefore, it is important to use biological controls to prospectively detect any variability upon a lab's replacement of lung function testing equipment.

The aim of this study was to compare variability in measurement of spirometry, diffusing capacity and body plethysmography between Medgraphics and Jaeger equipment by using biological control data.

Method: Spirometry, diffusing capacity and body plethysmography parameters, from four healthy, non-smoker technicians (three female & one male), were collected using Medgraphics Elite Full Body Plethysmograph and Jaeger Master Screen Body Plethysmograph with MS-PFT Analyser Unit lung function equipment. These results were compared to detect variation between Medgraphics and Jeager systems.

All of the biocontrol data were collected within the same calendar year. Means of FEV_1, FVC, D_LCO, V_A, FRC and TLC of individual subject were compared using t-test. Coefficient of variation in percentage (CV%) were compared using the Mann-Whitney U test.

Results: The comparison of CV% between Medigraphic and Jaeger systems showed no significant statistical differences in any of the investigated parameters. Spirometry: FEV_1 (2.41% vs 2.35%, $p > 0.05$) and FVC (2.12% vs 2.33%, $p > 0.05$), D_LCO (5.12% vs 4.4%, $p > 0.05$) and V_A (2.27% vs 2.69%, $p > 0.05$) and TLC (2.61% vs 1.93%, $p > 0.05$) and FRC (5.7% vs 5.19%, $p > 0.05$).

The mean of individual subject's above lung function parameters did not show significant differences.

Conclusion: The results showed no statistically significant differences in spirometry, diffusing capacity and body plethysmography parameters between Medigraphics Elite Body Plethysmograph and Jaeger Master Screen Body Plethysmography with MS-PFT Analyser Unit.

Key Words: biological control, spirometry, diffusing capacity, body plethysmography

Nomination for New Investigator Award: No
Grant Support: None

AP 007

LUNG FUNCTION BEFORE AND AFTER TREATMENT OF VOCAL CORD DYSFUNCTION (VCD)

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Introduction/Aim: Vocal cord dysfunction (VCD) often accompanies asthma. Effective treatment of VCD may improve lung function, especially measures of airway resistance. As part of a multidisciplinary VCD clinic, patients with confirmed VCD (via endoscopy and/or CT larynx) were evaluated before and after speech therapy and botulinum toxin injection.

Method: Patients with confirmed VCD (n=35) were assessed. Diagnosis of VCD was based on detection of inspiratory paradoxical vocal cord movement (PVCM) on at least on occasion. Pre and post spirometry were done, we also conducted resistance measurements and measured lung volumes via body plethysmography before and after treatments. Results were compared using paired t-tests.

Results: Speech therapy was provided to 35 patients and botulinum toxin injections were administered to 22 patients. Baseline patient demographics are shown in Table 1. All results reported are post bronchodilator (except LV). There were no significant changes to lung function or resistance measures after either speech therapy or botulinum toxin injection. There were changes in sGaw after both treatments that approached statistical significance.

Conclusion: Treatment of VCD with speech therapy and botulinum toxin injection do not improve airway function. However, absence of changes in physiology does not preclude improvements in symptoms and other features of VCD.

Table1. Patient demographic data pre and post speech therapy and botulinum toxin injection

	Speech Tx (n=35)			Botulinum Toxin (n=21)		
	Pre	Post	p	Pre	Post	p
Age	60.29±13.12	-	-	60.70±11.39	-	-
BMI	30.84±7.32	-	-	32.18±7.11	-	-
FEV1 (% ped)	78.50±21.62	81.0±22.0	0.84	78.50±21.62	80.70±22.82	0.95
TLC (% pred)	99.92±14.93	102.12±14.39	0.93	100.63±16.46	103.88±16.09	0.83
Raw	4.39±3.27	3.45±3.13	0.77	4.91±3.38	3.45±3.13	0.22
sGaw	0.11±0.07	0.16±0.10	0.07	0.11±0.08	0.24±0.28	0.08

AP 008

OUTCOMES IN VOCAL CORD DYSFUNCTION (VCD) AFTER SPEECH THERAPY AND BOTULINUM TOXIN INJECTION TREATMENTS

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Introduction/Aim: Vocal cord dysfunction (VCD) causes vocal cord narrowing during inspiration resulting in airflow obstruction and may contribute to breathlessness in asthma. Treatment is difficult, however speech therapy and botulinum toxin (Botox) injections can be effective. As part of a multidisciplinary VCD clinic, patients undergoing treatment were evaluated for symptom and healthcare outcomes.

Method: Patients with confirmed VCD (n=35) were assessed. VCD was diagnosed by detection (CT larynx and/or laryngoscopy) of inspiratory paradoxical vocal cord movement (PVCM) on at least one occasion. Patients were then treated with speech therapy (n=35) and if this failed with botulinum toxin injection (n=21). They were assessed pre and post treatment. Patient symptoms were evaluated using standardised asthma, dysfunctional breathing and VCD questionnaires (ACT ACQ, Nijmegen, VCDQ). Health care outcomes were assessed by questionnaire to determine emergency department (ED) and general practitioner (GP) visits in the year prior to and after treatment.

Results: There were no significant differences in the standardised questionnaires post speech therapy (ACQ: p=0.19; ACT: p=0.28; VCDQ: p=0.66; Nijmegen: p=0.68). Although GP visits were not significantly reduced post treatment (p=0.07), ED visits were significantly reduced post speech therapy (p=0.01). The 21 patients who had botulinum toxin injection had a significant reduction in GP visits (p=0.05) but no reduction in ED visits (p=0.11). There was also no significant difference in questionnaires (ACQ: p=0.13; ACT: p=0.14; VCDQ: p=0.66; Nijmegen: p=0.37).

Conclusion: Speech therapy and botulinum toxin injection did not improve patient symptom scores linked to asthma and VCD. However, important health outcomes (GP visits and ED admissions) were reduced. The reasons for the discordance between symptoms and health outcomes are unclear.

AP 009

AUDIT TO MONITOR AND IMPROVE THE QUALITY OF RESPIRATORY FUNCTION REPORTS AT EASTERN HEALTH

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Introduction/Aim: To address errors identified in respiratory function reports (RFRs) during TSANZ Laboratory Accreditation, we developed an audit tool to identify systematic or random errors, to monitor and improve the quality of our reports. Audit items included: demographic, clinical notes, technical comments, feasibility of results, transcription errors as well as interpretation concordance against current ATS/ERS interpretation guidelines.

Method: Eighty randomly selected RFRs (two/day for 8 weeks) from June to August 2016 were subsequently reviewed by both one of three Physicians and one of two Scientists. The auditing Physician/Scientist did not review their own reports to eliminate potential conflict of interest. The audit tool consisted of 49 questions including "Critical questions" eg gender correct? interpretation correct? and "Non-critical questions" eg. Spelling mistakes?

Results: Of the 80 randomly selected RFRs reviewed, we identified 0.6% errors (22 errors / (49 total no. questions x 80 reports). When we analysed the 33 Critical questions e.g. Correct gender?, we only identified 0.5% critical errors (12 errors / (33 critical questions x 80 reports). Of these 12 errors 2 (3.6%) were interpretation errors.

Conclusion: Overall, we detected an acceptable error rate for both critical and non-critical questions. The areas requiring improvement: 1. Quality of technical comments (4 non-critical errors); 2. Grammar/spelling mistakes in final report (5 non-critical errors) and 3. How we record document control. The audit results and areas for improvement were discussed with the Physicians / Scientists. The Physicians have now included methodical checking of lung volume subdivisions as part of their reporting strategy. The audit was a useful tool given that we had recently recruited new Physicians which not only consolidated their training in reporting, but an excellent opportunity to ensure their reporting style was standardized for Eastern Health. This audit will now be conducted annually.

FEV$_1$ REPRODUCIBILITY DURING BRONCHIAL CHALLENGE TO INHALED MANNITOL IN RELATION TO SEVERITY OF BRONCHIAL HYPERRESPONSIVENESS (BHR)

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Introduction: Protocols measuring BHR by administering methacholine using deep inhalations can lead to negative tests in mild BHR. Repeated deep inhalations may reduce bronchoconstriction due to airway smooth muscle (ASM) stretch. Measuring BHR using FEV$_1$, also a deep inhalation manoeuvre, may possibly cause ASM stretch leading to improved subsequent FEV$_1$ values in protocols where repeated FEV$_1$ values are required after each provoking dose.

Aim: To determine if there is evidence of increases in FEV$_1$ following provoking dose steps during a mannitol challenge in subjects with different severities of BHR.

Method: Subjects for occupational assessment for asthma using inhaled mannitol (n=67; median age 20yrs, range: 16-48yrs; 58M:9F) had FEV$_1$ manoeuvres assessed for quality, and the difference of the first FEV$_1$ compared to best second FEV$_1$.

Results: Subjects were analysed who had either moderate (n=20) or mild (n=30) BHR documenting a 15% fall in FEV$_1$, as well as subjects with borderline BHR who documented a maximum fall in FEV$_1$ of between 10%-15% (n=17).

Difference in best second FEV$_1$ - first FEV$_1$ (% change) post each mannitol dose

BHR	35mg	75mg	155mg	315mg	475mg	635mg
Moderate	+0.40.8	+0.50.8^	+0.51.1~			
Mild	+0.70.9*	+1.11.5*	+0.91.6*	+1.92.7*	+0.71.5^	
Borderline	+0.51.2	+1.31.4*	+1.01.2*	+1.92.1*	+2.12.9*	+2.11.6*

Data in table are presented as mean±SD. ~$p<0.05$, ^$p<0.01$, *$p<0.001$

The best second FEV$_1$ was consistently higher compared to the first FEV$_1$ at all doses in all severities of BHR, with larger differences observed in the final 3 (mild) provoking dose steps. Thus, if % fall in FEV$_1$ was calculated using the first FEV$_1$, 53% of subjects with borderline BHR (n=9) would be reclassified as having mild BHR.

Conclusion: There are small increases in FEV$_1$ with repeated FEV$_1$ manoeuvres for all severities of BHR to mannitol, with larger changes seen in those with borderline BHR. This suggests an FEV$_1$ manoeuvre may cause ASM stretch in asthmatics.

Key Words: mannitol, bronchial hyperresponsiveness

FEASIBILITY OF LUNG FUNCTION TESTING & RESULTS IN CHILDREN WITH SPINAL MUSCULAR ATROPHY TYPE II & III

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Introduction/Aim: Respiratory function testing is important for children with spinal muscular atrophy (SMA) as a way of monitoring disease progression and timing of interventions. However, it is unclear which tests are most appropriate for this patient group. Our objectives were (1) to assess feasibility of a variety of lung function tests in children with SMA type II and III, and (2) establish baseline data in this unique cohort for future clinical research.

Method: Subjects (n=18) were prospectively recruited when they had a respiratory outpatient appointment or overnight sleep study. Forced oscillation technique (FOT), Lung clearance index (LCI) via Multiple breath washout, spirometry, peak cough flow (PCF), sniff nasal inspiratory pressure (SNIP), maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) were attempted on all subjects.

Results: Subjects able to perform and achieve results with PCF, MIP and MEP were comparatively lower so data was excluded from analysis. Table highlights the difference in the number of patients able to adequately perform each test and subsequently achieve acceptable results. Median of all results reported (IQR).

Lung Function Test	Number Tested	No Results	Achieved Results	Results Median (IQR)
FOT Rrs$_8$ z score	15	5	10	2.4 (2.11 – 3.75)
FOT Xrs$_8$ z score	15	5	10	-2.03 (-2.51 – -0.86)
MBW LCI	16	5	11	7.34 (6.96 – 8.16)
Spirometry FVC (% Pred)	16	2	14	84 (34.8 – 92.9)
SNIP z score	9	0	9	-2.4 (-3.1 – -1.5)

Conclusion: Establishing which tests are more appropriate for children with SMA will help to improve the quality of lung function results and better optimise patient management. While MIP, MEP and PCF may have clinical relevance, subjects ability to perform these tests were more variable compared with reported results. This suggests that these tests may not be useful for monitoring patient progress.

Key Words: Respiratory function, Spinal muscular atrophy, feasibility

AP 012

USING IDEAL BODY WEIGHT TO ADJUST PREDICTED VO2

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Introduction: Peak VO2 is used to stratify patients with diagnosed chronic heart failure (CHF). CHF patients with a VO2%pred <50% or <14ml/kg/min have a three-fold increased risk of death within 6 months[1].

Aim: To assess whether adjusting predicted VO2 for ideal body weight (IBW) results in an increase of patients with a VO2 <50% predicted.

Method: A retrospective analysis of cardiopulmonary exercise tests (CPET) results between June 2014 and June 2017 was performed. 306 subjects (184 male) underwent CPET within the respiratory department. 107 of these subjects had a body mass index (BMI) > 30. A paired t-test and a chi-squared analysis were used to assess the difference between VO2% predicted using actual body weight and IBW.

Results: Without adjusting for IBW, 15 subjects had a VO2 <50% predicted. After adjusting for IBW, 40 patients had a VO2 <50% predicted. Significant differences were found in VO2% predicted between actual body weight and IBW ($p<0.01$).

Conclusion: Adjusting for IBW in patients with a BMI >30 results in an increase of patients with a VO2 <50% predicted, assisting with additional stratification for patients diagnosed with CHF.

Key Words: cardiopulmonary exercise test, VO2, IBW

Nomination for New Investigator Award:

Grant Support:

AP 013

A CULTURALLY APPROPRIATE INDIGENOUS SPIROMETRY TRAINING PROGRAM—A MEANS TO IMPROVE QUANTITY AND QUALITY OF SPIROMETRY PERFORMED IN PRIMARY CARE

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Introduction: Health workers (HW) trained and mentored in the Indigenous Health Worker spirometry training program (STP) and who are supported by their managers are more likely to do spirometry (spiro) and achieve quality test results.

Aim: To assess the quantity & quality of spiro performed by HW after attending the STP.

Method: HW in Indigenous primary care who were either already performing spiro or were being required to commence performing spiro attended our 2 day culturally appropriate STP. A number of tests performed before training (PreSTP) and after training (PostSTP) were submitted for quality assessment which included patient demographics, test acceptability and repeatability and technical comment inclusion (a total score out of 8). The average quality test score was calculated for a HW's portfolio and the mean±SD quality score was calculated for the group PreSTP & PostSTP.

Results: 28 HW submitted spiro tests either PreSTP and/or PostSTP (16 Indigenous). There was an increase in the number of HW doing spiro testing.

	Quality score	
	Pre STP	Post STP
Mean	4.5	5.3
±SD	1.78	1.57
*n	8	25

(*n = HW's who submitted spiro test results)

Conclusion: The Indigenous Health Worker spirometry training program increases the number of HW doing spiro. There is a trend towards improved quality of spirometry after training. Post workshop telehealth mentoring may further improve spiro quality.

Key Words: Spirometry training, Indigenous Primary Care

Nomination for New Investigator Award: No

Grant Support: Nil

AP 014

VARIABILITY OF COMPUTER ADJUSTMENT OR SCIENTIST ADJUSTED PHASE 3 SLOPES OF SCOND & SASCIN SLOPES IN ECO MEDICS EXHALYZER MULTI BREATH NITROGEN WASHOUT

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Introduction/Aim: The use of multi-breath nitrogen washout (MBNW) for the calculation of parameters of airways heterogeneity, Sacin and Scond is increasing in both adult and paediatric respiratory function laboratories. These indices may help detect early onset of diseases affecting small airways. Software within new MBNW device's calculates the slope of phase 3 of the washout curve. Software in earlier in-house equipment required the investigator to manually adjust slopes. This study aims to determine the difference in Scond and Sacin adjusted manually compared to those indices generated by the software with no manual adjustment.

Method: 3 groups (Normal, Asthma & COPD) with a smoking history <5pk yrs performed MBNW with controlled tidal breathing of 1L to 1.3L x 3 with FRC within $\pm10\%$ using the Eco Medics Exhalyzer® D Nitrogen Washout Bypass System. Scond and Sacin were compared when the slope phase 3 was manually adjusted by the same investigator and unadjusted, using mean differences and paired t test.

Results: 8 Normal, 8 Asthmatics and 8 COPD were studied. A paired T test showed that there was no statistically significance difference between adjusted and unadjusted Scond for any group (p=0.065, 0.169, 0.645). However for all groups Sacin showed a significance difference (p=0.003, 0.007, 0.010) between adjusted and unadjusted values.

	Scond ($\pm$SD)	Sacin ($\pm$SD)	Mean difference Scond Adjusted Vs Unadjusted ($\pm$SD)	Mean difference Sacin Adjusted vs Unadjusted ($\pm$SD)
Normal	0.018 (0.006)	0.084 (0.046)	0.002 (0.003)	0.024 (0.016)
Asthma	0.032 (0.022)	0.186 (0.078)	-0.154 (0.066)	0.046 (0.034)
COPD	0.046 (0.018)	0.437 (0.216)	0.002 (0.010)	0.067 (0.055)

Conclusion: This data suggests that adjustment of the phase 3 slope is not required for calculation of Scond but as Sacin differed significantly when adjusted by the investigator, compared to the unadjusted values, manual adjustment continues to be indicated. Although seeing a significant difference within this small group data, the effect is yet to be seen in larger groups.

Key Words: Multi-Breath Nitrogen Washout (MBNW), FRC, Phase 3 Slope

Nomination for New Investigator Award: No

Grant Support: No

AP 015

A REVIEW OF LUNG FUNCTION TESTS IN PATIENTS WHO HAVE UNDERGONE ENDOBRONCHIAL VALVE INSERTION

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Background: Endobronchial valves can help emphysema patients who suffer from hyperinflation by reducing lung volumes using minimally invasive procedures, rather than undergoing lung reduction surgery (Frank C. Sciurba et al. 2010, p.1233-1244).

Aim: To assess lung function improvement with physical functional improvement in patients who have had recent endobronchial valve insertion.

Method: Eight patients mean aged 72±7.5 years, 7 male and 1 female, were assessed over the course of 4 months pre and post endobronchial valve insertion. Lung function testing including Spirometry, Body plethysmography and 6 minute walk test distance were performed. The lung function tests were then analysed to determine if any results had an improvement greater than 12%, which is considered substantial.

	TLC%	RV%	RVITLC°k	FVC%	FEV1%	FVC/FEV	6MWT(M	SpO2%
Patient 1	**-17.87**	**-32.7**	**-18.5**	80	**64**	-8.3	7.1	-2
2	-5.95	**-24.3**	-19	**19.67**	**31.1**	6.67	-12.5	-1.04
3	-1.85	5.12	5.88	-6.67	0	12	0	0.06
4	4.52	6.59	1.92	4.87	-14.44	-20.83	-16.67	2.11
5	-1.43	-10	-10	6.79	1.33	-3.57	-14.29	0
6	-12.01	**-14.82**	-1.64	-10.28	0	14.81	100	2.2
7	**-19.3**	**-28.89**	-11.11	-3	**100**	**51.52**	-37.5	0
8	-2.67	-2.22	1.67	-3.33	0	3.85	-14.29	-1.06

For all the patients p=0.1503. For the three patients improvements p=0.2576.

Results: Table below contains the percentage change.

Mean change in FEV1 was 20±39% (median=0.6). Only patients 1, 2 and 7 achieved some improvement in their FEV1 values, with all three demonstrating a small reduction in hyper-inflation, as demonstrated by reduced RV values.

Whilst the three patients did show some improvement in their results, statistical analysis suggested no significant improvement occurred in these parameters (p=0.2574). There was also no functional improvement in the six minute walk distance (p=0.404).

Conclusion: Functional improvement was not achieved even in patients demonstrating some reduction in hyperinflation. However, given this small sample group, more studies regarding the mechanism for improvement following endobronchial valve treatment are required.

Key Words: Spirometry, Body Plethysmography, 6 Minute walk test, hyperinflation, Endobronchial valves

REFERENCE

Frank C. Sciurba, et al, 2010, 'A Randomized Study of Endobronchial Valves for Advanced Emphysema', The New England Journal of Medicine, 363:1233-1244

SUPPORT FOR SPIROMETRY OPERATORS BY AN ON-LINE SPIROMETRY ASSESSMENT TOOL

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Introduction: A Spirometry Assessment Tool (SAT) has been developed within the Spirometry Learning Module (SLM) training program allowing for remote evaluation of spirometry test quality by a designated respiratory scientist incorporating ongoing feedback to operators over time.

Method: The SAT is an interactive PDF document which allows operators to self-assess spirometry measurements against key ATS/ERS criteria; specifically test performance acceptability, measurement repeatability and spirometry interpretation.

The SLM online components are integrated within a Modular Object-Oriented Dynamic Learning Environment (MOODLE) open source software Learning Management System. Participants upload spirometry test reports with accompanying SATs via a drop-box within MOODLE. Submissions are made at regular intervals within the SLM 12-week review period to allow previous reviewer feedback to be incorporated into later spirometry assessments.

Reviewers are designated within MOODLE and receive email notification of submitted SATs. The SAT is opened with a PDF annotator which allows correct and incorrect responses to be 'marked' by green ticks and red crosses. Additional comments are added from a drop-down menu. Once reviewed, the operator is notified by email that a marked SAT is available for viewing.

Discussion: Use of the SAT provides an opportunity to positively reinforce the practical aspects of spirometry training with ongoing timely feedback to operators and allows them to identify suboptimal test quality specifically related to poor patient test performance. It also allows the uniform evaluation of test quality across multiple reviewers.

Conclusion: The Spirometry Assessment Tool is a simple, standardised, inexpensive and interactive approach to assess the practical application of operator knowledge seen as central in determining the practical outcomes of spirometry training.

Key Words: spirometry Assessment Tool; spirometry test quality; self-assessment

Nomination for New Investigator Award: No
Grant Support: None

TSANZ ORAL PRESENTATIONS

Respiratory Nurses

CABRINI SHARED CARE MODEL: EARLY REFERRAL AND ACCESS TO PALLIATIVE CARE FOR PATIENTS WITH COPD

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Introduction: Chronic obstructive pulmonary disease (COPD) is a significant cause of death in Australia but access to Palliative Care is limited. In addition, previous studies indicate that patients with chronic lung disease are more likely to have their first encounter with palliative care in a critical care setting.

Aim: Cabrini Hospital developed a shared model of early referral and access to palliative care for patients with advanced COPD integrated across the Respiratory Continuing care program and Palliative Homecare team, through: Enabling patients to live as actively as possible with focus on quality of life; Reducing time in hospital and optimizing utilization of continuing care services to support preferred place of care; Optimizing function and comfort physically, psychosocially, emotionally and spiritually; Minimizing physical and psychosocial symptoms.

Providing adequate knowledge and open communication for patients and carers to help timely and informed decision-making; Supporting carers throughout the person's illness; and Supporting patients and carers when death is inevitable and through the bereavement period.

Preliminary Results: Patient and families reported positive patient experience; improvement in preferred place of death; patients did not feel abandoned or "handed over' to another service; family end of life experience improved due to patient and family being well known to palliative homecare staff and respiratory nurses ; direct admission to inpatient palliative care services prevented a visit to emergency; prevention of hospital admission during final year of life improved quality of life; reduction in emergency calls to ambulance service due to breathlessness and anxiety;

Conclusion: A shared model of early referral and access to palliative care markedly improved quality of services for patients with advanced, non-malignant lung disease. Training is required to support palliative homecare nurses to deliver care to patients with non-malignant disease, and equally for chronic disease nurses to support and deliver a palliative care approach.

WITHDRAWING/WEANING NON INVASIVE VENTILATION IN PALLIATIVE CARE PATIENTS WITH RESPIRATORY FAILURE

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Introduction: Withdrawal of Non Invasive ventilation (NIV) at the end of life is extremely challenging with varying patient experience. There is little evidence describing medication titration prior to weaning/post NIV cessation, increasing the risk of an undignified death. St George Hospital palliative care service (SGHPS) receives referrals to assist in NIV withdrawal in patients failing to respond to treatment with both malignant and non-malignant disease. It was recognized that there was a need to develop a more consistent way of weaning each patients NIV and titrating their medications depending on their level of dependency on the NIV.

Methods: In 2015/2016, SGHPC received 64 respiratory failure patient referrals receiving NIV. 35 were specifically referred for end of life care where treatment was deemed futile and there was a change in the direction of care with NIV to be weaned and ceased. We have identified 3 levels of NIV dependency at end of life (EOL) requiring different doses of medications/adjustments to ventilation during the weaning process to ensure a symptom free death. This led to the provision of more specific education to the respiratory medical and nursing staff in the units that use NIV. Effective withdrawal of NIV requires an integrated team approach to provide best practice care

Results: Provision of regular education and support of staff improved staff confidence and competence in caring for patients during the weaning process of NIV. 100% patients dying were on regular opioids and benzodiazepines at time of death. Number of days from referral to death ranged from 0-8 with 25% dying on the referral day.

Conclusion: There is a need for further research and guidelines in palliative care NIV withdrawal with respiratory failure. A consistent collaborative approach from both the respiratory/palliative care services in optimal EOL management is encouraged.

TO 003

#O2THEFIX: SWIMMING BETWEEN THE FLAGS

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Introduction/Aim: Historically it has been common practice to administer oxygen regardless of need, without sufficient monitoring and adjustment. This has been consistently demonstrated by audits carried out at Waitemata District Health Board (Waitemata DHB) and other hospitals in New Zealand[1,2].

The Thoracic Society of Australia and New Zealand (TSANZ) recently released guidelines for the acute use of oxygen in adults that promote prescribing of oxygen therapy to target a level between a prescribed range of oxygen saturations[3]. For example between 92% to 96% is appropriate for most patients. For patients that retain carbon dioxide, such as those with chronic obstructive pulmonary disease (COPD), oxygen should be titrated to 88-92%

Methods: *#O2TheFix: Swimming Between the Flags* is an innovative multidisciplinary collaboration to improve the prescribing and safe administration of oxygen at Waitemata DHB. A campaign was planned to showcase the mix of utilising technology via electronic prescribing, social media and educational sessions sporting a catchy phrase: *"O2 the Fix, Aim 92-96. If high CO2, Aim 88-92"* to improve the awareness of oxygen with improved prescribing and administration.

Results: At baseline, only 12% of patients had their oxygen prescribed. The remaining patients were receiving oxygen without a prescription.

A re-audit six months later showed an increase of oxygen prescribing from 12% to 49%.

Staff also report increased understanding of important safety concepts regarding oxygen and their delivery devices.

Conclusion: #O2TheFix has improved patient safety by raising awareness of oxygen and device prescribing, including specified target saturations ranges. The #O2TheFix team will continue to monitor oxygen and device prescribing while continuing to spread the important safety message.

Grant Support: nil

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TO 004

INTEGRATED CARE REVIEW OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE INPATIENT MANAGEMENT

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Introduction/Aim: In 2014–15, 66,540 patients were hospitalised with an acute exacerbation of COPD (AECOPD) in Australia. National and international guidelines to optimise inpatient management of COPD exist, however compliance to these remains unclear. In 2015 Westmead Hospital implemented a COPD Integrated Care Team (ICT) to review and optimise inpatient and outpatient management of COPD. To review management of AECOPD in inpatients admitted to a tertiary teaching hospital.

Methods: We developed an evidence-based checklist to monitor the care of inpatients with AECOPD and the adherence to COPD national and international guidelines. We performed a retrospective chart review of checklist adherence for AECOPD admissions at Westmead Hospital from 2016 to 2017. ICT reviewed patients usually within 4 days of hospitalisation or step-down from high dependency, recorded compliance with the checklist, and then provided advice to inpatient teams regarding optimisation of COPD management.

Results: We reviewed 276 inpatients with AECOPD (55% male; mean age 69.9±10.4 years). We identified good adherence to oxygen prescription on medication charts, early antibiotic rationalisation, and spirometry measurement (all>75% compliance). However, we found inhaler prescription errors in 37% of reviews including incorrect or missing prescriptions and duplication of inhaler classes. 36% of patients were still on nebulised therapy at ICT review, 30% of patients were current smokers and only half had been offered smoking cessation measures. Respiratory vaccinations were not up-to-date in 62% of patients, and only 5% had been offered pulmonary rehabilitation.

Conclusion: ICT has identified areas for improvement in inpatient management of AECOPD including inhaler therapy prescriptions, smoking cessation measures, referral to pulmonary rehabilitation and assessment of immunisation. There is a role for ICT in education, ongoing monitoring, and optimisation of inpatient AECOPD management. Further research is needed to understand the impact of improved compliance to AECOPD guidelines on long-term ambulatory outcomes in patients with COPD.

INNOVATIVE MULTI-LINGUAL MOBILE APP TO IMPROVE KNOWLEDGE AND UNDERSTANDING OF ASTHMA AMONG INDIGENOUS CARERS OF CHILDREN WITH ASTHMA—PROTOCOL

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Introduction/Aim: Among Indigenous Australians, asthma is the most common self-reported chronic respiratory problem. Asthma related health outcomes are also poorer among Indigenous than non-Indigenous Australians. To address this, innovative interventions that are culturally-appropriate are needed. We have developed a multi-lingual mobile phone application (App) from our existing asthma flipchart, with 'voice-over' in local Indigenous languages, using a mixture of static and interactive formats. This study aims to evaluate whether the App improves health knowledge and understanding of asthma among Indigenous carers of children with asthma.

Methods: Evaluation of the app includes quantitative and qualitative methods in addition to the usability testing scheduled. The quantitative component involves a before and after study on asthma-related knowledge based on our previous flipchart study. Eighty Indigenous carers of children with asthma will be enrolled. Carers will undergo a pre-education questionnaire, followed by asthma education using the App. A post-education questionnaire will be administered immediately post-education session. A subset of carers will repeat the questionnaire two weeks later to determine short-term knowledge retention. In the qualitative component, Indigenous health professionals with and without asthma will participate in semi-structured interviews to ascertain perspectives of the functionality and usability of the App.

Results: Recruitment for this study will commence late October 2017 for 12 months.

Summary: Improving asthma related health outcomes is important, and requires a focused, multidisciplinary approach, particularly for at-risk groups such as Indigenous Australians.

Education in the form of mobile Apps is an innovative method of communicating health messages to culturally and linguistically diverse groups, that moves towards reducing language and context barriers particularly faced by Indigenous people in rural or remote settings. The asthma App has the potential to improve community knowledge by increasing access and usability of health education once only delivered in health centres.

Declaration of interest: Nil

Grant Support: Asthma Australia

HARNESSING HOPE, INSTILLING BELIEF: COPD SELF-MANAGEMENT

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Introduction/Aim: Chronic Obstructive Pulmonary Disease (COPD) has a significant impact on the healthcare system and patient. Although literature worldwide supports the efficacy of self-management, studies are traditionally entrenched in the economic model of supported self-management with the primary outcome of decreasing healthcare utilisation. There is limited literature in a rural setting that explores COPD self-management through the lens of patient experience.

This study aims to explore the concept of self-management through the eyes of the patient with COPD, living in rural Western New South Wales (NSW); what their understanding of self-management is and how they measure it?

Methods: A Heideggerian phenomenological inquiry formed the framework for this research, allowing exploration of the patients lived experience. In depth audio-recorded semi-structured interviews were conducted. A total of eight participants (four male, four female) with a reported diagnosis of COPD living in regional and rural Western NSW met the inclusion criteria. Interviews were transcribed verbatim, data was themed and analysed until thematic saturation was achieved (n=8).

Results: Findings unveiled four emerging themes: Adapt, Pace, Preserve and Ownership. Further exploration identified social, emotional and physical domains within the themes Adapt, Pace and Preserve. Exploring the phenomena through the patient lens, identified the true meaning of self-management and their measures of success.

Conclusion: Exploring the patient's lived experience of COPD self-management provides a meaningful and context-driven explanation of patient's perceptions of self-management, opening up the concept of subjective patient measures as an indicator of self-management.

Grant Support: This research was supported by the NSW Ministry of Health, Rural Research Capacity Building Program and Western NSW LHD.

Conflict of Interest: COPD Nurse Presenter for Lung Foundation Australia, funded by Menarini.

ARE INPATIENT SMOKERS CONSISTENTLY IDENTIFIED AND OFFERED SMOKING CESSATION INTERVENTIONS: A QUALITY IMPROVEMENT PROJECT

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Introduction/Aim: Each year, smoking kills an estimated 18,000 Australians and costs Australia $31.5 billion in health and economic costs. Smoking harms nearly every organ in the body, causing disease and reducing quality of life and life expectancy. An inpatient care episode represents an opportunity to identify smokers with current health needs and to intervene consistently to improve health care outcomes. NSW Health Policy requires consistent identification of smokers and, as a minimum, brief intervention to manage their nicotine dependence. As health care systems transition from paper to electronic records, it is possible that documentation quality may suffer in areas such as this. The purpose of this audit was to determine the quality of our practice in this important area and whether documentation was compromised in the transition to an electronic medical record(EMR).

Methods: Records of Respiratory Medicine inpatients from January to May 2017 (paper-based) and June-October 2017 (EMR) 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.

Results: 61 paper and 61 EMR records were analysed. 56(92%) of paper records identified smoking status. This fell significantly to 41(61%) [$p < 0.001$; chi^2 test] in EMR records. 7 of 13 smokers identified from paper records and 1 of 7 smokers from EMR were offered smoking cessation intervention[$p = 0.08$].

Conclusion: Smoking status could be more consistently identified and recorded. Provision and/or documentation of smoking cessation interventions is poor. Transition to EMR may be a risk for poorer health service provision or documentation.

The audit has shown that there is a need for improvement in documentation by health professionals if smoking interventions as per NSW government guidelines are to be achieved.

Conflict of Interest: There is no conflict of interest.

Grant Support: NIL

IRF7, CXCL9 AND CXCL10 PROTEIN LEVELS IN CHILDREN WITH ASTHMA

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Introduction/Hypothesis: Rhinovirus (RV) species C infection is associated with increased severity of acute wheezing and asthma compared with other RV species. RVC utilises a different host cellular receptor to RVA and B, but the mechanisms and pathways activated by RVC and their contribution to the severity of disease are unknown. We have previously identified gene expression differences in nasal cell samples from children with acute asthma and wheezing who were infected with RVC versus RVA. RVC-specific genes included *IRF7*, whereas *CXCL9* and *CXCL10* were identified in the RVA-specific response. We hypothesised that protein levels for each of these genes would be different in nasal fluid from children having a respiratory exacerbation and infected with RVC versus RVA.

Methods: Nasal fluid samples were collected from 21 children with RVA and 37 with RVC presenting to our tertiary children's hospital Emergency Department with acute respiratory illness. CXCL10 and CXCL9 protein were measured as part of a multiplex ELISA (*ThermoFisher*), whereas IRF7 protein was measured using a single ELISA kit (*Cusabio*). Urea was measured using a quantitative chromatic assay (*BioAssay Systems*) and used to standardise the ELISA measurements (presented here as pg protein per μg urea).

Results: CXCL9 levels were not significantly different (Mann-Whitney U=192, $p = 0.79$) between RVA (median 13.27, range 0.34-159.88, n=14) and RVC cases (median 20.66, range 0.37-248.44, n=29). CXCL10 levels were also not significantly different (Mann-Whitney U=234, $p = 0.90$) between RVA (median 0.48, range 0.04-11.41, n=16) and RVC cases (median 0.46, range 0.02-41.19, n=30). IRF7 levels did not differ (Mann-Whitney U=217, $p = 0.63$) between RVA (median 1.88, range 0.15-6.16, n=17) and RVC cases (median 1.62, range 0.19-21.78, n=28).

Conclusion: *CXCL9*, *CXCL10* and *IRF7* gene expression in nasal cell samples collected during RVC vs RVA-induced acute wheezing and/or asthma are different, but this has not translated to alterations in nasal fluid protein levels.

Declaration of Interest: none.

TO 009

GROWTH OF THE AIRWAY SMOOTH MUSCLE LAYER IN EARLY LIFE IS DUE TO CELL HYPERPLASIA

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Introduction/Aim: Thickening of the airway smooth muscle (ASM) layer is present in children with asthma which implicates a developmental origin. Little is known about the structural changes that occur in the airway and ASM layer from late gestation to adulthood. The aim of this study was to assess maturational changes in airway wall structure and examine mechanisms of ASM growth in terms of hyperplasia, hypertrophy and extracellular matrix (ECM).

Methods: Sheep were euthanized at late gestation (128 d), birth (150 d), post weaning (4 months) and sexual maturity (1 year). Lungs were fixed by instillation of formaldehyde and samples obtained from the trachea, main bronchus, segmental bronchus, sub-segmental bronchus and peripheral airways. The area of the ASM layer, inner and outer wall and perimeter of basement membrane (P_{bm}) were measured by planimetry. The number and size of ASM cells was assessed by stereology and fractions of muscle, ECM and 'other' within the ASM layer were determined by point counting.

Results: The predominant period of airway maturation was from birth to 4 months of age. Airway size (P_{bm}) and airway wall areas (including ASM) were all increased in the trachea ($p<0.05$), segmental bronchus ($p<0.05$) and sub-segmental bronchus ($p<0.05$). When wall areas were normalised to P_{bm}, there was no effect of age indicating that airway structure grew in proportion to airway size. Changes were less pronounced in more peripheral airways. The mechanism of ASM growth was due only to an increase in cell number and not as a result of cell hypertrophy or changes in the proportion of ECM.

Conclusion: Substantial airway growth occurs before weaning and this includes expansion of the ASM layer as a result of cell hyperplasia. Upregulation of ASM proliferation in infancy could facilitate thickening of the ASM layer and the development of asthma in childhood.

Declaration of Interest Statement: None.

TO 010

LUNG FUNCTION AT 6 WEEKS OF AGE IS ASSOCIATED WITH THE RISK OF DEVELOPING BRONCHIOLITIS IN INFANTS BORN TO MOTHERS WITH ASTHMA DURING PREGNANCY

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Introduction/Aim: FeNO-guided asthma management during pregnancy was associated with a reduction in bronchiolitis episodes in the first year of life (Mattes et al., Thorax 2013). The aim of this analysis was to investigate an association between infant lung function at 6 weeks of age and bronchiolitis in the first 6 months of life in a cohort of babies born to women with asthma during pregnancy.

Methods: Tidal breathing flow-volume loop (TBFVL) measurements were performed during quiet unsedated sleep in infants born to mothers who participated in an ongoing NHMRC-funded multi-centre RCT of FeNO-guided asthma management versus usual care (Breathing for Life Trial). All researchers remain blinded in regards to the pregnancy intervention.

Results: Of 324 babies recruited to date, 289 attended a clinical assessment and 261 remained in quiet sleep during testing. 232 had TBFVL attempted (44% female; age 6 weeks SD 1.2), of which 209 (90%) tests were technically acceptable. At the time of abstract submission, 140/209 (67%) were 6 months old.

Infants with one episode of bronchiolitis in the first 6 months of life had a mean of time to Peak Tidal Expiratory Flow/time Expiratory Flow % (tPTEF/tE%) of 28.5 (SD 6.8; n=30) at 6 weeks of age. Infants with >1 episode of bronchiolitis had a mean tPTEF/tE% of 22.79 (SD 4.46; n=6) while those without bronchiolitis had a mean tPTEF/tE% of 32.34 (SD 9.4; n=104). There were no difference in respiratory rate (RR) between groups (1 episode: mean RR 44 breaths per minute; >1 episode: mean RR 42 breaths per minute; no bronchiolitis: mean RR 44 breaths per minute).

Conclusions: Lung function may be associated with the risk of developing bronchiolitis which could provide a linking mechanism for the effect of FeNO-guided management on bronchiolitis prevalence.

ANTI G-CSFR ANTIBODY TREATMENT SUPPRESSES NEUTROPHILIC AND TYPE-2 LUNG INFLAMMATION IN AN ALLERGIC ASTHMA MODEL WORSENED BY NEONATAL CO-INFECTION

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Introduction/Aim: Early life respiratory infections are associated with the development of severe asthma, where the detection of both respiratory viruses and bacteria occur frequently in children with acute wheeze. However, the mechanistic interaction between neonatal respiratory infections and the establishment of allergic type-2 and neutrophilic lung inflammation remains poorly understood in severe asthma. Our aim is to investigate the role of neonatal exposure to infectious pathogens in the development of allergen-triggered asthmatic pathogenesis and airway remodelling.

Methods: Intranasal inoculation of *Streptococcus pneumoniae* (2000 CFU, EF3030)/saline and Influenza A virus (500 PFU, HKx31)/saline was performed on neonatal mice (female BALB/c) at the age of 8 days and 15 days respectively. At the age of 21 days, house dust mite (HDM)/saline was administered intranasally daily for 3 weeks.

In the therapeutic study, a separate cohort of mice was treated as described above. In the last week of HDM regime, 100 μg of anti-G-CSF receptor (G-CSFR) /isotype antibody was injected intraperitoneally every second day.

Results: HDM challenge in mice co-infected as neonates significantly increased pneumococcal lung infection, neutrophilic inflammation and mucus production. Neutrophilic lung inflammation was associated with an increase in interleukin-17A and granulocyte-colony stimulating factor (G-CSF). Blocking G-CSFR significantly reduced neutrophlic inflammation in the bronchoalveolar (BAL)-fluid and myeloperoxidase activity in lung tissue without increasing pneumococcal lung load. In addition, elevated markers of netosis including neutrophil elastase and double-stranded DNA were reduced in the BAL-fluid of anti-G-CSFR treated mice. Anti-G-CSFR therapy also potently reduced type-2 inflammation including BAL eosinophils, IL-33/IL-13 lung transcripts, CD4^{+}IL4^{+} T_H2 cells and mucus (muc5ac) production.

Conclusion: Disrupting G-CSFR significantly reduced neutrophil mobilisation and netosis without worsening pneumococcal lung infection and furthermore, reduced type-2 inflammation in allergic airways disease. Monoclonal antibodies against the G-CSFR may represent a novel therapeutic target for mixed granulocytic severe asthma.

GENETIC VARIANTS IN HUMAN RESPIRATORY VIRUS RECEPTORS WERE ASSOCIATED WITH INFECTION, RECOVERY AND RECURRENCE OF WHEEZING EXACERBATIONS IN CHILDREN

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Introduction/Aim: Human rhinoviruses (RV) and respiratory syncytial virus (RSV) are common respiratory viruses in children with acute wheezing illnesses. Viruses use human receptors to enter host cells. RSV uses nucleolin (NCL), and RV uses intercellular adhesion molecule 1 - (ICAM1), low density lipoprotein receptor (LDLR) or cadherin related family member 3 (CDHR3). We aimed to assess whether variants in viral receptor genes were associated with asthma severity.

Methods: Cohort: Children who presented to a tertiary children's hospital emergency department with acute asthma (n=50). Samples: Nasal samples for RV detection. DNA was extracted from peripheral blood. Analysis: Viral receptor genes were sequenced using Ion AmpliSeq primers (Thermo Fisher Scientific). Data collected included: (1) number of hours from presentation to discharge, (2) number of respiratory hospital presentations and admissions from birth and (3) number of salbutamol doses administered in the first 6 hours. Statistical analysis was completed using SPSS version 22. All analyses were adjusted for age and gender.

Results: The mean age of children was 8.44yrs, 60% male, 56% with detectable RV. Children with genotypes *CDHR3* rs34426483 GC or CC and *NCL* rs7598759 CC were 0.161-0.105 fold less likely to have rhinovirus detected at recruitment than children with the other genotypes (95% confidence interval (CI): 0.023-1.11; p-value: 0.064 and 95% CI: 0.009-1.24; p-value: 0.073, respectively). Children with *ICAM1* rs281437 TT genotypes had 17.0 fold more hospital visits before recruitment (95% CI: -0.062-23.5; p-value: 0.002) and took 2.52 fold longer to be discharged from hospital (95% CI: 7.81-129; p-value: 0.019) compared to children with CC genotypes. Children with *ICAM1* rs5498 GG genotypes had 0.593 fold fewer treatment doses in 6 hours (95% CI: -0.852-12.1; p-value: 0.013) than children with AA genotypes.

Conclusion: Gene variants in viral receptor genes may play a role in viral infection and treatment response, and thus recurrent respiratory illnesses requiring presentation to hospital.

Conflict of Interest: No.

Nomination: Nil.

TO 013

This abstract has been withdrawn

Paediatric

TO 014

ABNORMAL LUNG CLEARANCE INDEX (LCI) IN PRESCHOOL YEARS IS ASSOCIATED WITH LOWER SPIROMETRY LATER IN CHILDHOOD IN CYSTIC FIBROSIS (CF) CHILDREN

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Introduction/Aim: Availability of robust commercial multiple breath nitrogen washout (MBNW) equipment offers improved feasibility for wide-spread preschool lung function testing in Cystic Fibrosis (CF) clinics. Clinical utility is emerging with this commercial equipment but the prognostic value of performing preschool MBW (defined as age 2-6 years) remains unclear. We have previously shown an association between higher preschool Lung Clearance Index (LCI) values and greater medication use and incidence of bacterial isolation within our clinic. This study aimed to explore the association between those preschool LCI values and later spirometry, a well established clinical tool in older CF subjects.

Methods: Current spirometry values (FEV_1, FEV_1/FVC and FEF_{25-75}) were collated on the original 37 preschool children who had MBW performed at mean (SD) age 5.0 (1.2, range 2.8-6.9) yrs: median (range) LCI 8.0 (6.5-14.3). Spirometry results were expressed as z-scores (GLI reference equations). Abnormal preschool LCI was defined based on recently published preschool healthy control data using identical equipment and testing protocol[1] (ULN for LCI 8.0).

Results: Technically acceptable spirometry data were available in 35/37 (95%) (one had moved out of state, one has autism) at mean (SD; range) age 7.7 (1.4; 4.8-9.8) years, which was 2.7 (0.4; 1.0-3.3) years after the original MBW testing time point.

	Later spirometry (z scores)		
	FEV_1	FEV_1/FVC	FEF_{25-75}
Overall cohort (n=35)	-0.18 (1.28)	-0.80 (1.06)	-0.82 (1.43)
Abnormal preschool LCI (n=17)	-0.53 (1.53)	-1.28 (1.17)	-1.05 (1.63)
Normal preschool LCI (n=18)	-0.02 (0.91)	-0.62 (0.78)	-0.63 (1.04)
p value (abnormal vs. normal LCI)	0.07	0.02	0.03

Data presented as mean (SD).

Conclusion: Abnormal MBW-derived LCI values in the preschool years are associated with later spirometry deficits. This suggests prognostic utility of MBW testing in this younger preschool age range to predict later spirometry values.

[1] Stanojevic et al AJRCCM 2017;195:1216-1225

Conflict of interest: No conflicts of interest to declare.

CAN A BRONCHOSCOPICALLY DEFINED BRONCHITIS TOOL IN CHILDREN BE VALIDLY DEVELOPED?

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Introduction/Aim: Despite bronchitis being the most common finding at flexible bronchoscopy (FB) in many paediatric centres such as ours, no validated objective system exists. From previously recorded FB, we: (1) determined the correlation among the different macroscopic findings with airway neutrophilia (2) examined the inter-rater repeatability of these findings and, (3) developed an experimental model of an objective FB-derived bronchitis score (BScore$_{exp}$).

Methods: We reviewed 100 consecutive previous recordings (2016) from our database. 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. FB recordings were assessed (by 2 scorers independently,blinded to the clinical history) for 6 components: amount of secretions (scores 1-6 from previous validated score), colour of secretions (0-8 using BronkoTest), mucosal oedema (0-3), ridging (0-3), erythema (0-3) and pallor (0-3), based on pre-determined criteria on a pictorial chart. The various models of BScore$_{exp}$ were plotted against neutrophil% using a receiver operating characteristic (ROC) curve. Here we report our preliminary findings; on the first 65 children with valid FBs.

Results: Only secretion amount (r_s=0.272, p=0.03) and colour (r_s=0.342, p=0.005) significantly correlated with BAL %neutrophil but other macroscopic findings correlated with each other. For the 26 FBs examined for repeatability, kappa values for secretions (K=0.96, 95%CI 0.91-1.0) and colour (K=0.84, 95%CI 0.73-0.95) were excellent. Other K ranged from 0.38 to 0.67. Using BAL neutrophilia of 15% to define inflammation, the highest aROC (0.63, 95%CI 0.50-0.76) was obtained by the giving three times weightage to secretion amount and colour and adding it to the other 4 components except pallor.

Conclusion: A repeatable FB-defined bronchitis scoring system can be derived. However, a prospective study needs to be performed with larger numbers to further evaluate the different models to obtain aROC of >0.7.

Declaration of Interest statement: None.

PROTRACTED BACTERIAL BRONCHITIS (PBB)—LONG-TERM OUTCOMES AT FIVE YEARS: A COHORT STUDY

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Introduction/Aim: PBB is a common cause of paediatric chronic cough and is defined as chronic wet cough (>4-weeks) without specific signs or symptoms of an alternative cause which responds to 2-weeks of appropriate antibiotic therapy. In this first 5-year outcome data on children with PBB, we aimed to describe the long-term clinical outcomes in children with PBB.

Methods: 160 children (median age 25mths, range 2-163mths) were recruited and followed for 5-years with monthly contacts by research staff and when possible, annual physician clinical review. Flexible bronchoscopy, bronchoalveolar lavage and basic immune tests were performed at baseline. During follow-up, chest CT was performed if clinical features were suggestive of bronchiectasis. Bronchiectasis was diagnosed when paediatric radiology criteria and clinical features were present. Spirometry was undertaken at the final follow-up (5-years) when possible. We present data on the initial 101 children (n PBB=82, controls=19) of the cohort with 5-year follow-up data.

Results: Of the 82 children with PBB (median age 23mths, range 5-163mths; 65% boys), CT was undertaken in 26 children during the follow-up period; 7 had bronchiectasis (7/82=8.5%). All were diagnosed within 28-months. The frequency of recurrent PBB ($\geq$3/yr) decreased over the duration of the study from 54 (66%) at Yr-1 to 10 (12%) at Yr-5. Fifty-seven (70%) of children with PBB had tracheomalacia and/or bronchomalacia on bronchoscopy, whilst 25 (30%) had visible evidence of bronchitis. At the Year-5 point, the mean FEV$_1$ was 94% predicted (SD 15.8) in both the PBB and control groups.

Conclusion: PBB is associated with a subsequent diagnosis of bronchiectasis in a proportion of children recognised within 28 months of initial PBB diagnosis. While recurrent PBB decreases over time, those with recurrent episodes should be reviewed for bronchiectasis. Spirometry values remains in the normal range in children diagnosed with PBB at long-term follow-up.

TO 017

RESPIRATORY STATUS IN CHILDREN WITH SPINOMUSCULAR ATROPHY TYPE II & III

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Introduction: Spinomuscular atrophy (SMA) is an uncommon, progressive Neuromuscular Disorder (NMD) with significant respiratory morbidity and eventual respiratory failure. There are currently no clear guidelines for non-invasive ventilation (NIV) instigation in this condition. Newer treatment options are likely to change current clinical practices but improved respiratory assessment methods are needed. Our ***objectives*** in this cohort were to (**1**) analyse the patterns of sleep breathing measured by polysomnography (PSG) and (**2**) determine early clinical and lung function predictors of nocturnal hypoventilation.

Methods: We retrospectively reviewed clinical records and PSG data of all children with genetically-confirmed SMA II/III living in Queensland. Spirometry, Forced Oscillatory Technique (FOT), Lung Clearance Index (LCI), & respiratory muscle strength testing were prospectively performed/measured. The prospective arm of the study is ongoing with complete data collection expected by November 2017.

Results: 23 children (9F; 17 with SMA II, median age 108 months) were included. Median FVC% predicted (z score) was 61% (n=19, -3.32); Rrs_8 z-score: 2.19 (n=11); Xrs_8 z-score: -2.03 (n=11); SNIP z-score: -2.53 (n=10) & LCI: 7.36 (n=12). Median (IQR) REM related Apnea-hypopnea index (rAHI) was high at 5.9 (2.9-17.5;n=19). 10 children (9 with SMA II) required long-term nocturnal NIV initiated at a median age of 94 months; 5 (50%) after an acute respiratory illness. These children were older (127 vs 84 months; p=0.03) with significantly worse FVC-z scores (-4.8 vs -1.18; p<0.01); rAHI (26.5 vs. 4.2; p=0.05), LCI (8.8 vs. 7.1, p=0.01) & SNIP z-scores (-3.5 vs. -1.47 p=0.001). Predictors of NIV need will be analysed using a logistic regression model once the prospective arm is completed.

Conclusion: Most children with SMA II need nocturnal ventilatory support beginning in early childhood and FVC may be a predictor. FOT, SNIP and LCI were deranged and may help in predicting early respiratory insufficiency, particularly in early years.

Declaration of Interest: No conflicts of interest.

TO 018

AIRWAY SMOOTH MUSCLE CONTRACTION IS ENHANCED BY INTRA-AMNIOTIC LIPOPOLYSACCHARIDE AND SUPPRESSED BY POSTNATAL DEXAMETHASONE IN A PRETERM OVINE MODEL

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Introduction/Aim: Chorioamnionitis is associated with preterm birth and the development of airway disease in later life. Chorioamnionitis promotes lung inflammation, but its effect on airway smooth muscle (ASM) function is unknown. Postnatal steroids are given to preterm infants with severe lung disease and may have beneficial effects on airway development. This study examined the separate and combined effects of chorioamnionitis and postnatal steroids on ASM contraction in a preterm ovine model.

Methods: Chorioamnionitis was induced by ultrasound-guided intra-amniotic (IA) injection of lipopolysaccharide (LPS) into time-mated ewes (127d gestation; term=150d). Postnatally, LPS-exposed lambs received intravenous low-dose dexamethasone (LPS/Dex) or saline (LPS/Sal: n=6) commencing within 2 h of birth. Postnatal controls received IA saline at 127d gestation and daily intravenous low-dose dexamethasone (Sal/Dex: n=9) or saline (Sal/Sal: n=6) postnatally. Lambs were delivered via caesarean section at 129d gestation, receiving respiratory support as required, and euthanised after 7d (i.e., 136d postconceptional age). A fifth group of naïve fetal control lambs were euthanised immediately at 136d gestation as maturational controls. Bronchial rings were studied in organ bath chambers. Isometric force production to acetylcholine was measured and dose-response curves constructed to determine maximal response, slope and sensitivity. ASM thickness was determined histologically after Masson's Trichrome.

Results: Maximal response, slope and sensitivity were similar between maturational and postnatal (placebo) controls, indicating ASM contraction was unaffected by preterm delivery. Maximal response was increased by IA LPS administration (p<0.05) and not significantly affected by postnatal dexamethasone. Dose-response slope was reduced by postnatal dexamethasone (p<0.05) in LPS-exposed lambs. ASM thickness was lower in animals treated postnatally with dexamethasone, irrespective of prior exposure to LPS (p<0.05).

Conclusion: ASM contraction is enhanced in offspring born to chorioamnionitis-affected pregnancies, and this is suppressed by postnatal dexamethasone through reduced ASM thickness. Postnatal dexamethasone may reduce the incidence of future airway disease after chorioamnionitis.

CHARACTERISTICS OF CHILDREN WITH CHRONIC SUPPURATIVE LUNG DISEASE (CSLD): A PROSPECTIVE 10-YEAR STUDY

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Introduction/Aim: While largely preventable, CSLD (including bronchiectasis), remains highly prevalent amongst disadvantaged Indigenous populations in high income countries. Adult studies with CSLD have shown that persistent airway infection and inflammation, and longer duration of chronic productive cough result in poorer clinical outcomes. There are however, no prospective studies in children with CSLD in the last 50-years to help guide long-term clinical care and management. We evaluated the long-term clinical outcomes of Indigenous children with CSLD who participated in our previous study, 'Multicentre Bronchiectasis Study (BOS)' (2004-2012).

Methods: During 2015–17, we re-assessed as many children as possible from BOS (Australia n=97, Alaska n=41, New Zealand n=42). Research staff administered standardised questionnaires and undertook medical note review, clinical examination and spirometry. Medical history was extracted from the original dataset and current medical records. Based on their clinical assessment, physicians classified children into 4 overall categories (well, better, stable, worse).

Results: 120/180 (67%) children (current median age 11.5-years (IQR 5.9-18.6); 46% males) were reviewed. From birth until their current age, children had a median of 20 (IQR 14-30) community-treated acute lower respiratory infections and 4 (IQR 3-7) respiratory hospitalisations. Respiratory infections decreased with age. At examination, wheeze was present in 10%, wet cough in 26% and digital clubbing in 17% of children. The children's summary clinical status were: well (22%); better (32%); stable (46%) or worse (0%). Airway obstruction on spirometry was present in 36% and restrictive pattern in 19%, with only 45% having normal spirometry values within population norms.

Conclusion: In a 10-year follow-up of children with CSLD and on-going clinical care, most were stable or improved by adolescence. However, as many still experience respiratory symptoms and demonstrate impaired lung function, clinical follow-up is recommended during adolescence to optimise clinical management.

Declaration of interest: Nil

FREE FATTY ACID RECEPTORS 1 AND 4 MEDIATE DESENSITISATION-RESISTANT BRONCHODILATION AND ARE EXPRESSED IN ASTHMATIC AIRWAYS

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Introduction: Salbutamol opposes airway hyperresponsiveness in asthma but its efficacy is limited by β_2-adrenoceptor desensitisation. Free fatty acid receptors 1 and 4 (FFAR1, FFAR4) are expressed in mouse and human lungs (Mizuta *et al*., AJP Lung, 2015) and their agonists cause relaxation of mouse airways with greater efficacy than salbutamol (Bourke *et al*., AJRCMB, 2017).

Aims: To compare bronchodilation to salbutamol, GW9508 (FFAR1/FFAR4 agonist) and TUG891 (FFAR4 agonist) under conditions of β_2-adrenoceptor desensitisation, test potential FFAR1/FFAR4 desensitisation and assess FFAR expression in mouse airways from a model of chronic allergic airways disease and human airways from subjects with and without asthma.

Methods: Precision cut lung slices were prepared from 6-8-week-old male BALB/C mice. Airway relaxation to GW9508, TUG891, and salbutamol were compared after overnight incubation with 10μM salbutamol, 100μM GW9508, or vehicle. Immunohistochemistry for FFARs was performed on lung sections from saline control (C) and ovalbumin (OVA)-sensitised mice and airway biopsies from non-asthmatic (NA) and asthmatic (A) subjects.

Results: Salbutamol and FFAR agonists relaxed airways pre-contracted with methacholine (%relaxation: 10μM salbutamol 50±6%; 100μM GW9508 28±7%; 100μM TUG891 44±10%, n=7,4,6). Overnight incubation with salbutamol reduced subsequent relaxation to salbutamol (to 4±2%, n=7, p<0.0001 *cf* control), but not to GW9508 or TUG891 (27±6%, 42±10% respectively, n=6,5). GW9508 incubation did not affect salbutamol- or GW9508-mediated relaxation (44±6%, 26±7% resepectively, n=6,6). Both FFAR1 and FFAR4 expression was similar in C and OVA mouse airways (FFAR4 positive pixel count/mm^2: C 4.4±0.3x10^6; OVA 5.4±0.7x10^6, n=5,6) and both receptors were evident in airway smooth muscle and epithelium in NA and A human airways.

Conclusion: Relaxation to FFAR agonists was maintained under conditions of β_2-adrenoceptor desensitisation and resistant to homologous desensitisation. Expression of FFAR1 and FFAR4 in asthma context suggests that these receptors may be targeted for alternative or adjunct bronchodilator therapy.

TO 021

DETERMINANTS OF PHYSICAL ACTIVITY IN OBSTRUCTIVE AIRWAY DISEASES

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Introduction/Aim: Severe asthma (SA), chronic obstructive pulmonary disease (COPD) and bronchiectasis are obstructive airway diseases (OAD) that share clinical characteristics that are likely to impair patients' physical activity (PA) level. However, PA has not been extensively studied in OAD, outside of COPD. We aimed to describe the prevalence of PA impairment in different OAD compared to controls, and to test whether in the OAD group, PA is associated with shared clinical characteristics of these diseases.

Method: A cross-sectional study of adults with OAD (SA=62, COPD=67, bronchiectasis=60) and controls (n=63) was conducted. Participants underwent a multidimensional assessment involving measurement of body mass index (BMI), lung function, exercise capacity (6-minute walk distance (6MWD)), health status (SGRQ) and systemic inflammation (hsCRP). PA (steps/day) was measured using the ActiGraph wGT3X-BTaccelerometer.

Results: The OAD group included 189 participants (58.7% female), median [IQR] age 67 [58-72] years and mean FEV_1% predicted 69.4%. The control group included 63 participants (52.4% female), aged 55 [34-64] years. Compared to controls, those with OAD accumulated less steps/day: median difference -4630 (COPD), -2255 (SA), and -2289 (bronchiectasis) ($p \leq 0.001$ all results). Compared to COPD, both SA and bronchiectasis accumulated more steps/day: median difference 2375 and 2341, respectively ($p \leq 0.0001$). No statistically significant differences were found between the SA and bronchiectasis groups. In separate adjusted regression models, 6MWD, FEV1% predicted and SGRQ were all associated with physical activity in participants with OAD. In the full multivariable model, 6MWD, FEV_1% predicted and BMI remained significantly associated, explaining 47.4% of the adjusted variance of PA in people with OAD ($p<0.0001$).

Conclusion: People with OAD engage in lower levels of PA compared to controls. The degree of activity impairment differs by disease. Despite this, the level of activity is associated with shared clinical characteristics. Interventions to improve PA should be multifactorial, and target the OAD population, irrespective of diagnosis.

TO 022

IL-33 AND RHINOVIRUS EFFECTS ON IL-33 RECEPTOR EXPRESSION IN ASTHMA

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Background: Epithelial cell-derived interleukin-33 (IL-33) appears to have an important role in polarizing type 2 immune responses to allergens, though whether IL-33 can also modify responses to respiratory viruses in asthma is not clear.

Aim: Examine the effects of IL-33 on anti-viral cellular immunity in asthma, focusing on the role of the two chains of the IL-33 receptor, interleukin 1 receptor like 1 (IL1RL1; also known as ST2) and IL-1 receptor accessory protein (IL1RAP).

Methods: Peripheral blood mononuclear cells were isolated from 16 people with mild/moderate allergic asthma and 16 healthy donors, exposed to IL-33 (10ng/ml) and activated with rhinovirus (RV) serotype 16 for 24h. mRNA and protein expression were assessed by qPCR, flow cytometry and/or ELISA.

Results: In those with asthma, RV + IL-33 induced greater type 2 cytokine production, whereas in control subjects, IL-33 enhanced type 1 cytokine production. Both RV alone and RV + IL-33 induced upregulation of IL1RL1/ST2 mRNA and surface protein expression in asthma ($p=0.013$ and $p=0.034$ respectively), but not in healthy participants. This was due to enhanced IL1RL1/ST2 expression on both type 2 innate lymphoid cells (ILC2) and conventional T-cells. In contrast, neither RV nor IL-33 had any effect on expression of IL1RAP expression. ILC2 cells were the major source of IL-13 production.

Conclusion: These findings suggest dysregulation of the IL-33 receptor IL1RL1/ST2 in asthma, and provide a mechanism by which RV infections might exacerbate type 2 inflammation in an IL-33 rich tissue environment.

TO 023

This abstract has been withdrawn

TO 024

THE ROYAL MELBOURNE HOSPITAL THUNDERSTORM-ASTHMA COHORT

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Introduction/Aim: We aimed to characterise people affected by the catastrophic thunderstorm-asthma event in Melbourne, Australia in November 2016. We identified individual patient characteristics associated with hospital admission to inform research and practice in the management and prevention of the increasingly recognised and potentially fatal phenomenon of thunderstorm-asthma.

Methods: Cross-sectional, retrospective analysis of demographics of 240 patients presenting to The Royal Melbourne Hospital, an adult metropolitan university teaching hospital in Melbourne, and clinical characteristics of 70 of those patients who subsequently attended an outpatient clinic review.

Results: Patients were generally young adults (mean age 35 years), non-Caucasian (60%), with seasonal rhinitis (96%) and universally (100%) sensitised to ryegrass pollen. Forty-three patients (18%) required hospitalisation. Twenty-six (37%) of these patients had no prior diagnosis of asthma. Amongst known asthmatics, preceding the event, 79% had active asthma symptoms. Forty-four per cent of patients were receiving short-acting β-agonist therapy alone. Hospitalisation was associated with uncontrolled asthma symptoms in the month prior to the event (60%), and more symptomatic allergic rhinitis, lower lung function, higher total and ryegrass-specific IgE and higher peripheral blood eosinophil counts measured at review.

Conclusion: Thunderstorm-asthma affects people with seasonal rhinitis, ryegrass sensitisation and can occur without prior history of asthma, with a dramatic potential to rapidly inundate a healthcare system. Poor asthma control earlier in the hay fever season was associated with hospitalisation and inhaled corticosteroids should be considered prior to the high-risk season in strongly sensitised individuals.

A SINGLE BOUT OF MODERATE-INTENSITY EXERCISE REDUCES EOSINOPHILIC AIRWAY INFLAMMATION IN INACTIVE ADULTS WITH ASTHMA, WHILE VIGOROUS-INTENSITY EXERCISE HAS NO EFFECT

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Introduction/Aim: Exercise benefits general health, however its impact on asthma has received little attention, with the effects of exercise intensity not having been examined in this population. We previously found a single bout of moderate-intensity exercise decreased exhaled nitric oxide in physically inactive, but not in physically active, adults with asthma. The aim of this study was to examine the acute effects of exercise intensity on airway inflammation in adults with asthma, and to examine whether this differs by usual exercise levels.

Methods: In a randomised controlled trial, adults with asthma were randomised to complete either 45 minutes of moderate-intensity exercise (55-70% HRmax) on a cycle ergometer (n=19), 30 minutes of vigorous-intensity exercise (70-85% HRmax) on a cycle ergometer (n=19) or 30 minutes of rest (n=18). Sputum cell counts were obtained the day prior to and 4 hours-post exercise/rest.

Results: Sputum eosinophil count was lower following moderate-intensity exercise [0 (-26, 23)x10^6/mL) versus rest [9 (3, 42)x10^6/mL, p=0.0249]. However, sputum eosinophil count did not change following vigorous-intensity exercise [8 (-21, 47)x10^6/mL, p=0.380] versus rest. Participants who reported performing exercise causing breathlessness or sweating ≤once per week had a significant decrease in sputum eosinophil count [-3 (-89, 0) vs 7 (3, 142)x10^6/mL, p=0.006] and sputum %eosinophils [-0.3 (-0.7, 0)% vs 0.5 (0.1, 2.0)%, p=0.012] following moderate-intensity exercise, compared to rest. Participants who became breathless or sweaty during exercise ≥twice/week had no change in sputum eosinophil count (p=0.395) or sputum %eosinophils (p=0.449) following the exercise challenge.

Conclusion: This study demonstrates that an acute bout of moderate-intensity, but not vigorous-intensity, exercise reduces sputum eosinophils in adults with asthma. This change was only evident in physically inactive participants, suggesting that regular physical activity may protect against airway inflammation.

PRELIMINARY SAFETY AND EFFICACY OF TRIPLE-COMBINATION CFTR MODULATOR REGIMENS

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Introduction/Aim: Prior studies with cystic fibrosis transmembrane conductance regulator (CFTR) modulators in patients heterozygous for *F508del* and a minimal function (MF) CFTR mutation (*F508del*/MF) have failed. One strategy to enhance clinical efficacy is to add a second corrector to established corrector/potentiator regimens. Safety and efficacy of 3 such next-generation (NG) correctors (VX-440, VX-152, VX-659) in triple-combination therapy (TC) with tezacaftor (TEZ) and ivacaftor (IVA) were evaluated in patients with CF with *F508del*/MF or *F508del*/*F508del* genotypes.

Methods: Randomized, double-blind, placebo- or active-controlled studies of VX-440 and VX-152 (phase 2), and VX-659 (phase 1) in TC were conducted in CF patients with *F508del*/MF (n=80) or *F508del*/*F508del* genotypes (n=40; the latter with VX-152 and VX-440 only; after 4 weeks of TEZ/IVA pretreatment). Primary objectives were safety and tolerability; efficacy and pharmacodynamic effects were assessed by absolute change in ppFEV$_1$ and sweat chloride from baseline, respectively.

Results: Baseline characteristics were balanced. NG TC regimens were well tolerated; most adverse events (AEs) were mild or moderate. AEs leading to discontinuation included increased alanine aminotransferase/aspartate aminotransferase (VX-440 TC, n=1), pneumonia (VX-152 TC, n=1), and respiration abnormal/sputum increased (placebo, n=1). After 2 to 4 weeks, significant improvement from baseline in ppFEV$_1$ of 9.6 to 12.0 percentage points was seen with all 3 NG TC regimens in *F508del*/MF patients, and significant improvement from baseline of 7.3 to 9.5 percentage points was seen with VX-440 or VX-152 TC on top of TEZ/IVA in *F508del*/*F508del* patients (vs TEZ/IVA baseline). Significant reductions from baseline in sweat chloride were also seen with TC regimens vs placebo or TEZ/IVA alone.

Conclusion: This is the first demonstration of substantial improvements with NG TC regimens in patients with CF with *F508del*/MF genotype, in whom previous CFTR modulators have failed, and in patients with CF with *F508del*/*F508del* genotype. Ongoing studies will guide development of TC regimens.

Conflict of Interest: PW was an investigator for the Next Gen clinical trial and has taken part in advisory boards for Vertex Pharmaceuticals.

TO 027

A PERIPHERAL BLOOD TRANSCRIPTIONAL PROFILE PREDICTS DISEASE SEVERITY AND THE RISK OF FUTURE EXACERBATIONS IN ADULTS WITH CYSTIC FIBROSIS (CF)

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Introduction/Aim: To determine if a blood transcriptional gene signature could be used to predict risk of exacerbations in the next 12 months.

Methods: CF participants (n=21) were recruited when stable at annual review and followed for 12 months. Peripheral blood RNA was collected into Paxgene RNA tubes. RNA was extracted using the Paxgene Blood RNA Kit (Qiagen) and RNA quality and quantity was assessed using the Bioanalyser (Agilent Technologies). Transcriptional profiles were generated (Illumina HumanRef-8 V4) and analysed using Gene-Spring GX14.8.

Results: Participants had mean age 33years (13.5), mean FEV1 65% predicted (sd 22). Unsupervised hierarchical clustering of gene expression profiles revealed 2 distinct clusters. Cluster 2 (n=16) were characterised by significantly lower FEV1% predicted (p=0.036), higher residual volume % predicted (p=0.040), lower BMI (p=0.042), more frequent exacerbations requiring IV antibiotics (p=0.012), and increased presence of pseudomonas (p=0.011), compared with cluster 1 (n=5). This more severe phenotype in cluster 2 was associated with a reduction in the expression of 119 entities, including downregulation of immune regulatory genes such as IL-10, IL-17RD, and NLRP8.

Conclusion: Transcriptional profiles of peripheral blood can predict disease severity and future risk of exacerbations in the next 12 months.

Grant Support: n/a

TO 028

HYPERGLYCAEMIA IN YOUNG CHILDREN WITH CYSTIC FIBROSIS CORRELATES WITH INFECTION AND NEUTROPHIL BURDEN ON BRONCHOALVEOLAR LAVAGE

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Introduction: Cystic Fibrosis(CF) results in insulin deficiency from birth and progresses to Cystic Fibrosis-related diabetes (CFRD)[1]. CFRD has a significant impact on lung function, respiratory infections, and nutrition, and leads to an increase in mortality[2]. However, the prevalence of early hyperglycaemia and impact on respiratory tract infections in young children with CF remains unknown.

Aims: To determine the prevalence of hyperglycaemia in children with CF using Continuous Glucose Monitoring (CGM) To correlate hyperglycemia on CGM with presence of CF pathogen and neutrophil percentage in routine bronchoalveolar lavage (BAL).

Methods: A single-centre study of children with CF <5years. The CGM device (CGM Medtronic MiniMed) was inserted when clinically well during routine bronchoscopy/BAL and worn for 3 days. CGM outcomes included peak glucose, time spent >7.8mmol/L and Area Under Curve (AUC) >7.8mmol/L. BAL samples were cultured and cell count and differential determined. A t-test and regression analysis was undertaken to examine the relationship between hyperglycaemia and the presence of CF pathogen, and neutrophil percentage on BAL.

Results: 14 children (3 female) had CGMs performed, 12/14 had neutrophil percentage results available. Median age 2.44 years (range 1-5.5). 3 day glucose mean=5.89$\pm$0.49mmol/L (mean$\pm$ SD). 43% (6/14) had diabetic range (≥11.1mmol/L) glucose levels. Participants who had positive cultures spent a greater period of time >7.8mmol/L on CGM (mean time 9.9%) compared with culture negative participants (3%, p=0.02), and had a greater glucose AUC>7.8mmol/L (p=0.04). There was a positive correlation with peak glucose (r^2=0.4, p=0.02) and AUC>7.8mmol/L (r^2=0.4, p= 0.04) with neutrophil burden on lavage.

Conclusion: Young children with CF have demonstrated diabetic range hyperglycaemia on CGM. CF pathogens are more likely to be present when glucose abnormalities are more severe and a significant correlation between neutrophil count and hyperglycemia was demonstrated. Further research is underway to determine whether abnormalities on CGM in this cohort has an impact on nutrition, pulmonary inflammation and lung function.

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GREATER SLEEP FRAGMENTATION IS ASSOCIATED WITH LESS PHYSICAL ACTIVITY IN ADULTS WITH CYSTIC FIBROSIS

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Introduction/Aim: Sleep quality in people with cystic fibrosis (CF) is known to be poor, while regular physical activity participation is associated with less decline in lung function (FEV_1). The relationship between sleep quality and physical activity in people with CF is unknown. We aimed to explore any association between sleep pattern and physical activity participation in young adults with CF.

Methods: This is a secondary analysis of sleep and activity data collected via actigraphy. Adults with CF in stable health, participating in a study of physical activity (including assessment of exercise capacity), completed 7 days of activity and sleep assessment (SenseWear Armband (SWA), Bodymedia USA). Sleep characteristics were derived from accelerometer positional data and registration of sleep state by the SWA, determined by energy expenditure.

Results: Sleep and activity data were available for 47 participants (n=28 male; mean (SD) age 29(8) years; median (IQR) FEV_1 60 (50 to 82) %predicted). More fragmented sleep was associated with poorer exercise capacity (r_s=-0.303, p=0.04), time spent in moderate-vigorous physical activity (MVPA) (r_s=-0.337, p=0.020), and poorer FEV_1 (r_s=-0.344, p=0.018). In a stepwise multiple regression model that included age, sex, body mass index and FEV_1, models including wake after sleep onset (WASO) were significant for predicting total activity time and total MVPA time (R^2=0.30 and 0.26 respectively, p<0.02). Less WASO significantly predicted more total daily activity time (ß=-1.0, SE of ß=0.4, *p*=0.02), and trended toward significance for predicting greater MVPA time (ß=-0.3, SE of ß=-0.26, *p*=0.08). Greater total sleep time and sleep efficiency were related to better exercise capacity and lung function (p<0.05).

Conclusion: This analysis demonstrated a modest relationship between sleep parameters and physical activity and exercise capacity in adults with CF. Future studies of interventions to promote physical activity participation in this group should consider the relationship between sleep and activity performance.

NON-INVASIVE MUCOCILIARY TRANSIT ASSESSMENT IN LIVE PIG TRACHEA

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Introduction/Aim: The Imaging and Medical Beamline (IMBL) at the Australian Synchrotron was designed to be the world's widest synchrotron x-ray beam, to facilitate clinical imaging and therapeutic applications in humans, as well as for imaging large animal models. Our group is currently interested in imaging the airways of newly-developed CF animal models that display human-like lung disease, such as the CF pig. We hypothesise that the ability of the lung to clear inhaled particulates by mucociliary transit (MCT) can be used as an outcome measure for assessing the effectiveness of CF airway therapies. This study extends findings from *ex vivo* sheep and pig tracheal tissue studies previously performed at the IMBL, and was designed to determine whether the design of the IMBL is suitable for imaging pig airways.

Methods: A small sample of 200 μm diameter high refractive index (HRI) glass bead marker particles were delivered into the tracheal airway surface of eight live piglets. Automated analysis algorithms were used to track and quantify deposited-particle motion, including the response to aerosol delivery of hypertonic saline. A high-resolution computed tomographic (CT) whole-animal post-mortem scan of one pig was also performed to verify the large-sample CT capabilities of the IMBL.

Results: MCT tracking particles were visible in all animals, and our automated MCT tracking algorithms were able to identify and track particles. A CT of the whole animal was successfully acquired, and visualisations were successfully made from the CT dataset. Due to unexpected IMBL technical and equipment issues shuttering of the X-ray bean was sometimes poorly controlled, resulting in high radiation doses for some animals.

Conclusion: This study demonstrated that the IMBL is suitable for large animal tracheal MCT imaging and CT. Radiation doses must be carefully and reliably controlled for future non-recovery studies, and will enable estimation of the minimum achievable doses with this experiment design.

ABSENTEEISM AND PRESENTEEISM IMPACT WORK IN ADULTS WITH CYSTIC FIBROSIS

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Introduction/Aim: People with cystic fibrosis (CF) are living longer and thus facing issues related to work. The aims of this study were to, in people with CF living in Western Australia (i) report work status and self-reported absenteeism (absence from work due to illness) and presenteeism (loss of performance at work due to illness); and (ii) explore factors related to work status and absenteeism and presenteeism.

Methods: Secondary analyses of a larger study were conducted. Measures were collected of work status, absenteeism and presenteeism (World Health Organisation's Health Performance Questionnaire), airflow obstruction (FEV_1), health-related quality of life (HRQoL; CF Questionnaire-Revised) and level of education. Adults with CF were grouped by work status (full-time *versus* part-time/unemployed) and self-reported absenteeism/presenteeism (substantial *versus* no substantial). Between-group differences were explored and factors related to work status and absenteeism/presenteeism were evaluated using logistic regression.

Results: Of the 50 participants (30 [25-36]yr, percent predicted FEV_1 60±18[SD]%), 34 (68%) worked full-time. Participants reported working 30±14(SD)hr/week. Compared to those part-time/unemployed, participants working full-time were older (median [IQR] 33 [27 to 38]yr *versus* 26 [22 to 32]yr; p=0.048) and had higher levels of education (79% *versus* 31% completed university or other tertiary studies; p=0.002). Higher education level was associated with reduced odds of working part-time/being unemployed (OR 0.26 95%CI [0.11 to 0.64]). Substantial absenteeism and substantial presenteeism were reported by 47% and 16% of participants, respectively. Those reporting substantial absenteeism had worse HRQoL (median [IQR] role domain score 92 [75 to 100] no substantial absenteeism versus 83 [60 to 90] substantial absenteeism; *p*=0.018). No associations were found for substantial presenteeism.

Conclusion: Despite moderate disease severity, most participants reported working full-time. Cystic fibrosis may have a greater impact upon absenteeism than presenteeism; however, larger studies are needed to determine the reasons for this greater impact.

Declaration of Interest: Nil.
Declaration of Interest: Nil.

Occupational & Environmental Lung Disease / Population Health

SMOKING, FAMILY HISTORY AND ASBESTOS EXPOSURE ARE ASSOCIATED WITH IPF

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Introduction/Aim: Idiopathic Pulmonary Fibrosis(IPF) is a progressive scarring lung disease of unknown cause with limited treatment and a median survival of 2-3 years. Our aim was to identify potential occupational and environmental exposures associated with development of IPF in Australia.

Methods: Cases were recruited by the Australian IPF registry. Patients completed a questionnaire about demographics, smoking, family history, environmental and occupational exposures, and medical history. Clinical, radiological and histopathological data were reviewed by a multidisciplinary panel. Population based controls were recruited by random digit dialling, frequency matched on age, sex and state, and interviewed to collect comparable data. Multivariate logistic regression was used to assess associations with IPF as Odds Ratios(OR) and 95% confidence intervals(95%CI), adjusted for age, sex and smoking.

Results: Data were from 374 cases assessed by multidisciplinary discussion as definite, probable or possible IPF, and 902 controls. The mean±SD age of cases was 71.2±7.8 and controls 70.8±8.4 years. 72% cases and 69% controls were male. Current or past tobacco smoking was associated with increased risk of IPF: OR=2.24 (95%CI 1.72, 2.91), but marijuana use appeared protective: 0.43 (0.26, 0.70). A family history of pulmonary fibrosis was associated with 14.1 (7.14, 27.9) fold increased risk of IPF. No domestic environmental exposures were associated with increased risk, but pet birds or standing water appeared protective (OR=0.51; 0.34, 0.78 and 0.57; 0.36, 0.89 respectively). Self-reported occupational exposure to asbestos was associated with increased risk: OR=1.38 (1.06, 1.79), but silica appeared protective: 0.60 (0.42, 0.85). Self-reported occupational exposures to gases, fumes, chemicals or dust were not associated with IPF.

Conclusion: Preliminary findings suggest that the burden of IPF could be reduced by continued tobacco control measures and preventing ongoing exposure to asbestos. More detailed assessment of occupational exposures will be undertaken using the Finnish job exposure matrix (FINJEM).

TO 033

LONGITUDINAL SURVEILLANCE OF METROPOLITAN FIREFIGHTERS INDICATES NORMAL LUNG FUNCTION DECLINE

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Introduction/Aim: Longitudinal surveillance of firefighter lung function is highly valuable, especially considering its utility in determining changes in function following disastrous exposures. Studies investigating the long-term rate of change in lung function parameters of firefighters, however, have produced mixed findings. We aimed to determine the rate of change in FEV_1 and FVC of a contemporary cohort professional South Australian Metropolitan Fire Service (SAMFS) firefighters.

Methods: Spirometry was conducted in 5 stages between 2007 and 2016 on all available and consenting full-time firefighting staff, in accordance with ATS/ERS criteria using a Viasys MasterScreen® spirometry system. We examined serial FEV_1 and FVC measurements to determine the average rate of change using linear mixed effects modelling.

Results: Participation at each stage of data collection ranged from approximately 48-64%. Data from 838 individual male firefighters, each contributing an average of 2.6 ± 1.1 (range 1-5) measurements, were included in the analysis. Fifty per cent of included firefighters had at least three measurements. Preliminary analyses show that the proportion of firefighters below the lower limit of normal (LLN) at baseline was 0.7% for FEV_1, 0.0% for FVC and 14.2% for FEV_1/FVC, while longitudinally, FEV_1 (adjusted for baseline age and height) declined by 34 (95% CI, 30 to 37) mL/yr while FVC declined by 24 (95% CI, 20 to 29) mL/yr.

Conclusion: The SAMFS firefighters observed in this study showed normal levels of FEV_1 and FVC at baseline; unsurprising given that they are selected, in part, based on their physical fitness. Early results indicate that the cohort have a normal rate of change in FEV_1 and FVC, suggesting that their lung function remains relatively unaffected by their occupation.

TO 034

ASSESSING THE SUITABILITY OF FRACTIONAL EXHALED NITRIC OXIDE (FENO) CUT-OFF RANGES FOR ABORIGINAL AND/OR TORRES STRAIT ISLANDER CHILDREN AND YOUNG ADULTS

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Introduction/Aim: Fractional exhaled nitric oxide (FeNO) is used as a non-invasive measure of eosinophilic airway inflammation. It is unknown how appropriate the recommended FeNO cut-off ranges are for Aboriginal and/or Torres Strait Islander patients. Our aim was to assess the distribution of healthy Aboriginal and/or Torres Strait Islander FeNO results according to current American Thoracic Society cut-off guidelines.

Methods: We measured FeNO (using Aerocrine NioxMINO) in 991 Indigenous children and young adults (aged 3 to 25 years) from seven Queensland communities. Questionnaires and medical charts were reviewed to identify healthy participants (no respiratory and/or atopic illness ever).

Results: Acceptable FeNO measurements were achieved by 553 children (≤12 years) and 288 adults (>12 years). Participants with a history of respiratory and/or atopy conditions were excluded resulting in a healthy cohort of children (n=401, 72.5%) and adults (n=193, 67%). The geometric mean FeNO results for children and adults were 11.1ppb and 12.5ppb respectively. Table 1 summarises the distribution of healthy FeNO results for each ethnic group according to current cut-off ranges.

Conclusion: Although the majority of participants had FeNO results within the age-respective normal ranges, we found a proportion of healthy participants with elevated FeNO results in all groups. The greatest proportion of elevated results was seen in Torres Strait Islander children and adults, and Aboriginal/Torres Strait Islander children. This suggests that the recommended cut-off ranges may not be appropriate for these groups. Further investigation is still needed.

	Child ≤12 years (ppb)				Adult >12 years (ppb)		
	Normal ≤20	Intermediate 21-34	Inflammation ≥35		Normal ≤25	Intermediate 26-49	Inflammation ≥50
Aboriginal (n=112)	88%	7%	5%	(n=51)	90%	6%	4%
Torres Strait Is (n=134)	83%	6%	11%	(n=87)	83%	10%	7%
Both (n=155)	85%	8%	7%	(n=55)	87%	9%	4%

Is–Islander, Both=Aboriginal and Torres Strait Islander

LUNG CANCER SCREENING IN THE WESTERN AUSTRALIAN ASBESTOS REVIEW PROGRAM

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Introduction: Asbestos exposure increases the risk of lung cancer, especially in smokers. Western Australia (WA) has the highest rates of asbestos-related diseases in the world, due to crocidolite mining in the Pilbara town of Wittenoom and the widespread use of asbestos throughout WA. Early diagnosis utilising low dose CT (LDCT) scans have been shown to reduce mortality from lung cancer.

Aim: To analyse the efficacy of LDCT in detection of lung cancer in an asbestos-exposed population over a 5-year period.

Methods: In 2012, the Asbestos Review Program (based at Sir Charles Gairdner Hospital) began performing annual LDCT to screen an asbestos-exposed population for asbestos related lung disease and lung cancer. Population: Wittenoom miners and residents, other individuals with >3 months cumulative full time exposure. All participants had a prone LDCT scan with annual health questionnaire (including smoking status), spirometry and gas transfer.

Results: 5907 LDCT scans were performed on 1760 individuals with a median age of 70 years (IQR 63-76), 1490 (85.1%) were male and 1115 (63.7%) were ever-smokers. Lung cancer was diagnosed in 17 participants (0.97% of the cohort), 15 (pre-operative stage 1a or b) underwent treatment with curative intent, 2 underwent non-curative chemo-radiation. Lung cancer was prevalent in 10 (59%), and incident in 7 (41%) individuals (see Table 1). One participant died 4 months after surgery (found to have M1a disease during operation); no participants treated curatively have had reoccurrence to date. Mesothelioma was diagnosed in 7 other individuals. Asbestosis was present in 40.3% of the ARP population and 64.0% had pleural plaques, confirming significant asbestos exposure. The median radiation exposure per LDCT was 0.20mSv (IQR 0.14-0.52).

Conclusions: A carefully controlled LDCT screening program is effective at diagnosing and treating early-stage lung cancer in this population. Occupational exposure to asbestos should be accounted for in assessing risk for lung cancer.

Table. 1. Characteristics of ARP participants diagnosed with lung cancer

	n=	%
Total Participants	1760	
Total Scans	5907	
Lung Cancer	**17**	0.97
Smoking status		
Ex	11	64.7
Current	1	5.8
Never	5	29.4
Asbestos Exposure		
Lx-Wittenoom Worker	5	29.4
Lx-Wittenoom Resident	4	23.5
Other (mixed occupations)	8	47.0
Histology		
Adenocarcinoma	11	64.7
Squamous	4	23.5
Carcinoid	1	5.9
Small Cell	0	0
Risk Factors		
Lmphysema visible on LDCT	5	29.4
First degree relative - Lung Cancer	5	29.4
*Obstructive Spirometry**	7	41.2

LOCT = Low *dose chest CT scan; *(FEV$_1$/**FVC** ratio <0.7)*

TO 036

NITROGEN DIOXIDE IS ADVERSELY ASSOCIATED WITH TRANSFER FACTOR OF CARBON MONOXIDE IN A DOSE-RESPONSE MANNER

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Introduction/Aim: While air pollution exposure can contribute to the development of chronic obstructive pulmonary disease (COPD), previous studies have not examined lung function beyond the airways. We aimed to examine relationships between exposure to nitrogen dioxide (NO_2, a gaseous air pollutant) and complex post-bronchodilator (post-BD) lung function measures in middle-aged Australians.

Methods: Cross-sectional data were obtained from the Tasmanian Longitudinal Health Study (n=1,389) when participants were 45 years of age. Annual outdoor mean NO_2 concentrations at participants' residential addresses were estimated using a validated satellite-based, land-use regression model. Multivariable regression used post-BD spirometry, carbon monoxide transfer factor (T_Lco) and static lung volumes as continuous outcomes.

Results: Median NO_2 exposure was 3.66 [interquartile range 2.95, 5.22] parts per billion. Increasing exposure to NO_2 was associated with reduced T_Lco in a dose-response manner [p-for-trend<0.001]. Compared with the lowest quartile of NO_2 exposure, the reduction in T_Lco was equivalent to 7.7% of predicted for the highest NO_2 quartile (95%CI: −10.8 to −4.5) independent of smoking, and was significantly lower for those with current asthma [$p_{(interaction)}$=0.005]. There was a trend to reduced TLC [p-for-trend=0.02], and reductions in post-BD FVC for non- and past but not current smokers exposed to the highest NO_2 quartile [non-smokers −2.6% pred, p=0.042, $p_{(interaction)}$=0.056]. There were no statistically significant relationships with post-BD FEV_1/FVC, $FEF_{25-75\%}$ or gas trapping (RV/TLC).

Conclusion: We provide evidence for a moderate adverse association between NO_2 exposure and T_Lco at relatively low pollution levels, that varies with current asthma status. Other non-obstructive features favour a lung parenchymal process, although co-existent small airway narrowing may be masked by reduced FVC levels. This new knowledge supports environmental policy to reduce NO_2 levels to as low as feasible.

TO 037

MIDDLE-AGE LUNG FUNCTION DECLINE IS PREDOMINANTLY INFLUENCED BY ADULT FACTORS AND THEIR INTERACTIONS WITH CHILDHOOD AND GENETIC FACTORS

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Introduction/Aim: Accelerated adult lung function decline is a major pathway to chronic obstructive pulmonary disease. We sought to investigate associations and interactions between life span factors and lung function decline during middle age.

Methods: Post-bronchodilator lung function was measured at 45 and 53 years in 842 participants from the Tasmanian Longitudinal Health Study. We used multivariate linear regression to investigate associations of factors in adulthood (current asthma, smoking, atopy, BMI, BMI change, occupational exposures and traffic related air pollution), childhood (pneumonia, asthma, parental asthma and parental smoking) and Glutathione S-transferase gene polymorphisms, with the rate of lung function decline between 45 and 53 years. Interactions between factors were also investigated.

Results: Current asthma (-6; 95%CI: -11,-1 mL/year), current smoking (-16; -21,-10 mL/year), atopy (-5; -9,-0.7 mL/year), all at 45 years, lifetime occupational exposure to vapour/gas/dust/fumes (-6; -11,-1 mL/year) and increased BMI during the follow-up period (-2; -2.6,-1.5 mL/year per kg/m^{2} increase) were independently associated with accelerated FEV_1 decline after controlling for age, height, sex, socioeconomic status and lung function at baseline (45 years). Current smoking (-12; -18,-6 mL/year) and BMI change (-2.5; -3.2,-1.9 mL/year per kg/m^{2} increase) were associated with greater FVC decline. GTTM1 polymorphism modified the effect of occupational exposure (p=0.06 and 0.07), and heavy maternal smoking during childhood modified the effect of personal smoking (p=0.03 and 0.02) on both FEV_1 and FVC decline. The effect of occupational exposure was only significant for carriers of the GSTM1 null genotype, and the effect of personal smoking was augmented in those also exposed to maternal smoking.

Conclusion: Lung function decline in this middle-aged sample was predominantly influenced by adult factors. Exposure to maternal smoking during childhood and genetic susceptibility may predispose people to being more susceptible to adulthood exposures.

DECLARATION OF INTEREST STATEMENT

There is no conflict of interest.

Primary Care/ Palliative Care/ Tobacco

PERSONAL VAPORIZER E-JUICES AND AEROSOLS VARY WIDELY IN PHYSICOCHEMICAL PROPERTIES

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Introduction/Aim: Personal vaporizers ("electronic-cigarettes") aero-solise a liquid "e-juice" producing an aerosol which is inhaled. There is no regulation of e-juice ingredients. There are tens-of-thousands of different flavours, nicotine concentrations and excipient blends available from thou-sands of suppliers. Furthermore, while many ingredients are approved as food additives, inhalation toxicology data may be unavailable. We aimed to test the physico-chemical properties of a range of e-juices and aerosols to (i) identify potentially toxic substances and (ii) to see whether ingredi-ents match labelling.

Methods: 18 e-juices were obtained from Australian and US retailers. E-juice chemistry was analysed via GC-MS. Aerosols were generated using a custom-made device based on an Innokin MVP2 vaporizer / Inno-kin iClear30 cartomizers set at 2.1Ω and 4.2V. Aerosols were collected for 30 minutes using appropriate filters and collection tubes. We assessed levels of carbonyls, volatile organics, polycyclic-aromatics, nicotine, par-ticulate matter and metals. Aerosol mass and size distributions were mea-sured using an optical particle spectrometer.

Results: 28 different chemicals were detected in e-juices including known respiratory irritants such as 2-chlorophenol and 1,2,3-butantriol. Nicotine was detected in 6 apparently "nicotine-free" juices. Seven metals were identified in aerosols, including titanium, chromium and nickel. We also identified 7 carbonyls, however only formaldehyde, acetaldehyde and acetone were common. Sixteen volatile organics were identified. The solvents hexane and 2-ethoxy ethanol were ubiquitous in all samples. No poly-cyclic aromatics were detected. Aerosols contained particulate mat-ter at hugely varying levels (3.3 to 63mg/m^3) and particle size distributions also varied considerably, apparently based on the excipient mixture.

Conclusion: The physico-chemical properties of e-juices and aero-sols vary widely and hence their potential to impact health is also likely to vary. Importantly, nicotine was found in many "nicotine-free" juices, which has implications for addiction.

PHARMACIST-LED SMOKING CESSATION INTERVENTION IN AUSTRALIAN PRIMARY CARE TARGETING SMOKERS AT RISK OF DEVELOPING COPD

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Introduction: Tobacco smoking is the most preventable risk factor in the development of COPD. Approximately one in five patients attending general practice is a smoker. We describe a pharmacist-led smoking ces-sation intervention as part of an interdisciplinary model of care (RADICALS) aimed at reducing the burden of COPD and smoking in Australian primary care.

Methods: General practices (n=43) were block-randomised into ICG (interdisciplinary care group) or UCG (usual care group). Patients aged ≥40 years and self-reporting being current or ex-smokers with a smoking history of ≥10 pack years, and/or those who were managed as having COPD were invited to participate. Participants in UCG practices received routine care from their GP and Quitline referral, if appropriate. In ICG, indi-vidualised smoking cessation support was coordinated by a pharmacist on-site and offered to participants who were current smokers. Smoking cessation support was also provided by a consultant pharmacist during a home medicines review in participants with COPD. Pharmacotherapy was recommended and discussed with the participant's GP, if appropriate. Exhaled CO-verified 7-day point prevalence abstinence and changes in nicotine dependence at 6 and 12 months from baseline are outcomes.

Results: A total of 1,055 participants with a range of demographic and clinical characteristics were recruited. Of these, 693 (65.7%) were current smokers; almost all smoked daily (649, 93.7%). Median exhaled CO was 21ppm [IQR 13-28]. Smokers in ICG practices (n=373) were at various readiness-to-quit stages. Tailored pharmacist interventions ran-ged from motivational counselling/Quitline referral to advising on nicotine replacement therapy/varenicline use. Six month follow-ups are now com-plete (n=370); 12 month follow-ups will be completed by February 2018.

Conclusion: Pharmacists working with GPs can assist smokers attending general practices to quit using pharmacotherapy and non-pharmacological approaches.

TO 040

AUSTRALASIAN MALIGNANT PLEURAL EFFUSION (AMPLE)-1 RANDOMIZED CONTROLLED TRIAL OF INDWELLING PLEURAL CATHETER VERSUS TALC PLEURODESIS

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Introduction: Hospital admissions and multiple pleural interventions for symptom relief are often required in the management of malignant pleural effusions (MPEs). Current literature suggested that talc pleurodesis and indwelling pleural catheter (IPC) offer similar quality-of-life benefits, resulting in equipoise. No studies have previously examined hospitalization of MPE patients in their remaining lifespan as the principle endpoint, an outcome of significance to these patients who often have limited prognoses.

Method: An open-labelled, randomized controlled trial: ACTRN12611000567921. Nine units from Australia, New Zealand, Singapore and Hong Kong recruited 146 MPE patients randomized (1:1) to IPC or talc slurry pleurodesis; minimized by Australasia vs Asia, mesothelioma vs metastatic malignancies, and trapped lung (vs not). The primary endpoint is total days of hospitalization from treatment to death, or 12-month follow-up.

Results: The IPC group spent significantly fewer days in hospital than the Pleurodesis group: median (IQR) 10.0 (14) vs 12.0 (14) days, p=0.026, which represented 6.2 (13.8)% vs 11.1 (33.7)% of their remaining lifespan in hospital respectively, p=0.01. Mean reduction in hospitalization days was 3.6 days/patient: 12.7 (IPC) vs 16.3 (Pleurodesis) days. The reduction was mainly in effusion-related hospitalizations: median 1.0 (IPC) vs 4.0 (Pleurodesis) days, p<0.001, though fewer non-effusion related hospitalization days were observed with IPC treatment. Fewer IPC-treated patients required further invasive pleural drainages (4.1% vs 22.5%, 95% CI 7.7-29.2%). Both treatments provided significant improvement in breathlessness (assessed by Visual Analog Score) and quality-of-life (EQ5D), and had comparable complication rates.

Conclusion: Treatment of MPE with IPC can reduce lifetime hospitalization days and further invasive pleural procedures compared with conventional talc pleurodesis, without compromising on symptomatic improvement. These data will inform patients' decision on treating options. Extrapolating from this result, use of IPC (instead of talc slurry pleurodesis) for MPE can save up to 14,000 bed days in Australia each year.

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.

TO 041

PALLIATION AND THE USE OF DIAGNOSTIC TESTS IN PATIENTS DYING IN HOSPITAL FROM COPD

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Introduction/Aim: COPD is an incurable, progressive illness, with associated significant morbidity and mortality. Accurately determining prognosis in severe COPD is well-recognised to be challenging, as is diagnosing "active dying".

Aim: To audit the use of diagnostic tests in both recognising active dying and after establishing the "Goal of Care" (GOC) was palliation in COPD patients dying in hospital.

Method: A retrospective audit of 475 consecutive patients who died from COPD at an Australian teaching hospital between 2004-2016.

Results: Of 221 patients included: 136 (60%) male, median age 80 years; median respiratory function: FEV$_1$ 0.8L (41%), FVC 2.0L (73%) and DLco 9 (41%); and 109 (49%) used home oxygen. 63 (29%) patients had palliative care involvement prior to the final admission.

During the terminal admission patients received on average 7 episodes of venepuncture, 9 Arterial Blood Gas tests and 3 chest radiographs. Receiving increased diagnostic tests was associated with age <70years, admission under respiratory medicine team, ICU admission, and radiological evidence of pneumonia on admission.

For 187 (85%) patients, the GOC was documented as palliation during the final admission, a median of 1.8 days prior to death. 131 (70%) patients had diagnostic tests performed on the day palliation was initiated, and despite the change in GOC 22 (12%) patients had further tests following palliation. 70 (32%) had tests on the day they died.

Conclusion: Excessive, unnecessary diagnostic tests were performed in one third of inpatients dying from COPD, including those following a clear decision to palliate. Failure to clinically diagnose active dying imposes an unnecessary burden of diagnostic tests on those in their final hours.

Key Words: Palliation, COPD, diagnostic tests
Nomination for New Investigator Award: N/A
Grant Support: N/A

A CLUSTER RANDOMIZED TRIAL OF AN INTERDISCIPLINARY INTERVENTION FOR COPD IN AUSTRALIAN PRIMARY CARE

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Introduction: Interdisciplinary practice-based interventions could potentially benefit patients with COPD in primary care. We describe the RADICALS (Review of Airway Dysfunction and Interdisciplinary Community-based care of Adult Long-term Smokers) model of care delivered in Australian general practices.

Methods: General practices (n=43) were block-randomised into ICG (interdisciplinary care group) or UCG (usual care group). Patient participants with spirometry-confirmed COPD in UCG practices received routine care from their GP and Quitline referral, if appropriate. ICG participants received the RADICALS model of care, coordinated by a research assistant, GPs and staff at each clinic. The model comprised individualised smoking cessation support, a home medicines review (HMR) from a consultant pharmacist, and home-based pulmonary rehabilitation from specifically trained physiotherapists. The primary endpoint is change in Health Related Quality of Life (HRQoL), as measured by the St George's Respiratory Questionnaire (SGRQ), at 6 months from baseline. Other outcomes include changes in lung function, dyspnoea, COPD assessment test (CAT) score and EuroQol-5D at 6 and 12 months.

Results: A total of 275 patients with COPD were included – 161 in ICG and 114 in UCG. Their mean ($\pm$SD) age was 64.4 ($\pm$11.0) years; 171 (62%) were male and 168 (61%) were current smokers. Mean/median baseline SGRQ, CAT and mMRC scores were 32.3 ($\pm$18.2), 13.1 ($\pm$7.8) and 1 [IQR 0-2]. A total of 85 ICG participants received the HMR, 71 completed home-based pulmonary rehabilitation, and 62 received both components. Six month follow-ups are complete (n=208); 12 month follow-ups are in progress and will be completed by February 2018.

Conclusion: An interdisciplinary model of care for COPD has been developed, implemented and evaluated in general practice. HMR and home-based pulmonary rehabilitation had moderate acceptance as interventions by GPs and patients.

Conflict of Interest: Funding was received from Boehringer Ingelheim. Boehringer Ingelheim was involved in project discussions, planning and progress review, but had no involvement in the design of the intervention program and will not be contributing to decisions regarding data analysis and dissemination of findings.

LUNG FOUNDATION AUSTRALIA (LFA) CONSUMER SURVEY RESULTS 2017

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Introduction: LFA undertook a survey to gain insight into the key issues facing consumers and carers, and to understand how LFA meets - or can better meet – their needs.

Methods: 9,000 surveys were distributed (via email and post) to consumers with any lung disease that subscribe to the LFA network.

Results: 1700 surveys were completed, representing a response rate of approximately 19%. Of these, 65% were female, 57% were aged between 65-79 years, 87% had a lung disease and 13% were carers. Respondents indicated that 39% see family and friends less often, 29% feel isolated from society and 59% do the things they love less often because of their lung disease. When asked specifically about how they felt at time of diagnosis, 30% felt less deserving of help than people with other medical conditions, 23% felt shame, guilt or fear of being discriminated against, 41% felt stigmatised by the view that lung diseases are self-inflicted and smoking-related and 58% felt they had all the support they needed to deal with the diagnosis. Suggestions were received about additional LFA supports; responses highlighted the need for psychosocial support through more telephone, online and face-to-face connection with LFA and other consumers, as well as the need for additional education seminars and webinars, and more information on specific disease treatments and research.

Conclusion: People impacted by lung disease face many challenges. This survey has detailed the effect on community and social interactions, with feelings of isolation and less contact with loved ones highlighted. Also it demonstrates the shame, stigma and guilt some people may experience when diagnosed with a lung disease.

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TO 044

HDAC6 PROMOTES DDX1-MEDIATED ANTIVIRAL IMMUNITY AND IS IMPAIRED IN COPD

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Introduction/Aim: COPD primary bronchial epithelial cells (pBECs) are characterised with deficient innate antiviral response to influenza virus infection, leading to heightened viral replication. The molecular mechanisms underpinning this deficiency is unclear. HDAC6 is a unique cytoplasmic deacetylase, its roles in innate immunity is less well characterised. In this study we aim to determine the function of HDAC6 in antiviral immunity, and how HDAC6 expression/function is altered in COPD pBECs.

Methods: CRISPR-Cas9 HDAC6 Knockout plasmid and HDAC6-plasmid was transfected into a human minimally immortalised bronchial epithelial cell line BCi-NS1.1, and infected with H1N1. Protein interactions/expression levels were measured by immunoprecipitation, immunoblotting, and cytometric bead array. Viral replication was measured by plaque assay. pBECs from those with COPD (GOLD III-IV) and healthy controls were infected with H1N1. Similar measurements were performed.

Results: HDAC6 deficiency showed an overall reduction in antiviral response. Immunoprecipitation (IP) of HDAC6, mass spectroscopy, and co-IP identified that DDX1 is a direct binding target. DDX1 is an important viral RNA sensor. We found that HDAC6 deacetylated DDX1 and promoted DDX1-mediated type I and III interferon (IFN) induction. HDAC6 expression, DDX1 deacetylation, and antiviral responses were reduced in COPD pBECs. This reduction in HDAC6 expression in COPD pBECs was due to increased expression of miRNAs miR-141/-200a. Inhibition of miR-141/-200a increased HDAC6-DDX1-mediated antiviral response and decreased viral replication in both COPD and healthy control pBECs.

Conclusion: HDAC6 is essential in DDX1-mediated antiviral signaling to influenza viral infection, reduced HDAC6 expression and DDX1 deacetylation in COPD led to deficient antiviral signalings and increased viral replication, which could be restored by specific inhibition of miR-141/-200a.

TO 045

NONTYPEABLE HAEMOPHILUS INFLUENZAE (NTHI) EXPLOITS DEFECTS IN AIRWAY EPITHELIAL CELL XENOPHAGY AS A MEANS OF PERSISTENCE DURING COPD

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Introduction/Aim: NTHi infection causes approximately 50% of COPD exacerbations, inflammation, and FEV1 decline. Normally intracellular microbes are degraded by microbe-specific autophagy (xenophagy). We hypothesise NTHi exploits defects in xenophagy in COPD, potentiated by cigarette smoke, enabling infection and propagation between airway epithelial cells (AEC).

Methods: Cultures of bronchial AEC (bAEC) lines, and from control and COPD donors differentiated at an air-liquid interface (ALI) were exposed to 10% cigarette smoke-extract (CSE) and NTHi. Markers of xenophagic flux and intracellular NTHi were assessed using western analysis, immunofluorescence and transmission electron microscopy (TEM).
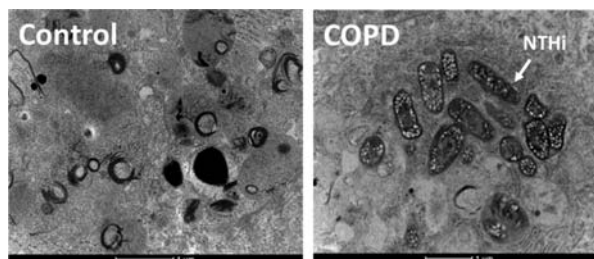

Figure 1   TEM of bAEC from control donors revealed no detectable NTHi, and considerable autophagic activity (evidenced by dark electron dense regions) within vesicular structures. Conversely, NTHi was readily evident in AEC derived from COPD donors and in close proximity to similar vesicular structures.

Results: AEC exposed to 10% CSE exhibit a block in autophagic flux and down-regulation of the xenophagy-microbial adapter protein NDP52. Immunofluorescence analysis resolved intracellular NTHi within AEC exposed to 10% CSE in proximity to the autophagic apparatus marker LC3. Importantly, control ALI cultures exposed to NTHi for 24h contained no detectable infection and evidence of normal autophagic activity, whereas COPD-derived bAEC contained multiple infective particles (Fig.1), some which remained intact within autophagosome-like vesicles. Further, TEM analysis demonstrated the expulsion of autophagosome-like vesicles.

Conclusion: NTHi is able to avoid xenophagic degradation in AEC exposed to 10% CSE or in cultures of COPD-derived AEC, and may usurp the defective autophagic apparatus as a mode of persistence and extracellular propagation. Hence, modes of therapeutic intervention which restore normal xenophagic activity in AECs will significant utility to improve the clearance of intracellular NTHi infection, and thereby decrease the influence of this damaging pathogen in the airways afflicted by COPD.

INTRANASAL DELIVERY OF THE TLR7 AGONIST, IMIQUIMOD, PROTECTS AGAINST INFLUENZA A VIRUS-INDUCED MORBIDITY IN MICE

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Introduction/Aim: Influenza is a significant global burden with 5 million cases per year, 10% of which are fatal and thus, there is an urgent need for new therapeutics. Toll like receptor 7 (TLR7) is a pattern recognition receptor, which drives a powerful anti-viral signalling pathway that helps clear virus infections. The aim of the present study was to determine the effect of the TLR7 agonist imiquimod on morbidity, lung inflammation, oxidative stress and antibody production caused by influenza A virus (IAV) infection in mice.

Methods: Saline or imiquimod (50μg/mouse) was delivered intranasally to anaesthetised male C57BL/6J mice one day (d-1) prior to infection with a low (10^3PFU/mouse) or high dose (10^5PFU/mouse) of the mouse adapted Hong Kong X31 virus strain and everyday thereafter until mice were culled day 3 (d3) or 7 (d7) post-infection for analysis. Bronchoalveolar lavage (BAL) was performed to assess airways inflammation, and inflammatory cell oxidative burst (by L-012 enhanced chemiluminescence). In addition, BAL fluid and serum was used to determine antibody titres. The lungs were then harvested and used to assess inflammation (H&E staining) and pro-inflammatory cytokine gene expression by qPCR. Bodyweights were recorded daily during the experimental process.

Results: Imiquimod significantly suppressed body weight loss caused by IAV infection with a maximum reduction of ~60% starting from day 4 (d4) (10^3 PFU/mouse, n=7-13, p<0.001). At d3 post infection, imiquimod treatment caused a significant reduction (~50-60%) in airway and peribronchial inflammation and BALF neutrophil populations (10^5 PFU/mouse, n=8-15, p<0.01) but had no effect on macrophage and lymphocyte populations, and the oxidative burst. TNF-α and IL-6 mRNA expression was supressed by ~60% (p<0.01 and p<0.05, respectively), whilst IFN-β and IL-1β mRNA expression were unaffected. Day 7 data showed a modest but significant increase in IgE, IgM, IgG1, and IgG2a (p<0.05) in BALF following imiquimod treatment compared to control. There were no changes in antibody titres within the serum.

Conclusion: Our findings highlight a potential of imiquimod as a therapeutic option for the treatment of influenza disease.

AIRWAY EPITHELIAL INNATE IMMUNE RESPONSES TO CORONAVIRUSES

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Introduction/Aim: Despite the recurring emergence of novel pathogenic coronaviruses (CoVs) SARS-CoV (2002) and MERS-CoV (2012), there is a lack of understanding of host immunity during respiratory infection with CoVs. In this study, we characterised the innate immune responses of differentiated primary bronchial epithelial cells (pBECs) to infection with related less-virulent OC43-CoV and 229E-CoV.

Methods: Human pBECs were grown at the air liquid interface (ALI) until differentiation was observed (25-30 days), and infected at a multiplicity of infection (MOI) 0.1 with OC43-CoV or 229E-CoV for 0, 24, 96 hours and 7 days. Supernatants and RNA were collected to measure pro-inflammatory- and anti-viral-cytokines and viral replication. Using microarray, the gene expression profile of OC43-CoV and 229E-CoV infection was analysed (n=1). A549 cells transduced to overexpress Interferon-induced transmembrane proteins (IFITM) 1, 2 and 3 were infected with OC43-CoV or 229E-CoV. Viral replication was measured at 0, 8, 24 and 48 hours post-infection.

Results: OC43-CoV and 229E-CoV demonstrated different viral replication kinetics. 229E-CoV replicated earlier and more efficiently, peaking at 24 hours. This was associated with a delayed but robust activation of the innate host response, with induction of type I and III interferons (IFN-β, IFN-λ1/3), IFN stimulated genes and IP-10. In contrast, replication of OC43-CoV peaked between 96 and 168 hours, with attenuated levels of IFN-β, IFN-λ1/3 and IP-10. Microarray data also identified IFITM protein upregulation during 229E-CoV infection. In A549 cells over-expressing IFITM 1, 2 or 3, 229E-CoV replication was suppressed by IFITM 1 and 3, while the IFITM2 clone displayed similar replication kinetics to the control. OC43-CoV replication was unhindered by over-expression of all IFITM proteins.

Conclusion: This study demonstrated that both OC43 and 229E-CoVs replicated in differentiated pBECs, but they induce a divergent innate immune response potentially linked to their different replication kinetics. Understanding the host-virus interaction for these less virulent coronaviruses will give insight into pathogenic mechanisms underpinning SARS-CoV and MERS-CoV-induced respiratory disease.

TO 048

VIRAL INFECTION IS EXACERBATED IN A CHRONIC MODEL OF INFLAMMATORY LUNG DISEASE

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Introduction/Aim: Infective exacerbations of chronic inflammatory lung diseases, such as asthma and chronic obstructive pulmonary disease (COPD), are associated with incremental scarring and fibrosis and gradual decrements in lung function. Central to this pathology is the pleiotropic cytokine transforming growth factor-beta (TGFB) that regulates cell proliferation, tissue remodelling and lung fibrosis. Our previous studies have demonstrated that TGFB suppresses the immune response, resulting in enhanced viral infection.

Methods: We have utilised a transgenic mouse model of lung-specific TGFB over-expression and established an acute and chronic model of inflammatory lung disease. We infected the mice with influenza A virus (IAV; strain HKx31) and examined disease severity, inflammatory and immune responses, and viral loads.

Results: In the acute model, TGFB was over-expressed for 2 days prior to IAV infection. These mice experienced more severe bronchitis and pneumonia, increased inflammatory cell infiltrates and enhanced cytokine and chemokine production in bronchoalveolar lavage (BAL) fluid compared to mice with normal TGFB levels. These mice also demonstrated a suppressed innate immune response that was associated with enhanced viral titres.

In the chronic model, TGFB was over-expressed for 8 weeks, which resulted in thickening of the respiratory bronchiole epithelium and surrounding smooth muscle, and an emphysematous appearance within the airspaces, resembling phenotypic changes characteristic of asthma and COPD. Preliminary results in this model demonstrate that IAV infection is more severe compared to mice with normal TGFB levels.

Conclusion: Our transgenic mouse model provides us with a unique tool to evaluate the direct effects of TGFB on viral infection, or in the context of chronic inflammatory lung disease, and to investigate potential therapeutic strategies to combat viral-induced disease exacerbation.

Declaration of Interest: none.

TO 049

DIFFERENTIATION BETWEEN APOPTOTIC AND NECROTIC CELL DEATH IN AIRWAY EPITHELIAL CELLS IN RESPONSE TO VIRAL INFECTION AND ANAEROBIC CONDITIONS USING FLOW CYTOMETRY

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Introduction/Aim: Necrosis of airway epithelial cells (AEC) resulting in airway inflammation 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. Current methodologies to measure apoptotic and necrotic cell death using flow cytometry in AEC are not adequate to completely differentiate between the two. The aim here was to determine whether a novel flow cytometry methodology described in other cell types could be optimized and adapted to AEC to sufficiently differentiate apoptotic and necrotic AEC.

Methods: Non-CF and CF AECs were permeabilised, infected with human rhinovirus for 24 hours (MOI 1 & 3), or incubated in a limited O_2 environment (0% O_2 for 15 hours). Cells were then collected and stained with Annexin-V (A5) and TO-PRO-3 (TP3) before analysis via flow cytometry. Data was analysed using a seven-step gating process to differentiate six different populations from AEC.

		A5+ Apoptotic	A5- Apoptotic	Necrotic	Apoptotic Bodies	Debris
		Viable				
non-CF	Control	82.43% 1.88%	0.50%	9.82%	3.92%	1.44%
	Permeabilised	3.01% 75.21%	0.23%	18.64%	3.16%	0.26%
	Virus	76.91% 1.97%	0.49%	11.01%	5.23%	3.51%
CF	Control	59.46% 8.83%	1.28%	17.92%	6.81%	2.56%
	Permeabilised	0.98% 60.43%	2.09%	26.94%	7.51%	0.89%
	Virus	58.10% 9.63%	1.88%	15.51%	8.31%	2.75%

Results: Flow cytometry using A5 and TP3 was able to differentiate viable, apoptotic, and necrotic cells, plus apoptotic bodies and cellular debris in stimulated and unstimulated epithelial samples.

Conclusion: Flow cytometry utilising A5 and TP3 in conjunction with a seven-step gating process is sufficient to differentiate six populations from both stimulated and unstimulated AEC of healthy and diseased individuals. Further studies utilising this technique will allow quantification of AEC necrosis in patients with and without CF, with the aim to investigate differences in mechanisms driving cell death and airway inflammation.

Chronic Obstructive Pulmonary Disease (COPD) 1

SMALL AIRWAY FIBROSIS ASSOCIATED WITH DECREASED LUNG FUNCTION IN COPD

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Aim: The primary source of airflow limitation in COPD is small airway (SA) fibrosis and obliteration. We previously showed that epithelial mesenchymal transition (EMT) is an active process in small airways contributing to fibrotic pathogenesis. Myofibroblast is highly active fibrotic cells that excessively secrete extracellular matrix (ECM). Here we explore the consequence of SA myofibroblast proliferation and relate them to physiological outcomes and airway remodeling in smokers and COPD patients.

Methods: SA lung resections, from non-smoker controls (NC), normal lung function smokers (NLFS), COPD current (CS) and ex-smokers (ES) were stained with anti-human αSMA, collagen-1, and fibronectin. αSMA+ cells were enumerated in Reticular basement membrane (Rbm), Lamina Propria (LP), and adventitia and represented as per mm of Rbm and mm^2 of the respective area surveyed. Collagen-1 and fibronectin are represented as a percentage change. All measurements including the sub-epithelial LP and adventitia thickness were measured using Image-proplus 7.0.

Results: We observed a general increase in sub-epithelial LP and adventitia thickness in all pathological groups compared to NC. Similar increases in αSMA+ myofibroblasts was observed in sub-epithelial Rbm, LP, and adventitia in the pathological groups compared to NCs, though the changes were prominently higher in the LP. Further, the increase in myofibroblast population in the LP was strongly associated with a decrease in lung function, and an increase in ECM proteins collagen-1 and fibronectin deposition in the LP. Finally, we observed EMT markers expressed in epithelial basal cells and Rbm, correlated to the increased SA myofibroblasts and airway thickness.

Conclusion: This is the first report that systematically characterizes the myofibroblasts in COPD based on their localization and statistically correlates them to lung function. The increase in myofibroblast population also directly related to pathological changes in ECM proteins. Driving these changes is likely to be EMT activity in the basal epithelial cells.

Conflict of Interest: Nil.

SKELETAL MUSCLE REGENERATION AND FUNCTION IS IMPAIRED IN EXPERIMENTAL COPD

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Introduction/Aim: Skeletal muscle wasting is a major comorbidity of COPD and a powerful predictor of mortality. Current therapeutic strategies aim to increase muscle mass by augmenting protein synthesis and reducing protein degradation. Muscle mass can also be increased through the activation of satellite cells, which play a pivotal role in skeletal muscle regeneration. However, the role of satellite cells in COPD is not fully understood. Thus, we explored whether muscle regeneration in response to injuring the Tibialis Anterior (TA) muscle is impaired in mice exposed to cigarette smoke (CS).

Methods: Male BALB/c mice were exposed to room air (sham) or CS generated from 9 cigarettes/day, 5 days/week for 8 weeks. After 8 weeks of CS exposure, the right TA muscle was injured by injection of 40μl barium chloride ($BaCl_2$). The mice were then exposed to CS for another 7, 14 and 21 days at which time the contractile properties of the right TA muscle were measured. Mice were then culled and both the uninjured left TA and injured right TA muscles dissected out, weighed and used to examine the expression of genes associated with muscle regeneration (e.g. Pax 7) and for histological assessment of muscle injury.

Results: $BaCl_2$-induced injury significantly decreased the weight of the TA muscle at 7 days post injury and this was further exacerbated in CS-exposed mice (n=10, p<0.05). $BaCl_2$ also caused significant muscle injury as demonstrated by centrally located nuclei and altered tissue architecture when assessed 7 days post injury. However, muscle injury was even greater in CS-exposed mice when compared to injured sham mice (n=8, p<0.05). Injured TA muscle from CS-exposed mice had at least a two-fold increase in Pax 7 mRNA expression compared to injured TA muscle from sham-exposed mice at 7 days post injury (n=8, p<0.001). Moreover, TA muscle contractile function was significantly impaired in the injured CS-exposed mice compared to the injured sham-exposed mice (n=7, p<0.05).

Conclusion: Skeletal muscle regeneration and function is impaired in experimental COPD.

TO 052

TRANSFORMING GROWTH FACTOR ALPHA PRODUCES AIRWAY REMODELLING AND REDUCES AIRWAY DISTENSIBILITY

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Introduction/Aim: Airway distensibility is reduced in patients with COPD. Transforming growth factor alpha (TGF-α) is increased in the serum of COPD patients and produces airway remodelling in mouse models. We hypothesised that TGF-α overexpression reduces airway distensibility. Our aim was to determine the effect of TGF-α and its regulatory gene, early growth response one (Egr-1), on airway thickness and distensibility.

Methods: Conditional expression of TGF-α in the airways of transgenic mice (Clara cell secretory protein-rtTA(+/-)/[tetO]$_7$-TGF-α(+/-)) was induced by doxycycline (Dox). Mice were Egr-1 homozygous (+/+) or heterozygous (+/-). At 4 weeks of age, mice were fed Dox in chow or a control diet for 3 weeks and then anaesthetised, mechanically ventilated and had lung function measured using low frequency force oscillation. Airway conductance (*G*) was measured at trans-respiratory pressures of 0 (G_0) and 5cmH$_2$O (G_5). Distensibility was calculated from the change in conductance (G_5-G_0). Lungs were fixed for morphometry and stereology.

Results: Dox-fed mice had increased thickness of the airway epithelium, inner and outer wall and airway smooth muscle layer. While the increase in thickness of the epithelium and inner wall was greater in Egr-1 +/- mice, other changes were not affected by genotype. Dox-fed mice had reduced airway distensibility independent of genotype.

Conclusion: Increased TGF-α expression within the airway wall is associated with increased wall thickness and reduced airway distensibility. The effects of TGF-α were largely unaffected by partial modification of the Egr-1 gene. Findings suggest that TGF-α signalling may contribute to airflow limitation in COPD by reducing airway distensibility.

Declaration of Interest Statement: None.

TO 053

LIPOSOMAL FORMULATION OF QUERCETIN AND RESOLVIND1 FOR TREATMENT OF STEROID RESISTANT AIRWAY INFLAMMATION

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Introduction/Aim: Steroids are the mainstay treatment targeting airway inflammation. However, in some patients increased oxidative stress could result in resistance to steroid treatment. Therefore, combining anti-inflammatory, resolvin D1 (RvD1), and antioxidant quercetin (Q) could be a promising therapeutic strategy. Here, we aim to prepare liposomal formulation of Q and RvD1 and investigate its effectiveness in human airway epithelial cells (BEAS-2B).

Methods: Blank, Q and QRvD1 liposomes were prepared and characterised. Cell uptake studies were performed using confocal microscope and antioxidant activity of the liposomes was determined.

Results: The results demonstrated a monomodal size distribution of 163.26 $\pm$ 1.69 nm, 158.16 $\pm$ 1.89 nm, 167.3 $\pm$ 0.8 nm for blank, Q and QRvD1 liposomes respectively.The concentration of Q encapsulated was found to be 4.99 $\pm$ 2.6 µg/ml and 2.5 $\pm$ 1.97 µg/ml in Q and QRvD1 liposomes respectively and concentration of RvD1 in QRvD1 liposomes was found to be 9.57 $\pm$ 0.01 pg/ml. There was a time-dependent uptake of liposomes (Q and QRvD1) observed over 6 hours following treatment with liposomes. The antioxidant activity of Q was found to be significantly higher ($P<0.05$) when formulated as liposomes (48.177 $\pm$ 6.99% for Q and 48.33 $\pm$ 5.626% for QRvD1) compared to free Q (30.79 $\pm$ 2.51%).

Figure 1. Uptake of Q liposomes into the Beas-2B cells 6 hours following treatment

Conclusion: In conclusion, liposomal formulations demonstrate acceptable characteristics for inhalation with significantly increased antioxidant properties when compared with the free Q. These liposomal formulations could potentially improve the therapeutic outcomes in steroid resistant patients. Further studies will investigate the anti-inflammatory activity of these liposomes in *in vitro* and *in vivo*.

CHARACTERISTICS OF PATIENTS WITH AND WITHOUT PERIPHERAL EOSINOPHILIA IN PATIENTS PRESENTING WITH AN ACUTE COPD EXACERBATION; GOLD COAST UNIVERSITY HOSPITAL EXPERIENCE

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Introduction/Aim: COPD patients with peripheral eosinophilia may have increased frequency of COPD exacerbations, respond better to oral corticosteroids and reduced mortality. Peripheral eosinophilia in COPD patients (eosinophil count of ≥ 2% of white blood cell count) has a prevalence in the range of 37-45%. To our knowledge, there is little epidemiological data of Australian COPD patients concerning peripheral eosinophilia, its prevalence and its association with rehospitalisation rates, steroid responsive disease and mortality rates. With this literature gap in mind, records of patients presenting with COPD exacerbations were audited retrospectively to determine the prevalence of peripheral eosinophilia in an Australian population.

Methods: Consecutive patients with spirometry confirmed COPD admitted to our institution with a COPD exacerbation during the period of July 2016 – December 2016 were considered for the study. These patients' records were subsequently followed up until June 2017. The variables recorded were white blood cell count, absolute and relative eosinophil count, readmission rate, decompensated type 2 respiratory failure rate, non-invasive ventilation initiation rate, intensive care admission rate and mortality rate.

Results: 240 patients were included for analysis and of these 37% had peripheral eosinophilia. Using Pearson's coefficient, there appeared to be a statistically significant correlation between increasing peripheral eosinophil count and increased number of readmissions (R=0.175, p=0.007) but not with decompensated type 2 respiratory failure, non-invasive ventilation initiation rate, intensive care admission rate or mortality rate. Two-sample t-Test for equal means when comparing those with peripheral eosinophilia ≥ 2% and those without was also in keeping with a statistically significant difference in readmission rates (t=-2.367, p=0.019).

Conclusion: Prevalence of peripheral eosinophilia in Gold Coast patients was similar to overseas cohorts. In congruence with findings in previous overseas studies, Gold Coast patients with eosinophilia were prone to readmission but not increased type 2 respiratory failure, non-invasive ventilation, intensive care admission or mortality. As such peripheral eosinophilia can be used in Australian COPD patient cohorts to predict rehospitalisation rate. Future studies should look to prospectively evaluate the effect inhaled corticosteroids have on readmission rates in patients with peripheral eosinophilia.

TARGETING APOPTOSIS SIGNAL-REGULATING KINASE 1 IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Introduction: Increased airway smooth muscle (ASM) mass is part of overall structural changes observed in COPD, and is correlated with severity of the disease and has been found to negatively impact lung function. Thus, there is clear unmet clinical need for finding new therapies for COPD which can target airway remodeling and disease progression. Apoptosis signal-regulating kinase 1 (ASK1) is a ubiquitously expressed MAP3K activated by various stress stimuli, including ROS, TNF-α, and LPS. However, the role of ASK1 in airway remodeling is not established. In this study, we aimed to determine the effects of ASK1 inhibition on ASM growth and pro-mitogenic signaling using ASM cells from well-established COPD patients.

Methods and Results: It is known that ASM cells from COPD patients have greater proliferative capacity to variety of mitogens *in vitro.* We used human lung tissue samples and primary human ASM cells obtained from COPD patients and healthy controls. IHC revealed increased expression of ASK1 in COPD lung when compared with non-COPD lung. Pre-treatment of human ASM cells with highly selective (IC50:14 nM) and orally available ASK1 inhibitor; TCASK10 resulted in a dose-dependent reduction in mitogen (FBS, 10%; PDGF and EGF; 10 ng/ml, 72 hours)-induced ASM growth as measured by CyQuant assay. Furthermore, ASK1 siRNA prevented mitogen-induced human ASM cell growth, while immunoblotting revealed that the anti-mitogenic effect of ASK1 inhibition or silencing is mediated by JNK and p38MAP kinase-signalling pathways evident by reduced phosphorylation of downstream effectors JNK1/2 and p38MAP kinase respectively with no effect on ERK1/2 signalling.

Conclusions: Collectively, these findings establish the anti-mitogenic effect of ASK1 inhibition and identify a novel pathway that can be targeted to reduce or prevent excessive ASM mass in COPD.

Key Words: COPD, airway remodelling**,** mitogen

OLIV 1

NOVEL ANTI-FXII ANTIBODY INHIBITS FXII-INDUCED PRO-FIBROTIC FUNCTIONS IN LUNG FIBROBLASTS

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Introduction/Aim: Excessive pro-coagulant activity drives recurrent inflammation and fibrosis in patients with Idiopathic Pulmonary Fibrosis (IPF). Coagulation factors promote healing during damage, but can also exert pro-fibrotic cellular effects. Coagulation factor XII (FXII) has been identified as a potential mediator of lung fibrosis. The aim of this study is to further define a role for FXII in fibrogenesis.

Methods: Blood from 35 IPF patients was collected repeatedly (0-15 months) and compared to age and gender-matched healthy controls. Plasma FXII and IL-6 were measured. Immunohistochemical analysis for FXII was performed on paraffin-embedded lung tissue from IPF patients and non-diseased controls (NDC). *In vitro* effects of FXII on primary IPF and NDC fibroblasts were evaluated for cytokine production, proliferation and migration. The effect of a novel, fully human monoclonal antibody against FXII (CSL312) was evaluated.

Results: Baseline and longitudinal levels of FXII in IPF patients with progressive disease was elevated compared to those with stable disease (27.7 vs 17.6μg/ml, p=0.04 baseline; 26.3 vs 20.6μg/ml, p=0.014 longitudinal) but were not increased in IPF compared to healthy controls. Baseline plasma IL-6 was elevated in IPF patients when compared to healthy controls (3.9vs 1.5 pg/ml, p=0.001). IHC analysis revealed significant FXII staining in IPF lung tissue with minimal staining observed in non-fibrotic lung tissue. Activated FXII induced IL-6 production and enhanced proliferation/migration in primary lung fibroblasts. Migration and IL6 production were effectively inhibited by CSL312.

Conclusion: FXII is elevated in the lungs of progressing IPF patients and can drive pro-fibrotic and pro-inflammatory functions of fibroblasts. An anti-FXII antibody (CSL312) can inhibit these activities. The ability of FXII to drive IL-6 production in lung fibroblasts may contribute to elevated IL-6 levels seen in IPF patients' blood. Blocking FXII activity may be novel avenue to treat IPF and other inflammation-driven interstitial lung diseases.

Grant Support: Nil
Conflict of Interest: Employee of CSL Ltd.

A SINGLE CENTRE, PROSPECTIVE, LONGITUDINAL STUDY OF THE HUMAN RESPIRATORY VIROME AFTER LUNG TRANSPLANTATION

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Introduction/Aim: Lung transplantation (LTX) provides a unique opportunity to investigate the dynamics of viruses present within the human pulmonary virome which is transplanted into the recipient within the donor lungs. The aim of our study was to elucidate interactions between viral species within the respiratory virome of the LTX recipient and describe their impact on allograft function.

Methods: A prospective, longitudinal study of viral dynamics after LTX. Multiple sample types were collected. Samples were processed and assayed using multiple uniplex PCRs for human rhinovirus (HRV), respiratory syncytial virus (RSV), influenza A and B, (Flu A, B), parainfluenza (PIV) 1,2,3 and human metapneumovirus. Clinical outcomes were analysed and compared with microbial detection.

Results: 52 consecutive LTX were recruited. Swabs of explanted lungs were positive for viruses in 18/52 despite recipient vaccination and negative recipient NPS. Day 1 BAL showed Flu A (n=28), HRV (n=9) and PIV (n=1). Donor swabs showed influenza (A=1, B=1), and HRV (n=3). Donor transmission of Flu A was observed. 47/52 recipients had BAL positive samples for viruses (38/47 on multiple BAL) and viruses persisted for up to 14 weeks.

114 paired transbronchial biopsies and viral PCR on BAL were performed. 21 patients showed evidence of acute cellular rejection on biopsy (Grade A2B0=3, Grade A1B1=6, Grade A1B0=12). Of these, 11/21 had viruses detected in the BAL collected concurrently. Conversely, in patients who showed no evidence of cellular rejection on biopsy, 51 were virus positive, while 42 were virus negative. Analysis using Fisher's exact test (2 tailed) indicated no significant correlation (p=1.00) between viral detection and the presence of acute cellular rejection.

Conclusion: The finding of frequent donor transmission and early acquisition of viruses (particularly influenza A) support the importance of respiratory virome surveillance after LTX to direct acute therapies. In this cohort, viral presence after LTX was not correlated with acute rejection events.

Grant Support: N/A

EXOSOMES AND PAH: THE ROLE OF CELLULAR COMMUNICATION IN BOTH DISEASE PROGRESSION AND THERAPEUTIC SUCCESS

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Introduction/Aim: Previously we reported the therapeutic effect of BMPR2 augmented endothelial progenitor cell therapy in a rat PH model. We know there is little direct cell integration into the pulmonary endothelium following intravenous injection, thus we attribute the positive physiological effects of our cell therapy to cell-to-cell communication via secreted factors such as exosomes (exos). In this study we look at comparing PAH-EPC and control-EPC protein profiles via mass spectrometry, and we assess their capacity to interact with and transport BMPR2 into endothelial cells (EC).

Methods: EPCs are isolated and cultured from 15mL of PAH or control peripheral blood. Cells were either transduced with AdBMPR2 or AdTrackLuc, or untransduced for subsequent exo isolations. Exosomes are isolated via differential centrifugation, and characterised with a Nano-Sight, TEM and SEM. Exosome protein profile was via mass spectrometry. Exo-Quick™ treated exos and GFP-exos labelled were used to view exo localisation within the target ECs both live and fixed via confocal microscopy. BMPR2-Exos were incubated on ECs for 48hrs before being washed off, and the cells lysed for western blot analysis.

Results: Exosomes were positively identified as 40-200nm via Nano-Sight, TEM and SEM. Protein profiling of exos showed differential protein expression in the PAH vs control for 326 proteins, including a relative down-regulation of BMPR2 in PAH exos. Exosome interaction with ECs demonstrated localisation around the nucleus of the cell, both in live and fixed EC samples. Additionally, BMPR2 expression was significantly increased in cells treated with BMPR2-Exos.

Conclusion: Differential protein expression between exos derived from PAH compared to control EPCs was shown. Additionally, we have characterised exos interaction with ECs and shown that they are involved in BMPR2 transfer from BMPR2 transduced EPCs to naïve ECs. These results indicate the potential role of exos in our BMPR2-cell therapy.

DORNASE ALFA DURING LOWER RESPIRATORY TRACT INFECTION POST LUNG TRANSPLANTATION

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Introduction/Aim: Lung transplant (LTx) recipients are at a high risk of lower respiratory tract infection (LRTI) secondary to immunosuppression, while altered respiratory physiology can make it difficult to clear secretions. Inhaled mucoactive agents alter mucus properties and/or facilitate mucocilliary clearance in suppurative lung disease. However there are no randomised controlled trials (RCTs) studying these effects post LTx. We aimed to evaluate the safety and efficacy of nebulised dornase alfa compared to isotonic saline during LRTI > 2 months post LTx.

Methods: Inpatient adults with LRTI and sputum production following bilateral sequential LTx were eligible for this assessor blinded RCT. Randomisation was stratified by LTx indication (±cystic fibrosis (CF)). Participants received either 5ml isotonic saline, or 2.5ml dornase alfa, nebulised once daily for 1 month followed by 2 months symptom diary only. The primary outcome was change in lung clearance index (LCI) measured by multi-breath washout. Secondary outcomes included adverse events; spirometry; quality of life; readmission; length of stay and self-reported exacerbations at baseline, 1 month and 3 months.

Results: 32 participated, 16 each group (18M,14F), mean(SD) age 50 ± 14, FEV1% 58 ± 22, median(IQR) length of stay 7 ± 5, days since LTx 1275 ± 2482. LTx indications included CF (n=11) and chronic obstructive pulmonary disease (n=11). There were no significant between-group differences in LCI at any time point (one month mean difference -0.34, 95% confidence interval (CI) -1.57 to 0.89; three months mean difference -0.76, 95% CI -2.29 to 0.78, both favouring dornase alfa). Secondary outcomes were not different between groups.

Conclusion: These results do not support the routine use of dornase alfa during LRTI in LTx recipients.

Conflict of Interest: No conflict of interests to declare.

VARIATION IN SENSITIVITY TO PIRFENIDONE AMONG FIBROBLASTS DERIVED FROM PATIENTS WITH AND WITHOUT IDIOPATHIC PULMONARY FIBROSIS

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Introduction/Aim: Lung fibrosis is the end-stage consequence of interstitial lung diseases (ILDs) which involve excessive numbers of activated lung fibroblasts with elevated alpha-smooth muscle actin (αSMA) expression. Pirfenidone is approved for use in patients with idiopathic pulmonary fibrosis (IPF), the most common and fatal of the idiopathic ILDs. Poor tolerability and large variation in efficacy of pirfenidone is a significant barrier to best patient outcomes. This study aims to investigate whether an in-vitro fibroblast test can identify patients most likely to benefit from pirfenidone therapy.

Methods: Primary lung fibroblasts were derived from the apex and base of the lungs from patients with IPF (N=10), patients with other end-stage non-IPF ILDs (N=10) and normal donors whose lungs were deemed unsuitable for transplantation (NDC)(N=10). Determined by in-cell western, αSMA and GAPDH levels in fibroblasts were measured before and after treatment with pirfenidone (0-1mM) and in the presence/absence of transforming growth factor-β (TGFβ) (0-10ng/mL). Sensitivity to pirfenidone was defined by a decrease in αSMA/GAPDH level from baseline by ≥10%.

Results: Treatment with pirfenidone decreased αSMA levels in N=9 fibroblast lines at 72 hours (Figure 1). Fibroblast αSMA levels correlated with the extent of αSMA decline in response to pirfenidone (Spearmans' R = -0.76, p=0.037). In patients with IPF, basal αSMA level of the fibroblast line correlated with forced vital capacity (FVC, % predicted) of the patient from whom the line was derived (Spearmans' R = 1, p=0.016).

Conclusion: The response of lung fibroblasts to pirfenidone may identify patients with IPF who would benefit from said treatment. Our data suggest that patients who have high numbers of αSMA+ fibroblasts would in particular benefit from pirfenidone therapy, although further screening is required. Variation in αSMA level of fibroblasts may be reflective of the overall lung fibrotic burden as it correlated with FVC.
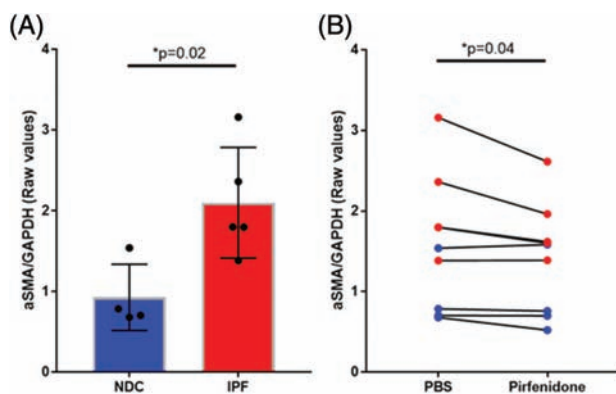
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Figure 1 Quantification of aSMA levels in primary lung fibroblasts pre and post Pirfenidone therapy by in-cell-western. Primary fibroblasts were derived from N=5 patients with idiopathic pulmonary fibrosis (IPF, red dots) and N=4 donors without lung disease (NDC, blue dots). (A) Fibroblasts derived from patients with IPF express greater levels of aSMA compared to fibroblasts from NDC donors. (B) Treatment with 1mM Pirfenidone (in PBS) decreased aSMA expression in lung fibroblasts. Each dot is an experimental triplicate.

CHARACTERISATION OF PULMONARY ARTERIAL HYPERTENSION ENDOTHELIAL PROGENITOR CELLS 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. Mutations in BMPR2 are causally linked to PAH. Endothelial progenitor cells (EPCs) are cells that can differentiate into endothelial cells, play a role in vascular repair and are dysfunctional in PAH patients. Hypoxia is thought to play a significant role in disease pathogenesis and is used to induce PAH in animal models of disease. This study aimed to characterise the differences in PAH and control EPCs in hypoxic conditions.

Methods: EPCs were isolated from PAH and control patient's peripheral blood (15mL). Following characterisation and expansion, cells were exposed to either normoxia ($5\%CO_2$/ atmosO_2) or hypoxia ($1\%O_2$/5% CO_2/94% N_2). Proliferation and apoptosis were assessed using MTT assays and flow cytometry. Protein analysis was conducted via western blots.

Results: EPCs originating from PAH patients proliferated at a similar rate to control EPCs in normoxia (increases of 198%±60% and 206%± 17% over 72hrs respectively). However, under hypoxic conditions proliferation of control cells was 88% less than PAH cells (7%±36% and 95%± 11% increase over 72hrs respectively). Preliminary data suggests this continued proliferation could be due to apoptosis resistance in PAH lines as assays revealed lower apoptosis levels after hypoxia exposure for 72hrs in PAH lines (2.8%) than in control lines (8.5%). Activated SMAD 1/5/8 was decreased by 68% in hypoxic PAH cells compared to controls.

Conclusion: EPCs isolated from peripheral blood of PAH patients are functionally different under hypoxic conditions to those isolated from control subjects. Most notably, the PAH EPCs appear to possess a higher resistance to apoptosis and hypoxia. These findings suggest EPCs could play a role in the pathogenesis of PAH as they can contribute to the aberrant proliferation, apoptosis and vascular remodelling seen in PAH.

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Ann Woolcock Young Investigators Award

RCT OF NHF THERAPY COMPARED WITH NIV IN HYPERCAPNIC COPD

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Introduction/Aim: Acute hypercapnic respiratory failure secondary to an exacerbation of COPD is associated with poor clinical outcomes and increased mortality. Non-invasive ventilation (NIV) is part of the standard of care but can be poorly tolerated.

We have shown Nasal High Flow therapy (NHF) produces a small reduction in transcutaneous CO_2 tension ($PtCO_2$) in stable COPD.

Our aim was to compare NHF and NIV in hypercapnic COPD.

Methods: *Design:* Single-blind randomised controlled two-way cross-over trial.

Setting: Single centre institute in New Zealand recruiting participants from hospital databases.

Participants: 24 participants with a doctor's diagnosis of COPD, FEV_1: FVC ratio <0.7, ≥40 years, smoking history of ≥10 pack years, $PcapCO_2$ >45.0mmHg, BMI <35kg/m^2 , no recent exacerbations and no diagnosis of obstructive sleep apnea or obesity hypoventilation syndrome.

Interventions: NHF at 45Lmin and BiPAP at 15/4cmH$_2$O, each for 60mins with a 15min washout in between.

Primary outcome measure: $PtCO_2$ at 60mins, adjusted for baseline.

Secondary outcomes included tolerability and the proportion of participants with a decrease in PtCO2 ≥4mmHg and ≥8mmHg at 60 minutes.

Results: $PtCO_2$ was 2.5mmHg (95% CI -4.5 to -0.5) lower with NIV compared to NHF, p=0.016.

The proportion of participants with a reduction of $PtCO_2$ ≥4mmHg with NIV versus NHF was 45.8% versus 25.0%. For a reduction in $PtCO_2$ ≥8mmHg it was 25% versus 8.3%. These differences were not statistically significant. Participants rated NHF significantly better for ease of application, comfort, fit and willingness to use in the future.

Conclusion: In stable COPD patients with chronic hypercapnia, NIV resulted in a small reduction in $PtCO_2$ compared with NHF, which is of uncertain clinical significance. NHF was better tolerated. NHF may be a therapeutic option for some people with hypercapnic respiratory failure and studies in acute exacerbations of COPD are required.

MULTIDIMENSIONAL AETIOLOGICAL ASSESSMENT IDENTIFIES CLINICAL PHENOTYPES AMONGST HOSPITALIZED ACUTE EXACERBATIONS OF COPD

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Introduction/Aim: Hospitalized AECOPD are heterogenous events of diverse aetiology. We hypothesized that comprehensive AECOPD evaluation would reveal clinical phenotypes amongst AECOPD.

Methods: Nasopharyngeal viral PCR, sputum culture, C-reactive protein, chest X-ray, troponin I (hs-TnI), N-terminal pro brain natriuretic peptide (NT-proBNP) and Hospital Anxiety and Depression Scale (HADS) were used to construct a cumulative aetiological phenotype for each AECOPD using a simple acronym: **A**=airway viral infection, **B**=bacterial infection, **C**=coinfection, **D**=depression/anxiety, **E**=embolism (pulmonary), **F**=failure (cardiac), **G**=general environment, **X**=unknown.

Results: Aetiologies identified among 155 unique AECOPD admissions were diverse (viral=35, bacterial=61, coinfection=8, no infection=44) and often multifactorial, with 1 aetiology in 31%, 2 in 48.4%, 3 in 5.2% and no identifiable aetiology in 5.8%.

Baseline lung function and symptoms were similar across exacerbation subtypes. Infective exacerbations were associated with lower eosinophils (p<0.001) and non-infective exacerbations with lower pH (p=0.004). NIV requirement was higher in non-bacterial v bacterial (p=0.03). AECOPD patients with no identifiable aetiology (X) were generally "frequent exacerbators" with severe acute presentations but prompt stabilization. Admissions ≤4 days were most common in non-infective groups (viral 22.9% v bacterial 39.3% v co-infection 12.5% v non-infective 47.7%, p=0.06). Subclinical cardiac dysfunction was highly prevalent in both infective and non-infective AECOPD with elevated hs-TnI in 27.3% and elevated NT-proBNP in 61.7% overall. Anxiety/depression was prevalent in all aetiological subgroups (overall population HADS mean/SD =16.7/8.7). Survival at 12 months post discharge was lower in non-viral versus viral AECOPD (p=0.03).

Conclusion: Hospitalized AECOPD are multidimensional and multifactorial. Subtyping by infection type identified significant differences in comorbidities, health care utilization, laboratory parameters, inpatient management and post exacerbation survival. Anxiety/depression and cardiac dysfunction appear prevalent but underdiagnosed. Our clinically oriented methodology provides a feasible framework for clinicians and researchers to address AECOPD complexity and target therapeutic interventions.

RELAXIN POTENTIATES SALBUTAMOL-MEDIATED AIRWAY RELAXATION IN MULTIPLE SPECIES

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Introduction: Treatment with β-adrenoceptor agonists may not overcome symptoms of severe asthma. Relaxin (rhRLX), an RXFP1 receptor agonist, exerts cardioprotective effects in acute heart failure and elicits vascular relaxation via RXFP1 and nitric oxide signalling. Although we have previously established its bronchodilator efficacy in rat airways (Lam et al., 2016), its effects in other species and its potential to enhance β-adrenoceptor-mediated relaxation have yet to be explored.

Aim: To compare the bronchodilator effects of relaxin alone and in combination with the β_2-adrenoceptor agonists, isoprenaline (ISO) or salbutamol (SAL) in multiple species.

Methods: Tracheal rings or bronchi were dissected and/or precision cut lung slices (PCLS) containing intrapulmonary airways were prepared from mice, rats, guinea pigs and marmosets and human lungs (unused donor). rhRLX alone and in combination with ISO or SAL were added to airways pre-contracted to MCh.

Results: rhRLX (100 nM) elicited partial relaxation in rat airways that was more rapid in PCLS than trachea but was ineffective as a direct bronchodilator in guinea pig trachea or mouse PCLS. rhRLX markedly increased the potency of ISO by 10-fold in rat PCLS without increasing maximum relaxation, and of SAL by 27-fold in guinea pig trachea. SAL only elicited partial relaxation in mouse PCLS but synergism was evident between rhRLX and SAL (maximum relaxation: rhRLX no response; SAL 41±5%; rhRLX/SAL 90±6%; n= 4-7; P<0.001). Preliminary data showed rhRLX elicited relaxation and potentiated SAL-mediated relaxation in marmoset and human small airways.

Conclusion: rhRLX elicits airway relaxation in some species and enhances responsiveness of both small and large airways to salbutamol across all species tested. Since rhRLX increases the potency of salbutamol, further investigations are warranted to define its therapeutic potential as an add-on asthma therapy in human lungs, particularly when responsiveness to current dilator therapy is limited.

ENDOSOMAL NOX2 OXIDASE INHIBITOR PROTECTS AGAINST HIGHLY PATHOGENIC INFLUENZA VIRUS MORBIDITY

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Introduction/Aim: Influenza A viruses cause respiratory tract infections that can lead to fatal outcomes when the virus spreads to the alveolar space, more predominantly observed with high pathogenic influenza virus strains. We have shown that influenza A viruses, irrespective of strain, cause a burst of reactive oxygen species (ROS) production via NOX2 oxidase that occurs in endosomes. Evidently, an endosome targeted NOX2 oxidase inhibitor called cholestenol conjugated gp91ds-TAT (Cgp91) abrogated disease caused by a seasonal strain of influenza A virus (IAV) in mice (1). The aim was to determine the effect of Cgp91 treatment on the lung pathology induced by a highly pathogenic strain of IAV.

Methods: Male C57Bl/6J mice were treated daily via intranasal administration with Cgp91 (0.2mg/kg) or DMSO (2%; control) over a 4-day period. Mice were infected with the PR8 (H1N1; 500 PFUs) strain of IAV or PBS control, one-day post initial drug treatment and analysed at day 3 post-infection. Bronchoalveolar lavage (BAL) fluid collected from mice was used to assess airway inflammation. Histopathological analysis of lung was assessed using H&E stain and scored for alveolitis, inflammatory cell infiltrate and peribronchiolar inflammation. Superoxide generation in the BAL was measured using L-012 enhanced chemiluminescence and changes in cytokine and viral mRNA expression in the lung were quantified using real-time QPCR.

Results: Cgp91 treatment significantly (P<0.05) reduced airway inflammation, neutrophil influx, and pulmonary inflammation as measured by the degree of alveolitis, inflammatory cell infiltrate and peribronchiolar inflammation. Additionally, Cgp91 attenuated ROS generation and influenza viral mRNA expression in PR8-infected mice.

Conclusion: The spatial inhibition of NOX2 in endosomal compartments with Cgp91 could be used as a potential treatment strategy for highly pathogenic influenza A virus infections.

(1) To *et al*. Nature Communications, 2017, **8**, Article number: 69.

AMOXYCILLIN-CLAVULANATE VS AZITHROMYCIN FOR RESPIRATORY EXACERBATIONS OF BRONCHIECTASIS IN CHILDREN: A MULTI-CENTRE DOUBLE BLIND NON-INFERIORITY RCT

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Introduction: Based on limited available data, amoxicillin-clavulanate is the current recommended first-line empirical oral-antibiotic treatment for non-severe bronchiectasis exacerbations in children. Azithromycin is an attractive alternative because of its long half-life, reduced dosing schedule, and good safety profile in children. We tested our primary hypothesis that oral azithromycin is non-inferior (within 20% margin) to amoxycillin-clavulanate at achieving resolution of exacerbation by day-21 of treatment in children with bronchiectasis.

Methods: We conducted a multicentre, parallel group, double-dummy, double-blind placebo-controlled RCT trial in 4 centres. At the start of an exacerbation, 179 children were randomised to receive either amoxycillin-clavulanate (22.5 mg/kg bd)/placebo or azithromycin (5mg/kg/day)/placebo for 21-days. Our primary outcome was resolution of exacerbation (defined as 'return to baseline') by 21-days. Study was powered for 90% (α=0.05, 1-sided) with 20% non-inferiority margin to detect 80% resolution rate by day-21. Secondary outcomes were cough-specific quality of life (PC-QoL) and duration of exacerbation. Generalised linear model was used to calculate relative differences between groups.

Results: Baseline characteristics of the 2 groups (amoxycillin-clavulanate n=97 and azithromycin n=82) were similar. By day-21, resolution was comparable between groups, relative risk 0.99 95%CI 0.84-1.17, falling within the a-priori calculated 20% non-inferiority margin. Between group differences for duration of exacerbation (2 days 95%CI -1.7, 5.3) and PC-QoL at day-21 compared to beginning of exacerbation was also within our non-inferiority margin (0.42, 95%CI -0.06, 0.89).

Conclusion: Azithromycin is non-inferior to amoxicillin-clavulanate for treating non-severe exacerbations of bronchiectasis in children. Azithromycin may be preferred to amoxicillin-clavulanate in selected settings e.g. adherence. However, its use needs to be balanced with risk of treatment failure (within 20% compared to amoxicillin-clavulanate) and inducing macrolide resistance.

LUNG ELASTIC RECOIL, INFLAMMATION AND PERSISTENT AIRFLOW LIMITATION IN ASTHMA

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Introduction/Aim: Persistent airflow limitation (PAL) may develop in older non-smokers with asthma however the mechanism is unknown. Reduced lung elastic recoil may contribute as this occurs with age and may occur in asthma. Neutrophilic airway inflammation is also more common in older people with asthma. We aimed to determine the relationship between lung elastic recoil, airway inflammation and airflow limitation. We hypothesise that reduced lung elastic recoil and neutrophilic airway inflammation are associated with PAL in older non-smoking asthmatics.

Methods: Non-smoking adults with asthma, treated with standardised high dose inhaled corticosteroid/long acting beta agonist for two months, underwent standard lung function, lung elastic recoil measurement using an oesophageal balloon to derive indices of loss of lung elastic recoil (increased K and reduced B/A), and bronchoscopy to obtain bronchoalveolar lavage fluid (BAL) for differential leukocyte count and T_H17 cytokine measurement. Spearman correlations were assessed and multiple linear regressions were used to adjust for age, BMI and disease duration.

Results: Nineteen subjects (11 male; mean$\pm$SD age 63$\pm$9 years, asthma duration 38$\pm$22 years) demonstrated moderate PAL ((mean$\pm$SD z-score) post-bronchodilator FEV_1 -2.05$\pm$0.75, FVC -0.61$\pm$0.95, FEV_1/FVC -2.46$\pm$0.90). Reduced lung elastic recoil was demonstrated in 8/18 subjects (median (IQR) z-score K 1.57(-1.08–3.43), B/A -1.18(-1.65–-0.02)). FEV_1/FVC correlated negatively with K (r=-0.53, p=0.023) independent of age, BMI and disease duration. Neutrophilic airway inflammation was not demonstrated (mean$\pm$SD: neutrophils 9.1$\pm$18.1%, n=10). Lung elastic recoil did not correlate with BAL neutrophil count or T_H17 cytokines.

Conclusion: Loss of lung elastic recoil contributes to PAL in older non-smokers with asthma. This may be due to lung tissue changes in addition to airway remodeling. Despite the lack of relationship with airway inflammation in this exploratory study, the underlying cellular mechanisms require further investigation. An alternate paradigm of 'lung remodeling' would have potential implications on preventing PAL in this population.

TOL 001

LUNG CELLS FROM PEOPLE WITH COPD ARE HYPER RESPONSIVE TO E-CIGARETTE VAPOUR

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Introduction/Aim: E-cigarettes are proposed as an alternative to smoking and as nicotine replacement therapy. There is confusion around the safety and efficacy of E-cigarettes as smoking cessation aids stemming from contradictory findings across multiple studies. The aim of this study was to determine the inflammatory response of both Chronic Obstructive Pulmonary Disease (COPD) and non-COPD cells to E-vapour under realistic physiological conditions.

Methods: Primary human airway smooth muscle cells were stimulated with increasing concentrations of 18mg/ml nicotine and 0mg/ml nicotine (tobacco and menthol flavoured, Vaper empire) E-vapour extract for 24 hours. An MTT assay was performed to determine cytotoxicity and ELISA was used to assess IL-6 and CXCL8 production. Cells were isolated from explanted and resected lung tissue from COPD patients and smokers without COPD.

Results: All 4 E-vapour extracts were cytotoxic to cells (n=9-14, $p \le 0.0001$), cytotoxicity of E-vapour was increased in aerosols created at higher temperatures. All 4 E-vapour extracts stimulated CXCL8 production compared to unstimulated controls (n=14, $p < 0.05$). Cells from people with COPD were hyperresponsive to E-vapours, with 18mg/ml nicotine tobacco flavoured E-vapour stimulating significantly greater CXCL8 production from COPD cells compared to non-COPD cells (n=7, $p < 0.05$). IL-6 production was not stimulated.

Conclusion: E-cigarettes have the potential to contribute to the pathology of COPD. Cytotoxicity can cause cell death and ineffective repair, as seen in both the airways and parenchyma in COPD. Increased CXCL8 would contribute to the proinflammatory environment in the lung. Our data suggests that COPD patients should not use them as a smoking cessation aid or cigarette replacement.

Grant Support: None

TOL 002

DOES ASTHMA CONTROL IN PRESCHOOLERS PREDICT THE LIKELIHOOD OF DISEASE REMISSION?

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Introduction/Aim: Many preschoolers with asthma experience disease remission. As the first 5 years of life may offer a window of opportunity to modify long-term outcomes, we explored the relationship between the likelihood of remission and asthma control in the two years following the diagnostic of asthma in preschoolers.

Methods: We assembled a retrospective birth cohort of children born between 1990-2013 in four Canadian provinces (Quebec, Manitoba, Saskatchewan, British Columbia). Preschool asthma was defined by one hospitalisation or 2 medical visits within a 2-year period for asthma in children aged less than 5 years. Remission was assumed after two years without any asthma-related drug claims, medical visit or hospitalization. The main exposure was asthma control in the 2 years following diagnosis, measured on the validated 4-level Pediatric Pharmacoepidemiology Asthma Control Index (PPACI) and ascertained over 4 consecutive 6-month periods. Cohort exit occurred at death, loss of medical or drug coverage, or date of last available data. Within each province, a Cox regression model served to estimate the strength of association between the PPACI stability over 2 years post diagnosis and remission, after adjusting for potential confounders and covariates, namely demographics (e.g., sex, social assistance), disease characteristics (e.g., age, atopy), therapy (e.g., first controller therapy). A random-effects meta-analysis aggregated the province-specific results.

Results: Of 1.3 million live births in the 4 provinces, 118,785 children less than 5 years met the definition of asthma; 63% were male, 69% were aged less than 3 years at diagnosis. The pooled rate of remission was 7.74 (95% CI: 7.67, 7.81)/100 person-years. Poorer asthma control over the 2 years following diagnosis was associated with incrementally lower likelihood of asthma remission (Table).

PPACI 2 years post-dx	Adjusted HR *(95% CI)
Controlled throughout	reference
Improving control	0.80 (0.68, 0.95)
Varying control	0.59 (0.52, 0.68)
Worsening control	0.50 (0.42, 0.59)
Out of control throughout	0.31 (0.27, 0.36)

*Adjusted for demographic and disease characteristics (3 provinces)

Conclusion: Poorer asthma control in the two years following diagnosis is associated with an incrementally lower rate of remission. Better asthma control appears as a promising target to modify long-term outcomes of asthmatic preschoolers.

AN ASSESSMENT OF EARLY LIFE EXPOSURE TO COAL MINE FIRE SMOKE AND CHILDREN'S LUNG HEALTH

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Introduction/Aim: In 2014, emissions from a fire in an open cut coal mine caused markedly increased concentrations of fine particulate matter ($PM_{2.5}$) in the Latrobe Valley of Victoria, Australia, for approximately six weeks. We aimed to evaluate the impacts of infant (<2 years of age) exposure to mine fire emissions on lung function measured three years after the fire.

Methods: Hourly $PM_{2.5}$ from the fire at 1x1 km^2 was derived from an atmospheric transport model. Daily average and maximum $PM_{2.5}$ were assigned to participants' residential address during the fire. Lung function was evaluated using the forced oscillation technique (FOT), which generated z scores for resistance (Rrs) and two measures of reactance as follows: (1) Reactance at a frequency of 5Hz, (Xrs) and (2) area under the reactance curve (AX). We used generalised linear models, adjusted for maternal smoking in pregnancy and maternal stress during the fire to assess associations between $PM_{2.5}$ exposure and lung function.

Results: 71 children, with a mean age of 4.3±0.6 (SD) years were included. Median [IQR] daily $PM_{2.5}$ exposures were 6.8 [1.9-12.7] μg/m^3 (average) and 107.4 [60.4-167.0] μg/m^3 (maximum). The baseline mean (SD) z scores were Rrs 0.6 (0.8), Xrs 0.8(0.9) and AX 0.7(1.0). A 10μg/m^3 and 100μg/m^3 increase in average and maximum $PM_{2.5}$ respectively was independently associated with z scores for AX coefficient (95%CI): Average $PM_{2.5}$: 0.23 (0.02 to 0.44); Maximum $PM_{2.5}$: 0.13 (0.00 to 0.25), but not with the other measures of lung function. Maternal smoking was strongly associated with Xrs_5: 1.15 (0.60 to 1.69) and AX: 0.89 (0.30 to 1.48), while maternal stress during the fire was protective for Xrs_5: -0.62 (-1.19 to -0.06).

Conclusion: Exposure to coal mine fire emissions during infancy may be associated with reduced lung reactance. Further research is required to validate these findings.

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LUNG DIFFUSING CAPACITY IN YOUNGER SMOKERS WITH NORMAL SPIROMETRY

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Introduction/Aim: The prevalence of Chronic Obstructive Pulmonary Disease (COPD) has been extensively studied, however limited evidence exists for the role of lung diffusing capacity for carbon monoxide (DLCO) in the management of COPD. Various predicted equations have been used in the interpretation of DLCO. Recently the Global Lung Initiative (GLI) has been established with new reference equations for calculating DLCO. We aimed to assess the prevalence of low DLCO in younger smokers with normal spirometry using the GLI predicted equations.

Methods: We performed a cross-sectional analysis of subjects who have had both spirometry and TLCO measured at the Respiratory Laboratory at Monash Lung and Sleep, Monash Health. Subjects included males and females, aged 40 to 60 years with normal spirometry and significant smoking history. As sub-study, CT scanning was used to assess the prevalence of parenchymal lung diseases in this group. Initially, the ROCA (Roca J, 1990) predicted equations were used in the calculation of lower limit of normal (LLN). Subsequently the results were reanalysed with the GLI equations and both sets of data were compared.

Results: We screened 15,226 lung function tests and identified 470 subjects aged between 40 and 60 with normal spirometry and a significant smoking histories. Of this cohort, 290 subject (60% of the group) had a TLCO below their lower limit of normal when using the ROCA equations. Subjects with the low DLCO had higher prevalence of emphysema and bronchiectasis on CT scanning. When GLI equations were applied, there was a markedly lower prevalence of low DLCO, with 24.3% of subjects in this cohort having a DLCO below LLN.

Conclusion: A low transfer factor for carbon monoxide (DLCO) is prevalent amongst younger smokers with normal spirometry. This low TLCO may be an important early indicator of potential lung damage in COPD.

Grant Support: NA

Cystic Fibrosis 2

EFFECT OF LUMACAFTOR/IVACAFTOR ON CT SCORES: EXPLORATORY IMAGING SUBSTUDY

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Introduction/Aim: To evaluate lumacaftor (LUM) and ivacaftor (IVA) combination therapy on lung morphology with CT scanning in patients aged 6-11 years with cystic fibrosis (CF) homozygous for the *F508del-CFTR* mutation.

Methods: Baseline CT scans were obtained in 19 patients (12 LUM/IVA, 7 placebo) from the phase 3 trial (NCT02514473), and 24-week CT scans were completed in 7 active treatment and 3 placebo patients. CT scans were obtained at total lung capacity and at residual volume (RV). CT scans were scored by 2 independent readers blinded to all patient and time point information using the Brody score, which evaluates extent and severity of multiple aspects of CF lung disease, including bronchiectasis and air trapping. Scores are presented as mean $\pm$ SD; no statistical testing was performed for this preliminary study.

Results: Mean total CT score (sum of the subcomponent scores) decreased from 20.6 to 12.5 (mean change $\pm$ SD, 8.1$\pm$13.6) in the LUM/IVA group and increased from 32.8 to 41.4 (8.6$\pm$14.6) in the placebo group. Mean bronchiectasis score decreased from 3.2 to 2.5 (0.7$\pm$1.3) in the LUM/IVA group and increased from 6.4 to 8.1 (1.7$\pm$2.1) in the placebo group. Additionally, there was a suggestion that several ectatic bronchi decreased in size in patients on active treatment. Mean air trapping score decreased from 7.8 to 5.9 (1.9$\pm$6.8) in the active group and increased from 9.8 to 14.5 (4.7$\pm$11.7) in the placebo group.

Conclusion: This is the first report to describe CT lung findings after CFTR corrector/potentiator therapy in patients 6-11 years of age homozygous for *F508del*. In this 24-week exploratory analysis, bronchiectasis and air trapping scores improved in patients treated with LUM/IVA and worsened in the placebo group. These data suggest that LUM/IVA may reduce CF disease-related changes in lung morphology and support the need for further study.

LONGITUDINAL ASSESSMENT OF CT REGIONS OF LOW ATTENUATION REVERSIBILITY IN YOUNG CHILDREN WITH CYSTIC FIBROSIS

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Introduction: Low attenuation regions (LAR) on chest CT are an important component of end-stage lung disease and reflect small airways disease in cystic fibrosis (CF). However, the extent of LAR reversibility in young children is unknown. We aimed to assess localised changes in LAR distribution over time in relation to CF-lung disease outcomes. We hypothesised that a proportion of LAR is irreversible in young children with CF and indicative of clinical severity.

Methods: Children in the AREST CF cohort contributed CT scans and clinical data from annual consecutive visits. Localised changes in LAR distribution were assessed using specialised image analysis software by matching CT lung images from two time points and measuring the lung volume proportion of new (%LARnew), reversed (%LARreversed) and stable (%LARstable) LAR. Linear mixed effects models adjusted for age and multiple visits, assessed differences between LAR outcomes and their association with clinical predictors. These include: age, pancreatic sufficiency, bronchiectasis extent determined from the PRAGMA-CF method and pulmonary inflammation and infection measured by bronchoalveolar lavage.

Results: The entire cohort comprised 139 CT scans from 45 CF patients with mean age (range) of 4.5(2.0-6.8) years. Approximately one-third of total LAR was stable over time. Age-corrected log%LARnew (0.49 [0.31, 0.66]; p<0.001) and log%LARreversed (0.59[0.41, 0.76]; p<0.001) were significantly higher than log%LARstable. Log%LARnew was inversely correlated with pancreatic sufficiency (-0.702[-1.197, -0.208]; p=0.006) and log%LARreversed was associated with the presence of neutrophils in the previous year (0.016 [0.008, 0.024]; p<0.001). Log% LARstable was associated with pancreatic sufficiency (-0.769[-1.386, -0.151]; p=0.016) and the previous detection of neutrophilic inflammation (0.011[0.003, 0.0184]; p=0.009).

Conclusion: CT-detected LAR is present in early life and around one-third of LAR is irreversible over time. Progressive LAR is associated with pancreatic insufficiency and neutrophilic inflammation in children with CF, which suggest a role for LAR as a secondary imaging endpoint.

SCHOOL-AGED OUTCOMES OF INFANT LUNG FUNCTION IN CYSTIC FIBROSIS

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Introduction/Aim: Studies show that a significant proportion of infants with cystic fibrosis (CF) have diminished lung function within the first 2 years of life. However, it is unknown whether lung function tests in infancy have the potential to predict worse prognosis and determine which infants are most likely to benefit from treatment early in life. This study aims to investigate whether diminished lung function detected in infants diagnosed following newborn screening is associated with worse lung function when re-measured at school-age.

Methods: Lung function was assessed in 58 individuals with CF diagnosed after newborn screening (0-2 years) and again at school age (7–10 years). The raised volume rapid thoraco-abdominal compression (RVRTC) technique and multiple breath washout (MBW) test was performed at infancy, and spirometry and MBW performed again at school-age. Mixed-effects models were used to determine if outcomes from RVRTC such as forced expiratory volume in 0.5 second ($FEV_{0.5}$) and FVC, as well as lung clearance index (LCI) from the MBW test were associated with FEV_1, FVC and FEV_1/FVC measured by spirometry, and LCI at school-age.

Results: Age and height-adjusted $FEV_{0.5}$ and FVC and height-adjusted LCI at infancy were not associated with $zFEV_1$, zFVC and $zFEV_1$/FVC and LCI at school-age. The coefficients, 95% confidence intervals and p-values of the mixed-effects models are shown below.

	Infant LCI	Infant $FEV_{0.5}$	Infant FVC
$zFEV_1$	0.13 (-0.66, 0.91) p=0.742	-0.27 (-1.66, 1.12) p=0.696	0.25 (-1.40, 1.91) p=0.760
$zFEV_1$/FVC	0.45 (-0.22, 1.12) p=0.186	-0.02 (-1.18, 1.13) p=0.967	-0.26 (-1.63, 1.11) p=0.703
LCI	0.60 (-0.55, 1.74) p=0.300	-1.89 (-4.85, 1.08) p=0.206	-3.29 (-6.80, 0.21) p=0.065

Conclusion: Lung function measured in infancy is not associated with lung function outcomes at school-age. Other factors such as respiratory infections and clinical status should be investigated and may be better predictors of worse lung function at school-age.

Conflict of Interest: All authors have no conflict of interest to declare.

PREVALENCE OF NONTUBERCULOUS MYCOBACTERIA (NTM) IN POTABLE WATER

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Introduction/Aim: NTM is an emerging respiratory infection in people with cystic fibrosis (CF) with one species, *Mycobacterium abscessus* complex (MABSC), causing concern. The mode of acquisition is unknown but their prevalence in potable water may be a risk factor in people with CF. This study is investigating if NTM can be recovered from the potable water systems of The Prince Charles Hospital (TPCH) and Queensland homes.

Methods: Water was collected from showers and sink taps of two respiratory wards at TPCH across five time points (2014 to 2017). Water was collected from homes in Queensland from four groups: 1) People with CF who had active MABSC respiratory infection (<2 years since positive sputum culture); 2) People with CF and past MABSC respiratory infection (>2 years since positive sputum culture); 3) People with CF never infected with NTM; 4) People with no lung disease. The hospital and home water samples were filtered, inoculated into growth media and incubated for 8 weeks. DNA was extracted from presumptive NTM isolates and sent for whole genome sequencing.

Results: The water sampling recovered 257 presumptive NTM isolates (hospital, n=69; home, n=188). To date, 94 presumptive NTM isolates have been sequenced. Two isolates were contaminants. Thirty-nine isolates from the hospital water were identified as *Mycobacterium kansasii* (n=25), MABSC (n=7), unidentified *Mycobacterium* (n=5) and *Mycobacterium avium* (n=2). Fifty-five isolates from the home water were identified as MABSC (n=29), *M. kansasii* (n=10), unidentified *Mycobacterium* (n=10) and *M. avium* (n=4). These water isolates are being compared to CF MABSC respiratory isolates as well as other environmental isolates.

Conclusion: NTM species can be found in potable water systems of homes and a hospital. The most dominant NTM species were *M. kansasii* in the hospital water and MABSC in the home water.

HIGH FREQUENCY HEARING LOSS IN CYSTIC FIBROSIS ADULTS

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Introduction/Aim: Cystic Fibrosis (CF) is characterised by chronic lung infections often with *Pseudomonas aeruginosa,* requiring repeated aminoglycoside therapy. Aminoglycosides are recognised to cause both acute and chronic damage to the inner ear with sensorineural hearing loss (SNHL), especially of the higher frequencies. This study examined hearing in CF adults at Westmead Hospital, comparing pure tone audiometry (PTA) with high frequency audiometry (HFA).

Methods: Asymptomatic CF adults were recruited from the outpatient CF clinic. In a quiet room, PTA examined frequencies of 500Hz to 6000Hz, whilst HFA tested frequencies of 8000Hz to 16000Hz. Hearing loss severity was categorised as follows: 26-40dB (slight), 41-60dB (moderate), 61-80dB (severe), and 81+dB (profound), recording the worst 2 consecutive frequencies in standard and high ranges.

Results: A total of 134 CF adults, mean (SD) age 26.7 (8.7) years were recruited. Standard PTA detected hearing loss in both ears with 5 showing slight, 3 moderate and 2 severe impairment. HFA detected more hearing loss with 20 having slight, 16 moderate, 9 severe and 4 profound impairment. All those with hearing loss at standard frequencies exhibited similar or worse abnormalities at high frequencies. Older patients showed more hearing abnormalities both at standard and high frequencies.

Conclusion: These preliminary results suggest that HFA is more sensitive than standard PTA for measurement of potential hearing loss in the CF population. Comparison of these results with the cumulative doses of aminoglycosides is being undertaken in this cross-sectional study.

A REVIEW OF PERIPHERALLY INSERTED CENTRAL CATHETER-ASSOCIATED DEEP VENOUS THROMBOSIS IN ADULT CYSTIC FIBROSIS PATIENTS IN WESTERN AUSTRALIA

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Introduction: Peripherally inserted central catheters (PICC) have an integral role in managing pulmonary exacerbations in Cystic Fibrosis (CF). They allow effective delivery of intravenous antibiotics both in inpatient and outpatient settings. With repeated use of PICC lines, however, the incidence of complications rises. One such complication is deep venous thrombosis (DVT) and treatment with anti-coagulation can prove challenging in the setting of haemoptysis or CF related liver disease.

Aim: A retrospective audit was undertaken at Sir Charles Gairdner Hospital of all PICC line insertions in patients with CF between January 2016 and February 2017. The objectives were (i) to assess current practice of PICC insertion and (ii) to determine the frequency of PICC-associated DVT.

Methods: Information was obtained through computer records and included basic patient demographics, prior history of haemoptysis or venous thrombosis, complications and outcomes.

Results: A total of 121 4Fr PICC insertions in 63 patients (33 males and 30 females) took place during the study period. Twenty-eight percent of patients had a history of haemoptysis and one fifth (13/63; 20.6%) had a prior history of DVT or pulmonary embolus. The majority of patients had PICC lines inserted by a Radiologist (55.4%) and the rest were performed by Nurse Practitioners (44.6%). Symptomatic DVT (or pulmonary embolism) occurred in 6/121 (4.96%).

Conclusion: Our audit shows that the rate of PICC-associated DVT in adults attending the WA adult CF centre is equivocal to that reported in the literature of between 3.5 – 16.4%. It is well recognised that factors including PICC size, the thrombotic state of patients with CF and history of DVT can impact the likelihood of PICC-associated DVT. Following this audit we plan to assess the role of enoxaparin prophylaxis, particularly in the outpatient setting, aiming to further minimise the risk of PICC associated DVT.

Interventional Pulmonology / Bronchology 1

PLEURAL EFFUSION AND SYMPTOM EVALUATION (PLEASE) STUDY ON THE PATHOPHYSIOLOGY OF BREATHLESSNESS IN PATIENTS WITH SYMPTOMATIC PLEURAL EFFUSIONS

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Introduction/Aim: Breathlessness is common in patients with pleural effusion, but its pathophysiology is unclear. PLEASE is a comprehensive study assessing physiological and symptom responses to pleural effusion drainage and aims to i) identify etiologic factors that correlate with breathlessness and ii) determine incidence and factors influencing symptomatic benefit from fluid drainage.

Methods: Consecutive 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 three separate grading systems; 3) 6-minute Walk Distance (6MWD) capacity; 4) Spirometry; and 5) Diaphragm morphology and motion with ultrasonography.

Results: The 145 patients (median age 69; 55% male) most commonly (63%) had malignant effusions and heart failure effusions (15%). Most (93%) effusions were moderate- or large-sized (≥25% hemithorax on CXR) and had 1680 [median, IQR 1100–2600] mL drained.

All breathlessness measurements improved significantly after effusion drainage: Visual Analog Score by 30.0mm (minimal clinical important difference=14mm); Dyspnoea-12 score by -10; Borg score by 0.62 (all $p<0.05$). Respiratory and heart rates, 6MWD (increase by 26m), FEV_1 and FVC (by 8% and 6.6%) all improved ($p<0.05$). Abnormal diaphragmatic morphology (flattened or inversion, 50%) and motion (paralysed or paradoxical, 48%) were common pre-drainage, and normalized in 94% and 73% of patients, respectively, post-drainage. Most (73%) reported significant relief of breathlessness (by VAS).

Conclusion: The pathophysiology of breathlessness in patients with pleural effusion is complex and multifactorial. Drainage of pleural effusion improves symptoms, functional capacity, and spirometry and normalises diaphragm morphology and motion.

Conflict of Interest: All authors declare no conflict of interests.

RELATIONSHIPS OF PLEURAL FLUID PH AND GLUCOSE LEVELS: A MULTI-CENTRE STUDY OF 2971 CASES

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Introduction/Aim: Pleural fluid pH and glucose levels are both recommended in current guidelines as investigations in the workup of pleural effusions. Both parameters are reduced in inflammatory and/or metabolically active conditions. Whether pleural fluid pH and glucose levels provide duplicated information or independent knowledge is unclear. We aimed to investigate the relationships between pleural fluid pH and glucose levels in unselected pleural effusions, and the incidences of discordance in their levels.

Methods: *Setting*: Pleural services of three centres in Spain, UK and Australia.

Data: Clinical information and pleural fluid pH and glucose levels were collected.

Analyses: i) To assess the relationship between pH and glucose using smooth curves from restricted cubic spline models; ii) Concordance between pH and glucose for varying cut-off levels was assessed.

Results: Pleural fluid samples (n=2971) were separated into four categories: malignant (n=1045), bacterial infection (n=1133), TB pleuritis (n=544) and other benign effusions (n=249). The mean pH was 7.38 (SD 0.22) and median glucose was 5.99 (range 0-29.4) mmol/L. Linear regression modelling of the relationship between glucose (log-transformed) and pH with a restricted cubic spline showed linear ($p<0.01$) and nonlinear effects ($p<0.01$). Most (91.6%; n=2720) of the samples were concordant in pH and glucose levels (i.e. at cutoffs of 7.20 and 3.3mmol/L respectively). Concordance was the lowest in the TB group (80.7%) and highest in the other benign pleuritis group (98.2%). Patients with a low pH but high glucose (n=99) were more likely to be diabetic (31% were diabetic *vs* 8% of those with low glucose and high pH), $p<0.001$, and have bacterial infection.

Conclusion: Pleural fluid pH and glucose correlate and are concordant in the majority of cases. Either test below its cut-off level can be used to aid diagnosing infection. Pleural fluid glucose should be interpreted with care in diabetic/hyperglycaemic patients.

TO 076
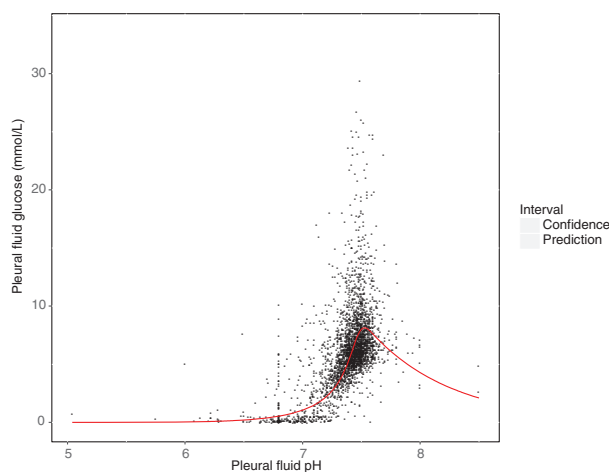
COMPARISON OF THE 19-GAUGE AND THE 21/22-GAUGE ASPIRATION NEEDLE IN ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL NEEDLE ASPIRATION (EBUS-TBNA) IN DIAGNOSING MEDIASTINAL LESIONS

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Introduction/Aim: This study aims to examine whether there is a difference between the 19 and 21/22-G EBUS-TBNA needles in obtaining adequate tissue for diagnosis and ancillary testing, as well comparing their safety.

Methods: This was a retrospective review of EBUS-TBNA cases done at the Lyell McEwin Hospital between June 2016 to September 2017. We included 25 cases done with the 19-G needle. For comparison, we randomly selected the same number of cases using the 21 or 22-G needle. Data collection included the patients' demographic data, diagnosis based on fine needle aspiration (FNA) samples, average size of lymph nodes biopsied, number of needle passes, sample adequacy for immuno-histochemistry (IHC) and molecular mutation testing in cases of primary lung adenocarcinoma (EGFR and ALK), sample quality and procedure complication data. Results were analysed and compared statistically using the Fisher's test.

Results: With the 19-G needles, the diagnostic yield was 96% and 80% with the 21/22-G needles (p= 0.19). Sample adequacy was obtained with IHC in 90% in the 19-G compared to 50% in the 21/22-G group (p= 0.04). In both groups, molecular mutation testing was achieved in 100% of patients with primary lung adenocarcinoma. Average size of lymph nodes was significantly larger in the 19-G group compared with the 21/22-G group (30mm $\pm$ 10.5mm cf. 18mm $\pm$ 9.8mm, p= 0.0006) However, there was slight increase in bleeding in the 19-G group (20% cf. 4%, p= 0.19).

Conclusion: There was no significant difference between the 2 needle sizes used in EBUS-TBNA with regards to diagnostic yield and sample adequacy for molecular mutation testing. However, in this study, there was a significant difference between sample adequacy for IHC testing. This comes at a slight increased risk of bleeding.

TO 077

INTRAPLEURAL TPA WITH DNASE FOR IPC RELATED PLEURAL INFECTION

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Introduction/Aim: Indwelling pleural catheter (IPC) is an effective treatment for recurrent, especially malignant, pleural effusions. Pleural infection, though uncommon, remains physicians' major concern in the use of IPCs. Intrapleural tPA/DNase therapy has revolutionized care of pleural infection, but its use in IPC-related pleural infection has not been the subject of prior reports.

Methods: Single centre, retrospective review of patients with IPC-related pleural infection treated with tPA/DNase in our tertiary pleural unit. Demographics, interventions and outcomes of treatment were described. Treatment success is defined as survival to hospital discharge and avoidance of surgery. Data are presented as percentages or median [IQR] as appropriate.

Results: Nineteen patients (63% male, age 68 [59-73] years) received intrapleural tPA/DNase. Most had malignant effusions from mesothelioma (68.4%) or non-small cell lung carcinoma (15.8%). Median time from IPC insertion to diagnosis of pleural infection was 162 [57-363] days. Median follow-up was 262 [124-453] days. One patient died before 30-day follow-up from cancer progression. Fever (73.7%), dyspnoea (42.1%) and decreased fluid drainage (36.8%) were the commonest presenting complaints. Staphylococcus aureus and gram-negative bacilli were the most common organisms found in pleural fluid culture. tPA/DNase therapy successfully cured 90% (17/19) of cases. The remaining two patients underwent surgery because of inadequate clinical improvement. Three patients required additional chest drain or thoracentesis. CRP improved from 170 [135-250]IU/L pre-tPA/DNase to 17 [10.1–66.0] IU/L at outpatient follow-up and WCC from 11.8 [8.5–14.3] x10^9/L to 8.8 [6.5-10.2]x10^9/L, p=0.001 and 0.036 respectively. Pleural opacity on CXR improved in most (84.2%) patients. Post-infective pleurodesis developed in 11 patients allowing IPC removal. Length of hospital stay was 7 [6-9] days. No significant complications (including bleeding) associated with tPA/DNase therapy were observed.

Conclusion: Intrapleural tPA/DNase therapy can be safely administered via IPC for pleural infection and provides a high cure rate.

TO 078

PREVIOUS PLEURAL INJURY INCREASES PNEUMOTHORAX RISK POST-ENDOBRONCHIAL VALVE INSERTION FOR BRONCHOSCOPIC LUNG VOLUME REDUCTION

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Introduction/Aim: Bronchoscopic lung volume reduction (BLVR) via endobronchial valve (EBV) insertion is an accepted treatment for patients with severe emphysema. The most common complication of EBV insertion is pneumothorax, with a reported incidence of up to 25%. The aim of this study was to determine if previous pleural injury, or paraseptal/panlobular emphysema morphological subtype, would contribute to pneumothorax risk post-EBV insertion.

Methods: EBV insertion for BLVR that occurred in Adelaide, South Australia over the period 2014 to September 2017 were examined in 3 centres: the Royal Adelaide Hospital, The Queen Elizabeth Hospital, and ChestCare Clinic.

Emphysema subtype was determined by evaluating pre-EBV CT chest scans. The presence of pleural injury was determined by assessing patients for previous pneumothorax, pleural instrumentation, and pleural plaques/nodules in their pre-EBV CT chest scans.

Results: 86 procedures were completed within the study timeframe. 13 (15.1%) procedures resulted in pneumothorax. Mean age at EBV insertion was 67.31 years. 54.6% (47/86) of EBV insertions occurred in male patients. Statistical analysis was undertaken via logistic regression.

Previous pleural injury significantly increased the risk of pneumothorax post-EBVI (OR 22.55, 95% confidence interval 2.51-202.51, p = 0.005,). Gender, age at EBV insertion, and paraseptal/panlobular emphysema subtypes did not significantly increase pneumothorax risk.

Conclusion: This is the first Australian study to examine risk factors for pneumothorax incidence in EBV insertion. Previous pleural injury significantly increases the pneumothorax risk after EBV insertion. This data will contribute to our ability to predict pneumothorax in patients evaluated for EBV insertion, thus allowing improved risk assessment, and facilitating discharge planning post-EBV insertion. We plan further studies evaluating other possible risk factors, including quantitative CT scoring of pleural adhesions.

TO 079

EPITOME (EARLY PLEURODESIS VIA INDWELLING PLEURAL CATHETER WITH TALC FOR MALIGNANT EFFUSIONS): A PILOT STUDY OF THE STATE-OF-THE-ART MANAGEMENT ALGORITHM

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Introduction: Talc pleurodesis (TP) and indwelling pleural catheter (IPC) are recognized treatments for malignant pleural effusions (MPEs); each with its own advantages. Combining them can potentially provide best fluid control, facilitate early IPC removal, minimize re-intervention, hospitalization, long term IPC costs and complications.

Methods: A single-centre pilot study of a new treatment algorithm, EPIToME. All patients with symptomatic MPEs requiring definitive treatment were offered inpatient IPC (unless contraindications) insertion. Upon complete drainage (usually overnight), CXR was performed. If the lung full re-expanded, talc slurry (4g) was instilled via the IPC and patient discharged the following day with daily IPC drainage using suction-bottle for 10-14 days (longer if continual reduction of drainage volumes). IPCs were removed if pleurodesis was successful (defined as fluid drainage <50ml for 3 consecutive drainages without significant residual effusion on imaging). Patients with trapped lung, or contraindication to talc, were discharged with IPC and drainage when symptomatic. Data were presented as median [IQR].

Results: Patients with MPE (n=40: 60% male, median age 70) from metastatic cancers (47.5%) or mesothelioma were included. A median volume of 2.5 [1.9-3.5] litres were drained within 24 hours of IPC insertion. Sixteen patients fulfilled the criteria and received talc instillation via the IPC, usually one day post-IPC insertion. The median total hospitalization was 3 [2-3] days. Nine patients (56%) achieved pleurodesis after median of 14 days [11-27] and underwent catheter removal with no evidence of recurrence; median follow-up 116 [81-55] days. Talc was not administered in 24 patients due to trapped lung (50%), prior failed talc pleurodesis (21%), etc. Complications of talc included reversible tube blockage (n=2), self-limiting fever (n=2) and subsequent development of symptomatic loculations (n=3 successfully managed tube drainage ± intrapleural tPA).

Conclusion: The EPIToME protocol combining IPC and talc pleurodesis is feasible, safe and has potential advantages over individual therapies.

Pulmonary Physiology & Sleep 1

TO 080

OBSTRUCTIVE SLEEP APNOEA EPIDEMIOLOGY IN THE BUSSELTON HEALTHY AGEING STUDY (BHAS)

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Introduction/Aim: Obstructive sleep apnoea (OSA) is common and associated with significant morbidity and mortality. There are few objective prevalence data in Australia, particularly for women. In Busselton, Western Australia, the prevalence of OSA (respiratory disturbance index >15) was estimated in 1990 at 4.7% in men, and in 2007 (N=793) at 12.4% in men and 5.7% in women (apnea-hypopnea index (AHI)>15 in participants without known OSA). We assessed OSA prevalence in the Busselton Healthy Ageing Study, a comprehensive health study of both sexes aged 46-64 years.

Methods: Between 2010 and 2015, all residents on the Busselton Shire electoral roll born 1946 to 1964 were invited to participate, with 75% participation (N=5,082). Dual channel ApneaLink devices for home sleep study were issued to 3,745 participants (73.7%) and 2,707 (53.3%) collections were suitable for analysis. The prevalence of OSA was defined by the AHI obtained from the ApneaLink automated event scoring algorithm, and its relation to demographic data and co-morbidities was assessed. Moderate and severe OSA were defined as AHI≥15 and ≥30 respectively.

Results: The prevalence of OSA (AHI>15) 20.4% in men and 10.1% in women (see table). Increasing OSA severity was associated with increased BMI and alcohol use in both sexes, and with sleepiness in men only.

	Men			**p**	**Women**			**P**
AHI	<15	15-29.9	≥30		<15	15-29.9	≥30	
n (%)	958 (79.6)	183 (15.2)	63 (5.2)		1352 (90)	121 (8.1)	30 (2)	
BMI, kg/m2	27.9 ±3.7(SD)	29.7 ±4.4	31.3 ±5.3	<0.001	27.7 ±5.2	31.1 ±6.5	32.3 ±8.5	<0.001
Alcohol, glasses/wk	15.1 ±14.5	17.4 ±16.2	21.8 ±19.3	<0.001	6.9 ±8.2	5.2 ±8.8	5.0 ±6.7	<0.001
ESS	6.0 ±3.7	6.6 ±4.1	7.2 ±4.0	0.01	5.6 ±3.7	6.2 ±3.8	5.9 ±3.5	0.165

Compared with AHI<15, an AHI>15 was associated with: hypertension in both sexes (p<0.001); with current depression in men only (20.3% vs 13.3%, p=0.005); and with diabetes (11.3% vs 5%, p=0.002) and cancer (22.5% vs 14.9%, p=0.014) in women only.

Conclusion: The prevalence of OSA in Busselton has increased, and the prevalence in women is higher than previously reported. Sex-based differences in comorbidities are observed.

CORTICAL CONTRIBUTION TO QUIET BREATHING IN COPD IS ASSOCIATED WITH AGEING

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Introduction/Aim: Current evidence indicates that inspiratory loads engage cortical mechanisms to defend ventilation. A cortical contribution to breathing is determined via the presence of a Bereitschafts (readiness) potential – a low amplitude negativity which begins ~1s before inspiration. In chronic obstructive pulmonary disease (COPD), changes in the lung, chest wall and respiratory muscles induce an inspiratory load. We hypothesised that there is a cortical contribution to quiet breathing in COPD and that a cortical contribution to inspiratory threshold loading is related to dyspnoea – a major symptom of COPD.

Methods: Electroencephalographic activity (EEG) was recorded in 15 COPD patients (10 males; age: 57-87) and 30 healthy controls (15 age-matched and 15 young) during quiet breathing and inspiratory threshold loading (10% maximal inspiratory pressure). Two blinded observers evaluated the presence of Bereitschaftspotentials prior to inspiration from ensemble averages of 80 or more epochs of EEG at Cz and FCz. Dyspnoea was rated using a modified Borg scale.

Results: The incidence of a cortical contribution to quiet breathing was significantly greater in the COPD patients (7/15) than the young (0/15) ($P < 0.01$), but not the age-matched (5/15) ($P = 0.46$), controls. A cortical contribution to inspiratory threshold loading was associated with higher Borg scores in the young ($P < 0.05$), but not the age-matched controls ($P = 0.25$) or the COPD patients ($P = 0.43$).

Conclusion: This study provides evidence that age, rather than COPD, is associated with a cortical contribution to quiet breathing. A cortical contribution to inspiratory threshold loading may be associated with more severe dyspnoea, at least in healthy young people.

USE OF CLOUD BASED TECHNOLOGY TO OPTIMISE CPAP INITIATION IN OSA

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Introduction/Aim: Despite advances in technology of Continuous Positive Airway Pressure (CPAP) in the treatment of Obstructive Sleep Apnea (OSA) and well validated benefits in quality of life and health outcomes, long term adherence remains a major challenge. Remote access cloud based technology has become a standard feature of new CPAP devices. Currently, this feature may not be optimally utilised to improve compliance and patients' experience with CPAP.

We sought to determine whether, remote based assessment of CPAP usage at regular intervals with follow up telephone assessment could improve CPAP usage and Epworth sleepiness score (ESS) in patients commencing CPAP therapy for OSA through a well-supported sleep service.

Methods: We sought to prospectively assess 50 consecutive patients commencing CPAP therapy for OSA. Each patient had CPAP usage remotely assessed at weeks 1, 3, 6 and 9 post commencement. Telephone assessment with a standardised questionnaire was carried out at each interval if CPAP usage was <4/hrs per night. CPAP usage and final ESS were compared to 50 consecutive retrospective controls. Current preliminary data includes 37 of target 50 patients in the intervention group.

Results: The mean age was 56.1 ± 14.5 years (SD) vs 52.5 ± 14.4, Body mass index (BMI) 37.0 ± 9.1 vs 37.7 ± 7.4 kg/m^2, Apnea Hypopnea Index (AHI) 46.5 ± 29.0 vs 46.2 ± 29.0 events/hour and baseline ESS 8.8 ± 5.3 vs 10.6 ± 5.3 in control and intervention groups, respectively.

There was no significant difference in CPAP usage between control group and intervention group at 1week: 5.0 ± 2.6 vs 4.4 ± 2.7 hours (SD) (p=0.55); 3weeks: 4.8 ± 2.6 vs 4.2 ± 2.6 hours (p=0.49); 6weeks: 4.6 ± 2.5 vs 4.4 ± 2.8 hours (p=0.90); or 9weeks: 4.3 ± 2.5 vs 5.2 ± 2.8 hours (p=0.23), respectively. Additionally, there was no significant difference in change in ESS score -0.6 ± 5.6 vs -2.7 ± 4.3 (p=0.24), respectively.

Conclusion: Regular interval remote based assessment of CPAP usage in OSA, in addition to usual care, does not improve 2-month CPAP usage or ESS.

TO 083

RETROSPECTIVE CASE-CONTROLLED STUDY OF OBSTRUCTIVE SLEEP APNOEA IN DOWN SYNDROME

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Introduction/Aim: Down syndrome (DS) is associated with multiple health issues including obstructive sleep apnoea (OSA). Dysmorphic craniofacial features inherent to DS predispose to OSA. The aims of this study were to ascertain the prevalence and severity of OSA in DS adults and identify possible barriers/enablers to treatment by comparing demographic and polysomnography (PSG) indices, continuous positive airway pressure (CPAP) prescription rates and adherence in DS adults matched to a group of non-DS adults referred for a sleep study at Repatriation General Hospital.

Methods: Data were collected from electronic and paper-based records. DS patients with OSA were identified by case review and compared to a randomly selected matched gender, age (± 3), body mass index (BMI) ($\pm 3 kg/m^2$) and study date (± 90 days) (ratio1:3). Between group comparisons were conducted using independent samples t-tests and Mann-Whitney U tests for continuous data and Fisher's or Chi^2 tests for categorical variables.

Results: 30 DS were matched with 58 non-DS patients for gender, age (mean$\pm$SD 38.8$\pm$12.5 versus 41.4$\pm$12.4 years) and BMI (34.9$\pm$9.1 versus non-DS 32.8$\pm$6.8 kg/m^2). 28 (93%) DS had OSA compared to 32 (55%, p<0.001) non-DS patients. 25 DS (92.8%) and 15 non-DS (46.9%) patients with OSA were commenced on CPAP (p<0.001). DS had more severe OSA (total apnoea hypopnoea index 56.4[28-73.8] (median [IQR]) versus controls 15.5[4.4-17.6]). CPAP adherence at 6 months: average hours use DS 4.6$\pm$0.7 (mean$\pm$SEM) versus controls 6.4$\pm$0.6 in controls (p=0.044). There was similar intensity of follow up visits in the first year after CPAP initiation: DS 5.0$\pm$0.5 (mean$\pm$SEM) versus controls 4.1$\pm$0.6 (p=0.288). DS patients with higher intensity of supervision overnight had better CPAP compliance.

Conclusion: DS patients had significantly more severe OSA but reduced CPAP adherence. Further research is required to elucidate barriers to treatment and potential solutions to improve CPAP compliance amongst DS patient with OSA.

Declaration of Interest: Nil

TO 084

ARTIFICIAL INTELLIGENCE HELPS DETECTING LUNG DISEASE WITH PULMONARY FUNCTION TESTS

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Introduction/Aim: Pulmonary function testing (PFT) is a main tool to evaluate the function of the respiratory system. However, used alone, it hardly leads to disease diagnosis. Based on artificial intelligence (AI) we aimed to develop a smart software which improves the clinical reading of a lung function and suggests a respiratory disease diagnosis if possible.

Methods: Data of 1430 subjects with respiratory symptoms were taken from 33 Belgian hospitals to develop the algorithm. The final diagnosis (healthy, asthma, COPD, ILD, neuromuscular disease, chest wall or pleural disease, pulmonary vascular disease, other obstructive disease) was obtained from clinical history, lung function and all additional tests, and confirmed by an expert panel. A cloud-based solution was incorporated into clinical setting to validate the accuracy of the algorithm on a random sample of 136 new subjects. Finally, the software diagnoses were compared with the diagnostic opinions of 85 pulmonologists (from 11 different European hospitals) provided with PFT and clinical data of 50 new subjects.

Results: At development, software presented a high accuracy of 74% after 10-fold cross-validation when detecting lung diseases (8 possible disease categories). During validation, the high accuracy was maintained in a real clinical setting (76%). At the external multicentric validation, the software-based automated diagnoses (82% accuracy) were superior over the suggested diagnoses of 85 pulmonologists (44.6 $\pm$ 3.7 % mean accuracy). Great disagreement between readers is observed with a low kappa score of 0.34.

Conclusion: AI can be used to identify different lung diseases. Due to its superiority and work consistency, such software can provide a powerful decision support system in daily clinical routine.

Asthma & Allergy 3

THE ASSOCIATION BETWEEN REGIONAL LUNG DISTENSION AND GENE EXPRESSION DURING MECHANICAL VENTILATION

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Introduction/Aim: Mechanical ventilation, a lifesaving therapy for patients with respiratory failure, contributes to mortality by inducing inflammation, which can lead to multisystem organ failure. Different regions of the lung have been shown to heterogeneously respond to mechanical ventilation, however, the association between this variation in regional lung distension and regional lung inflammation is unknown. The aim of this study was to assess this association in the healthy lung.

Methods: We ventilated two groups of adult BALB/c mice (n = 8 per group) for 2 h using a protective [low tidal volume with moderate positive end expiratory pressure (PEEP)] or injurious [high tidal volume with zero PEEP] ventilation strategy. RNA levels of 19 genes were quantified regionally by qPCR array. Gene expression was correlated with regional FRC, tidal volume and distension (FRC + tidal volume). FRC and tidal volume were obtained from analysis (cross-correlation-based velocimetry) of dynamic high-resolution (phase contrast) 4DCT lung images at baseline and after two hours of ventilation.

Results: Two genes had differential regional expression that varied between ventilation strategies (IL-6, P=0.02 and Ccl-2, P<0.01). The expression of these genes was positively correlated with regional tidal volume and distension (P<0.05 for all correlations). The expression of Cxcl2, Tnf-α, Wnt1, c-fos and Nfe2l2 also varied between ventilation strategies (P<0.01), but they did not appear to be associated with FRC, tidal volume or distension.

Conclusion: We have demonstrated associations between regional gene expression and tidal volume. Our results provide critical insight into the regional lung response to mechanical ventilation. In particular, these results highlight the importance of the balance between under-ventilation and over-stretch (tidal volume) and how each of these can contribute to lung inflammation and, potentially, patient outcomes.

ORAL CORTICOSTEROID USE IN ASTHMA PATIENTS: AN EASY WAY OUT

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Introduction/Aim: Although significant progress has been made in asthma management, 5-10% of patients have severe asthma (SA) that is associated with increased morbidity, mortality and an economic burden. Within this group, 30-40% of patients are prescribed continuous or near-continuous oral corticosteroids (OCS) to achieve or maintain asthma control. However, in primary care, a subset of these patients may exist with poor asthma management practices and thus less severe disease, relying on OCS to achieve asthma control instead of regular inhaled preventer medication. The aim of this study is to identify patterns of medication taking behaviour and describe the respiratory status of people with asthma in primary care. This will allow for the development of a framework that identifies patients based on asthma severity through medication records.

Methods: Patient data (n=493) was utilised from a quality-controlled community pharmacy database. Correlational analysis and regression modelling were employed to determine potential predictors of asthmatic oral corticosteroid users (n=72) based on asthma severity, lung function, symptom control, comorbidities, adherence, inhaler technique and medication management.

Results: Fifteen percent of asthmatics recruited were prescribed OCS in the last 12 months. Ninety-three percent of OCS users were classified as having poor asthma control, 96% identified potential barriers to non-adherence (determined by the Brief Medication Questionnaire (Svarstad BL et al. 1999)), and 86% had incorrect inhaler technique. Significant relationships were found between OCS users and ownership of an asthma action plan (p<0.00), the existence of depression (p=0.002) and eczema (p=0.02), potential for non-adherence (p=0.018), poor asthma control (p<0.00), poor lung function test (p=0.04) and a higher prescribed rate of inhaled combination therapy (p<0.000), including a higher rate of visits to the doctor regarding asthma (p=0.044).

Conclusion: This research has uncovered a heterogeneous group of people with asthma in primary care, with less severe disease who put themselves at risk of exacerbations due to their medication taking behaviour. By better understanding the behaviour of individuals in the context of their day-to-day management, we will be able to tailor interventions for these patients reflecting current guidelines.

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WORKING WHILE UNWELL: WORKPLACE IMPAIRMENT IN PEOPLE WITH SEVERE ASTHMA

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Introduction/Aim: Severe asthma substantially impairs quality of life and may impair workplace productivity, although this has rarely been quantified. The aim of this study was to compare workplace impairment in severe and non-severe asthma over time, and identify characteristics associated with presenteeism in severe asthma.

Methods: Patients were enrolled in the Severe Asthma Web-based Database (SAWD), an ongoing observational registry of 434 patients with severe refractory asthma and 102 with non-severe controlled asthma from 26 sites across Australia, New Zealand and Singapore (18 to 88 years; 59% female). Participants provided baseline clinical and questionnaire data and were followed-up every 6 months until 24 months. Workplace absenteeism (% time absent from work), presenteeism (% self-reported impairment at work) and activity impairment (% self-reported impairment in daily activities outside work) in the past week were derived from a validated questionnaire.[1]

Results: Half of participants were employed at baseline. A quarter of workers reported absenteeism and two-thirds reported presenteeism. People with severe compared with non-severe asthma were 3.15 times more likely to report presenteeism (95%CI 1.75-5.69) and 2.26 times more likely to report daily activity impairment (95%CI 1.44-5.54). Having poorer asthma control or more exacerbations in the previous year was associated with greater absenteeism, presenteeism and activity impairment (all p<0.05). Worsening asthma control scores were associated with increasing presenteeism over time (time interaction p=0.011). In participants with severe asthma, worse asthma control (p<0.001), asthma-related quality of life (p<0.001), depression symptoms (p=0.001) and anxiety symptoms (p=0.002) were associated with greater odds of presenteeism.

Conclusion: Impaired work and non-work functioning are important components of the disease burden of severe asthma. Optimising workplace productivity requires improvement in asthma control and attention to mental health. Absenteeism and presenteeism may be key metrics for assessing intervention efficacy among people with severe asthma of working age.

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CASEIN KINASE 1DELTA/EPSILON: A NOVEL PATHWAY SENSITIZING GLUCOCORTICOID ACTIVITY

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Introduction/Aim: Glucocorticoids (GCs) remain central to treatment of asthma, but therapeutic responses are impaired in severe asthma and during asthma exacerbation. Our laboratory found TGF-β1 *per se* impairs GC activity, and is a key mediator of viral infection-induced GC insensitivity in airway epithelium. The key CLOCK component CK1δ/ϵ, implicated in TGF-β1 signalling, also regulates GCs activity. In the current study, we demonstrate that targeting CK1δ/ϵ prevents TGF-β1-indcued GC insensitivity, and attenuates virus mimic Poly (I:C)-induced inflammatory responses.

Methods: Differential expression of CK1δ/ϵ was assessed by IHC in human asthmatic cohort. GC responsiveness of bronchial epithelial cells (BEAS-2B, air-liquid interface (ALI)-differentiated primary human bronchial epithelial cells (HBEC)) in the presence of TGF-β1 was assessed by RT-qPCR and GRE-SEAP. Poly (I:C)/TNF-α-induced inflammatory responses in BEAS-2B cells was assessed by ELISA. The potential involvement of CK1δ/ϵ in the above experimental settings was determined using pharmacological (PF670462) and genetic (siRNA) approaches.

Results: CK1δ expression was significantly higher in the airway wall of severe asthmatics compared to well-controlled asthma and healthy subjects. In BEAS-2B cells and ALI-HBECs, TGF-β1 suppression of GC-induced GRE activity and endogenous gene expression was prevented by CK1δ/ϵ (3μM PF670462). Poly (I:C)/TNF-α-induced pro-inflammatory cytokines (IL-6, IL-8 and GM-CSF) were attenuated by inhibition of CK1δ/ϵ using 3μM PF670462 and CK1δ/ϵ-targeting siRNAs.

Conclusion: We have identified CK1δ/ϵ as a novel target with therapeutic potential to restore anti-inflammatory efficacy of GCs in severe asthma and asthma exacerbation.

A SPUTUM SIX GENE SIGNATURE PREDICTS INFLAMMATORY AND EXACERBATION PHENOTYPES IN UNCONTROLLED MODERATE-TO-SEVERE ASTHMA: AN AMAZES SUB-ANALYSIS

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Introduction/Aim: Improved diagnostic tools for predicting airway inflammatory phenotype and future exacerbation frequency in asthma are required. We previously demonstrated a sputum gene expression signature of 6 biomarkers (6GS) could predict inflammatory phenotype and corticosteroid responsiveness in stable asthma. We recently demonstrated that azithromycin add-on treatment in uncontrolled moderate-to-severe asthma significantly reduced asthma exacerbations (AMAZES clinical trial). We aimed to test whether the 6GS predicts airway inflammatory and future exacerbation phenotypes in a subpopulation of the AMAZES clinical trial. We also tested whether 48 weeks of azithromycin treatment altered 6GS expression compared to placebo.

Methods: 142 patients (73 placebo-treated, 69 azithromycin-treated) produced adequate sputum for differential cell count and PCR of 6GS markers at baseline and after 48 weeks of treatment. Logistic regression and ROC analysis was performed on baseline results to compare the predictive value of 6GS and conventional biomarkers for airway inflammatory phenotype and future exacerbation frequency.

Results: The 6GS significantly predicted airway inflammatory subtype at baseline, outperforming systemic biomarkers peripheral blood eosinophils (PBE) and fractional exhaled nitric oxide (FENO). 6GS significantly predicted future exacerbation phenotype, was numerically superior to all biomarkers examined (sputum eosinophils, sputum neutrophils, PBE and FENO), and identified patients who would go on to experience frequent ($\geq$ 2/year) severe exacerbations. Azithromycin treatment did not significantly alter 6GS expression compared to placebo, nor did it affect the prediction of exacerbation phenotype using the 6GS.

Conclusion: The sputum 6GS is useful as a diagnostic tool for inflammatory phenotyping and predicting future frequent severe exacerbations. The 6GS retains this predictive capacity in azithromycin-treated asthma, suggesting a novel therapeutic mechanism independent of known exacerbation-associated inflammatory factors.

THE EFFECT OF TREATMENT WITH OMALIZUMAB ON ANTIVIRAL RESPONSES IN ADULTS WITH SEVERE ALLERGIC ASTHMA

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Introduction/Aim: Severe asthma is characterised by frequent exacerbations, that lead to poor asthma control and worsened quality of life. Tthe majority of these exacerbations are triggered by viral respiratory tract infections. Poorly controlled asthma is associated with impaired antiviral immune responses. Treatment of severe allergic asthma with Omalizumab, a monoclonal antibody against IgE, has been shown to improve asthma control and reduce exacerbation risk. We sought to determine if treatment with Omalizumab resulted in improvement in antiviral innate immune responses to influenza A (IAV) and rhinovirus (RV).

Methods: We recruited 10 adults, with poorly controlled allergic asthma; atopic to one or more aeroallergens, on maximal dose inhaled corticosteroid/ long acting bronchodilators, with persisting poor asthma symptom control, exacerbations requiring oral corticosteroids and a serum total IgE >30IU/ml. They were compared to healthy aged matched controls with no asthma or atopy. Participants were assessed prior to commencing treatment with Omalizumab and then 6 months later at the time effectiveness of treatment was assessed. Blood was drawn and peripheral blood monocytes (PBMCs) were isolated. PBMCs were then exposed for 48 hours to IAV, and RV.. Response was assessed by ELISA/bead arraywith release of interferon (IFN)-α, IFN-λ, IFN-γ, IL-6, IL-10, IL-5 and IL-13.

Results: At baseline visit subjects with severe allergic asthma compared to healthy controls demonstrated impaired IFN-α, and IFN-λ release in response to IAV ($p<0.001$) and RV ($p=0.003$). Following 6 months treatment, 9/10 demonstrated an improvement in asthma symptom control to continue treatment. In the clinical responders there was a significant increase seen in IFN-α, and IFN-λ to IAV and a trend towards improvement to RV.

Conclusion: Adults with severe allergic asthma demonstrate impaired systemic innate immune responses to IAV and RV. Treatment with Omalizumab, that results in improved asthma control is associated with improvement in innate antiviral responses.

SEVERE ASTHMA TREATABLE TRAITS: PREVALENCE AND EXACERBATION PREDICTION

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Introduction/Aim: Treatable traits (TT) have been proposed as a new approach for airway disease management, however supporting data are currently limited. We aimed to determine if identification of TT is possible using a severe asthma registry, to assess their prevalence in severe compared to non-severe asthma, and to assess the relationship between TT and future exacerbation risk.

Methods: The Severe Asthma Web-based Database is an observational registry of 434 severe asthma patients and a comparison group of 102 patients with non-severe asthma from 26 sites in Australasia (18-88 years, 59% female). Participants were characterised at enrolment and followed for 24 months. Published traits[1,2] were mapped to registry data fields and prevalence determined. Bayesian model averaging was applied to identify traits that best predicted future exacerbation risk.

Results: Seven pulmonary, 13 extrapulmonary and 4 behavioural risk-factor traits were identified. More pulmonary and extrapulmonary traits were expressed in severe than non-severe asthma (p<0.001). Traits significantly more common in severe asthma were incompletely reversible airflow limitation (58% vs. 39%, p=0.002), frequent exacerbations (51% vs 6%, p<0.001), neutrophilic airway inflammation (23% vs 4%, p=0.023), obesity (49% vs 27%, p<0.001), systemic inflammation (41% vs 13%, p<0.001), reflux (49% vs. 36%, p=0.021), inhaler-device polypharmacy (29% vs. 18%, p=0.018) and Aspergillus sensitisation (39% vs 19%, p<0.001). During follow-up, patients with severe asthma reported more exacerbations (median [IQR]: 2 [0-4]) than non-severe (0 [0-2]; IRR 2.33, p<0.001). Each additional trait was associated with a 13% increase in exacerbation risk (p<0.001). Previous exacerbations, inhaler-device polypharmacy, sleep apnea and depression best predicted exacerbation risk.

Conclusion: A registry-based systematic characterisation of asthma may be used to assess TT. We report traits that predict exacerbation risk and confirm greater burden associated with severe asthma. Trials evaluating the efficacy and cost-effectiveness of the TT approach are needed.

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THE UNFOLDED PROTEIN RESPONSE VARIES BETWEEN INFLAMMATORY PHENOTYPES OF ASTHMA

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Introduction/Aim: Asthma is a chronic inflammatory airway disease which is characterized by recurrent attacks of breathlessness and wheezing. The pathogenesis of asthma is complex and still unclear. The unfolded protein response (UPR) of the endoplasmic reticulum (ER) has recently been identified as playing a decisive role in inflammatory diseases. Worsening of asthmatic condition can be brought on by stimuli such as oxidative stress, pathogenic infection, and allergen exposure. All of which can induce ER stress and activate UPR. Activated arms of UPR induce different inflammatory pathways and dysregulate the innate immune response. However, how UPR is associated with asthma is unclear. Here we investigate the UPR signature in different inflammatory phenotypes of asthma using human clinical samples.

Methods: Broncho alveolar lavage fluid (BALF), endobronchial biopsies and induced sputum samples were collected from eosinophilic, neutrophilic, paucigranulocytic asthma patients, and from healthy individuals. The expression of UPR associated genes in BALF cells, and biopsy samples were analysed by qPCR. UPR related protein expressions was analysed by immunoblot. UPR gene expression in sputum cells were analysed by microarray.

Results: UPR genes (GRP78, CHOP, XBP1s, and PDIA4) in lung immune cells were significantly induced (p<0.05) in eosinophilic asthma while neutrophilic asthma demonstrated an increased trend. GRP78 and CHOP protein expression were significantly higher in both eosinophilic and neutrophilic groups. Microarray data from sputum cells demonstrated an upregulation of various UPR genes mostly in the eosinophilic asthma group, but not in paucigranulocytic or mixed granulocytic groups. UPR gene expression in lung biopsies did not show significant differences between groups. However, bronchial epithelial cells (BECs) treated with asthma allergens demonstrated an increased trend of UPR.

Conclusion: UPR is heightened in eosinophilic and neutrophilic asthma. Airway immune cells have a major role in regulating UPR in airways of asthma.

PLASMA CELL AND REGULATORY B CELL-INFILTRATION IN THE LUNGS OF BLEOMYCIN-TREATED MICE

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Introduction: STAT3 and B cells are implicated in the development of lung fibrosis. We have previously demonstrated that hyper-activated STAT3, B cell-deficient gp130[757F];$\mu MT^{-/-}$ mice are protected from bleomycin (BLM)-induced lung fibrosis suggesting that B cells are important in the regulation of STAT3-mediated fibrosis.

Hypothesis: We hypothesise that the pro-fibrotic effects of STAT3 involve B cell-mediated immune regulation.

Methods: The effect of anti-CD20 therapy in bleomycin-treated wild-type and gp130[757F] mice on lung fibrosis and immune cell composition was examined. Mice were given two 100μg doses of anti-CD20 antibody (Genentech Inc USA) or IgG2a isotype control i.p. either 7 days prior to and 7 days after bleomycin or on day 10 and day 19 post-bleomycin treatment (following the initiation of fibrosis), and the extent of fibrosis measured at 28 days.

Results: FACS analysis of blood taken on days 0, 7 and 28 days post-bleomycin-treatment revealed an almost complete depletion of CD19 + B cells in the circulation of wildtype mice but not gp130[757F]. However, the extent of fibrosis, assessed using micro-CT imaging and HPLC analysis of hydroxyproline levels was not significantly different between treatment groups. Histological analysis revealed an abundance of CD5+ B cells and CD138+ (plasma cells) in the lungs of the anti-CD20-treated mice. FACS analysis identified an expansion of CD138+ (days 7 and 28) and CD5+ cells in the lungs of bleomycin treated mice at day 28.

Conclusion: Although antibody depletion of follicular B cells had no effect on bleomycin-induced fibrosis, residual CD138+ plasma cells and CD5+ B are abundant in the lungs of bleomycin-treated mice. The activity of these B cell subsets may contribute to the fibrotic phenotype.

THE EFFECT OF THE DIETARY ω-6 POLYUNSATURATED FATTY ACID, ARACHIDONIC ACID, ON AIRWAY INFLAMMATION AND REMODELING IN COPD

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Introduction/Aim: Obesity appears to have protective effects on lung pathology and inflammatory responses in COPD, however, the underlying relationships between obesity, diet and disease outcomes in COPD are not fully understood. This study explored the relationship between the dietary ω-6 polyunsaturated fatty acid (PUFA) arachidonic acid (AA) and airway inflammation and remodeling, in primary human pulmonary fibroblasts *in vitro* from people with and without COPD. Also, the effect of body mass index (BMI) on the inflammatory response was assessed.

Methods: Primary human lung fibroblasts derived from COPD patients and non-COPD patients were challenged with BSA-conjugated AA for 48hr. Release of the pro-inflammatory cytokines, IL-6 and CXCL8, was measured using ELISA. Messenger RNA (mRNA) expression of the extracellular matrix (ECM) proteins, fibronectin (FN), collagen I (COL I) and tenascin (TNC) was measured using quantitative PCR.

Results: We found that challenge with AA results in increased IL-6 and CXCL8 release from fibroblasts, however IL-6 ($p<0.001$) and CXCL8 ($p<0.05$) release in COPD (*n=12*) was lower compared to non-COPD (*n=24*). Regression analysis revealed no relationship between BMI and cytokine release in COPD. AA reduced basal FN ($P<0.01$) and COL I ($P<0.05$) mRNA expression in fibroblasts from COPD patients (*n=5*).

Conclusion: This study demonstrates that AA, commonly found in obese diets, affects inflammatory processes and ECM deposition in COPD. COPD cells compared to non-COPD cells are hyporesponsive to AA, suggesting that in COPD meals rich in ω-6 PUFAs are not as potent in the induction of inflammatory responses compared to other lung diseases. However, the reduced capacity to produce ECM proteins could negatively affect healing processes which is likely to manifest as perturbed and excessive tissue remodeling in COPD.

TO 095

LYMPHOCYTE SENESCENCE IN COPD IS ASSOCIATED WITH DECREASED SIRT1 EXPRESSION IN STEROID RESISTANT PRO-INFLAMMATORY LYMPHOCYTES

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Introduction: Class III NAD-dependent histone deacetylase (HDAC) sirtuin 1 (SIRT1) is an important regulator of senescence, aging and inflammation through de-acetylation of chromatin histones thereby silencing inflammatory gene transcription. We have reported increased steroid resistant senescent pro-inflammatory CD28nullCD8+ T cells in patients with COPD. We hypothesized that expression of SIRT1 would be reduced in these cells in COPD and that treatment with SIRT1 activators (resveratrol) and agents that prevent NAD depletion (theophylline) would upregulate SIRT1 expression and reduce pro-inflammatory cytokine expression in these steroid resistant cells.

Methods: Blood was collected from COPD patients and aged matched controls and expression of CD28, SIRT1 and pro-inflammatory cytokines determined in CD8+ and CD8- T and NKT-like cells cultured in the presence of $\pm$ 1μM resveratrol $\pm$ 5.0mg/mL theophylline $\pm$ 1 μM prednisolone using flow cytometry.

Results: Decreased SIRT1 expression was identified in CD28nullCD8+T and NKT-like cells compared with CD28+ counterparts from both patients and controls (eg., CD28null 7$\pm$3% vs. CD28+ 55$\pm$5%). Loss of SIRT1 was associated with increased production of IFNγ and TNFα and steroid resistance. SIRT1 expression was upregulated in the presence of 1μM resveratrol and 5.0mg/mL theophylline and was associated with a decrease in steroid resistance and IFNγ and TNFα production by CD28nullCD8+T and NKT-like cells.

Conclusion: Steroid resistance in pro-inflammatory CD28nullCD8+ T and NKT-like cells is associated with decreased SIRT1 expression. Combination resveratrol and/or theophylline treatment increases SIRT1 expression, restores steroid sensitivity and inhibits pro-inflammatory cytokine production from these cells and may reduce systemic inflammation in COPD.

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TO 096

ESTROGEN AFFECT THE IMMUNE SYSTEM AND LEADS TO MORE SEVERE ASTHMA IN FEMALES

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Introduction/Aim: Women have a higher incidence of asthma compared to men and exacerbations in women are often more severe and correlate with high estrogen levels. Using an experimental animal model for asthma, we have observed that female rats with experimental asthma also develop more severe exacerbations compared to male rats. The aim of the study was to investigate if the female sex hormone estrogen can impact the asthma response and identify the immunological mechanism for this effect.

Methods: By implanting estrogen-releasing pellets into male rats prior to ovalbumin-sensitisation and re-challenge we investigated how estrogen-exposed males responded compared to untreated males and females. We used multi parameter flow cytometry to investigate proportion and activation of antigen presenting dendritic cells, responding T effector and regulatory T cells in airways before and after allergen re-challenge.

Results: We discovered that estrogen was sufficient to induce a female-like disease phenotype during exacerbations in male rats. Interestingly, male and female rats also displayed significant differences in CD4+/CD8+ T cell ratios in airway draining lymph nodes and this was directly impacted by estrogen exposure. In addition, female and estrogen treated male rats, but not male rats, displayed signs of recruitment of CD4+ cells into the airways following allergen re-challenge which most likely contributed to the exacerbated response.

Conclusion: Our data suggest that estrogen is sufficient to induce female like asthma symptoms in male rats and appears to alter the T cell balance promoting allergic responses.

PERSONALIZED CELL CULTURE MODEL FOR HIGH-THROUGHPUT SCREENING FOLLOWING CFTR CORRECTION

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Introduction and Aims: Small molecules can correct CFTR production or function and greatly improve CF outcomes. Rarer mutations are hindered by the lack of appropriate primary culture models. Modifying primary airway epithelial cells (AECs) from children with CF modified to express a fluorescence marker that allows functional CFTR assessment would provide a culture-based high-throughput screening platform. We compared methodologies to achieve stable fluorescence in primary AEC.

Methods: Primary AECs were obtained from children (CF and non-CF) by bronchial brushing and cultured using a conditional reprogramming methodology. Cells were transfected with a pcDNA3.1 plasmid via Lipofectamine® or Nucleofector™ device. Alternatively, AEC were transduced by a replication-deficient retroviral vector with fluorescent tag. After 48 hours, cells expressing fluorescence were selected by fluorescence activated cell sorting (FACS) flow cytometry and then expanded further in culture to assess stability of gene expression.

Results: Primary AECs were amenable to all three methodologies. Transfection by Lipofectamine® was 24.1% efficient and the best electroporation protocol achieved a slightly higher efficiency (30.0%). Replication deficient retrovirus was most effective with 78.9% positive cells. There was no difference in transfection efficiency observed between non-CF and CF AECs. Cells could be successfully cultured after FACS selection, but only AEC transduced by retroviral vector maintained their fluorescence through two passages of cultures.

Conclusion: Retroviral vector could stably induce fluorescence into primary AECs. We are constructing a retroviral vector containing the YFP gene and validating the CFTR functional assay across a range of CFTR mutations.

Chronic Obstructive Pulmonary Disease (COPD) 2

MANAGEMENT OF ACUTE COPD EXACERBATIONS: DO WE FOLLOW THE GUIDELINES?

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Introduction/Aim: Chronic Obstructive Pulmonary Disease (COPD) is the second leading cause of avoidable hospital admission in Australia, but to date no national data exists that compares the recommendations of clinical practice guidelines for inpatient management of acute exacerbations against actual practice. We aimed to compare contemporary management against the recommendations of the COPD-X guidelines.

Methods: A prospective audit of COPD hospital admissions from five tertiary care hospitals in five states in Australia was conducted. A standardised audit tool was used to collect data. Telephone follow-up at 28 days after discharge assessed readmission and health-status. Data were assessed against the COPD-X guidelines.

Results: Prospective data were obtained for 207 admissions in 171 patients between October 2012–April 2013. The mean±SD age was 70.2 ± 9.9 years, 50.3% were male, and 95.3% caucasian. The mean number of comorbidities per patient was 3.6 ± 1.9, with hypertension (48.5%), gastrointestinal disease (37.5%), ischaemic heart disease (28.5%), psychiatric/anxiety/depression disorders (28.1%) the most prevalent. Over half were ex-smokers (58.6%) and lived at home with another (56.2%). Of the 171 patients, 21.1% were readmitted within 28 days, there were 2 inpatients deaths (1.2%), and a further 9 deaths (5.3%) within 28 days of discharge.

Concordance to the COPD-X recommendations varied. Prescription of oral corticosteroids (95.1% [inter-hospital range 90-100%]), antibiotic therapy (89.2% [42.9-94.9%]), and performance of chest x-ray (99.5% [87.5-100%]) was high. However, performance of spirometry 22.3% (range 0-52.4%), written inpatient prescription of acute oxygen therapy 27% (range 3.2-76.9%), and referral to pulmonary rehabilitation 29.1% (range 10.3-50.8%) were poor.

Conclusion: Important gaps in management were seen nationally when compared against clinical practice guidelines.

Declaration of Interest: We declare that we have no conflicts of interest related to the above project.

ASSOCIATIONS OF TYPE-SPECIFIC PHYSICAL ACTIVITY WITH MORTALITY RISK IN COPD

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Introduction/Aim: To examine the dose-response associations between specific types of physical activity (PA) and mortality risk in people with chronic obstructive pulmonary disease (COPD).

Methods: A prospective cohort study was used. People with COPD aged ≥40 years were identified from the 1997 Health Survey for England and the 1998 and 2003 Scottish Health Survey cohorts. Self-reported walking, domestic PA, and sport/exercise were assessed at baseline, and were classified into three groups: 1) No participation in that type of PA (the referent group); 2) below the median level of activity of the cohort ('Low'); or 3) equal to or above the median level of activity of the cohort ('High'). The medians were 5.25 metabolic equivalent (MET)-hours/week for walking, 5.70 MET-hours/week for domestic PA, and 8.00 MET-hours/week for sport/exercise. Cox proportional hazards models were used to examine the association between PA and mortality risk.

Results: 2398 participants with COPD were included in the analysis (mean age (SD) 62.6 (11.5), mean FEV1% predicted 73.4% (25.4), 52% men). Over 8.5 (3.9) years follow-up, there were 571 deaths. Dose-response associations with mortality risk were demonstrated for walking and sport/exercise, but not for domestic PA. Compared to the referent group, participants in the 'High' walking group had a reduced mortality risk (hazard ratio (HR) 0.70, 95% confidence interval (CI) 0.56 to 0.88), as did participants in the 'High' sport/exercise group (HR 0.69, 95% CI 0.51-0.93). No significant mortality risk reductions were observed in the 'Low' groups for walking or sport/exercise.

Conclusion: Walking and structured exercise should be encouraged in people with COPD to gain mortality benefit, but the effects of domestic PA on mortality remain unclear.

OXYGEN SUPPLEMENTATION DURING EXERCISE TRAINING IN COPD: A RCT

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Introduction/Aim: Approximately 47 % of people with chronic obstructive pulmonary disease (COPD), referred to pulmonary rehabilitation, desaturate during exercise.

The aim was to determine whether supplementary oxygen during exercise training was more effective than medical air in improving exercise capacity and health-related quality of life in people with COPD who desaturate to < 90% during the six-minute walk test.

Methods: Multi-centre randomised controlled trial with randomisation (independent, concealed allocation), blinding (participants, exercise trainers and assessors) and intention-to-treat analysis. Participants were randomised to either an Oxygen Group (OG) or Air Group (AG). Both groups received the respective gas from a concentrator via nasal prongs at 5 litres/minute during exercise training of treadmill and cycle exercise, three times/week for eight weeks. Primary outcome measures were the endurance shuttle walk test (ESWT) and the Chronic Respiratory Questionnaire (CRQ). The study had ethics approval and trial registration.

Results: 111 participants (60 males), mean (SD) age 69 (7) years, FEV_1/FVC 0.43 (0.13), FEV_1 46 (17) % predicted were recruited and 97 completed (OG n=52; AG n=45). Within-group changes at 8 weeks were significant for ESWT, CRQ Total (T), CRQ Dyspnoea (D) (ESWT: OG mean difference [95%CI]: 163 s [76, 249]; AG 149 s [56, 242]; CRQ T: OG 0.4 points(pts) [0.2, 0.7]; AG 0.5 pts [0.2, 0.7]; CRQ D: OG 0.6 pts [0.3, 0.9]; AG 0.7 pts [0.3, 1.0] (all p<0.01). There were no between group differences with p> 0.05 for all outcomes.

Conclusion: Exercise capacity and health-related quality of life improved significantly in both groups, with no greater benefit from training with supplemental oxygen than with medical air. This is the largest rigorous RCT to report such findings.

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REDUCTION IN THE RATE AND RISK OF MODERATE OR SEVERE EXACERBATIONS WITH ONCE-DAILY INDACATEROL/GLYCOPYRRONIUM COMPARED WITH TWICE-DAILY SALMETEROL/FLUTICASONE IN A SUBSET OF GOLD GROUP D COPD PATIENTS WITH A HISTORY OF ≥2 EXACERBATIONS OR 1 HOSPITALIZATION: THE FLAME STUDY

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Introduction: The FLAME study demonstrated the superiority of indacaterol/glycopyrronium (110/50 μg, once daily), in reducing exacerbations, improving lung function, and health status versus salmeterol/fluticasone in moderate-to-very severe COPD patients with a history of exacerbations.[1] We assessed the effect of indacaterol/glycopyrronium versus salmeterol/fluticasone on the rate and risk of moderate or severe exacerbations in a subset of GOLD Group D patients who had a history of ≥2 exacerbations or 1 hospitalization for exacerbation from the FLAME study.

Methods: FLAME was a 52-week, randomized, double-blind, double-dummy, parallel-group study. Patients with moderate-to-very severe COPD, post-bronchodilator FEV_1 ≥25% to <60% predicted normal, and a history of ≥1 exacerbation in the previous year were randomized (1:1) to receive either indacaterol/glycopyrronium (110/50 μg) once-daily or salmeterol/fluticasone (50/500 μg) twice-daily. The rate and time to moderate or severe exacerbations were analyzed in the subset of GOLD Group D patients.

Results: Of the 3362 patients randomized, 2514 were categorized as GOLD Group D. The mean post-bronchodilator FEV_1 was 44.1% of the predicted normal value and 56.3% patients were on ICS at screening. Indacaterol/glycopyrronium demonstrated superior efficacy over salmeterol/fluticasone in reducing the rate of moderate or severe exacerbations (rate ratio, 0.86;**Table**). Indacaterol/glycopyrronium delayed the time-to-first moderate or severe exacerbation compared with salmeterol/fluticasone (median days: 291 versus 215;**Table**). The patients treated with indacaterol/glycopyrronium had a 19% lower risk of a moderate or severe exacerbation compared with salmeterol/fluticasone.

Conclusion: Indacaterol/glycopyrronium was superior to salmeterol/fluticasone in reducing the rate and risk of moderate or severe exacerbations in subset of GOLD Group D patients with a history of ≥2 exacerbations or 1 hospitalization for exacerbation, confirming its use as a preferred treatment option for COPD patients at high risk of exacerbations.

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Table 1 Effect of indacaterol/glycopyrronium versus salmeterol/fluticasone on moderate or severe exacerbations in the subset of GOLD Group D patients with a history of ≥2 exacerbations or 1 hospitalization for exacerbation

Annualized rate

	Indacaterol/glycopyrronium (n=531)	Salmeterol/fluticasone (n=503)
Rate (95% CI)	1.26 (1.06 to 1.51)	1.47 (1.24 to 1.75)
Rate ratio* (95% CI)	0.86 (0.74 to 1.00)	
P value	0.05	

Time-to-first exacerbation

	Indacaterol/glycopyrronium (n=536)	Salmeterol/fluticasone (n=511)
Patients with event, n (%)	281 (52.4)	299 (58.5)
Patients without event, n (%)	255 (47.6)	212 (41.5)
Time at risk (days), median (range)	247.5 (1 to 419)	181 (2 to 386)
Time-to-event (days), median (95% CI)	291 (254 to 352)	215 (175 to 261)
Hazard ratio*(95%CI)	0.81 (0.69 to 0.96)	
P value	0.013	

* indacaterol/glycopyrronium versus salmeterol/fluticasone

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PARENTAL RESPIRATORY DISEASE IS ASSOCIATED WITH REDUCED OFFSPRING LUNG HEALTH AT AGE 45 VIA PATHWAY OF MATERNAL AND PERSONAL SMOKING

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Introduction: Familial aggregation of chronic lung conditions may result from a combination of genetic susceptibility and exposure to risk factors throughout life. We used a life-course approach to investigate factors contributing to the relationship between parental respiratory disease history and Reduced Lung Health (RLH) in adulthood using data from the 1958 British Birth Cohort Study.

Methods: Cohort participants (n=6304) were characterised in terms of RLH (presence of respiratory symptoms at 42yrs and airway obstruction [FEV1/FVC<0.7 at 45yrs]) and parental history of respiratory disease (at offspring age 0,11,16yrs).

Life-course factors evaluated were maternal smoking (0yrs), living with smoker (16,23,33,42yrs), social class (0,7,16,23,33,42yrs), respiratory illness (7,11,16,23,33,42yrs), smoking status (23,33,42yrs), and occupational exposure to dust or fumes (33,42yrs), operationalised for life periods (birth, childhood [7,11,16yrs], adulthood [23,33,42yrs]). Path analysis was used to investigate the mediating role of life-course factors in the relationship between parental respiratory disease history and RLH, adjusting for gender, asthma and recent chest infection.

Results: Within this cohort, 3.7% had a parental respiratory history and 6.3% of offspring had RLH. Parental respiratory history was positively associated with RLH (p=0.023). Maternal smoking during pregnancy, personal smoking in adulthood, social class (0, 23 and 42yrs) and occupational exposure to dust or fumes were the only factors related to both parental history and RLH. Mediating pathway testing indicated that the sequence through maternal and adulthood smoking contributed most to model fit (indirect effect p=0.015), explaining 30% of the parental history-RLH relationship.

Conclusion: An association between parental history of respiratory disease and offspring RLH at 45yrs was partly mediated by a sequence of exposure to maternal smoking and being a smoker during their adulthood. A large proportion of the relationship between parental history-RLH remains unexplained by smoking, suggesting that assessing parental history of respiratory disease may provide insights into earlier diagnosis and intervention.

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ASSOCIATIONS OF ACTIVITY PHENOTYPES WITH HEALTH OUTCOMES IN COPD

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Introduction/Aim: To examine the association of four activity phenotypes with mortality and cardiometabolic risk factors in people with Chronic Obstructive Pulmonary Disease (COPD).

Methods: A prospective cohort was analysed. People with COPD aged >40 years who were current or ex-smokers were identified from the 2003 Scottish Health Survey and grouped into one of the following activity phenotypes based on their self-reported activity levels: 1) 'Couch Potatoes': insufficiently active with high leisure-based sitting time and/or no domestic physical activity (PA); 2) 'Light Movers': insufficiently active with some domestic PA; 3) 'Sedentary Exercisers': sufficiently active with high leisure-based sitting time; or 4) 'Busy Bees': sufficiently active with low leisure-based sitting time. 'Sufficiently active' involved adhering to PA recommendations of ≥ 7.5 metabolic equivalent (MET) hours per week. 'Low leisure-based sitting time' was defined as ≤ 200 minutes of recreational screen time per day. Associations between the phenotypes with mortality and cardiometabolic outcomes was made using Cox proportional hazards models or binary logistic regression models respectively.

Results: The sample comprised 584 participants (mean age (SD) 63.8 (11.5) years, 52% male). Over 5.5 (1.3) years follow-up, there were 81 all-cause deaths from 433 COPD participants with available data. Compared to the 'couch potatoes', there was a reduced risk of all-cause mortality in the 'busy bees' (hazard ratio 0.26, 95% confidence interval (CI) 0.11-0.65) with a trend towards a reduction in mortality risk in the other phenotypes (p-trend = 0.02). There was a reduced risk of diabetes in the 'busy bees' compared to the 'couch potatoes' (odds ratio 0.14, 95% CI (0.03 to 0.67).

Conclusion: This analysis demonstrated a mortality benefit and reduced risk of diabetes in people with COPD when leisure-based sitting time was low and PA guidelines were adhered to, indicating the health benefits of PA and the importance of measuring these activity outcomes in the COPD population.

Pulmonary Physiology & Sleep 2

CLINICAL OUTCOMES IN COPD PATIENTS ATTENDING PULMONARY REHABILITATION ARE PREDICTED BY FORCED OSCILLOMETRY

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Introduction/Aim: In COPD, lung hyperinflation reduces inspiratory reserve, thereby limiting exercise. Respiratory system reactance (Xrs) measured by forced oscillation technique (FOT) reflects heterogeneous airway narrowing and closure in COPD, and may relate to clinically important outcomes. We hypothesized that Xrs relates to quality of life, hyperinflation and exercise capacity in COPD.

Methods: 15 COPD subjects from the Royal North Shore Hospital Pulmonary Rehabilitation department underwent spirometry, plethysmographic lung volumes, St. George's Respiratory Questionnaire (SGRQ) and 6-minute walk distance (6MWD). Xrs was measured at 5Hz by FOT during 60s of tidal breathing followed by 3 deep inspirations, from which mean Xrs over the recording (Xmean), Xrs during inspiration only (Xinsp), the expiratory decrease in Xrs as an index of expiratory flow limitation (EFLI), and inspiratory capacity were derived. FOT, SGRQ and 6MWD were repeated at rehabilitation completion and 3 months later.

Results: Participants were (mean$\pm$SD) 75.2 ± 6.1years old with FEV1 $51.8\pm17.4\%$predicted. Xinsp correlated with SGRQ (r=-0.60, p=0.04) and IC (r=0.80, p<0.001) but was unrelated to 6MWD at baseline. EFLI was unrelated to either IC or 6MWD. Xinsp and 6MWD improved significantly post-rehabilitation (-2.35 ± 0.98 cmH$_2$O*s*L^{-1} to -2.04 ± 0.82cmH$_2$O*s*L^{-1}, p=0.008 and 399 ± 99m to 451 ± 123m, p=0.005, respectively). IC did not change. Both, baseline Xinsp and baseline EFLI predicted improvement in 6MWD, 3 months after completion of rehabilitation (r=0.59, p=0.04 and r=-0.62, p=0.03, respectively).

Conclusion: Reactance during inspiration (Xinsp) and EFLI reflect different aspects of mechanical impairment of the respiratory system in COPD and have different clinical correlates. The correlations between Xinsp and quality of life and hyperinflation suggest it may be a useful clinical parameter in managing COPD, and this deserves further evaluation in larger prospective studies. EFLI does not add any further information above that of Xinsp, within the context of the present study. Therefore, separating Xrs into its inspiratory and expiratory components may be more clinically useful than using the mean value, in COPD.

THE PHYSIOLOGICAL PROPERTIES OF THE KANGAROO AIRWAY

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Introduction/Aim: Comparative physiology is a powerful approach to help understand the relationship between structure and function. The kangaroo exhibits a unique breathing mechanism when hopping: respiration depends more on motional forces and less on active contraction of the diaphragm. We asked how structural and mechanical properties of the kangaroo airway might accommodate the respiratory pressures generated during hopping. This study compared mechanical and structural properties of airways from kangaroos and sheep, the latter of which is not subject to the same motion-driven movement of air.

Methods: Bronchial segments from kangaroos (n=8) and sheep (n=12) were mounted in an organ bath chamber. Pressure-volume curves were obtained between -10 and 20 cmH$_2$O before and after theophylline. Airway stiffness was calculated from the change in pressure over normalized volume (Δ volume/initial volume). Closing pressure (pressure required for airway collapse) and airway wall morphology were also assessed. Data is mean$\pm$SEM.

Results: The stiffness of kangaroo airways was less than in sheep (kangaroo, 6 ± 2 cmH$_2$O; sheep, 16 ± 4 cmH$_2$O; p<0.05). Theophylline caused a reduction in sheep airway stiffness (p<0.05) but had no effect on kangaroo airway stiffness, suggesting a role for smooth muscle tone in the former. Kangaroo airways also required a less negative pressure for collapse compared with sheep airways (kangaroo, -15 ± 3 cmH$_2$O; sheep, -30 ± 3 cmH$_2$O; p<0.05).The kangaroo airway had a thicker inner (p<0.05) and thinner outer wall (p<0.05) compared with the sheep airway. While the total thickness of cartilage was comparable between groups, there were a greater number (p<0.05) of smaller (p<0.05) cartilage plates in the kangaroo airway.

Conclusion: Kangaroo airways have low stiffness and are more collapsible compared with sheep airways. Fragmented cartilage plates and absence of smooth muscle tone contributes to the lower stiffness. Low airway stiffness may maintain functional residual capacity during hopping in response to large variations in respiratory pressures.

Declaration of Interest Statement: None.

FORCED OSCILLATION TECHNIQUE REFLECTS COMMUNICATING LUNG VOLUME (VA/TLC RATIO), BUT NOT TOTAL LUNG CAPACITY, IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Introduction/Aim: The lung in COPD demonstrates expiratory flow limitation, airway closure and ventilation heterogeneity. Reactance at 5 Hz (X5) measured by the forced oscillation technique (FOT) is influenced by each of these pathophysiological phenomena, but is also dependent on lung volume. In the presence of airway closure, where oscillating pressure waves are not able to penetrate all lung segments, X5 may not relate to the total thoracic gas volume. Single-breath alveolar volume (VA), measured during the diffusing capacity test, estimates the communicating gas volume by dilution during a breath hold. The ratio of VA to plethysmographic total lung capacity (TLC), or VA/TLC, is therefore reduced in obstructive airways disease due to incomplete gas mixing and gas trapping. We hypothesised that X5 would relate to VA/TLC but not TLC in COPD.

Methods: 15 subjects with mild-moderate COPD (11 male, mean (range) age 68 (58-79), mean $\pm$ SD %pred FEV1 64 $\pm$ 17) were tested using FOT (Thorasys tremoFlo c100) during 60 s normal tidal breathing. Spirometry, body plethysmography and the single-breath diffusing capacity test were then performed according to standard quality criteria. Spearman rank correlation coefficients were determined before and after adjustment for known covariates from published reference equations.

Results: X5 was moderately correlated with VA/TLC (r = 0.66, p = 0.008) and VA (r = 0.58, p = 0.03) but not with TLC. After adjustment for known covariates, X5 Z-score remained moderately correlated with VA/TLC (r = 0.60, p = 0.02) but not VA or TLC Z-scores. VA/TLC correlated with the severity of airflow obstruction measured by FEV1/FVC ratio Z-score (r = 0.77, p = 0.001).

Conclusion: In COPD, X5 measured by FOT during normal tidal breathing reflects the communicating lung volume rather than the total lung volume. FOT therefore may compliment traditional lung function measurements.

PHYSIOLOGICAL RESPONSES TO THE SIX MINUTE WALK TEST AND MAXIMAL EXERCISE TESTING IN PULMONARY HYPERTENSION

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Introduction/Aim: The six minute walk test (6MWT) remains the most commonly used clinical measure of exercise capacity in pulmonary hypertension (PH). Whilst maximal exercise testing using a cardiopulmonary exercise test (CPET), remains the gold standard estimate of exercise capacity, this test is much less common in clinical practice. The purpose of this study was to compare the physiological responses to the 6MWT and CPET in a group of PH subjects.

Methods: Eighteen individuals with Group I/IV PH patients (Functional Class I-III) completed a CPET on a cycle ergometer and a 6MWT on separate days. During both tests, gas exchange was measured using a calibrated portable metabolic system (Cortex, Metamax). Oxygen uptake (VO_2), carbon dioxide production (VCO_2), ventilation (V_E), heart rate (HR), oxygen (O_2) pulse, V_E/VCO_2, end tidal carbon dioxide ($P_{ET}CO_2$), oxygen saturation (S_PO_2) and breathlessness (Borg, 0-10) were averaged over the final 30s and compared between the 6MWT and CPET. In a subgroup of 8 participants, end exercise lactate (HLa) was also measured using a portable lactate analyser (Lactate Scout).

Results: The mean peak power achieved by participants was 74 $\pm$ 20 W, whilst the mean 6MWT distance was 574 $\pm$ 89m. There was no significant difference between CPET and the 6MWT for peak VO_2 (CPET: 16.3$\pm$6.6 vs 6MWT: 15.5$\pm$3.8 ml.kg^{-1}.min^{-1}), V_E (54.7$\pm$13.8 vs 49.7$\pm$15.8 L.min^{-1}), HR (136$\pm$22 vs 143$\pm$27 beats.min^{-1}), O_2 pulse (6.8$\pm$1.3 vs 7.0$\pm$1.7 ml.beat^{-1}), $V_E/VCO2$ (35$\pm$6 vs 36$\pm$5), $P_{ET}CO_2$ (30$\pm$5 vs 29$\pm$4 mmHg) or SpO2 (88$\pm$11 vs 87 $\pm$ 14%). Peak VCO_2 (1.43$\pm$0.46 vs 1.20$\pm$0.31 L.min^{-1}), breathlessness (5.5$\pm$2.2 vs 3.6$\pm$1.9) and lactate (8.5$\pm$1.5 vs 5.0$\pm$1.9) were all significantly higher(p<0.05) with CPET.

Conclusion: We found that the physiological responses to CPET and 6MWT in our group of PH participants were similar. This would suggest that the 6MWT is similar to a peak exercise challenge the PH population.

EFFECTIVENESS OF A SUBMAXIMAL CYCLE TEST TO PRESCRIBE TRAINING INTENSITY

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Introduction/Aim: In pulmonary rehabilitation (PR), cycle training is recommended at 60% peak oxygen uptake measured during cardiopulmonary exercise testing (CPET). However, access to CPET is limited and estimation of an equivalent intensity from the 6-minute walk distance (6MWD) using published equations is associated with substantial variation. This study aimed to investigate whether a submaximal cycle exercise test (SMCT) can prescribe appropriate cycle training intensity and whether initial training intensity estimated from 6MWD and SMCT is similar.

Methods: Retrospective data was collected from patients who attended PR over the previous 12 months. Each patient routinely performed a 6-minute walk test at baseline and completed a SMCT during the second exercise session. In the subsequent exercise session, cycle training was prescribed at 50% of peak work (Watts) achieved on SMCT. Initial intensity was considered appropriate if the patient could complete 15 minutes as prescribed with a reported dyspnoea and/or RPE score of 3-4 on the Borg 0-10 score.

Results: Forty-three patients (23 male) with chronic lung disease (23 COPD, 10 ILD, 10 other) were included, with mean (SD) age of 70(11), 6MWD 437(86) metres and SMCT peak work of 60(22) watts. Eight one percent of patients achieved the target intensity, 16% found the initial workload too easy and 2% were unable to maintain the target intensity. There was a moderate correlation between work rate predicted from 6MWD 35(8) Watts and SMCT 30(11) Watts (r= 0.71, p<0.001). Estimating cycle training intensity from 6MWD over-predicted (>5 Watts) appropriate training in 44% patients and under-predicted in 7%.

Conclusions: In chronic lung disease, prescribing cycle exercise intensity at 50% of SMCT peak work achieves an appropriate training intensity that was tolerated by > 80% of patients. Prescribing work rate from SMCT and 6MWD results in similar training loads, although SMCT may provide more accurate cycle training intensity.

FATTY ACIDS DO NOT ALTER BOVINE TRACHEALIS MUSCLE CONTRACTILITY

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Introduction/Aim: Increased dietary fat is associated with an increased risk of asthma and airway hyperresponsiveness. A single high fat meal reduces the efficacy of salbutamol, suggesting that dietary fatty acids may alter airway smooth muscle (ASM) contractility. Therefore our aim was to determine the effect of fatty acids on *in vitro* bovine trachealis smooth muscle responsiveness to relaxant and contractile stimuli.

Methods: Oleic acid, linoleic acid, alpha-linolenic acid, palmitic acid, stearic acid and elaidic acid were compared at $10^{-4.5}$M. Bovine trachealis muscle strips (n = 7/group/experiment) were mounted in tissue baths with warmed, aerated Krebs solution. All experiments were done in the presence of tetradotoxin (10^{-6}M). To test sensitivity to relaxant stimuli, muscle strips were contracted with acetylcholine (half maximal effective concentration, EC_{50}) before addition of vehicle or fatty acid and cumulative dose-response curves to isoproterenol (10^{-9}M to 10^{-4}M) performed. To test sensitivity to contractile stimuli, separate muscle strips were incubated with vehicle or fatty acid for 20min before cumulative dose-response curves to acetylcholine (10^{-9}M to 10^{-2}M) were performed.

Results: In the relaxation experiment, ASM force following acetylchoine was not affected by addition of any of the fatty acids. Similarly, there was no effect of fatty acid on the EC_{50} concentration to isoproterenol (RANOVA p = 0.52). In the contraction experiment, baseline force was unaltered by addition of any of the fatty acids. Similarly, there was no effect of fatty acid on the EC_{50} to acetylcholine (RANOVA p = 0.86).

Conclusion: Dietary fatty acids do not alter bovine trachealis ASM function.

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QUANTIFICATION OF PIPERACILLIN AND TAZOBACTAM IN PLASMA AND PLEURAL FLUID MEASURED BY A NOVEL LC-MSMS ASSAY

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Introduction: Piperacillin (PIP) with tazobactam (TAZ) is commonly used for treatment of pleural infection, the pleural pharmacokinetics however, have not been reported. We developed and validated a rapid and sensitive ultra-performance liquid-chromatography with tandem mass-spectrometry assay for quantification of PIP/TAZ.

Methods: Both drugs were extracted from human plasma and pleural fluid by protein precipitation in methanol containing internal standards (IS) piperacillin-d_5 and sulbactam. 5uL of sample was mixed with 125uL of methanol containing IS, vortexed and centrifuged. Supernatant was diluted into mobile phase containing 10mM of ammonium bicarbonate and water. The chromatographic separation was achieved using an Acquity BEH C-18 column.

This method was applied to two patients with pleural infection. Six pleural fluid and blood samples were obtained at steady-state before and over 6-hours post-infusion of 4500mg-PIP/TAZ.

Results: Electrospray ionisation in positive mode and multiple reaction monitoring (MRM) were used for PIP and piperacillin-d_5 at the transitions m/z 518.2→143.2 and m/z 523.2→148.2 respectively and in negative mode for TAZ and SUL at the transitions m/z 299.1→138.1 and m/z 232.4→140.1. Linearity was observed over the concentrations of 0.25-352mg/L and 0.25-50.5mg/L for PIP and TAZ respectively. Complete method validation was performed according to US FDA guidelines for selectivity, specificity, precision, accuracy, matrix effects and stability; results were within acceptable limits.

In both patients, the time to maximum concentration (C_{max}) for PIP and TAZ in pleural fluid were delayed compared to plasma. The C_{max} for PIP in pleural fluid reached 63mg/L and 59mg/L at 90 and 150-minutes in each patient. This was 77% and 52% of the C_{max} achieved in plasma for each patient respectively.

Conclusion: The two cases had notably different concentration-time profiles for both drugs in pleural fluid but did not differ in systemic elimination of PIP/TAZ. The assay is feasible to use for future pharmacokinetic studies.

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HIGH LEVELS OF HOSPITAL HEALTH CARE UTILIZATION ASSOCIATED WITH BRONCHIECTASIS

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Introduction/Aim: Bronchiectasis not related to cystic fibrosis (non-CF BEx) is an increasingly recognised cause of chronic lung disease that can occur in isolation or with other lung diseases including asthma and COPD. In other settings bronchiectasis is associated with significant health care utilisation but its impact in both Australia and New Zealand is poorly understood, including for Indigenous populations. We aimed to described the impact of non-CF BEx on inpatinet hospital care in this setting

Methods: A multicentre Australian and New Zealand retrospective audit of hospital admission data relating to patients with non-CF BEx admitted once or more to five hospitals in Melbourne, Sydney and Alice Springs (Australia) and Auckland (New Zealand) was undertaken. The number and length of stay (LOS) of respiratory admissions was determined. For Melbourne, Alice Springs and Auckland additional information was obtained regarding the requirement for ventilatory support.

Results: Data regarding hospitalisation are presented below.

(95% CI)	AUSTRALIA			NEW ZEALAND	
	Alice Springs Indigenous	Melbourne	Sydney	Auckland Indigenous	Auckland non-Indigenous
Number of participants	85	79	37	157	85
Admission	2.9	0.7	0.4	0.7	0.7
(no/pers.yr)	(2.7-3.1)	(0.6-0.8)	(0.3-0.4)	(0.6-0.8)	(0.6-0.8)
LOS (day/pers.yr)	16.9	6.4	3.1	4.1	4.0
	(16.4-17.3)	(6.1-6.7)	(2.9-3.3)	(4.0-4.3)	(3.8-4.2)
LOS	4	6	7	4.5	4
(med, IQR)	(3-7)	(4-11)	(5-11)	(3-7)	(3-7)
Ventilate %	50.6	19.0	-	7.6	2.4
	(39.5-61.6)	(11.0-29.4)		(4.0-13.0)	(0.3-8.2)
non-invasive	37.6	17.7	-	5.7	1.2
	(27.4-48.8)	(10.1-27.9)		(2.7-10.6)	(0.0-6.4)
invasive	8.2	5.1	-	0.0	0.0
	(3.4-16.2)	(1.4-12.5)		(0.0-2.3)	(0.0-4.2)

Conclusion: Health care utilisation for non-CF BEx is substantial. The number of admissions varies substantially by site as does the cummulative LOS. Average LOS also varies and Australian patients have longer LOS compared to NZ patients. Indigenous Australian patients have a shorter LOS compared with non-Indigenous counterparts despite more frequent admission and overall greater hospitalisation days. LOS is comparable to COPD (ranging from 4.1-7.3 days in Australia) and the frequency of admission for non-CF BEx is likely to be the major factor driving hospital-based health care utilisation. The utilisation of ventilatory support varies by country and is particularly high in Indigenous Australians. The impact and optimal level of admission frequency, LOS and ventilatory support on susequent representation to hospital, quality of life and survival should be a focus of further investigation.

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RIFAMPICIN MONO-RESISTANT TUBERCULOSIS IN QUEENSLAND, AUSTRALIA

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Introduction/Aim: Drug resistant tuberculosis (TB) is an emerging problem. Rifampicin resistance is rare and is usually seen in multi-drug resistant (MDR) TB. Rifampicin mono-resistant (RMR) TB is less common.

The World Health Organization recommends RMR-TB should be treated as per MDR TB guidelines. This requires prolonged treatment with second line agents including intravenous aminoglycosides, and is associated with increased risk of toxicity and cost. The evidence to support this recommendation in RMR-TB is lacking.

We predicted MDR TB regimens are not commonly used in Queensland for RMR-TB and to confirm this we carried out a study to examine the clinical features, treatment regimens and outcomes of RMR-TB in Queensland, Australia.

Methods: This retrospective case series identified all cases of RMR-TB in Queensland from 2000 to 2016. Data was gathered through the Notifiable Conditions System database with cross-reference using medical records.

Results: Twelve cases of RMR-TB were identified. The mean age was 29.1 years. All patients were overseas born. Nine cases (75%) had pulmonary disease.

Drug susceptibility testing confirmed isolates were resistant to Rifampicin and sensitive to other first line agents (Isoniazid, Pyrazinamide and Ethambutol).

Complete data on treatment and outcomes were available for 8 cases. No patients were treated with a MDR TB regimen. All patients who completed treatment in Queensland were cured. The mean duration of treatment was 14.6 months. The majority of patients were treated with the first line agents plus Moxifloxacin was added to the regimen in 5 cases. Only 1 patient received intravenous Amikacin.

Conclusion: This study confirms RMR-TB is rare in Queensland but is not being managed with MDR TB regimens. Generally an extended regimen with first line agents +/- a Fluroquinolone was used. These regimens achieved good outcomes with 100% cure rates. Management of RMR-TB requires further studies to determine the optimal treatment regimen, however based on this data extended courses with MDR type regimens are not necessary.

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5-YEAR OUTCOME AND RAPID SCORE: AN AUSTRALIAN PLEURAL INFECTION COHORT

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Introduction/Aim: Mortality from pleural infection (PI) remains high. Many patients die after successful treatment of their PI. Few studies report on longer term outcomes and cause of death; one US study reported 76% 5-year mortality. The RAPID score is a recently introduced risk stratification tool for PI, encompassing 5 parameters - age, renal function, pleural fluid purulence, infection source and serum albumin. We aimed to validate the RAPID score in our single centre cohort, and examine longer term outcomes and cause of mortality.

Methods: All cases of PI treated at Nambour General Hospital 1st July 2007 – 1st July 2012 were reviewed. PI was defined by positive pleural fluid gram stain or culture *or* complicated parapneumonic effusion. Data until date of censor (1st July 2017) was extracted from hospital records and electronic pathology database. In-hospital and 5-year mortality and cause of death were recorded. GP practices were contacted to confirm death data.

Results: 41 cases where included. Mean age was 58 (18). 68% were male. 61% were hospital-acquired PI. 76% were culture positive. In-hospital mortalty was 17.1% and 5-yr mortality 46.3%. Most cases were stratified as medium-risk by RAPID score (low n=12, medium n=21, high n=8). In-hospital mortality for low-, medium- and high-risk groups was 0%, 28.6%, 12.5%. 5-yr mortality for low-, medium- and high-risk groups was 0%, 66.7%, 62.5%. Cause of death for cases that were discharged but deceased at 5 years (n=12) included chronic liver disease, malignancy, myocardial infarction, bowel obstruction, cellulitis and aspiration pneumonia. These patients had a median of 4 comorbidities at the time of their PI.

Conclusion: In our cohort, the RAPID score accurately stratified the low risk group.

Poor longer term outcomes post PI likely relates to significant patient co-morbidities.

Addressing co-morbidity management at the time of PI is important.

HIGH IMPACT OF INFLUENZA ON HOSPITALISATION RATES IN CHILDREN WITH CHRONIC LUNG DISEASES: A POPULATION-BASED STUDY

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Introduction/Aim: Severe influenza infection in children with chronic lung diseases results in, unscheduled hospital presentations and substantial burden to the health system. National influenza burden data in children with chronic lung diseases are limited. Such data are crucial to monitor burden of disease and evaluate effectiveness of influenza vaccination program. We conducted a retrospective population-based cohort study to measure the impact of influenza on hospitalisation rates in children with chronic lung diseases.

Methods: We performed a retrospective cohort study using population-based linked administrative data for all children born in New South Wales between 2001-2010 with complete follow-up until December 31st 2011. The cohort was divided in to two groups: i) children with chronic lung diseases including all children with asthma, bronchopulmonary dysplasia, cystic fibrosis, and congenital lung disorders; and ii) all other standard-risk children.

The primary outcome was any episode of influenza associated hospitalisation (ICD codes J.09-J11). Incidence rates for influenza hospitalisation were calculated for 2001-2011. We used Poisson estimation to calculate 95% confidence interval around incidences.

Results: Our cohort comprised of 9,708 children with chronic lung diseases and 877,240 standard-risk children. The adjusted rate/1000 child-years of influenza hospitalisation in children with chronic lung diseases was 5.21 (95% CI 2.57-7.84) and for all other standard-risk children was 0.92 (95% CI 0.46-1.38). During 2001-2011, the rate in children with chronic lung diseases ranged between 0.20-12.57/1000 child-years. The rate/1000 child-years was similar in male and female children with chronic lung diseases and was 5.45 (95% CI 2.63-8.26) for boys and 5.15 (95% CI 2.41-7.89) for girls.

Conclusion: Our study has demonstrated that children with chronic diseases are at least five times more at risk of being hospitalised with influenza than standard-risk children. Future studies investigating the effectiveness of universal vaccination program for these and all other children may help reduce the burden.

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THE SPREAD OF PSEUDOMONAS AERUGINOSA INFECTION IN BRONCHIECTASIS AND COPD

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Introduction/Aim: Pseudomonas aeruginosa (Pa) is the dominant respiratory pathogen in people with cystic fibrosis (CF) and can be released as viable aerosols during coughing. These aerosols can travel for at least 4 metres and remain airborne for at least 45 minutes. There is no research to determine if people with other chronic lung conditions can release Pa in cough aerosols. This project aimed to determine if people with non-CF bronchiectasis (nCFB) and chronic obstructive pulmonary disease (COPD) release Pa aerosols during cough.

Methods: Twenty participants with nCFB (n=16) and COPD (n=4) and Pa lung infection were recruited. Participants underwent testing in two validated aerosol-sampling devices to measure Pa viability at 2 and 4 m (distance) and at 5, 15 and 45 min (duration) during voluntary cough. Aerosols from each test were sampled using a 6-stage Andersen Cascade Impactor. Quantitative sputum counts and aerosol cultures were performed with the total number of colony forming units (CFUs) determined.

Results: Twenty participants with mean (SD) age of 62.5 (11.0) years, FEV_1 56.7 (20.7)% predicted and BMI 25.3 (4.3) kg/m^2 were recruited. On the day of testing, 1 participant did not culture Pa in their sputum. Nine participants completed all five cough tests. Viable Pa was detected in cough aerosols from 6/19 (31.6%) participants at 2m, 6/19 (31.6%) participants at 4m, 2/15 (13.3%) participants at 5 minutes and 2/15 (13.3%) participants at 15 minutes. No participants produced Pa cough aerosols at 45 minutes. The concentration of Pa in the sputum did not correlate with the Pa CFU in the aerosol cultures.

Conclusion: Pa can be released as viable cough aerosols in people with nCFB and COPD, although at lower CFU compared to people with CF. These results highlight the importance of respiratory hygiene and infection control strategies in hospitals.

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DISCORDANT PERCEPTIONS OF ASTHMA CONTROL AND RELIEVER DEPENDENCE AMONG USERS OF SHORT-ACTING BETA-AGONISTS

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Introduction/Aim: Overuse of short-acting beta-agonists (SABA) can compromise asthma control and increase burden of disease, especially among those with poorly-controlled symptoms. This study assessed perception of control and dependence on reliever medication among patients who were taking SABA alone.

Methods: Cross-sectional population-based internet survey of participants with current asthma aged >16 years. Using Likert-type questions (ranging from strongly disagree to strongly agree), the survey captured attitudes about asthma and asthma treatment. Asthma control was assessed using the Asthma Control Test (ACT: Poorly-controlled <20; Well-controlled 20-25).

Results: SABA-only respondents who had poor symptom control (n=374) compared with SABA-only users with well-controlled symptoms (n=632) were almost 3 times more likely to agree/strongly agree that they felt anxious without a reliever when out (30.6 vs. 11.6%, respectively; p<0.0001), and almost twice as likely to feel anxious when without a reliever around triggers (36.9 vs. 19.2%, respectively; p<0.0001). Additionally, those with poorly-controlled vs. well-controlled symptoms were more likely to agree/strongly agree that they relied on their reliever for their asthma (50.9% vs. 39.9%, respectively; p<0.0001), and that their reliever was "a life-saver" (43.6% vs. 24.4%, respectively; p<0.0001). Half of respondents in both groups agreed/strongly agreed that their reliever gave them control over their asthma (49.7% vs 52.2%, respectively; p=0.74).

Conclusion: Patients with poor symptom control appeared overly reliant on SABA compared to patients with well-controlled asthma. While optimal asthma control in this population requires preventative treatment, half of SABA-only respondents viewed their reliever as their means of achieving control over their asthma. Given this, public messages such as "you can control your asthma" that are aimed at encouraging preventer use may inadvertently give the opposite message to many people. These data call into some question the preventer-reliever-control paradigm as currently used. Terminology that interacts better with patients' thoughts and beliefs may be more effective.

FETAL GROWTH RESTRICTION CAUSES FUNCTIONAL AND STRUCTURAL ABNORMALITIES OF THE AIRWAY WALL IN ADULT MOUSE OFFSPRING

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Introduction/Aim: Intrauterine growth restriction (IUGR) is associated with increased risk of asthma in later life. Developmental changes to airway structure and function may impact susceptibility to subsequent disease. This study used a maternal hypoxia-induced mouse model of IUGR to assess changes in airway smooth muscle (ASM) contractility and thickness in male and female adult offspring.

Methods: Pregnant BALB/c mice were housed under hypoxic conditions (10.5% O_2) from gestational day (GD) 11-GD17.5 (IUGR group; term=GD21). Following hypoxic exposure, mice were returned to a normoxic environment (21% O_2). A second group of pregnant mice were housed under normoxic conditions throughout pregnancy (Control). Weights of offspring were recorded until 8 weeks of age at which point they were euthanized and a tracheasectomy was performed. Trachea segments were studied in an organ bath chamber to measure isometric force production to carbachol and subsequently fixed for morphometry. Maximal active tension and stress were calculated from force normalised to segment length and ASM cross-sectional area respectively.

Results: The IUGR offspring were lighter at birth (Control, n=60; IUGR, n=58; p<0.05) and remained lighter at 8 weeks of age compared with Controls (Control, n=21; IUGR, n=21; p<0.05). Active tension (p<0.05) and stress (p<0.05) were reduced in male IUGR offspring compared with Controls with no difference in ASM thickness. There were no statistical differences in active tension or stress in IUGR female offspring despite a reduction in ASM thickness (p<0.05). Sensitivity of ASM to contractile agonist was not altered by IUGR.

Conclusion: There are persisting effects of IUGR on the mature airway wall which favour reduced contraction of the ASM layer, including lower ASM contractility in male offspring and a thinner ASM layer in female offspring. Findings suggest that altered development of the fetal airway can impact susceptibility to future airway disease through changes in ASM structure and function.

INTRINSIC AIRWAY SMOOTH MUSCLE TONE IN PERIPHERAL AIRWAYS IS DETERMINED BY THE VOLUME FRACTION OF MUSCLE AND EXTRACELLULAR MATRIX

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Introduction/Aim: Abnormalities in small airways are implicated as a primary cause of functional impairment in obstructive airway disease. Contraction of the airway smooth muscle (ASM) layer in the absence of an exogenous stimulus is termed 'intrinsic tone' and may contribute to air-flow limitation. The aim of this study was to assess the underlying structural determinants of ASM intrinsic tone in peripheral human airways.

Methods: Subjects (12M:6F, 37-85 years) undergoing lung resection surgery were recruited and baseline lung function assessed prior to surgery. Peripheral airways were dissected from resected tissue and further cut into bronchial rings (1-4 rings/subject) for measurement of force in organ bath chambers. Length-tension curves were constructed to KCl (60 mM) to establish optimum length (L_O) for contraction and subsequently adapted to repeated KCl stimulation. All experiments were performed at L_O. Tension (mN/mm) in the ring was determined before and after complete relaxation to theophylline (10^{-2}M) and then fixed for stereology. Sections (0.5 μm) were stained using Masson's trichome technique and relative fractions of ASM (VV_{ASM}) and ECM (VV_{ECM}) within the ASM layer measured by point counting. Muscle tension was converted to stress (mN/mm^2) after normalising to muscle thickness.

Results: Subjects had a pre-bronchodilator FEV_1(%Pred) of 89.4±4.5 and FEV_1/FVC of 0.72±0.03. Bronchial rings exhibited a mean intrinsic stress of 20.1±3.4mN/mm^2. Intrinsic stress (n=18) was negatively correlated with VV_{ECM} (r=-0.47, p<0.05) and positively correlated with VV_{ASM} (r=0.51, p<0.05). There was also a non-significant trend for a decrease in FEV_1 (%Pred) with increasing intrinsic stress (r=-0.56, p=0.07). There was no association between lung function and VV_{ECM} or VV_{ASM}.

Conclusion: The presence of intrinsic stress in the peripheral ASM layer is determined by the underlying layer composition, increasing with greater muscle fraction and decreasing with ECM fraction respectively. We propose that muscle composition affects lung function through regulation of intrinsic tone.

ASSOCIATIONS BETWEEN THE DIETARY INFLAMMATORY INDEX AND LUNG FUNCTION IN MIDDLE-AGE DIFFER BY ASTHMA STATUS

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Introduction/Aim: A pro-inflammatory diet may contribute to poor lung function and, in turn, the development and/or progression of chronic inflammatory lung diseases. Few studies have assessed the relationship between the dietary inflammatory index (DII®), a literature-derived measure of the inflammatory potential of the diet, and lung function. We aimed to investigate this relationship in a population-based sample of middle-aged adults.

Methods: A random sample of middle-aged adults (45-72 years) from inner south-east Melbourne were assessed by spirometry and questionnaires (n=1183). An energy-adjusted DII was calculated for each participant from a semi-quantitative food frequency questionnaire. Regression methods were used to model relationships between DII quintiles and lung function outcomes, adjusting for age, gender, height, energy intake, BMI, asthma, atopy and smoking. Asthma status was also examined as an effect modifier.

Results: Associations between DII and FEV_1 and between DII and FVC differed by asthma status (p=0.001 and <0.001, respectively). Current asthmatics with a diet in the highest DII quintile had a mean FEV_1 516ml lower than those in the lowest DII quintile (95%CI 212, 819ml; P_{trend}=0.003) and a mean FVC 588ml lower (95%CI 249, 926ml; P_{trend}=0.006). Remitted asthmatics with a diet in the highest DII quintile had a mean FEV_1 364ml lower than those in the lowest DII quintile (95% CI 81, 646ml; P_{trend}=0.02) and a mean FVC 391ml lower (95%CI 76, 706ml; P_{trend}=0.01). For those who had never had asthma, there were no associations between DII and any of the lung function measures. There were also no associations between DII and FEV_1/FVC in any asthma category.

Conclusion: A pro-inflammatory diet was associated with poorer lung function in current and remitted asthmatics. If this association is causal, it argues for a low inflammatory diet for people with a history of asthma.

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A MULTIDISCIPLINARY TEAM (MDT) CLINIC FOR VOCAL CORD DYSFUNCTION (VCD)

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Introduction/Aim: Vocal cord dysfunction (VCD) is often mistaken for severe asthma and accurate diagnosis is crucial – but difficult. Treatment is complex and dedicated follow-up is essential. To examine optimal overall management of VCD a Multidisciplinary Team (MDT) clinic was initiated and operationalized. This type of clinic has not yet been described.

Methods: Patients with suspected VCD (n=80) were referred by Respiratory physicians (n=76) and ENT surgeons (n=4). The clinic was staffed by a Respiratory physician, ENT surgeon (laryngologist), Speech therapist and Respiratory Nurse specialist. Patients completed questionnaires, had spirometry and dynamic CT larynx prior to review. At review by the team a history was obtained, physical examination conducted and laryngoscopy performed. Diagnosis of VCD was based on detection (CT larynx or laryngoscopy) of inspiratory paradoxical vocal cord movement (PVCM) on at least one occasion. The team finally reviewed all data, a likely diagnosis was formulated and treatment was selected in consultation with the patient.

Results: A total of 80 patients are reported of whom 61 (76%) had established asthma. A diagnosis of VCD was established in 53/80 cases (67%) and 44 elected to access speech therapy services. Based on symptoms speech therapy was gauged unsuccessful in 29/44 patients (65%) and 22/29 individuals elected to have botulinum toxin injection. In a second group of 17/80 cases (21%) a diagnosis of VCD was considered unlikely. In this group 13/17 patients had poorly controlled asthma and 4/17 patients had other diagnoses. In a third group of 10/80 patients (12%) VCD was strongly suspected but not confirmed. All patients were offered speech therapy and success was achieved in 7/10 cases.

Conclusion: A VCD MDT clinic was established providing an integrated multidisciplinary approach to diagnosis and management of VCD. Our experience indicates that this strategy is feasible and can be employed to optimise management of this problematic condition.

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MULTIDIMENSIONAL ASSESSMENT OF TREATABLE TRAITS IN SEVERE ASTHMA AND COPD

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Introduction/Aim: Treatable traits have been proposed as a new paradigm for airway disease management. Our aim was to determine the prevalence of traits in severe asthma and COPD compared to healthy controls and to compare trait prevalence by diagnostic label.

Methods: Participants with severe asthma, COPD and age-matched healthy controls were recruited to this cross sectional study and underwent a clinic-based multidimensional assessment to characterise their treatable traits.

Results: Recruited were 140 severe asthma, 45 COPD and 67 healthy control participants. Overall the mean±SD age was 56.6 ± 16.2 years, and 57.5% were female. COPD participants were older compared to those with severe asthma and healthy controls, $p < 0.001$. Post-bronchodilator FEV_1 % predicted was lower in COPD (53.0 ± 19.8) compared to severe asthma (74.7 ± 21.1) and healthy controls (99.0 ± 13.8); $p < 0.001$. Of the 23 possible traits, significantly more were identified in COPD (10.6 ± 2.4) and severe asthma (9.0 ± 2.8) compared to healthy controls (2.4 ± 1.4); $p < 0.001$, with a significant difference between COPD and severe asthma; $p < 0.001$. However, the number of comorbidities was not different between disease groups (COPD 6.8 ± 3.1 versus severe asthma 5.9 ± 2.7). Traits that were more prevalent in COPD compared to severe asthma were dyspnoea; $p < 0.01$, exertional O_2 desaturation; $p < 0.001$, mucous-hypersecretion; $p < 0.05$ and airflow limitation; $p < 0.001$. Those with severe asthma had significantly more daytime-sleepiness; $p < 0.01$, musculoskeletal problems; $p < 0.01$, obesity; $p < 0.05$, upper-airway diseases; $p < 0.001$ and dermatitis; $p < 0.001$. Airway-eosinophilia was more common in severe asthma and airway-neutrophilia and systemic inflammation in COPD, $p < 0.05$, $p < 0.001$, respectively. The prevalence of frequent chest infections, pathogen colonisation, smoking, non-adherence, inhaler-polypharmacy, dysfunctional breathing, reflux, anxiety or depression did not differ between COPD and severe asthma.

Conclusion: This study confirms the heterogeneity of COPD and severe asthma. Multidimensional assessment in chronic airway disease allows for the detection of traits that can be targeted using a precision medicine approach. Trials testing these approaches are needed to advance management.

Declaration of Interest: No interest to declare.

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MICRORNA SIGNATURES IN MALIGNANT PLEURAL MESOTHELIOMA EFFUSIONS

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Introduction/Aim: Malignant pleural mesothelioma (MPM) is an incurable cancer of the pleura that can be difficult to diagnose. Bio-markers for an earlier and/or easier diagnosis are urgently needed. The powerful gene regulators microRNA, have become popular diagnostic targets due to their stable expression within the body. Studies have examined microRNA in MPM and control samples, however it is still unclear which microRNA are potential biomarkers for MPM. Approximately 90% of patients develop pleural effusions which are an ideal source of diagnostic targets as sample collection is minimally invasive. The biomarker potential of microRNA in MPM frozen/fresh effusions is yet to be determined. We hypothesise that microRNA expressed in effusions are potential biomarkers for MPM.

Methods: Taqman OpenArray profiling and real-time quantitative PCR were used to analyse microRNA in a cohort (Cohort 1) of 48 effusion cell and supernatant samples from MPM, lung adenocarcinoma and benign pleural disease patients. The potential microRNA biomarkers were then analysed in a second cohort (Cohort 2) of 60 MPM and lung adeno-carcinoma samples.

Statistics: MicroRNA expression was determined to be significantly different between diseases on a volcano plot with a 2 or more-fold change and a $p < 0.05$. MicroRNA combinations were analysed using logistic regression and diagnostic efficiency was assessed using receiver operating characteristic curves.

Results: An effusion cell signature based on the combination of miR-143, miR-210 and miR-200c for the diagnosis of MPM was identified in Cohort 1 (AUC – 0.92) and validated in Cohort 2 (AUC – 0.71).

Conclusion: MicroRNA expressed in effusion cells are potential biomarkers for differentiating MPM from lung adenocarcinoma.

Declaration of Interest: No conflicts of interest.

TRANSCRIPTIONAL PROFILING OF EPITHELIUM REVEALS SIMILAR COMPOSITION, BUT PARTIALLY DIFFERING ORGANIZATION BETWEEN THE UPPER AND LOWER AIRWAY

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Introduction/Aim: Emerging evidence suggests that the upper and lower airway are unified and that under disease settings, a pathological process in one region of the airway would affect the function of the entire airway. However, direct evidence supporting this is extremely limited and only inferred by the fact that the respiratory tract is continuous lined with epithelial cells and clinical observations of improved outcomes for lower airway disease following management of upper airway disease.

Methods: Here, we directly tested this hypothesis by performing RNA-sequencing on predominantly matched nasal and bronchial epithelial brushings from 63 children with or without atopy or asthma. We then used a combination of differential gene expression, and gene co-expression analyses to determine similarity of the transcriptional landscape between the upper and lower airway.

Results: Overall, we report ~50% homology and ~50% divergence between the two sites, independent of disease phenotype and atopy. We identified sixteen modules of co-expressed genes (enriched for specific biological functions) to be conserved across nasal and bronchial epithelium. However, almost half of these were differentially expressed between the two regions.

Conclusion: Our findings suggest that in part the upper and lower airway do share a similar transcriptional composition, but also exhibit significant differences that is reflective of their region-specific functions. With significant interest in biomarker development, our data suggests that in certain settings nasal epithelial cells, may inform on lower airway disease and thus has considerable clinical implications.

Conflict of Interest: No conflict of interest.

MITOCHONDRIAL DYSFUNCTION REINFORCES THE SENESCENT PHENOTYPE IN IPF LUNG FIBROBLASTS

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Introduction/Aim: Increasing evidence highlights that cellular senescence contributes to idiopathic pulmonary fibrosis (IPF). The DNA damage response (DDR) in senescence also leads to escalated mitochondrial superoxide production to reinforce senescence. This study characterises senescence in lung fibroblasts from IPF patients (IPF-LFs) and age-matched controls (Ctrl-LFs), delineating the role of mitochondria in senescence stabilization.

Methods: Fibroblast senescence was assessed using a composite set of markers, including p21 expression and senescence-associated-β-galactosidase activity, which were measured by PCR and cytochemical staining, respectively. The DDR was detected by formation of phosphorylated-p53 nuclear foci using immunofluorescence. A senescent-associated secretory phenotype (SASP) was characterised by measuring increases in cytokine production and inflammatory gene expression with ELISA and Nanostring technology, respectively. Mitochondrial dysfunction was monitored by increases in mitochondrial stress, mass and superoxide using the fluorogenic dyes, n-nonyl-acridine orange, Mitotracker Green and MitoSOX, respectively.

Results: Even at early passage, IPF-LFs were more senescent-like than Ctrl-LFs, exhibiting an intensified DDR, a SASP and mitochondrial dysfunction. The DNA damaging agent etoposide augmented senescence in Ctrl-LFs accompanied by heightened mitochondrial stress, mass and superoxide production. However, it had no effect on IPF-LFs. Mitochondrial perturbation by rotenone also evoked a DDR and senescence in Ctrl-LFs. Inhibition of mTORC1, a regulator of mitochondrial function or incubation with the antioxidant, *N*-acetyl cysteine attenuated pharmacological-induced senescence.

Conclusion: IPF-LFs exhibit senescent-like features and mitochondrial dysfunction reinforces the senescent phenotype. Understanding the mechanisms by which mitochondria contribute to fibroblast senescence in IPF has potentially important therapeutic implications.

NOTCH3 INHIBITION SIGNIFICANTLY REDUCES MUC5AC IN HUMAN AIRWAY EPITHELIAL CELLS

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Introduction: Mucus overproduction in patients with asthma is linked to increased hospitalisations and morbidity. The Notch family of receptor proteins regulate airway mucus production via differentiation mechanisms that direct cells towards secretory or ciliated morphology. However little is known regarding Notch's role during mucus production, following differentiation.

Aim/Hypothesis: To examine the impact of inhibiting Notch signalling on mucus production in fully differentiated primary bronchial epithelial cells (pBECs) from control subjects as well as patients with asthma. We hypothesize that Notch inhibition will downregulate mucus production.

Methods: pBECs from 5-6 donors of each cohort were grown at air-liquid interface (ALI) culture for 25 days to promote multicellular differentiation. At this time, cells were treated with dibenzazepine (DBZ), a potent inhibitor of Notch signalling for a further 96h during which, apical lining fluid was collected every 24h for assessment of MUC5AC release. At the completion of the experiment, samples were also collected for protein, mRNA and histological analysis. To assess the direct role of Notch3 on MUC5AC, siRNA knockdown of Notch3 was also performed in monolayer cultures of human epithelial cells.

Results: DBZ treatment significantly reduced MUC5AC expression and release in all phenotypes as assessed by qPCR, ELISA and IHC. Western blotting/qPCR revealed significant reduction of NOTCH3 intracellular domain (NICD3) and Notch3 mRNA in pBECs from all donor phenotypes. Notch3 siRNA knockdown significantly reduced MUC5AC protein. Finally, the goblet cell marker protein CLCA1 was unchanged across all treatments.

Conclusion: Notch3 inhibition reduced MUC5AC expression and secretion from differentiated pBECs, independent of goblet cell number. This reduction is NOTCH3 dependent and occurs in pBECs from asthmatics and non-asthmatics. This suggests that Notch3 regulates MUC5AC production outside of Notch's well characterised role during secretory cell differentiation.

INVESTIGATING THE ROLE OF HISTONE ACETYLATION IN TGF-β INDUCED FIBROSIS IN COPD

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Introduction/Aim: Fibrosis and thickening of the airway smooth muscle (ASM) layer are components of airway remodeling and have been attributed to an increase in the ECM fraction in the ASM layer[2]. It has been shown that epigenetic changes occur in COPD (immune cells and peripheral lung tissue)[3] but it is not known if airway mesenchymal cells are reprogrammed. This project aims to identify differentially expressed ECM proteins and investigate the effect of epigenetic inhibition on protein expression.

Methods: Primary human ASM cells were isolated from lung tissue of COPD and non-COPD smoking patients. ASM cells were grown in culture and stimulated with TGF-β (10ng/ml) +/- histone deacetylase inhibitor Trichostatin A (TSA), bromo- and extra terminal domain (BET) protein inhibitor (+)JQ1, or histone acetyltransferase inhibitor Curcumin. Cell lysates were collected after 48 hours of treatment. Microarray analyses were carried out to identify basal differences in expression of ECM and epigenetic gene targets between COPD and non-COPD smokers. qPCR carried out to confirm microarray analyses and determine effect of epigenetic inhibitors.

Results/Conclusion: ASM cells from COPD patients show augmented *col5a1*, *col15a1* and *TNC* expression in response to stimulation with TGF-β (10ng/mL) when compared to cells of smokers without COPD. Inhibition with TSA had no effect on *col5a1,* or *TNC* expression in cells from both patient groups, whilst inhibiting *col15a1* expression in COPD. (+)JQ1 treatment significantly abrogated expression of *col15a1* COPD and non-COPD groups, whilst *col5a1* expression was abrogated in COPD and *TNC* in non-COPD. *Col5a1* expression was significantly repressed with Curcumin treatment in non-COPD group only. The different responses between non-COPD susceptible smokers and COPD group highlights the epigenetic differences in disease, and that targeting histone acetylation may be a therapeutic option of small airway fibrosis in COPD.

DYSREGULATED NOTCH SIGNALING DURING ASTHMATIC AIRWAY EPITHELIAL REPAIR

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Introduction/Aim: The airway epithelium is a key driver in asthma pathogenesis, partly due to its dysregulated response to injury. Notch signalling and potential crosstalk with integrins, modulate epithelial cell migration and repair. Therefore, it was hypothesised that aberrant Notch signalling in asthmatic epithelium would result in defective repair by airway epithelial cells(AEC) via regulation of integrins.

Methods: Tracheobronchial airway brushings of non-asthmatic (n=18; age range: 1.2-15.6yr; 8 males) and asthmatic (n=14; 3.3-16.9yr; 12 males) children were utilised for AEC isolation and culture. Notch receptor and ligand gene expression was investigated by qPCR (mean-±SEM; arbitrary units, AU). Notch signalling in cultures was inhibited with gamma secretase inhibitor, DAPT(N-[N-(3,5-Difluoro-phenacetyl)-L-ala-nyl]-S-phenylglycine-t-butyl ester) over a dose-range (1nM-10μM). Linear wounds were performed on AEC to assess repair (IncuCyte ZOOM®, Essen Bioscience). Integrin α5β1 protein expression was investigated by In-Cell™ Western.

Results: Notch receptors (*NOTCH1-4*) and ligands (*JAG1-2, DLL1, 3, 4*) were found to be expressed in *ex vivo* AEC from non-asthmatic and asthmatic children, however only *NOTCH2* and *JAG1* gene expression were differentially expressed in AEC from asthmatic children (*NOTCH2*, 10-fold downregulation[p<0.01]; *JAG1*, 3.5-fold upregulation[p<0.01]; n=6). Following *in vitro* wounding, *NOTCH2* (2.92±0.11AU) and *JAG1* (3.35±0.14AU) mRNA levels were induced within 48hr in AEC of non-asthmatic children. However, an earlier induction of both *NOTCH2* (2.58±0.10 AU) and *JAG1* (4.19±0.09 AU) at 24hr post wounding was observed in AEC from asthmatic children. Global inhibition of Notch signalling resulted in a 40% reduction in wound repair and an inability to close the wound, observed at the maximal dose, 10μM. Furthermore, Notch signalling inhibition resulted in a reduction of α5 integrin protein expression of 30% at 500 nM DAPT, but not β1 integrin protein expression.

Conclusion: Findings suggest dysregulated expression of Notch signalling molecules, in conjunction with its role in regulating integrin expression, contribute to the defective wound repair of the asthmatic airway epithelium.

Chronic Obstructive Pulmonary Disease (COPD) 3

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PULMONARY REHABILITATION DOES NOT IMPROVE OBJECTIVE MEASURES OF SLEEP QUALITY IN PEOPLE WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Introduction/Aim: More than 50% of people with chronic obstructive pulmonary disease (COPD) report poor sleep quality which has been associated with increased morbidity and mortality. There are varying reports of the effect of pulmonary rehabilitation (PR) on self-reported sleep quality. We aimed to assess the effect of PR on objectively measured sleep quality in people with COPD.

Methods: This is a secondary analysis of data collected as part of an RCT comparing home-based to centre-based PR for COPD. Sleep quality was assessed objectively using the SenseWear Armband (SWA, Bodymedia USA), worn for 7 days before and after an 8-week PR programme. Sleep characteristics were derived from accelerometer positional data and registration of sleep state by the SWA, determined from energy expenditure.

Results: 33 participants (17 male; mean$\pm$SD age 68$\pm$11 years, FEV_1 56$\pm$21 %predicted) had paired pre and post PR sleep data. Twenty participants received centre-based PR and n=13 were allocated to home-based PR.

Pre-PR median [interquartile range] sleep onset latency (SOL) was 25 [9, 41] minutes, total sleep time (TST) 390 [339, 421] minutes and wake after sleep onset (WASO) 74 [43, 106] minutes. Sleep efficiency (SE) was low (75% [64, 84]).

No significant differences were seen in any sleep parameter (SOL, TST, WASO, SE) after PR (all p>0.10), between intervention groups (all p>0.20), or within PR groups (all p=0.13). There was no association between sleep parameters and measures of quality of life or function before or after PR. Attendance at a greater proportion of PR sessions was moderately associated with more TST at end rehabilitation (r_s=0.5, p=0.009).

Conclusion: Sleep quality, measured objectively using actigraphy, did not improve after an 8-week PR programme in individuals with COPD. Whether ongoing participation in regular exercise training beyond the duration of PR may influence sleep quality is yet to be determined.

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IMPACT OF THE 2017 GOLD STRATEGY ON TIOTROPIUM +OLODATEROL RESPONSE

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Introduction/Aim: In the 2017 GOLD COPD strategy, treatment choices are guided by patient classification based on assessment of symptoms and exacerbation history. The previous strategy also included lung function. Here, we investigated the effect of the 2017 classification on an analysis of the efficacy of tiotropium+olodaterol (T+O) in GOLD stage A/B patients with COPD.

Methods: Patients from the Phase III, replicate 52-week TONADO studies (NCT01431274, NCT01431287), who received T+O or the monocomponents, were classed as GOLD A/B or C/D by the 2017 (exacerbation history) or 2014 (lung function and exacerbation history) criteria. Distinction between A and B was not possible as mMRC Dyspnoea Scale and COPD Assessment Test had not been used. St. George's Respiratory Questionnaire (SGRQ) and transition dyspnoea index (TDI) were analysed.

Results: More patients are classified as GOLD A/B with 2017 criteria than with 2014 guidelines. T+O was superior to monotherapy for SGRQ and TDI in 2017 A/B population (Table).

Conclusion: Using exacerbation history alone (GOLD 2017), rather than combined with lung function, results in more patients classified as GOLD A/B, leading to more statistical power to investigate differences between T+O and monotherapies. Using the 2017 strategy, T+O had a greater impact on SGRQ and TDI than monotherapies in GOLD A/B patients.

Table

	2017 GOLD A/B			2014 GOLD A/B		
	n	Adjusted mean ±SEM	Responders n(%)[a/b]	n	Adjusted mean ±SEM	Responders n(%)[a/b]
SGRQ total score change from baseline						
T+O 5/5μg	739	−6.9±0.4	428(58)	390	−6.4±0.6	219(56)
Tiotropium 5μg	719	−5.0±0.4	343(48)	393	−5.2±0.6	195(50)
Olodaterol 5μg	744	−5.1±0.4	332(45)	412	−6.2±0.6	198(48)
Mahler TDI focal score						
T+O 5/5μg	751	1.95±0.11	400(53)	396	2.12±0.15	219(55)
Tiotropium 5μg	737	1.50±0.11	351(48)	395	1.93±0.15	204(52)
Olodaterol 5μg	768	1.51±0.11	358(47)	425	1.88±0.14	213(50)

[a]SGRQ is ≥4.0 units better than baseline; [b]Mahler TDI is ≥1.0 unit better than baseline

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THE IMPACT OF PULMONARY REHABILITATION ON PEOPLE WITH MILD CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A RANDOMISED CONTROLLED TRIAL

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Introduction/Aim: People with mild chronic obstructive pulmonary disease (COPD) experience exercise intolerance, dyspnoea and poor health-related quality of life. However, the role of pulmonary rehabilitation in this group is unclear. This randomised controlled trial aimed to explore effects of home-based pulmonary rehabilitation (PR) in people with mild COPD.

Methods: People with mild COPD (FEV_1/FVC<70%; FEV_1>80%predicted) with a smoking history of $\geq$ 10 packet years were randomised to either 8-weeks of home-based PR (one home visit and seven once-weekly telephone calls) or attention control (weekly social telephone calls). Six-minute walk distance (6MWD), modified Medical Research Council (mMRC) dyspnoea score and Chronic Respiratory Questionnaire (CRQ) scores were compared between groups post intervention and at 6-months.

Results: A total of 58 participants (34 females, mean age 68 (SD 9) years, FEV_1 90 (7) %predicted, 6MWD 496 (105) metres) were included with 29 participants randomised to home-based PR. Participants attended an average of 6.8 of the eight scheduled sessions, ranging from three to eight sessions. Both groups showed improvements in exercise capacity, symptoms and health-related quality of life over time, however there was no between-group differences in the primary outcome of 6MWD at end-intervention (mean difference 1.4 metres, 95% confidence interval (CI) -28.7 to 31.4 metres) or six months (9.8 metres, 95% CI -30.5 to 50.2 metres). At 6-months follow-up home-based PR participants were more likely to have clinically important improvements in CRQ emotional function (50% of home PR vs 0% control, *p*<0.001) and CRQ total score (45% vs 17%, *p*=0.05), however there were no other differences in symptoms or other aspects of health-related quality of life.

Conclusion: For people with mild COPD, home-based pulmonary rehabilitation did not improve exercise capacity or health-related quality of life more than weekly social telephone calls.

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NO ADDITIONAL BENEFITS FOR PULMONARY REHABILITATION INCLUDING COGNITIVE BEHAVIOURAL THERAPY

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Aim: This pragmatic randomised controlled trial aimed to determine whether comprehensive pulmonary rehabilitation (CPR) including cognitive behaviour therapy (CBT) for the sensation of breathlessness significantly improved health outcomes beyond those achieved with CPR alone.

Methods: People with COPD (FEV_1 < 80 % pred, $FEV1/FVC$ <70%, GOLD Grade $\geq$ 2) were block randomised to eight weeks of CPR with or without CBT (BREVE). Primary (six minute walk test (6MWT), Hospital Anxiety and Depression scale (HADs)) and secondary outcomes (breathlessness in daily life (Dyspnoea-12 (D-12), Multidimensional Dyspnoea Profile (MDP), quality of life (Chronic Respiratory Questionnaire (CRQ) and habitual daily activity (accelerometry)) were assessed before and one, six and 12 months post intervention. Differences between groups were assessed with latent growth models (non-linear change) with and without covariates (age, sex, BMI, GOLD grade, comorbidity, smoking status and CPRP attendance) using both intention to treat (ITT) and per protocol (PP: commenced intervention and valid 6MWT) approaches with p$\leq$0.05 significant.

Results: 101 participants (mean age 70 $\pm$ SD 8.5, 54 males, FEV_1 % pred 47.7 $\pm$ 16.3) enrolled in the trial (n=88 for PP analysis). With the exception of CRQ and MDP subdomain scores, groups did not differ significantly in either trajectory or assessment points for primary or secondary outcomes (ITT, PP with and without covariates). For ITT, improvements in CRQ-Dyspnoea favoured CPRP + BREVE (unadjusted model p = 0.03) whereas reductions in MDP-Emotional Response favoured CPRP alone (adjusted model p = 0.03). For PP with and without adjustment for covariates, differences between groups for CRQ and MDP favoured CPRP alone (CRQ-Mastery p = 0.04; MDP-Immediate Perception p = 0.03; MDP- Emotional Response p = 0.04).

Conclusion: In this cohort of people participating in CPRP, there was no clear additional short or longer term benefit of combining CPRP with CBT for breathlessness.

Clinical Trial registration: Australian New Zealand Clinical Trials Registry (ANZCTR12611000292976)

AN AUDIT OF ACTIVITY AND OUTCOMES OF THE AUSTIN RESPIRATORY HIGH DEPENDENCY UNIT

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Introduction/Aim: There is a paucity of literature documenting Respiratory High Dependency Unit (HDU) outcomes. We present demographic and outcome data for patients undergoing care in the Austin Hospital Respiratory HDU, which provides single organ support for patients with acute respiratory failure.

Methods: This retrospective audit describes all admissions to the Respiratory HDU during January to December 2016. Logistic regression was used to identify factors related to in-hospital mortality.

Results: 82 patients, mean age 67.3 years (SD 16.83,) underwent 83 HDU admissions. 53% (44 patients) were male. Mean HDU length of stay (LOS) was 2.17 days (SD 2.15, 95% CI 1.71-2.63.) The main precipitating causes for respiratory failure were exacerbation of chronic obstructive pulmonary disease (n=25, 30.12%) and infection (n=23, 27.7%.) 25 admissions (30.12%) were for management of hypoxic respiratory failure, 9 of which were treated with non-invasive ventilation (NIV). N=18 (21.69%) admissions occurred following a ward MET call and had an average HDU LOS of 1.5 days (SD 0.99, 95% CI 1.11-2.03.) 7 patients (8.4% of admissions) did not survive to hospital discharge. A higher age-adjusted Charlson comorbidity score was associated with higher in-hospital mortality (OR 1.41, p=0.021, 95% CI 1.05-1.89.)

Conclusion: The HDU has a high turnover of patients, including post-MET call care. Outcomes are generally good, however increased comorbidity as reflected by a higher age-adjusted Charlson score was associated with in-hospital mortality. A proportion of hypoxaemic patients received NIV, raising an opportunity for review of current practice.

Grant Support: None.

ALPHA-1 ANTITRYPSIN TREATMENT SLOWS EMPHYSEMA PROGRESSION INDEPENDENT OF BASELINE FEV1

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Introduction/Aim: Patients with alpha-1 antitrypsin deficiency (AATD) develop pulmonary emphysema prematurely. RAPID, a randomized placebo-controlled trial, showed that treatment with A_1-PI (Zemaira/Respreeza) slows emphysema progression. Based on observational data, which showed a reduced loss in FEV_1 in a subgroup of patients, current guidelines recommend treatment with A_1-PI when FEV_1 is between 30 and 65% predicted. However, the relationship between the effect of treatment on lung structure preservation and FEV_1 is unclear. The aim was to assess the effect of treatment in relation to baseline FEV_1 % predicted as measured by change in computed tomography (CT) lung density in 180 patients randomized in RAPID with baseline FEV_1 between 27% and 79% predicted.

Methods: Changes in annual CT lung density decline rates for both active and placebo treated patients were calculated at 2 years. A random slope intercept model with baseline FEV_1 and treatment group as covariates was used to analyse the influence on treatment effect.

Results: Baseline lung function impairment did not affect long-term changes in lung density (p=ns), the regression line was flat. Active treatment was associated with lung density preservation (P<0.0001) and the regression line was parallel to that of placebo treated patients. The regression line for rate of annual lung density decline vs baseline FEV1% was flat with no interaction between treatment group and baseline FEV_1.

Conclusion: These data demonstrate that patients with AATD who are treated with A_1-PI therapy derive an equal benefit in terms of lung tissue preservation over 2-years that is independent of their pre-treatment FEV_1%.

Interventional Pulmonology / Bronchology 2

DIAGNOSTIC ACCURACY OF BRONCHOSCOPY WITH CONSCIOUS SEDATION VERSUS GENERAL ANAESTHETIC IN A RANDOMISED PROSPECTIVE COHORT

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Introduction/Aim: To assess for non-inferiority of diagnostic accuracy for conscious sedation (CS) compared with general anaesthetic (GA) for bronchoscopic procedures.

Methods: We report on a further analysis of a prospective randomised patient group. Patients undergoing therapeutic and diagnostic procedures within the RBWH were considered for trial entry and randomization. Procedures included standard bronchoscopy, endobronchial ultrasound (EBUS) with transbronchial node aspiration (TBNA) or EBUS Guide Sheath. Patients were randomized to either CS or GA, stratified for Charlson Comorbidity Index. GA was defined as the use of a Laryngeal mask airway and/or propofol usage. Diagnosis obtained at bronchoscopy was compared to the final clinical diagnosis.

Results: 93 patients were randomised. 49 of these received CS of which 32 were diagnostic procedures, with 14 being EBUS TBNAs. In the GA group these numbers were 44, 32 and 14 respectively. A final diagnosis of malignancy was made in 12 cases in the CS group (38%) and 18 cases in the GA group (56%). For all diagnostic procedures there was no significant difference in diagnostic accuracy between CS and GA, 93.3 vs 87.5% (p=0.67). Regarding EBUS TBNA diagnostic accuracy was 100 vs 92.9% (P=1.00). 24 lymph nodes were sampled in the CS group, 46% paratracheal, 17% subcarinal and 38% hilar. 21 nodes were sampled in the GA group, 24% paratracheal, 29% subcarinal and 48% hilar. Average passes per node were 3.28 $\pm$0.79 and 3.00 $\pm$1.00 respectively (p=0.29). For the CS cases only 2 drugs were used: Midazolam (mean dose 4.4mg $\pm$1.0) and Fentanyl. A variety of anaesthetic agents were used in the GA group. There was no significant difference regarding mean fentanyl dosage of 90.6mcg $\pm$16 for CS vs 86.2mcg $\pm$52.9 for GA (p=0.60).

Conclusion: CS is not inferior to GA in terms of diagnostic accuracy, including EBUS TBNA from a wide range of nodal stations.

Grant Support: Nil

SAFETY AND DIAGNOSTIC PERFORMANCE OF CRYOBIOPSY IN MELBOURNE, AUSTRALIA

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Introduction/Aim: Cryobiopsy is an emerging technique with mounting utilisation in the settings of diffuse parenchymal lung disease (DPLD) and neoplasia. The safety and usage pattern of cryobiopsy is not well established in the Australian setting. At our tertiary institution, we routinely perform cryobiopsy with general anaesthesia, endotracheal intubation and fluoroscopy guided 1.9mm cryoprobe via ERBECRYO 2 with routine bronchial blocker balloon deployment. We thus set out to establish the safety and usage patterns of our cryobiopsy service.

Methods: Following institutional ethics approval, we conducted a retrospective audit of our institution's cryobiopsy register (November 2015-September 2017). Records missing from our electronic records were supplemented by a hand search, and by contacting referrers. Results were cross-checked by two authors (CD, LS), verified by a third (PL) and are presented are mean$\pm$SD.

Results: 49 patients underwent cryobiopsy in the audit period, with 2.6$\pm$1.1 biopsies performed per patient, and targets as follows: right lower lobe 23, right upper lobe 15, left lower lobe 12, left upper lobe 11 and endobronchial 4. The predominant indication for cryobiopsy was suspected DPLD (43/49) with possible malignancy accounting for the remaining cases. The mean FVC was 88$\pm$17% predicted (lowest 57%) and DLCO 59$\pm$17% predicted (lowest 35%). Same day discharge was achieved in 42/49, with 2 further uncomplicated cases staying overnight for social reasons. There were no cases of severe bleeding. Bleeding was moderate (controllable with endobronchial interventions) in 5 cases; 4 cases had pneumothoraces of whom 2 required intercostal catheter insertion. Physicians agreed or strongly agreed that cryobiopsy was helpful in 45/49 patients. Cryobiopsy was suggestive or diagnostic of DPLD in 39, infection in 1 and malignancy in 6. No abnormality was present in 2, 1 of whom was referred for surgical lung biopsy.

Conclusion: Cryobiopsy appears to have an acceptable safety profile with a good diagnostic yield.

Key Words: cryobiopsy, bronchoscopy, interstitial lung disease

Grant Support: Nil

UTILITY OF RADIAL EBUS CRYOBIOPSY IN DIAGNOSIS OF SOLITARY PULMONARY NODULES

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Introduction/Aim: Forceps biopsy through a guide sheet after locating the lesion using radial probe EBUS is an established technique in diagnosis of solitary pulmonary modules (SPN). The yield, however, drops significantly if the lesion is not concentric. Furthermore, the 1.7mm forceps often provide small samples which occasionally fall short of providing all the information required in malignancies. Using a cryoprobe in combination with radial EBUS could potentially provide larger samples and increase the yield in non-concentric lesions.

Methods: All patients who underwent radial EBUS cryobiopsy for diagnosis of SPN at Concord and Macquarie University hospitals in Sydney were included in this study. A retrospective audit was undertaken to obtain demographic, baseline physiological and procedural data. Complications and length of stay were recorded. Yield was determined by histopathology and clinical data.

Results: A total of 9 patients (3 female, mean age 73.4 years) have so far been included in the study. All procedures were performed under general anesthesia, with rigid intubation used in 8 cases. The lesion was located in all cases using an EBUS radial probe with only one eccenteric lesion. Most targets were located in the upper lobes (66.6%). An average of 3.1 biopsies were obtained. No cases of pneumothorax or severe bleeding were observed. Only two patients stayed overnight after the procedure. Average diameter of specimens was 5mm. Definite malignant pathology was diagnosed in 5 cases with an overall yield of 7/9 (77.7%)

Conclusion: Radial EBUS cryobiopsy is a feasable alternative in diagnosis of SPN. The yield is comparable to previously reported techniques, however the larger specimens obtained by cryobiopsy could potentially provide invaluable data in malignant conditions.

Grant Support:

TRANSBRONCHIAL CRYOBIOPSY IN INTERSTITIAL LUNG DISEASE—A RETROSPECTIVE AUDIT

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Introduction/Aim: Histolopathology is often required to achieve a multidisciplinary diagnosis in diffuse parenchymal lung disease. Surgical lung biopsy (SLB) remains the gold standard but is associated with significant morbidity and mortality. Recent emergence of transbronchial cryobiopsy (TBCB) as a potential alternative to SLB, promising less complications and a comparable yield, has divided the world of interventional pulmonology. There have been numerous publications reporting different and occasionally contradicting outcomes. Despite relative popularity of TBCB in our region, so far there have not been any published series from Australia.

Methods: All patients who underwent TBCB at Concord, Macquarie University and Liverpool Hospitals in Sydney for diagnosis of diffuse parenchymal lung disease between August 2013 and June 2017 were included. A retrospective audit was undertaken to obtain demographic, baseline physiological and Procedural data. Complications and length of stay were recorded. Diagnostic value of TBCB was assessed by its histopathological and clinical impact. All biopsy specimens were reviewed by a single investigator to record size, presence of artefact, percentage of alveolar area and presence of pleura or proximal airway structures.

Results: A total of 46 patients (25 male, average age 62.2) were enrolled in this study. All cases were performed under general anaesthesia with rigid bronchoscope access. An average of 6.1 biopsies were obtained from 1-3 lobes. Most patients were discharged home the same day (65.7%) with average length of stay of 1.05 nights. Pneumothorax was observed in 10.5% of the patients with severe endobronchial bleeding in 5.2%. There were no deaths reported within 30 days of the procedure. Histopathological data as well as yield are currently being analysed.

Conclusion: Our preliminary data suggests that TBCB is a relatively safe procedure with an acceptable yield which could be considered as an alternative to SLB.

Grant Support:

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STUDY OF ENDOBRONCHIAL VALVES INSERTION FOR ADVANCED EMPHYSEMA AT THE ROYAL BRISBANE AND WOMEN'S HOSPITAL IN QUEENSLAND AUSTRALIA

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Introduction/Aim: Emphysema is a leading cause of disability and death. Its current medical treatment shows certain limitations in the advanced stage of the disease. Also, there is limited evidence in the Australian setting regarding therapeutic interventions for reducing hyperinflation, including endobronchial valves insertion (EBV). This study examined the outcomes of EBV insertion in patients with severe emphysema at the Royal Brisbane and Women's Hospital.

Methods: This is a retrospective review of patients with severe emphysema who underwent EBV insertion from 2011-2017. The primary outcomes were change in exercise tolerance as measured by the six-minute walk test (6MWT) and quality of life (QoL) as measured by the St. George's Respiratory Questionnaire (SGRQ) and direct questioning. Variables of interest were measured pre- and post-EBV placement.

Results: Of the 31 patients included in the study, 15 were females. Age ranged from 50 to 80 years (median age=67 years). Sixteen patients had no complications, and 9 patients had multiple complications. Three patients were readmitted within 30 days and 2 died mainly due to old-age co-morbidities. Ninety-day mortality rate was 0%. Pre and post values for 6MWT were obtained for 18 patients, SGRQ for 10 patients, and QoL data for 24 patients. Patients with complete data (25) showed improved mean values of SGRQ, 6MWT, and lung function. Mean SGRQ was reduced by 24 units (p=0.001), and 6MWT was increased by 78 metres (p=0.001). Mean FEV1 was increased by 4% (p=0.006), and residual volume and TLC were reduced by 25% and 11% (p=0.009 and 0.01), respectively. Significant improvement in QoL was reported in 13 patients while 11 reported improvement/slight improvement.

Conclusion: EBV is an effective and safe therapy that improves lung function, exercise capacity, and QoL in selected patients with emphysema. Further studies on a larger population need to confirm our findings.

Grant Support: Nil

Conflict of Interest: None.

Keywords: Severe emphysema, endobronchial valve, quality of life

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BRONCHIAL THERMOPLASTY REDUCES GAS TRAPPING IN SEVERE ASTHMA

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Introduction/Aim: In randomized controlled trials, bronchial thermoplasty (BT) has been proven to reduce symptoms in severe asthma. The mechanisms by which this is achieved are still uncertain as no improvement in spirometry is observed in most studies. We postulated that BT might improve lung mechanics by altering airway resistance in the small airways of the lung in ways not measured by FEV1. This study aimed to evaluate changes in measures of gas trapping particularly the Residual Volume (RV).

Methods: A prospective cohort of 32 consecutive patients with severe asthma who were listed for BT at two tertiary institutions (Frankston Hospital and Macquarie University Hospital) were evaluated at three time points, namely baseline, and then 6 weeks and 6 months post completion of all procedures. At each evaluation, medication usage, symptom scores (Asthma Control Questionnaire, ACQ-5) and exacerbation history were obtained, and lung function was evaluated by (i) spirometry (ii) gas diffusion (DLCO) and (iii) static lung volumes by body plethysmography.

Results: ACQ-5 improved from 3.0 ± 0.8 at baseline to 1.5 ± 0.9 at 6 months (mean$\pm$SD, p<0.001). Daily reliever salbutamol usage improved from 8.3 ± 5.6 to 3.5 ± 4.3 puffs per day (p<0.001). Exacerbation frequency and maintenance oral corticosteroid usage also significantly declined (p<0.001), but no changes in any spirometric parameter were demonstrated. DLCO was also unaltered by BT treatment. However, a significant reduction in gas trapping was observed with RV falling from $146\pm37\%$ predicted to $136\pm29\%$predicted (p,0.002, paired t test). Significant improvements in TLC and FRC were also observed. These changes were evident at the 6 week time period and maintained at 6 months. The change in RV was negatively correlated with the baseline FEV1, r=-0.474, p=0.006, indicating that the greatest improvement was evident in the most obstructed patients.

Conclusion: Bronchial thermoplasty appears to improve gas trapping and this effect is greatest in the most severely obstructed patients. The improvement may relate to changes in the mechanical properties of small airways that are not measured with spirometry.

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Lung Cancer

EPITHELIAL MESENCHYMAL TRANSITION (EMT) AND NON-SMALL CELL LUNG CANCER (NSCLC): A MUTUAL ASSOCIATION WITH AIRWAY DISEASE

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Introduction/Aim: COPD and smoking play a vital role in development of NSCLC. Local progression and metastasis of NSCLC has been associated with epithelial mesenchymal transition (EMT), which is implicated in COPD pathogenesis.

Methods: We have investigated EMT biomarkers (S100A4, Vimentin, and N-cadherin), an epithelial activation marker (EGFR) and a vascularity marker (Type-IV collagen) in surgically resected tissue from patients with NSCLC (adeno- and squamous cell carcinoma), and compared them with corresponding non-tumorous airways.

Results: EGFR, S100A4, vimentin, N-cadherin expression was higher in tumour cells, at the peripheral leading edge of NSCLC when compared with centrally located tumour cells of same subjects (P<0.01). Same was with Type-IV collagen expressing blood vessels. EGFR and S100A4 expression was related to differentiation status (P<0.05) and TNM stage (P<0.05) of NSCLC. Moreover, EMT markers in the leading edge were significantly related to airway EMT activity, while peripheral edge vascularity of squamous cell-carcinoma only was significantly related to large airway Rbm vascularity (P<0.05).

Conclusion: EGFR and EMT-related protein expression was remarkably high at peripheral leading edge of NSCLCs and related to tumour characteristics associated with poor prognosis. The relationships between EMT-related tumour bio-marker expression and those in the airway epithelium and Rbm, provides a background for utility of airway changes in clinical settings.

Conflict of Interest: Authors declare no conflict of interest.

HEALTH-RELATED QUALITY OF LIFE - QUEENSLAND LUNG CANCER SCREENING STUDY

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Introduction/Aim: Lung cancer screening has a high false positive rate, carrying the potential for negative psychological impact. We report health-related quality of life (HRQoL) from the first year of screening in the Queensland Lung Cancer Screening Study (QLCSS).

Methods: QLCSS screened 256 healthy volunteers aged 60-74 with extensive current or former smoking history (pack years ≥30, quit <15 years prior). Scan results were defined based on 12 months follow-up: false-positive scans (FP) were lung cancer–free at 1 year; true-positives (TP) were not. There were no false negatives. Global health status (physical and mental function) was assessed using a 4-week recall period at baseline (pre-screening), 1 month, 6 months and 12 months after baseline screening scan using the Short Form 12 version 2.0 (SF-12). SF-12 contains twelve questions. Aggregate summary measures (Mental Component Summary (MCS) and Physical Component Summary (PCS)) were calculated using factor weights derived from a 1998 US general population sample. MCS and PCS range between 0 and 100; higher values indicate better health. The Minimally Important Difference determined clinically meaningful differences (MID = half of a standard deviation (SD) of the mean).

Results: Response to each questionnaire was ≥88% (table 1). Baseline mean (SD) for MCS and PCS were 54.82 (6.83) and 49.90 (7.72) respectively. MCS was above or at the general population norm in 91%; PCS was above or at the norm in 76%. Small changes, below MID, were seen in FP and Negative groups at most time-points (Figure 1). Larger changes were seen in TP group, however, the number of responses was very small.

Conclusion: Screening was associated with small measurable changes in global HRQoL. There was no clinically meaningful difference between participants with negative or FP scans.

Table 1   Respondents, time point by baseline scan result

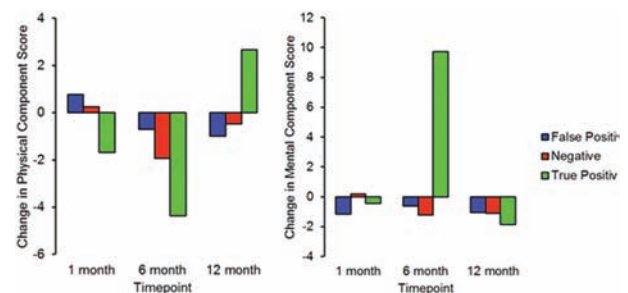| Scan result	Base-line	1 month	6 month	12 month
False Positive	123	112	112	115
Negative	127	120	111	119
True Positive	5	5	1	2
Missing	1	19	32	20
Response rate %	100	93	88	92

Figure 1   Mean change in Physical Component Score and Mental Component Score from baseline.

PLEURAL FLUID CHOLESTEROL IS USEFUL IN DISTINGUISHING EXUDATES FROM TRANSUDATES

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Introduction/Aim: Light's criteria is the gold standard for distinguishing between exudative and transudative pleural effusions (98% sensitivity, 80% specificity). The usefulness of pleural fluid cholesterol to improve diagnostic accuracy compared to Light's criteria is unclear. This study aims to determine i) the level of pleural fluid cholesterol and triglyceride and b) its use in distinguishing exudates from transudates.

Methods: Pleural fluid was prospectively collected from 110 consecutive pleural effusion cases. The fluid was analysed by an accredited laboratory (PathWest, WA) for protein, lactate dehydrogenase (LDH), cholesterol and triglycerides. Aetiology of the effusion was independently verified based on clinical, radiological and pathological assessment. The effusion was classed as an exudate (89) or transudate (21) based on final aetiology.

Results: Exudates were mainly due to malignancy (68 including 13 lung, 6 breast, and 26 mesothelioma effusions), pleural infections (6) and benign pleuritis (5). Transudates were secondary to heart failure (16), hepatic hydrothorax (4) and peritoneal dialyses (1). Exudates had higher pleural fluid protein [median 41.5 (IQR 36-46) g/dL], LDH [314 (203-611) mmol/L], cholesterol [2.08 (1.67-2.61) mmol/L] and triglycerides [0.36 (0.24-0.57) mmol/L] compared to transudates with fluid protein [21 (13-26)], LDH [88 (72-115)], cholesterol [0.66 (0.45-0.97)] and triglycerides [0.2 (0.16-0.33)]. Cholesterol and triglyceride were highest in malignant [mean 2.18 (SD 0.76) and 0.47 (0.36), respectively] and parapneumonic [1.93 (0.47) and 0.35 (0.09)] effusions. Strong Spearman correlation was found between fluid cholesterol and protein (0.798, $p<0.0001$) as well as fluid:serum protein ratio (0.752, $p<0.0001$). Exudates were identified with a high discrimination (accuracy 95.5%, sensitivity 96.7% and specificity 90.5%) when fluid protein (>35), LDH (>225) and cholesterol (>1.5) with modified cut-offs were combined.

Conclusion: Pleural fluid cholesterol and triglyceride levels are higher in exudates, particularly malignant and parapneumonic effusions. A combined fluid protein, LDH and cholesterol criteria is useful in distinguishing exudates from transudates.

Conflict of Interest: All authors declare no conflict of interests.

SIX-WEEK EXERCISE INTERVENTION IN PATIENTS WITH MALIGNANT PLEURAL DISEASE IMPROVES PHYSICAL FUNCTION, MUSCULAR STRENGTH AND APPENDICULAR LEAN MASS

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Introduction/Aim: To investigate the feasibility and efficacy of exercise to improve physical functioning, body composition, and patient-rated outcomes in patients with malignant pleural disease (MPD).

Methods: Thirty-three patients with MPD were recruited to complete an exercise training intervention. The exercise intervention included progressive resistance exercise training three times/week for six-weeks. Outcomes assessed at baseline and post-intervention included muscular strength (1-repetition maximum leg press), functional capacity (6-Minute Walk Test), physical functioning (Timed Up and Go), body composition (DXA scan), quality of life (Short-Form 36 Health Survey), ratings of intervention burden and acceptability (7-point Likert scale; 1, not at all, to 7, very much). Paired T-test or Wilcoxon Signed Rank Test was used to assess changes over time.

Results: Mean participant age was 64 (SD =11) years. The majority had mesothelioma (93%), ECOG performance status 0-1 (97%), and were male (70%), and sarcopenic (56%). Twenty-six participants (79%) completed the intervention; 24 (73%) completed all post-intervention assessments. Median adherence to supervised exercise was 100% (range 6%-100%). Median ratings of trial evaluation were high (i.e., 7/7 for all measures) and intervention burden were low (i.e., <1.5/7 for all items). Post intervention, significant improvements were found for mean six-minute walk distance (+59 m; 95% CI 24-93; $p<0.05$), 1-repetition maximum leg press (+17 kg; 95% CI 11-23; $p<0.001$), timed up and go (-0.51 sec; 95% CI -0.94 - -0.08; $p<0.05$), chair rise (-1.5 sec; 95% CI -2.2 - -0.9; $p<0.001$), and appendicular lean mass/height squared (+0.19 kg/m^2; 95% CI 0.04 – 0.34; $p<0.05$). For patient-rated outcomes, only the mental health subscale of SF-36 changed significantly (median change +2.6, IQR 0.0, 5.2; $p<0.05$).

Conclusion: Progressive resistance exercise training is a feasible intervention with measurable health benefits for patients with MPD.

Conflict of Interest: All authors declare no conflict of interests.

TARGETED PROFILING OF EBUS BRUSHINGS IDENTIFIES MOLECULAR DRIVERS IN NSCLC

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Introduction/Aim: Radial Endobronchial Ultrasound (EBUS) bronchoscopy in conjunction with rapid-on-site examination (ROSE) is a procedure that routinely achieves an adequate diagnostic yield to identify malignant cells. This study aims to improve the diagnostic value of EBUS bronchial brushings by screening these specimens for molecular changes that can identify therapeutic targets. More specifically, to assess the feasibility of using EBUS bronchial brushings to detect differentially expressed tumour markers using Taqman Low Density Array (TLDA) RT-qPCR.

Methods: Single pass radial EBUS brushings from Non-Small Cell Lung Cancer (NSCLC) patients (n=15) were collected following ROSE confirmation of the malignant site at the Royal Melbourne Hospital. Final diagnoses included adenocarcinoma (n=10) and squamous cell carcinoma (SCC, n=5). As a control, benign brushings were collected from clinic-radiologic confirmed interstitial lung disease patients (n=14). Isolated DNA and RNA from individual brushings were used for TLDA gene expression analysis to determine the fold change of several tumour markers (FGFR1, PD-L1, PTEN, RICTOR, MET and MMP-9) and Next Generation Sequencing (NGS) using the Illumina TruSight 15 panel. Statistical significance was assessed by performing Mann Whitney t tests to compare unpaired groups.

Results: Fold change values were higher for PD-L1 (mean±SEM: 6.24±1.73, $p<0.04$), FGFR1 (3.44±1.30, $p<0.02$), RICTOR (1.51±0.23, $p<0.02$) and MMP-9 (33.79±7.38, $p<0.0001$) in the malignant brushings relative to the benign brushings. According to tumour type a fold increase in PD-L1 (8.50±2.26, $p<0.02$), RICTOR (1.84±0.28, $p<0.003$) and MET (3.51±1.38, $p<0.005$) were observed in adenocarcinomas vs. SCCs. FGFR1 levels were higher (6.86±4.5 fold, $p<0.02$) and PTEN levels were lower (0.64±0.12 fold, $p<0.001$) in SCCs vs. adenocarcinomas. The malignant nature of the lesions were confirmed by NGS, identifying common mutations in p53 (10/15 patients), Kras (2/15), EGFR (2/15) and PI3K (3/15).

Conclusion: These findings demonstrate that targeted RT-qPCR profiling can identify molecular abnormalities in EBUS bronchoscopy brushings collected from ROSE confirmed malignant lesions. Further investigation is warranted as to whether RT-qPCR can be used clinically to guide individualised therapeutic options.

RADIATION THERAPY AUGMENTS THE EFFICACY OF IMMUNOTHERAPY IN NON-SMALL CELL LUNG CANCER: A CASE-CONTROLLED STUDY

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Introduction/Aim: Preclinical studies have demonstrated that radiation acts as an immune stimulus, facilitating immune mediators to enable anti-tumour responses. Impact of previous radiation therapy to the chest on the efficacy and safety of nivolumab in patients with advanced non-small cell lung cancer (NSCLC) is unknown.

Methods: Consecutive series of patients who received nivolumab for advanced NSCLC on an intention-to-treat basis over a 30 months period between January 2015 and June 2017 at a large thoracic-oncology unit were identified. Outcomes in patients who had received radiation therapy to the chest as part of previous treatment prior to commencing nivolumab (RT group, n=20) were compared to an age, gender, tumour histology and performance status matched cohort of patients who did not receive previous radiation therapy (non-RT group, n=20).

Results: The RT group had received a mean 53.3Gy (SD 12.3) at a median of 12.4 months prior to commencing nivolumab. The median progression free survival (PFS) was 3.4 months (95%CI 2.2-4.5) in the RT group compared to 1.3 months (95%CI 1.0-1.7) in the non-RT group (p=0.01). The median overall survival was 8.4 months (95%CI 5.1-11.6) in the RT group compared to 4.2 months (95%CI 1.0-7.7) in the non-RT group (p=0.08). The disease response on the initial assessment following starting nivolumab included nine (45%) patients who had stable disease or partial response in the RT group compared to five (25%) in the non-RT group after a median of four cycles of therapy. Rate of immune related complications were 35% (n=7) and 15% (n=3) in the RT and non-RT groups respectively (p=0.1). The RT group had a higher mean smoking pack years.

Conclusion: This study demonstrates a novel finding of previous radiation therapy to the chest resulting in significantly higher PFS in patients treated with nivolumab for advanced NSCLC. A trend towards a higher rate of immune related adverse effects seen in the RT group may due to increased activity of the immunotherapy in these patients.

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NINTEDANIB LONG-TERM EFFICACY IN IPF IS MAINTAINED IRRESPECTIVE OF DOSE

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Introduction/Aim: In Phase III INPULSIS® trials, nintedanib significantly reduced annual rate of FVC decline versus placebo in patients with IPF (−113.6 versus −223.5 mL/year). In an extension trial (INPULSIS-ON), patients who completed treatment and follow-up visit in INPULSIS® could receive open-label nintedanib. In INPULSIS-ON, patients receiving nintedanib or placebo 150mg twice-daily (bd) at the end of INPULSIS® received nintedanib 150mg bd; patients receiving nintedanib or placebo 100mg bd received nintedanib 100mg bd or 150mg bd, based on discussion between the patient and the investigator. Dose reduction to 100mg bd was allowed to manage adverse events; re-escalation to 150mg bd was permitted. We assessed the influence of nintedanib dose on FVC decline in INPULSIS-ON.

Methods: Annual rates of FVC decline over 96 weeks in INPULSIS-ON were assessed in patient subgroups (treated with nintedanib 150mg bd; 100mg bd; or both). Slope of FVC decline was calculated using all available FVC measurements collected between baseline and week 96 in INPULSIS-ON. The first patient was enrolled in July 2012. Analyses were descriptive, based on a data snapshot in October 2015.

Results: Of 734 patients treated, 436 (59.4%), 53 (7.2%) and 245 (33.4%) received 150mg bd, 100mg bd and both doses, respectively. Adjusted annual rates±SEM of FVC decline over 96 weeks were −116.4±8.9, −79.0±30.1 and −126.2±11.4 mL/year in patients treated with nintedanib 150mg bd, 100mg bd and both doses, respectively. Annual rates of FVC decline in all subgroups were consistent with annual rate of FVC decline over 96 weeks in all treated patients (−117.8±6.8 mL/year).

Conclusion: Annual rate of FVC decline was similar in patients treated with nintedanib 150mg bd, 100mg bd or both. Long-term efficacy of nintedanib in reducing disease progression was maintained in patients with IPF who required dose adjustments to manage adverse events.

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HIGH RESOLUTION CT-BASED CHARACTERIZATION ANALYSIS OF IDIOPATHIC PULMONARY FIBROSIS

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Introduction/Aim: Idiopathic pulmonary fibrosis (IPF) is the most aggressive and frequent form of idiopathic interstitial pneumonias. Progression of IPF is variable between individuals and no established quantitative tools exist to assess its development. This work aims to integrate information from volumetric imaging with pulmonary function tests using a predictive computational model under the hypothesis that abnormalities on volumetric are not sufficient to explain increased lung stiffness and decreases in DLCO.

Methods: Tissue regions in HRCT images from 8 patients with IPF were quantitatively analysed. Tissue abnormalities were classified using CALIPER (Computer-Aided Lung Informatics for Pathology Evaluation and Ratings) software. Tissue density (TD) distribution and volume of tissue (classified as reticular, ground-glass, normal and emphysema in each lung) were calculated. The classified data were mapped to a statistical shape model, which allows consistent comparison of regional tissue properties between patients or within one patient at different time points. Ventilation distribution and gas exchange were simulated in a computational model that was parameterised to each subject's lung tissue characterisation, to predict the relationship between V-Q matching, DLCO and disease distribution.

Results: Fibrosis usually has a consistently higher TD (0.34/0.41 for reticular/ground-glass) compared to normal tissue (0.28), and presents predominantly in lower lobes (72%, 58%, 65% for honeycomb, reticular, ground-glass). In contrast, emphysema has lower density (0.08) and appears predominantly in upper lobes (73%). Model predictions of ventilation distribution and DLCO show that V-Q mismatch occurs due to redistribution of ventilation away from diseased regions, contributing to observed DLCO decreases.

Conclusion: A quantitative analysis of the spatial distribution of IPF disease coupled with functional models provides a potential tool to improve assessment of the contributors to decline in IPF patient status over time. Decline in DLCO is a function of regional lung stiffness due to disease location combined with a redistribution of ventilation to 'normal' lung tissue.

THE INTERSTITIAL LUNG DISEASE MULTI-DISCIPLINARY MEETING: 3 YEAR REVIEW OF A NOVEL STATEWIDE TELEMEDICINE MODEL

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Introduction/Aim: A multidisciplinary meeting (MDM) model of care is recommended by TSANZ for the diagnosis and initial management of interstitial lung disease (ILD). In order to ensure equity of access to the required expertise, we established an ILD-MDM at Prince Charles Hospital (TPCH) in Brisbane which facilitated telemedicine and active participation of sites from elsewhere in Queensland.

Methods: We reviewed all cases presented at the ILD-MDM from July 2014 to June 2017. The ILD-MDM included a minimum of 2 expert thoracic physicians, 1 radiologist and 1 histopathologist.

Results: 313 referrals from 38 clinicians and 11 institutions were discussed. 38.3% were female, mean age 67 years, and 24.9% were from outside TPCH, including 1.9% from private practice. Mean FVC was 74.0% and carbon monoxide diffusion capacity 51.5%. Overall, 111 cases (35.5%) were classified as idiopathic pulmonary fibrosis (IPF) and 17 (5.4%) as combined pulmonary fibrosis and emphysema, with the majority eligible for antifibrotic medication. 18 (5.8%) were classified as connective tissue disease, 12 (3.8%) chronic hypersensitivity pneumonitis, whilst 18.2% remained unclassifiable. There were 105 (33.5% patients) surgical lung biopsies (SLB) reviewed with 79% performed prior to first MDM presentation. In patients with a first presentation diagnosis of IPF, 65.6% had not had a prior SLB. 71 cases (22.7%) had high-resolution computed tomography (HRCT) reported as usual interstitial pneumonia (UIP), a further 130 (41.5%) as possible UIP and 4.5% had inadequate imaging. Of 61 SLB showing definite UIP pattern, 63.9% had possible UIP and 19.7% UIP pattern on HRCT. In 22% of initial case presentations (n=69), further investigations were recommended including surgical lung biopsy (n=30), HRCT (n=26), bronchoscopy (n=4) and extended autoimmune screen (n=9).

Conclusion: A telemedicine model is feasible and can facilitate equity of access for patients and clinicians where a low volume ILD caseload &/or absence of expertise precludes local establishment of the ILD-MDM.

Declaration of interest: None.

ACHIEVING THE MINIMAL IMPORTANT DIFFERENCE FOLLOWING EXERCISE IN ILD

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Introduction/Aim: Exercise training delivers significant short-term improvements in functional exercise capacity, symptoms and quality of life, across the range of interstitial lung diseases (ILD)s, but to what extent do individuals experience a clinically significant benefit? This study aimed to establish the proportion of patients achieving the minimal important difference (MID) in 6-minute walk distance (6MWD) and in the dyspnoea and fatigue domains of chronic respiratory questionnaire (CRQ).

Methods: Data from 142 participants with ILD [61 idiopathic pulmonary fibrosis (IPF), 22 asbestosis, 23 connective tissue disease-related ILD (CTD-ILD) and 36 with ILD of other aetiologies] randomised to either eight weeks of supervised exercise training or usual care were reviewed. We compared the percentages of patients who achieved the MID for 6MWD for ILD (29-34m), CRQ dyspnoea (2.5 points) and CRQ fatigue (2.0 points) between exercise training and control group for the entire ILD population and each subgroup (IPF, asbestosis and CTD- ILD) using Pearson chi[2].

Results: Following exercise training at least a third of participants achieved improvements in 6MWD that exceeded the MID, increasing to 43% and 55% in the IPF and asbestosis subgroups respectively (see Table). Compared to the control group, a greater percentage of participants achieved improvements that exceeded the MID for CRQ dyspnoea and fatigue for the entire ILD sample, IPF and asbestosis; this was significantly greater than the control group for CRQ fatigue. Improvements that exceed the MID were limited in CTD-ILD and more likely occur in CRQ dyspnoea and fatigue than 6MWD.

Conclusion: A third to a half of participants with ILD achieve clinically meaningful improvement following exercise training, including those with IPF, the most devastating of all ILDs. Fatigue and 6MWD appear more responsive to change than dyspnoea.

Table 1 Percentage of participants who achieved the MID following the intervention

	Whole ILD		IPF		Asbestosis		CTD ILD	
6MWD								
Control	15%	p =0.01	11%	p=0.05	0%	p=0.006	9%	p=0.1
Exercise training	33%		43%		55%		10%	
CDRQ Dyspnoea								
Control	30%	p=0.1	35%	p=0.1	27%	p=0.6	18%	p=0.3
Exercise training	42%		53%		57%		40%	
CDRQ Fatigue								
Control	23%	p<0.001	27%	p=0.03	18%	p=0.07	36%	p=0.8
Exercise training	55%		57%		55%		40%	

p <0.05 compared to control group; ILD, interstitial lung disease; CTD ILD, connective tissue disease-related ILD; IPF, idiopathic pulmonary fibrosis.

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CARDIOVASCULAR SAFETY OF NINTEDANIB IN SUBGROUPS BY BASELINE CARDIOVASCULAR RISK

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Introduction/Aim: Tyrosine kinase inhibitors may be associated with an increased risk of arterial thromboembolic events. The efficacy and safety of treatment with nintedanib versus placebo in patients with idiopathic pulmonary fibrosis were assessed in the Phase II TOMORROW trial and 2 Phase III INPULSIS® trials. Exclusion criteria included: myocardial infarction in the previous 6 months, unstable angina in the previous month or stroke in the previous year. We assessed the effect of cardiovascular (CV) risk at baseline on the CV safety of nintedanib 150mg twice-daily.

Methods: Incidence rates of major adverse CV events (MACE) in subgroups of patients with a history of atherosclerotic CV disease (CVD) and/or ≥1 CV risk factor (hypertension, dyslipidemia, body mass index >30 kg/m^2, current/former smoking and diabetes) at baseline (higher CV risk) and patients with no history of atherosclerotic CVD and no CV risk factors at baseline (lower CV risk) were analysed using pooled data from the TOMORROW and INPULSIS® trials.

Results: At baseline, 1107 (89.9%) patients (656 nintedanib, 451 placebo) had higher CV risk and 124 (10.1%) patients (67 nintedanib, 57 placebo) had lower CV risk. In patients with higher CV risk, incidence rates (95% CI) of MACE were 3.88 (2.58, 5.84) and 3.49 (2.10, 5.79) per 100 - patient–years in the nintedanib and placebo groups, respectively (Figure). In patients with lower CV risk, incidence rates (95% CI) of MACE were 4.78 (1.54, 14.82) and 5.37 (1.73, 16.65) per 100 patient–years in the nintedanib and placebo groups, respectively (Figure).

Conclusion: In pooled data from the TOMORROW and INPULSIS® trials, the incidence of major adverse CV events was similar between nintedanib and placebo groups both in patients with higher and lower CV risk at baseline.
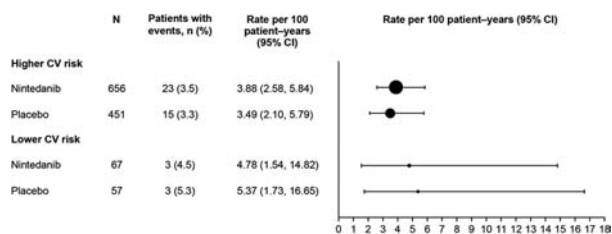
Figure 1

MULITPLE PROGRESSION EVENTS IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS (IPF)

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Introduction/Aim: Declines in forced vital capacity (FVC), declines in 6-min walk distance (6MWD) and respiratory hospitalizations are events associated with disease progression and mortality in IPF. The incidence of multiple events in the context of a 52-week study and in patients (pts) receiving antifibrotic treatment with pirfenidone (PFD) is unknown. To determine the incidence of multiple progression events and the proportion of pts with death subsequent to a progression event in the first 12 months of PFD treatment vs placebo (PBO).

Methods: All pts from the pooled Phase III trials (PFD n = 623; PBO n = 624) were analyzed for incidence of events, defined as relative decline in %predicted FVC ≥10%, absolute decline in 6MWD ≥50 m; respiratory hospitalization, or death from any cause.

Results: The incidence of progression events was driven by declines in FVC (total events, 202 PFD vs 304 PBO) and 6MWD (265 PFD vs 348 PBO). A lower proportion of pts had > 1 event with PFD vs PBO (17.0% vs 30.1%; P < 0.0001; Figure 1). Death following ≥ 1 progression event occurred less often with PFD vs PBO (2.1% vs 6.3%; *P* = 0.0002).
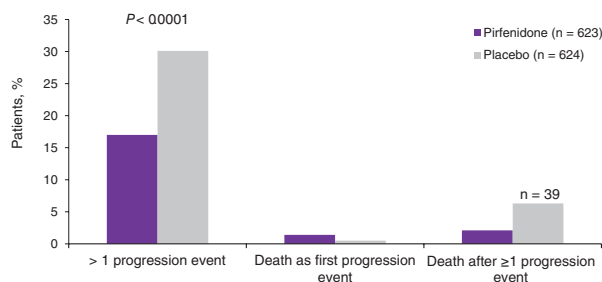

Figure 1 Multiple progression events and death as a first or subsequent progression event in the pooled CAPACITY and ASCEND phase 3 trials (N = 1247). CAPACITY-004, NCT00287716; CAPACITY-006, NCT00287729; ASCEND, NCT01366209.

Conclusion: PFD significantly reduced the incidence of multiple progression events and death subsequent to a progression event at 12 months vs PBO. A multiple events–driven approach may have relevance for the design of future IPF clinical trials.

INTERVENTIONS FOR PROMOTING PHYSICAL ACTIVITY IN PEOPLE WITH COPD: A COCHRANE SYSTEMATIC REVIEW

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Introduction/Aim: Increasing awareness of the deleterious health impacts of physical inactivity in people with chronic obstructive pulmonary disease (COPD), coupled with technological developments permitting more accurate measurements, has led to a dramatic increase in studies that aim to improve physical activity participation. This systematic review aimed to evaluate the effectiveness of interventions to promote physical activity in people with COPD.

Methods: Randomised controlled trials of interventions designed to increase physical activity for people with COPD using objective measures for physical activity were identified from the Cochrane Airways Group's Specialised Register (to March 2017). Two review authors independently assessed studies for inclusion and risk of bias, then undertook data extraction. Results are for the primary outcome of steps/day at program completion, using published data.

Results: 1950 references were screened, 189 papers assessed and 32 of 72 included studies reported steps/day. The greatest improvements were seen with physical activity counselling and a pedometer (compared to counselling alone, 1 study, mean difference 2942 [95%CI 1881 to 4002] steps/day) and telecoaching (compared to advice alone, 1 study, 1548 [1045 to 2051] steps/day). Significant improvements were also demonstrated with telephone counselling and a pedometer (compared to pedometer alone, 1 study, 1419 [698 to 2140] steps/day) and endobronchial valves (compared to usual care, 1 study, 1400 [655 to 2145] steps/day]). A deterioration in step count was seen following singing classes (compared to film workshops, 1 study, -1774 [-2848 to -700] steps/day). Risk of selection and detection bias was generally low, with high or unclear ratings for reporting bias.

Conclusion: A range of interventions, particularly those involving physical activity counselling, can improve physical activity as measured by daily steps. These results suggest that targeted interventions may be useful to improve physical activity in people with COPD.

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PERIPHERAL VENOUS BLOOD GAS ANALYSIS VERSUS ARTERIAL BLOOD GAS ANALYSIS FOR THE DIAGNOSIS OF RESPIRATORY FAILURE AND METABOLIC DISTURBANCE IN ADULTS

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Introduction/Aim: Whilst arterial blood gas (ABG) is the gold standard for the diagnosis of respiratory failure and metabolic disturbance, the peripheral venous blood gas analysis (PVBG) is increasingly being used. We sought to compare the performance (accuracy) of both tests to diagnose these target conditions.

Methods: We performed an extensive electronic and manual search of the literature for case-control or consecutive series studies that directly compared the index test (PVBG) to the reference standard (ABG). No language restrictions were applied. Included studies provided outcome data for specified target conditions (pO_2, pCO_2, pH, HCO_3) using generally accepted cut points. Quality assessment was conducted using the QUADAS-2 tool. The statistical analysis utilized 2x2 tables for each outcomes' positive and negative results and Stata 12 software (*Statacorp 2011*). The published protocol is available at the Cochrane Database of Systematic Reviews. Article No:CD010841.

Results: We identified 7207 articles with our search strategy following the removal of duplicates. There were 16 studies meeting the inclusion criteria, however only 6 could provide sufficient data for the statistical analysis. Two authors evaluated the quality for these studies which were generally considered a low risk of bias. For (any) respiratory failure, 2 studies demonstrated poor accuracy of the PVBG compared to the ABG. The diagnostic odds ratio (DOR) was 2.73 with 95% confidence intervals 0.14-55.2. For isolated hypercarbia (6 studies) and metabolic disturbance (3 studies), the PVBG performed well (DOR 35.5 with 95% CI 9.7-130.2 and DOR 5.8 with 95% CI 1.5- 22.2). Meta-analysis was only able to be performed for hypercapnia. The PVBG showed high sensitivity (95.4%) but low specificity (33.6%) with a high false positive rate (45.8%).

Conclusion: Limited data suggests the PVBG is useful in diagnosing metabolic disturbance but not respiratory failure. For isolated hypercarbia the PVBG has high sensitivity but poor specificity.

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DIAGNOSTIC YIELD AND APPROPRIATENESS OF COMPUTED TOMOGRAPHY PULMONARY ANGIOGRAM

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Introduction/Aim: International guidelines recommend Computed Tomography Pulmonary Angiography (CTPA) as the gold standard imaging modality for suspected Pulmonary Embolism (PE). Royal College of Radiologist suggests PE should be detected in 15% of CTPA scans. Appropriate requesting of CTPA is important to both establishing an accurate diagnosis and minimizing unnecessary testing and radiation exposure. International and Waikato Hospital guidelines recommend pre-test probability scoring and D-dimer assay to stratify patients prior to performing CTPA.

We aimed to determine the overall and departmental diagnostic yield of CTPA at Waikato Hospital. We also aimed to identify whether CTPA were ordered according to current guidelines.

Methods: Medical records of 200 consecutive patients who underwent CTPA for suspected PE from 01 March to 31 May 2017 were retrospectively reviewed. Patient demographics, referral source, clinical risk factors, D-dimer levels, diagnostic yield and additional CTPA findings were recorded. We utilized an age-adjusted D-dimer cut-off. CTPA images were obtained using either a Siemens 128 or 256 slice multidetector CT scanner. Results were compared with international guidelines as well as similar local studies.

Results: 41 (20.5%) patients had PE. Orthopaedics had the highest yield (36.4%), followed by Respiratory (32.9%) and General Surgery (18.8%). According to the Wells Score, 74 (37%) patients were low risk while 134 (63%) were High Risk. D-dimer was done in 108 (54%) patients. 34 (44.7%) patients in the low-risk group did not have D-dimer. Two patients who had low wells score and negative D-dimer received CTPA, neither had PE. Of the 14 patients referred by cardiology, none had positive scans. On review, only one patient had CTPA requested inappropriately (low wells score, D-dimer not done).

Conclusion: Diagnostic yield of CTPA in Waikato Hospital is consistent with international standard. D-dimer has not been adequately used as a rule out test. Adherence to diagnostic protocol could potentially improve positive yield.

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This abstract has been withdrawn

Asthma & Allergy 1

PATIENT PERSPECTIVES ON SEVERE ASTHMA EPISODES: ATTACKS, FLARE-UPS OR EXACERBATIONS?

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Introduction/Aim: Severe asthma exacerbations are common and have major impacts on outcomes. The 2017 Lancet Asthma Commission[1] called for zero-tolerance on exacerbations and has recommended replacing the terms 'exacerbation' or 'flare-up' with 'attack'. The aim of this study was to explore patients' perspectives on episodes of severe asthma and the terminology used.

Methods: Semi-structured qualitative interviews were conducted with 14 adults with severe asthma. Interviews explored individuals' experiences with severe asthma episodes and their perspective on language used. Sampling was purposive and interviews continued until no new themes emerged. Data were analysed using a modified thematic analysis.

Results: Participants had a mean±SD age of 59±12 years and 57% were female. Mean±SD FEV_1% predicted and ACQ6 were 61±25% and1.8±1.2 units, respectively. Most (71%) lived with family. Participants described attacks of asthma as frightening events that had major impacts on the their lives: '*it's an attack on your life*'. The use of the term 'exacerbation' was perceived as being used by health professionals to '*medicalise*' their asthma. Patients considered exacerbations and flare-ups as a transient, often common increase in their symptoms that might last hours or days but generally led to a return to baseline. These were viewed as being less severe events. The term 'attack' however had a different meaning. Participants used this to describe serious life-threatening events: '*It's an attack when it's completely out of control*'. The use of the term exacerbation by health professionals was described as '*insulting*' as it trivialised their experience.

Conclusion: Exacerbation and flare-up have a different meaning to patients with severe asthma than how they are intended. These data provide important person-centred support to the recommendations of the Lancet commission[1] in regard to the use of the term attack. The term attack better reflects the severity of events from the patient perspective.

1. Pavord ID. Lancet 2017, Sept 11.

Grant Support: The study was supported by the Centre of Excellence in Severe Asthma and the John Hunter Charitable Trust.

Declaration of Interest Statement: Nothing to declare

ASTHMA SELF-MANAGEMENT FOR AUSTRALIAN CHILDREN AND THE ROLE OF APPS?

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Introduction/Aim: Smartphone apps can deliver self-management programmes for children with asthma, however the literature reports heterogeneous outcomes. Consumers' perspectives are yet to be investigated despite being crucial for uptake and effectiveness. This project aimed to: 1. explore the self-management strategies and needs of children with asthma and their carers; and 2. understand the content, design features and usability of existing asthma apps.

Methods: Children with asthma aged 6-11 years and their carers participated in focus groups which incorporated a group discussion followed by user-testing of 7 asthma apps. Focus groups were recorded, transcribed and analysed thematically.

Results: Participants (children: n=41, carers: n=38) took part in one of 31 focus groups. Carers reported being heavily involved in selfmanagement activities including symptom and medication management and communication with health professionals. Carers wanted children to take on more self-management responsibility but expressed concern about relinquishing control. Carers and children both expressed frustration over asthma negatively impacting social factors including a strong desire to not be seen as different. Most carers felt positive about the potential of an app to build awareness of their child's experience of asthma and to improve their child's asthma self-management. App features found particularly useful by participants included customisation, recording and tracking information (e.g. symptom monitoring), education, reminders (e.g. medication), icons and visuals and information sharing with health professionals. Missing, desired features included multiple personnel entry options, automation, intuitive design for young children to navigate, parent and child portals, information sharing between child and carer, and social networking. No single asthma app tested met all needs identified as important by participants.

Conclusion: These findings have significant implications for the future design and implementation of acceptable and effective asthma self-management apps, and indicate the need for greater end-user involvement in app design.

Grant Support: This study was supported by NHMRC Partnership Grant no.1065898.

PREVALENCE OF DIFFERENT TREATABLE TRAITS IN SYMPTOMATIC AIRWAYS DISEASE

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Introduction/Aim: The concept of treatable traits has been proposed as an alternative approach to the classification of airways diseases. This approach does not rely on diagnostic labels such as asthma or COPD but on the presence of specific treatable characteristics to guide management. Many candidate treatable traits have been suggested but their prevalence among people with symptoms of airways disease is unknown.

Methods: Data on the presence of treatable traits were derived from the previously reported New Zealand Respiratory Health Survey. Participants aged 18-75 with symptoms of wheeze and breathlessness, recruited from a random population sample, underwent detailed characterisation including symptom and medical history questionnaires, measurement of lung function, gas exchange, and biomarkers including blood eosinophils and exhaled nitric oxide (FeNO). Participants were not required to have a previous diagnosis of asthma or COPD.

Results: 389 participants had complete data and were included in the analysis.

Airflow limitation, defined as a baseline FEV1:FVC ratio <0.7, was present in 161/389 (41%) of participants. 108/389 (28%) demonstrated ≥12% reversibility to salbutamol. Impaired gas exchange (corrected KCO <80% predicted) was seen in 77/389 (20%).

Elevated blood eosinophils (≥0.3) were seen in 133/389 (33%) and a raised FeNO (≥50) was present in 68/389 (17.5%).

The prevalence of other treatable traits was as follows: rhinitis 74%, reflux 50%, obesity (BMI≥30) 37%, recurrent chest infections 22%, biomass exposure 19%, workplace-related symptoms 16%, current cigarette smoking 15% (ex-smoker 34%), non-steroidal anti-inflammatory use 13%, beta-blocker use 4%. Rates of doctor diagnosed co-morbidities were: hypertension 26%, depression 21%, anxiety 17%, cardiovascular disease 15%.

Conclusion: Retrospective review of data from participants with symptoms of wheeze and breathlessness has allowed the prevalence of multiple treatable traits to be determined.

COUGH SENSITIVITY TO MANNITOL INHALATION CHALLENGE IDENTIFIES SUBJECTS WITH COUGH

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Introduction/Aim: It is unknown whether cough sensitivity to mannitol identifies subjects with cough and whether it correlates with subjective cough severity.

Method: Subjects with cough as the primary symptom (n=17), with other airway symptoms (n=52) and healthy subjects (n=15) performed mannitol challenge and completed the Leicester Cough Questionnaire (LCQ).

Results: The mean (95%CI) number of provoked coughs divided by the cumulative dose of mannitol (CDR) was 21.1 (12.6 – 35.4) in subjects with cough, 6.25 (4.15 – 9.40) in those with other symptoms and 2.80 (1.3 – 6.10) coughs/100 mg in the healthy subjects (p<0.001). Area under the receiver-operating characteristic curve comparing cough subjects against healthy subjects was 0.95 and when comparing cough subjects against healthy controls and subjects with other symptoms it was 0.80. There was a significant correlation between CDR and LCQ total score (r_s= -0.50, p=0.04) within the cough group, as well as when combining both subjects with cough and other airway symptoms (r_s= -0.43, p<0.001).

Conclusion: Cough sensitivity to mannitol identifies subjects with cough and correlates with subjective cough severity. Since mannitol challenge can be performed without complicated equipment or trained personnel in a standardised fashion, it is a promising diagnostic test for cough hypersensitivity syndrome.

Key Words: cough hypersensitivity, mannitol

PRESENCE OF DYSFUNCTIONAL BREATHING IS ASSOCIATED WITH WORSE ASTHMA STATUS AND MORE COMORBIDITIES IN A DIFFICULT ASTHMA POPULATION

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Introduction/Aim: Dysfunctional breathing (DB) is poorly defined however it is a common and potentially treatable comorbidity in difficult asthma patients and confers significant morbidity. Little is known about the factors associated with DB in a difficult asthma population and we hypothesized that these patients are likely to have poorer baseline asthma status and more frequent comorbidities. This study aimed to better define the DB population within a difficult asthma cohort.

Methods: 163 consecutive patients evaluated through a systematic difficult asthma assessment in a teaching hospital were identified. DB was assessed using the Nijmegen Questionnaire (scores >23 indicating DB). Patient demographics, baseline asthma status, lung function, and comorbidities (allergic rhinitis, anxiety, depression, chronic rhinosinusitis, obstructive sleep apnoea, reflux) were evaluated.

Results: 73 patients with elevated Nijmegen scores were identified. They were predominantly females (70%) with elevated BMI ($32kg/m^2$+/-8) and compared to those without DB were significantly more likely to be unemployed (66% versus 39%, p=0.04), have poorer asthma control (ACQ6 2.8 versus 2.1 p=0.001), more exacerbations in the prior 6 months (3 versus 2.3 p=0.037) and poorer quality of life (AQLQ 3.8 versus 4.6 p<0.001). There was no difference in IgE, blood eosinophils, age or lung function. DB patients were also more likely to have comorbid sleep apnoea, reflux, current symptoms of allergic rhinitis and chronic rhinosinusitis, a psychiatric history, and current symptoms of anxiety and depression.

Conclusion: Patients with DB in a difficult asthma population have worse asthma control, more exacerbations and worse quality of life. The presence of DB is associated with other asthma comorbidities.

Grant Support: Nil funding

## PARENT'S PERSPECTIVES ON ASTHMA MEDICATION MANAGEMENT: A SOCIAL NETWORK ANALYSIS

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Introduction/Aim: Despite the input of multiple health care professionals (HCPs), patients often establish their own health sources, health advice and support outside the HCP domain[1]. The overall aim of this study was to gain an understanding of the relative significance of health care professionals, personal contacts and any other sources of advice/information on the parent's asthma medication management of their child's asthma.

Methods: In-depth, semi structured interviews were conducted with parents of children (aged 4 to 18 years) with asthma (self-reported) from Sydney, Australia. Participants were recruited from several points including asthma clinics, general practice clinics and community pharmacies. Quantitative social network analysis provided structural insight into the asthma networks while qualitative social network analysis assisted in interpretation of network data.

Results: A total of 26 interviews were conducted. A wide variety of individuals and resources were identified by all parents to a be part of their ongoing management of their child's asthma medications. Figure 1. represents the collated asthma networks of these parents. While general practitioners (GPs) and paediatricians were participant's principal choice of healthcare professionals (HCPs), community pharmacists were less regarded. Each parent included at least one family member, friend or other mother with a child who has asthma in their asthma networks, with 9 of the parents mentioning their spouse as a significant contributor to their child's asthma medication management.
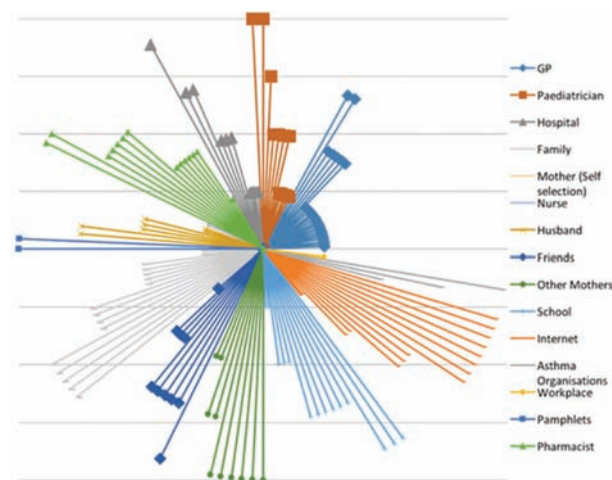
Conclusion: Parents have developed their own health networks to aid them in the management of their children's asthma medications, often consisting of multiple individuals and resources apart from the traditional HCPs. This research highlights the need to consider parent's health contacts and how they may drive and influence children's asthma outcomes. Further research is required to explore factors impacting parent's network choices and their influence on their management of their children's medications.

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PATTERNS OF PRESCRIBED ASTHMA MEDICINE USE IN AUSTRALIAN CHILDREN: A POPULATION-BASED STUDY

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Introduction/Aim: Despite the widespread availability of asthma management guidelines, variation in asthma medicine prescribing practices has been observed in the paediatric population. We aimed to characterise the utilisation of asthma medicines subsidised by the Pharmaceutical Benefits Scheme (PBS) in Australians aged <18 years.

Methods: We used a 10% sample of individual-level PBS claims (July 2012-December 2016) for Australian children dispensed asthma medicines to examine annual trends in incident and prevalent use (for 2014-2016). We used a 12-month lookback period to define incident use and applied one tenth of the Australian Bureau of Statistics midyear population of residents ≤18 as the denominator for incidence and prevalence per 100 estimates

Results: During 2014-2016, 160,632 children were dispensed an asthma medicine; 72,159 (45%) were girls and the median age was 5 years (IQR 2-10 years). Annually, an average of 81,404 children were dispensed at least one asthma medicine. The annual incidence of asthma medicines use ranged from 8.5-8.9% and annual prevalence's ranged from 13.5-14.6%.

The proportion of children who initiated fixed dose combination inhalers (FDC) annually was 1.2%, 1.1% and 1.0% for 2014, 2015 and 2016 respectively. Similarly the proportion of children who initiated inhaled corticosteroid (ICS) was 1.7%, 1.9% and 1.8% for 2014, 2015 and 2016. The proportion of children who initiated FDC without ICS in the preceding 12 months was around 1% annually. The total market share for the entire period for FDC was 12.43% amounting to a total of AUD 66,629,640.

Conclusion: Our data suggest that while the proportion of Australian children using asthma medication remained constant, a large proportion of children initiated FDC without a preceding ICS indicating prescribing of asthma medications not consistent with national guidelines.

EOSINOPHILIA AS A TREATABLE TRAIT IN THREE PATIENTS WITH ASTHMA/COPD

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Introduction/Aim: The combination of asthma and COPD in an individual presents significant challenges to achieving satisfactory outcomes. Recently, the concepts of precision medicine and the treatable trait, as opposed to homogenous management based on disease labels, have arisen as promising tools to improve care for this group of patients. In this series, we present three cases of patients with features of both asthma and COPD, in addition to peripheral blood eosinophilia, which was successfully targeted as a treatable trait.

Methods: We performed a retrospective chart review of three patients with chronic airways disease, with features of both asthma and COPD. These patients were selected for this case series based on prior therapeutic choices targeted at suppressing peripheral blood eosinophil count. Medical records were reviewed to compare the outcomes featured in Table 1 reported for each patient before and after the initiation of targeted treatment.

Results: All three patients were male ex-smokers, aged 68-74, with severe airflow obstruction, and CT evidence of emphysema, with either a positive response to bronchodilator on spirometric testing or demonstrating excess variability of FEV_1 between visits, and peripheral blood eosinophilia. Oral corticosteroids were successfully used in all three to suppress peripheral blood eosinophil counts below 0.4×10^9 cells/L, and titrated down to the lowest dose to accomplish this. This resulted in significant benefits to all three patients, including improvements in symptoms (using CAT scores), and lung function, and, a marked decline in hospital admission and exacerbation rates, as demonstrated in Table 1.

Conclusion: This case series demonstrates the ability to apply the concept of the treatable trait in the real world to the complex population of patients with chronic airways disease with features of both asthma and COPD. Importantly, this highlights the need to see through the labels of these diseases to the individual traits that reflect therapeutic targets.

Table 1

Outcome	Case	Pre-OCS	Post-OCS
Post-BD FEV_1 (L) and (% predicted)	1	0.54 (18)	2.27 (74)
	2	0.54 (17)	0.74 (27)
	3	1.23 (43)	2.03 (71)
Exacerbation rate	1	2	0
	2	8	2
	3	2	0
Hospital admission rate	1	2	0
	2	8	0
	3	1	0
CAT Score	1	26	11
	2	28	5
	3	24	16
6MWD	1	343	520
	2	256	466
	3	50	505

Post-BD = Baseline post-bronchodilator

A RETROSPECTIVE REVIEW OF THE MANAGEMENT OF HOSPITAL PRESENTATIONS DUE TO EXACERBATIONS OF ASTHMA

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Introduction/Aim: Effective asthma management involves addressing educational, environmental, pharmacological, and psychosocial factors, and this also applies to inpatient management of acute exacerbations. Hospital admission provides a good opportunity to clarify a patient's diagnosis and optimise their long term control. Society guidelines recommend that a review of the patient's medications, and inhaler technique, and provision of an action plan, should be performed prior to discharge, and failure to do so may contribute to future risk of exacerbation and fixed airway obstruction. This study aims to evaluate the management of patients with acute asthma presenting to the Gold Coast health service, with particular attention to diagnostic clarification and the evaluation of patient self-management skills.

Methods: A retrospective review of patients presenting to hospitals within the Gold Coast health service, with a diagnosis of an acute asthma exacerbation, from July 2016, to June 2017, was performed.

Results: 149 presentations with acute asthma were evaluated (80% female). 47 patients (32%) were managed by a specialist respiratory team, and 102 (68%) were manged by general medicine or emergency medicine. Patients under the care of a respiratory team at the time of discharge were more likely to be objectively evaluated for airflow obstruction via spirometry or peak flow (72% vs 22%; P=<0.001), were more likely to have inhaler technique scrutinised (62% vs 25%; P = <0.001) and their written action plan reviewed (60% vs 28% P = <0.001), and more likely to receive education from a specialised respiratory nurse (57% vs 23%; P = <0.001).

Conclusion: Referral of patients presenting to the Gold Coast health service with acute asthma exacerbations to an inpatient respiratory team improved adherence to guideline recommendations regarding inpatient asthma management, including diagnostic clarification and self-management strategies. The institution of a formal acute asthma management pathway would be expected to improve adherence further.

PREMATURITY, LUNG FUNCTION AT 6 WEEKS OF AGE AND BRONCHIOLITIS IN BABIES BORN TO MOTHERS WITH ASTHMA DURING PREGNANCY

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Introduction/Aims: Asthma is common during pregnancy and can result in adverse pregnancy outcomes. The aim of this analysis was to explore for an association between preterm delivery, infant lung function at 6 weeks of age and the development of bronchiolitis in the first 6 months of life in a cohort of babies born to women with asthma during pregnancy.

Methods: We performed tidal breathing flow-volume loop (TBFVL) measurements during quiet unsedated sleep in infants born to mothers who participated in an ongoing multi-centre RCT of FeNO-guided asthma management versus usual care (Breathing for Life Trial). All researchers remain blinded in regards to the pregnancy intervention.

Results: 324 babies have been recruited to date, of which 289 attended clinical assessment and 261 remained in quiet sleep during testing. 232 TBFVL were attempted (44% female; mean (SD) age 6 (1.2) weeks and 209 (90%) tests were technically acceptable. Mean time to Peak Tidal Expiratory Flow/time Expiratory Flow % (tPTEF/tE%)in preterm infants (n=19) was 25.9 (SD 4.8) versus those who were born at term 32.6 (SD 9.9). Mean respiratory rate (RR) was 47 breaths/ per minute in preterm babies vs 44 breaths/ per minute in fullterm babies. At the time of abstract submission, 140/209 (67%) were 6 months old and 36/209 (17%) had at least one bronchiolitis episode. 37% of preterm babies developed bronchiolitis during the first 6 months of life compared to 22% full-term babies.

Conclusion: Prematurity resulted in lower tPTEF/tE % at 6 weeks of age in babies born to asthmatic mothers which may be associated with the subsequent development of bronchiolitis.

TPL 001

12-MONTH FOLLOW-UP OF 2016 EPIDEMIC THUNDERSTORM ASTHMA PATIENTS WITHOUT PRIOR DIAGNOSIS OF ASTHMA ASSESSING SYMPTOMS, PREVENTER USE, ASTHMA ACTION PLAN OWNERSHIP AND HEALTH CARE UTILISATION

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Introduction/Aim: Epidemic thunderstorm asthma(ETSA) severely affected Melbourne in November 2016. There is scant literature on the natural history of individuals affected by ETSA. This is a 12-month follow-up study of Eastern Health ETSA patients without prior asthma diagnosis assessing their symptomology and behaviours.

Methods: A standardised telephone questionnaire was developed and administered between 4th-15th December 2017 to individuals affected by 2016 ETSA(n=232). The questionnaire assessed asthma symptoms, preventer prescription and adherence, asthma action plan ownership and healthcare utilization.

Results: 86.2%(n=200) of individuals responded. 57.5%(115) had never been diagnosed with asthma before. On follow-up, 21.7%(25) were asymptomatic, 48.7%(56) described infrequent episodic symptoms(up to 1/month), 10.4%(12) had frequent episodic symptoms(>1/month but <1/week) and 19.1%(22) reported persistent symptoms(≥1/week).

Preventer prescription was 54.5%(12) in patients with persistent symptoms and <40% in the other groups. Adherence was poor with only 58.3% (7) of patients with persistent symptoms using their inhaler for ≥5 days/week, and none of the patients in the asymptomatic group.

Asthma action plan ownership was <50%, with only 22.7%(5) ownership in patients with persistent symptoms. Urgent visits to GP, ED or hospitalization was required in 12.5%(7) of the infrequent episodic group, 25%(3) of the frequent episodic group and 31.8%(7) of the persistent group.

67.3%(33) of patients who had never experienced wheeze, chest tightness or dyspnoea prior to November 2016 had developed asthma symptoms during follow-up. This compared with 86.4%(57) of patients who reported at least one symptom prior to November 2016.

Conclusion: Majority of patients affected by 2016 ETSA without a prior diagnosis of asthma reported symptoms suggestive of current asthma on follow-up. This included the majority of patients who had never experienced prior symptoms suggestive of asthma. Preventer use and asthma action plan ownership were low, even in patients with persistent symptoms. Concerningly, a significant proportion sought urgent healthcare over the follow-up period. Better recognition of undiagnosed asthma and optimisation of asthma management may help to improve symptom control and healthcare utilization before and after an ETSA event.

TPL 002

RESIDENTIAL NO$_2$ EXPOSURE IS ASSOCIATED WITH RECENT URGENT HEALTHCARE UTILISATION IN CURRENT ASTHMATICS ADMITTED TO EASTERN HEALTH DURING A THUNDERSTORM ASTHMA EPIDEMIC

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Introduction/Aim: There is increasing interest in the role of traffic-related air pollution (TRAP) in allergic airway diseases. The Melbourne 'thunderstorm asthma' event in November 2016 provided an opportunity to investigate the relationship of annual average residential NO2 exposure and living closer to major roads, proxy markers of TRAP exposure, with risk of recent asthma exacerbation requiring urgent health healthcare utilisation in the last 12 months in those with current diagnosed asthma.

Methods: Patients who presented to the three Eastern Health Emergency Departments with asthma symptoms on the 21st or 22nd November 2016 were identified and contacted using a standardised questionnaire. Current asthma was defined as diagnosed asthma with symptoms within the last 12 months, with further identification of urgent healthcare utilisation for asthma within this period. Residential addresses were geocoded and the annual average NO2 exposure for each patient was assigned through a validated satellite-based land use regression model. Residential distance to the nearest major road was calculated using ArcGIS.

Results: A total of 88 patients with current asthma were analysed from 263 thunderstorm asthma patients. The mean (SD) annual residential NO2 exposure for patients with urgent health care utilisation was 6.7 (1.5) ppb, compared with 5.8 (1.7) ppb in those without (p=0.02). The difference in the mean (SD) distances to nearest road for patients with health care utilisation was 321 (262) m, compared with 411 (609) m in those without health care utilisation, respectively, was not significant.

Conclusion: Annual average residential NO2 exposure was associated with asthma exacerbation requiring urgent health care utilisation for asthma exacerbation in the last 12 months amongst Eastern Health thunderstorm asthma patients with current diagnosed asthma. While those who required urgent health care utilisation lived closer to a major road, the difference was not statistically significant, which may be related to the study power.

Cell, Immunology & Molecular Biology of the Lung 1

PHYSIOLOGICAL STIFFNESS IS CRITICAL FOR EMULATION OF GLUCOCORTICOID RESPONSES

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Introduction/Aim: Respiratory diseases, including severe asthma and chronic obstructive pulmonary disease (COPD), are conditions with significant unmet need. However, many drug developments have failed, despite showing impressive efficacy in preclinical models. Biomechanical characteristics of the preclinical *in vitro* models have been highlighted as important influences on cell morphology, proliferation, and other physiological functions, including the homeostasis of matrix stiffness in respiratory system. We provide evidence in the current study that the glucocorticoid response of airway epithelial cells *in vitro* is conditioned by the stiffness, with softer microenvironments showing more relevance to the pattern of responses in animal models.

Methods: Cells were cultured in plates of defined stiffness for 24h, and treated with Dexamethasone (Dex) for 4h. Mice were treated with bleomycin and/or Dex for 14 days. GC-responsive gene expression was measured by RT-qPCR. Lung sections were stained with ENaCα, GILZ and MKP-1.

Results: Glucocorticoids induced expression of GILZ and MKP-1 in culture settings across the range of stiffness from physiological (0.5-1.0 kPa) to fibrotic (16-64 kPa). However, the induction of ENaCα was attenuated in softer culture microenvironments and the baseline level of expression was increased 10 fold. These latter findings with ENaCα emulate the elevated expression and lack of GC response in mouse lung.

Conclusion: GC response is related to extracellular matrix stiffness; culture on a physiologically soft substrate is inherently more likely to provide physiological relevance and better predictive value for drug screening .

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THE EFFECT OF DIETARY FATTY ACIDS ON INFLAMMATION IN PRIMARY LUNG MESENCHYMAL AND EPITHELIAL CELLS

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Introduction/Aim: Obesity is an important risk factor for developing severe asthma. Dietary fatty acids which are increased in sera of obese individuals and after high fat meals, activate the innate immune system, induce inflammation and impair responses to treatment in the airways. This study investigated whether dietary fatty acids directly cause inflammation and/or synergise with obesity-induced cytokines in primary human pulmonary fibroblasts *in vitro* and the underlying mechanisms.

Methods: Fibroblasts were challenged with BSA-conjugated ω-6 polyunsaturated fatty acids (PUFAs), ω-3 PUFAs or saturated fatty acids (SFAs) with or without TNFα. Release of the pro-inflammatory cytokines, IL-6 and CXCL8, was measured using ELISA. To investigate underlying mechanisms, specific inhibitors were used to block signaling pathways. Activation of two main pathways, p38 and NF-κB, were investigated using western blotting. To investigate whether other structural lung cells respond the same as pulmonary fibroblasts, selected experiments were repeated in airway smooth muscle (ASM) cells and human bronchial epithelial cells (BEAS-2Bs).

Results: We found that ω-6 PUFA arachidonic acid (AA), but not ω-3 PUFAs or SFAs up-regulates IL-6 and CXCL8 release from fibroblasts. Combined AA and TNFα challenge resulted in substantially greater IL-6 and CXCL8 release than either alone, demonstrating synergy. Synergistic upregulation of IL-6, but not CXCL8 was mainly mediated *via* cyclooxygenase (COX). Inhibition of p38 mitogen-activated protein kinase reduced CXCL8 release induced by AA and TNFα alone, but not in combination. Synergistic CXCL8-release following AA and TNFα challenge was not medicated via a single signaling pathway (MEK1, JNK, PI3K and NF-κB), nor by hyperactivation of NF-κB or p38. Similar effects in ASM were found, but not in epithelial cells.

Conclusion: This study suggests that diets rich in ω-6 PUFAs might promote airway inflammation via multiple pathways, including COX dependent- and independent pathways, and in an obese person may lead to more severe airway inflammation.

TP 013

THE CD1B LIPID ANTIGEN PRESENTATION PATHWAY IN COPD IS ASSOCIATED WITH OXIDIZED AIRWAY LIPIDS AND SPHINGOLIPID SIGNALING

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Introduction/Aim: Reduced alveolar macrophage (AM) clearance of apoptotic cells and a build-up of oxidised lipid in the airway have been described in COPD. We showed that CD1b, a lipid antigen presenting molecule, is altered in COPD AM, and by oxidised airway epithelial cell lipid. We hypothesised that CD1b contributes to defective macrophage function and that this occurs via sphingolipid signalling.

Methods: CD1b expression by (a) AM from never-smoker, ex-smoker and current-smoker controls, and current- and ex-smoker COPD patients and (b) MDM exposed to cigarette smoke (CS) $\pm$ FDA approved sphingolipid modulator FTY720 was measured by flow cytometry $\pm$ immunofluorescence. Oxidation states of lipid films produced from mechanically detached and CS-exposed 16HBE bronchial epithelial cells were measured by spectrophotometry. Phagocytosis was measured by flow cytometry using the intracellular pH-sensitive pHrodo stain.

Results: AM from COPD patients and smokers showed higher expression of CD1b than controls (current-smoker COPD 15.8%; ex-smoker COPD 9.6% vs. control 1.8%). CD1b expression significantly correlated with FEV1. Epithelial-derived lipids were oxidised by CS (average increase of 272% vs. controls). Treatment with CS-oxidised airway epithelial lipid increased CD1b in MDM (87% vs. 69%) and also significantly decreased phagocytosis (8.7% vs 16.5%). FTY720 reversed these effects.

Conclusion: A build-up of oxidised lipids from uncleared apoptotic airway cells may cause decreased phagocytosis in COPD and be presented by CD1b, potentially identifying an autoimmune-like component which could be exploited in future treatment strategies targeting the sphingolipid pathway.

TP 014

TOLL-LIKE RECEPTORS IN VIRUS-INDUCED STEROID RESISTANCE IN BRONCHIAL EPITHELIAL CELLS

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Introduction/Aim: Airway viral infection is a major cause of acute respiratory disease, which responds inadequately to anti-inflammatory glucocorticoids (GC). Virus can be recognised by pattern recognition receptors, including the Toll-like receptors (TLRs). TLR2 and TLR4 can be activated by viral protein; TLR3 recognizes viral double-strand (ds) RNA intermediate; and TLR7 recognizes viral single-strand (ss) RNA. We recently found that the virus-induced glucocorticoid (GC) resistance in human bronchial epithelial cells was mediated by TLR3 dependent release of TGF-β (Xia, 2017). The present study explores the presence and function of other TLRs members to GC response in bronchial epithelial cells.

Methods: The expression of TLRs (TLR1-TLR10), on bronchial epithelial cell line BEAS-2B cells was examined by RT-PCR. The cells were challenged with TLR2 agonist Zymosan A, TLR3 agonist polyinosinic-polycytidylic acid (Poly (I:C)), TLR4 agonist lipopolysaccharide (LPS) and TLR7 agonist imiquimod for 24 hours. Glucocorticoid transactivation was measured through examination of GC Response Element (GRE)-dependent promoter activity with 24 hours dexamethasone treatment; and GC-responsive gene expression with 4 hours dexamethasone treatment.

Results: All the ten members of TLRs were detectable expressed in BEAS-2B cells albeit at varying levels. Activation of TLR3 inhibited GC-induced GRE activation and impaired the GC-responsive genes. Activation of TLR4 also impaired the GC activity, but to a lesser extent than TLR3, whereas activation of TLR2 and TLR7 had no detectable effect on GC-induced GRE activity or GC-responsive gene expression in the BEAS-2B cells.

Conclusion: The bronchial epithelial cells express various TLRs, which are important in airway inflammation and immunity. Activation of TLR3 and TLR4, but neither TLR2 nor TLR7 impaired the GC activity in bronchial epithelial cells. Better understanding of the viral infection pathway that is involved in the GC resistance may provide new targets for treating viral infection-induced bronchiolitis or asthma/COPD exacerbations.

IN VITRO EXPOSURE OF AIRWAY EPITHELIAL CELLS TO SOY BIODIESEL EXHAUST IS LESS TOXIC COMPARED WITH MINERAL DIESEL EXHAUST

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Introduction/Aim: As biodiesel usage increases worldwide, concerns have been raised over the impact of exhaust exposure on human health. The aim of this study was to compare the effects of exposure to exhaust generated by the combustion of mineral diesel (ULSD), 100% soy biodiesel (B100) or a blend of 20% biodiesel to 80% ULSD (B20) on human airway epithelial cells *in vitro.*

Methods: Human airway epithelial cells obtained from 6 healthy volunteers (2.7-5.4yrs; 4 males) were exposed for 1, 2 or 4 hours to diluted exhaust generated by a diesel engine running on ULSD, B100 or B20 fuel. Exhaust was characterised for toxic gas levels and the physico-chemical properties of the particulate matter were analysed. Cells were incubated for 24 hours after exposure before health outcomes were assessed.

Results: All exposures resulted in cell death and the release of inflammatory mediators compared to untreated controls, however there were few overt trends with respect to exposure time. Across all time-points, cells exposed to ULSD exhaust were significantly less viable compared with cells exposed to soy biodiesel exhaust (e.g. ~50% cell death for ULSD exhaust exposure compared with ~25% cell death for B100). The majority of cell death was via apoptosis, with a smaller proportion of cells undergoing necrosis.

Exhaust gases varied significantly with respect to gas levels. B100 exhaust contained the highest concentrations of NOx, CO_2 and SO_2, ($p < 0.01$) all of which are known respiratory irritants. Particle size spectra also varied between exhaust types.

Conclusion: Soy biodiesel exhaust exposure was less harmful to human airway epithelial cells *in vitro* compared with ULSD exhaust exposure. This is contrary to our previous findings for canola based biodiesel (which was more toxic than ULSD), suggesting that the base-oil biodiesel is made from can significantly impact health outcomes.

ESTABLISHMENT OF A DOXORUBICIN DETOXIFICATION ASSAY TO MEASURE ATP BINDING CASSETTE SUBFAMILY A MEMBER 3 (ABCA-3) FUNCTION IN NASAL EPITHELIAL CELLS DERIVED FROM CHILDREN WITH ABCA-3 DEFICIENCY

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Introduction/Aim: The *ABCA3* gene encodes a lipid transporter, expressed in respiratory epithelial cells, essential for pulmonary surfactant homeostasis. Children with disease-causing mutations in *ABCA3* suffer severe respiratory disease, and this rare condition is often fatal. Development of potential therapeutic agents targeting ABCA-3, requires the *in vitro* demonstration of ABCA-3 function before and after drug exposure. The transporter function of ABCA-3 confers resistance to the antineoplastic chemotherapy drug, doxorubicin and has been used previously to demonstrate decreased viability in HEK293 cells expressing mutant ABCA-3. The present study aimed to adapt and optimise the doxorubicin detoxification assay for application in patient-derived nasal epithelial cells, as we have previously demonstrated *ABCA3* gene expression in nasal epithelium.

Methods: Nasal epithelial cells were obtained by cytological brushing of the nasal turbinate from children with (n=2; median (range) age 4.9 (2.2-7.6) years; males: 1) and without (n=4; age 2.9 (2.7-5.4) years; males: 4) ABCA-3 deficiency and used to establish conditionally-reprogrammed primary cultures. Mutations in *ABCA3* were confirmed and identified: c.920C>T/c.920C>T in Patient 1 and c.838C>T/c.3997_3998delAG in Patient 2. Cell viability after three-hour exposure to doxorubicin (0 – 10 µM) was assessed using the MTS assay.

Results: Over the concentration range assessed, there was no significant effect of doxorubicin on cell viability in healthy control cells, $0.50 < p < 0.80$ (n=12). Cell viability for Patient 1 (n=3) was reduced by 25.2% $\pm$ 2.7% (SD), $p < 0.001$, and 30.35% $\pm$ 2.6% (SD), $p < 0.001$, after treatment with 5 µM and 10 µM doxorubicin, respectively, compared to healthy controls. Cell viability for Patient 2 (n=3) was reduced by 11.3% $\pm$ 0.3% (SD), p=0.02, by 5 µM doxorubicin and 7.8% $\pm$ 8.1% (SD), p=0.24, by 10 µM doxorubicin compared to healthy controls.

Conclusion: Doxorubicin detoxification function was impaired in ABCA-3 deficient nasal epithelial cells, relative to cells from healthy controls. Effects were patient-specific, indicating that genotype may influence effect size.

EXPRESSION OF AUTOPHAGY MARKERS IN THE HUMAN ASTHMATIC EPITHELIUM

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Introduction/Aim: Asthma affects more than 300 million people worldwide and poses a huge economic burden on the healthcare system. Current anti-asthma therapies are effective in ameliorating asthma-related symptoms but fail to target structural changes in the lung also known as airway remodelling. Airway remodelling in patients with asthma has been associated with progressive loss of lung function. Macroautophagy (autophagy) is a fundamental process that occurs in all eukaryotic cells and can be referred to as the cell recycling mechanism. Autophagy regulation is linked to fibrotic remodelling in the heart, liver and kidneys. The aim of our study is to explore the role of autophagy in asthma by investigating autophagy markers in the epithelium of large airways of asthmatics *vs.* non-asthmatics.

Methods: Tissue from asthmatics and non-asthmatics were immunostained for autophagy markers; ATG5, Beclin1 and p62. The percentage area of positive staining was enumerated in the epithelium using ImageJ software.

Results: Expression of Beclin-1 was significantly higher ($p<0.05$) in the epithelium of non-asthmatic tissue compared with asthmatic tissue. There were no statistically significant differences observed in degree of p62 and ATG5 staining in the tissues. Furthermore we found increased Beclin-1 positive staining in cilia of asthmatic patients. Comparatively, the cilia of non-asthmatic patients completely lacked Beclin-1 staining.

Conclusion: The reduction in expression of Beclin-1 indicates that autophagy is possibly impeded or impaired in the large airway epithelium of asthmatics. Strong cilia positivity for Beclin-1 in asthmatics highlight that autophagy-dependent regulation of cilia (ciliophagy) may be active in asthma. Our study is the initiation of our ongoing research into the role and effect of autophagy in asthma.
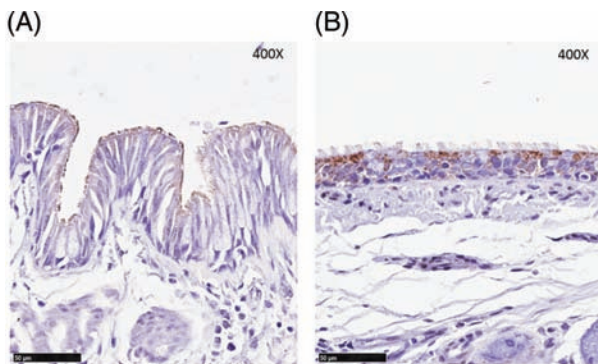

Figure 1 Cilia in the large airways of asthmatics (A) are positively stained for the autophagy marker Beclin-1, whilst cilia in the large airways of healthy patients (B) are devoid of Beclin-1 staining.

A PILOT STUDY ASSESSING THE WOUND REPAIR CAPACITY OF THE UPPER AIRWAY EPITHELIUM OF CHILDREN BORN PREMATURELY

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Introduction/Aim: Premature birth is the leading cause of mortality among children under 5 years of age; primarily from lung complications. The airway epithelium protects the body from the external environment, eliciting rapid repair when injured to reinstate barrier integrity. However, in some disease states this mechanism is potentially defective. In this study we aimed to characterise the repair mechanisms of the airway epithelial cells in preterm infants.

Methods: Upper airway nasal epithelial cells (NECs) obtained by cytological brushing of the nasal turbinate from 10 children born very preterm (25-31 weeks gestational age) at 1.07-1.22yrs corrected age (8 males; 3 BPD) and 6 full-term children (2.4-6.5yr; 4 males) were used to establish primary cell cultures. Twenty four hours prior to wounding, cell monolayers were cultured in restricted media and subsequently wounded (Essen CellPlayer® WoundMaker®). Monolayers were washed to remove cellular debris and media replenished every 48h. Time-lapse images were captured and analysed every 30 minutes with the IncuCyte® ZOOM. Wound recovery was calculated by manual tracing of the new wound edge at each time interval and comparing the wound width to that of the originally created wound edge. Calculated values were then expressed as a percentage of total wound recovery over the period to achieved full repair.

Results: Healthy full-term NECs were found to fully repair wounds by 36 hrs. In contrast, the preterm NECs only completed 37.5% repair on average at the same time point. At 72 hours post injury, two preterm NECs exhibited significantly dysregulated repair (20-30% repair), five achieved 50-80% wound closure, 1 >90 repair with 2 achieving full repair.

Conclusion: Data generated suggests that there is an inherently delayed ability of preterm infant upper airway AEC to successfully repair which may contribute to their increased susceptibility to environmental pathogens.

Declaration: No conflict of interest

TRACE ELEMENT CONCENTRATIONS IN HUMAN PLEURAL EFFUSIONS

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Introduction/Aim: Pleural effusions are common and contain abundant nutrients and growth factors. Trace elements are increasingly recognized for their potent and diverse range of biological roles. For example, we recently found that manganese is important in *Streptococcus pneumoniae* proliferation in empyema. Trace elements have rarely been investigated in pleural diseases. This study aimed to determine the presence and concentrations of trace elements in human pleural effusions.

Methods: We analysed 119 pleural fluid samples which included 71 malignant (39 mesothelioma), 16 parapneumonic (including empyema), 14 heart failure and 16 other miscellaneous benign effusions. Iron (Fe), manganese (Mn), copper (Cu), zinc (Zn), cobalt (Co) and molybdenum (Mo) were assayed by a NATA accredited hospital laboratory (PathWest, WA). Clinical diagnoses of the effusions were verified by a respiratory specialist.

Results: All trace elements were detected in the pleural effusions: median (IQR) levels of Fe 8.02 (3.96-16.80) umol/L; Mn 10.71 (5.64-18.04) nmol/L; Cu 9.05 (5.98-14.77) umol/L; Zn 5.84 (3.26-8.67) umol/L; Co 1.58 (1.05-2.63) nmol/L and Mo 7.91 (5.38-15.82) nmol/L. Strong (Spearman) correlations were found between Fe and Mn as well as Zn and Cu levels (0.742 and 0.745, both $p<0.000001$). Pleural fluid protein correlated weakly with Zn and Cu (Spearman 0.442 and 0.506, both $p<0.000001$) but not with other elements. No strong correlations were found between pleural fluid pH or glucose with any trace elements measured. Fe levels were significantly higher in malignant than benign effusions (median 10.07 vs 5.54 umol/L, $p<0.001$). Conversely, benign pleural fluids contained higher levels of Mo (median 12.18 vs 6.96 nmol/L, $p<0.001$) and Co (1.84 vs 1.58 nmol/L, $p<0.001$) than malignant effusions. Co levels were higher in parapneumonic effusions than in other etiology groups.

Conclusion: Trace elements are present (and differentially accumulated) in various pleural effusions. Their roles in normal and pathological pleural conditions need investigations.

Declaration: All authors declare no conflict of interests.

THE EFFECT OF VIRAL INFECTION ON GLUCOCORTICOID SENSITIVITY IN BRONCHO-ORGANOIDS

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Introduction/Aim: Viral infection, such as respiratory syncytial virus (RSV) and rhinovirus (RV) is a major cause of acute respiratory disease, which responds inadequately to anti-inflammatory glucocorticoids (GC). We recently found that the endogenous TGF-β partially explained virus-induced GC resistance in human bronchial epithelial cell line BEAS-2B cells and in the air-liquid interface (ALI) differentiated primary human bronchial epithelial cells (HBEC) (Xia, 2017).bIn the current study, we further investigate virus-induced GC resistance in the broncho-organoids.

Methods: Immortalized human airway basal cell line, BCi-NS1 (expression of hTERT), or primary bronchial epithelial cells (Lonza) were mixed with 5% Corning® Matrigel® in bronchial epithelial cell growth medium (BEGM™, Lonza), seeded on a layer of 25% or 40% Matrigel® in BEGM, to enable the formation of the broncho-organoids. The cell viability of the organoids was tested by CellTiter-Glo® luminescent assay. The organoids were infected with virus for 48 hours by microinjection. The selective ALK5 (TGFβRI) inhibitor, SB431542 was used to test the involvement of TGF-β. Glucocorticoid transactivation was measured through examination of GC-responsive gene expression with the last 4 hours dexamethasone treatment.

Results: Formation of the broncho-organoids was observed within approximately one week. The size of the organoids increased in the first week. The lumen was visible within two weeks. The cells within the organoids maintained a differentiated state with a pseudostratified epithelial structure with the apical surface projecting towards the lumen by week two to three. Beating cilia and mucus were visualized under microscope. The effect of virus infection on the broncho-organoids in terms of GC sensitivity is being investigated.

Conclusion: Virus infection impairs GC-inducible genes and protein expression in BEAS-2B cells and ALI-HBECs. The effect of virus infection to the bronchial epithelium was further investigated in a newly established physiologically relevant model, broncho-spherical organoids.

TP 021

PROGNOSTIC SIGNIFICANCE OF THE NEUTROPHIL-TO-LYMPHOCYTE RATIO IN PLEURAL FLUID

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Introduction/Aim: Predicting survival of patients with malignant pleural effusions (MPEs) is notoriously difficult. A robust prognostic marker can guide clinical decision making. The neutrophil-to-lymphocyte ratio (NLR) in blood has been shown to predict survival in many cancers. Pleural fluid bathes the malignant pleural tissues, thus the NLR of the pleural fluid may closer reflect the local tumour environment.

Methods: *Setting*: tertiary pleural referral service at SCGH.

Subjects: patients who had pleural fluid drained and a matching blood leucocyte count (within 24 hours of the fluid collection) were included. Those with recent chemotherapy or pleurodesis were excluded.

Data: Neutrophil and lymphocyte counts in effusions were performed by manual review of cytospin cell preparations by trained observers. Clinical data were extracted from a state-wide hospital database.

Results: Paired blood and effusion samples (n=141: 117 malignant and 24 benign) were analysed. Mesothelioma accounted for 55% of cases. There were significantly fewer neutrophils (expressed as percentage of total leukocyte count) in pleural fluids than in blood (9% vs 73%; p<0.001). The NLR was significantly lower in pleural fluids than in corresponding blood: median [IQR] = 0.20 [0.04-1.18] vs 4.9 [3.0-8.3], p<0.001. In univariate analysis, NLR in malignant pleural fluid was predictive of survival (HR=1.026 [1.004-1.048]; p=0.018), and remained significant after adjustment for age, sex, presence of chest drain and cancer type (1.027 [1.005-1.050]; p=0.021). The NLR in blood was also predictive of survival (1.05 [1.02–1.07]; p<0.001) in MPE patients. Patients with blood NLR ≥5 had a median survival of 130 (95%CI 64-195) days from sample collection, *vs* 479 (95%CI 289-669) days if NLR <5, p<0.001. No correlation was observed between the NLR of pleural fluids and blood.

Conclusion: This is the first study to show that NLR in malignant effusions can predict survival, despite no correlation with blood NLR.

TP 022

SHORT TERM EXPOSURE TO WILDFIRE SMOKE EXTRACT POTENTIATES AUTOPHAGIC INSUFFICIENCY AND BARRIER DYSFUNCTION IN EX VIVO MODELS OF THE AIRWAY EPITHELIUM

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Introduction/Aim: Climate change wildfire events are becoming more frequent and increasingly encroaching on urban areas. Thus, many more individuals are likely to be exposed to wildfire smoke than ever before, yet the body of evidence on the health consequences of such exposure remains small. Here we examine markers of fragility and barrier function in models of human airway epithelium exposed to wildfire smoke-extract (WFSE).

Methods: Submerged cultures of Small Airway Epithelial Cells (SAEC) and differentiated air-liquid interface (ALI) cultures of bronchial AEC (bAEC) were exposed for up to 6h with 1-10% WFSE generated from plant species found in the Australian bushland. Autophagy (LC3-II and Sequestosome), apoptosis (Poly-(ADP)-Ribose Polymerase cleavage) and tight junction proteins were measured using western analysis. Barrier function was assessed using fluorescein tracers and trans-epithelial resistance (TER). The production of inflammatory cytokines were assessed using ELISA.

Results: SAEC exposed to 10% WFSE exhibited a significant blockade in autophagy as evidenced by an increase in LC3-II coupled with a concomitant elevation in Sequestosome abundance (both $P<0.05$). These conditions also induced significant PARP cleavage indicative of apoptotic changes. ALI cultures of bAEC treated with 5% WFSE demonstrated barrier dysfunction with significant increases in paracellular molecular permeability and ionic conductance (both $P<0.001$), and a reduction in the abundance of the tight junction proteins ZO-1 and Claudin-1 (both $P<0.01$). These cultures also exhibited an increase IL-6 secretion, which is consistent with an epithelial inflammation and repair response. The responses to WFSE were consistently elevated in comparison to parallel exposures of cigarette smoke-extract.

Conclusion: Relatively short exposures to WFSE potentiated a block in autophagic flux and barrier dysfunction in models of human airway epithelium. This scenario is commonly observed in the airways during COPD. As autophagy is a central regulator of cellular repair, viability, and inflammation, targeting the block in autophagic flux may ameliorate the consequences of wildfire smoke-exposure, particularly for individuals with pre-existing respiratory conditions.

COI Statement: The authors have no conflicts of interest to declare.

PULMONARY SURFACTANT ACTIVITY IS REDUCED IN MUCOPOLYSACCHARIDOSIS TYPE IIIA MICE

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Introduction/Aim: Mucopolysaccharidosis type IIIA (MPSIIIA) is a lysosomal storage disorder caused by a deficiency in the activity of the lysosomal hydrolase sulphamidase, normally involved in heparan sulphate (HS) degradation. This results in primary storage of partially degraded HS and secondary lipid storage in tissues. We recently showed HS storage and changes in lipid metabolism in MPS IIIA mouse lung tissue. Here we determine the *in vitro* surface activity of alveolar surfactant harvested by bronchoalveolar lavage of normal (Norm), heterozygous (Het) and MPSIIIA mice.

Methods: Bronchoalveolar lavage fluid (BALF) (4-6 mice/genotype) was centrifuged to remove immune cells and the supernatant frozen and shipped on dry ice to Madrid. Samples were sequentially defrosted and centrifuged at 105,000g to pellet surfactant material. The pellets were reconstituted in 0.9% NaCl to a final concentration of 20mg/ml phosphatidylcholine and analysed fresh on a Captive Bubble Surfactometer.

Results: For all measurements, results for MPSIIIA animals were more variable, with many individuals performing more poorly. Nevertheless, under static conditions, surfactant demonstrated similar initial adsorption among all genotypes lowering equilibrium surface tension (γ_{eq}) to ~20mN/m. However, under dynamic conditions (30 cycles/min) surfactant from MPSIIIA animals was unable to reach a low surface tension at minimum bubble size (γ_{min}) even after 20 cycles compared with Norm and Het animals (γ_{min}: Norm: 1.6±0.7; Het: 1.3±0.3; MPSIIIA: 8.6±6.0mN/m; mean±SD; p<0.0001). Similarly, the surfactant of MPSIIIA animals also had a higher γ_{max} at maximum bubble size (γ_{max}: Norm: 29.0±0.8; Het: 29.6±1.6; MPSIIIA: 36.8±8.5mN/m; mean±SD; p<0.0001). In addition, the change in area required to reach γ_{min} was significantly greater in MPSIIIA animals (Δ(area): Norm: 0.10±0.06; Het: 0.09±0.02; MPSIIIA: 0.38±0.16; mean±SD, p<0.001).

Conclusion: These data show that surface activity in MPS IIIA mice is inhibited either by changes in surfactant protein composition (lipids are unchanged) or by factors in the alveolar compartment. The latter likely relates to increased storage of heparan sulphate in lung tissue, which may enter the alveolus and either inhibit surface activity directly or indirectly by eliciting an immune reaction. A reduction in surfactant activity has significant implications for the lung function of MPSIIIA patients.

ASSOCIATIONS BETWEEN TIME USE AND BODE INDEX SCORE IN PEOPLE WITH COPD

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Introduction/Aim: Few data are available describing use-of-time patterns in people with COPD and the relationship between use of time and COPD severity remains unclear. This study aimed to describe use-of-time patterns across a typical day for a person with COPD and to explore associations between BODE index scores and time use patterns.

Methods: Using a cross-sectional design, people with clinically stable moderate to severe COPD had their demographics, objective measures of function, and self-reported COPD-related impairment recorded. Habitual activity was recorded using a seven-day accelerometry protocol and use-of-time recall interviews. Use-of-time recall interviews record 24-hour habitual activity profiles, combining activities that share similar context into one of eight domains. Compositional profiles were created using both energy expenditure bands (accelerometer data) and activity domains (use-of-time data). Compositional linear regression models described the relationship between BODE index scores and the compositional profiles. Models also predicted time use (min/d) across BODE index scores.

Results: 135 people were recruited (Age 70.7 ± 8.1 yrs., FEV1 50% ± 17%, females 40%[n=57]). In both accelerometer and use-of-time compositional models, significant differences in time use were observed across the BODE index. Relative to remaining components, as BODE index scores increased so did time spent in sedentary activities, quiet time and screens. The cumulative increases were strongly significant (p<0.001) and totalled 296 min/d (sedentary), 131 min/d (quiet time) and 155 min/d (screens). Corresponding cumulative and significant reductions in chores and household administration totalling 206 min/d (p<0.001) and 50 min/d (p=0.015) respectively were also observed.

Conclusion: In people with COPD, use-of-time patterns differ across BODE index scores. BODE index scores correlated strongly with time spent in chores, screen and/or quiet time.

TP 024

PARTICIPATION IN PULMONARY REHABILITATION DID NOT SIGNIFICANTLY ALTER TIME USE PATTERNS IN PEOPLE WITH COPD

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Introduction/Aim: Whether participation in comprehensive pulmonary rehabilitation programs (CPRP) changes habitual time use in people with COPD is equivocal. This study aimed to explore whether time use patterns changed in the twelve months after CPRP participation.

Methods: Using a non-randomised clinical trial design, adults with clinically stable moderate to severe COPD were recruited into an eight-week CPRP or Usual Care cohort. Baseline demographics, objective measures of function, self-reported COPD-related impairment and use-of-time recall interviews (24-hour profiles of habitual activity) were assessed at baseline and one, six and 12 months post CPRP. Activities sharing similar context were grouped into one of eight domains (chores, household administration, quiet time, screen time, self-care, sleep, socio-cultural, sports/exercise), which were then used to create compositional profiles representing an average day. Between compositions and between compositional components (at group and time point level) comparisons were conducted using ANOVA models and isometric log ratio differences respectively.

Results: 89 people (mean age 69.7 $\pm$ 9.7 yrs. FEV_1 51% $\pm$ 9) were recruited into CPRP (n=49) or Usual Care (n=40). With the exception of FEV_1 %$_{pred}$ (CPRP 47% $\pm$ 19% vs. Usual Care 55% $\pm$ 16% [p=0.032]), baseline demographics were similar. Both cohorts exhibited similar time use patterns where there were no statistically significant differences in time use patterns evident between cohorts or time points.

Conclusion: This study found CPRP did not significantly influence patterns of habitual time use in people with COPD. Given the observed similarities in use-of-time profiles between cohorts, this data suggests changing habitual patterns of time use in people with COPD requires more than enrolment, and participation in, an eight week CPRP.

TP 025

'LET'S START THE CONVERSATION…'—THE PERSPECTIVES OF HEALTH CARE PROFESSIONALS ON PHYSICAL ACTIVITY PRESCRIPTION FOR PEOPLE WITH COPD

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Introduction/Aim: Clinical practice guidelines recommend that people with chronic obstructive pulmonary disease (COPD) should be encouraged to be more physically active. However, it is not clear how guidelines are applied in practice. Reporting the perspectives of respiratory health care professionals (HCP) regarding physical activity (PA) advice and prescription would assist translation of PA recommendations into clinical practice.

Methods: An interview-based qualitative study including 30 respiratory HCP was conducted. Interviewed HCP (12 physicians, 10 physiotherapists, four nurses and four exercise physiologists) all provide care for patients with COPD. Semi-structured interviews were conducted, transcribed verbatim and analysed by two independent researchers using thematic analysis.

Results: Six overarching themes emerged from synthesis of the interviews. (1) Respiratory HCP acknowledged the importance of PA for people with COPD and identified it as a key component of management. (2) HCP were conscious of low PA levels; however, few specifically address this issue in practice. (3) Physicians described limitations including time constraints, pharmacological treatment prioritisation and perceived lack of expertise; as a result they preferred to refer to physiotherapists or nurses for more comprehensive assessment and advice regarding PA. (4) Most HCP viewed pulmonary rehabilitation as an essential intervention to enhance COPD outcomes, but PA was poorly differentiated from exercise training. (5) Although HCP were aware of guidelines regarding prescription of PA, few were able to recall specific recommendations for people with COPD. (6) HCP perceived that there were few evidence based strategies to enhance PA.

Conclusion: Respiratory HCP perceive that enhancing PA is a key element of COPD care, however this is not always addressed in practice. A structured approach to assessment and prescription of PA could assist HCP to discuss PA during clinical consultations.

PULMONARY REHABILITATION AND SLEEP QUALITY IN PATIENTS WITH COPD

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Introduction/Aim: Poor sleep quality is a common complaint reported by patients with COPD. Exercise has been shown to improve sleep quality. However, the relationship between pulmonary rehabilitation (PR) and improved sleep quality is unknown. We examined sleep quality in patients with COPD before and after PR, to identify factors associated with improvement in sleep quality following PR.

Methods: We performed a retrospective chart review of all patients with COPD who completed PR in Western Sydney from January 2012 to May 2017. Our primary outcome was sleep quality measured by Pittsburgh Sleep Quality Index (PSQI). We identified patients with poor sleep quality at baseline (PSQI>5 units), and compared baseline and post-PR characteristics of patients whose PSQI improved following PR by ≥3 units (responders) with those who did not (non-responders). Data were compared using paired t-tests within group, and Mann-Whitney tests between groups. Data presented as mean±SD. $p<0.05$ was significant.

Results: Data were available for 329 patients (52% male, 69.5±8.9 years, FEV_1% predicted 48±16%). 219 (67%) had poor sleep quality. Following PR, group mean PSQI decreased by 0.95±3.14 units ($p<0.0001$). 88 of 219 patients with poor sleep quality at baseline improved PSQI by ≥3 units following PR. There was no difference at baseline between responders and non-responders for age, gender, lung function, 6MWD, mood or quality of life (QOL) (all $p>0.05$). However, following PR, responders had a greater 6MWD compared with non-responders by 38.3m and an improved QOL score by 5.3 units (both $p=0.005$).

Conclusion: Sleep quality improves following PR for COPD, but is highly variable between individuals. Greater gains in 6MWD and QOL were also seen in association with a clinically significant improvement in sleep quality following PR. Future intervention studies targeting improved sleep quality for patients with COPD may help to maximise the benefits of a PR program.

FEASIBILITY AND EFFICACY OF NOVEL TRANSITIONAL RESPIRATORY EXERCISE GROUP

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Introduction/Aim: Pulmonary rehabilitation programs (PRPs) are integral in the care of chronic respiratory disorders for improvements in quality of life, exercise capacity and reduction in hospitalisations. 1 Exercise is a key component of PRP but the efficacy of other components is yet to be determined. 2 Port Macquarie Base Hospital (PMBH) has developed an abridged PRP, without education, to provide greater access to PRPs for in a timely fashion with limited resources. The Transitional Respiratory Exercise Group (TREG) is a hospital based program incorporating 6 weekly exercise sessions with rolling intake.

We aimed to assess the feasibility and efficacy of performing TREG.

Methods: We conducted a retrospective review of outcome data for all patients enrolled in TREG March 2016 - August 2017. This was compared to data from the PMBH PRP for the 12 months prior to TREG. The mean difference between 6MWT, oxygen saturations were determined using the Paired T-Test.

Results: 50 COPD admissions for occurred between March 2015 and March 2016. 12 (24%) were enrolled into the traditional PRP.

46 COPD admissions for occurred between March 2016 and March 2017. 29 (63%) were enrolled in TREG. Another 30 participants were referred to TREG from external sources to make up 59 patients total. Average time from hospital discharge to enrolment in TREG was 30 days with an average completion rate of 81%.

TREG group had significant improvement in 6MWT with mean increase of 42.5 m ($p < 0.05$). Oxygen saturations had a mean decrease of 0.004% ($p < 0.05$).

40 readmissions (Range 0-2) occurred following TREG (9 month average follow-up post, range 5-12m) compared to 61 readmissions (Range 0-3) in the 12 months prior to TREG ($p < 0.05$).

Conclusion: TREG is a feasible and efficacious means to provide timely access to an exercise rehabilitation program following hospitalisation.

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TP 028

PAIN COEXISTING WITH CHRONIC LUNG DISEASE ASSOCIATED WITH EMPLOYMENT STATUS

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Aim: Australian data on pain prevalence among those with chronic lung disease (CLD) is limited. This study aimed to: 1) determine pain prevalence for people with and without self-reported CLD in Australia; and 2) identify respondent characteristics associated with the presence of pain among people with self-reported CLD.

Methods: A cross-sectional analysis was undertaken on data obtained from adult respondents to the Australian Bureau of Statistics National Health Surveys in 2011/12 (n=15,136) and 2014/15 (n=14,510). Participants who self-reported a diagnosis of chronic bronchitis or emphysema lasting at least six months were classified as having CLD. A single survey item recorded the severity of any and all pain experienced by respondents in the previous four weeks, which was dichotomised as: 1) no pain/pain; 2) none-mild pain/moderate-very severe pain. Logistic regression was used to assess age- and sex-adjusted associations between pain and respondent socio-demographic characteristics for those with CLD.

Results: Overall prevalence of CLD across both surveys was 3.6% (95% CI 3.4%-3.9%; n=1,081). Those with CLD more commonly reported any pain compared to those without (83.5% (95% CI 49.8-55.8) vs. 68.9% (95% CI 68.4-69.4), p<0.001), and more commonly reported moderate to very severe pain compared to those without CLD (52.8% (95% CI 49.8-55.8) vs. 27.4% (95% CI 26.9-27.9), p<0.001). Among those with CLD, being employed was associated with a lower probability of experiencing at least moderate pain (2011/12: OR=0.51, 95%CI 0.34-0.78, p=0.002; 2014/15: OR=0.52, 95%CI 0.34-0.80, p=0.003), after accounting for age and sex. No other factors were consistently associated with pain in adjusted models.

Conclusion: Pain was commonly experienced by people with CLD. In addition, employment was the only factor consistently associated with the experience of at least moderate pain among people with CLD. This finding may indicate functional impairment contributing to an inability to work among those experiencing pain and CLD.

TP 029

LIMITED SPECIFIC GUIDANCE FOR PAIN IN COPD CLINICAL PRACTICE GUIDELINES

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Aim: Pain is highly prevalent in people with moderate to severe COPD, with up to 85% of people experiencing pain in everyday life. This systematic review aimed to describe how pain (prevalence, assessment, management) is reported in COPD clinical practice guidelines (CPGs).

Methods: A systematic search of databases (Medline, Scopus, CiNAHL, EMbase, clinical guideline), reference lists and websites identified current versions of CPGs for the management of COPD published in any language from 2006 to 2016. Two independent reviewers extracted data on frequency and context (verbatim) of the word "pain". Pain context was synthesied into common categories including statements of prevalence, and stratergies for assessment and management.

Results: 39 CPGs were included in this review (English n=20; translated n=19). "Pain" was mentioned 55 times across 24 CPGs; ranging from no (15 CPGs) to 11 mentions within a single CPG (Dutch). Three CPGs reported "pain" in the context of prevalence: '30-70% in advanced COPD' (Finnish); 'main symptom in year before death' (German); 'patients believe that they will experience less pain than people with other chronic conditions' (Dutch). In the context of pain assessment, there were 13 mentions across nine CPGs (23%): as a need for differential diagnosis (n=12) or self-report questionnaires for problematic sputum causing painful cough (n=1). In the context of pain management, there were seven mentions across six CPGs, all suggesting palliation as the management strategy, of which two specifically suggested opioids. Further mentions of "pain" related to adverse drug reactions (n=22), contraindications to lung function assessments (n=6), or specific to surgical management (n=4).

Conclusion: Pain is common in people with COPD and has negative consequences for symptoms and quality of life. While the majority of COPD management CPGs (62%) mention pain, there was limited specific guidance for the assessment and management of pain over the life-course of COPD.

HOME-BASED PULMONARY REHABILITATION IN THE "REAL" WORLD

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Introduction: Pulmonary rehabilitation is an effective intervention for people with chronic lung disease; however, centre-based program access and uptake are poor. A home-based model has demonstrated equivalent outcomes in a clinical trial; this study aimed to evaluate the clinical implementation of this model.

Methods: Since December 2016, Hospital Admissions Risk Program (HARP) clients with chronic lung disease referred for pulmonary rehabilitation have been offered the option of a home-based program (one home visit in week 1, 7 once-weekly phone calls); or a traditional centre-based program (8 weeks, twice-weekly sessions). Baseline and end-rehabilitation assessments include exercise capacity (6-minute walk test) and health-related quality of life. Home-based program completion was defined as participating in 70% of phone calls and attending a final assessment.

Results: Of the 110 clients referred, 34 (31%) chose to undertake a home-based program (21 female, mean age 69 [SD 13] years, FEV_1 59 [24] % predicted, baseline 6-minute walk distance 375 [179] metres). Diagnoses included chronic obstructive pulmonary disease (n=23), bronchiectasis (n=5), asthma (n=3) and interstitial lung disease (n= 3). Reasons for choosing the home-based program included transport issues (n=16) and work commitments (n=11); of these working clients, none had been previously able to undertake pulmonary rehabilitation. Twenty-seven participants stated that they would not have attended a centre-based program. To date, 30 people have attended an initial assessment for the program, and 21 people have completed the program. There was a significant improvement in 6-minute walk distance following home-based pulmonary rehabilitation (mean 23 [CI 7-38] metres).

Conclusion: Home-based pulmonary rehabilitation provides access to an effective intervention alternative for people with chronic lung disease who are not able to participate in a centre-based model.

PHYSICAL EXERCISE DURING ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A SURVEY OF AUSTRALIAN PHYSIOTHERAPY PRACTICE

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Introduction/Aim: Some debate surrounds the role of physical exercise for patients admitted to hospital due to acute exacerbation of chronic obstructive pulmonary disease (AECOPD). Little is known regarding the practice and opinions of physiotherapists regarding exercise and physical activity prescription and evaluation for this patient group. This study aimed to evaluate current Australian physiotherapy practice.

Methods: A national paper-based survey of 123 'large' or 'principal referral' Australian public hospitals was conducted in 2016-17. The custom survey evaluated rates of prescription, outcomes used to measure treatment effectiveness, referral practices to pulmonary rehabilitation and factors related to service delivery. Response options were typically multiple choice or Likert scales. Results were compared between groups defined according to </>5 years cardiorespiratory experience via Chi square test.

Results: 176 physiotherapists from 89 hospitals returned surveys (response rate 72%). Most physiotherapists (n=161, 91%) prescribed physical exercise for 60-100% of patients and felt their role was very or fairly important (n=42, 81%). The most frequently prescribed exercise modalities were non-treadmill walking (n=165, 94%), sit-to-stand lower limb endurance training (n=156, 89%), and non-equipment based lower limb strengthening (n=138, 78%), while aerobic capacity (n=127, 72%) and function (n=121, 69%) were most common assessed via the 6-minute walk test (n=69, 39%) and sit-to-stand tests (n=55, 31%). Most physiotherapists (n=97, 55%) did not offer physiotherapy evaluation during follow-up outpatient clinic reviews but frequently referred patients to follow-up pulmonary rehabilitation (n=121, 69%). The rate of referral was higher in those with less experience compared to those with greater experience (p=0.031).

Conclusion: Australian physiotherapists frequently prescribe simple physical exercise training modalities for patients with AECOPDs and perceive their role to be important in their overall management.

Conflicts: None to declare

CLINICIAN AND PATIENT TREATMENT PREFERENCES FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN AUSTRALIA: A DISCRETE CHOICE EXPERIMENT

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Introduction/Aim: To identify patient and clinician preferences for the treatment of chronic obstructive pulmonary disease (COPD) and the significance of attributes and values on decision making.

Methods: An online discrete choice experiment was conducted between July and October 2017 to evaluate patient and clinician preference for bronchodilators that co-administer long-acting antimuscarinic agent (LAMA) and long-acting beta 2-agonist (LABA) fixed dose combination (FDC) as inhaled therapy. A total of 200 patients with COPD currently taking a LAMA/LABA FDC; 40 respiratory specialists and 100 General Practitioners (GPs) participated in the survey. The survey evaluated hypothetical treatments of ten attributes derived from the literature. For each scenario, patients were asked to choose between their current treatment and three new treatment options based on mode of administration. GPs and respiratory specialists were asked to choose between their most prescribed treatment and three new treatment options based on mode of administration. A latent class model was used to estimate the relative priority patients and clinicians place on different attributes and estimate their willingness to pay for new treatments.

Results: Cost, improvement in symptoms and side effects primarily influenced the treatment decisions of clinicians. This was similar for the majority of COPD patients. Mode of administration (metered dose inhaler) and the ability to use a spacer were significant determinants of choice for a proportion of patients and a smaller segment of clinicians.

Conclusion: The results of this study suggest that whilst patients and clinicians share similar treatment preferences in COPD, differences were observed. Patients are more willing to trade off other attributes, risks and cost when considering a new mode of administration for COPD medications.

ADVANCE CARE PLANNING IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE ASSESSED FOR LONG TERM OXYGEN THERAPY

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Introduction/Aim: An Advance Care Plan (ACP) is a communication between patient and clinician about end-of-life care, and has been shown to improve outcomes for patients and their families. Despite the incurable nature of Chronic Obstructive Pulmonary Disease (COPD), poor long term prognosis and proven benefit of ACP, uptake in this patient group is low, and discussion surrounding patients' values, goals and palliative care are rarely addressed in an outpatient setting. This study examined patients with COPD on Long Term Oxygen Therapy (LTOT) to determine rates of uptake of ACP and factors associated with presence of an ACP in this population.

Methods: Data was retrospectively collected from consecutive patients with COPD assessed for continuation or commencement LTOT who attended Oxygen Clinic at a tertiary hospital in Melbourne between 1st July 2015 and 30th June 2016. Factors recognised to be associated with ACP were analysed using independent t-tests for continuous variables and Chi-squared tests for ordinal variables.

Results: 79 patients were included; age (mean $\pm$ SD) 71$\pm$11years, FEV1%predicted 38$\pm$15%, PaO_2 60$\pm$11mmHg, $PaCO_2$ 45$\pm$10mmHg, arterial pH 7.43$\pm$0.04, Body Mass Index 28$\pm$8kg/m^2. 21.5% had an ACP. 40.5% were on continuous home oxygen, 36.7% intermittent oxygen, 11.4% nocturnal oxygen and 11.4% did not qualify/oxygen not advised for safety reasons/refused oxygen. 43.0% lived at home with community supports, 35.9% home with family, 12.7% family and supports, 3.8% home alone, 5% not known. 26.6% died within the study period. The only factor significantly associated with the presence of an ACP on univariate analysis was number of hospital admissions within the preceding 12 months (p<0.002).

Conclusion: This study demonstrated a low ACP rate, despite high mortality, in patients with COPD assessed for LTOT. Patients who were hospitalised within the last 12 months were more likely to have an ACP in place.

EXACERBATION STATUS IS LINKED TO DYSFUNCTIONAL PHAGOCYTOSIS IN STABLE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) PATIENTS BUT NOT TO PULMONARY FUNCTION

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Introduction/Aim: Chronic obstructive pulmonary disease (COPD) is a significant and increasing public health challenge. Much of the disease burden and economic cost of COPD is associated with acute exacerbations and resulting bacterial colonisation of the airways. The aim of this study is to determine whether the bactericidal functions of phagocytic cells (monocytes and neutrophils) are impaired, predisposing COPD patients to increased bacterial infections.

Method: Spirometry and venous blood were collected from COPD patients across the GOLD2015 spectrum and a group of healthy controls were recruited for comparison. Flow cytometry was used to determine differential counts for a range of leukocytes and internalisation of fluorescently labelled S*treptococcus pneumoniae* in whole blood phagocytes. Groups were compared by ANOVA and post hoc tests.

Results: Results demonstrated that peripheral blood monocytes ($p=0.04$) and neutrophils ($p=<0.0005$) in exacerbation prone COPD patients had significant reductions in both bactericidal activity against *S. pneumoniae* ($p=0.01$) and internalisation of inert microparticles ($p=0.01$) compared to healthy controls and also stable COPD patients. Data collection remains ongoing.

Conclusion: This study has demonstrated that defective phagocytosis in COPD patients prone to exacerbations is irrespective of disease severity (according to GOLD2015). Thus dysfunctional cellular activity of blood monocytes and neutrophils, and a failure to mount an appropriate immune response to infection, may enable bacteria to overwhelm host defences leading to further lung tissue damage.

Grant Support: Institutional (JCU) funds to CR supported this project.

Declaration of interest: all of the named authors have no significant competing financial, professional or personal interests that might have influenced the performance or presentation of the work described in this submission.

COMMENCEMENT OF PULMONARY REHABILITATION DURING HOSPITAL ADMISSION INCREASES RATES OF ATTENDANCE AMONG PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD): RANDOMISED CONTROLLED TRIAL

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Introduction: Early implementation of pulmonary rehabilitation (PR) after an Acute Exacerbation of COPD (AECOPD) is safe and effective, however the optimal time to implement PR remains unknown.

Aim: To compare PR attendance and completion rates for participants commencing PR at various time points relative to a hospital admission for AECOPD.

Methods: Participants admitted to hospital with an AECOPD were randomly allocated to commence PR either (i) at time of hospital admission, (ii) four weeks or (iii) eight weeks post discharge. Primary outcome measures were attendance and completion rates. Secondary outcome measures include 6-minute walk test (6MWT) and hospital re-presentation within 8 weeks post discharge. Primary outcomes were analysed using Chi Square and odds ratio. Secondary outcomes were analysed with ANCOVA. Significance was set at $p<0.05$.

Results: Sixty-two participants (mean(SD) age 68(12.9), baseline FEV1%predicted 47(19.4)) were recruited to the trial. 80% of those commencing PR at time of hospital admission attended at least one session of PR, compared to 65% of those commencing at 4 weeks post, and 50% of those commencing at 8 weeks post discharge (X^2(df)=4.1(2), p=0.1). Participants were more likely to attend PR at time of hospital admission compared to 4 weeks (OR(95% CI)=0.5(0.1 to 1.9), p=0.3) and 8 weeks (OR(95% CI)=0.25(0.1 to 0.9), p=0.048) post discharge. 60% of participants commencing PR at time of hospital admission completed the program, compared to 40% of the 4 weeks group, and 46% of the 8 weeks group (X^2(df)=1.7 (2), p=0.4). There were no significant differences in hospital presentations (F=1.2, p=0.3) or readmissions (F=0.7, p=0.5), and all groups showed a tendency for improvement in 6MWT (F=1.6, p=0.22).

Conclusion: Patients who commence PR at time of hospital admission are significantly more likely to attend, but just as likely to complete and improve exercise capacity, as those commencing at 8 weeks post admission.

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Declaration of Interest Statement: We hereby declare that there are no known conflict of interest in this project.

Word count: 300 words

OLIV

CXCR4 AND SDF-1 ARE EXPRESSED IN THE HONEYCOMB CYSTS OF PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

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Introduction/Aim: The presence of "honeycomb lung" on CT is a diagnostic most commonly but not exclusively associated with idiopathic pulmonary fibrosis (IPF). CXCR4 is a transmembrane-receptor activated by SDF-1 and present on epithelial cells. Conflicting reports in the literature, describing honeycomb cysts as having both airway origin and parenchymal/alveolar origin highlights the need for further investigation into the cells of the honeycomb cysts and their immediate microenvironment.

Methods: Sixty paraffin embedded samples of human lung tissue (n=30 (non-diseased control, NDC, n = 10; IPF, n = 10 and non-IPF interstitial lung disease, n = 10) from patients were included in this study. Staining patterns of CXCR4, SDF-1, CD20, CD45, E-Cadherin, and alpha-smooth muscle actin (α-SMA) were determined by immunohistochemistry. Total collagen in the tissue sections was determined by Masson's trichrome staining. Regions of examination on the apical and basal lobes of each patient included distal airways, small blood vessels, and alveolar spaces of the parenchyma where honeycombing is found.

Results: Brightfield microscopy performed on (N=4) patients with IPF and (N=4) non-diseased control (NDC) donors demonstrated strong CXCR4 and SDF-1 expression in honeycomb regions of IPF tissue compared to mild or absent staining in the normal parenchyma of NDC tissue (Figure 1). Prominent CXCR4 expression was also observed in distal airway epithelium. Co-staining of CXCR4 and e-cadherin or CD45 by immunofluorescence suggested the presence of 2 populations of CXCR4 + cell; one epithelial (CXCR4+/e-cadherin+) and one bone marrow derived (CXCR4+/CD45+).

Conclusion: Honeycomb changes are most commonly, but not exclusively seen in patients with IPF. CXCR4 expression within both honeycomb cysts and distal airway epithelium is suggestive of an airway origin of honeycombing, however, CXCR4 expression was also observed occasionally in small vessels within fibrotic interstitial tissue.
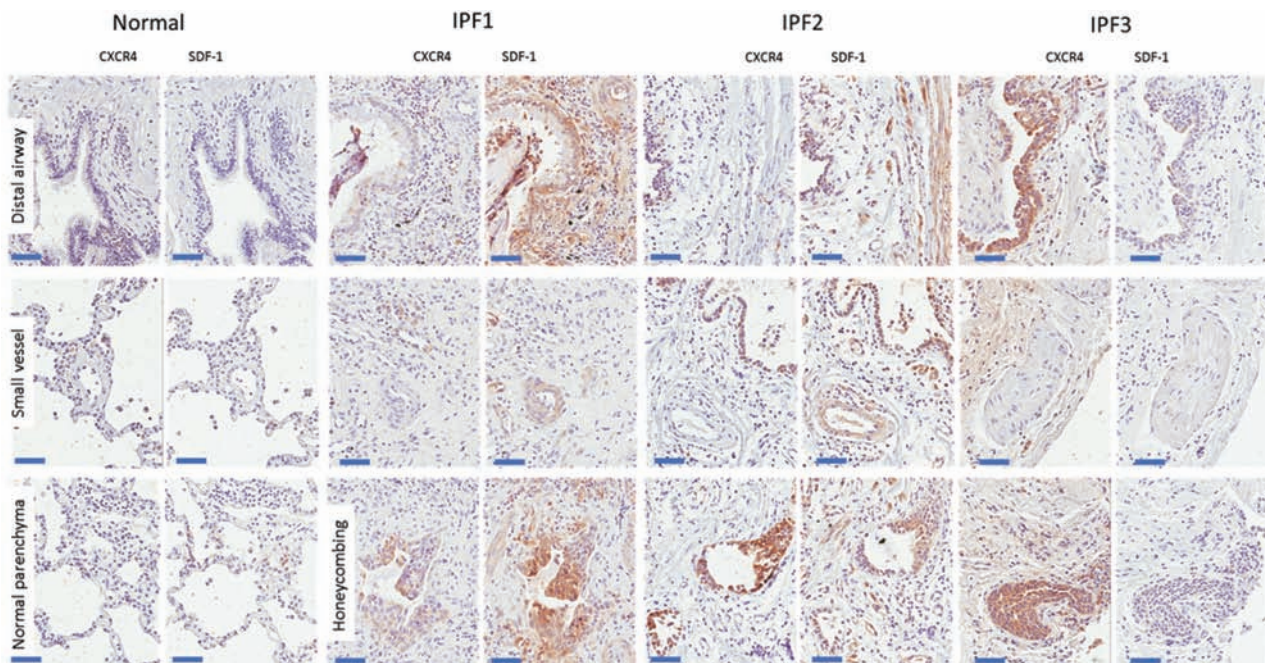
Figure 1 Immunohistochemistry on lung tissue from patients with/without idiopathic pulmonary fibrosis (IPF). Tissue sections were probed with antibodies to CXCR4 and SDF-1.

CYCLOPHOSPHAMIDE FOR CONNECTIVE TISSUE DISEASE–ASSOCIATED INTERSTITIAL LUNG DISEASE

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Introduction/Aims: Decision-making in the treatment of connective tissue disease associated interstitial lung disease (CTD-ILD) is difficult due to lack of evidence of benefit and high risk of side effects.

The objectives were to assess the efficacy and safety of cyclophosphamide in the treatment of CTD-ILD.

Methods: Searches for randomised controlled studies on CENTRAL, MEDLINE, EMBASE, CINAHL, and Web of Science to May 2017 were performed.

Results: Four trials with 495 participants (mostly systemic sclerosis) were included. The evidence was low quality, as participants had mostly non-progressive disease, the withdrawals were high in the intervention groups, and there were wide confidence intervals with small effect sizes.

There was a small significant impact on lung function using cyclophosphamide compared with placebo (FVC% mean difference (MD) 2.83; 95% CI 0.80 to 4.87; p=0.006) but not in DLCO % (MD -1.68; 95% CI -4.37 to 1.02; p=0.25; two trials, 182 participants).

There was a clinically and statistically significant improvement in breathlessness and in quality of life in one trial favouring cyclophosphamide compared with placebo. There was an increased risk of adverse events, and no impact on mortality.

There was no significant impact on lung function using cyclophosphamide compared with mycophenolate (FVC% MD -0.68, 95% CI -5.44 to 4.08; p=0.78; two trials, 149 participants), however there was an increased risk of adverse events.

Conclusions: Further studies are required, adequately powered to compare outcomes within different subgroups, including by radiological severity, and in other forms of CTD; with cyclophosphamide compared with other anti-fibrotic agents, and in those with evidence of progressive fibrotic disease, who may benefit the most.

ANTIFIBROTICS FOR TREATMENT OF IDIOPATHIC PULMONARY FIBROSIS IN THE REAL WORLD: A SINGLE CENTRE EXPERIENCE

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Introduction/Aim: Idiopathic Pulmonary Fibrosis (IPF) is the most common interstitial lung disease (ILD), however until recently, there was no effective treatment. In May 2014, landmark trials of antifibrotic medications (nintedanib and pirfenidone), demonstrated slowing of disease progression in IPF. There is however, limited data outside of clinical trials regarding long-term effects of these medications. In this study, we describe the experience with these medications in the population of IPF patients at Royal Prince Alfred Hospital (RPA).

Methods: We retrospectively reviewed the ILD multidisciplinary meeting (MDM) diagnosis of all patients and included any patient with a diagnosis of IPF. All patients received follow-up with serial pulmonary function and six-minute walk tests. Patients on antifibrotic medications had doses and adverse events recorded at each clinic appointment.

Results: Of the 500 patients reviewed, IPF was the most common diagnosis with 32% (n=160). They were mostly male (115, 71.9%), older (71.3±9.7 years) with mild impairment (FVC 73.65%±15.95%; DLCO 55.75%±18.17%. 36% (n=57) of these IPF patients received antifibrotic treatment (pirfenidone n=29; nintedanib n=28). This population was largely similar to those who did not start treatment. 7 patients reported no side-effects. Severe side-effects occurred in 12 resulting in a cessation of antifibrotic. 24 had a pause in treatment and then restarted at the same (n=6) or lower dose (n=18) of the same antifibrotic. 6 patients were switched from one antifibrotic to the other. The most common adverse events for both medications combined included weight loss / anorexia (52.4%), nausea (49.2%) and diarrhoea (36.5%).

Conclusion: IPF was the most common diagnosis made at the RPA ILD-MDM. 36% of IPF patients commenced antifibrotic therapy. Side effects were common but only led to treatment changes in 57.1% (n=36). Overall, there appeared to be more side effects in this population compared with clinical trials.

TP 036

IDENTIFYING INTERSTITIAL LUNG DISEASE PATIENTS WHO PRESENT WITH AUTOIMMUNE FEATURES

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Introduction/Aim: A long recognised subgroup of patients with interstitial lung disease (ILD) and autoimmune features don't fulfil a specific autoimmune disease diagnosis. Recently, scoring criteria have been proposed to categorise these patients, who are said to have interstitial pneumonia with autoimmune features (IPAF).

Aim: We sought to determine how many ILD patients presented at our ILD multidisciplinary meeting fulfil the criteria for this designation, and describe their features.

Methods: A retrospective study was performed of patients presented in the ILD multidisciplinary meetings at Concord Hospital from 2014 to 2017. Case summaries from the meetings were reviewed and IPAF patients were identified using a data collection checklist.

Results: 200 cases were reviewed, of which 24 patients (12% of cases) satisfied the criteria for IPAF. The mean age was 69.5 (range 50 to 88 years), and 14 were female. The diagnosis of ILD was overwhelmingly based on HRCT abnormality, only 1 patient underwent a surgical lung biopsy. Clinical criteria for IPAF were only present in 2 patients but all had serological abnormalities. The most common serological abnormality was positive ANA in 15 cases. The most common chest HRCT appearance was NSIP (16 cases), followed by OP (6 cases). 8 patients were being treated with steroid/ immunosuppressive therapy and 16 were being monitored. Of those being treated, prednisone provided symptomatic relief.

Conclusion: The diagnosis of IPAF is heavily based on abnormal serology in patients with an NSIP pattern on chest CT scanning. At presentation, most were deemed sufficiently well to monitor only. The appropriateness of this and further information on disease trajectory in this group is required.

TP 037

COMPOSITE PHYSIOLOGIC INDEX IN IDIOPATHIC PULMONARY FIBROSIS: EFFECTS OF NINTEDANIB

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Introduction/Aim: In the Phase III INPULSIS® trials, nintedanib 150mg twice daily slowed disease progression in patients with idiopathic pulmonary fibrosis (IPF) by significantly reducing the annual rate of decline in FVC. Patients with FVC ≥50% predicted, diffusing capacity of the lung for carbon monoxide (DLco) 30–79% predicted and FEV_1/FVC ≥0.7 were eligible for inclusion. The composite physiologic index (CPI), calculated based on percent predicted values for FVC, DLco and FEV_1, is a measure of the extent of pulmonary fibrosis in patients with IPF. We assessed the effect of nintedanib on change in CPI.

Methods: The measures required to calculate CPI were taken at baseline, Week 24 and Week 52. *Post-hoc* analyses were conducted on the effect of nintedanib on change from baseline in CPI at Weeks 24 and 52 using pooled data from both INPULSIS® trials. Adjusted mean difference versus placebo at Week 52 was assessed based on a mixed model for repeated measures (MMRM).

Results: 1061 patients were treated in the INPULSIS® trials (638 with nintedanib, 423 with placebo). Mean±SD CPI at baseline was 45.9±10.9 and 46.3±11.0 in the nintedanib and placebo groups, respectively. At Week 24, mean±SD changes from baseline in CPI were 2.1±8.3 in the nintedanib group and 2.2±7.0 in the placebo group. Based on MMRM, the adjusted mean±SEM change from baseline in CPI at Week 52 was 2.8±0.4 in the nintedanib group and 3.9±0.5 in the placebo group (difference –1.1 [95% CI: –2.3, 0.1]; p=0.0676).

Conclusion: Based on data from the INPULSIS® trials, nintedanib was associated with a marginal treatment effect on change from baseline in CPI at Week 52. This may be due to the high variability in DLco assessments in multi-centre clinical trials and the influence of factors other than extent of fibrosis on DLco.

CHRONIC HYPERSENSITIVITY PNEUMONITIS: A PROSPECTIVE COHORT ANALYSIS OF AN UNDER-RECOGNISED CLINICAL ENTITY

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Introduction/Aim: Chronic hypersensitivity pneumonitis (CHP) is an immune mediated interstitial lung disease, caused by an antecedent exposure to an offending agent. It can be difficult to accurately diagnose, but may improve with immunomodulatory treatment. Little is currently known about patient characteristics and prognosis.

We sought to determine what characteristics accurately conferred a diagnosis of CHP, and what factors might influence disease trajectory and mortality.

Methods: We collected data from all patients with a consensus diagnosis of CHP from the Alfred ILD Registry: a prospective, longitudinal cohort registry commenced in 2002.

Results: Fifty-five patients with a consensus diagnosis of CHP were identified (mean age 55±10yrs; 43% male). Dyspnoea was the most common symptom at disease onset, clubbing likely (40%) but not crackles (9%). Over 50% had a clinical exposure identified, including 30% with avian exposure, however, only 37% underwent avians precipitans testing and none were positive. Multi-disciplinary meeting (MDT) clinical diagnostic confidence was only definite in 10%, probable in 61% and equivocal in 30%. Ground glass changes were the most common radiological feature. Multinucleated histiocytes the predominant histopathological feature on biopsy (27%) or explant (21%). Immunomodulatory treatment was used in 70% of patients, most commonly prednisolone (45%). Oxygen supplementation was used in 20%. Nine-percent were deceased at time of follow up, and 5% underwent lung transplantation. The average rate of decline per year was FEV1 150±10mL, FVC 117±29mL, and %TLCO 2±18%. The rate of decline was not affected by identification of clinical exposure (p=0.7) or immunomodulatory treatment (p=0.4).

Conclusion: This data describes the natural history of CHP patients, however is limited by small patient numbers. Further larger registry research is required to aid more accurate MDT diagnosis, predict prognostic factors, and response to treatment.

Grant Support

LONG-TERM NINTEDANIB TREATMENT IN IPF: NEW DATA FROM INPULSIS-ON

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Introduction/Aim: The efficacy and safety of nintedanib 150 mg twice daily in patients with idiopathic pulmonary fibrosis were assessed in the 2 Phase III INPULSIS® trials. Patients who completed the 52-week treatment period and follow-up visit 4 weeks later in INPULSIS® could receive open-label nintedanib in the extension trial INPULSIS-ON. We assessed the long-term efficacy and safety of nintedanib based on an interim analysis of INPULSIS-ON in October 2016.

Methods: Patients treated with placebo in INPULSIS® initiated nintedanib in INPULSIS-ON; patients treated with nintedanib continued nintedanib.

Results: 734 patients were treated in INPULSIS-ON (430 continuing nintedanib; 304 initiating nintedanib). At this interim analysis, mean±SD exposure in INPULSIS-ON was 27.7±15.1 months. Mean±SD (minimum–maximum) total exposure for patients treated with nintedanib in INPULSIS® and INPULSIS-ON was 40.7±14.6 (11.9–63.1) months. In INPULSIS®, mean±SD change in FVC from baseline to Week 52 was −89±264 mL in the nintedanib group and −203±293 mL in the placebo group; the annual rate±SEM of decline in FVC was −114±11 mL/year and −224±13 mL/year in these groups, respectively. In all patients treated in INPULSIS-ON, mean±SD change in FVC from baseline of INPULSIS-ON to Week 144 of INPULSIS-ON was −305±365 mL; the annual rate-±SEM of decline in FVC over 144 weeks was −131±6 mL/year. The adverse event profile of nintedanib in INPULSIS-ON was consistent with that in INPULSIS®.

Conclusion: Data from INPULSIS-ON indicated that the effect of nintedanib on reducing disease progression is maintained over the long term. Nintedanib treatment (up to 63 months) had an acceptable safety and tolerability profile.

Grant Support: The study was funded by Boehringer Ingelheim.

TP 040

1-YEAR GOOD, 5-YEARS NOT SO: ERA EFFECT ON SHORT AND LONG TERM SURVIVAL AFTER LUNG TRANSPLANTATION

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Introduction/Aim: While short term survival after lung transplantation has improved over time, mortality at 5 years remains higher than other solid organ transplants. We examine the effect of era on 30-day, 1-year and 5-year conditional survival after lung transplantation.

Methods: We compared baseline characteristics, 1-year survival and 5 year conditional survival in adult lung transplant recipients at St Vincent's Hospital across 3 decades: 1990-1999, 2000-2009, 2010-2016. We also examined the change in cause of death at 1 year over time.

Results: A total of 860 patients met our inclusion criteria. Survival was 96%, 88% and 61% at 30 days, 1 year and 5 years respectively. There was a strong association between improved 30-day mortality rate and increasing era of transplantation (85.8/100 patient years (pyrs) in 1990-1999, 36.3/100pyrs in 2000-2010, 27.0/100pyrs in 2010-2016, p=0.006). There was also a strong association between increasing era of transplantation and 1-year mortality rates (19.4/100pyrs in 1990-1999, 11.23/100pyrs in 2000-2009, 9.7/100pyrs in 2010-2016, p=0.0045). However, there was no association between transplantation era and 5-year conditional survival (7.6/100pyrs in 1990-1999, 6.3/100pyrs in 2000-2010, 8.2/100pyrs in 2010-2016, p=0.97). Causes of death at 1 year have also evolved over time, with more technical failures occurring in the early era compared to the more recent era.

Conclusion: While there have been significant improvements in short term survival after lung transplantation over time, there have been no significant improvements in conditional 5-year survival. In order to improve conditional 5-year survival, we must focus on optimal candidate selection and improving the prevention, detection and management of (a) chronic allograft dysfunction, in its various phenotypes, (b) acute cellular and antibody mediated rejection (c) infection prophylaxis and (d) post-transplant malignancy.

TP 041

IN SIGHT BUT OUT OF MIND: THE HIDDEN RISK OF HUMAN PAPILLOMA VIRUS IN MALES AFTER LUNG TRANSPLANTATION

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Introduction/Aim: In contrast to other solid organ transplant recipients, lung transplant (LTX) patients are often within their reproductive years. We reported previously that high grade human papilloma virus (HPV) lesions are more frequent in females after LTX. Herein we explored factors which influence rate and severity of HPV related morbidity in male LTX recipients including the potential role of HPV vaccination.

Methods: Single centre, anonymous, cross sectional survey to ascertain sexual health experiences of male LTX recipients.

Results: 101 consecutive bilateral LTX recipients (age 47 ± 15 years, mean $\pm$SD, range 21-77 years) attending outpatient clinic were recruited at 5.9 ± 5.9, range 0.5-23 years post LTX. Indications were cystic fibrosis (n=32), interstitial lung disease (n=29), emphysema (n=28) and other (n=12). Only 1% had completed HPV vaccination. 9% reported penile lesions comprising warts (n=6) and penile intraepithelial neoplasia (PIN) / cancer (n=3). Therapy comprised topical preparations (33%), ablation (33%) and partial penectomy (33%). Only 24% recorded always using barrier prophylaxis with a casual partner while 49% recorded no use. In comparison, 10% recorded always using barrier prophylaxis with a stable partner while 53% recorded no use. Traditional risk factors, including age of first sexual intercourse and number of partners were not significant nor was time post LTX.

Conclusion: Even accounting for recollection bias, HPV causes significant and diverse morbidity after LTX occasionally requiring extensive surgery. In addition to HPV vaccination in both males and females, an ongoing education and surveillance program is critical to limit morbidity, prevent mortality and preserve reproductive potential with a focus on self-examination and prompt reporting to effect successful therapies.

OUT OF SIGHT, OUT OF MIND: THE HIDDEN RISK OF HUMAN PAPILLOMA VIRUS IN FEMALES AFTER LUNG TRANSPLANTATION

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Introduction/Aim: Unlike other solid organ transplant recipients, lung transplant (LTX) patients are often females with reproductive potential. We reported previously that high grade human papilloma virus (HPV) lesions are more frequent after LTX. Hence we explored factors which influence rate and severity of HPV related morbidity including the role of HPV vaccination.

Methods: Single centre, anonymous, cross sectional survey, to ascertain sexual health experiences of female LTX recipients.

Results: 143/144 consecutive LTX recipients attending clinic (bilateral: heart lung = 140:3) (age 47 $\pm$ 15 years, mean $\pm$SD) were recruited at 5.9$\pm$4.2, range 0.5-23 years post LTX. Indications were cystic fibrosis (n=48), interstitial lung disease (n=16), emphysema (n=49) and other (n=30). 17% had completed HPV vaccination. 30% reported abnormal Pap smears. Rates of warts, vulval intraepithelial neoplasia, vaginal intraepithelial neoplasia, and anal intraepithelial neoplasia were 4.9%, 4.2% and 3.5% respectively. Therapy comprised observation (33%), loop excision of the transformation zone (LETZ) / long LETZ (23%), cervical cone biopsy (22%) and hysterectomy (5%). Traditional risk factors, including age of first sexual intercourse (p=0.001) and number of partners (p<0.001) were significant as was time post LTX (p=0.020). Smoking history was not (p= 0.444). Only 48% recorded always using barrier prophylaxis with a casual partner while 28% recorded no use. In comparison, 16% recorded always using barrier prophylaxis with a stable partner while 47% recorded no use.

Conclusion: Even accounting for recollection bias, HPV causes significant and diverse morbidity after LTX. In addition to HPV vaccination, an ongoing education and surveillance program is critical to limit morbidity, prevent mortality and preserve reproductive potential.

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WHAT A CHANGE A FEW DECADES CAN MAKE: IMPROVEMENTS IN 1-YEAR SURVIVAL AFTER LUNG TRANSPLANTATION

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Introduction/Aim: Post-transplant survival in adult lung transplant recipients has improved over time. We examine the effect of era on survival after lung transplantation, adjusting for baseline donor and recipient factors.

Methods: We compared baseline characteristics and 1-year survival in adult lung transplant recipients at St Vincent's Hospital across 3 decades: 1990-1999, 2000-2009, 2010-2016. We used a Cox proportional hazards model to determine risk-adjusted era effect on mortality.

Results: Of 860 patients meeting inclusion criteria, 826 had sufficient follow-up data for 1-year survival analysis. Survival was 88% at 1 year. There was a strong association between transplant era and 1-year mortality (RR 0.58 in 2000-2009 with p=0.02 and RR 0.50 in 2010-2016 with p=0.005 compared to 1990-1999). Other predictors of 1-year mortality on crude analysis included older age, gender, higher patient baseline BMI, transplant type, indication for transplantation, operation duration, older donor age, increased donor to recipient weight ratio, and female donor to male recipient transplants. Patients in more recent years were also older and more overweight/obese. In multivariate regression, the association between era of transplant and 1-year mortality was even stronger (HR 0.35 in 2000-2009 and HR 0.17 in 2010-2016 compared to 1990-1999, p<0.0001). Other variables included in multivariate regression for prediction of 1-year mortality were older patient age at transplant (HR 1.40, p=0.079), older donor age (HR 2.31 for donors aged >56 vs 0-17 years, p=-0.063), longer operation duration (HR 1.39, p=0.006) and transplantation for interstitial lung disease (HR 2.31 compared to cystic fibrosis, p=0.042).

Conclusion: Despite increasing baseline risk profiles of patients, risk-adjusted mortality at 1-year post-transplant has improved over time.

RETROSPECTIVE RISK STRATIFICATION PREDICTS EVENTUAL OUTCOMES IN PATIENTS PRESENTING WITH ACUTE PULMONARY EMBOLISM

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Introduction/Aim: The Pulmonary Embolism Severity Index (PESI) score is a risk prediction score that estimates the 30 day mortality risk of a patient presenting with an acute pulmonary embolism (PE), as well as identifying low risk patients who may be a candidate for early discharge and home therapy. This study aims to audit the adherence to society guideline recommendations that a risk assessment score should be performed for patients presenting with acute PE, and to retrospectively calculate the patient's risk to assess how this correlated with eventual outcomes, including length of stay (LOS), and mortality.

Methods: A retrospective review was performed of adult patients presenting the Gold Coast Health Service, with acute PE over a two year period. Patients with incidentally-detected PE, or those who developed a PE while an inpatient for another reason, were excluded. The PESI score was calculated from clinical information documented at admission.

Results: 288 patients were included (60% male). 14 (5%) had a PESI score documented by the treating team. There is a significant correlation between retrospectively calculated PESI score and length of stay (R^2 = 0.312; P = <0.001). Average LOS (days) for each PESI category was Very Low = 3.5, Low = 4.3, Intermediate = 5.7, High = 7.8, Very High = 9.1. There is a correlation between PESI score and mortality at 30 days (R^2 0.286; P = <0.001), 90 days (R^2 0.373; P = <0.001), and 1 year (R^2 0.439; P = <0.001).

Conclusion: This study demonstrates that a PESI score calculated from clinical parameters at admission for acute PE predicts length of stay and mortality, and is therefore a useful risk stratification tool which could encourage early discharge for low risk groups, or more intense observation, investigation, and counselling for high risk groups.

A CASE OF DYSPNOEA—HEPATOPULMONARY SYNDROME

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Introduction: Hepatopulmonary syndrome (HPS) is characterized by abnormal arterial oxygenation from intrapulmonary vascular dilatations (IPVD) in the setting of chronic liver disease particularly those with portal hypertension or congenital portosystemic shunts and rarely in acute liver disease. Its prevalence ranges from four to 47 percent.

Method/Case Report: A 61 years old male presented with progressively worsening shortness of Breath for years. He was found to have platypnoea and orthodeoxia and was diagnosed to have Child pugh B chronic liver disease secondary to alcohol excess.

He had long standing background history of anaemia and thrombocytopenia under investigation, subdural haematomas and asbestos exposure. He was an ex-smoker with ten pack year history of smoking.

Preliminary investigations for chest pain and dyspnoea were negative. He was discharged with home oxygen. Patient continued to drink alcohol despite constant encouragement to quit and wasn't interested for liver transplant.

Results: Transthoracic echocardiogram Exercise stress test and myocardial perfusion scan were unremarkable. Spirometry and lung volumes within normal limits however there was severe reduction in CO diffusion which didn't correct for alveolar volume. There was no evidence of CT pulmonary thromboembolism and significant parenchymal lung disease. Ultrasound liver showed fatty liver with possible cirrhosis but normal spleen size. Agitated saline test did not show any interatrial shunt, however left atrial opacification occurred only after seven cardiac cycles post initial right atrial opacification.

Conclusion: Development of HPS doesn't correlate with the severity of the liver disease so recognising this condition early will prevent concerns and minimise excessive investigations.

A COORDINATED MULTIDISCIPLINARY CLINIC MODEL OF CARE FOR CHILDREN AND ADULTS WITH PRIMARY CILIARY DYSKINESIA (PCD) IN SYDNEY, AUSTRALIA

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Introduction: Diagnosing and treating a rare multi-system disease such as Primary Ciliary Dyskinesia (PCD) requires specialist expertise and multi-disciplinary support. A multidisciplinary service for children and adults with PCD was established in 2013 at Concord Hospital, Sydney to provide patients with an annual health review and plan. The clinic aims to ensure patients are managed according to PCD guidelines, and have access to coordinated specialist respiratory, ear nose and throat, audiology, and physiotherapy expertise on annual basis. The clinic was established through a collaboration of paediatric and adult respiratory physicians and physiotherapists, ENT specialists, nursing and respiratory scientists. The clinic is conducted quarterly at Concord Hospital and the benefits of the model of this clinic include opportunities to conduct research/ quality improvement, provide education and support for local services, provision of health information for patients and families, and importantly a seamless transition of care from child to adult services.

Aims: To determine how many patients are being seen within the clinic

To describe the proportion of paediatric patients that will be followed through the transition period to adult services.

Methods: A retrospective review of clinic bookings over a 4 year period (January 2014 to October 2017), was undertaken. The number of patients seen in clinic were determined and results presented using descriptive statistics.

Results: Within the 4 years examined, 57 patients with PCD have been seen (19/57, 30% children). 34/57 (60%) of all patients were seen on more than one occasion.

Conclusion: This clinic model has established a transition pathway for multidisciplinary care for patients with PCD. This may be a useful model for other complex, rare chronic conditions requiring care from multiple services. Further research is being undertaken to examine quality of life around the time of transition within this clinic model.

RANDOMISED CONTROLLED TRIAL OF AMBULATORY OXYGEN VERSUS AIR VIA PORTABLE CONCENTRATOR IN CHRONIC INTERSTITIAL LUNG DISEASE

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Introduction/Aim: Ambulatory oxygen therapy (AOT) is often provided to patients with interstitial lung disease (ILD) and exertional desaturation, although evidence supporting benefit is limited. Lightweight portable oxygen concentrators are an alternative to portable compressed oxygen cylinders and are more acceptable to people with ILD. This study aims to examine the impacts of ambulatory oxygen using portable concentrators on health outcomes in people with ILD who experience dyspnoea and exertional desaturation.

Methods: This double-blind, placebo-controlled trial aims to recruit 73 participants with ILD from two tertiary institutions. Participants are randomised to 3-month supplemental oxygen or air delivered via portable concentrators at the maximal setting of six. Assessments are performed at baseline, during intervention (Week 4), post intervention (Week 12) and at follow-up (Week 18). The primary outcome is change in 6-minute walk distance (6MWD) post intervention. Additional outcome measures include disease-related symptoms, health-related quality of life, physical activity, systemic oxidative stress and inflammatory markers, and device utilisation. The feasibility of study design and recruitment strategies will also be evaluated.

Results: To date, 17 participants (four idiopathic pulmonary fibrosis) have been randomised, with median FVC 68 (range 50-92)% predicted and TLCO 33 (28-62)% predicted. The median baseline 6MWD was 466 (209-663) m. The median resting and nadir oxyhaemoglobin saturation during 6MWT at baseline were 96 (93-99)% and 84 (74-89)%, respectively. The median duration of device usage at Week 4 was 101 (19-864) minutes per week. Three participants withdrew from the study after randomisation: two due to clinical deterioration, and one for personal reasons.

Conclusion: This prospective study will provide important information regarding the role of AOT in ILD, with the potential to influence clinical practice and facilitate evidence-based discussion with patients.

Respiratory Infectious Diseases

PASTEURELLA MULTOCIDA PNEUMONIA—COMING BACK TO BITE?

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Introduction: *Pasteurella multocida* is a zoonotic infectious organism that is most-commonly associated with animal bites and local soft-tissue infections. *P multocida* has been isolated in the human respiratory tract as a commensal and rarely causes serious infections such as pneumonia, empyema and abscesses. In patients with an underlying lung disease such as COPD, infection has a high mortality rate approaching 30%[1].

Case Report: We present a case of a 78-year-old man admitted with a three-day history of dyspnoea and low-grade fever, on a background of COPD on continuous home oxygen. He had a chronic cough productive of yellow sputum but no previous documentation of *Pseudomonas* spp. *or Pasteurella* spp. He was in type 1 respiratory failure but blood tests failed to show a raised white cell count (6) or C-reactive protein (26.9) and his chest x-ray showed only a few increased markings bilaterally. He was treated as per a non-infective exacerbation of COPD. Subsequent sputum cultures grew *Pasteurella multocida* and on day 2 of the admission, he deteriorated with oxygen saturations down to 62% on a FiO2 of 28%. He was promptly commenced on intravenous antibiotics with Benzylpencillin and Doxycycline and made a rapid recovery with discharge on day 5. On further history, he revealed he had close contact with his two dogs and a cat. There was no history of bites or scratches.

Conclusion: We associate Pasteurella infections with animal bites but there have been cases of serious infections after non-bite exposure usually with close animal contact and inhalation of secretions. Obtaining a detailed history of animal exposures especially in our chronic lung disease patient group is essential to promptly diagnose and treat with a penicillin-based agent. We need to advice patients with underlying lung disease to avoid close contact with pets for preventing serious, life-threatening infection.

USE OF INTERFERON GAMMA RELEASE ASSAYS (IGRA) IN A REGIONAL HOSPITAL

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Conflicts of interest: none

Introduction/Aim: IGRAs represent an alternative to the tuberculin skin test (TST) in diagnosing latent tuberculosis (TB). All guidelines emphasise that it should not be used to test for active TB due to poor sensitivity and specificity. As with the TST, results should be interpreted with other relevant information (e.g. age, Bacillus Calmette–Guérin status, country of origin, travel history and contact with TB). This audit examines the use of IGRAs in a regional hospital and thus identifies gaps in clinicians' knowledge in regards to these guidelines.

Methods: Retrospective audit of patients who had IGRA performed at Cairns hospital from 1/1/16 to 1/1/17. Patients were identified by Auslab records. Clinical notes were reviewed to assess indications for the test, documentation of other relevant factors and actions taken on the IGRA result.

Results: 190 tests were performed. 37.4% of the cases were attempting to diagnose active TB, 60% latent TB and in 2.6% the reason was unclear or insufficient history was documented. Of the patients that were tested to investigate latent TB, 20/114 (17%) were inappropriate e.g.: screening for patients on insufficient immunosuppression to risk conversion to active tuberculosis.

In only 36.6% cases was appropriate history taken. General medicine, infectious diseases, neurology and gastroenterology specialties were most likely to use the test inappropriately. Worryingly, even if results were positive, the majority were overlooked; 10/15 cases that were positive and 15/16 'indeterminate' results were never further investigated.

Conclusion: IGRAs are widely used by non-respiratory specialists in our regional hospital and seem to be poorly understood, often being used inappropriately to diagnose active TB. Frequently no further action is taken even if the result of the test is positive.

LOW UTILITY OF MICROBIOLOGY TESTING IN COMMUNITY ACQUIRED PNEUMONIA

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Introduction/Aim: Community-acquired pneumonia (CAP) is a common cause of admission to Australian hospitals. The aim of this study was to evaluate yield and utility of microbiological investigations in the management of patients who presented to a tertiary cardio-thoracic hospital with a diagnosis of CAP.

Methods: A retrospective audit was performed on patients who presented to the Prince Charles Hospital (TPCH) from 1st July 2016 to 31st March 2017 with a discharge diagnosis of pneumonia. The following data were gathered:—patient demographics, antimicrobial allergy, microbiology results including sputum, blood cultures, urine antigens for *Streptococcus pneumoniae* and *Legionella*, nasopharyngeal swab for respiratory viruses and atypical serologies including *Mycoplasma*, *Chlamydophila* and *Legionella* species.

Results: 85 cases were identified for audit. Mean age was 70 with 49% being male. 99% had either radiographical or clinical signs consistent with pneumonia. 39% of cases had documented allergies to first line beta lactam antimicrobials. The yield of microbiology investigations for identifying a respiratory pathogen were as follows: sputum culture 8%, blood cultures 4.5%, nasopharyngeal swab 6%, urine *pneumococcal* antigen 7%, *Mycoplasma* serology 11%. There were no positive results for urine *Legionella* antigen, *Chlamydophila* serology and *Legionella* serologies. Overall, causative pathogens were identified in only 16.4% of cases.

Conclusion: Microbiology investigations performed for patients who present to TPCH with a discharge diagonosis of CAP showed low yields. This result indicates that these investigations should be performed on a more selective group of patients to aid aetiological diagnosis and management.

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LEPTOSPIROSIS-ASSOCIATED PULMONARY HAEMORRHAGE IN FAR NORTH QUEENSLAND: A CASE SERIES

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Introduction/Aim: This is an observational, descriptive study of all cases of pulmonary haemorrhage admitted to the Cairns Hospital between 1998-2016. This study aims to describe the prevalence of pathognomonic presenting features of those with Leptospirosis-associated pulmonary haemorrhage, including demographics and serovar. The prevalence of those requiring intensive care admission, vasopressor therapy and intubation is also described.

Method: Retrospective chart review of 24 cases of pulmonary haemorrhage admitted to the Cairns Hospital

Results: 22 cases were male (92%). Median age was 37yrs. The most prevalent serovar was Leptospira sp. Australis in 9 cases (36%). At presentation, 19 (79%) of cases had low platelets (<150 x10^9/L), 20 (83%) had elevated creatinine and 13 (54%) had elevated bilirubin. 17 (71%) had positive findings on chest auscultation and 16 (67%) had an abnormal chest radiograph. 22 (92%) had >10x10^6/L erythrocytes on urinalysis. At any time during admission, 22 (92%) cases were admitted to the intensive care unit, half of these required vasopressor therapy and 7 (29%) required intubation. There were no deaths from pulmonary haemorrhage in this cohort.

Conclusion: Pulmonary haemorrhage is a serious complication of leptospirosis, a zoonotic infection of global importance and most commonly encountered in Australia in the states of Queensland and Victoria. This case series describes the prevalence of common presenting features of the disease in 24 cases who developed pulmonary haemorrhage in the last 2 decades in Far North Queensland.

Key Words: Leptospirosis, pulmonary haemorrhage, tropical infections, diffuse pulmonary airspace opacities, thrombocytopenia

Grant Support: Nil

Declaration of Interest: Nil

RESPIRATORY INFECTIONS WITHOUT RADIOLOGICAL FINDINGS- ARE WE OVER TREATING THEM?

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Introduction/Aim: Lower respiratory tract infection(LRTI) is a common reason for hospital admission. Adherence to Australian therapeutic guidelines for antibiotic selection is variable. Data is lacking for inpatients with LRTI without radiological findings. The DISPNOEA study evaluated antibiotic use in non-immunosuppressed patients without chronic lung disease admitted with LRTI and normal chest x-ray(CXR).

Methods: Retrospective audit of patients admitted to Alfred Hospital in 2016 with discharge diagnoses of LRTI, chest infection, bronchitis, pneumonia or influenza. Patients with COPD, emphysema, bronchiectasis, asthma, cystic fibrosis, immunosuppression and hospital acquired pneumonia were excluded. Patient demographics, SMART-COP and CORB scores, laboratory results and antibiotics were reviewed.

Results: For 231 patients, median age was 82 years with average LOS of 3 days. The mean Charlson score was 5. The discharge diagnosis was LRTI in 60% and pneumonia in 35%. The median white cell count and C-reactive protein was 9 and 39 respectively. Sputum samples were obtained in only 44 patients yielding no growth(n=18) or oral flora (n=13), allowing targeted therapy in 13 patients only. Nasopharyngaeal viral PCRs were performed in 64 patients with 40 positive results (influenza in 8). The mean total length of antibiotics was 7 days with an average of 2 days of intravenous antibiotics followed by 5 days of oral therapy. 85.3% were classified as low severity by the SMART-COP score. Despite this, 91.3% were started on intravenous therapy including ceftriaxone with azithromycin(n= 67) or ceftriaxone with doxycycline(n= 35) or benzylpenicillin with doxycycline(n=34). There were no admissions to intensive care and a mortality rate of 3.5%.

Conclusion: Inpatients with LRTI with low severity scores and normal CXR were often over-diagnosed as pneumonia and over-treated with intravenous antibiotics. Few patients were treated as per the therapeutic guidelines and this study highlights the importance of using severity scores to guide treatment.

Grant Support: Nil

IDENTIFYING THE GAPS: BRONCHIECTASIS CARE IN A GENERAL RESPIRATORY UNIT

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Introduction: Bronchiectasis is a heterogenous condition associated with high mortality, morbidity and reduced quality of life. TSANZ Bronchiectasis Guidelines[1] suggest optimal management involves specialised multidisciplinary care; however, many patients attend general respiratory clinics.

Aim: To describe patient characteristics and review current bronchiectasis management at an Australian teaching hospital.

Methods: A retrospective medical record audit was undertaken for all patients with a diagnosis of bronchiectasis, excluding traction bronchiectasis, attending respiratory outpatient clinics at the Royal Melbourne Hospital, between 1/1/2015 and 31/12/2016.

Results: Of 145 patients with bronchiectasis, aetiology was documented for 58 (40%) patients. The cohort was predominantly female (54%), of mean age 65 years (range 21-93), and mean Body Mass Index 26.1 (range 15.6-57.9). Comorbid asthma or chronic obstructive pulmonary disease was present for 87 (60%). Smoking status was documented for 139 (96%), with 60 (43%) current or previous smokers.

Patients had a mean of 1.4 exacerbations per year with 70% of exacerbations managed in the community. Modified Medical Research Council dyspnoea scores were inferred for 126 patients (86%), with 43 patients (34%) scoring 3-4.

Spirometry was available for 142 (97%) patients. The mean FEV_1 was 70% predicted (SD 28.8%), and mean 6MWT distance 383m (SD 191m). Chest Computerised Tomography was available for 131 (90%) patients, of which 59 (45%) had 3-5 lobes involved. Immunoglobulin levels were measured in 74 (52%). Of 117 (80%) patients with sputum microbiology available, 26 (22%) were colonised with *P. aeruginosa*.

Long term antibiotics were prescribed for 56 (38%) patients. Few had documentation of accessing chest physiotherapy (n=78, 54%) or pulmonary rehabilitation (n=28, 19%). Vaccination status was infrequently documented against *Influenza* (n=73, 50%) and *Pneumococcus* (n=37, 26%). Action plans were documented for 43 (30%) patients.

Conclusion: While many aspects of care were good, a significant proportion did not appear to receive all recommended elements of multidisciplinary care, particularly physiotherapy.

Grant Support: Nil

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CHARACTERISING THE TREATMENT AND PREVENTION OF DRUG RESISTANT TUBERCULOSIS IN NSW

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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: The 1st part of the study is a retrospective cohort study to analyse the demographics, TB diagnosis, treatment, outcomes and treating facility information for patients with bacteriologically confirmed MDR-TB diagnosed between 2000 and 2016 in NSW. 2nd part of the study is a cohort study of contacts of patients with MDR-TB identified by index patients during the contact investigation. It aims to evaluate the characteristics between the index and contact patients and the prevalence of latent TB infection (LTBI). The quality of the MDR-TB cases management will be assessed by an Expert Clinical Panel and compare with identified international standards to achieve improvements to MDR-TB control and management in Australia.

Results: 76 patients with MDR-TB diagnosed between 2000 and 2016 are identified via The Institute for Clinical Pathology and Medical Research (ICPMR) Mycobacterium Reference Lab from 6 hospitals in NSW. The demographics, duration of treatment, outcomes of the patients and the infection control facilities of the treating facility are presented. We also described the prevalence of LTBI and management of the contact patients.

Conclusion: The study highlighted the importance of adopting health system approaches to improve management of MDR-TB. Contact investigation provides an important opportunity for prevention of drug resistant disease in Australia.

Grant Support: Nil

IN ADULTS HOSPITALISED WITH COMMUNITY-ACQUIRED PNEUMONIA STEP COUNT IS REDUCED IN THOSE WITH GREATER CLINICAL FRAILTY AND THOSE WHO HAVE A PLEURAL EFFUSION

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Aim: In adults hospitalised with community acquired pneumonia, to explore relationships between daily step count and possible influencing factors of; (i) clinical frailty, (ii) pleural effusion and, (iii) occasions of physiotherapy service.

Methods: A prospective observational study design. Adults hospitalised with community acquired pneumonia were identified from electronic databases. Throughout their admission, participants wore a StepWatch Activity Monitor. Details related to clinical management were recorded. For analyses, participants were grouped according to disease severity using pneumonia-specific CURB score (scores of 0 and 1 = less severe disease and 2 and 3 = more severe disease) and clinical frailty scores (scores of 1 to 3 = mild frailty and 4 to 7 = moderate-to-severe frailty).

Results: Of the 148 participants recruited to the study, 88 wore the StepWatch for more than 24 hours. These participants were aged 66 ± 18 (SD) years and had a length of stay of 3 [4] [IQR] days. Daily step count was 883 [1008] steps. In a logistic regression model three variables were found to influence daily step count. Higher frailty, the presence of a pleural effusion and two or more occasions of physiotherapy service were associated with lower step count. Overall these variables contributed to 25% of the variance with clinical frailty being the main contributing factor (15%).

Conclusion: Greater clinical frailty and the presence of a pleural effusion were associated with lower daily step counts, suggesting that physiotherapy should target frailer patients and those with a pleural effusion for mobilisation programs. Current physiotherapy practice is targeted at those patients who are less mobile.

Grant Support: Australian Government Research Training Program Scholarship.

Declaration of Interest Statement: No conflicts of interest to declare.

MICROBIOLOGICAL PROFILE AND LONG-TERM ANTIBIOTIC USE IN A LARGE NSW METROPOLITAN COHORT OF ADULT PATIENTS WITH BRONCHIECTASIS: EARLY DATA FROM THE AUSTRALIAN BRONCHIECTASIS REGISTRY

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Introduction/Aim: The burden of bronchiectasis for Australians is not well described. As part of the ABR we recruited from 2 tertiary centres in Sydney to describe the severity of disease, impact of airway microbiolog, and antibiotic use.

Methods: Eligible participants (bronchiectasis on CT, no CF) were recruited from Concord and Royal Prince Alfred Hospitals. Data were collected into the ABR dataset. Recruitment began in April 2015.

Results: 243 patients have been recruited to date; 71% female, mean age 64.2years [95%CI 62,66]. Aetiology was mainly post-infective (26.8%) or idiopathic (24.7%). 51% had FEV1/VC <0.7, and mean FEV1 was 74%pred [70.5,77.7]. The mean number of affected lobes was 2.95 [2.7-3.2]. 66% produced sputum daily;mean sputum/day 33mls [25-42]. Mean exacerbations/year were 1.6 [1.3,1.8], mean hospitalisations/year 0.44 [0.32,0.57]. 23% were taking long-term macrolides (azithromycin 29%, clarithromycin 25%), 9% were on alternative long-term oral antibiotics (doxycycline) and 4% were on nebulised antibiotics.

21% had chronic *Haemophilus influenzae,* (HI), 20.5% had chronic *Pseudomonas aeruginosa* (PA) and 8.2% had chronic NTM (93% female;75%MAC;1 MABSC).

Patients with chronic PA had significantly (p<0.05 for all) lower lung function (mean FEV1 63%pred [52.5,73.6]), higher sputum volumes (mean 49mls/day [23.2,75.0]), more exacerbations/year (mean 3.1 [2.4,3.8]) hospitalisations/year (mean 1.9 [1.5,2.4]), and lobes affected (mean 4.3 [3.8,4.8]). They were more frequently taking macrolide (42%) and/or nebulised antibiotics (21%).

Patients with chronic HI, compared to those with PA, were younger (mean 54.4yrs [48.6,60.1]), with less exacerbations/year (mean 2.2 [1.8,2.6]) and hospitalisations/year (mean 1.2 [1.1,1.3]), however had no significant differences in lung function, number of lobes affected, sputum volume, QOLB or mMRC scores. They were more frequently taking doxycycline (19.4%);36% on macrolide, 8% on nebulised antibiotic.

Conclusion: PA colonisation is associated with greater disease burden, supporting a role for sputum surveillance and attempted eradication. HI is an important colonising organism in younger patients.

COMPARISON OF PAST AND PRESENT PLEURAL INFECTION MICROBIOLOGY AND OUTCOMES

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Introduction/Aim: Pleural infection (PI) rates are increasing and mortality remains high despite intrapleural tPA/DNAse and surgery. Microbiological patterns vary worldwide and may influence outcome, and few Australian studies have reported data. We aimed to 1) examine microbiology at our centre in Queensland and 2) compare outcomes past and present.

Methods: All PI cases treated at Sunshine Coast Hospital and Health Service between 1st July 2007 – 1st July 2012 (period A) and 1st October 2016 – 1st October 2017 (period B) were reviewed. PI was defined by positive pleural fluid culture *or* complicated parapneumonic effusion. Cases were identified by ICD coding and review of positive pleural fluid cultures on a pathology database.

Results: 67 cases were included; period A n=41, period B n=26. Mean age was 63 (17). Community-acquired PI accounted for 56.7%. 65.7% of cases were culture positive. The commonest pathogens of community-acquired PI were Streptococcal species (29.0%), especially Streptococcus milleri; Staphylococcal species (34.5%), especially Staphylococcus aureus, were most common in hospital-acquired PI.

Patients in Period B were older (71(13) vs 58(18) years, p<0.05) and had more community-acquired PI (84.6 vs 39.0%; p<0.05). The culture positive rate was lower in period B (53.9 vs 76.0%). Of positive cultures, Period B had a greater percentage of gram negative organisms (42.9 vs 23.3% p=0.51). In Period B, 46.2% of cases were treated with intrapleural tPA/DNAse. Compared to Period A, surgical referral was lower, 4.8 vs 29.2%; p=0.04. However, median hospital stay (16(9-27) vs 21(10-37) days) and in-hospital mortality (14.3 vs 17.1%) were not significantly changed.

Conclusion: The incidence of pleural infection has increased.

Mortality rate remains high in the modern era.

Surgical referrals have significantly reduced following introduction of a tPA/DNAse protocol.

Streptococcal species were the most common community-acquired PI and Staphylococcal species the most common hospital-acquired PI.

MYCOBACTERIUM TUBERCULOSIS COMPLICATED BY EMPYEMA NECESSITANS

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Empyema necessitans is a rare complication of a complicated pleural effusion and describes the extension of purulent pleural fluid through the parietal pleura with resultant formation of an abscess in the extrathoracic soft tissues (1). Factors influencing the development of empyema necessitans include the virulence of the organism, or previous trauma or thoracic surgery (2). Pleural effusion with associated empyema necessitans is typically caused by Mycobacterium tuberculosis, accounting for 70% of cases (3). Other causative organisms include Actinomyces spp, Blastomycosis spp, Aspergillus and Nocardia.

Empyema necessitans secondary to pleural tuberculosis is rarely seen in the twenty-first century, particularly in an immunocompetent host situated in a geographical area with a low prevalence of tuberculosis. We present the case of a 37 year old female who presented with back pain and a subcutaneous lump of 12 months duration. Subsequent investigations, including imaging with plain films, computed tomography and magnetic resonance imaging demonstrated a small pleural collection with extension through the intercostal space in the absence of parenchymal lung disease. A biopsy confirmed fully sensitive Mycobacterium tuberculosis. Management included standard short course antituberculous chemotherapy and was complicated by drug induced liver injury and rupture of the collection through the chest wall within 2 weeks of commencing therapy.

Mycobacterium tuberculosis infection is uncommon in non-indigenous Australian born patients with no known exposure history. This organism needs to be considered when evaluating patients with pleural effusions.

ANTIPHOSPHOLIPID SYNDROME PRESENTING WITH LARGE CAVITATING PULMONARY EMBOLISM IN A TEENAGER

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Introduction/Aim: Antiphospholipid syndrome is associated with arterial and venous thromboembolic disease. Pulmonary embolism is quite common in patients with antiphospholipid syndrome but large pulmonary embolism leading to infraction and systemic inflammatory response are quite rare. We report a case of large cavitating pulmonary embolism in a teenage due to previously undiagnosed antiphospholipid syndrome.

Methods: An 18 year old man presented with pleuritic chest pain, fever and haemoptysis. Chest X-ray revealed a consolidation and it was initially thought to be a bacterial pneumonia. No response to appropriate antibiotics led to a CT scan which confirmed large pulmonary embolus and cavitatory infarct. A bronchoscopy was performed for microbiological sampling with no particular growth. Serological test confirmed presence of the lupus anticoagulant. Very low positive titre of anti GBM antibody prompted renal assessment for any involvement. There was no eveidence of microscopic haematuria or proteinuria. A transcutaneous core lung biopsy did not reveal any vasculitis in the lung lesion. A repeat sample of anti GBM antibody from a different laboratory was negative and a diagnosis of Goodpasture disease was refuted.

Results: Systemic anticoagulation with enoxaparin followed by warfarin lead to resolution of his symptoms along with clinical and radiological improvement.

Conclusion: A teenage presenting with large pulmonary embolus leading to infarction and cavitation. Such unusual presentation should raise possibility of underlying systemic disorders and should be appropriately investigated and treated.

TPL 007

IMPACT OF THE 2017 INFLUENZA SEASON IN A VICTORIAN RURAL HOSPITAL

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Introduction/Aim: Influenza activity in Australia was highest in 2017 since 2009. Overall, severity was lower, however, with 8.9% of hospitalised patients admitted to ICU nationally based on sentinel hospital data. Limited data exists on the impact of influenza on rural hospitals. We report our experience of the 2017 influenza season at Mildura Base Hospital (MBH), a 165-bed rural Victorian hospital with 5 intensive care beds. This information may contribute to future pandemic planning in resource-limited settings in Australia.

Methods: We conducted a retrospective audit of patients hospitalised during the period 01/04/17 to 07/10/17 with positive influenza PCR. Patient demographics, influenza subtype, oseltamivir and antibiotic use, biochemical markers and outcome were recorded and severity scores (SMART-COP, CURB-65) were calculated. Data was analysed using SPSS.

Results: 58 patients (median age 67) with average LOS 7 days were identified. Influenza A (non-subtyped) was the predominant infection (65.5%) with 8.6% H1N1 subtype, and 25.9% influenza B. Community acquisition accounted for 72.6%, with 13.8% acquired in hospital/facility. Median SMART-COP and CURB-65 scores were 1 and 1. 41.4% cases were appropriately isolated on/before influenza diagnosis. 55.2% received oseltamivir with median time to commencement 2.5 days. 84.5% received concurrent antibiotics. 32.8% required ICU admission; 34.5% had pre-existing lung disease. Mean Charlson co-morbidity index was 4. 86.2% patients were discharged home, with 4 deaths and 1 transfer.

Conclusion: Influenza burden was high, consistent with national trends; our centre experienced higher use of ICU resources. Understanding factors affecting the rural experience of influenza season is essential with future planning in resource-limited settings.

Grant Support: Nil

References

Cystic Fibrosis

TP 060

INFECTION CONTROL IN AUSTRALIAN AND NEW ZEALAND CYSTIC FIBROSIS CENTRES

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Introduction/Aim: In people with cystic fibrosis (CF), new research has demonstrated that the spread of respiratory infections may be via aerosol transmission. To prevent the spread of aerosol transmission in people with CF, updated infection control guidelines for managing people with CF during hospital visits have been published. We wanted to investigate the current infection control practices used in CF centres in Australia and New Zealand.

Methods: Two online surveys were developed for distribution to the Australian and New Zealand CF centres. One survey was developed for the Medical Directors and CF Lead Nurse and the second survey was developed for the CF Lead Physiotherapists. Both surveys included sections on general demographics, outpatient care infection control guidelines, inpatient care infection control guidelines and mask wearing protocols (if used).

Results: The surveys were distributed to 50 centres providing CF care. The surveys opened on 27th September 2017 and to date, a total of 45 responses (medical and nursing responses, n=39; physiotherapy responses, n=6) have been received. The final results will be presented at TSANZ Conference.

Conclusion: The high response rate for this survey within a short opening time (<3 weeks) demonstrates that understanding infection control practices in CF centres is a priority.

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TREATING PARENTS OF CHILDREN WITH CYSTIC FIBROSIS WITH UNRESOLVED GRIEF

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Introduction/Aim: Diagnosis of CF in a child can cause parental grief, and if parents do not adjust well the grief can remain unresolved. Parental unresolved grief may be associated with emotional distress, and may impact on a child's health outcomes.

Aims were: to identify parents with unresolved grief, depression and anxiety at an Australian paediatric CF centre; to compare the effectiveness of insight oriented therapy vs. CF education for the treatment of unresolved diagnosis grief (UDG).

Method: Parents of children with CF aged 6months-18years were screened for UDG and randomised to receive either 5 hours of insight oriented therapy or 5 hours of disease and treatment related education from a multi-disciplinary CF team over 5 weeks. UDG, anxiety and depression were measured before and after the intervention with the Reaction to Diagnosis Interview (RDI), the Depression, Anxiety, Stress Scale(DASS), the Parent Stress Index(PSI) and the Impact of Events Scale-Revised questionnaire(IES-R).

Results: Overall, 44 parents were screened, of which 21(48%), 15(34%), 13(30%) had UDG, anxiety and depression, respectively. Anxiety and depression were significantly more prevalent in parents with UDG n=10 (48%), n=8 (38%) respectively (p=0.0002). The median duration of UDG was 5 years. Fourteen parents with UDG received intervention: six received insight-oriented therapy and eight received education. Grief resolved in 3 (50%) parents with insight-oriented therapy and 6 (75%) parents who received education. Levels of anxiety and/or depression reduced in 3 (50%) parents receiving insight-oriented therapy and 5 (63%) parents receiving education.

Conclusion: Unresolved grief around CF diagnosis remains prevalent for parents well after diagnosis of their child and is significantly associated with anxiety and depression. This preliminary interim analysis suggests that parental insight-oriented therapy and/or CF education may partially mitigate the parental grief and emotional distress associated with a child's CF diagnosis.

Key Words: unresolved grief, parents, Reaction to Diagnosis Interview, trauma

PERCEPTIONS OF BODY MASS INDEX AMONG YOUTH WITH CYSTIC FIBROSIS: AN EXAMINATION OF ACCURACY AND ITS RELATION TO QUALITY OF LIFE

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Introduction/Aim: Adherence to the dietary regimen is a crucial aspect of managing cystic fibrosis (CF). Our primary aim was to examine the accuracy in youths' perceived body image compared to Body Mass Index (BMI) and its relation to quality of life (QOL) in youth with CF.

Methods: A total of 54 patients with CF (M_{age}=13.61, SD=2.32; 53.7% female) were recruited from two pediatric pulmonary clinics. Anthropomorphic data and pulmonary function test results were obtained via medical chart review. BMI percentile was classified using CDC weight status categories. Patients completed the Figure Rating Scale (FRS) to assess body size perception and the Cystic Fibrosis Questionnaire—Revised to measure quality of life (QOL).

Results: Paired-samples t-tests revealed a significant difference between observed BMI percentile scores ($M = 44.67\%$, $SD = 29.48\%$) and BMI percentile scores converted from the FRS ($M = 31.04\%$, $SD = 12.90\%$) across all youth, $t (53) = 4.14$, $p < .05$. Results of independent samples t-tests indicated a significant difference in respiratory-related QOL scores between participants who underestimated and those who overestimated their BMI, $t (51) = 2.67$, $p = .01$. Youth who underestimated their BMI reported significantly higher respiratory-related QOL scores ($M = 82.26$, $SD = 14.87$) compared to youth who overestimated their BMI percentile scores ($M = 67.49$, $SD = 24.10$).

Conclusion: Results indicate that youth were not very accurate in identifying their actual BMI compared to objective measurement. Further, findings suggest among youth with CF, those with higher QOL related to respiratory function tend to underestimate their BMI. Future research is needed to evaluate the relation between perceived body size and adherence to medical regimens.

TP 063

COMPARATIVE EFFICIENCY OF HA AND VSV-G PSEUDOTYPED LENTIVIRAL VECTORS FOR CYSTIC FIBROSIS AIRWAY GENE THERAPY

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Introduction/Aim: Lentiviral (LV) vectors are a promising option for treating cystic fibrosis airway disease by delivering a functional copy of the CFTR gene into airway epithelial cells. We have developed a unique dosing technique that involves conditioning the airway with lysophosphatidylcholine (LPC) prior to LV vector delivery. However, the choice of vector pseudotype is important to ensure that the correct cells are efficiently targeted. The aim of the project was to examine the gene transfer levels that result when the LV vector is pseudotyped with the VSV-G or HA envelope proteins, which target airway receptors on the basolateral and apical surfaces, respectively.

Methods: The lungs of normal C57Bl/6 female mice were conditioned with 10 μl of LPC (n=12) or PBS (control; n=12), followed one hour later by two 15 μl aliquots of a VSV-G (n=12) or HA (n=12) pseudotyped LV vector containing the Luciferase reporter gene. Bioluminescence imaging (BLI; Xenogen, IVIS) was performed at 1 week, 1, 2, 3, 4 and 5 months after LV vector instillation to assess lung luciferase gene expression levels over time.

Results: Lung luminescence was detected by BLI at all imaging time points in the LPC and PBS conditioned mice that received either pseudotyped LV vector. At one week, the VSV-G pseudotype group had significantly higher expression levels that the HA group, regardless of whether LPC airway conditioning was used ($p > 0.0001$, Tukey's multiple comparison). From the 1-5 month time points there was no quantifiable difference in luminescence between LPC and PBS, or VSV-G and HA.

Conclusion: The addition of LPC conditioning has shown not to be more effective in targeting basolateral or apical airway cell receptors in lung airways of mice for up to 5 months. Monthly imaging of the treated mice will continue to occur for approximately 12-18 months.

TP 064

DOES EPITHELIAL ABLATION IN THE NASAL AIRWAYS OF MICE IMPROVE STEM CELL ENGRAFTMENT?

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Introduction/Aim: Cell transplantation therapy has proven successful for treating some immune disorders and this approach has potential to correct the airway disease phenotype associated with cystic fibrosis. This project assessed whether conditioning the mouse nasal airway with the agent polidocanol (PDOC) enhanced the rate of human basal epithelial cell (HBEC) engraftment.

Methods: Normal HBEC (LONZA, USA: CC-2540S) were seeded onto collagen-coated flasks, expanded to 75% confluency, and exposed to a lentiviral vector containing the luciferase transgene at a MOI of 10. To prepare the mouse nasal epithelium for cell transplantation the airway epithelium was first exposed to 2% PDOC (Polyoxyethylene-9 lauryl ether), which removes most of the epithelial cell layer. Normal female C57Bl/6 mice received 4 μl of either PBS (control (n=10)) or PDOC (n=7) into the right nostril. Two hours later, three 10 μl aliquots of HBEC-Luciferase were delivered to the treated nasal passage within a period of 30 mins. Bioluminescence imaging (BLI; Xenogen, IVIS) of animals was performed at 1, 3, 5 and 8 weeks after cell transplantation to assess HBEC engraftment via luminescence of Luc-expressing cells.

Results: Mice that received PDOC ablation prior to HBEC-Luciferase cell transplantation showed significant luminescence for up to 3 weeks ($p < 0.01$, RM ANOVA vs PBS control), as detected by BLI. Nasal luciferase gene expression declined at the 5 week time point, and was below detectable levels by 8 weeks. No luciferase expression was detected by BLI at any time point in the PBS conditioned (control) animals.

Conclusion: This data suggests that the PDOC airway conditioning procedure can produce initial and persisting Luc-expressing cell engraftment in the airways. While these results are encouraging, further studies are warranted to confirm cell engraftment using histological analyses before testing the potential of a therapeutic cell therapy in a CF animal model.

ADHERENCE TO A SMARTPHONE APPLICATION FOR REPORTING SYMPTOMS IN CF

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Introduction/Aim: In people with cystic fibrosis (CF), respiratory exacerbations impair lung function and health-related quality of life, and increase healthcare costs. Delayed reporting of symptoms can result in more severe exacerbations and worse outcomes. We have developed a smartphone application used to report symptoms suggestive of a respiratory exacerbation, and are now investigating its impact on health outcomes in a randomised controlled trial (RCT). As part of this study, we report on the current adherence to the weekly use of the smartphone application amongst participants.

Methods: Participants in the intervention group of the RCT were required to use the smartphone application weekly, or sooner if they felt their symptoms had worsened. If the smartphone application responses were not received during any given week, a text message reminder was sent to the participant. Adherence, defined as the number of weeks used versus number of weeks enrolled in the RCT (as a percentage), is reported on participants who have used the smartphone application for a minimum of 6 months.

Results: Twenty-nine participants (17 female, aged (mean $\pm$ SD) 31 ± 10 years, FEV_1 $58 \pm 18\%$ predicted) were allocated to the intervention group. Nineteen participants (66%) have completed the 12 month intervention, with a further 10 having used the smartphone application for a minimum of 6 months. Adherence to the weekly use of the smartphone application was mean (range) 77% (31 to 100%). Adherence was greater than 90% in 8 (28%) participants, and less than 50% in 2 (7%) participants.

Conclusion: We have demonstrated, on average, good adherence to the weekly use of a smartphone application used to report symptoms to the CF team. Complete adherence data will be available at the end of the RCT.

AIRWAY CLEARANCE BY EXERCISING IN MILD CYSTIC FIBROSIS: CLINICAL OUTCOMES

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Introduction/Aim: Guidelines generally recommend that patients with CF perform daily airway clearance techniques. Many patients report using exercise as one of their forms of airway clearance despite there being a paucity of studies supporting this practice. This study aimed to determine the feasibility of a research protocol investigating the medium-term effectiveness of exercise as a stand-alone form of airway clearance, and collect preliminary data on clinical outcomes.

Methods: A prospective, single blinded, randomised controlled feasibility trial was conducted at the Royal Adelaide Hospital with recruitment open for 12 months for adults with mild CF ($FEV_{1\%pred} > 70\%$). All participants completed a wash-in period comprising four weeks of PEP and exercise. Participants who adhered with the wash-in protocol were randomised to a three month intervention period of either PEP and exercise or exercise alone for airway clearance. Clinical outcomes were respiratory function, respiratory exacerbation rates and quality of life as measured by the Cystic Fibrosis Questionnaire (Revised) (CFQR) and the Leicester Cough Questionnaire (LCQ).

Results: 57 eligible patients were identified, 17 were recruited (59% male, mean$\pm$SD age 25$\pm$5yrs, $FEV_{1\%pred}$ 93$\pm$12%, 41% F508del homozygote). Of the 17 recruited, 13 (76%) were randomised after the four week wash-in period and 13 completed the final assessment. The changes (mean$\pm$SD) in clinical outcomes over the three month intervention period were:

	PEP + Exercise (n=6)	Exercise Only (n=7)
FEV_1 (L)	0.03$\pm$0.21	0.12$\pm$0.54
Total number of exacerbations	3	4
CFQR (respiratory)	7.6$\pm$4.5	7.9$\pm$12.8
LCQ (total)	1.0$\pm$1.6	0.6$\pm$0.4

Conclusion: Clinical outcomes appeared similar between groups. Given the recruitment and randomisation rates observed, further refinement of the protocol is required prior to expansion to a multi-centre study.

ULTRASHORT ECHO TIME MRI CAN EVALUATE TREATMENT EFFECT OF LUMACAFTOR/IVACAFTOR

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Introduction/Aim: To evaluate feasibility of ultrashort echo time (UTE) MRI in a subset of patients aged 6-11 years with cystic fibrosis (CF) who were homozygous for the *F508del* mutation treated with lumacaftor (LUM) and ivacaftor (IVA) combination therapy in a phase 3 trial (NCT02514473).

Methods: UTE MRI scans were obtained at study baseline (n=10); a second scan was completed at week 24 in 9 patients (4 LUM/IVA, 5 placebo) at 3 institutions using MRI hardware from 2 vendors. One vendor platform was 3D radial UTE[1]; the other was 3D "stack of stars" UTE.[2] Scans were obtained during 5 minutes of tidal breathing without use of IV contrast. MRI scans were scored by 2 independent readers using the Brody score after supervised training on UTE MRI scans. Readers were blinded to time point and treatment arm. Scores are presented as mean $\pm$ SD; no statistical testing was performed.

Results: Despite the lower image quality of MRI compared with CT, potential treatment effects were seen on UTE MRI. Mean total Brody score with treatment decreased from 41.1 to 32.5, a change from baseline ($\pm$ SD; %) of 8.4$\pm$11.2 but increased from 31.3 to 34.6, a change from baseline of 3.3$\pm$8.2 with placebo. Mucus plugging subscore decreased by 5.0$\pm$5.1, from 8.5 to 3.5 with treatment but increased by 1.4$\pm$4.4 from 4.2 to 5.6 with placebo. There were no noticeable changes in other subscores (bronchiectasis, peribronchial thickening, parenchymal opacities, or hyperinflation).

Conclusion: In this analysis from an exploratory substudy in patients with CF aged 6-11 years homozygous for *F508del*, UTE MRI was a feasible approach for detecting the effect of LUM/IVA, despite the small sample size, short duration of treatment, and limitations in image quality. As optimization of UTE MRI technology improves image quality, monitoring disease course in patients with CF may also improve.

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SAFETY AND EFFICACY OF LUMACAFTOR/IVACAFTOR IN PEDIATRIC CYSTIC FIBROSIS PATIENTS

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Introduction/Aim: Lumacaftor/Ivacaftor (LUM/IVA) was well tolerated and improved lung function and other efficacy endpoints in patients with cystic fibrosis (CF) aged ≥6 years homozygous for *F508del* in two 24-week phase 3 studies (NCT01897233; NCT02514473). A preplanned interim analysis was conducted after all patients reached week 24 of a subsequent 96-week open-label extension (OLE; NCT02544451).

Methods: Patients continued LUM/IVA (LUM 200 mg/IVA 250 mg q12h [6-11 years] or LUM 400 mg/IVA 250 mg q12h [≥12 years]), or if previously receiving placebo, were assigned to LUM/IVA regimens by age. Primary endpoint was safety (up to OLE week 72); secondary endpoints included absolute change from baseline in lung clearance index (LCI$_{2.5}$), sweat chloride, body mass index (BMI), and percent predicted FEV$_1$ (ppFEV$_1$).

Results: Of 260 eligible patients, 240 enrolled in the OLE and 229 completed ≥24 weeks. Most adverse events (AEs) were mild (36.8%) or moderate (48.5%); the most common were cough (47.3%), infective pulmonary exacerbation (30.1%), pyrexia (18.8%), nasal congestion (16.3%), and headache (15.5%). Serious AEs were reported in 40 patients (16.7%); 6 (2.5%) discontinued because of AEs. Predefined respiratory events were more frequent in placebo patients initiating LUM/IVA vs those continuing LUM/IVA (19.8% vs 8.4%); all were mild or moderate, and none led to discontinuation. Twenty-eight patients (11.7%) had AST or ALT >3×ULN. LCI$_{2.5}$ and ppFEV$_1$ improvements were maintained after 48 weeks in patients continuing LUM/IVA: absolute mean change from week 0 (95% CI): -1.07 (-1.49, -0.65), $P<0.0001$ and 2.8 (0.7-4.9), $P=0.0090$, respectively; patients previously receiving placebo had similar significant, rapid, sustained improvement in LCI$_{2.5}$: -0.97 (-1.48, -0.47); $P=0.0002$. Improvements in sweat chloride and BMI occurred in all patients.

Conclusion: LUM/IVA treatment for up to 48 weeks was well tolerated and led to durable improvements across multiple endpoints. Safety profile was consistent with phase 3 studies, with no new safety concerns.

THE CLINICAL SIGNIFICANCE OF OROPHARYNGEAL CULTURES IN YOUNG CHILDREN WITH CYSTIC FIBROSIS

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Introduction: For young children with cystic fibrosis (CF), bacterial surveillance is commonly performed using oropharyngeal swabs (OPS). We evaluated the associations between *P. aeruginosa* (*PsA*) from OPS and lung disease in young children with CF.

Method: Paired OPS, bronchoalveolar lavage (BAL) samples were obtained annually in children in the AREST CF program between 2005 and 2017. Test characteristics of OPS were calculated using BAL as gold standard. Culture results were related to lung inflammation (BAL neutrophil elastase and interleukin-8), structural lung disease (chest CT scored using PRAGMA CF method) and hospital admissions for respiratory exacerbations, accounting for repeated measurements and adjusting for age and pancreatic insufficiency.

Results: Six hundred and ninety paired OPS-BAL cultures were obtained from 181 patients. Prevalence of *PsA* in BAL was 7.4%. Sensitivity of OPS for BAL result was 23.5% ($CI_{95\%}$, 12.8%-37.5%), specificity 90.9% ($CI_{95\%}$, 88.4%-93.0%), the post-test probability of positive BAL culture changed only marginally on the basis of OPS results (from 7.4% to 6%). *PsA* on OPS was not associated with increased risk for BAL *PsA* the following year (odds ratio (OR) 2.03 $CI_{95\%}$ 0.85-4.87, p=0.11). *PsA* on OPS was not associated to any lung disease parameter studied. In contrast, *PsA* on BAL was associated with positive neutrophil elastase (OR 4.6 $CI_{95\%}$ 2.14-9.88, p<0.001), increased interleukin-8 (p<0.001), increased PRAGMA-CF CT scores at baseline (p<0.001) and progression of PRAGMA-CF CT scores in the following year (p<0.05). Patients with *PsA* on BAL but not OPS had an increased risk of admission for respiratory exacerbations in the following year (Incidence Rate Ratio 3.73 $CI_{95\%}$ 2.06-6.76, p<0.001).

Conclusion: OPS were not associated with current or progression of lung disease or an increased risk for exacerbations in young children with CF. Alternative non-invasive techniques are required for early detection of lower airway *PsA* infection.

Key Words: Cystic Fibrosis, oropharyngeal swabs, *P. aeruginosa*

Nomination for New Investigator Award: No

GENERATION OF NEW CYSTIC FIBROSIS RAT MODELS IN AUSTRALIA

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Introduction/Aim: Animal models are fundamental to the development of therapies for cystic fibrosis (CF). A major disadvantage of CFTR-defective mouse models has been the lack of CF pathology in the lungs. The first CF knock-out rat model was reported to have excessive mucus production that was later shown to enable development of lung pathology (Birket S, 2015; Tuggle K, 2014). We have established a Sprague Dawley strain CF rat model in collaboration with the Australian Phonemics Network (Monash University).

Method: Founder animals were generated using CRISPR/Cas9 genome editing, with HDR used to delete the codon aligning to 508 in the human CFTR gene sequence (Phe508del, the most common human CF-causing mutation). Two animals harbouring the targeted mutation and one animal harbouring an off-target mutation (causing termination early in the coding sequence), were selected as colony founders. The CF rat colony is maintained through the breeding of mutation-matched CF-heterozygous pairs, and a limited number of animals have been used for post-mortem analyses to date.

Results: To date the Adelaide CF rat colony has generated more than 50 CF-affected individuals; most survive past the age of weaning, while approximately 25% succumb to gut complications within their first few weeks. Observed out to 12 weeks of age, the CF rats that reach adulthood typically appear active, without signs of distress, although they are considerably smaller than their unaffected littermates and they show abnormal tooth development. Consistent with reports on the USA-based CF rats, the respiratory histology of the Australian CF rats remains similar to normal at 8 weeks old.

Conclusion: By March 2018 we expect to report on respiratory outcomes out to 6 months of age. Once established and characterised, the Australian CF rat will be used in our studies of CF airway gene correction, and will be available to other research groups.

Key Words: Animal models, cystic fibrosis, CRISPR/Cas9, genome editing.

PARAPNEUMONIC EFFUSION IN AN ADULT WITH CYSTIC FIBROSIS (CF): A CASE STUDY

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Introduction: We report an uncommon case of complicated parapneumonic effusion in an adult with CF managed with intercostal catheter and intravenous antibiotics.

Method: Retrospective review of clinical notes.

Result: SH is a 23-year old man with moderate CF lung disease and chronic infection with *Pseudomonas aeruginosa* and Methicilline resistant *Staphylococcus aureus.* He presented with a three-day history of breathlessness, left-sided pleuritic chest pain, fevers and night sweats. On examination, he had a low grade temperature with bilaterally reduced breath sounds, increased vocal resonance and percussion dullness in the left base. Chest X-ray showed left lingular and lower lobe consolidation and a small left-sided pleural effusion. The patient was treated with intravenous timentin and tobramycin but continued to spike temperatures. CT chest on day 3 showed a large, complex loculated pleural effusion adhered to the left superior anterior chest wall with underlying consolidation. A pigtail catheter was inserted with drainage of 500 millilitres of straw-coloured exudate. No bacteria were cultured. Intravenous Vancomycin was added. Repeat CT after 10 days of drainage showed persistence of multiple thick-walled pleural locules which was managed conservatively. The patient improved and was discharged after 19 days. Subsequent X-rays demonstrated resolution of the effusion and consolidation.

Discussion: Parapneumonic effusions/ empyemas are rare complications in adults CF pre-transplant. In our patient, the loculated effusion on the initial X-ray was obscured by underlying lobar consolidation which further delays diagnosis. The negative bacterial culture on pleural fluid analysis was attributable to the delay in diagnostic aspiration after commencement of antibiotics. Given a high rate of discordance between sputum and pleural microbiology has been reported in CF empyemas, timely diagnostic aspirate is crucial for microbiological identification and antibiotic optimization in CF empyemas. Our case highlights the importance of vigilant detection, early diagnosis and treatment for this rare, but serious, CF complication.

Declaration of Conflict of Interest: *Nil*

PATIENT PERCEIVED EFFECTIVENESS OF AUTOGENIC DRAINAGE COMPARED WITH OTHER AIRWAY CLEARANCE TECHNIQUES IN CYSTIC FIBROSIS

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Introduction/Aim: Cystic Fibrosis (CF), the most common inherited disease in Australia is characterised by abnormally thick airway secretions causing chronic lung infections. Airway clearance techniques have been shown to maintain lung function and slow the progression of lung disease in children and adults with CF. Autogenic drainage (AD) is an effective technique for mobilising peripheral sputum up the airway and can be performed without the use of any devices. However, AD can be difficult for both the physiotherapist and patient to learn and teach effectively. This study aimed to compare the patient perceived effectiveness of AD with other airway clearance techniques used on a daily basis.

Methods: Adults with CF at outpatient physiotherapy appointments or admitted into hospital were taught AD in multiple sessions. Once familiarised, the AD technique was used in comparison to their usual airway clearance technique such as positive expiratory pressure (PEP) or percussion with postural drainage. A questionnaire using a visual analogue scale (VAS) was completed for the different physiotherapy techniques used in each session, where 0 indicates a positive perception towards treatment whilst 10 a negative perception.

Results: 16 adults with CF were recruited, median age of 24.6 (range 19-35). 15 adults found AD to be more effective than their previous treatment. The vast majority of adults with CF (14 of the 16) indicated that AD required higher concentration than their previous technique and 10 adults found their previous treatment regimen easier to perform. However, because of its perceived effectiveness, despite these difficulties 13 of the 16 adults still chose to continue with AD.

Conclusion: AD was perceived to be effective in clearing sputum in the recruited cohort. Patients found AD difficult to complete as it required high concentration levels, but once they felt the benefits of this technique they were more motivated to continue with this treatment.

Evidence-Based Medicine & Practice

PULMONARY EMBOLECTOMY: AUDIT OF PATIENT CHARACTERISTICS AND OUTCOMES

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Introduction/Aim: Optimal management of high risk submassive and massive pulmonary emboli (PE) is unclear with treatment options including systemic anticoagulation, catheter directed lysis, systemic thrombolysis and surgery. Until evidence is available to recommend a specific therapy for each circumstance, we have taken a multidisciplinary approach. Patients who underwent pulmonary embolectomy after the introduction of a PE management pathway at a tertiary centre were audited.

Methods: Retrospective review of medical records of all pulmonary embolectomies done at Sir Charles Gairdner Hospital between January 2016 and February 2017.

Results: 13 pulmonary embolectomies were undertaken during audit period. Median age was 65 (37-79) and median body mass index was 34 kg/m^2 Most patients had a PE severity index of 4 or 5 (n=8) and European Society of Cardiology Risk Class of Intermediate-high or High (n=11). 2 patients had surgery provoked PE, 3 had immobility provoked PE and 1 had a thrombophilia.5 required cardio-pulmonary resuscitation pre-operatively with 1 undergoing thrombolysis. 12 underwent a CT pulmonary angiogram; all showed features of right heart strain. 12 had a pre-operative echocardiogram (ECHO) which showed right heart failure. Estimated pulmonary artery systolic pressure ranged from 44-105 mmHg (n=5). Median intensive care length of stay (LOS) was 5 days (2-22 days) and median hospital LOS was 20 days (7-35 days). Patients needed endotracheal intubation and an intercostal catheter for a median of 3 days and 3 had acute kidney injury post-operatively. 1 patient died during hospital stay. Of those discharged, all survived at 6 month follow up. At hospital discharge, 8 patients had normal or mild impairment of right ventricular (RV) function. 8 had ECHO at clinic follow up and all had normal RV function.

Conclusion: Pulmonary embolectomy is associated with morbidity but has a clear place in the management of high-risk PE. A multidisciplinary team approach may assist in ensuring the best treatment is matched to individual patients. Comparison with a non-surgical series on RV outcomes is needed.

AUDIT OF PLEURAL PROCEDURES AT WAIKATO HOSPITAL

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Introduction/Aim: Pleural procedures are commonly performed in the acute clinical setting. We conducted an audit of our procedures at Waikato Hospital using the BTS 2015[1] audit criteria to establish the number of procedures performed on medical/respiratory patients, the complication rate and whether our current practice adheres to international guidelines.

Methods: We conducted a retrospective audit on medical/respiratory inpatients who underwent pleural procedures between January to December 2016. Patients were identified from clinical coding. Data was extracted from clinical notes and electronic records and entered onto MS Excel spreadsheet. Specific data were extracted: patient demographics, procedure indication, procedure type, consent process, thoracic ultrasound usage for procedure, working hours (08h00 - 16h00) or after hours (16h01 - 07h59) when procedure was conducted, appropriate coagulation profile management and any post-procedural complications.

Results: 92 pleural procedures were performed. 55 (59.8%) intercostal drains and 37 (40.2%) pleural aspirates. 60% male. Mean age was 66.6 years old. 32% of the indications were for undiagnosed effusions and 27.2% were for infective cause. Consents was documented in 49 cases (53.3%). Bedside ultrasound was performed in 50 cases (54.4%). 48 procedures (52.2%) were performed during working hours. Pre-procedural coagulation profile was checked in 82 cases (89.13%), where relevant, patient on anticoagulant were managed accordingly to Haematology guidelines in 94.5% of time. Most common immediate complications for intercostal drain was pain, 24 cases (44.4%); Most common delayed complications was blocked intercostal drain, 16 cases (29.6%) and 1 case (1.9%) of pneumothorax. For pleural aspirate, most common complications was pain, 27%. There doesn't appear to be significant difference in complication rates between procedure conducted during hours and after hours in our population.

Conclusion: Pleural procedures are commonly performed at Waikato Hospital. Our audit demonstrates a need for standardisation of pleural procedures, improving our consent process, increase usage of pre-procedural thoracic ultrasound and peri-procedural pain management.

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THROMBOEMBOLIC DISEASE: UNDER-DIAGNOSED IN CLINICAL PRACTICE

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Introduction: CTEPH is a largely underdiagnosed disorder and majority of cases had ineffective clot resolution from acute PE [3].

Aim: To improve awareness of early diagnosis needed for this unique, fatal but potentially curable condition.

Case 1: A 47-year-old man presented with a week history of exertional dyspnoea. He has hypertension, hypertensive heart disease and chronic renal impairment. His troponin assay was elevated at 0.102 (less than 0.01 ng/ml) with recent normal coronary angiogram. Myocardial perfusion scan and cardiac MRI which did not identify the cause. Subsegmental left lower lobe pulmonary emboli were found on V/Q scan. There was no features of pulmonary hypertension or right heart dysfunction. He was commenced on oral anticoagulant and to be followed up at thoracic outpatient.

Case 2: An 80-year-old lady presented with rapid atrial fibrillation, dyspnoea and right sided chest pain. Her medical history includes chronic atrial fibrillation, hypertension, moderate aortic stenosis, renal impairment, metastatic ovarian cancer. V/Q scan revealed multiple segmental pulmonary emboli in right upper lobe. Given her risks of recurrent thromboembolism and CTEPH, lifelong anticoagulation with warfarin was recommended.

Discussion: The natural history of CTEPH remains unclear [1]. Progressive pulmonary hypertension, right ventricular dysfunction and death ensure if the condition is left untreated [1]. V/Q scan and echocardiography are initial screening investigations in suspected cases followed by pulmonary angiography and right heart catheterization to confirm the diagnosis and assess the surgical suitability [2]. In patients with operable CTEPH, pulmonary endarterectomy is the treatment of choice [2]. All patients should receive lifelong anticoagulant treatment with warfarin or its equivalent [2].

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CTPA PRACTICE AT A REGIONAL NZ HOSPITAL: PE YIELD, ALTERNATIVE DIAGNOSES AND INCIDENTAL FINDINGS

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Introduction: CT Pulmonary Angiography (CTPA) is the most commonly used investigation to diagnose a pulmonary embolus (PE). There is an ongoing global initiative to reduce unnecessary tests across all specialities[1]. The aim of this study was to determine the usefulness of CTPA in a real world setting.

Methods: All inpatient CTPA requests at Rotorua Hospital during 2016 were included. Radiology reports, blood test results, discharge summaries and clinic letters were reviewed for each patient.

Results: 197 CTPAs were included for analysis. Of these 33 (16.8%) were positive for PE. In 50 of the other 164 scans (30.5%) an alternative diagnosis was evident that was not reported in the preceding chest x-ray. Most commonly these were infective changes. 86.8% of all the CTPA reports yielded additional findings compared with the chest x-ray. The majority of these were not clinically relevant and unrelated to the current presentation.

12 patients (6.1%) had follow up imaging arranged for incidental findings unrelated to the admission diagnosis (5—Lymphadenopathy, 4—Nodules, 1—Kidney lesion, 1–Thymus mass, 1–Thyroid mass).

121 patients had a D-Dimer performed as part of their initial workup. The PE yield significantly increased with the D-Dimer value:

D-Dimer (ug/L)	PE positive/Total scans
≤999	0/36 (0%)
1000-1999	2/45 (4.4%)
2000-4999	12/26 (46.2%)
≥5000	8/14 (57.1%)

Conclusion: The PE yield of CTPA at Rotorua Hospital is comparable to similar studies in Australasia with a significant amount of alternative diagnoses and a low rate of incidental findings requiring follow up. The PE yield increased significantly with higher D-Dimer values. This information can be used to better inform clinicians and patients of the possible outcomes of a CTPA request.

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PRIORITIES AND EXPECTATIONS OF PATIENTS ATTENDING A MULTIDISCIPLINARY INTERSTITIAL LUNG DISEASE CLINIC

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Introduction/Aim: A sub-specialist multidisciplinary interstitial lung disease (ILD) clinic was established at the Royal Prince Alfred Hospital (RPAH) in 2010. The RPAH-ILD clinic is a referral centre for patients with suspected ILD from throughout NSW, enabling patients to see expert physicians, specialist nurses and physiotherapists in the one visit. Our study aimed to determine the expectations and priorities of patients attending the RPAH-ILD clinic. In particular, we sought to determine how important the multidisciplinary aspect of the clinic was to the patients, and which aspects were most valued.

Methods: An 18 item survey was sent to a sample of 100 patients who had previously attended the RPAH-ILD clinic. The survey collected anonymous demographic data as well as both quantitative and qualitative data regarding patient's experiences when attending the RPAH-ILD clinic.

Results: To date, 38 (41%) patients have returned the survey (age 66 ± 13 yrs; male 21 (55%)). 23 (63%) of patients were from Sydney, with the remaining patients from other areas of NSW and ACT. ILD diagnoses ranged from IPF (n=12, 31.6%) to connective tissue disease associated ILD (n=7, 18.4%) and 14 patients (37%) were uncertain of their ILD diagnosis.

Obtaining an accurate diagnosis, multidisciplinary care, education and access to medications all ranked very highly, with 76%, 66%, 67% and 66% of patients listing these issues as top priority. Patients rated access to a respiratory physician and specialist nurse as extremely important with 84% and 59% listing these as top priority, respectively. Other patient education tools, including written material, attending education courses or enrolling in clinical trials were very important to a subset of patients. Attending the ILD clinic, was an important support mechanism for patients, further signalling the benefit of its multidisciplinary approach.

Conclusion: Patients appear to place high value on the multidisciplinary approach to the management of ILD. Further work will focus on thematic analysis of qualitative responses.

AN AUDIT OF NON-INVASIVE VENTILATION USE IN A REGIONAL HOSPITAL: A CLINICAL OUTCOMES AND RESOURCE UTILISATION ANALYSIS

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Introduction/Aim: The advent of non-invasive ventilation (NIV) has reduced intubation rates and mortality in acute respiratory failure. This audit aims to look at clinical outcomes, adherence to practice guidelines, and resource utilisation in a Victorian regional hospital.

Methods: A retrospective analysis of all patients >18 years of age receiving NIV as an inpatient over a 3-month period (01 January to 31 March 2017) was performed. We excluded patients receiving home NIV who did not receive additional NIV.

Results: A total of 34 patient were included in the audit. The most frequent indications were acute pulmonary oedema (47%), pneumonia (26%), and exacerbation of chronic obstructive pulmonary disease (COPD) (21%). 97% of patients received NIV in the emergency department, intensive care unit, or both, with 3% receiving it on the ward. Of the COPD exacerbations, 57% were confirmed to have acute hypercapnia. In terms of duration of NIV use, 50% received <4 hours, 41% between 4-48 hours, and 9% >48 hours. With regards to guiding ongoing therapy, 62% did not have documented oxygen saturation targets and 32% did not get repeat blood gases. In terms of clinical outcomes, 76% of patients were successfully weaned off NIV, 18% intubated and 6% palliated. None of the patients that received NIV for 4-48 hours required intubation.

Conclusion: Our avoidance of intubation rate is similar to published data. Our indications for using NIV align with established guidelines, however better patient selection would have avoided unnecessary application of NIV, particularly in COPD patients who did not have acute hypercapnia. Compliance with setting oxygenation targets and monitoring response with repeat blood gases was poor. These issues could be addressed by provider education. The group of patients receiving NIV for 4-48 hours are a potential target for patients who could be managed on the ward.

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CARDIAC EVENTS IN PATIENTS WITH RESPIRATORY INFECTIONS WITHOUT RADIOLOGICAL FINDINGS

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Introduction/Aim: Lower respiratory tract infection(LRTI) is a common reason for hospital admission. Cardiovascular events occur in 14-19%[1] following admissions with community acquired pneumonia (CAP). However there is no similar data for LRTI without radiological consolidation. The DISPNOEA study evaluated the outcomes of patients admitted with LRTI without chronic lung disease and normal chest-xray (CXR).

Methods: Retrospective audit of patients admitted to Alfred Hospital in 2016 with discharge diagnoses of LRTI, chest infection, bronchitis, pneumonia or influenza. Patients chronic lung disease, immunosuppression and hospital acquired pneumonia were excluded. Patient demographics, cardiac history, SMART-COP and CORB scores, in-hospital cardiac events and 30-day re-admission data was obtained from medical records.

Results: For 231 patients (103=Male), median age was 82 years with average LOS of 3 days. The mean Charlson co-morbidity index was 5 with past history of Ischaemic heart disease (IHD) and heart failure documented in 25% and 12% respectively. 34.6% were on anti-platelets on admission. 85.3% were classified as low severity of infection by the SMART-COP score. Inpatient stay was complicated by a cardiac event in 17.7% (n=41). Acute decompensated heart failure(ADHF) occurred in 13.9% (n=32) which was a new diagnosis in 24 patients. Other events include new atrial fibrillation in 4.8%(n=11) and myocardial infarction in 3.9% (n=9). There were no ICU admissions however inpatient mortality rate was 3.5%(n=8). The 30-day re-admission rate to the same hospital was 13.9% (n=32), 40.6% of them secondary to cardiovascular complications (n=13) of which ADHF was most common(n=10).

Conclusion: Our study revealed that nearly 20% of patients admitted with LRTI with normal CXR suffered subsequent cardiac events, often resulting in high readmission rates. These results are comparable with prior studies of patients with CAP. This highlights the need for close follow-up of these patients post hospital discharge and adequate optimisation of their cardiac risk factors.

Grant Support: Nil

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AUDIT OF HIGH FLOW NASAL CANNULAS IN AN AUSTRALIAN TERTIARY HOSPITAL

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Introduction: High flow oxygen via nasal cannulas (HFNC) deliver humidification and a higher FiO2 and flow rate than other modalities of oxygen delivery and has been traditionally used in high dependency and intensive care units (HDU/ICU). In recent years use of HFNC has become commonplace in medical and surgical wards.(1) However, evidence for improvement in outcomes over traditional devices is lacking and further large randomised controlled trials are required, particularly outside of the ICU and neonatal setting.(2, 3) Furthermore, the ability to deliver high fractions of inspired oxygen has the propensity to cause harm in patients at risk of hypercapnia.(4)

Methods: The medical records of all patients treated with HFNC during the winter months on the medical and surgical wards was retrospectively reviewed. Patients were excluded if they were immediately admitted to the ICU without first being admitted to a medical or surgical ward.

Results: 55 patients were included. The mean age was 61.6 with 45% males. The most commonly prescribing specialties were General Medicine (23%), Respiratory (18%) and the surgical specialties (36%). The most common indications were hypoxic respiratory failure (22%), Obstructive Sleep Apnoea (22%), for increased work of breathing (18%) and there were two patients treated for hypercapnic respiratory failure with HFNC. 77% of patients had identified risk factors for hypercapnia but only 31% had arterial blood gas measurement before or after starting HFNC. Only 45% of patients had a formal oxygen prescription and 13% were assessed as complying with the oxygen guidelines set out by the Thoracic Society of Australia and New Zealand.

Conclusion: In our cohort of patients there was a wide range of indications for commencing HFNC, many which fell outside the supporting literature. There was poor utilisation of arterial blood gas measurement despite most patients having risk factors for hypercapnia. There was also poor utilisation of formal oxygen prescriptions despite there being a hospital wide mandate for such documentation. Further education of medical staff prescribing HFNC may improve safety and in some cases, result in prescription of more cost-effective delivery devices.

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DIAGNOSIS OF DYSPNEA: A LITERATURE REVIEW

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Introduction/Aim: Dyspnea or breathlessness is a common presenting symptom among patients attending primary care services. In Australia 1.8 million people have breathlessness that chronically limits exertion. We undertook a narrative literature review to determine if there are clinical tools that can be incorporated into a clinical decision support system for primary care for efficient and accurate diagnosis of causes of dyspnea.

Methods: We conducted a systematic search in MEDLINE, EMBASE and Google Scholar of all literature published between 1946-2016. Studies that evaluated a clinical decision support system in assessment of dyspnea in patients of any age group presenting to physicians with chronic dyspnea were included.

Results: We identified 125 abstracts, 44 papers were reviewed, six were included. The age of the patients was between 20-80 years, 60% were women (752 women, 494 men). Duration of dyspnea was three weeks to 25 years. The studies undertook a stepwise or algorithmic approach to assessment of dyspnea. The initial stage included physical examination, history taking, and screening tests such as spirometry, electrocardiography, chest x-ray, thyroid function test and full blood count. If undiagnosed by the initial assessment, the subsequent stage included more specialised investigations such as Echocardiogram, lung volume measurement, bronchial provocation, and cardiac exercise stress test. The third stage of assessment included invasive investigations such as bronchoscopy and cardiac catheterization.

Initial assessment ascertained a cause for dyspnea for 35% of the patients. Stage 1 and stage 2 in combination diagnosed 65% and more than 90% of the dyspnea cases were diagnosed by initial assessment and the advanced invasive tests.

Conclusion: Our review suggest that, while there is a paucity of literature, a stepwise approach using simple tests and then more expensive or invasive tests only when the initial steps fail, can achieve an accurate diagnosis in the majority of patients with dyspnea.

ASSESSMENT OF NON-CARDIAC PULMONARY HYPERTENSION AT IPSWICH HOSPITAL

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Introduction: Pulmonary hypertension (PH) is a heterogeneous condition with a wide range of aetiology. The diagnosis is often delayed or missed. The prognosis is usually poor without appropriate and timely management.

Aim: To evaluate whether patients with evidence of non-cardiac PH are adequately investigated at Ipswich Hospital.

Method: A retrospective audit of patients who underwent echocardiogram between 1st January 2016 to 31st June 2016 was conducted. Patients were screened for echocardiographic signs of PH (right pulmonary systolic pressure of $\geq$ 40mmHg, right ventricular dysfunction or enlargement, right atrial enlargement and flattening of interventricular septum). Patients with obvious cardiac dysfunction (left ventricular dysfunction, cardiac valvulopathy and congenital cardiac defects) were excluded. A review was conducted to find if these patients had further work up of their PH (pulmonary function test, overnight oximetry or polysomnogram, VQ scan/CTPA and autoimmune tests). A second review was done to identify follow up of these patients.

Results: Of the 851 echocardiograms performed at Ipswich Hospital between January and June 2016, 63 had evidence of non-cardiac PH. The mean age was 70 years with standard deviation of 14 years. 31 (49.2%) patients had no investigations performed.18 (28.6%) patients had only one investigation and 14 (22.2%) had more than 2 investigations performed. 17 (27%) patients were identified to have a probable aetiology for their PH. 13 patients (20.6%) had appropriate follow up.

Conclusion: In our centre, a considerable number of patients with non-cardiac PH did not get adequate evaluation of their PH in the period audited. Majority of patients were not appropriately followed up or referred to a specialist. Further intervention is necessary to improve our current management strategy of PH.

Asthma & Allergy 2

NLRC4 GENE VARIANTS ARE ASSOCIATED WITH mRNA EXPRESSION LEVELS IN CHILDREN HAVING AN ASTHMA EXACERBATION

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Introduction/Aim: Asthma results from interactions between environmental and genetic risk factors. We identified five genes (*NLRC4*, *MNDA*, *THBS1*, *CD163* and *IFTIM3)* that fulfilled at least two criteria including: altered mRNA expression in peripheral blood mononuclear cells (PBMC) and/or nasal epithelial cells in children with asthma and/or wheezing exacerbations compared to (1) convalescence and/or (2) healthy controls; and/or (3) contained rare variants associated with recurrent asthma exacerbations. During asthma and/or wheezing exacerbations, we found children with minor homozygote genotypes in these genes had altered exacerbation severity, incidence of rhinovirus infection and recurrent hospital visits compared to common genotypes. We aimed to identify whether these genotypes had altered mRNA expression in PBMC collected during asthma and wheeze exacerbations.

Methods: Cases were children who presented to hospital with an asthma or wheezing exacerbation (n=85). PBMC were isolated from peripheral blood samples, RNA was extracted and mRNA expression measured by microarray using Affymetrix U133 Plus 2.0. In these five genes, 39 variants were genotyped by Australian Genome Research Facility. Statistical analysis was completed using R version 3.2.2.

Results: Mean age was 2.31 years and 32.9% were male. Children with *NLRC4* rs212721 TT genotypes had lower mRNA expression (mean 5.14) than children with CT (mean 5.93; p=0.024) and CC genotypes (mean 5.90; p=0.028). Children with *NLRC4* rs212736 AA genotypes had lower mRNA expression (mean 4.68) than children with AG (mean 5.99; p=<0.001) and GG genotypes (mean 5.78; p=0.003). Children with *NLRC4* rs7562653 TT genotypes had lower mRNA expression (mean 4.58) than children with the CT (mean 6.07; p=<0.001) and CC genotypes (mean 5.78; p=<0.001). No association was observed in the other four genes.

Summary/Conclusion: NLRC4 is involved in intracellular pathogen detection and inflammasome complex formation. Taken together, our results suggest *NLRC4* gene variants alter gene expression and may contribute to asthma and wheezing exacerbations in children.

COMBINED FLOW CYTOMETRY AND GENE EXPRESSION PROFILING OF MAST CELLS AND BASOPHILS IN ASTHMATIC SPUTUM

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Introduction/Aim: Quantification of immune cell populations in sputum can inform asthma prognosis and treatment. Mast cells (MCs) and basophils are pathophysiologically relevant cells present in low numbers in sputum, making their study challenging. MCs and basophils express both unique and overlapping surface markers and gene signatures, which may be useful for development of biomarkers of their activity. Indeed, MC and basophil-associated genes are often amongst the most differentially expressed in transcriptomic analyses of sputum and bronchial brushings in asthma. Here, we aimed to use flow cytometry and mRNA profiling to develop reliable biomarkers for these two cell types in sputum.

Methods: Sputum cell suspensions were prepared using conventional dispersion methods and undispersed sputum plugs were stored for subsequent RNA isolation and analysis. MC and basophil populations were identified using flow cytometry. Sputum microarray data was used to test for differential expression of published MC and basophil gene signatures across asthma inflammatory phenotypes. Differentially expressed MC and basophil genes were selected for qPCR analysis in matched flow cytometry-characterised sputum samples.

Results: MCs and basophils were increased in eosinophilic asthma compared to both healthy control and non-eosinophilic asthma. Sputum microarray analysis of published MC and basophil gene signatures revealed upregulation in eosinophilic asthma. qPCR measurement of these genes in sputum samples also tested by flow cytometry allowed ranking of these genes as sputum biomarkers for MCs and basophils.

Conclusion: Here we combine flow cytometry with microarray and qPCR analysis for the first time to develop reliable, potentially clinically applicable biomarkers of MCs and basophils in induced sputum. We show that MCs and basophils are increased in eosinophilic asthma. Further analysis will focus on the clinical outcomes associated with MC/basophil-high asthma, and aim to characterise the functional roles of these cells in driving inflammation and pathology in asthma.

ABNORMAL MiRNA-22 EXPRESSION AFTER INFLUENZA INFECTION FACILITATES EPITHELIUM REMODELING IN ASTHMA

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Introduction/Aim: Specific miRNAs play essential roles in airway remodelling in asthma. Influenza A virus-induced exacerbations may also magnify pre-existing airway remodelling in asthma. Epithelium of asthmatics display dysregulated differentiation. miR-22, is a differentiation specific miRNA and has been proposed to suppress different genes with potential roles in airway remodelling including, CD147(a MMP inducer) and HDAC4 (an epigenetic regulator of EMT). We hypothesised that the impaired miR-22 expression after H1N1 exacerbates epithelium abnormalities in asthmatics. Our aims were to determine the expression and role of miR-22 in responses in the context of airway remodelling in epithelial cells of asthmatics, in the absence of any stimulus and after H1N1 infection.

Methods: Primary bronchial epithelial cells (pBEC) obtained from severe asthmatics were cultured under ALI condition. Cells were incubated with H1N1 (MOI 5). miRNAs and mRNA were isolated using RNAeasy mini kit with some modifications and subjected to Taqman miR-22 and mRNA assays.

Results: Basal expression of miR-22 was similar in pBEC of asthmatics and non-asthmatics. However miR-22 expression increased significantly at 24 h after H1N1 infection in pBECs from non-asthmatic but expression was unchanged in asthmatics. mRNA expression of the miR-22 targets, CD147 and HDAC4 were reduced during infection cells from non-asthmatics. *CD147* expression increased whereas *HDAC4* remained un-changed in asthmatics. The expression of regulators of miR-22 and its targets; *c-Myc* and *SP1*, also increased during H1N1 infection in pBEC of asthmatics which may result in induction of CD147.

Conclusion: The different profile of miR-22 expression in differentiated epithelial cells from asthmatics and non-asthmatics highlight a novel mechanism through targeting CD147 and HDAC4. The consequent reduction of CD147 and HDAC4 following H1N1 infection in healthy cells may indicate a self-defence mechanism against further epithelium aberrant responses which is not present in asthmatics.

CHANGE IN TYPE-2 INFLAMMATORY BIOMARKERS FOLLOWING SEVERE EXACERBATIONS OF ASTHMA

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Introduction/Aim: Blood eosinophils, fraction of exhaled Nitric Oxide (FeNO), serum periostin and serum IgE are biomarkers of Type 2 inflammation in asthma. We aimed to identify the time course of these biomarkers during and after severe exacerbations to understand how a recent exacerbation may affect their clinical utility in identifying patients likely to benefit from monoclonal antibody therapy directed against IgE, IL-4Rα, IL-5 and IL-13.

Methods: 34 adults with asthma were recruited within 24 hours of starting systemic corticosteroid therapy for a severe asthma exacerbation. Blood eosinophils, FeNO, serum periostin and serum IgE levels were measured at six visits over 12 weeks. Mixed linear models were used to compare reference biomarker measurements at 12 weeks with those at each previous visit, under the assumption that levels would return to previous stable readings by study end.

Results: Mean blood eosinophil level was lowest at week zero ($0·07$ vs $0·33$ x10^9/L), difference 0.25x10^9/L (95% CI 0.15-0.36), $P<0·001$; median FeNO was lowest at week two (23 vs 33 ppb), ratio of geometric means (RGM) $0·79$ (95% CI 0·63-1·01), $P=0·06$; median serum periostin was lowest at week one (45·9 vs 50·9 ng/ml), RGM $0·86$ (95% CI 0·82-0·92), $P<0·001$; median serum IgE was highest at week zero (339 vs 249 U/L), RGM $1·32$ (95% CI 1·22 to 1·43), $P<0·001$.

Conclusion: The time course of change for each of these Type 2 biomarkers are different following treatment for severe exacerbations of asthma. A delay of up to four weeks following a severe exacerbation is required if these biomarkers are used to identify patients likely to benefit from monoclonal antibody therapy.

Conflict of Interest: Funding for the study was provided by Genentech Inc.

TP 087

DE-RECRUITMENT IN ASTHMATIC AND HEALTHY SUBJECTS ASSESSED VIA FOT

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Introduction/Aim: De-recruitment plays an important role in asthma given its strong relationship with clinical parameters. Recently, the forced oscillation technique (FOT) has been used to identify surrogate measures of airway closure via reactance (Xrs) lung volume relationships. In this study, we tested the hypothesis that there are two independent lung volume markers of de-recruitment: 1. where de-recruitment is initiated (DR1) and 2. where rapid de-recruitment commences (DR2). We also hypothesize that these lung volumes correlate with different physiological and clinical markers.

Methods: Asthmatic (n=20) and control (n=19) subjects were included in the study. DR1 and DR2 were identified on the Xrs percentage lung volume relationship via an automatic algorithm. DR1 and DR2 were compared to other physiological measurements obtained via spirometry, multiple breath nitrogen washout and the ACQ6 asthma questionnaire, by obtaining the correlation coefficients and p values.

Results: Asthmatics had higher values of $DR1_{vol}$ and $DR2_{vol}$ (p<0.001) indicating the de-recruitment was at a higher lung volume. The rate of de-recruitment of the asthmatics was also significantly slower than the control group (p<0.01). In the control group, $DR1_{vol}$ and $DR2_{vol}$ were positively correlated with age (r=0.79 and r=0.73 respectively). In the asthmatic group $DR1_{vol}$ both and $DR2_{vol}$ were highly correlated (r>0.4 and p<0.01) with symptoms and physiological markers of disease (Scond, Sacin, ACQ6), while only $DR1_{vol}$ correlated with spirometry parameters (FEV1, FRC and FER).

Conclusion: This study demonstrates that two different de-recruitment volumes are evident via Xrs percentage lung volume relationships. Also, the initiation and rate of de-recruitment are altered in subjects with asthma.

This abstract has been withdrawn

TP 089

BELIEFS ABOUT MEDICINES AND ADHERENCE TO ASTHMA MEDICATION IN PREGNANCY

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Introduction/Aim: Non-adherence to inhaled corticosteroids (ICS) is a significant issue in pregnancy; however the reasons for this are unknown. This study aims to characterise beliefs about medicines in pregnant women with asthma and determine whether an association with ICS adherence exists.

Methods: Pregnant women (n=284) completed the validated Beliefs about Medicines Questionnaire (BMQ), consisting of 10 questions about asthma medicines (characterised into "necessity" questions about maintaining health, or "concern" questions about adverse effects), and 8 general medicine questions, each scored on a 5-point Likert Scale. The Necessity-Concerns differential (N-C) was calculated, with positive scores indicating that the patient perceives the benefits of medicines to outweigh the costs.

Results: 88 women used ICS, with 46 (52%) self-reporting adherence (≥80% of prescribed doses taken in past week) and 42 (48%) non-adherence. 30% of participants agreed or strongly agreed that they sometimes worry about becoming too dependent on their asthma medication. The majority (80%) believed that their asthma medication would protect them from becoming worse. 21.1% believed that doctors use too many medications, and 16% believed that if doctors had more time with patients they would prescribe fewer medicines. The median N-C was 8 and 5 for women who were adherent and non-adherent, respectively (P=0.008).

Conclusion: Approximately half of all pregnant women were nonadherent to ICS. Pregnant women with asthma who report non-adherence to asthma medicines also express negative concerns about their treatment. Interventions which target beliefs and attitudes about asthma medication use in pregnancy are needed.

PASSIVE INTRINSIC AND INDUCED ACTIVE TONE TO ACETYLCHOLINE AND HISTAMINE IN HUMAN SMALL AIRWAYS IN VITRO

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Introduction/Aim: Passive intrinsic tone is the tension generated by the airway smooth muscle in the absence of any exogenous stimuli. Human large airways (3-12mm inner diameter) *in vitro* exhibit an intrinsic tone of approximately 50 percent of the maximal contractile response. Given the current interest in small airway diseases such as asthma and chronic obstructive pulmonary disease (COPD), it is important to establish what is normal in regards to airway responsiveness and tone in these airways. This study explored the baseline parameters for assessing contraction of small airways *in vitro.*

Methods: Resected lung tissue was acquired from five adult cancer patients (3 female; age 68 ± 13 years) with normal lung function. Small airway rings (1-4mm) internal diameter; n=17 tissues) were dissected free from the parenchyma and mounted into a wire myograph chamber. Optimal tissue length (L_O) was determined by measuring force generated to 60mM KCl at increasing tissue lengths. At L_O concentration-response curves were generated to acetylcholine (ACh) and then to histamine in the presence of atropine ($1\mu M$). Finally to determine intrinsic airway tone, theophylline (10mM) was added to fully relax the airways.

Results: Mean internal diameter (ID) at L_O was 2.8 ± 0.9mm. Maximal active wall tension to ACh and histamine were 2.5 ± 0.7mN/mm and 2.4 ± 0.75mN/mm, respectively. Active wall tension to ACh and His were highly correlated to each other (P<0.0001). Potency to ACh and histamine were $1.7\mu M$ 95% CI [1, $3\mu M$] and 154nM 95% CI [92, 258nM], respectively (histamine approximately 10 fold more potent). Potency/sensitivity for ACh and His were positively correlated with ID, r=0.53 (P=0.03) and r=0.50 (P=0.04), respectively. The intrinsic passive tone as a percentage of maximal active tone was $12\pm8\%$.

Conclusion: Small human airways exhibited increased sensitivity to histamine compared with ACh and considerably less intrinsic airway tone (~12%) than that reported previously for large airways (~50%).

TNF AND LPS EXERT DIFFERENTIAL EFFECTS ON THE REACTIVITY OF INTRAPULMONARY AIRWAYS AND ARTERIES IN MOUSE PRECISION CUT LUNG SLICES

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Introduction: Inflammation-induced increases in airway and vascular reactivity contribute to diseases such as asthma and pulmonary hypertension. Whilst *in vitro* exposure to bacterial lipopolysaccharide (LPS) or the inflammatory cytokine tumour necrosis factor alpha (TNFα) have been shown to affect reactivity of large airways and pulmonary arteries, their influence on small intrapulmonary airways and arteries have yet to be defined.

Aim: To use the precision-cut lung slice (PCLS) technique to determine the effect of *in vitro* treatment with LPS or TNFα on responses to broncho/vasoconstrictors in intrapulmonary airways and arteries.

Methods: 8-week old male C57BL6 mice were culled and lungs were inflated with agarose and collected for preparation of PCLS. Multiple PCLS from each mouse were cultured overnight in the absence or presence of $10\mu g/mL$ LPS or 10ng/ml TNFα. Contraction of intrapulmonary airways and arteries (80-200μm) in response to the thromboxane mimetic U46619 and endothelin-1 (ET-1) were assessed *in situ* under phase contrast microscopy and expressed as % reduction in lumen area.

Results: After LPS treatment, contraction to ET-1 increased in both airways (maximum contraction (%): untreated $61 \pm 4\%$ n=11; +LPS $81 \pm 7\%$ n=4, p<0.05) and arteries (untreated $35 \pm 6\%$ n=9; +LPS 33%, 100% n=2). Incubation with TNFα increased vasoconstriction to U46619 (untreated $23 \pm 3\%$ n=11; +TNFα $45 \pm 10\%$ n=7, p<0.05) but not to ET-1, while airway responses to both contractile agonists were unaltered with TNFα treatment.

Conclusion: This study demonstrates differential effects of inflammatory mediators on airway and artery contractile responses in PCLS. Further insights into the disease-specific drivers and mechanisms underlying altered reactivity may identify novel approaches for therapeutic targeting of small intrapulmonary airways and arteries in lung diseases.

This abstract has been withdrawn

DUPILUMAB IMPROVES ACQ-5 ITEMS IN CRSWNP PATIENTS WITH COMORBID ASTHMA

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Introduction/Aim: Dupilumab is a fully human monoclonal antibody, directed against the shared IL-4Rα subunit, that inhibits interleukin (IL)-4 and IL-13, which are key drivers of type 2-mediated inflammation. Dupilumab is approved in the USA and EU for the treatment of adults with moderate-to-severe atopic dermatitis. In a phase 2a study (NCT01920893), dupilumab improved endoscopic, radiographic, and clinical endpoints in patients with chronic rhinosinusitis with nasal polyposis (CRSwNP) and comorbid asthma. This post hoc analysis evaluates the effect of dupilumab on each of the 5 items of the Asthma Control Questionnaire (ACQ-5) in patients with CRSwNP and asthma.

Methods: CRSwNP patients refractory to intranasal corticosteroids were assigned to weekly doses of subcutaneous dupilumab 300 mg or placebo, with mometasone furoate nasal spray. Asthma control was assessed using ACQ-5 at baseline and at Week 16.

Results: Of 60 patients enrolled, 58.3% had asthma and used asthma medications. Dupilumab showed clinically relevant improvements in total ACQ-5 (Table). Differences vs placebo were significant for each of the 5 items assessing asthma symptoms (shortness of breath; wheezing time; awake in the morning with symptoms; activity limitation; and nighttime awakenings). Asthma-control improvement correlated with improvement in patient-reported outcomes (visual analogue scale; 22-item Sino-Nasal Outcome Test) and nasal polyp score. Injection-site reactions, headache, and nasopharyngitis were the most frequently reported adverse events with dupilumab.

Conclusion: In CRSwNP patients with asthma, dupilumab significantly improved all asthma-related measures. Improvement correlated with reduced nasal polyp burden.

ACQ-5	Measure	Mean score (SD) at baseline		LS mean change (SE) from baseline to Weak 16			Incidence of patients achieving MCID of 0.5 based on change from baseline to Week 16, n (%)	
		Placebo (n =19)	Dupilumab (n = 16)	Placebo (n = 19)	Dupilumab (n = 16)	LS mean difference (95% CI)	Placebo (n =19)	Dupilumab (n= 16)
Overall	Total score	1.63 (0.87)	1.55 (1.11)	-0.10(0.20)	-1.19(0.19)	-1.09 (-1.54,-0.63)***	3 (15.8)	10 (62.5)* odds ratio 9.50 (95% CI 1.13, 80.03)
1	Woken at night by asthma	1.00 (1.10)	0.88 (1.45)	0.08 (0.24)	-0.91 (0.23)	-0.99 (-1.55, -0.42)**		
2	Awake in the morning with symptoms	2.00 (1.37)	1.69 (1.25)	0.01 (0.22)	-1.46 (0.20)	-1.46 (-1.94, -0.99)***		
3	Limited in activities	1.38 (1.20)	1.25 (1.13)	-0.11 (0.23)	-0.93 (0.21)	-0.83 (-1.34, -0.32)**		
4	Shortness of breath	2.19 (1.33)	1.94 (1.24)	-0.29 (0.29)	-1.33 (0.27)	-1.04 (-1.77, -0.31)**		
5	Wheezing time	1.56 (0.63)	2.00 (1.90)	-0.54 (0.36)	-1.50 (0.34)	-0.96 (-1.81, -0.12)*		

*P ≤ 0.05 vs placebo; **P ≤ 0.01 vs placebo; ***P < 0.001 vs placebo. CI, confidence interval; LS, least-squares; MCID, minimal clinically important difference; SD, standard deviation; SE, standard error.

DUPILUMAB IMPROVES FEV$_1$ AND EXACERBATIONS IN ASTHMA WITH ALLERGIC RHINITIS

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Introduction/Aim: Allergic rhinitis (AR) is a common type 2 comorbidity in asthma patients. In addition to having higher exacerbation rates and healthcare costs, asthma patients with AR (vs those without AR) have worse asthma disease control, symptoms, and quality of life (QoL). Dupilumab is a fully human monoclonal antibody, directed against the shared IL-4Rα subunit, that inhibits interleukin (IL)-4 and IL-13, which are key drivers of type 2-mediated inflammation. Dupilumab is approved in the USA and EU for the treatment of adults with moderate-to-severe atopic dermatitis. In a pivotal phase 2b study (NCT01854047), dupilumab improved lung function and QoL measures, reduced severe asthma exacerbations, and was generally well tolerated in adults with uncontrolled persistent asthma on medium-to-high-dose inhaled corticosteroids plus a long-acting β$_2$-agonist (ICS+LABA). This post hoc analysis assessed efficacy findings in asthma patients with self-reported ongoing comorbid AR.

Methods: Patients received dupilumab 200/300 mg every 2 weeks (q2w; currently being investigated in phase 3 [NCT02414854]) or 4 weeks, or placebo. Change from baseline to Weeks 12 and 24 in forced expiratory volume in 1 second (FEV$_1$; L and %) and annualized severe asthma exacerbation rate over the 24-week treatment period are reported.

Results: Dupilumab 200 and 300 mg q2w improved FEV$_1$ (L) ($P<0.05$ vs placebo) at Weeks 12 and 24. The severe exacerbation rate was lower ($P<0.05$ vs placebo) with both dupilumab doses (Table).

Conclusion: In asthma patients with ongoing AR, dupilumab added to ICS+LABA improved FEV$_1$ and reduced severe asthma exacerbations. Future studies are required to further investigate the benefit of dupilumab in this subgroup.

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	Week 12			Week 24		
	Placebo (n =158)	Dupilumab 200 mg q2w (n =150)	Dupilumab 300 mg q2w (n = 157)	Placebo (n = 158)	Dupilumab 200 mg q2w (n = 150)	Dupilumab 300 mg q2w (n = 157)
Patients with ongoing AR at baseline, n	99	95	92	99	95	92
FEV,(L)						
Mean (SD) at baseline	1.84 (0.56)	1.84 (0.54)	1.87 (0.54)	1.84 (0.56)	1.84 (0.54)	1.87 (0.55)
Patients, n	97	89	90	92	86	89
LS mean change from baseline (SE)	0.16 (0.04)	0.31 (0.041)	0.28 (0.04)	0.16 (0.04)	0.28 (0.04)	0.28 (0.04)
LS mean difference vs placebo (95% CI)	-	0.15 (0.04-0.25)	0.11(0.00-0.22)		0.11 (0.00-0.22)	0.12 (0.01-0.23)
P value vs placebo	-	0.0077	0.0417	-	0.0410	0.0282
LS mean percent change from baseline (SE)	9.13 (2.37)	17.00 (2.45)	17.84 (2.46)	8.24 (2.32)	15.25 (2.39)	17.69 (2.39)
LS mean difference vs placebo (95% CI)	-	7.88 (1.29-14.47)	8.71 (2.12-15.31)	-	7.01(0.57-13.44)	9.44 (3.01-15.87)
P value vs placebo	-	0.0192	0.0097	-	0.0329	0.0041
Annualized rate of severe exacerbations	-	-	-			
Patients, n	-	-	-	99	93	92
≥ 1 exacerbation in the 24-week treatment period, n (%)	-	-	-	23 (23.2)	10 (10.8)	12 (13.0)
Adjusted annualized severe exacerbation event rate estimate (95% CI)	-	-	-	0.894 (0.573-1.393)	0.269 (0.137-0529)	0.302 (0.160-0.570)
Risk reduction vs placebo, %	-	-	-	-	69.9	66.2
P value vs placebo	-	-	-		0.0027	0.0044

CI, confidence interval; LS, least-squares; SD, standard deviation; SE, standard error.

This abstract has been withdrawn

Chronic Obstructive Pulmonary Disease (COPD) 2

12-MONTH FOLLOW-UP OF 2016 EPIDEMIC THUNDERSTORM ASTHMA PATIENTS WITH PRIOR ASTHMA DIAGNOSIS ASSESSING SYMPTOMS, PREVENTER USE, ASTHMA ACTION PLAN OWNERSHIP AND HEALTH CARE UTILISATION

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Introduction/Aim: Epidemic thunderstorm asthma(ETSA) severely affected Melbourne in November 2016. There is scant literature on the natural history of individuals affected by ETSA. This is a 12-month follow-up study of Eastern Health ETSA patients with prior asthma diagnosis assessing their symptomology and behaviours.

Methods: A standardised telephone questionnaire was developed and administered between 4th-15th December 2017 to individuals affected by 2016 ETSA(n=232). The questionnaire assessed asthma symptoms, preventer prescription and adherence, asthma action plan ownership and healthcare utilization.

Results: 86.2%(n=200) of ETSA patients responded. 42.5%(85) had a prior diagnosis of asthma with 70.6%(60) and 29.4%(25) categorized as "current asthma" or "past asthma" (symptoms within or longer than 12 months before ETSA presentation) respectively.

3%(2) of patients with "current asthma" were asymptomatic on follow-up, with 50%(30) reporting infrequent episodic (up to 1/month), 11.7%(4) frequent episodic (>1/month but <1/week) and 35%(21) persistent symptoms (≥1/week). 12%(3) of patients with "past asthma" remained asymptomatic with 60%(15) reporting infrequent episodic, 12%(3) frequent episodic and 16%(4) persistent symptoms.

Amongst those with a prior asthma diagnosis, 88%(22) of those with persistent symptoms were prescribed preventers, with 72.7%(16) demonstrating adherence (≥5 days/week). This compared with 60%(36) of those in the other groups combined, with 55.6%(20) adherent.

Asthma action plan ownership was 52%(13) in those with persistent symptoms and 43.3%(26) in those without. 32%(8) of patients with persistent symptoms utilised healthcare services (urgent visit to GP, ED presentation or hospitalization) during the follow-up period compared to 20%(12) in the other groups combined.

Conclusion: The majority of patients affected by 2016 ETSA with a prior diagnosis of asthma had ongoing symptoms on follow-up. Those without persistent symptoms had suboptimal preventer use and adherence. Furthermore, nearly a quarter of all patients required urgent healthcare review for asthma in the follow-up period. Optimisation of preventer usage and action plan ownership may improve asthma control and healthcare utilisation in patients with ETSA.

BARRIERS AND FACILITATORS TO THE IMPLEMENTATION OF COPD SCREENING IN AUSTRALIAN PHARMACIES: A QUALITATIVE ANALYSIS

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Introduction/Aim: Studies demonstrate that COPD case-finding by community pharmacists is feasible and effective. A pharmacist-delivered case finding service recently conducted in New South Wales (using evidence based criteria, micro-spirometry and referral of at-risk patients to GPs) produced a diagnostic yield of 15% which may have been limited by by not all participating pharmacists reaching the target number of screened patients.We aimed to investigate the barriers and facilitators encountered by the pharmacists in the NSW COPD case-finding service to facilitate the wider adoption of this service model.

Methods: Community pharmacists participated in semi-structured telephone interviews within three months of case-finding service completion. Interviews were recorded and transcribed verbatim. Data were analysed thematically and managed using NVivo version 11 software (QSR International Pty Ltd.).

Results: Fifteen of 21 pharmacists (male 53%; age 39.8±8.6yrs, rural 47%) in the NSW case-finding service participated in a telephone interview. In general, the pharmacists engaged positively with the service. Our analysis revealed three 'barrier themes': *'challenges of patient recruitment'*, *'poor community awareness of pharmacy services'* and *'poor interdisciplinary collaboration'* and three 'facilitator themes': *'pharmacist adaptation/entrepreneurship'*, *'training opportunities'* and *'professional satisfaction'.* Suggestions for future implementation included training all pharmacy staff (not just the pharmacist providing the service), creating public awareness about pharmacy services to increase their acceptability, providing pharmacists with remuneration, and streamlining referral logistics to improve GP referral uptake.

Conclusion: Improving COPD diagnosis and treatment requires the involvement of all segments of primary health care, including community pharmacy. Data from this study identifies the main barriers and facilitators to provision of a feasible and effective COPD screening service in Australian pharmacies. Future research is recommended into the benefits of digital tools and electronic decision support algorithms for COPD case-finding screening to support service provision.

THE CHRONIC RESPIRATORY QUESTIONNAIRE HAS A HIGHER RESPONSIVENESS TO PULMONARY REHABILITATION COMPARED TO THE COPD ASSESSMENT TEST

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Introduction/Aim: Assessment of disease-specific quality of life is a key component of pre- and post-pulmonary rehabilitation (PR) outcome measurements. The PR programme at Alfred Health, Melbourne, has traditionally utilised the Chronic Respiratory Questionnaire (CRQ) for this assessment, however recently, the COPD Assessment Test (CAT) has become increasingly popular. Whether the CAT is equally responsive to PR as the more established CRQ, is unclear.

Methods: Over 3-years, CRQ and CAT scores were routinely collected pre and post PR. All PR participants with pre and post CRQ and CAT results were included in the analysis. Mean change scores were compared using paired t-tests. The number of individuals who achieved the minimal important difference (MID) for each measure was calculated, along with correlations between change scores using Spearman's Rho. Responsiveness of each tool was evaluated using standard response means (SRM).

Results: Participants (n=92) were 49 males, mean age 69 (SD 13) years, COPD n=44 (48%). CAT and CRQ scores improved from baseline (all p<0.05). Only 50% of individuals achieved the MID for the CAT and 45% for the CRQ total score. There was a weak negative correlation between the change scores generated by the CAT and CRQ total (r_S=0.4, p<0.001). Responsiveness was moderate for CRQ dyspnoea domain (SRM=0.7) and the total CRQ score (SRM=0.6), however the CAT was less responsive to PR (SRM=0.3).

Conclusion: The CRQ demonstrated greater responsiveness compared to the CAT tool in people with chronic respiratory disease undergoing PR. The CRQ and CAT were weakly correlated, suggesting the tools measure different constructs and are not interchangeable. The CRQ may better reflect changes in dyspnoea-related quality of life following PR.

Grant Support: None to declare.

RECRUITING ADULT OFFSPRING OF PEOPLE WITH COPD TO EXPLORE INTERGENERATIONAL LUNG HEALTH: FEASIBILITY STUDY

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Introduction/Aim: Parental history of COPD increases the likelihood of the same condition occurring in their adult offspring. Despite this, familial associations have not generally been a focus of early examination of lung health. Proband-initiated recruitment is a screening/case-finding strategy used to recruit family members of people with conditions that have well-known genetic components. This study aimed to test the feasibility of using this recruitment method to investigate lung health in adult offspring of parents diagnosed with COPD.

Methods: People with confirmed COPD (proband) were identified and contacted by mail from four hospital/clinic databases or face-to-face during a pulmonary rehabilitation program. Ethical considerations required that interested probands be invited to pass on study information to their adult offspring, who if interested, could then contact the researchers. Any comments volunteered by potential participants were recorded.

Results: 645 proband were contacted through mail (n= 546) or face-to-face (n=99), resulting in four offspring recruited (1% offspring response rate).

Fifty-eight (11%) proband invited by mail made contact with the researcher; 16 agreed to pass information on to their adult offspring and four offspring consented to participate.

Of those approached face-to-face, forty-one (41%) eligible proband indicated interest in the study. One contacted the researcher regarding passing information onto their adult offspring, who later declined to participate.

Common reasons that proband (n=74) declined to pass information onto their offspring include: offspring lives interstate/overseas (39%), no offspring (28%), perception that their offspring are too busy (14%) or would not be interested (7%).

Conclusion: Low recruitment of adult offspring by contacting people with diagnosed COPD indicate that this process was not feasible to investigate offspring exposures and lung health. Some known parent-related barriers were identified that include possible low prioritisation of lung health as an issue but offspring-related barriers remain unknown.

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DELAYED TIME TO FIRST AND SUBSEQUENT EXACERBATIONS INDEPENDENT OF SEASON WITH INDACATEROL/GLYCOPYRRONIUM COMPARED WITH SALMETEROL/FLUTICASONE: THE FLAME STUDY

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Introduction: Seasonal differences have been identified in the pattern of COPD exacerbations.[1]

We compared the efficacy of indacaterol/glycopyroonium (IND/GLY) vs salmeterol/fluticasone (SFC) in reducing exacerbations across seasons and in reducing the risk of multiple exacerbations in patients with moderate-to-very severe COPD.

Methods: FLAME was a 52-week, double-blind, double-dummy study, randomised (1:1) patients (with past year history of ≥1 exacerbation) to IND/GLY 110/50 μg once daily or SFC 50/500 μg twice daily[2]. Here, we assessed the rate of moderate/severe exacerbation, and time to first and subsequent exacerbations.

Results: Of the 3362 patients randomised, 82.2% completed the 52 weeks of study treatment. IND/GLY significantly reduced the rate of moderate/severe exacerbation in both spring/summer and fall/winter seasons vs SFC (Table). IND/GLY significantly delayed the time to 1st, 2nd, and 3rd exacerbation (moderate/severe), with a 22% (95% CI, 14 to 30%; $P<0.001$), 24% (95% CI, 11 to 34%; P<0.001), and 29% (95% CI, 9 to 44%; $P = 0.006$) reduction in risk vs SFC, respectively.

Conclusion: IND/GLY was more effective than SFC in reducing COPD exacerbations in both seasons and should be considered as the preferred first-line treatment option in COPD patients at high risk of exacerbations.

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Table 1 Annualized rates of moderate/severe exacerbations during 52 weeks of treatment with IND/GLY vs SFC by season

Season	Exacerbation Outcomes	Annualized rate[1] (95% CI)		Rate ratio (95% CI)
		IND/GLY 110/50 μg o.d. (N=1675)	SFC (50/500 μg b.i.d. (N=1679)	
Spring/Summer	Rate of moderate or severe COPD exacerbations	0.79 (0.68-0.92)	0.95 (0.82-1.09)	0.84 (0.73-0.96) P=0.010
Fall/Winter	Rate of moderate or severe COPD exacerbations	1.11 (0.98-1.26)	1.35 (1.19-1.52)	0.83 (0.74-0.92) P<0.001

[1]Rate per 365 days of the season group. b.i.d., twice-daily; IND/GLY, indacaterol/glycopyrronium; o.d., once-daily; SFC, salmeterol/fluticasone

POST-HOSPITALISATION SHORT-TERM OXYGEN THERAPY: A RETROSPECTIVE STUDY

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Introduction/Aim: Home oxygen therapy is commonly prescribed for patients who remain hypoxaemic at hospital discharge, although there is a lack of evidence supporting this practice. The aim of this study was to evaluate the prescription and follow-up of patients who were discharged with home oxygen therapy following hospitalisation in a tertiary hospital setting.

Methods: A retrospective audit of patients who were discharged with home oxygen following hospitalisation from January 2011 to December 2015 was conducted. A designated clinical pathway for prescription of home oxygen therapy and follow-up following hospital discharge was present during the study period. Chart review was performed to collect patient demographics, comorbidities, oxygen assessment and prescription, follow-up re-assessment and mortality.

Results: Over 5 years, 205 patients were prescribed home oxygen therapy at hospital discharge. The study population was male predominant (58%) with a median age of 75 years. The majority of patients were admitted under Respiratory Medicine (29%), General Medicine (20%) and Medical Oncology (20%). Only 71 (35%) patients had detailed oxygen assessments prior to therapy prescription. Common indications for therapy were chronic lung disease (54%) and palliation (26%). Among the 118 patients who attended their scheduled review appointment 4 to 6 weeks after discharge, 47 (40%) did not fulfil the criteria for long-term oxygen therapy. The 1-year cumulative survival rate for the study population was 56%.

Conclusion: For those patients who were discharged with home oxygen therapy, a significant proportion either failed to attend reassessment following hospital discharge or did not fulfil the criteria for long-term oxygen therapy at reassessment. The assessment for patients who were prescribed with home oxygen therapy at hospital discharge was inadequate. Adherence to the clinical pathway and education for both clinicians and patients should be emphasised.

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OUTCOMES OF IMPLEMENTATION OF AN INTEGRATED MULTIDISCIPLINARY INPATIENT COPD PATHWAY

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Introduction/Aim: To assess the effect of an integrated clinical management pathway in chronic obstructive pulmonary disease (COPD) exacerbations on hospital length of stay, readmission rate and clinicians and patients' satisfaction with the pathway.

Methods: A clinical management pathway for COPD exacerbations was developed and implemented at the Lyell McEwin Hospital as a trial from February to December 2016. We evaluated the effectiveness of the COPD pathway by calculating the average length of stay (ALOS) and readmission rate during the implementation of the COPD pathway, and this was compared to baseline data obtained 12 months prior to the trial. Clinicians' satisfaction was assessed using an online survey and patients' satisfaction was evaluated by telephone survey 28 days following discharge of patients during the trial.

Results: Baseline data indicated an ALOS for COPD exacerbations of 4.31 days and a 28-day readmission rate of 18.90%. Implementation of the COPD pathway was associated with a reduction in ALOS of 0.31 days and a decrease in readmission rate by 1.3%. Extrapolating this data, in our institution, use of the pathway over the 2016 calendar year would have equated to a possible reduction in 286 occupied bed-days, with indicative savings of approximately $314 000. Survey data collected indicated that staff felt instructions were clear, and patients were confident in using their COPD action plan and emergency pack of medications.

Conclusion: An inpatient multidisciplinary COPD pathway is effective in reducing length of stay for pulmonary exacerbations, and is generally well received by staff and patients. It is less effective in reducing 28-day re-admissions and further work is required for this outcome

BETA-BLOCKER USE IN COPD PATIENTS WITH CARDIOVASCULAR DISEASE IN A MAJOR SYDNEY HOSPITAL

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Introduction/Aim: In Australia, about 30% of patients with Chronic Obstructive Pulmonary Disease (COPD) die from heart disease. Beta-blockers remain one of the most affordable and efficacious classes of medications to reduce cardiac-related morbidity and mortality. However, despite increasing evidence for the safety of beta-blockers in COPD, their use in COPD patients with known cardiac indications remains inconsistent. We reviewed all admissions to a major Sydney hospital in patients with both a history of COPD and co-morbid cardiac disease over a 12 month period to determine beta-blocker prescription rates in COPD patients.

Methods: A retrospective cohort study was conducted across all patients admitted to Concord Repatriation General Hospital (CRGH) from May 2016 to May 2017 with a history of either an acute exacerbation or stable COPD, and a known or new cardiac condition for which a beta-blocker is indicated. Patient demographics recorded included age, sex, length of stay, beta-blocker prescription and whether the patient either died in hospital or was readmitted within 28 days.

Results: 198 patients meeting criteria were admitted to CRGH within the study period. The mean age was 79 ($\pm$ 10.5) and 59% were male. Overall only 75 (37.9%) of patients with an indication for beta-blocker therapy were prescribed such. The most commonly prescribed beta-blockers were bisoprolol (38.7%), metoprolol (24.0%) and carvedilol (14.7%). Only 4 patients (2.0%) were commenced on beta-blocker therapy during admission. Furthermore, of the 47 patients that were readmitted within 28 days, 32 (68.1%) were still not prescribed a beta-blocker.

Conclusion: Our results show that beta blockers are under-prescribed in the COPD population at a major Sydney hospital.

FACTORS ASSOCIATED WITH READMISSION AFTER CHRONIC OBSTRUCTIVE PULMONARY DISEASE RELATED HOSPITALISATION

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Introduction/Aim: Acute exacerbations of Chronic Obstructive Pulmonary Disease (COPD) are associated with increased morbidity and mortality. Readmission within 30 or 60 days of discharge remains common. The purpose of this study was to identify factors in COPD admissions that are associated with readmission at two Melbourne teaching hospitals.

Methods: Admissions where COPD was the principal diagnosis between August 1st and December 31st 2016 were retrospectively reviewed through the electronic database of Western Health. Information pertaining to the patient, COPD severity and treatment, as well as to the admission itself was recorded. Admissions were not recorded if they were incomplete, if follow-up was not possible, or if the admission concluded with death. Data was analysed through STATA (v14.2).

Results: 211 admissions were included. The outcome 30-day readmission occurred 39 times (19.0%) and the outcome 60-day readmission occurred 60 times (28.4%). Patients who were readmitted were generally older and male. Univariate analysis demonstrated that the risk of 30-day readmissions was higher in patients with more previous COPD or total admissions, lower FEV_1, higher bicarbonate levels, abnormal chest x-rays, admissions to Footscray Hospital, higher number of regular medications, and a recent history of pulmonary rehabilitation or Hospital Admission Risk Program participation.

Multivariate analysis showed that a higher number of regular medications, a recent COPD admission, a higher white blood cell count, and higher bicarbonate levels on admission were associated with 30-day readmissions (corrected for age, sex, and hospital site). Similar associations were observed for 60-day readmission.

Conclusion: Readmission within 30 and 60 days of discharge after admission for AECOPD are common in the Western Health population. Several factors were significantly associated with readmission, in particular those related to COPD severity.

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FEASIBILITY OF NHF FOR ACUTE HYPERCAPNIC RESPIRATORY FAILURE IN COPD

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Introduction/Aim: Non-invasive ventilation (NIV) is part of the standard of care for the management of acute hypercapnic respiratory failure in patients with acute exacerbation of COPD (AECOPD). However, NIV is often poorly tolerated. Nasal high flow therapy (NHF) is effective in non-hypercapnic respiratory failure but its utility in hypercapnic respiratory failure is unknown. We aimed to determine the feasibility of a randomised controlled trial of NHF in patients with AECOPD and acute hypercapnic respiratory failure.

Methods: Patients presenting to the Emergency Department (ED), Wellington Hospital, were enrolled and received protocolised standard medical care. Baseline paired arterial and venous blood gas measurements were recorded. Participants with an initial pH 7.25 to 7.34 had a further ABG after a 60 minute optimisation period. Enrolment and data collection was by ED staff. Consent to use data was sought once participants had capacity.

Primary outcome: The proportion of patients with protocol defined treatment failure after 60 to 90 minutes. *Secondary outcomes* included recruitment and eligibility rates.

Results: During the four month study period 120 people were admitted with a primary diagnosis of AECOPD, of whom 56 (47%) received an initial ABG as per study protocol. 7/56 (12.5%) participants were acidotic on initial ABG, 4/56 (7%) had an initial pH in range for the study and 3/56 received a second ABG after the optimisation period. Care deviated from the agreed protocol in 1 of 3 enrolled participants. Only 2 enrolled participants received the second ABG after 60 minutes, both had protocol defined treatment failure.

Conclusion: Lower than expected rates of ABG sampling and of hypercapnic respiratory failure mean that an RCT comparing NIV and NHF is unlikely to be feasible with this design. Factors which may affect enrolment include the presence of dedicated research staff in the ED and the requirement for ABG sampling.

Grant Support: None

CARDIAC EVENTS AND MORTALITY FOLLOWING ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE: AN AUDIT OF FOUR NEW ZEALAND HOSPITALS

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Introduction/Aim: Cardiac comorbidities are common in patients with COPD and COPD exacerbations are often associated with acute cardiac conditions. We assessed the frequency of cardiac events and mortality in the 2-years following admission for an exacerbation of chronic obstructive pulmonary disease (COPD) in four New Zealand hospitals.

Methods: A review of the clinical notes of 100 consecutive patients admitted with a primary diagnosis of an exacerbation of COPD during 2011/2012 was performed at Middlemore, Waikato, Wellington and Christchurch hospital. We recorded subsequent cardiac events, occurring either during or after the index admission, and further hospitalisations for exacerbations of COPD, and mortality of any cause within 2 years of the index admission.

Results: 400 patients' clinical notes were reviewed. The mean age on admission was 70 years and 54% were women. In total, 19.8% of patients experienced a cardiac event in the 2 years following the index admission and 61% had a further hospitalisation for exacerbation of COPD. Only 3.3% died during the index admission, but 36.5% of patients died within 2 years (*Figure*).
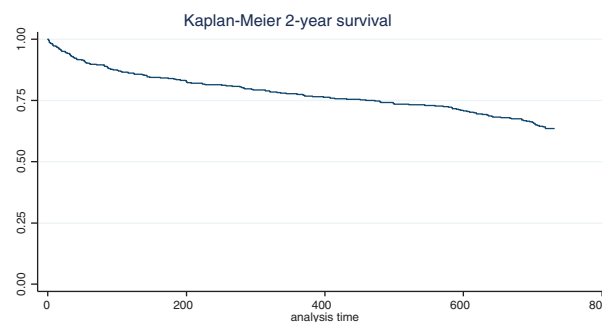

Figure 1   Survival after COPD exacerbation.

Conclusion: Although the inpatient mortality is low in New Zealand, over a third of patients die within two years of an admission for an acute exacerbation of COPD. Further hospitalisations for COPD exacerbations are very common and one fifth of patients had a cardiac event within 2 years of admission.

POTENTIAL EFFECTS OF REVISED PRESCRIBING CRITERIA ON AMBULATORY OXYGEN TESTING

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Introduction/Aim: Clinical utility of ambulatory oxygen in COPD patients with mild-moderate desaturation is lacking. Furthermore, the use of blinding in walk tests to determine suitability for ambulatory oxygen is variable but still recommended by TSANZ.

The aim is to estimate the effect of revised prescribing and use of 'gold standard' testing on respiratory laboratory costs and time.

Methods: A literature review was conducted and identified that the highest quality ambulatory oxygen assessment includes blinded, 3-step testing with room air, medical air and oxygen. Additionally revised prescribing criteria were proposed, based on the recent trial data[1] and known placebo effect of intranasal air versus oxygen, namely restriction to those patients that desaturate below SpO2 80%. The effect on cost and laboratory testing time was compared with the currently used 2-step room air/-oxygen assessment. 63 out of 65 COPD patients and 50 out of 52 patients in the non-COPD group were analysed from the records of the RHH Respiratory Function Unit from 2014-2016. 4 patients were excluded because of incomplete data.

Results: Modelling of revised prescribing criteria and adoption of a 3-step ambulatory oxygen test when applied to previous testing may result in a reduction in testing time of 10.3% for COPD and 15% in non-COPD patients. This equates to 10 minutes saved per test for a consecutive testing cohort of 100 patients. Potential cost savings of $13K and $6K in the COPD and non-COPD groups were calculated over a three-year period. Cost savings of $178 per patient from each 100 consecutive tests may be achieved.

Conclusion: Applying best evidence-based practice to ambulatory oxygen testing and prescribing in COPD and non-COPD patients is above cost-neutral, may generate savings of $178 per patient tested with modest improvement in laboratory testing time. Laboratories with higher testing volume may generate even greater efficiencies.

Grant Support: No funding received for this clinical audit.

SAFETY OF BI-WEEKLY INTRAVENOUS THERAPY WITH ALPHA-1 ANTITRYPSIN

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Introduction/Aim: Infusion of human alpha-1 proteinase inhibitor (A_1-PI) effectively slows the progression of emphysema in patients with alpha-1 antitrypsin deficiency (AATD). Nonetheless, weekly infusions of 60 mg/kg body weight are time consuming, costly and inconvenient, particularly when a patient plans to travel. The aim was to assess the safety of bi-weekly infusions of 120 mg/kg A_1-PI compared with weekly 60 mg/kg infusions.

Methods: The adverse event (AE) profile 7 days before a 120 mg/kg infusion was compared with the AE profile 7 days after the infusion.

Results: A placebo controlled trial of A_1-PI (Zemaira/Respreeza; RAPID-RCT), which randomised 180 patients, was followed by an open-label extension trial (RAPID-OLE) in which bi-weekly treatment with A_1-PI was permitted to cover holidays. The infusion adjusted event rate (IAER) of any treatment emergent AE was numerically higher in the 120 mg/kg A_1-PI and placebo groups compared with the corresponding 60 mg/kg groups (Table). However, AEs within the first 24 and 72 hours after infusion were comparable between all subgroups. The majority of reported AEs were infections of the upper and lower respiratory tract and exacerbations of COPD.

	933 infusions in 137 patients		374 infusions in 137 patients	
	A1-PI 60 mg/kg	A1-PI 120 mg/kg	Placebo 60 mg/kg	Placebo 120 mg/kg
Any TEAE	0.1029	0.1222	0.0960	0.1230
IAER 24 h	0.0354	0.0322	0.0321	0.0267
IAER 72 h	0.0568	0.0579	0.0535	0.0561

Conclusion: The IAER was similar between A_1-PI and placebo infusions. Doubling the dose, and thus the infusion volume, did not increase the IAERs after 24 and 72 h, the time in which volume effects would be expected to occur. No difference in tolerability between the two doses was detected.

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PREDICTORS OF CPAP ADHERENCE IN CHILDREN AND ADOLESCENTS WITH OBSTRUCTIVE SLEEP APNOEA

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Introduction/Aim: Obstructive Sleep Apnoea (OSA) is a common condition effecting 2-4% of children. Children are being increasingly treated with continuous positive airway pressure (CPAP), though its use is limited by poor adherence. The purpose of this study was to identify and describe the factors associated with adherence to CPAP.

Methods: We retrospectively reviewed the records and Polysomnography (PSG) scoring of children on CPAP for OSA during 2016 with a minimum of 6-month of CPAP usage data available. We studied the association of adherence (defined as median CPAP use per night of 4-hours or more for at least 6-months) with age, gender, obesity, Apnoea-Hypopnea Index (AHI) at diagnosis, change in AHI post treatment, socio-economic status (SES) and underlying aetiology.

Results: 85 children (28F) were included with a median age (IQR) at CPAP initiation of 5.8 years (2.6-12.2). 33(39%) were obese; 12 had Down's syndrome and 8 had Achondroplasia. AHI at diagnosis (n=76) was 14.35 (6.9-47.9) with a median improvement of 10.7 (4.4-40.8) with treatment. 57/78 (73%) children were considered adherent. Males were more likely to be adherent compared to females (80% adherence vs. 61%). Higher proportion of children with Achondroplasia were non-adherent (38% vs. 27%) though this difference was not statistically significant. Age, obesity, socio- economic status based on postcode, AHI at diagnosis and change in AHI with treatment did not predict adherence to CPAP therapy.

Conclusion: In this retrospective study, CPAP adherence was variable, though high proportion were adherent. Boys reported higher adherence rates though severity of OSA and degree improvement with treatment did not predict adherence. Prospective qualitative research is needed for better understanding of adherence governing factors, including data on patient and parent education at CPAP initiation and follow up.

Declaration of Interest: No conflicts of interest

OXYGEN EFFECT ON BREATHING PATTERN IN MULTIPLE BREATH NITROGEN WASHOUT PERSISTS INTO PRESCHOOL YEARS BUT IS OF SMALLER MAGNITUDE THAN FOUND IN INFANTS

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Introduction/Aim: Multiple breath inert gas washout (MBW) offers strong feasibility across all age ranges. Inert gas choice includes resident (e.g. Nitrogen, N_2) and non-resident gas options (e.g. Sulfur hexafluoride, SF_6). We have recently demonstrated detrimental effects of 100% oxygen (O_2) exposure on breathing pattern during N_2MBW in infants (Gustafsson et al JAP 2017): decreased tidal volume (V_T), minute ventilation (V_E) and increased end-tidal CO_2 ($ETCO_2$) most pronounced during initial O_2 exposure. In this study we investigated the persistence of this effect within the preschool age range (defined as 2-6 years of age).

Methods: Preschool subjects, experienced in MBW, were recruited from clinically indicated MBW tests at a tertiary paediatric centre (CHW). N_2MBW was performed in triplicate, with facemask interface, using commercial equipment (Exhalyzer D, Eco Medics AG, Switzerland). Standard test protocol (ERS/ATS consensus guidelines) was modified to contain an extended prephase (prior to 100% O_2 exposure, 30-60s) to ensure good estimation of baseline breathing pattern. Changes in V_T, V_E, $ETCO_2$, respiratory rate (RR), inspiratory drive ($V_T$in/V_T) were examined.

Results: Data collated from 20 subjects to date: mean (SD) age 4.3 (1.1) years, 75% cystic fibrosis, mean (SD) Lung clearance index 8.0 (1.3). Percent change in breathing pattern indices, compared to baseline, during initial O_2 exposure, in comparison to previously published infant cohort (tested on identical equipment) summarised below.

	Infant (n=10)	Preschool (n=20)
V_T	40% decline	11% decline
V_E	40% decline	14% decline
RR	no change	no change
Inspiratory drive ($V_T$in/V_T)	25% decline	7% decline
$ETCO_2$	5% increase	2% increase

Conclusion: Detectable differences in breathing pattern with 100% O2 exposure persist into the preschool age range but are of lesser magnitude than that observed in infants. Further work will examine whether magnitude also decreases with increasing age within this age range.

Conflict of Interest: No conflicts of interest to declare.

SINGLE VERSUS TRIPLICATE MEASUREMENTS IN ASSESSING DAY-TO-DAY FOT VARIABILITY

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Introduction: Objective tools for monitoring childhood asthma are urgently required, yet conventional lung function tests (e.g. spirometry, peak flow) are limited in this setting by their effort-dependent nature and limited insight into asthma control. The Forced Oscillation Technique (FOT) is a novel test performed during tidal breathing and assesses airway calibre and lung stiffness by measuring airway resistance (Rrs) and reactance (Xrs), respectively. We previously related day-to-day FOT variability to asthma control using triplicate measurements[1]; other work suggest single measurements may be sufficient to characterise this variability. We aimed to assess the effect of the number of measurements on estimation of day-to-day variability of FOT outcomes.

Methods: Data was analysed from 10 subjects, who performed 3x60-s technically acceptable FOT measurements daily using a commercial FOT system, under parent supervision over a 3-4 month period. FOT outcomes examined were Rrs and Xrs at 5 Hz, AX (area under the reactance curve), and resonant frequency. Variability of Rrs and Xrs was calculated from the running coefficient of variation over the past 7 days. Only technically acceptable runs were included. Values obtained using the first run vs. the mean of triplicate values were compared using Pearson correlations, paired t-tests, and Bland-Altman plots.

Results: Single versus mean-of-triplicate values were strongly correlated across all FOT outcomes (R>0.99, p<0.001). Magnitude and variability of all FOT outcomes obtained from single measurements were statistically higher compared to mean-of-triplicate measurements. The differences, however, were very small (<0.1 cmH$_2$O s L^{-1} or <4% of mean values for Rrs and Xrs) compared to known day-to-day variability and unlikely to be clinically relevant. Bland-Altman plots revealed no evidence of proportional bias.

Conclusion: A single measurement may be acceptable to quantify day-to-day FOT variability in trained children. This may increase overall feasibility of FOT for monitoring in the home and field settings.

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CAN WE DEVELOP A PAEDIATRIC APPROPRIATE BRONCHIECTASIS SEVERITY SCORE?

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Introduction/Aim: The 'Bronchiectasis Severity Index' (BSI) and the 'FACED' scores assess severity of disease in adults with bronchiectasis and have been validated in determining prognosis. However, a number of the clinical parameters are irrelevant to children.

Aims: 1.: To develop a disease severity score relevant for children with bronchiectasis.

2. To determine validity by comparing to other parameters associated with severe disease; antibiotic courses & clinic visits within a 12 month period.

Methods: We adapted the adult scoring systems to children with categories of; age, extension of disease, chronic infection, hospital admissions, presence of co-morbidities (total score 9), with the addition of lung function in a subgroup (total score 11). We separately recorded number of clinic visits within the previous year (scheduled by the clinical team; annual mild, 2 moderate, 4 or more severe) and the numbers of antibiotic courses picked up per year with an apriori definition (mild <2/year, moderate 2-4, severe >4). We then reviewed children in the database under current care at the Starship Bronchiectasis Clinic.

Results: There were 257 children appropriate for scoring, mean age 9.4 years (range 1.7 to 17.5 years) with a mean severity score of 4.4 (range 1-9) with 35 mild, 146 moderate & 76 severe. There was only moderate correlation between these categories and those determined by antibiotic pick-up, and clinic visits. With the addition of FEV1 there were 139 children (mean age 11.9 years, range 4.4 to 17.5 years), with a mean score 4.6 (range 1-11) with 18 mild, 104 moderate, & 17 severe.

Conclusion: In all parameters 28-40%of children have severe bronchiectasis. The clinical score correlated moderately with two other disease severity indicators meaning some adjusted weighting may be needed. The score also needs assessment in determining it ability to predict future outcomes.

TECHNOLOGY ENABLED LEARNING FOR SCHOOL STAFF ASTHMA TRAINING

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Introduction/Aim: One in 10 children in Australia is diagnosed with asthma. With children spending on an average 30% of their day at school, school staff are an important population who may be called upon to provide asthma first aid. Our aim was to investigate whether a technology enabled teaching resource improved asthma first aid knowledge and self-confidence among school staff.

Methods: We conducted a prospective randomised parallel study. School staff across Sydney were randomly assigned to receive asthma management training via the Asthma First Aid Management in Schools eBook, or standard face to face training. Each participant completed a 14 item asthma first aid knowledge questionnaire (AFAKQ) and a 4 item, 10 point Likert scale asthma management self-confidence questionnaire pre and post training.

Results: There was significant increase in mean score in asthma knowledge and 4 areas of asthma management self-confidence post training compared to pre-training in the eBook group (Table 1). There was no significant difference between the mean score changes in asthma knowledge and asthma management self-confidence when comparing both training groups.

Table 1

Variable	Pre-training Mean (SD)	Post-training Mean (SD)	Mean Change (95% CI)*
Score in AFAKQ	9.78 (3.10)	11.72 (1.67)	1.94 (1.20 -2.70)
Correctly using a spacer device with puffer	6.69 (2.97)	9.28 (1.24)	2.59 (1.93-3.24)
Recognise an asthma attack	6.74 (2.54)	9.14 (1.00)	2.40 (1.78-3.02)
Managing an asthma attack	6.29 (2.71)	9.10 (1.07)	2.81 (2.20-3.42)
Correct asthma first aid procedure	5.90 (2.81)	9.10 (1.12)	3.21 (2.60-3.82)

*Mean change significant at $p < 0.00001$

Conclusion: Both the Asthma First Aid Management in Schools eBook and standard face to face training increase asthma knowledge and self-confidence in school staff. The eBook is an effective alternative to face to face training in settings where human resources for health education are limited or for school staff unable to access training due to geographical location.

Grant Support: N/A

SPECIFIC VENTILATION IMAGING USING OXYGEN ENHANCED MRI IN ADOLESCENTS WITH CYSTIC FIBROSIS

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Introduction/Aim: Specific ventilation imaging (SVI) is a ***novel*** pulmonary imaging technique utilising magnetic resonance imaging (MRI) to evaluate the regional distribution of ventilation. The SVI technique developed by Prisk et al in San Diego relies on the paramagnetic properties of oxygen and signal change in MRI seen in the lungs during alternating cycles of room air (21% oxygen) and 100% oxygen.[1] Feasibility to date has been demonstrated only in adults. Our study aims to establish the technique and determine feasibility in both adult and adolescent patients at our center.

Methods: General Electric (GE) 1.5 T MRI SVI sequence used by Prisk et al, was adapted to a Philips 1.5T MRI. To reduce equipment-related dead space volume, a bias flow plumbing circuit with Solenoid switching valve system was developed (including 3-D Printed MRI-safe components) to deliver alternating 100% O_2 at 120L/min and room air through a Hans Rudolph face mask, sealed with putty. Chest coil used as receiver.

Results: Adult feasibility was demonstrated in five patients (2 male), age range 27- 36 years, with technically acceptable results achieved in all subjects. Adolescent feasibility was demonstrated down to 10 years: Four healthy adolescents (3 male, ages 10-16 years) and four cystic fibrosis patients (4 male, ages 15-18 years) with mild lung disease (abnormal LCI, normal FEV_1). SV quantification and mapping able to be performed on all subjects. Differences in vertical distribution in SV seen between healthy and CF participants.

Conclusion: SVI sequence specifications can be translated from GE to Philips MRI scanners. Strong feasibility was demonstrated in adults and, for the first time in adolescents down to 10 years of age at our centre.

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CLINICAL PROFILE OF CHILDREN WITH BRONCHIECTASIS UNDERGOING FLEXIBLE BRONCHOSCOPY (FB) AND CHEST COMPUTED TOMOGRAPHY SCANS (CT) IN THE NORTHERN TERRITORY: PROSPECTIVE CROSS-SECTIONAL 10-YEAR STUDY (2007-2017)

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Introduction/Aim: Indigenous children in the Northern Territory (NT) have high rates of repeated acute lower respiratory infections, associated with a future diagnosis of bronchiectasis. There is however, little data among non-Indigenous children and the trend over the years is unknown. We aimed to determine whether the clinical profile of children investigated for suspected bronchiectasis has changed between 2007-11 and 2012-17.

Methods: Demographics, clinical and medical history were obtained in children aged 3 months to 10 years undergoing FB and CT scans at the Royal Darwin Hospital.

Results: 304 children were enrolled (n=126 - 2007-11; n=178 - 2012-17); median age 2.4 years (IQR 1.6-3.9). CT confirmed bronchiectasis and age remained similar. However, the number of children with suppurative airways (p=0.02), chronic cough (p=0.008) and non-Indigenous ethnicity (p=0.04) increased (Table) between the two cohorts. In 2012-17, doctor visits for cough in the past year was high with 75% with >5 visits (5-10 visits=45/127, 35%; 10-20 visits=29/127, 23%; >20 visits=9/127, 7%).

	2007-11 n=126	2012-17 n=178	Total n=304
Age (yrs) (median)	2.4 (1.7-4.2)	2.3 (1.6-3.8)	2.4 (1.6-3.9)
Indigenous: non-Indigenous, n (%)	116 (92) : 10 (8)	150 (84) : 28 (16)	266 (88) : 38 (12)
Males, n (%)	75 (59.5)	94 (52.8)	169 (56)
Chronic Cough (>4 weeks)	67/109 (62)	94/167 (56)	161/277 (58)
CT confirmed bronchiectasis, n (%)	115/125 (92)	155/171 (91)	270/296 (91)
Suppurative airways, n (%)	88/126 (70)	100/174 (58)	188/300 (63)

Conclusion: The persistently high frequency of bronchiectasis in Indigenous children, increasing number of non-Indigenous children with bronchiectasis, higher prevalence of children with chronic cough, suppurative airways and frequent doctor visits in the later cohort require further evaluation and resources in the NT. This includes education at the primary care level for parents/carers and health professionals.

Conflict of Interest: None.

PARENTAL PERCEPTION OF QUALITY OF LIFE IN CHILDREN WITH BRONCHIECTASIS

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Introduction/Aim: Children with acute exacerbations of bronchiectasis are known to have a poorer health-related quality of life (HR-QOL) compared to peers without respiratory disease. However, during the stable state, the child-specific and the corresponding parental-proxy HR-QOL and the impact of bronchiectasis on the parents' psychological status are unclear. We aimed to determine the impact of bronchiectasis on (i) HR-QOL in clinically stable children compared to age-matched peers and (ii) the parent/caregivers' anxiety and depression.

Methods: Children (aged 5 to 18 years) with bronchiectasis while in a stable clinical state were recruited from two Australian tertiary hospitals. The children and their parents completed the child-specific and parent-proxy (respectively) versions of the Pediatric QOL inventory (PedsQL), a generic HR-QoL. Parents also completed the Hospital Anxiety and Depression scale (HADS) and the Centre for Epidemiological Studies Depression scale (CES-D). Age-matched control children (with no diagnosis of a respiratory condition) and their parents also completed these questionnaires.

Results: 29 children with bronchiectasis (mean$\pm$SD FEV$_1$ 91.5$\pm$14.5% predicted, age 10$\pm$4 years, their parents and 43 age-matched controls and their parents were enrolled. Children with bronchiectasis and their parent had significantly lower PedsQL scores compared to their peers (mean difference [MD] of raw scores 18.1 points, 95%CI 9.5 to 26.7; 24.8 points, 95%CI 16.2 to 33.4 respectively). Compared to parents of controls, parents of children with bronchiectasis were more anxious (MD 3.5 points [95%CI 1.8 to 5.2]) and more depressed according to both the HADS and CES-D (both p<0.001).

Conclusion: Children with bronchiectasis in the stable state have poorer HR-QoL. Their parents report higher levels of anxiety and depression. Attention to, and strategies to improving the HR-QoL and parental mental health are required in children with bronchiectasis.

THE IMPACT OF THE 13 VALENT CONJUGATE PNEUMOCOCCAL VACCINE ON PNEUMOCOCCAL SEROTYPES CAUSING CHILDHOOD EMPYEMA IN AUSTRALIA

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Introduction: The 13-valent conjugate pneumococcal vaccine (13vPCV) replaced the 7vPCV on the national immunisation schedule in Australia in mid-2011.

Aim: To determine the impact of 13vPCV on *Streptococcus pneumoniae* (Sp) serotypes causing childhood empyema.

Methods: Pleural fluid was collected from children with empyema presenting to 11 paediatric hospitals across Australia before (2007-2009) and after (2015-2017) the introduction of 13vPCV. Sp serotypes were identified on empyema fluid by PCR and sequencing.

Results: Pre 13vPCV: 143 children, 81 male, median age 4.9 (range 0.4-15.5) years were recruited. Sp was identified by PCR in 73 of 143 (51%) of cases. Post 13vPCV: 167 children, 85 male, median age 3.5 (range 0.6-15.8) years were recruited. Sp was identified by PCR in 95 of 167 (56.9%) of cases (Table).

Conclusion: The 13vPCV has not been effective against pneumococcal serotypes 3 and 19A. These data will help inform future national pneumococcal vaccination strategies.

Grant Support: NHMRC grant
Declaration of Interest: No

Serotype	2007-2009 (N=143)	2015-2017 (N= 167)	
	No. (%) specimens		13vPCV vaccination status Not (N), Partial (P), Full (F) (%)
PCV13 serotypes	50 (35%)	47 (28%)	
3	18 (32.7)	34 (58.6)	P 2 (6), F 32 (94)
19A	20 (36.4)	13 (22.4)	P 1 (7.7) F 12 (92.3)
1	8 (14.5)	0	-
7F/7A	2 (3.6)	0	-
14	1 (1.8)	0	-
9V/9A	1 (1.8)	0	-
Non vaccine serotypes	5 (3.5%)	11(6.5%)	
11A	0	3 (5.2)	F 3 (100)
25F/25A, 38	0	3 (5.2)	F 3 (100)
9N	0	2 (3.4)	N 1 (50), F 1 (50)
22F/22A	2 (3.6)	0	-
15A	0	1 (1.7)	F 1(100)
22F	0	1 (1.7)	F 1(100)
35B/35C	0	1 (1.7)	P 1(100)
6C	1 (1.8)	0	-
15F	1 (1.8)	0	-
21	1 (1.8)	0	-

The proportions of 13vPCV serotypes were not statistically different in the 2 time periods. (Z-Score = 1.2065, p=0.226).

EVALUATION OF AN INTEGRATED PAEDIATRIC ASTHMA MANAGEMENT PROGRAM: PRELIMINARY DATA

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Introduction/Aim: In 2016, The Sydney Children's Hospitals Network launched the Asthma Follow Up Integrated Care Initiative to address repeated presentations by children with non-complex asthma to the Sydney Children's Hospital (SCH) Emergency Department (ED). The aim was to reduce ED presentations, through better management of their asthma and increased engagement with their general practitioners (GPs).

Methods: Starting in January 2017, children aged 2-16 years, presenting to SCH ED with non-complex asthma, for ≥4 times in a 12 month period, were approached by Kids GPS Care Coordinators for enrolment in the program. Parents of enrolled children were, requested that their child have a review with their GP, and also offered referral to asthma education sessions. An extra layer of support was introduced in April 2017, a letter was sent to the child's GP advising of the child's recent hospital presentation. This letter suggested steps to improve the child's asthma management including influenza vaccination, review of asthma action plan, preventer medication and referral to a paediatrician if necessary. We compared the number of asthma ED presentations for these children six months pre and post enrolment using Wilcoxon signed-rank test.

Results: A total of 51 children have been enrolled in the program; 29 children were enrolled for >6 months. The median age of the children was 4 years (IQR 3-5 years). The median numbers of ED presentations in the six months preceding enrolment in the program was 2 (IQR 2-3) and post enrolment was 1 (IQR 0-1). There was significant reduction in the median frequency of ED presentations post implementation of the Asthma Follow Up Integrated Care Initiative (z=3.25, p =0.001).

Conclusion: Our preliminary data suggest that a comprehensive integrated approach to management of non-complex paediatric asthma may reduce frequent ED presentations due to exacerbation of asthma symptoms in children.

Grant Support: This work was funded by the NSW Health

LUNG CLEARANCE INDEX AS A MARKER OF SEVERE ASTHMA IN A PAEDIATRIC POPULATION

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Introduction/Aim: Lung clearance index (LCI) derived from nitrogen multiple breath washout (MBW) ventilation inhomogeneitVI). LCI airway disease severe asthma severe asthma.

Methods: This retrospective analysis 16 patients reviewed in The Severe Asthma Clinic (SAC) at John Hunter Children's Hospital between 2014 and 20172 to 15 years (6 females). All patients were uncontrolled on maximum doses of inhaled steroids plus long-acting beta agonist or montelukast to meet eligibility criteria. Relevant investigations performed included (where possible) spirometry, body plethysmography, exhaled nitric oxide (FeNO), asthma control test (ACT) scores, and measured in accordance with international recommendations.

Results: Nine of the total 16 patients (56.2%) ean LCI 11.7 (3.68.9-13.1), which was markedly higher than in two cohorts of healthy children at our site (mean LCI 7.1, Dunn et al., Ped Pulmonology 2017; mean LCI 7.3, Mandaliya et al. BMC Pulm Med 2015). Asthma control test scores 14.4 (5.111.0-19.5)FEV1 69.3 (16.957-78) FeNO 26.5 (24.87-38). Preliminary analysis suggest a correlation between improved clinical parameters and reduced LCI.

Conclusion: LCI airways disease in severe asthmain and management of more severe asthma.

Primary Care/ Palliative Care/ Tobacco

DEVELOPMENT AND VALIDATION OF A BRONCHOSCOPICALLY DEFINED BRONCHITIS TOOL IN CHILDREN

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Introduction/Aim: No validated tool exists for scoring bronchitis (i.e. airway inflammation) during flexible bronchoscopy (FB) despite potential clinical and research usefulness. Thus, we aimed to develop a bronchoscopically defined bronchitis scoring system in children (Bscore).

Methods: We used methods from our retrospective study; FB recordings were assessed for 6 components: amount of secretions (scores 1-6), colour of secretions (BronkoTest, 0-8), mucosal oedema (0-3), ridging (0-3), erythema (0-3) and pallor (0-3) based on pre-determined criteria. BScore was derived using several models developed from various combinations of the each of the 6 components that best related to airway neutrophilia (in BAL). We also determined the correlations (Spearman) between each component with BAL neutrophil%. Clinical history was obtained from parent(s) who consented for study inclusion before the FB undertaken. A clinician blinded to the child's history scored the FB. The various models of BScore were plotted against neutrophil% using a receiver operating characteristic (ROC) curve. Here we report our preliminary findings; we plan to enrol >100 children.

Results: Chronic/recurrent cough was the commonest indication for FB in the 30 children enrolled (median age=3-years). Secretion amount and colour had the strongest correlation with BAL neutrophil%, (r=0.409, p=0.025 and r=0.401, p=0.028 respectively). With inflammation defined as BAL neutrophilia >15%, the highest aROC (0.68, 95%CI 0.45-0.91) was obtained by tripling the secretion scores (amount and colour) and excluding pallor. aROC for the model derived from our retrospective study was 0.63 (95%CI 0.50-0.76). The highest aROC (0.86, 95%CI 0.71-1.00) was with neutrophils of >10% using the BScore obtained by each of the 6 components.

Conclusion: A validated bronchoscopic defined bronchitis scoring system can be obtained from visualization of airway secretions (amount and colour) and mucosa appearances (erythema, ridging and oedema). Further data is however required.

ASTHMA BEST PRACTICE (ABP): A NATIONAL ASTHMA EDUCATION PROGRAM CHANGING PRIMARY HEALTH CARE PRACTICE

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Introduction/Aim: In 2001 the Australian Government funded the National Asthma Council Australia (NAC) to establish an ongoing, national asthma education program focused on providing best-practice asthma management guidelines to primary health care professionals (PCHP). Aiming to reinforce and increase awareness of best-practice asthma management guidelines by PCHP through provision of peer education, via small group workshops across Australia.

Methods: An independent evaluator was appointed to assess program outcomes. Participants were asked to complete an evaluation survey. Follow-up telephone surveys were conducted with volunteer participants 6 months later to assess change in practice.

Results: From 2001-2016, 13,333 PHCP attended 828 workshops across Australia. The immediate post-workshop evaluation survey response rate was 78%. Across all workshop types, most respondents (91%) felt attending the workshop had increased their knowledge of evidence-based best practice, 89.4% increased their practical skills to support their application of evidence-based practice in asthma care, and 87% expected improvement in their asthma management practices.

The response rate of the 6-month follow-up survey in the 2013-2016 program was 22%. All responders reported they had 'entirely' or 'partially' retained knowledge from attending an NAC workshop. Confidence in exercising practical skills six-months post workshop ranged between 78%-97%, depending on skill area and workshop.

Conclusion: The ABP education program is a targeted, national program and a successful model for providing evidence-based asthma management guidelines and education to PCHP. It highlights a change in practice following participation.

ARE WE ASKING THE RIGHT QUESTIONS? USING DRAWINGS TO EXPLORE HEALTHCARE PROFESSIONALS' AND PATIENTS' PERCEPTIONS OF ASTHMA

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Introduction/Aim: Differences between healthcare professionals' (HCPs) and patients' views of asthma can influence communication, rapport, treatment provision and consequently clinical and psychosocial outcomes. This study aimed to explore the alignment between HCPs' and patients' perceptions of asthma.

Methods: HCPs and adults with asthma independently participated in a one-on-one semi-structured interview which was followed by a creative expression exercise (drawing). A qualitative approach utilising a coding process was used to cluster thematic material. Data were compared between the HCP and patient transcripts and drawings. The HCPs were also shown drawings which were made by patients and feedback regarding their impressions were sought.

Results: HCPs' drawings (N = 19) were clinically focussed and indicated little evidence of emotional content. In contrast, patients' drawings and interviews (N = 18) highlighted the prominence of the emotional burden of asthma and its often profound impact on their lives. Of note, the HCP data showed minimal exploration of patients' psychosocial experiences of being diagnosed with or managing asthma. HCPs revealed that patients would not offer information when it was not directly elicited, and that they frequently received a neutral response when they asked how patients were generally going with their asthma. When viewing the patients' drawings, HCPs were often surprised by the intensity of the emotions portrayed and expressed that they found this exercise insightful.

Conclusion: HCPs can more effectively explore the patient's perspective by asking targeted questions, as this may help to reduce patients' psychological burden and engage them to take an active role in the management of their asthma. This also raises the issue of the expectations that both HCPs and patients have regarding what could be discussed during clinical encounters. Creative methods for eliciting patients' lived experiences may offer a window into how asthma affects their lives personally.

PALLIATIVE AND SYMPTOMATIC CARE OF PATIENTS WITH FIBROTIC INTERSTITIAL LUNG DISEASE

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Introduction: Fibrotic interstitial lung diseases (ILD) are often progressive and incurable with limited treatment options. Patients experience significant symptom burden with refractory dyspnoea and cough. Current guidelines recommend early palliative care referral.

Aim: To examine the end of life care delivered to fibrotic ILD patients during the terminal hospital admission.

Methods: A retrospective audit was performed for all patients who died from progression of fibrotic ILD, at two Australian teaching hospitals over 5 years from 2012 to 2016.

Results: Of 55 patients who died from fibrotic ILD, 37 (67%) had Idiopathic pulmonary fibrosis. Median age was 78 years and 30 (55%) were male. The average number of comorbid conditions was 4.7. Median respiratory function: FEV_1 69.0% predicted (IQR 58.5-79.0%), FVC 64.0% predicted (IQR= 48.0-76.5%) and DLCO 36.5% predicted (IQR= 31.0-45.0%). 37 (67%) patients were prescribed domiciliary oxygen.

Prior to the terminal admission, 21 (38%) patients reported severe breathlessness (MMRC score: 3 or 4) and 16 (29%) used outpatient opioids for symptom relief. 25 (45%) patients received specialist palliative care and 18 (33%) had completed Advanced Care Planning.

During the terminal admission: 51 patients (93%) had their goal of care changed to comfort care. Nine patients (16%) were admitted directly under Specialist Palliative Care and 25 (54%) were subsequently referred. Palliative care referral occurred on average 1 day prior to death.

52 (95%) patients received inpatient opioids and 41 (75%) received benzodiazepines for symptom management. Median starting and final doses were 10mg to 20mg oral morphine equivalent/24hr; and 10mg to 12.5mg oral diazepam equivalent/24hr. These were commenced at 1 and 2 days prior to death respectively.

Conclusion: Although most ILD patients were identified as actively dying in the final admission, the referral to Palliative Care and commencement of palliative medications occurred just prior to death. Similarly the minority of patients accessed symptom palliation and palliative care earlier in their illness.

A NEW INTEGRATED RESPIRATORY AND PALLIATIVE CARE MODEL: PATIENTS/CARERS PERCEPTIONS

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Introduction/Aim: The Advanced Lung Disease Service (ALDS) is a unique, new model of integrated respiratory and palliative care for patients with advanced, non-malignant, lung disease.

Methods: All current ALDS patients and their carers were invited to complete an anonymous, confidential questionnaire with an independent researcher.

Results: Eighty-eight responses were received, from 24 carers and 64 (80.0%) of 80 eligible patients. Respondent patients' median age was 75 years, 34 (53.1%) male, 25 (39.1%) lived alone and 58 (90.6%) had severe COPD. The median number of ALDS clinic visits was 9, and 52 (81.3%) patients saw both respiratory and palliative care staff in the clinic.

66 (75.0%) respondents rated the ALDS as excellent, 18 (20.5%) as very good and 85 (96.6%) would recommend the ALDS. 88 (100%) respondents found the ALDS helpful, with 87 (98.9%) feeling more confident managing their symptoms, and 87 (98.9%) reporting the ALDS team listened to them carefully.

Aspects of the ALDS which were important to respondents included: continuity of care from the same doctors and nurses - 82 (93.2%), long term care - 77 (87.5%), access to urgent clinic reviews - 63 (71.6%), and respiratory nurse home visits - 53 (60.2%).

Common themes were staff kindness and friendliness, optimal disease management, self-management education, and opportunities to discuss all aspects of care, including future care wishes.

Conclusion: ALDS patients and their carers express high levels of satisfaction with this model of integrated respiratory and palliative care.

Grant Support: n/a

Declaration of interest: No competing interests.

INVESTIGATION BURDEN IN PATIENTS WITH FIBROTIC INTERSTITIAL LUNG DISEASE IN THEIR TERMINAL ADMISSION

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Introduction: The prognosis of fibrotic Interstitial Lung Disease (ILD), in particular idiopathic pulmonary fibrosis (IPF), is poor. Therefore referral to palliative care should be considered early. Patients may still be undergoing burdensome investigations despite being at the end of life.

Aim: To examine the number and types of investigations fibrotic ILD patients experience during their terminal hospital admission.

Methods: A retrospective audit was performed for all patients who died from fibrotic ILD, across two Australian teaching hospitals over 5 years from 2012 to 2016.

Results: Data from fifty-five patients were analysed; median age was 78 years (IQR=74-84 years), 30 (55%) were male and mean number of comorbid conditions was 4.7. Median respiratory function: FEV_1 69.0% predicted (IQR=58.5-79.0%), FVC 64.0% predicted (IQR=48.0-76.5%) and DLCO 36.5% predicted (IQR=31.0-45.0%). 37 (67%) patients were prescribed domiciliary oxygen. 25 (45%) patients had previous specialist palliative care involvement.

During the final admission, the average length of stay was 4 days (IQR=2-9 days). For 51 (93%) patients the goal of care was changed to comfort care. Excluding ten patients who died within 24 hours of admission, referral to Palliative Care occurred on average 1 day prior to death. 6 (11%) patients underwent further tests after institution of comfort care.

The mean number of investigations ordered was associated with ICU admission, activation of the Medical Emergency Team response and admitting team, with significantly more investigations when admitted by General Medicine (17.4 tests/person), compared to Respiratory Medicine (9.8 tests/person) and Palliative Care (0.8 tests/person).

Conclusion: Most fibrotic ILD patients received appropriate palliation at the end of life in hospital, however, a significant minority continued to receive unnecessary and burdensome investigations after the decision for comfort care. Practices varied widely between treating units.

Grant Support: Nil

BACTERIAL COLONIZATION OF INDWELLING PLEURAL CATHETERS IN PATIENTS WITH MALIGNANT PLEURAL EFFUSIONS

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Introduction/Aim: Indwelling pleural catheter (IPC) is increasingly used in malignant pleural effusion (MPE) care. IPCs often remain *in situ* for patients' remaining life, hence bacterial colonization and/or pleural infection can occur. Separating colonization from infection can be challenging. This report is the first to provide clinical data on patients with bacterial colonization of IPCs.

Methods: All patients with MPEs treated with IPCs at our tertiary pleural unit between 26/8/2009 and 31/5/2015 were included. Pleural fluid cultures were collected routinely at clinic follow-up. Clinical and microbiological data up to the censor date (1/12/2016) was retrospectively reviewed. *Definitions*: Patients with bacterial colonization or infection had at least one pleural fluid culture yielding microbes. Patients included in the Infection Group (IG) had clinical features compatible with active infection and were treated with antibiotics. Those in the Colonization Group (CG) did not require antimicrobial treatment.

Results: 183 MPE patients had IPCs inserted: mean age 69, 67% male, 59% right-sided. Of these 52 (28.4%) patients had positive pleural fluid cultures of which 38 (20.7%) were colonizations and 14 (7.7%) were pleural infections. Median time to first positive culture was shorter in CG [18 (0-125) *vs* 97 (39-269) days in IG]. No pre-specified baseline criteria differentiated colonization from infection. Gram-positive organisms (76%) accounted for most cases of colonization. Coagulase-negative Staphylococci (55%), Propionibacterium species (18%) and mixed microbes (13%) were the commonest organisms. The CG has lower inflammatory indices in pleural fluid and blood (*vs* IG): median pH 7.26 *vs* 7.05; LDH 535 *vs* 1630 IU/L; glucose 2.3 *vs* 0.5 mmol/L; serum CRP 140 *vs* 150 IU/L and total blood leukocyte count 10 *vs* 12 x10^9/L.

Conclusion: Bacterial colonization can occur with IPC use and does not require treatment/eradication. Clinical judgement, blood and pleural fluid parameters can help distinguish colonization from active infection.

Grant Support: NHMRC and Cancer Council WA (RT & YCGL); NSW Dust Diseases Board (YCGL); Sir Charles Gairdner RAG (YCGL); Raine Foundation and WA Dept of Health (EF).

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.

ELECTRONIC CIGARETTE AWARENESS, USE, AND PERCEPTION OF HARMFULNESS IN MIDDLE-AGED ADULTS: THE BUSSELTON BABY BOOMER STUDY

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Introduction/Aim: Despite emerging evidence suggesting that chronic e-cigarette use may be harmful to lung development and function, information on contemporary public perception and knowledge about the safety and use of e-cigarettes among Australian adults is not well known. We aimed to assess; *1)* awareness, *2)* usage *(ever or recent)* and *3)* perceived harmfulness of e-cigarettes among a community sample of middle-aged adults residing in Busselton, Western Australia.

Methods: Adults aged 51 – 71 years attending phase II of the longitudinal Busselton Baby Boomer Study in 2016/17 completed e-cigarette-related items from the US National Tobacco Survey (NATS) 2013-2014 questionnaire.

Results: E-cigarette awareness among 812 Baby-boomers surveyed (46.6% never smokers, 48.5% ex-smokers, 4.9% current smokers) was high with over 80% of respondents having heard of them and 30% of current smokers indicating they had tried them. However current or recent usage of e-cigarettes among adult smokers was low with only 3% reporting use over the last 30 days. Over 30% of current smokers believed e-cigarettes were less harmful than regular cigarettes compared with 16% of never- or ex-smokers. 15% of all respondents believed e-cigarettes were equally or more harmful than regular cigarettes. Over 60% of Baby-boomers felt they did not know enough information about e-cigarettes to compare harmfulness with regular cigarettes.

Conclusion: These results indicate that despite the sale of e-cigarettes being illegal in Western Australia a high number (1 in 3) of middle-aged smokers have tried e-cigarettes on at least one occasion. Recent or regular use of e-cigarettes among adult smokers in Busselton however is low, possibly reflecting State Government restrictions on sale and supply. The higher prevalence of lower perceived harmfulness of e-cigarettes among current smokers coupled with emerging evidence showing adverse effects on lung function suggest public education campaigns on e-cigarette safety may be warranted.

Grant Support: The Busselton Baby Boomer Study is supported by grants from the WA Government Office of Science and Department of Health.

PROFILES OF YOUTH AND PARENT INFORMATION MANAGEMENT STRATEGIES: AN EXPLORATORY LOOK AT ADOLESCENT ELECTRONIC CIGARETTE USE

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Introduction/Aim: The use of electronic cigarettes (e-cigs) among U.S. adolescents has tripled in recent years; however, there is limited research on parent and youth information management strategies (i.e., monitoring, control, knowledge, solicitation, disclosure, and secrecy) as they relate to this use. The current study uses a profile-based analytic procedure (cluster analysis) to explore patterns among these variables and investigate relations to adolescent e-cig use.

Methods: A total of 569 students (ages 13-18) were recruited from four high schools and one adolescent clinic in rural and suburban areas in Ohio, Pennsylvania, and West Virginia. Participants completed the *Youth Behavior Risk Survey* (YRBS) to assess tobacco use, and measures of parent and youth information management. Responses resulted in 223 youth (Mage = 16.25, SD = 1.16) identified as e-cig users. User status was defined as any use, even one puff, in the student's lifetime. Analyses include hierarchical and k-means cluster analyses, chi-squares with post-hoc testing, ANOVA, and MANOVA procedures.

Results: Consistent with current literature, 57% (n = 127) of students were identified as a dual user (e-cigs & conventional cigarettes) and 43% (n = 96) were identified as e-cig only user. A preliminary cluster analysis suggested a four-cluster solution, with each cluster representing significantly different combinations of parental and youth strategies. User group was found to be significantly related to cluster profile, X^2 (3) = 15.92, $p <$ .001, such that patterns of strategies for users particularly related to youth secrecy, youth disclosure, and parental knowledge.

Conclusion: Results suggest the potential of bidirectional associations between parental and youth information management strategies and differences in profiles for e-cig and dual users. These findings have the potential to clarify policy, particularly regarding eliciting parent help in reducing e-cig use among adolescents. Results also have the potential to inform youth-focused education and preventative efforts.

EXPECTED COSTS AND BENEFITS MEDIATES THE RELATION BETWEEN PEER USE AND SELF-REPORTED USE OF ELECTRONIC CIGARETTES IN ADOLESCENTS

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Introduction/Aim: Preliminary research has identified peer use as a salient risk factor of adolescent e-cigarette use, but have not expanded on the mechanism of this association. The aim of this study is to examine a mediation model of the effect of adolescent expectations of benefits and costs of e-cigarette use on the relation between peer- and self-reported e-cigarette use.

Methods: For this study, 569 adolescents (Ages 13-18, M=15.96, SD=$\pm$1.38; 42% male) were recruited from an adolescent medicine clinic and schools in rural and suburban areas of the mid-Atlantic U.-S. Participants completed the *Youth Behavior Risk Survey* (YRBS) to assess e-cigarette use, and the *Smoking Expectancy Scale for Adolescents* (SESA) to measure beliefs about the potential consequences of e-cigarette use. Mediation analyses were conducted in SPSS utilizing the PROCESS version 2.15 add-on (Hayes, 2013).

Results: An analysis of direct and indirect effects demonstrates that peer use has a significant direct effect on self-reported use of e-cigarettes $b = -.850$, $p < .05$. Benefits had an indirect effect of self-reported use, $b = -.071$, 95% CI [-.118, -.035]. Costs had an indirect on self-reported use, $b = -.134$, 95% CI [-.197, -.077]. The effect of the mediator indicates that increased report of benefits is associated with a 58% reduced chance of being in the non-user group and that an increased report of costs is associated with a 27% increased rate of being in the non-user group.

Conclusion: These findings support previous research claims that peer use is a significant risk factor for adolescent e-cigarette use and adds to the literature by suggesting that expectations about consequences of e-cigarette use (perceived costs and benefits) may play an important role in the association between peer and self-reported use. Additionally, this study informs future targeted strategies (e.g., social pressures or perceptions) to reduce youth e-cigarette use.

'CIGARETTES OR E-CIGARETTES?': A SURVEY OF YOUNG AUSTRALIANS ATTITUDES AND PERCEPTIONS OF EMERGING TOBACCO PRODUCTS

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Introduction/Aim: Young people are thought more likely to use electronic cigarettes (e-cigarettes) than adults, but their reasons for uptake and their attitudes toward e-cigarette safety and regulation are unknown. This study aimed to explore this.

Methods: An online survey was conducted among Australians aged 18-30 years, recruited through university mailing lists and social media pages. Participants were asked questions about how they first heard of e-cigarettes, the perceived safety of e-cigarettes and the regulations surrounding e-cigarette use.

Results: 124 participants (73% Female, Mean age 21.2 (SD±2.60) years, 95.2% University students) completed the survey, of whom 27% were past/current e-cigarette users and 32% were past/current tobacco cigarette smokers. Participants most commonly reported that their first exposure to e-cigarettes was via social media (56%), friends (54%) and/or the internet (48%). Among past/present users, the most common reason for initiating e-cigarette use was curiosity (94%), friends using them (36%) and/or considering them better for health than tobacco cigarettes (27%). Indeed, 85% of all respondents thought nicotine e-cigarettes had lower health risk than tobacco cigarettes and only half (55%) thought nicotine e-cigarettes could cause similar damage to their lungs. Moreover 53% of participants thought cannabis and 57% thought fast food carried less risk than nicotine e-cigarettes. More respondents agreed nicotine e-cigarettes are bad for your health than non-nicotine e-cigarettes (76% vs 33%). A number of respondents thought e-cigarettes could be used in places where they are currently banned in Australia, such as outdoor dining areas (24%).

Conclusion: Many young people consider e-cigarettes comparatively safe, with lower health risks than smoking, cannabis or fast food. They consider non-nicotine e-cigarettes safer than nicotine e-cigarettes, though current evidence contradicts this. The lack of understanding of potential health risks indicates the poor public health communication and confusion around e-cigarettes which must be urgently addressed.

Grant Support: None

SHORT ACTING BETA AGONIST OVERUSE: AN UNACKNOWLEDGED/MASKED PROBLEM IN AUSTRALIA

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Introduction/Aim: Research shows that in Australia, approximately 50% of people with asthma are poorly controlled; with overuse use of short Acting Beta Agonist (SABA) being reported. The drivers for overuse of SABA and the interactions between patients and treatable traits in Australia where SABA are available over the counter, is unknown, however, may hold the key to the unsatisfactorily high level of poorly controlled asthma. The aim of this study is to identify and characterise the clinical asthma status, behaviour and attitudinal clusters and patterns of SABA use in the asthma population.

Methods: In this observational study data was collected from people who purchased SABA in the pharmacy along the following domains: asthma control, medication use and side effects, comorbidities, smoking status, action plan ownership, device use, healthcare utilisation. Inclusion criteria was a SABA user over 18 who could self-complete the questionnaire.

Results: Data from 154 community base pharmacy patients were collected, mean age 43.1 (+/- 1.42), with an equal distribution of males and females (51%). Twenty percent had good control and 64 % self-reported good control. The mean number of SABA inhalations used per week was 1-4 puffs, three or more times a week, the proportion of SABA users who reported using a preventer every day was 30%, however 62% acknowledge being prescribed one. Fifty-four percent reported that they have never had their inhaler technique checked by a HCP. There was a statistically significant difference between patients who used preventer versus those who only used SABA in regards to asthma symptom control ($p<0.001$).

Conclusion: Twenty percent of people using SABA have never had a diagnosis of asthma; 70% have had it confirmed with spirometry. Patients are taking advantage of OTC availability of SABA and this preliminary data suggests that they self-medicate/manage in ways which puts a high proportion of them at risk.

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CLINICAL CHARACTERISTICS OF DYSFUNCTIONAL BREATHING IN DIFFICULT ASTHMA

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Introduction/Aim: Dysfunctional breathing (DB) is poorly defined, common in asthma patients and confers worse asthma control and quality of life. Little is known about phenotypes of asthma patients with DB and we aimed to describe the clinical characteristics of dysfunctional breathers in a difficult asthma cohort to help better define this group.

Methods: Consecutive patients with DB undergoing physiotherapy assessment and breathing retraining referred from the difficult asthma clinic at a university teaching hospital were identified. Asthma control, quality of life and comorbidities were examined. These patients were also evaluated for the presence of common DB features including mouth breathing, thoracic dominance, hyperventilation, musculoskeletal and postural abnormalities. Pre- and post- Nijmegen questionnaires were performed.

Results: Of the 29 patients, 59% were female with mean age 49 years, BMI 31 and FEV1 71% predicted. Asthma control was poor at baseline with mean of 3.1 severe exacerbations in the 6 months prior to review and ACQ6 2.4, and quality of life was poor with mean AQLQ 3.9. Comorbidities were common including a psychiatric history in 62% and vocal cord dysfunction in 66%. Mean baseline Nijmegen scores was 28.8. On assessment of breathing pattern thoracic dominance was the most common form of DB, present in 86%. Mouth breathing was present in 28%, hyperventilation 45%, spinal abnormalities 10%, abnormal neck position 10% and scalene muscle use at rest in 24%. All underwent breathing retraining and 59% responded with significant improvement in symptoms and/or reduction in asthma medication requirements. Of those with data available (n=6) there was a significant improvement in mean Nijmegen score post breathing retraining (21.5, p=0.006).

Conclusion: Thoracic dominance is the commonest phenotype seen in the difficult asthma population with DB however this overlaps significantly with mouth breathing and hyperventilation. Postural and musculoskeletal abnormalities are common. The majority of patients responded to breathing retraining.

ASTHMA SELF-MANAGEMENT EDUCATION AND PERCEIVED ASTHMA MEDICATION RISK DURING PREGNANCY

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Introduction/Aim: Women might discontinue or reduce their asthma medication during pregnancy, sometimes without physician consultation. One reason for this behaviour may be their perceived risk of asthma medication on the fetus. Providing education to pregnant women about their medication might lower this perceived risk. The aims of this study were to (i) determine baseline perceived risk of asthma medication on the fetus during pregnancy and (ii) determine the number of repeat education sessions needed to reach maximum benefit.

Methods: Data was extracted from the Managing Asthma in Pregnancy study, conducted between 2007-2010. Participating women completed a questionnaire at four visits during pregnancy. Perceived risk was assessed using three identical visual analogue scales for reliever medication, preventer medication and oral corticosteroids (OCS) ranging from 0% (no side effects, healthy baby) to 100% (severe side effects, e.g. deformity). At each visit, women were provided education about their asthma medication regarding treatment effect, safety and risks. Data were analysed using one-way ANOVA repeated measures with post-hoc pairwise comparison.

Results: Three hundred eleven women completed at least one questionnaire, the number of questionnaires declined from 268 (Visit 1) to 229 - (Visit 5). Baseline perceived risk was $14.4\pm3.1\%$ for reliever medication (n=267), $30.7\pm4.0\%$ for preventer medication (n=232), and $48.6\pm4.8\%$ for OCS (n=144). After one education session, perceived risk was significantly lower for all medications (p<0.05). Although perceived risk of OCS appeared to lower further after each session (p>0.05), additional education sessions did not significantly lower perceived risk further for any medication.

Conclusion: Perceived risk of OCS was highest among pregnant women followed by preventer and reliever medication. One educational session was required to reach maximum benefit in lowering perceived risk of preventer and reliever medication. Further research is needed to understand the reasons for this high level of perceived risk, to better inform education strategies.

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FVC RESPONSE TO TIOTROPIUM RESPIMAT® IN ADULTS WITH SYMPTOMATIC ASTHMA

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Introduction/Aim: To investigate the impact of tiotropium Respimat® (tioR) treatment on different measures of lung function in adult patients with symptomatic asthma across different severities.

Methods: Lung function data from 5 Phase III clinical trials, namely, pooled PrimoTinA-asthma® (severe asthma: 2x48-week, tioR5µg/placebo, once-daily [QD], added-on to inhaled corticosteroid [ICS] ≥800µg budesonide/equivalent + long-acting β2-agonist ± additional controller medications), pooled MezzoTinA-asthma® (moderate asthma: 2x24-week, tioR2.5µg/tioR5µg/placebo QD, added-on to ICS 400–800µg budesonide/equivalent) and GraziaTinA-asthma® (mild asthma: 12-week, tioR2.5µg/tioR5µg/placebo QD, added-on to ICS 200–400µg budesonide/equivalent) were compared in this post hoc analysis.

Results: TioR provided significant improvements in peak $FEV_{1(0–3h)}$ and trough FEV_1 versus placebo in severe (Week 24), moderate (Week 24) and mild (Week 12) asthma (Table). Peak and trough FVC were significantly improved with tioR versus placebo in the severe and moderate groups (Week 24). In patients with mild asthma, FVC improvements following tioR versus placebo were generally smaller; statistical significance was reached for tioR2.5µg (Week 12).

Conclusion: TioR as add-on to maintenance asthma therapy improves FEV_1 and FVC with a greater impact in patients with more severe asthma, possibly due to airway remodelling and hyperinflation seen in more severe persistent disease.

Table 1

Lung function analyses	Adjusted mean difference from placebo, mL(95%CI)	
	tioR5µg	**tioR2.5µg**
PrimoTinA-asthma®† (severe): N=907		
Peak FEV_1	110(63, 158)***	-
Trough FEV_1	93(50, 137)***	-
Peak FVC	87(26, 148)*	-
Trough FVC	118(62, 175)***	-
MezzoTinA-asthma®† (moderate): N=2081		
Peak FEV_1	185(146, 223)***	223(185, 262)***
Trough FEV_1	146(105, 188)***	180(138, 221)***
Peak FVC	95(53, 138)***	141(98, 183)***
Trough FVC	80(35, 125)**	107(62, 152)***
GraziaTinA-asthma®‡ (mild): N=464		
Peak FEV_1	128(57, 199)**	159(88, 230)***
Trough FEV_1	122(49, 194)**	110(38, 182)*
Peak FVC	57(–25, 140)	106(23, 188)*
Trough FVC	66(–19, 151)	98(13, 183)*

***p<0.0001; **p<0.001; *p<0.05
Results at †Week 24 and ‡Week 12

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"[SEVERE ASTHMA] IS CONSTANTLY WITH ME… EVERY DAY IS A BIT OF A STRUGGLE" A QUALITATIVE STUDY OF PEOPLE'S EXPERIENCES OF LIVING WITH SEVERE ASTHMA

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Introduction/Aim: Severe asthma is diagnosed when high doses of conventional treatment are required to prevent it from becoming uncontrolled or it remains uncontrolled despite such treatment and good patient adherence. There is a considerable body of literature on the clinical management of severe asthma, yet there is little empirical data on how it affects patients' lived experience. We aimed to explore the personal experiences of people living with severe asthma.

Methods: Rigorous qualitative research methods using in-depth semi-structured interviews, collected by maximum sampling variation. Participants were included if they were >18 years old and diagnosed with severe asthma. Participants were asked to give a narrative of their experience living and managing severe asthma. Interviews were mainly conducted in participants' homes and were video recorded. The data were transcribed and coded into categories and themes. These categories and themes were based on areas that were identified by the participants as important to them.

Results: From twenty-one interviews, our findings revealed that, for most participants, living with severe asthma affects their physical and mental health, relationships with family and friends, and limits work and activities. Participants wrestled with everyday decisions such as taking life-saving medications in the face of experiencing often debilitating side effects. Notably, for some people, their views and understanding of what their respiratory condition meant to them did not align with the diagnostic 'label' of severe asthma.

Conclusion: Barriers to self-management of severe asthma include taking medications and communication with healthcare providers. Healthcare providers need to know what people living with severe asthma understand about their condition, how they attempt to self-manage and address their concerns. This could potentially be a barrier to seeking appropriate care.

Grant Support: Seed Grant from the NHMRC Centre for Research Excellence in Severe Asthma.

Declaration of Interest: None.

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PEF DIURNAL VARIABILITY WITH TIOTROPIUM RESPIMAT® IN SYMPTOMATIC ADULT ASTHMA

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Introduction/Aim: We investigated diurnal variability in peak expiratory flow (PEF) following add-on treatment with tiotropium Respimat® (tioR), delivered as two puffs once daily (QD) across asthma severities.

Methods: *Post hoc* analysis of PEF diurnal variability from 5 Phase III trials was conducted: PrimoTinA-asthma® (pooled 2x48-week trials, tioR5µg/placebo QD [morning], added onto maintenance inhaled corticosteroids [ICS]≥800µg budesonide/equivalent+long-acting β_2-agonists±additional controller medications); MezzoTinA-asthma® (pooled 2x24-week trials, tioR2.5µg/tioR5µg/placebo QD [evening], added onto maintenance ICS 400–800µg budesonide/equivalent); and GraziaTinA-asthma® (12-week trial, tiotropium tioR2.5µg/tioR5µg/placebo QD [evening], added onto maintenance ICS 200–400µg budesonide/equivalent). Pre-dose PEF was self-monitored at home using the asthma monitor AM2+/3®.

Results: TioR improved morning and evening PEF in all studies. Mean baseline PEF variability was 14.14%, 13.51% and 12.08% in PrimoTinA-asthma®, MezzoTinA-asthma® and GraziaTinA-asthma®, respectively. Adjusted mean changes from baseline in PEF variability at Week 24 for tioR2.5µg/tioR5µg and placebo were small (Table).

Conclusion: The differences between tioR and placebo were generally small and variable (albeit the trials showed significant improvements in peak [0–3 hours post-dose] FEV_1, trough FEV_1 and PEF am/pm versus placebo). In these trials where tioR was added onto other maintenance asthma therapy, PEF diurnal variability was not a sensitive measure of bronchodilation.

Table 1

Study (Asthma severity, Treatment duration)	N	Change in PEF diurnal variability*, % adjusted mean±SEM	Treatment versus placebo, adjusted mean difference±SEM (95% CI)
PrimoTinA-asthma® (Severe, 24 weeks)			
tioR5µg	453	−0.33±0.35	0.54±0.50 (−0.44, 1.51)
Placebo	454	−0.87±0.35	
MezzoTinA-asthma® (Moderate, 24 weeks)			
tioR5µg	513	−0.32±0.30	0.70±0.43 (−0.15, 1.54)
tioR2.5µg	515	−1.78±0.30	−0.77±0.43 (−1.61, 0.07)
Placebo	518	−1.01±0.30	
GraziaTinA-asthma® (Mild, 12 weeks)			
tioR5µg	155	−0.37±0.52	0.15±0.72 (−1.26, 1.56)
tioR2.5µg	154	−0.52±0.52	<0.01±0.72 (−1.41, 1.42)
Placebo	155	−0.52±0.51	

*Absolute difference between morning and evening PEF divided by mean of the two values

LOW-DOSE MEPOLIZUMAB EFFECTIVELY TREATS CHRONIC RELAPSING EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS

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Introduction/Aim: Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare systemic vasculitis characterised by asthma, eosinophilia and multi organ disease. In its chronic form long term oral steroid treatment is required. Early evidence suggests Mepolizumab, a monoclonal antibody directed against IL5, may be a useful treatment. A single randomised placebo control trial has shown efficacy for 50% of patients treated with 300mg of Mepolizumab 4 weekly, subcutaneously. We sought to determine the efficacy of 100mg of Mepolizumab in a cohort of patients with chronic relapsing EGPA.

Methods: Six patients with a long term diagnosis (mean10.7 years) of EGPA (American College of Rheumatology Criteria) who were unable to wean off prednisolone due to multiple episodes of relapse were treated with 100mg of Mepolizumab 4 weekly over a period of 9-11 months. Patients were monitored 4 weekly by asthma control questionnaire (ACQ), clinical review, eosinophil counts, spirometry, exhaled nitric oxide (ExNO) and respiratory resistance using a Forced Oscillometry Technique (FOT). Prednisolone doses were tapered after three months according to clinician discretion.

Results: Pre-treatment, the average prednisolone dose was: 9 mg/day. All patients responded to Mepolizumab and were successfully weaned off prednisolone after 4 to 9 months. Eosinophils fell from an average of 0.7×10^9/L to 0.1×10^9/L and ExNO fell from 48ppb to 23ppb. FEV1 (%predicted) improved by 12% from baseline and airway resistance (FOT R5) improved from 185% to 127%. ACQ improved from a baseline reading of 2.9 to 0.3. There were no episodes of disease relapse, all patients reported improving clinically and Mepolizumab was well tolerated by all.

Conclusion: Mepolizumab therapy is a safe and efficacious therapy for patients with chronic relapsing EGPA at doses of 100mg 4 weekly. Mepolizumab is a more targeted immunomodulatory therapy allowing chronic patients to discontinue and avoid the long term complications of steroid therapy.

Conflict of Interest: No conflicts of interest

ASTHMA MEDICATION MANAGEMENT PRACTICES: UNDERSTANDING THE INFLUENCES ON PARENTS WHEN CARING FOR CHILDREN WITH ASTHMA

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Introduction: Preliminary research has indicated that parents consult with a range of health care professionals (HCPs) and lay contacts when considering the medication management of their children with asthma; with a preference for general practitioners (GPs), family and spouses. It remains unknown however as to why parents choose specific connections and on what basis parents selected specific sources for health advice. Further, it is unknown as to how parent's non-HCP advisor's may impact on the support parents seek or receive advice from HCPs.

Objective: The overall aim of this study was to explore the key elements contributing to the nature and development of parent's health connections with regards to the management of their children's asthma medications.

Methods: In-depth, semi structured interviews were conducted with parents of children (aged 4 to 18 years) with asthma (self-reported) from Sydney, Australia. Participants were recruited from several points including asthma clinics, general practice clinics and community pharmacies. Face-to-face interviews were audio recorded, transcribed verbatim, independently reviewed by three authors and analysed using a qualitative approach.

Results: A total of 26 interviews were conducted. Parents established a combination of HCP, personal and impersonal health connections around their perceptions of their children's medication needs and for advice and support. These needs were based on the provision of effective medications, including their ongoing management and education, regular monitoring of symptoms and physical and emotional support. Parent's trust in relationships, their circumstances at a present time, the convenience of health advice and their perceptions of the role of specific health connections in the management of their children's medications contribute towards the nature and development of parent's health networks.

Conclusion: This research has provided a greater understanding of the dynamics of parent's health connections and their potential impact on children's asthma management.

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IN PAEDIATRIC ASTHMATIC SUBJECTS, DAY-TO-DAY VARIABILITY IN HOME-BASED FORCED OSCILLATION TECHNIQUE (FOT) MONITORING IS INCREASED IN SUBJECTS EXPERIENCING EXACERBATIONS

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Introduction/Aim: Objective tools for monitoring childhood asthma are urgently required, yet conventional lung function tests (e.g. spirometry, peak flow) are limited in this setting by their effort-dependent nature and limited insight into asthma control. The Forced Oscillation Technique (FOT) is a novel test, performed during tidal breathing, assessing airway calibre and lung stiffness by measuring airway resistance (Rrs) and reactance (Xrs), respectively. In this study we sought to extend previously published utility of physician-supervised FOT day-to-day variability in the asthma camp setting[1] by examining these relationships with asthma control and exacerbations in the parent-supervised home setting over a longer period.

Methods: Asthmatic children (8-18 years) with asthma exacerbations over the preceding year are being recruited from tertiary hospital respiratory clinics (total intended n=25). Following FOT training and device (tremoFlo™, Thorasys Ltd, Canada) set-up in the child's home, daily FOT was collected over 3-4 months. Rrs and Xrs dy-to-day variability was calculated (as Coefficient of variation, CoV) and compared between and within subjects. Asthma symptoms, control and quality-of-life questionnaires were performed at regular intervals. Medication adherence was assessed using Smartinhalers™ (Adherium, New Zealand).

Results: Recruitment and data collection is ongoing: 12/12 completed home-based monitoring to date. Feasibility rates >90% have been achieved across several subjects. Data collected have highlighted: (1) ability to detect exacerbations, (2) increased day-to-day Rrs and Xrs variability in brittle asthma, compared to well-controlled asthma (R5: CoV 33% vs 17.4%; X5: CoV 41% vs 33%) and (3) detrimental impact of asthma preventer medication non-adherence on day-to-day variability compared to periods of good adherence (R5: CoV 28% vs 12%).

Conclusion: Home-based day-to-day FOT variability, under parental supervision, is feasible and observations during initial data collection support potential clinical utility of this approach in paediatric asthma. Ongoing data collection will seek to confirm the above patterns in other subjects.

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Key Words: Forced Oscillation Technique, variability, asthma

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SEVERE EOSINOPHILIC AASTHMA IN AUSTRALIA: THE AUSTRALIAN MEPOLIZUMAB REGISTRY

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Introduction/Aim: Mepolizumab is a monoclonal anti-interleukin 5 antibody for the treatment of severe eosinophilic asthma. Aim: to describe the baseline characteristics and clinical responses of patients treated with mepolizumab and entered in the Australian Mepolizumab Registry (AMR).

Methods: AMR, a multi-centre web-based post-marketing surveillance registry, was established to characterise the use, efficacy and adverse effects of mepolizumab (NUCALA) for the treatment of severe eosinophilic asthma. Patients with severe eosinophilic asthma who were prescribed mepolizumab were characterised prior to the commencement of therapy and at predetermined 4 and 7 month follow-up visits.

Results: Of 46 patients registered, the median(Q1,Q3) age was 58 (53,65) years, 23 were male and 61% were never smokers. They had a mean pre-bronchodilator FEV_1 %predicted 55.1 ± 16.3(SD), mean Asthma Control Questionnaire-5 score of 3.52 ± 0.87(SD) and 20% had required hospitalisation for an exacerbation in the 12 months prior. The median(Q1,Q3) peripheral blood eosinophil level was 0.7 (0.4,0.9) $\times10^9$/L. The median(Q1,Q3) IgE was 150 (51,427) IU/mL and 56% were atopic. Upper airways disease was common: rhinitis 57%, nasal polyposis 39%. 57% of patients were taking maintenance oral corticosteroids (mOCS) at baseline. The group not prescribed mOCS had a greater proportion of ex-smokers (55% vs 23%, p=0.048) and had attended more non-scheduled doctor visits for exacerbations in the previous 12 months (50% compared to 19%, p=0.027). Patients prescribed mOCS reported a higher Hospital Anxiety and Depression scale depression score [mean 6.8(3.82) compared to 4.21(2.97), p=0.042] and significantly poorer asthma-related quality of life in the Juniper emotions domain (2.82(1.6) vs 4.03(1.75), p=0.045).

Conclusion: People with severe eosinophilic asthma have a high disease burden. Psychological symptoms are worse in people prescribed mOCS. Reducing the use of mOCS may be of benefit in this population.

COMPARATIVE RESPONSES IN LUNG FUNCTION MEASUREMENTS IN MODERATE SYMPTOMATIC ASTHMA

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Introduction/Aim: We investigated (post-hoc) the comparative responses of several lung function measurements in adults and adolescents with moderate symptomatic asthma following tiotropium Respimat® (tioR) treatment.

Methods: Data from Phase III trials in adults (MezzoTinA-asthma®: two replicate, pooled, 24 week trials [NCT01172808/NCT01172821]) and adolescents aged 12–17 years (RubaTinA-asthma®: 48-week trial [NCT01257230]) were analysed. Both trials involved patients with moderate symptomatic asthma. Lung function measurements (FEV_1, FVC, FEV_1/FVC ratio and peak expiratory flow [PEF]) were analysed at Week 24 from patients receiving tioR2.5µg/tioR5µg/placebo once-daily added-on to at least 400–800µg budesonide/equivalent.

Results: In adults, significant improvements in tioR versus placebo were observed consistently across lung function measurements (Table). In adolescents, while significant improvements in peak $FEV_{1(0-3h)}$ were observed for both tioR doses, the difference for trough FEV_1, FEV_1/FVC and morning and evening PEF was significant only for tioR5µg. Peak $FVC_{(0-3h)}$ and trough FVC responses were non-significant for either tiotropium dose in adolescents.

Conclusion: Add-on tioR improves lung function in adults and adolescents with moderate symptomatic asthma. Adolescents demonstrated numerically smaller improvements than adults; statistically significant improvements were noted primarily for FEV_1 and PEF, and not for FVC, indicating larger flow than volume response in adolescents compared to adults.

Table 1

Parameter	tioR5µg		tioR2.5µg	
	MezzoTinA-asthma® Adults N=513	RubaTinA-asthma® Adolescents N=134	MezzoTinA-asthma® Adults N=515	RubaTinA-asthma® Adolescents N=125
Peak $FEV_{1(0-3h)}$, mL	185(146, 223)***	174(76, 272)**	223(185, 262)***	134(34, 234)*
Trough (pre-dose) FEV_1, mL	146(105, 188)***	117(10, 223)*	180(138, 221)***	84(−25, 194)
Peak $FVC_{(0-3h)}$, mL	95(53, 138)***	72(-37, 182)	141(98, 183)***	88(−24, 200)
Trough FVC, mL	80(35, 125)**	35(-80, 150)	107(62, 152)***	63(−55, 181)
FEV_1/FVC, %	2.7(1.9, 3.4)***	2.5(0.8, 4.2)*	3.3(2.6, 4.0)***	1.0(−0.8, 2.7)
PEF morning, L/min	24.3(17.9, 30.7)***	15.8(2.3, 29.3)*	25.4(19.0, 31.7)***	9.7(−4.1, 23.5)
PEF evening, L/min	23.2(16.9, 29.5)***	16.7(3.4, 30.0)*	22.1(15.8, 28.4)***	12.2(−1.3, 25.8)

***$p<0.0001$; **$p<0.001$; *$p<0.05$

CASE STUDY: MEPOLIZUMAB AND VEDOLIZUMAB EFFECTIVELY, AND SAFELY USED IN A PATIENT WITH SEVERE EOSINOPHILIC ASTHMA AND CROHN'S DISEASE

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Introduction: Mepolizumab (IL-5 inhibitor), a newly PBS-approved treatment for severe eosinophilic asthma (SEA) has changed the landscape of severe asthma. However, its safety-profile and potential drug-interactions in real-life patient settings require ongoing surveillance. Here, we present a unique case of a patient safely, and effectively treated with dual monoclonal therapies using mepolizumab and vedolizumab ($\alpha_4\beta_7$-integrin blocker).

Case: 30-year-old man with asthma was diagnosed in his early teens with multiple ICU admissions. Deterioration in asthma control was noted in the last 2 years with frequent exacerbations treated with high dose oral steroid with difficult weaning despite optimal adherence to maximal therapy (Seretide, Alvesco, Spiriva and Singulair). In the setting of persistent peripheral-eosinophilia, non-specific HRCT changes, raised ANCA-PR3, the diagnosis of EGPA vasculitis was finally confirmed on lung biopsy.

He also has Crohn's disease since age 13, severe, with histologic evidence of pancolitis. Over the last decade, he remained refractory to oral steroids and conventional immunosuppressive medications with abdominal pain and diarrhoea ($\geq$20 bowel motions per day) with persistent weight loss. Vedolizumab was started in November 2016 with gradual but significant symptomatic benefit and well-tolerated.

While high dose oral prednisolone was helpful in alleviating his asthma symptoms, it leads to intolerable side effects. After 6-months therapy of Mepolizumab, improvements noted in asthma symptoms (ACQ 4.5 to 1.6), FEV_1 (2.43, 56 %predicted to 3.65, 70 %predicted), FeNO (127 to 48), peripheral-eosinophil (1.9 to 0.03) and Anti-PR3 levels 3.2 to 1.6 (normal<1.8). He became exacerbation-free while prednisolone was weaned.

Both monoclonal therapies were well tolerated with no notable adverse event. His liver function remains stable despite background diagnosis of primary sclerosing cholangitis.

Conclusion: In this case, mepolizumab was highly effective in treatment of SEA secondary to EGPA. More importantly, it was safe to use in combination with vedolizumab ($\alpha_4\beta_7$-integrin blocker) in a patient with multiple autoimmune conditions.

GAVAGE EXACERBATES AIRWAY HYPER-RESPONSIVENESS IN AN ALLERGIC AIRWAYS DISEASE MODEL

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Introduction/Aim: Gavage is the most widely used method for precise oral dosing in experimental studies involving rodents. In the hands of a skilled operator, it is rapid and allows for a precise dose to be delivered directly to the stomach Gavage requires conscious, or lightly anesthetised experimental animals to be restrained, and thus it is also technically challenging. Instances of eosophageal trauma, aspiration and other complications are not uncommon. In this study, we aimed to investigate the effects of repeated gavage on lung function in a mouse model of allergic airways disease.

Methods: Adult male C57BL/6 mice were gavaged with saline 3 times per week from week 5 to week 9 of life (total of 15 gavages). Control mice were handled in the same way, but were fed saline by pipetting drops of it into their mouths. Mice were sensitised and challenged with ovalbumin. Seven days after the final gavage/feed, we assessed pulmonary inflammation, lung volume, lung function and responsiveness / sensitivity to the bronchoconstrictor methacholine.

Results: There was no effect of repeated gavage on any cell type identified in lavage fluid (p > 0.214 in all cases). There was no effect of repeated gavage on lung volume (p > 0.657) or any parameter of lung function at FRC (p > 0.243 in all cases). Mice subjected to repeated gavage were significantly more hyper-responsive to methacholine with respect to airway resistance compared with non-gavaged mice (p = 0.016).

Conclusion: Repeated gavage exacerbates measurements of airway responsiveness in a mouse model of allergic airways disease. This may be a result of the gavage needle causing physical trauma to the adjacent trachea, however further research is required to identify the mechanism. The results of this study have important implications for studies assessing lung function after repeated gavage.

GENERAL PRACTITIONERS (GPS) EXPERIENCES OF ASTHMA MANAGEMENT IN CULTURALLY AND LINGUISTICALLY DIVERSE (CALD) POPULATIONS

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Introduction/Aim: To explore how Australian GPs deal with CALD patients who have asthma.

Methods: Semi-structured interviews guided by a schedule of questions were conducted with GPs who deal with CALD patients with asthma. These GPs were recruited from medical practices in Melbourne, Australia.

Results: The study included 18 GPs have been interviewed so far. Preliminary thematic analyses of the interview transcripts highlighted five key emergent themes: self-management, miscommunication, accessibility and engagement, trust issues and cultural issues. Many participants highlighted CALD patients do not self- manage their asthma. Miscommunication was mentioned by some participants because of linguistic barriers. Other issues resulting in lower accessibility to health care was social isolation and financial stress. Trust issues among CALD resulted from unfamiliarity with the Australian health care system. Cultural attitude of CALD patients affected treatment, for example with conservative CALD patients refusing some physical tests (e.g.: Chest examination).

Conclusion: GPs perceive that treating CALD patients with asthma is difficult and there many key barriers observed to affect treatment. Cultural competence training for health professionals as well as improving asthma and health system awareness in CALD patients with asthma and their carer are key interventions that may address asthma management gaps in CALD patients.

Key Words: CALD, Asthma, General Practitioners, Asthma Management.

Nomination for New Investigator Award

PROFILING INNATE LYMPHOID CELLS IN THE CORD BLOOD OF INFANTS BORN TO MOTHERS WITH ASTHMA IN PREGNANCY

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Introduction/Aim: Perinatal risk factors for allergic disease such as maternal asthma, birth season and even birth order can be linked to detectable alterations in cord blood immune cells. Innate lymphoid cells (ILCs), have been implicated in the development of allergic diseases and are capable of regulating eosinophilic inflammation. Their potential role in the development of asthma is of great interest but remains poorly understood. Here we examine the cord blood cell profile in infants born to mothers with asthma in pregnancy taking part in the NHMRC funded Breathing for Life Trial (BLT).

Methods: Cord blood from 29 BLT participants was collected into EDTA tubes and processed within 6 hours of birth. Cells were stained in whole cord blood: Eosinophils (CD 45^+CD16^-CD193^+), ILC1(Lin$^-$ CD127^+ CD161^+ CD117^- CD294^-), ILC2 (Lin$^-$ CD127^+ CD161^+ CD294^+), ILC3 natural cytotoxic receptor (NCR)$^-$ (Lin$^-$ CD127^+ CD161^+ CD294^- CD117^+ NKp44$^-$), ILC3 NCR$^+$ (Lin$^-$ CD127^+ CD161^+ CD294^- CD117^+ NKp44$^+$). Cells were fixed overnight, samples were acquired on a BD LSRFortessa X-20 flow cytometer and analysed using FlowJo software.

Tidal breathing flow-volume loop (TBFVL) measurements during quiet sleep were performed in infants at 6 weeks of age.

Results: In this preliminary analysis, there were correlations between ILC1, ILC2 and (NCR)$^-$ ILC3s in cord blood (r=0.54-0.74, p<0.005; n=29). No significant correlations were found with NCR$^+$ positive ILC3. Eosinophils weakly correlated with ILC2 (r=0.38 p=0.04) and were inversely correlated with lung function (tPTEF/tE%) at 6 weeks (r=-0.83, p=0.005, n=10).

Conclusion: The study of ILC subtypes in cord blood is feasible and ILC1, ILC2 and ILC3 NCR$^+$ numbers in cord blood show strong correlations with each other. The apparent correlation between ILC2 and eosinophils in cord blood and the potential association with lung function at 6 weeks of age warrants further investigation in this ongoing study.

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ALVEOLAR SURFACTANT PHOSPHOLIPID CONTENT IS REDUCED IN MUCOPOLYSACCHARIDOSIS TYPE IIIA LUNGS

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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, normally involved in heparan sulphate (HS) degradation. This results in primary storage of partially degraded HS and secondary lipid storage in brain and liver. We recently showed HS storage and increased lipids, including cholesterol and selected species of GM1, 2 and 3, and bis-(monoacylglycero) phosphate (BMP) in MPS IIIA mouse lung tissue. Here we determine the phospholipid composition and rate of newly synthesised phosphatidylcholine in lung tissue and bronchoalveolar lavage fluid (BALF) of normal (Norm), heterozygous (Het) and MPS IIIA mice.

Methods: Mice received 100μl intraperitoneal injections of *methyl*-9-deuterated choline chloride (10mg/ml) and were sacrificed at 0, 1.5, 3, 6 and 24h (n = 3-14 per time point/group) after labelling. Phospholipid composition and enrichment of d9 choline in surfactant phosphatidylcholine (PC) in lung tissue and BALF were determined by electrospray ionisation mass spectrometry (ESI-MS/MS).

Results: At time 0 (no label), there was no difference in PC molecular species composition of either lung tissue or BALF between the three genotypes. Similarly, there was no difference in the overall phospholipid composition (i.e. %phosphatidylcholine, -glycerol, -ethanolamine, -serine or sphingomyelin) between the three genotypes. However, there was an approximate halving in the amount of total phospholipid content (nmol/lung) of the BALF in MPSIIIA animals compared with both normal and heterozygous animals (Norm: 259.9±64.3; Het: 271.4±100.4; MPSIIIA: 134.6±36.7nmol; mean ± SD, n=3-14; ANOVA, p=0.0003). In addition, the % enrichment in d9 choline chloride into newly synthesised PC in lung tissue was reduced at 3h in MPS IIIA animals (Norm: 1.32±0.31%; Het: 1.19±0.14; MPSIIIA: 0.96±0.30; mean±SD, ANOVA, p=0.01).

Conclusion: These data suggest that the pulmonary surfactant synthetic capacity of the lung in MPS IIIA mice is reduced. In addition, there may be changes in the rate of secretion or uptake of phospholipids to and from the alveolar compartment. A halving in the surfactant phospholipid content has significant implications for the lung function of MPS IIIA patients.

DIFFERENTIAL NLRP3/AIM2 INFLAMMASOME ACTIVATION IN COPD AND RESPONSE TO CIGARETTE SMOKE

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Introduction/Aim: The reasons for chronic airways inflammation in COPD are poorly understood. We hypothesised that one mechanism involves differential NLRP3/AIM2 inflammasome activation in the distal (alveoli) and proximal (bronchial) airways.

Methods: Lung tissue sections and bronchial brushing-derived epithelial cells from human COPD subjects and controls, and lung sections of mice chronically exposed to cigarette smoke were examined by immunofluorescence and confocal microscopy. Ten variants of human AIM2 amino acid sequences deposited in the NIH Gene Database were analysed for Nuclear Prediction Score (NucPred Score) and prediction of importin-alpha-dependent nuclear localization signals (NLS).

Results: In smoked mice we demonstrated significantly increased NLRP3 (p<0.05) only in the distal epithelial cells (>2-fold increase of % AIM2-positive), while AIM2 was increased in both distal (>3-fold) and proximal airways (>4-fold increase of particulate AIM2 immunofluorescence at the epithelial apex), with nuclear-to-cytoplasmic/apical translocation. These changes were accompanied by significantly increased cleaved IL-1β, IFNγ and PARP, and nuclear translocation of NFκB.

In both lung tissue and proximal epithelial cells from COPD patients vs. controls we observed nuclear-to-cytoplasmic/apical translocation of AIM2, supported by bioinformatics analysis which revealed NucPred Scores varying from 0.17 to 0.58, the highest in the full-length variant containing a NLS at aa336. Double-stranded DNA-transfected epithelial cells showed nuclear exit of AIM2, but single-stranded DNA or LPS induced only increased nuclear AIM2.

Conclusion: Our data suggest that the AIM2 inflammasome is a key mediator of chronic inflammation in the small airways of COPD patients and in response to cigarette smoke

SENESCENT LUNG FIBROBLASTS ATTENUATE ALVEOLAR EPITHELIAL CELL PROLIFERATION AND MIGRATION IN IPF

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Introduction/Aim: Idiopathic pulmonary fibrosis (IPF) is a progressive lung disease characterised by excessive accumulation of fibroblast (Fbs) and collagen in lung parenchyma. Our laboratory has shown that, in comparison to age-matched controls, lung Fbs from IPF patients *in vitro* exhibit increased characteristics of senescence including growth arrest and an activated secretome. We hypothesised that senescent Fbs disrupt alveolar epithelial regeneration following injury to perpetuate fibrosis in IPF. The aim of this study was to examine the effect of senescent lung Fbs on the growth and wound repair responses of alveolar epithelial cells.

Methods: Primary Fb cultures were established from lung tissue of patients with IPF (IPF-Fbs) and age-matched controls (Ctrl-Fbs). Ctrl-Fbs were treated with H_2O_2 (150 μM, 2h) followed by recovery for 72 h, to induce senescence. Senescence was detected by increased senescence-associated β-galactosidase activity and p16/p21 expression. IPF-Fbs or senescence-induced Ctrl-Fbs were co-cultured with A549 alveolar epithelial cells maintained in transwell inserts in the presence of 5% foetal bovine serum. After 48 h in co-culture, A549 cells were harvested for cell counting and cell-cycle analysis, or migration was analysed using a 'scratch-wound' assay. Furthermore, the effects of conditioned media (CM) from Fbs on A549 cell growth and wound repair were evaluated.

Results: A549 cell proliferation was attenuated when either co-cultured with or grown in CM from senescence-induced Ctrl-Fbs, as compared to non-senescent Ctrl-Fbs ($P < 0.05$, n=3). Cell-cycle analysis showed that A549 cells co-cultured with senescent Fbs were arrested in G2/M phase of cell cycle. A549 cell migration and wound healing was attenuated in the presence of IPF-Fbs but amplified with Ctrl-Fbs.

Conclusion: Senescent Fbs inhibit the proliferation and migratory capacity of alveolar epithelial cells. These data suggest that senescent Fbs may contribute to IPF pathogenesis by impeding re-epithelialisation.

Conflict of Interest: Authors declare no conflict of interest

DIFFERENTIAL EFFECTS OF EXOGENOUS IGF-1 ADMINISTRATION ON YOUNG ADULT AND GERIATRIC MICE FOLLOWING PNEUMONECTOMY

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Introduction/Aim: The murine unilateral pneumonectomy (PNX) model induces growth of new alveolar tissue in the remaining lung, increasing lung mass and volume 14d after surgery. This compensatory lung growth response declines as mammal's age. We aimed to determine whether infusion of Insulin-like Growth Factor (IGF)-1 could enhance lung growth in young adult mice and very old mice following PNX.

Methods: Groups of 5 – 8, female C57BL6/J mice aged 12 weeks or 23 months, received both a left sided PNX and also the subcutaneous insertion of an osmotic pump, delivering either rhIGF-1 or PBS. To determine changes in lung volume, mice were imaged by micro-Computerised Tomography at days 4,7,14 and 21 and then sacrificed, the right lung inflated, embedded and examined by immunohistochemistry.

Results: Following PNX in 12 week old mice, there is a rapid increase in lung volume which approaches pre-operative volumes by d4. IGF-1 supplementation following PNX in 12 week old mice significantly increased Ki67+ and Ki67/SpC+ lung cell numbers, at day 21 post-surgery, but did not affect magnitude of lung volume change compared to PBS treated mice. In contrast in old mice, there was a much less pronounced increase in total lung volume of the right lung following surgery. IGF-1 supplementation following PNX surgery significantly increased the volume of air in the lungs compared to PBS treated old mice, but not to the level of preoperative lung volumes and had no effect on tissue content or cell proliferation.

Conclusion: Exogenous IGF-1 treatment does not accelerate or increase lung growth in 12 week old mice or induce lung growth in old mice, following PNX. IGF-1 treatment did significantly increase the lung volume and reduce the lung density in old mice.

ESTABLISHING AN EPITHELIAL AIRWAY MODEL OF BACTERIAL-VIRAL POLYMICROBIAL INFECTION

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Introduction/Aim: Infections of the respiratory airway rarely involves a single pathogen aetiology. Modelling the human respiratory epithelium has been a challenge due to its complex structure multiple cell types. Using juvenile epithelial brushings, we generated a polarised epithelial layer using the Air-Liquid Interface (ALI) method and infected or inoculated two common but significant respiratory pathogens, namely Respiratory Syncytial Virus (RSV) and nontypeable *Haemophilus influenzae* (NTHi) to assess the impact on respiratory airway epithelial cells of sequential infection by the virus on NTHi biofilms and *vice versa,* characterise their behaviour through various functional, immunological, bacterial and viral endpoints.

Methods: Red fluorescent tagged RSV (A2 strain, rrRSV-BN1, 1 x 10^6 pfu) and Green fluorescent tagged NTHi (86-028 NP, 2.5 x 10^7 CFU) were inoculated individually, concurrently or sequentially onto differentiated and polarised human airway epithelial cells. RSV infection and/or NTHi colonisation were allowed to proceed for 7 days before three washes of 0.2ml 1X PBS were performed on the apical epithelial surface. Washes are used to determine bacterial and viral loads via qPCR, as well as cytokine profiles determined via multiplex. Apical and basal insert surfaces were fixed with Hoechst 33342, excised, mounted cell surface up with ProLong Gold antifade mountant and overlayed with coverslips. Five confocal microscopy field-of views of the inserts were obtained on a C2+ system (Nikon), and 1.2μm Z-stacks thickness used to reconstruct 3-dimensional images of the epithelium. Biofilm structural analysis was performed using the COMSTAT program. Image stacks were examined for: biomass thickness (μm), surface area (μm^2), and surface area to biomass ratio.

Event	Infection Groups					
	1 (NTHi only Control)	2 (RSV only Control)	3 (NTHi, RSV)	4 (RSV, NTHi)	5 (Concurrent NTHi+RSV)	6 (-ve Control)
Day 0 - Inoculation/Infection	GFP tagged-NTHi 86-028NP-pRSM2211 (2.5x10⁷ CFU)	RFP tagged-rrRSV-BN1 (1x10⁶ PFU)	GFP tagged-NTHi 86-028NP-pRSM2211 (2.5x10⁷ CFU)	RFP tagged-rrRSV-BN1 (1x10⁶ PFU)	GFP tagged-NTHi 86-028NP-pRSM2211 (2.5x10⁷ CFU) + RFP tagged-rrRSV-BN1 (1x10⁶ PFU)	20µl 1X PBS
Day 4-Post 1° Inoculation/Infection			RFP tagged-rrRSV-BN1 (1x10⁶ PFU)	GFP tagged-NTHi 86-028NP-pRSM2211 (2.5x10⁷ CFU)		
Day 7-Post 1° Inoculation/Infection						
Confocal Microscopy:	Green fluorescence (NTHi) on epithelial cells.	Red fluorescence (RSV) in susceptible epithelial cells	Only Green fluorescence (NTHi) on epithelial cells	Green fluorescence (NTHi) on epithelial cells. Red fluorescence (RSV) in susceptible epithelial cells	Green fluorescence (NTHi) on epithelial cells. Red fluorescence (RSV) in susceptible epithelial cells	No Green or Red Fluorescence observed
Z-Stacks (NTHi Biofilm Thickness (µm)	50-100	Absent	50-100	50-100	50-100	Absent
Density of NTHi Biofilm	+++	Absent	+++	++	++	Absent
Density of RSV infected epithelial cells	Absent	+++	+	+++	+	Absent

Results: Red fluorescence from RSV absent in epithelial cells inoculated four days earlier with NTHi when examined through confocal microscopy (at Day7-post primary inoculation/infection).

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

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IMMUNOFLUORESCENCE IS A USEFUL ADJUNCT TO TRANSMISSION ELECTRON MICROSCOPY FOR THE DIAGNOSIS OF PRIMARY CILIARY DYSKINESIA

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Introduction/Aim: Primary Ciliary Dyskinesia (PCD) is a rare autosomal recessive disorder characterised by dysfunction of motile cilia. Diagnosis of PCD has historically been made on the basis of the demonstration of impaired ciliary beating (using light microscopy) and abnormal ciliary ultrastructure (using electron microscopy) in patients with a suggestive phenotype and low nNO. Recent advances in molecular genetics have identified that up to 30% of affected individuals demonstrate normal ciliary ultrastructure. Transmission Electron Microscopy (TEM) is costly, labour intensive and limited to specialised units. We have been exploring direct immunofluorescence (IF) as a method for confirming TEM abnormalities with known protein defects with a view to extending to patients with a strong pre-test probability of PCD, but no abnormality demonstrable on TEM.

Methods: Consecutive patients with a history suspicious for PCD were referred for diagnostic ciliary studies. Nasal nitric oxide (nNO) levels were measured. Samples of ciliated nasal epithelium were then obtained using standard methodology using a cytology brush. The cells were suspended in Medium 199 and examined immediately using high-speed video microscopy. Further samples were prepared for IF and labelled using a panel of 4 antibodies (DNAH5, DNALI1, RSPH4 and GAS8). The rest of the cells were fixed with glutaraldehyde and prepared for TEM.

Results: 20 patients had ciliary brushing for TEM and IF.

M=12 ;F= 8. Mean age - 17.5 yrs (range 1-49). Mean nNO 502 ppb.

	Electron Microscopy		
Immunofluorescence	PCD Positive	PCD Negative	Unsatisfactory
PCD positive	4	1	0
PCD negative	0	8	3
Suspicious for PCD	0	1	0
Unsatisfactory	0	2	1

Conclusion: IF demonstated abnormal axonemal proteins in 1 case where TEM did not.

IF demonstrated normal axonemal proteins in 3 cases where TEM was inconclusive. IF added sensitivity and specificity to our PCD diagnostic algorithm.

CHARACTERISATION OF B CELL SUBSETS IN THE BLOOD AND LUNG OF PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

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Idiopathic pulmonary fibrosis is the most common of the idiopathic interstitial pneumonias and is typically associated with prominent lymphoid aggregates of CD3^{+} T cells and CD20^{+} B cells within the lung tissue that are located near sites of active fibrosis. The presence of lymphoid aggregates outside of primary and secondary lymphoid tissues is a prominent feature of many autoimmune diseases and the presence of lymphoid foci can precede the onset of clinical disease. We have examined the B cell profile of IPF patients and aged matched healthy controls using multicolour flow cytometry and analysed the serum for the presence of B cell cytokines BAFF and April, and CXCL13 a chemokine that promotes B cell migration to lung tissue. In contrast to healthy controls IPF patients show an accumulation of plasma B cells in the peripheral blood and a subset of patients show a rise in CD5+ CD23+ transitional B cells. Immunohistochemical staining of lung tissue from IPF patients revealed synchronous accumulation of CD138+ plasma cells and CD5+ B cells within the lymphoid aggregates of IPF patients. IPF patients showed a trend toward increased serum levels of BAFF, April and CXCL13. The presence of plasma cells and CD5+ B cells in the blood and lung tissue of IPF patients raises the important question as to the role of B cells in IPF disease pathogenesis.

SERUM AMYLOID A (SAA), TNFα AND INTERFERON γ IN SARCOIDOSIS

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Introduction/Aim: Sarcoidosis is a multisystem inflammatory disorder characterised by non-caseating granulomas which express SAA, TNFα and interferon (IFNγ). Definitive diagnosis requires a biopsy. Target organ biomarkers in e.g. exhaled breath condensate (EBC), blood and saliva may aid development of less invasive methods of diagnosis and monitoring. This study compared SAA, TNFα and IFNγ levels in EBC, peripheral blood and saliva of sarcoidosis patients and healthy controls.

Methods: EBC, blood and saliva were collected from sarcoidosis patients and healthy controls. SAA, TNFα and IFNγ expression in EBC, blood and saliva samples from sarcoidosis patients and healthy controls were measured using enzyme-linked immunosorbent assays. Total protein levels in EBC and saliva were measured using the Bradford protein assay.

Results: See table. Results are presented as median (range).

	Controls	Patients	*p*-value
Plasma SAA (ng/ml)	357 (124-724) n=13	526 (168-676) n=16	0.034 (<0.05)
Total salivary protein (μg/ml)	464 (313-1036) n=16	759 (313-1697) n=18	0.0276 (<0.05)

No differences were seen in levels of TNFα and IFNγ expression in any of the samples, but were generally at the limit of detection of the assays.

Conclusion: SAA was increased in the plasma of sarcoidosis patients, which probably reflects the total body burden of sarcoid granulomas. More sensitive assays may help establish non-invasive patterns of biomarkers that are suitable for the diagnosis and monitoring of sarcoid activity.

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TRANSCRIPTOMIC ANALYSIS OF HEALTHY PRIMARY TISSUE RESPONSE TO RHINOVIRUS INFECTION

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Introduction/Aim: Acute respiratory illness (ARI) caused by viral infection is a significant health burden in young children, especially those with underlying respiratory disease such as asthma. Human Rhinovirus (RV) is the most prevalent respiratory virus in children, however, there are no therapeutics effective at minimising adverse outcomes from RV. We applied a systems biology analysis to healthy epithelium infected with RV to fully describe the normal cellular response as a reference point for future studies.

Methods: Primary airway epithelial cells (AECs) were obtained from 17 healthy children (age 3.8 ± 1.5 years; 9 male). Cells were infected with RV1B (multiplicity of infection: 12.5) for 24 hours. RNA-sequencing was performed using Illumina Hi-Seq2500. Alignment and quality control was performed via an in-house pipeline. Differential gene-expression analysis was then conducted using Ballgown. Gene interaction was modelled by Network Analyst and upstream drivers identified using Ingenuity Pathway Analysis (QIAGEN, Germany).

Results: There were 329 differentially expressed genes in response to RV1B infection, of which 253 were upregulated. Genes not previously reported in RV response studies included interferon signaling mediators EPSTI1, IDO1, CMPK2 and HELZ2. Genes with high connectivity and betweenness which are known as hub—bottleneck nodes include STAT1, ISG15, NFκB2, PML and IRF1. Gene pathways were associated with interferon alpha/beta signaling, negative regulators of RIG-I/MDA5 signaling, interferon signaling, interferon gamma signaling and interleukin-6 signaling. Network analyst identified three key modules namely; interferon signaling, inflammation response and inhibition of viral translation and transcription.

Conclusion: Results demonstrate that applying a systems biology analysis to relevant primary samples uniquely inform whole cell responses to infection and is therefore an ideal platform for identifying new therapeutic targets in respiratory diseases.

TP 153

STAT3 ACTIVATION REINFORCES SENESCENCE IN HUMAN LUNG FIBROBLASTS

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Background: Idiopathic pulmonary fibrosis (IPF) is a chronic fibrosing interstitial pneumonia of unknown cause and has a median survival of only 3 years. We have shown that fibroblasts derived from IPF-lungs clearly display characteristics of senescent cells. Senescent cells are crucial for tissue homeostasis but in overwhelming numbers are thought to drive the pathology of diseases such as IPF. The question of what is driving abnormally high numbers of fibroblasts into senescence remains unanswered. Dysregulated activation of the transcription factor STAT3 has previously been shown to correlate with IPF progression and has the potential to drive the phenotypic divergence observed in lung fibroblasts (LFs) in IPF.

Hypothesis: Inhibiting STAT3 activation after oxidant-induced senescence will attenuate characteristics of the senescent phenotype.

Aim: To determine the effect of inhibiting STAT3 activation on the development of fibroblast senescence.

Methods: Primary cultures of LFs were established from macroscopically normal lung tissue of thoracotomy patients. Senescence was induced by exposing cells to H_2O_2 (150 μM) for 2hr and confirmed by measuring senescence-associated-β-galactosidase (SA-β-Gal), IL-6 production, and cell-cycle arrest protein p21 by cytochemistry, ELISA, and immunoblotting respectively. STAT3 activation was inhibited using the pharmacological inhibitor STA-21 (10 μM), cellular characteristics were subsequently assessed via Immunoblot, fluorescence, and the Seahorse Mito Stress test.

Results: The induction of senescence resulted in increased SA-β-Gal activity, p21 levels, and IL-6 production. Mitochondrial analysis revealed increases in mitochondrial volume, superoxide production, and proton leak. Targeting STAT3 activity after senescence induction attenuated IL-6 production and prevented senescence-associated increases in mitochondrial mass, reduced superoxide production, and inhibited proton leak.

Conclusion: Our data suggests that activated STAT3 plays a role in reinforcing fibroblast senescence, particularly through regulating mitochondrial activity.

EFFECT OF ALTERNATIVE DIESEL FUELS ON HUMAN BRONCHIAL EPITHELIAL CELLS

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Introduction/Aim: A potential alternative approach to reduce air pollution from diesel emissions is to substitute a portion of the diesel fuel with an alternative fuel, such as biodiesel (WCO), other biofuels (butanol) or with an additive (xylene or toluene). However, very little is known about the potential adverse health effects of these alternative fuels. The aim of this study was to compare the effects of diesel and alternative fuel emissions exposure on cell viability and inflammation of primary human bronchial epithelial (pHBECs) cells *in vitro*.

Methods: pHBECs were cultured at an air-liquid interface (ALI) and exposed to different diesel emissions for 30 minutes. This study compared seven diesel mixes made from four substitutes including butanol (Bu20, 20%), toluene (T20, 20%), xylene (X20, 20%) and waste cooking oil (B20, 20%; B50, 50%; B90, 90%; B100, 100%). As a negative control, pHBECs were exposed to filtered laboratory air for 30 minutes. After exposure, cell viability (cell proliferation, live cell percentage and CASP3 mRNA expression) and inflammation (IL-8 and IL-6 secretion) were measured. Statistical analysis was performed using a one-way ANOVA with a Tukeys multiple comparison post-test.

Results: Exposure to toluene- and xylene-diesel emissions significantly increased cell proliferation and CASP3 mRNA expression. Exposure to waste cooking oil biodiesel significantly increased cell proliferation, decreased live cell percentage, increased CASP3 mRNA expression and increased cytokine secretion.

Table 1 pHBEC response data to exposures

	D100	Bu20	T20	X20	B20	B50	B90	B100
Cell proliferation (%)	40.2[#] ±6.4	105.3 ±5.8	108.5* ±13.8	130.2* ±39.8	89.7* ±23.4	91.0 ±11.3	220.8*[#] ±64.1	73.8 ±18.5
Live cells (%)	3.7 ±1.2	7.0 ±2.5	17.8 ±17.6	9.4 ±24.36	26.2 ±7.8	79.0* ±33.3	64.6* ±11.2	53.3* ±12.4
CASP3 exp. (Log2 of ΔΔCt)	-9.3 ±1.1	-1.7 ±0.9	-6.3 ±1	3.0* ±0.6	10.3* ±0.9	3.3* ±1.5	4.2* ±1.1	-2.9* ±0.4
IL-8 secretion (Log2 fold change)	0.5 ±0.2	-0.8 ±0.3	0.8 ±0.7	-0.4 ±0.2	1.4 ±0.2	1.3 ±0.2	3.1* ±0.9	2.1 ±0.4
IL-6 secretion (Log2 fold change)	0.7 ±0.5	-0.4 ±0.1	1.8 ±0.7	-0.6 ±0.2	1.4 ±0.4	0.3 ±0.6	8.4* ±3.9	1.3 ±0.3

[#]indicates a statistically significant difference when compared to the filtered air control.

*indicates a significant difference when compared to diesel emissions exposure.

Conclusion: Exposure to these specific alternative fuel emissions had some adverse effects on cellular responses of pHBECs, compared to diesel emissions. These findings suggest that further research is warranted to characterise health effects of alternative fuels, more importantly biofuels before their implementation in diesel cars.

TP 155

ALVEOLAR MACROPHAGE ZINC HOMEOSTASIS IS DYSREGULATED BY EXPOSURE TO CIGARETTE SMOKE

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Introduction/Aim: Zinc homeostasis in the lung microenvironment is dysregulated in chronic inflammatory lung diseases associated with decreased zinc in the airways. Cigarette smoke exposure impairs the capacity of alveolar macrophages (AM) to phagocytose apoptotic airway epithelial cells (efferocytosis). We hypothesise that this impairment occurs by dysregulation of zinc homeostasis.

Methods: THP-1 macrophages were differentiated under various zinc conditions (0μM, 4μM or 20μM) and exposed to 10% cigarette smoke extract (CSE). Zinc transporter expression was assessed by qPCR, and intracellular labile zinc (FluoZin-3: Live cell stain) and efferocytosis using flow cytometry. Lung tissue sections from mice chronically exposed to cigarette smoke were examined by confocal microscopy; mean fluorescent intensity (MFI) for labile zinc (Zinpyr-1: Fixed cell stain) and zinc transporter ZnT4 (immunofluorescence) was compared to control mice (n=5).

Results: THP-1 macrophages differentiated in 0μM zinc medium did not have significantly altered intracellular labile zinc but were significantly ($p<0.05$) less able to efferocytose apoptotic cells (5.4%) vs control (9.2%). Differentiation in 20μM zinc significantly increased intracellular zinc to 50.7% positive vs control 30.2%, efferocytosis was also significantly ($p<0.05$) increased to 12.1%. THP-1 macrophage exposed to CSE interestingly showed significantly increased gene expression of vesicle zinc transport protein, ZnT4 (2-fold, $p<0.001$).

Corresponding with CSE-exposed THP-1 macrophages, AM from smoke-exposed mice had significantly increased ZnT4 protein detected by immunofluorescence, 256 ± 33 to 815 ± 123 (MFI$\pm$SEM, $p<0.01$). AM ZnT4 protein expression was negatively correlated with the ability of AM to efferocytose ($R^2=0.432$; $p<0.05$) and with Zinpyr-1 staining of labile zinc in the airways ($R^2= 0.723$, $p<0.001$). Airway labile zinc was positively correlated with AM efferocytosis ($R^2= 0.514$, $p<0.05$)

Conclusion: AM zinc homeostasis is influenced by exposure to cigarette smoke, potentially leading to the impaired efferocytosis and increased inflammation in patients with chronic inflammatory lung diseases.

Interventional Pulmonology / Bronchology

TP 156

DIAGNOSIS OF PULMONARY EMBOLISM DOES NOT INCREASE LONG-TERM RISK OF ADVERSE CLINICAL EVENTS

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Introduction/Aim: We aimed to assess the long term risk of serious clinical events (SCE) in patients investigated for pulmonary embolism (PE). SCE were defined as composite of mortality, malignancy, cardiovascular events, recurrent venous thromboembolism (VTE) and chronic thromboembolic pulmonary hypertension, and analyse associated risk factors.

Methods: We prospectively recruited 501 consecutive patients presenting with clinical suspicion of PE to Christchurch Hospital in 2002-2003. These patients were followed-up until 01/03/2015. The data were analysed descriptively.

Results: The mean ($\pm$SD) age at presentation was 62 (±18) years and 42.1% of patients were male. 104 (20.8%) patients were diagnosed with PE by CT pulmonary angiography or ventilation-perfusion scanning. Of these, 18 (17.3%) patients had un-provoked PE. The median follow-up was 11.9 years, 56.0% patients completing over 10 years of follow-up, and 286 patients developed SCE (61.5% in PE group, 55.9% in Non-PE group, P=0.3).

Two hundred and thirty patients (45.9%) died during follow-up; 43.3% in PE and 46.6% in Non-PE group (P=0.5). Using multi-variate analysis, the predictors of mortality were age (P<0.01), diagnosis of malignancy (P<0.01) and congestive heart failure (P<0.01). Diagnosis of PE itself was not associated with increased risk of death (P=0.52). A total of 48 patients (9.6%) developed malignancy during the follow-up period (13.5% in PE compared to 8.6% in Non-PE group, P=0.13), with age being the only risk-factor (P<0.01). Recurrent symptomatic VTE was diagnosed more commonly in patients with PE (10.6%) compared to Non-PE group (1.76%) (P<0.01).

Conclusion: We demonstrate that underlying comorbidities, and not diagnosis of PE is associated with increased risk of serious clinical events.. Recognition and management of underlying medical comorbidities is the key to improve long-term outcomes in patients with suspected or proven PE.

PLEURAL MANOMETRY DURING SIMULATION OF LUNG EXPANSION

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Introduction/Aim: Medical pleuroscopy is often used to investigate undiagnosed pleural effusions. Some of these require definite management using talc pleurodesis or placement of an indwelling catheter. The decision to use talc depends on the proceduralist's ability to predict lung expansion. This has been proven to be inaccurate in the literature. Simulation of lung expansion has already been described as a technique to directly visualize lung expansion when negative pressure is applied to the pleural space at the end of medical pleuroscopy.

The aim of this study is to demonstrate whether changes in intrapleural pressure during this manoeuver respond differently in expandable and non-expandable lung.

Methods: Patients undergoing diagnostic medical pleuroscopy for exudative pleural effusions were enrolled in the study. At the end of the procedure a 1.8mm catheter was introduced into the pleural cavity via the semi-rigid pleuroscope's working channel (Olympus LTF-160) while the pleural space was sealed. Pressure of -50mmHg was applied via wall suction and changes in intrapleural pressure were continuously monitored.

Results: A total of 6 patients have so far been enrolled including 4 expandable and 2 non-expandable lungs on direct visualization during the manoeuver. The slope of decline in pleural pressure was calculated in two phases: 1) from when the suction is applied to when the suction is released, 2) from when the suction is released to when the seal is broken.

Conclusion: Preliminary results indicate that the gradient of the slope of pleural pressure decline is different during both phases in expandable compared to non-expandable lung. This could further validate the use of visualization of lung expansion simulation during pleuroscopy as a predictor of succes of talc pleurodesis.

PROSPECTIVE OBJECTIVE AUDIT OF SAFETY OF TRANSBRONCHIAL CRYOBIOPSY IN A SINGLE AUSTRALIAN CENTRE USING THE BRONCHOFLEX ENDOTRACHEAL TUBE

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Introduction/Aim: Transbronchial cryobiopsy (cryo-TBB) is emerging as a minimally invasive technique to bronchoscopically acquire diagnostic tissue samples from lung parenchyma. Significant complications have been described. We utilise a technique to minimise bleeding complications and have included an objective measure of blood loss in all cases to validate safety.

Methods: The study had RBWH Ethics Committee approval and patients gave informed consent. Patients underwent general anaesthesia with a 'bronchoflex' endotracheal tube (Rüsch, Germany) which includes a side sleeve for a bronchial balloon blocker. This balloon (diameter 10-11mm) is placed in the target lobar bronchus prior to 1.9mm cryoprobe (Erbe, Germany) deployment through a standard bronchoscope (Olympus BF-1TH190, Japan). A seven second freeze cycle approximately 2cm from the pleural surface is employed, utilising a skin marker to maximise clarity of lateral probe movement. Upon sampling, the probe and bronchoscope is removed promptly en bloc, followed by inflation of the tamponade balloon. Blood loss is measured at a trap connected directly to the bronchoscope by weight. All patients undergo chest radiograph to exclude pneumothorax following the procedure.

Results: Twenty-four patients underwent cryo-TBB in July 2016-October 2017. Biopsy locations were from the upper lobe (10/24), middle/lingular (6/24) and lower lobe (10/24). Laterally directed segments were preferred. Procedural time was 33 minutes +/- 9 minutes. Mean measured blood loss was 16.7g (+/- 34.6g standard deviation). Clinically 3 patients experienced significant bleeding requiring further intervention (eg cold saline and adrenaline). In all cases this was due to inadvertent displacement of the balloon particularly from the upper lobe and was followed by change in deployment technique. 4 patients had pneumothoraces (3 requiring ICC insertion).

Conclusion: We have accurately demonstrated typical amounts of blood loss for cryo-TBB which include events due to balloon displacement. Care with this placement has improved our technique, and overall this has improved our concerns regarding the safety of the technique.

MASSIVE PULMONARY HAEMORRHAGE WITH A COMPLEX, PLEXIFORM BLOOD SUPPLY

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Massive haemoptysis is a life threatening emergency. It may be defined as >100mL blood in an hour or >500mL in 24 hours. There are a variety of causes, most commonly related to lung cancer, bronchiectasis and in some settings tuberculosis.

Bronchopulmonary sequestration (BPS) is a rare cause of massive haemoptysis. It is a developmental abnormality that comprises between 0.15 to 6.4% of all congenital abnormalities of the lower respiratory tract, which themselves have an incidence ranging from 1 in 10,000 to 1 in 35,000 live births. It is defined as a region of lung parenchyma that has an incomplete or no connection to the airways, and is supplied by an aberrant artery arising from the aorta or one its branches. Most occur in the lower lobes and the commonest form, intralobular sequestration, is equally found in men and women.

BPS is often diagnosed in childhood but may not be detected until adulthood. Presentations include recurrent infection, haemoptysis, or as an incidental finding on chest radiology.

We present the case of a 38 year old male who presented to hospital with life threatening haemoptysis and received immediate care within the limitations of a regional environment prior to transfer to a tertiary centre. This included CT scanning that showed a right lower lobe necrotic lesion supplied predominantly by enlarged bronchial arteries. Following transfer, a bronchial angiogram demonstrated the right lower lobe lesion with a bronchial artery to pulmonary vein shunt and vascular supply originating from the right bronchial artery, right intercostal artery and a branch from the abdominal aorta. Following discussion at multidisciplinary team meeting between the respiratory team, cardiothoracic surgeons and interventional radiologists, embolisation of these vessels was performed.

BRONCHOSCOPIC REMOVAL OF FOREIGN BODIES: PRESENTATION OF TWO UNUSUAL CASES

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Introduction/Aim: The incidence of foreign body aspiration is rare, but when occurs, Respiratory Physicians may be expected to manage difficult and unique airway issues. We highlight some of the challenges associated with foreign body removal at our health service.

Methods: We present two case reports of foreign body aspiration over six months at the Alfred Hospital.

Results: *Case One*: A 42 year old male presented with chest tightness following aspiration of a cockroach. During flexible bronchoscopy under sedation, the cockroach was identified in the ligula and extracted using biopsy forceps. Upon withdrawal of the bronchoscope, the patient had significant oxygen desaturation (nadir 65%) requiring a period of bag mask ventilation. On completion of the procedure, the patient expectorated further segments of the cockroach. Subsequent rigid bronchoscopy extracted a final hind-wing from the trachea.

Case Two: An 89 year old male with a history of dysphagia aspirated a capsule endoscope ('Pillcam') whilst being investigated for iron deficiency anaemia. The pillcam lodged in his bronchus intermedius. Flexible bronchoscopy with anaesthetic support and laryngeal mask airway was performed, and extraction of the pillcam was successful using an electrosurgical snare (used in gastrointestinal procedures). This complication of capsule endoscopy is reported with increasing frequency.

Conclusion: Adult respiratory physicians need to have the skills to manage unexpected foreign body aspiration. Our case series highlights the importance of anaesthetic support and airway management skills during foreign body extraction and draws attention to the under recognised issue of capsule endoscope aspiration.

Picture A: Cockroach within lingual

Picture B: Pillcam within right main bronchus

(A)   (B)
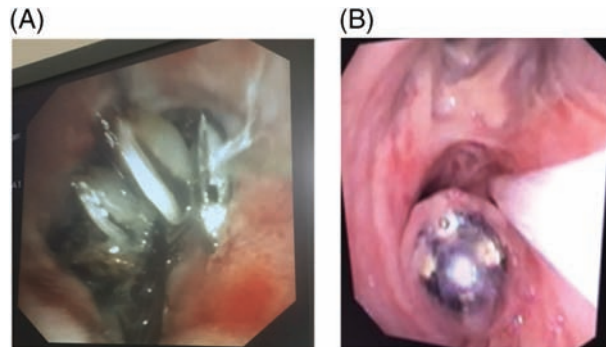
HIGH DIAGNOSTIC YIELD OF TRANSBRONCHIAL CRYOBIOPSY INCLUDES FOCAL PATHOLOGIES AND IS ENHANCED BY EBUS

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Introduction/Aim: Transbronchial cryobiopsy is emerging as a minimally invasive technique to bronchoscopically acquire diagnostic tissue samples from lung parenchyma. Most reports focus on yield of interstitial pneumonias however we here audit our experience with both diffuse and localised infiltrates and masses to improve yield. Including the additional use of endobronchial ultrasound to localise the cryoprobe.

Methods: Here, we report on the diagnostic outcomes of an ethics approved prospective series of 24 patients undergoing transbronchial cryobiopsy between July 2016 and October 2017 at The Royal Brisbane and Women's Hospital. All patients gave informed consent.

Results: Patients were aged 58 years (+/- 14.6 std dev), 42% were female. Radiographic changes showed diffuse abnormality in 13/24 (54%), focal infiltrate in 8/24 (33%) and focal lesion in 3/24 (13%). Radial probe endobronchial ultrasound was used to assist biopsy location in 6/24 (25%). Mean cryobiopsy specimen size was 8mm in maximal dimension. Broncholaveolar lavage was done in 16 cases as well as other conventional biopsies however pathologically the cryobiopsies were the most revealing. Breakdown of final diagnoses by cryobiopsy were diffuse interstitial lung disease 7/24, inflammatory conditions 13/24 (including cases of complex vasculitis, Bronchiolitis Obliterans Organising Pneumonia, and sarcoidosis which had defied previous forms of pathologic diagnosis), malignancy 3/24. Only 3 cryobiopsy biopsy specimens were reported as normal. Two cases had dual pathology with inflammatory and malignant features.

Conclusion: In addition to diffuse processes, cryobiopsy facilitates diagnosis of localised pathologies including complex masses, and is facilitated by EBUS.

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AUDIT OF THORACOSCOPIES PERFORMED IN A NEWLY-ESTABLISHED PLEURAL MEDICINE UNIT

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Introduction/Aim: Medical Thoracoscopy is increasingly utilised as a procedure of choice for investigation of undiagnosed exudative pleural effusion. This audit was performed to create a data pool relating to demographics and outcomes of patient undergoing Medical Thoracoscopy at Fiona Stanley Hospital (FSH). This data also serves as an initial comparator for future audits to improve service delivery.

Methods: Data was collected from the hospital database and patient medical records for all patients undergoing thoracoscopy at FSH since its establishment in January 2015 to August 2017. Outcomes assessed included length of inpatient stay, procedure-related complications, diagnosis post-procedure, other procedures performed at time of thoracoscopy, recurrence of effusions and patent mortality.

Results: 30 thoracoscopies were performed on 29 patients in the timeframe assessed. Only 1 of 6 extended admissions (>4 days) was associated with procedure-related complications. All procedures were performed in relation to investigation of pleural effusion. 23 patients (85%) were successfully diagnosed following thoracoscopy, with 16 diagnosed with malignancy, 7 diagnosed with non-malignant process while four patients had no diagnosis found. Only 8 patients received talc pleurodesis during their thoracoscopy, and 50% had recurrence of pleural effusion post-pleurodesis. All patients with recurrence had a diagnosis of mesothelioma. 11 (58%) of the 19 patients with malignant diagnosis have passed away since their procedure, with 6 patients passing away within 6 months of the procedure.

Conclusion: Similar to international data, thoracoscopy at our tertiary centre has been associated with low complication rates, and is effective in establishing the diagnosis of a pleural effusion. Success rate for pleurodesis at our centre is lower than the quoted published success rates (50% vs 77-100%), however our sample size is small in comparison.

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MANAGEMENT OF EMPYEMA AND COMPLICATED PARAPNEUMONIC EFFUSION IN CHRISTCHURCH

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Introduction: Empyema and complicated pleural effusion (CPE) carry significant morbidity and mortality. White cell morphology and pH are used to predict the risk of infected pleural fluid, as microbiological yield is often low. Empiric antibiotic therapy is usually commenced prior to culture results.

Aim: To establish a baselinemicrobiological yield from pleural fluid culture in patients with empyema/CPE. Secondary aims were to assess factors for empyema/CPE,fibrinolytic therapy use and further surgical intervention.

Methods: This study retrospectively evaluated consecutive patients requiring a chest drain insertion from January 2015 to December 2016. CPE was defined as an exudate by Lights criteria and a pH<7.2. Empyema was defined as gram stain or culture positive, or frank pus.

Results: Thirty eight patients from 333 had an empyema/CPE. Forty-five total chest drains were inserted, n=28(62.2%) left and n=17(37.8%) right. Patient age ranged from 17 to 91 years (median 69). The majority of chest drains were 12 French n=26(57.8%). Twenty five cases had more than 50% polymorphic white cells and gram stain was positive in 17(38%) cases. Organisms were cultured in 19(42%) cases, however antibacterial activity was detected in 16 out of 25(64%). Risk factors for developing an empyema/CPE included underlying lung disease n=22(58%), diabetes mellitus n=5(13%), immunosuppression n=5(13%), and current/ex-smoker n=24(63%). Fibrinolytic therapy was used in 26(57.8%) cases and surgical intervention was required for 3(7.9%) cases but 2 had prior fibrinolysis.

Conclusion: In our setting, 38 patients had an empyema/CPE; gram stain was positive in 38% and an organism was identified in 42% of cases. Polymorphic white cells is a strong marker for empyema/CPE. Lung disease and smoking history appears to have an associated risk for empyema/CPE. Surprisingly, immunosuppression and diabetes mellitus were less so. Very few patients required surgical management post fibrinolytic therapy.

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MEDICAL CHEST DRAIN INSERTIONS IN CHRISTCHURCH HOSPITAL

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Introduction/Aim: With the event of more effective therapeutic interventions like tunnelled pleural catheters (TPC), talcum pleurodesis and fibrinolytic therapy; the number of chest drain insertions appears to have increased. The aim is to review local chest drain insertions, use of fibrinolytics, the success rate of talcum pleurodesis, and compare this to international data.

Methods: This observational study included all patients admitted to the respiratory unit from January 2015 to December 2016 requiring chest drain insertion. We analysed patient characteristics, type of drain inserted, pleural fluid biochemistry, culture, cytology, pleurodesis and fibrinolytic therapy(alteplase and dornase).

Results: A total of 486 chest drains were inserted for 333 patients, with a median age of 69 years. The majority were male n=201(60%). Of these drains, 227(46.7%) were inserted on the left and 259(53.3%) on the right. The main indications for chest drain insertion were malignancy n=260(53.5%), non-malignant pleural exudate n=97(20%) and pneumothorax n=70(14.4%).

Drain size was 12 French n= 303(62.4%), central venous catheters n=69(14.2%), TPC n= 53(10.9%), 24 French n=25(5.1%), 18 French n=15(3.1%), 16 French n=2(0.4%), 28 French n=1(0.2%), and surgical drain n=2(0.4%). Interventional radiology inserted n=16(3.3%).

Talcum pleurodesis for malignant pleural effusion was used in 43 cases with a success rate of 72.1%. Fibrinolytics were used in 31(32%) cases of non-malignant pleural exudates. Twenty two patients required surgical intervention; pneumothorax n=14(4.2%), empyema/CPE n=3 (0.9%), hydropneumothorax n=3(0.9%) and other indications n=2(0.6%).

Conclusion: Mainly 12 French drains or central venous catheter lines were used in Christchurch whilst large bore drains were reserved for empyema, complicated pleural effusions and post thoracoscopy. Fibrinolytics were used for parapneumonic effusions and empyema. Our success rate of talc pleurodesis is in keeping with international data.

PULMONARY ARTERIO-VENOUS MALFORMATIONS: THE PRINCE CHARLES HOSPITAL EXPERIENCE

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Introduction/Aim: Pulmonary Arterio-Venous Malformations (pAVMs) are an uncommon lung pathology that can be isolated or associated with hereditary haemorrhagic telangiectasia (HHT). They may present with symptoms including dyspnoea, orthodeoxia and life-threatening haemoptysis, or incidentally found on thoracic imaging. They may also present due to complications including cerebrovascular accidents or abscess due to their right-to-left shunt function. Management approaches include expectant, intravascular coiling or resection. Regardless patients with pAVMs benefit from multi-disciplinary management involving respiratory physicians, cardiologists, interventional radiologists, clinical geneticists and specialist nursing staff.

Methods: We performed a literature review and retrospective analysis of all individuals with International Classification of Disease codes of either HHT or peripheral arteriovenous malformation who presented to the Prince Charles Hospital between July 1999 and July 2014 to gain further insight into their spectrum of symptoms and complications, biochemical markers, extent of association with HHT and management strategies.

Results: 62 unique patients presented during this interval. Data was available for 46 patients with the remainder excluded due to incorrect coding, chart loss or destruction.

Our data demonstrates that 45% of patients had a confirmed diagnosis of HHT. The most common presenting complaints were epistaxis and haemoptysis, with the incidence of complications including need for nasal cautery, hypoxia and intracranial haemorrhage being seen in 26%, 32% and 6% percentage of people respectively. Of our cohort 41% underwent at least one endovascular intervention with no acute or long-term complications documented within this group. One patient had partial recanalization and was treated with Onyx with good effect.

We have also collated information including demographics, biochemistry, haematinics and family screening to further explore the characteristics of this patient population.

Conclusion: To our knowledge this is the largest single centre cohort of pAVM patients in the Asia-Pacific region and it represents an insightful resource into common management strategies and complications within this region.

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Dr B Gerhardy has no conflicts of interest to declare.

Dr L Krebs has no conflicts of interest to declare.

Dr P Masel has no conflicts of interest to declare.

MASSIVE HAEMOPTYSIS IN A PATIENT WITH PROXIMAL PULMONARY ARTERY INTERRUPTION SYNDROME

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Introduction: Proximal pulmonary artery interruption syndrome (PPAIS) is a rare developmental anomaly which is commonly associated with other cardiovascular abnormalities. It is usually diagnosed in childhood and adult patients are usually asymptomatic. Symptoms can be frequent pulmonary infections or haemoptysis. Diagnosis of this condition can be very challenging. There is no consensus regarding treatment of PPAIS. Aim of this case report is to discuss diagnosis and treatment strategies in this rare entity.

Case report: This case is of a 45 year old previously fit and healthy woman who presented to hospital with 3 episodes of massive haemoptysis of approximately 1000ml. She was haemodynamically stable despite a 30g/ L drop in the haemoglobin level. Patient was further investigated with a CT bronchial angiogram which revealed complete occlusion of the left lower lobe pulmonary artery with associated bronchial arterial hypertrophy. Given the risk of recurrent life threatening haemorrhage , she underwent an elective left lower lobectomy. Histopathology revealed possible proximal pulmonary artery interruption syndrome.

Conclusion: Patients presenting with massive haemoptysis, even if it has spontaneously resolved, should always be investigated further to determine the aetiology. Medical colleagues are encouraged to publish similar cases in the medical literature to identify different clinical presentations, diagnosis and management strategies on these rare entities.

PARATHYROID ADENOMA DIAGNOSED WITH ENDOSCOPIC ULTRASOUND WITH BRONCHOSCOPE (EUS-B) GUIDED BIOPSY IN ASYMPTOMATIC PATIENT WITH PRIMARY HYPERPARATHYROIDISM

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Introduction: Endobronchial Ultrasound (EBUS) is being increasingly used to sample the hilar and mediastinal lymph nodes along with other accessible soft tissue masses through the tracheal and bronchial wall. Some mediastinal lesions are more accessible through the oesophagus. When EBUS scope is passed through the oesophagus to sample mediastinal structures, it is termed as EUS-B (Endoscopic ultrasound with bronchoscope).

Methods: We report a first case of atypical parathyroid adenoma diagnosed using Endoscopic Ultrasound with Bronchoscope (EUS-B) guided biopsy. 48 year old patient presented with dysphagia. A provisional diagnosis of oesophageal intramural mass was made based on a CT scan with subsequent normal oesophagoscopy. EBUS along with EUS-B was performed. Given the location of the lesion just below the vocal cord, it was more accessible through the oesophageal wall using EUS-B. Initial aspiration of the cystic lesion followed by fine needle aspiration (FNA) was performed.

Results: The histology was consistent with parathyroid adenoma. Subsequent biochemical investigations revealed asymptomatic severe hypercalcaemia due to undiagnosed primary hyperparathyroidism which was initially medically managed. Further study with a sestamibi scan showed activity in that lesion which was surgically excised and found to be consistent with atypical parathyroid adenoma. EUS-B is very valuable skill to sample mediastinal lesions which are otherwise could be difficult to access through the trachea.

Lung Cancer

RISK FACTORS AND RATE OF PNEUMOTHORAX FOLLOWING CT-GUIDED PULMONARY BIOPSY: A RETROSPECTIVE AUDIT OF A SINGLE TERTIARY LUNG CANCER CENTRE

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Introduction/Aim: Computer tomographic-guided biopsy (CTGB) is a widely used technique for obtaining a tissue diagnosis of pulmonary lesions, but is commonly complicated by pneumothorax. The aim of this single centre study was to describe the rate, independent risk factors and outcomes of post-procedural pneumothorax following CTGB.

Methods: A retrospective analysis was conducted of all patients undergoing CTGB of pulmonary lesion at Fiona Stanley Hospital during 2016. We excluded patients undergoing pleural or mediastinal biopsies and those in which the procedure was abandoned before introduction of the needle into the pleural space. Data were obtained using electronic medical records and included patient demographics, lesion size and type, needle size and type (co-axial, fine needle aspirate, core), number of passes, length of lung traversed (mm) and post-procedure pneumothorax. Univariate and multivariate analyses were then performed.

Results: One hundred procedures were performed in 94 patients. Forty-nine patients had a post-procedure pneumothorax (any size and defined on any modality), with 24 requiring admission and 12 requiring intercostal chest drain insertion. The presence of emphysema/bullae surrounding the biopsied lesion (aOR 5.11 [1.21-35.0]; p=0.05) and average size of the lesion (0.97 [0.95-0.99; p=0.02) were independent predictors of post procedural pneumothorax. This can be interpreted as a 3% reduction in risk of pneumothorax for each 1mm increase in size of the lesion. No peri-procedural factors were associated with risk of pneumothorax.

Conclusion: In patients undergoing CTGB there is an increased risk of pneumothorax in those with small lesion size and with emphysema/bullae surrounding the lesion. Peri-procedural factors did not appear related to pneumothorax risk in our study. As the main risk factors identified are unmodifiable, careful patient selection is warranted and must be balanced against the potential benefits of new less toxic cancer therapies available.

Key Words: CT-Guided Pulmonary Lesion Biopsy, Pneumothorax.

Grant Support: Nil declared

ACTIVE SCREENING FOR LUNG CANCER INCREASES SMOKING ABSTINENCE– 5 YEAR OBSERVATIONAL DATA FROM THE QUEENSLAND LUNG CANCER SCREENING STUDY (QLCSS)

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Introduction/Aim: Screening for lung cancer promotes smoking cessation behaviours and may represent a "teachable moment" in smoking abstinence. We report 5-year smoking outcomes from the QLCSS.

Methods: The QLCSS screened 256 participants at baseline, Year 1 and 2 using Low-Dose Computed Tomography (LDCT) and collected annual health status questionnaires over 5 years. 121 participants were self-reported current smokers or quit smoking <6 months prior trial enrolment; 135 were former smokers who quit >6 months prior. Smokers received brief intervention (<5mins counselling by the research team plus printed Quitline materials) and were advised to contact their GP and Quitline for further support. Self-reported prolonged smoking abstinence was ascertained annually by the following yes/no questions: "Do you NOW smoke cigarettes (one or more cigarettes per week)?" and "In the past 6 months, have you smoked any cigarettes?". Quitters were defined as answering "No" to both questions. Complete case analysis was performed. Sensitivity analyses for missing data used two models: 1) missing data coded as current smokers and 2) last observed status carried forward—LOSCF.

Results: Complete case analysis showed an increasing proportion of quitters up to 37% in Year 3 followed by a plateau. Worst case scenario (Model 1) showed a similar trend but overall lower proportion of quitters to Year 3 followed by a reduction. Model 2 suggested a continued increase across 5 years (Table 1).

Conclusion: Using a stringent definition of prolonged abstinence, we observed high levels of smoking cessation consistent with prior studies and the 'teachable moment'. Missing data limit the detailed analysis beyond Year 3; however, even in a worst-case scenario the rates of quitting remained high during active LDCT screening. This possibly reflects increased quit motivation through regular contact with the study team which diminished in the passive follow-up phase.

Table 1 Annual Proportion of Prolonged Smoking Abstinence Analysed in Complete Cases, Cases with Missing Smoking Status Interpreted as Continued Smokers and LOSCF

Year	Complete Cases[§] Quitters / Smokers n (%)	Model 1[ß] Quitters / Smokers n (%)	Model 2[◇] Quitters / Smokers n (%)
1	18 / 105 (17)	18 / 112 (16)	20 / 112 (18)
2	29 / 98 (30)	29 / 105 (28)	29 /105 (28)
3	34 / 92 (37)	34 / 103 (33)	26 / 103 (25)
4	30 / 85 (35)	30 / 103 (29)	34 / 103 (33)
5	19 / 57 (33)	19 / 101 (19)	41/ 101 (41)

[§]Complete cases: participants who did not develop lung cancer, did not withdraw from study and who completed self-reported smoking status at that time point (had returned follow-up form and had indicated smoking status).

[ß] Model 1: participants who had missing self-reported smoking status at that time point (either did not return follow-up form or did not fill in smoking status) were counted as continued smokers.

[◇]Model 2: participants who had missing self-reported smoking status at that time point (either did not return follow-up form or did not fill in smoking status) were assumed to have the same smoking status as at their last prior recorded observation.

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CURCUMIN IS TOLERABLE IN VIVO WHEN APPLIED INTRAPLEURALLY IN RATS

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Introduction/Aim: Curcumin, a polyphenol found in the spice turmeric, is cytotoxic towards mesothelioma cells *in vitro and in vivo* stimulating a number of pathways of programmed cell death including apoptosis, autophagy and pyrotosis. Difficulties with clinical translation exist as curcumin is poorly absorbed into the circulation via the intestinal mucosa and undergoes rapid biotransformation in the blood. We propose that curcumin could be instilled into the pleural cavity of patients with mesothelioma through tunneled indwelling pleural catheter for a direct internal topical treatment. Our aim was to evaluated the safety of curcumin treatments *in vivo*, when applied to the pleural cavity in healthy rats.

Methods: Curcumin (80 mg/kg) was injected into the pleural cavity of male and female Fischer 344 rats (n=6). Blood was taken at 1.5 h, 24 h, 48 h, 7-days, 14 days and 21 days. Rats were euthanized at 48 h, 1 week and 3 weeks (n=2). Parietal pleura, lung, kidney, liver brain and heart tissues were obtained and examined for signs of gross tissue damage and histopathological changes. Ultra performance liquid chromatography - mass spectrometry was uesed to determine systemic distribution of curcumin following intrapleural treatments.

Results: Encapsulated curcumin deposits were observed in the pleural cavity of rats at 1 and 3 weeks following curcumin administration. Histological analysis revealed focal reactive mesothelial hyperplasia and a histiocytic response towards curcumin. Lung, liver, heart, brain and kidney tissues all display normal histological appearances. Curcumin was detected in the plasma samples of rats receiving intrapleural curcumin with peak concentration observed at 1.5 h post curcumin treatment (387-100 µg/ml). Curcumin could still be detected 2-weeks after curcumin administration.

Conclusion: Preliminary data suggests that intrapleural curcumin treatments could be tolerable in patients with mesothelioma and is under consideration for cllinical trial.

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EXERCISE TRAINING IN ADVANCED LUNG CANCER: A COCHRANE SYSTEMATIC REVIEW

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Aim: To investigate the effects of exercise training on exercise capacity, health-related quality of life (HRQoL), dyspnoea, fatigue, feelings of anxiety and depression and lung function in people with advanced lung cancer.

Methods: We searched the Cochrane Central Register of Controlled Trials, PubMed, EMBASE, CINAHL, SPORTDiscus and PEDro up to July 2017. Randomised controlled trials (RCTs) were included in which study participants with advanced lung cancer (stage IIIB or IV) were allocated to receive either exercise training or a control group that received usual care. Two review authors independently screened and assessed studies for inclusion. Risk of bias was assessed using the Cochrane seven evidence-based domain table Meta-analyses were conducted were possible.

Results: Five RCTs involving 109 participants were identified. Overall, the risk of bias in the included studies was high. Pooled data from the included studies demonstrated that, compared to usual care, exercise training improved exercise capacity (SMD 0.76; 95% CI 0.30 to 1.23) and HRQoL (SMD 0.41; 95% CI 0.00 to 0.81). No between-group difference were found for dyspnoea (SMD -0.26; 95% CI -0.77 to 0.25), fatigue (SMD -0.12; 95% CI -0.56 to 0.33), feelings of anxiety (SMD -0.38; 95% CI -1.86 to 1.10), depression (SMD -0.46; 95% CI -1.44 to 0.53) or forced expiratory volume in one second (SMD 0.34; 95% CI -0.24 to 0.92).

Conclusion: Exercise training appears to improve exercise capacity and HRQoL in people with advanced lung cancer. The findings of this review should be interpreted with caution due to disparities between the studies, methodological limitations, risk of bias and small sample sizes. This systematic review emphasises the need for larger RCTs.

Declaration of interest: Nil.

HOPE: A TERTIARY CENTRE EXPERIENCE WITH INDWELLING TUNNELED PLEURAL CATHETERS

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Introduction/Aim: Flinders Medical Centre (FMC) is the first tertiary hospital in South Australia with a dedicated pleural service, the HOPE (Home Pleural Effusion) Program, established in 2013. The aim of this study was to determine the complication rate and outcomes of patients with a tunneled indwelling pleural catheter (TIPC) placed at Flinders Medical Centre (FMC).

Methods: A retrospective audit was conducted of all patients undergoing a TIPC insertion at FMC from Sept 2013 to Sept 2017. Time of insertion, TIPC removal and death were recorded along with complication and pleurodesis rates. Statistical analysis was performed using the Fisher's exact test.

Results: A total of 75 TIPC were inserted at FMC in 71 patients. Three patients required repeat TIPC insertion after initial drain dislodgement (n=2) or removal (n=1) and 2 patients had bilateral TIPCs. The majority of TIPCs were inserted for malignant pleural effusions (n=68) with n=7 inserted for benign recurrent pleural effusions. Average length of stay post insertion was 5.32 (+/-5.87 SD) days. The overall survival following TIPC insertion was 104 days (+/-117SD). The time from TIPC insertion to removal (n=20) was an average of 156.6 days (+/-113.13 SD) with the most common reason being pleurodesis (n=11). The overall rate of pleurodesis was 20% (15/75 TIPCs). Overall infection rate was 12/75 TIPCs with 8 patients developing an empyema, all of which were treated with good outcome. The rate of empyema appeared higher in those patients receiving concurrent chemotherapy (16.7% compared with 6.3%), however this was not statistically significant (p=0.24).

Conclusion: TIPCs are an effective and safe treatment for recurrent pleural effusions. Our complication rates are similar to those reported in the literature. Our observed rate of pleurodesis is lower than expected which may be due to symptom guided drainage.

Grant Support: None

PREVALENCE AND PET FEATURES OF ANTHRACOSILICOTIC LYMPHADENOPATHY IN PATIENTS UNDERGOING INVESTIGATION FOR MALIGNANCY

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Introduction/Aim: Anthracosilicosis is a known cause of FDG-avid thoracic lymphadenopathy in patients under investigation for malignancy. In patients with known or suspected malignancy, we aim to describe the patient factors and PET imaging findings of FDG-avid thoracic lymph nodes proven to contain silica and/or anthracotic material.

Methods: We conducted a retrospective analysis of 66 patients from Sir Charles Gairdner Hospital between 2014 and 2016 who underwent both PET scanning *and* EBUS-guided biopsy of thoracic lymphadenopathy for known or suspected malignancy, with subsequent biopsy proven anthracosilicosis. Each PET scan was reviewed by a nuclear medicine physician to obtain values for lymph node SUVmax/mean/peak, node SUV compared to liver/mediastinal blood pool/primary lung tumour and nodal stations/distribution.

Results: 22% of patients who underwent EBUS-guided nodal biopsy and PET scan for malignancy were found to have anthracosilicosis. A total of 107 lymph nodes contained anthracosilicosis. Mean age 66±11.5 years, M:F = 46:20, 78% current/former smokers. 61% of patients were undergoing investigation for lung cancer, 39% for other malignancies. 71% of patients had both hilar and mediastinal uptake on PET imaging. The mean SUVmax of these nodes was 4.45±2.88, and the mean SUV ratios between the lymph node and the liver (1.57), lymph node and atrial blood pool (2.18) and lymph node to primary tumour (0.58) were also calculated and compared to criteria proposed in the literature.

Conclusion: Anthracosilicosis was prevalent in our Western Australian population, and reinforces the value of invasive staging methods to ensure appropriate cancer treatment. Most patients with anthracosilicosis have both hilar and mediastinal disease, and the PET features listed above do not predict the absence of malignancy in our population, using previously validated criteria. Our results are preliminary at this time, however final results will include greater numbers and a comparison group of malignant lymph nodes.

Grant Support: Nil

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SURVIVAL OUTCOMES AND DISEASE RESPONSE IN ADVANCED NON-SMALL CELL LUNG CANCER WITH NIVOLUMAB: A SINGLE CENTRE EXPERIENCE

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Introduction/Aim: Clinical trials have shown promising results with nivolumab in advanced non-small cell lung cancer (NSCLC), however the efficacy in real-life clinical setting is less well defined. This study aims to determine the efficacy and safety of nivolumab at a large thoracic-oncology unit.

Methods: Consecutive series of patients who received nivolumab for advanced NSCLC over 30 months period between January 2015 and June 2017 were identified. Main outcomes were overall survival (OS) and progression free survival (PFS). Objective response and complications were also analysed.

Results: Intention-to-treat study population included 54 patients (median age 62 years). Median OS was 8.8 months (95%CI 4.4 to 13.2) and 23 patients (42.6%) were alive at 12 months after initiation of nivolumab. Median PFS was 2.6 months (95%CI 0.9 to 4.4). Patients with better performance status had significantly higher PFS with a median of 4.5 months for ECOG status one and 1.1 months for ECOG status two (p=0.02). Patients who had complications from nivolumab had higher median PFS compared to others (4.3 vs 1.6 months, p=0.049). Serum lactate dehydrogenase level (LDH) had a negative correlation with PFS (R= -0.32, p=0.02) but not OS. Disease response on initial assessment following starting nivolumab included six patients (11.1%) with partial response, 12 (22.2%) with stable disease, three (5.6%) with a biphasic response and 31 with progressive disease (57.4%) after a median of three cycles of therapy. Out of the patients who had either a partial response or stable disease initially, 16 (88.9%) continued to have stable disease at a median of 8.3 months. Fifteen patients (28.8% (95% CI 18.3 to 42.4)) had adverse events related to nivolumab.

Conclusion: The survival rates with nivolumab were higher than expected with conventional second line chemotherapy, with a favourable complications rate. The performance status and serum LDH levels predicted PFS. Patients who had a favourable response on initial assessment continued to have a sustained benefit.

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PNEUMONITIS AND OTHER IMMUNE RELATED COMPLICATIONS FROM NIVOLUMAB THERAPY IN PATIENT WITH NON-SMALL CELL LUNG CANCER: A DESCRIPTIVE STUDY

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Introduction/Aim: Nivolumab has had promising results in clinical trials in the treatment of advanced non-small cell lung cancer (NSCLC). Immune-related adverse event such as pneumonitis can be a major concern in patients with lung cancer who may already have pre-morbid lung disease. This study describes the rates and effects of immune-related complications with nivolumab in a large thoracic-oncology unit.

Methods: Consecutive series of patients who received at least one cycle of nivolumab for NSCLC over a 30 months period were identified. Demographic, clinical, histological and radiological data of the patient who had immune-related adverse effects were analysed.

Results: Fifty-two patients were initiated on nivolumab therapy for advanced NSCLC. The median number of treatment cycles was six (range 1 to 34) at a median dose intensity of 99% (range 98% to 100%) at a dose of 3mg/kg. Fifteen patients (28.8%, 95%CI 18.3 to 42.4) had adverse events. Three (5.8%) patients developed grade two or three pneumonitis with one patient requiring intravenous methyprednisolone, oral prednisolone and mycophenolate. The second patient was managed with intravenous methylprednisolone and oral prednisolone and third patient required oral prednisolone only. All three patients had moderate to severe underlying interstitial lung disease or emphysema. Nivolumab was ceased in the first two patients and one of whom died from hypoxic respiratory failure secondary to pneumonitis. Other immune related adverse events that required treatment included: myasthenia gravis, thyroiditis, hypothyroidism, colitis and hepatitis. Six patients had vasculitic rash, constipation, diarrhoea, xerositis, hypertensive urgency and a haemorrhagic stroke which did not require specific treatment. There were no statistically significant predictors of adverse events from nivolumab therapy.

Conclusion: The rates of immune related complications from nivolumab in NSCLC in real-life setting is comparable to clinical trial data. Pneumonitis was associated with underlying pre-morbid lung disease, and had significant morbidity and mortality in patients with poor baseline lung reserve.

RADIAL-EBUS INVESTIGATION OF PERIPHERAL PULMONARY LESIONS: A NEW ZEALAND PERSPECTIVE

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Background: Radial-probe endobronchial ultrasound (radial-EBUS) is becoming a key investigation for peripheral pulmonary lesions (PPLs), with growing international evidence supporting its use. This approach is still new to New Zealand, performed in only two centres nationally.

Aims: This study aimed to investigate the diagnostic yield (confirmed malignancy or benignity subsequently confirmed), predictors of success and radial-EBUS safety in New Zealand.

Methods: We performed a retrospective analysis of all cases (n=68) from Middlemore Hospital, Auckland, undergoing sheath-guided radial-EBUS for PPL from March 2015 to August 2016. Diagnostic yield from radial-EBUS was determined and associations with demographic and clinical variables were tested for. Logistic regression on complete records (n=54) was used to build a model predicting successful radial-EBUS.

Results: Overall diagnostic yield of radial-EBUS was 66.2% (95% confidence interval (95CI): 53.7-77.2). It was diagnostic in 57.4% (95CI: 43.2-70.8) of malignant cases with 81.0% (95CI: 58.1-94.6) of diagnostic samples sufficient for mutational analysis when required. Pneumothorax occurred in 4.4% (95CI: 0.9–12.4), none requiring chest drain insertion. There were no cases of pulmonary haemorrhage requiring blood transfusion. Distance from hilum (p-value=0.0020), air-bronchogram (p-value=0.0388) and concentric positioning (p-value=0.0054) were individually associated with diagnostic yield. A model predicting diagnostic yield with 85.3% (95CI: 68.9-95.0) sensitivity and 85.0% (95CI: 62.1-96.8) specificity was attained.

Conclusion: Radial-EBUS was shown to be safe with high diagnostic yield, similar to international reports. It should become common practice in the diagnostic work-up of PPLs in New Zealand. There were promising results allowing for the use of models to predict the yield.

Grant Support: There was no funding provided for this study and no conflicts of interest to be disclosed.

ROLE OF PRE-CLINIC MULTIDISCIPLINARY TRIAGE MEETINGS IN LUNG CANCER MANAGEMENT

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Introduction/Aim: Lung cancer is one of the leading cause of cancer related morbidity and mortality worldwide. Prolonged waiting periods before diagnosis and treatment can lead to poor outcomes. Our aim is to assess impact of thoracic multidisciplinary triage meetings on time to diagnosis and to treatment.

Methods: We organised thoracic multidisciplinary triage meetings which included respiratory physicians and thoracic radiologist. All referrals with suspected thoracic malignancy were assessed on a weekly basis for three consecutive months; further investigations or procedures were tentatively booked in advance and all patients were seen in clinic before they underwent any further procedures. We assessed impact on time to *a)* Lung cancer triage category clinic waiting periods and *b)* Time to diagnosis and relevant specialist appointment for further treatment. Data are expressed as mean±SD and outcomes were compared using unpaired t-test with previous two consecutive years for the same three month period.

Results: We identified 80 patients who were referred over a three month period in 2017; 37% male and age 71±12.6 years. 23.3% had adenocarcinoma, 20% benign, 16.6% squamous cell carcinoma, 3.3% small cell lung cancer and 36.8% other malignancies. Average time to when patients were seen in clinic, time to diagnosis and time to treatment is outlined in table 1.

Table 1

	2017 (mean±SD) days	2016 (mean±SD) days	2015 (mean±SD) days
Time to clinic	19±11	19.1±18.8	18.5±35.2
Time to diagnosis	25±18.1	49.2±59.5	38±48.1
Time to treatment	52±23.5	74.7±44.7	57.7±56.6

At the end of the three months average time span to diagnosis and treatment reduced by 24.2 (p-value 0.0008) and 22.7 days (p-value 0.01) respectively when compared to 2016 and 13 (p-value 0.03) and 5.7 days (p-value *0.6*) respectively when compared to 2015.

Conclusion: Multidisciplinary triage meetings appear to have a useful role to expedite diagnosis and treatment in patients with thoracic malignancy.

Grant Support: Nil

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CORE NEEDLE BIOPY VERSUS FINE NEEDLE BIOPSY IN A LARGE METROPOLITAN HEALTH NETWORK

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Introduction: Lung cancer is the world's leading cause of cancer related death. Early and accurate diagnosis is essential for prompt treatment to reduce morbidity and mortality. The aim of the large retrospective study was to compare the efficacy of radiologically guided core needle biopsy (CNB) and fine-needle aspiration (FNA) of lung lesions by analysing outcomes and complications.

Methods: Study analysis of 241 consecutive CT-guided CNB or FNA performed with the step and shoot approach between January 2007 and December 2013. For core biopsies 16-20G Quickcore needles and for FNA 22G Chiba needles were used. Specimens were sent for histopathological or cytological analysis. Immediately post procedure, a low dose CT scan was performed to exclude pneumothorax, followed by chest radiography two hours later to assess for complications.

Results: Of the 241 biopsies, 177 (73.44%) were CNB and 64 (26.56%) were FNAs. FNAs were more frequently performed on non-peripheral lesions than peripheral (60.94% vs 39.06%) compared to core biopsies (38.42% vs 61.58%). Core biopsies demonstrated higher yield (90.40% vs 65.63%) and diagnosed malignancy more often (70.06% vs 37.50%). Pneumothorax occurred 75 times (31.12%) and were more common non-peripheral (70.67% vs 29.33%), yet only 5.81% of biopsies and only one peripheral pneumothorax required further management. FNAs had a higher rate of pneumothorax than CNBs (43.75% vs 26.55%). Haemorrhage complicated 7.05% of biopsies and occurred more in CNB than FNA (8.47% vs 3.12%).

Conclusion: Core biopsy appears to be a more efficacious method of sampling tissue in the investigation of a solid pulmonary nodule. Our study demonstrated a higher diagnostic yield, lower pneumothorax rate and overall similar complication rate in CNB compared to FNA.

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INTERSTITIAL LUNG ABNORMALITIES IN THE QUEENSLAND LUNG CANCER SCREENING COHORT

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Introduction/Aim: Non-nodule incidental findings are common in lung cancer screening trials. We present preliminary data on the prevalence and progression of incidentally-detected interstitial lung disease in the Queensland Lung Cancer Screening Study (QLCSS) cohort.

Methods: 256 healthy volunteers underwent screening (low-dose, supine) (aged 60-74, >= 30 pack years smoking history and FEV1 >=50% predicted). Electronic search of baseline (T0) and two year follow-up (T2) Computed Tomography reports identified candidate cases using pre-specified interstitial lung disease terms. Candidate CTs were reviewed on PACS workstations in a randomised order by an experienced radiologist and senior respiratory medicine trainee blinded to the existing reports. Scans were scored for the presence and extent of interstitial abnormalities using an in-house score. A provisional diagnosis based on the radiology features was made where possible.

Results: 66 (25%) candidate cases were identified from reports. Single observer (JM) review of CT images of candidate cases identified 42 participants (16%) with an interstitial abnormality. Minor basal reticulation was the most common finding (43%) and usually involved less than 5% of the entire lobe. Fifteen cases (6%) demonstrated evidence of focal or more diffuse ground glass opacity. One participant met ERS/ATS radiological criteria for probable usual interstitial pneumonia with reticulation, traction bronchiectasis and honeycombing. Most participants showed no progressive change on T2 scan.

Conclusion: Minor interstitial abnormalities are common incidental findings in our lung cancer screening cohort. The majority of cases did not progress on short-term interval imaging and are unlikely to be of any clinical significance, however, longer-term assessment would enable more accurate prognostication.

This abstract has been withdrawn

CASE REPORT—A PULMONARY GLOMUS TUMOUR WITH MALIGNANT TRANSFORMATION

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Case Description: A 68-year-old female presented with an increased cough, exertional dyspnoea and chest tightness. A CT chest demonstrated a partially occlusive mass evident in the right bronchus intermedius. A bronchoscopy demonstrated a large, partially necrotic vascular tumour at the origin of the bronchus intermedius. Biopsies demonstrated features suggestive of a Glomus tumour. A PET CT scan of her chest showed a non FDG avid lesion in the right bronchus intermedius with no evidence of locoregional or metastatic disease defined.

She proceeded to an uncomplicated right middle and right lower lobe lobectomy. The histopathological findings were consistent with a malignant glomus tumour. Follow up CT scans now one year after the procedure have not demonstrated evidence of recurrence to date.

Discussion: The Glomus body is a neuromyoarterial apparatus in the dermis and contributes to body temperature regulation. Glomus tumours are rare solitary neoplasms that usually occur in the distal extremities. Occasionally glomus tumours can be found at ectopic sites such as gastrointestinal tract, respiratory system, female reproductive tract and cardiovascular system. Pulmonary Glomus tumours are extremely rare and most commonly arise from trachea and bronchial airways. There are less than 60 cases reported worldwide. Most pulmonary glomus tumours are benign and from the literature research at the time of writing, only 20% cases were malignant and less than 1% were with distant metastasis.

It is difficult to differentiate glomus tumours from other solid tumours in the lung preoperatively. It is also difficult to differentiate benign and malignant glomus tumours based on imaging features. Therefore the gold standard therapy for suspicious glomus tumour is operative management. The clinical prognosis of benign glomus tumours is excellent, while malignant tumour can have local and nodal invasion.

Conclusion: For glomus tumours that have malignant transformation or malignant potentials, close monitoring with regular follow up is warranted.

Grant Support: Nil

Occupational & Environmental Lung Disease / Population Health

VALIDATION OF AN ASBESTOS JOB-EXPOSURE MATRIX: EXPOSURE-RESPONSE RELATIONSHIPS FOR MALIGNANT MESOTHELIOMA

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Introduction/Aim: A Job-Exposure Matrix (AsbJEM) to estimate cumulative asbestos exposure for Australian jobs has been published[1]. However, certain assumptions in the calculations were questioned[2]. The aim of this study was to validate the AsbJEM by evaluating exposure-response relationships between various exposure estimates and the incidence of malignant mesothelioma (MM).

Methods: Subjects were people with a history of at least 3 months occupational asbestos exposure participating in a health surveillance program. Cumulative asbestos exposure estimates were calculated using duration of employment, intensity and frequency of exposure. Various exposure estimates were calculated by manipulating the intensity of exposure and duration of peak exposures. Cox proportional hazards models were fitted to analyze the association between MM incidence and each of the calculated cumulative exposures.

Results: Data was collected from 1897 (1843 males) subjects. Of these 42 developed mesothelioma. Ten exposure estimates were calculated, using two exposure intensities (50th and 75th percentile of the mode exposure) and 5 peak durations (5, 15, 30, 60 and 120 minutes). There were significant associations between MM incidence and cumulative asbestos exposure for all estimates. The strongest association, based on the β-coefficient estimated from the proportional hazards models, was found for the published AsbJEM assumptions (50th percentile of mode exposure and 15 minute duration of peak exposure). Using these assumptions the hazard ratios for mesothelioma were 1.93, 2.99 and 4.65 for a cumulative asbestos exposure of 0.83, 1.94 and 10.38 fibres/ml-years, respectively, compared with the reference exposure of 0.04 fibres/ml-years.

Conclusion: The AsbJEM seems to be a valid way of estimating risks of occupational asbestos exposure in Australia and may be useful for identifying exposure-MM relationships for low dose occupational exposures.

[1]van Ouyen et a, Ann Occ Hyg, 2015, 59, 737-748.

[2]Kottek and Kilpatrick. Ann Occ Hyg, 2016, 60, 531-532.

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PRELIMINARY OCCUPATIONAL REVIEW OF QUEENSLAND MINERS WITH DUST-INDUCED LUNG DISEASE

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Introduction/Aim: To review the occupational history of recently diagnosed cases of dust-induced lung disease in Queensland.

Methods: A single centre, retrospective analysis of 20 current or retired Queensland coal mine workers with a dust-induced lung disease. The workers included had occupational dust exposure in either underground mines or open-cut mines. Occupational histories were collected in consultation with the treating physician.

Results: The majority of workers had a diagnosis of silicosis (40%) or mixed dust pneumoconiosis (40%), reflecting respiratory silica exposure. Four patients (20%) had a diagnosis of coal workers pneumoconiosis, reflecting heavy coal dust exposure. Typically cases occurred in workers who were currently or previously employed in underground coal mining (90%) rather than above ground coal mining (10%). Some workers reported periods of prior employment in non-coal mines, or in the mining industry interstate or overseas. Occupational dust exposure history was broad, ranging from 10 to 42 years. Occupational roles associated with heavy dust exposure such as working; at the longwall or coal face; with conveyor belt systems; and roof bolting, were over represented.

Conclusion: This study reviewed the largest case series of dust-induced lung disease in Queensland miners in three decades. Commonalities amongst cases included long dust exposure histories, underground mining and crystalline silica dust exposure. This case series highlights the importance of understanding the complexities and prevalence of occupational lung disease in mining within Australia and the need to better understand the relationship between specific occupational roles and the development of dust-induced lung disease.

The authors have no conflicts of interest to declare.

Grant Support: none at the time of writing

THE RESPIRATORY INFLAMMATORY POTENTIAL OF PYRITE RICH COAL PARTICLES

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Introduction/Aim: The resurgence of coal workers' pneumoconiosis (CWP) in Australia is a significant public health concern. The geographic clustering of cases suggests that the local physico-chemical characteristics of coal dust may be contributing to CWP risk. The aim of this study was to compare the inflammatory potential of Australian coal dust with low and high reactive pyrite content.

Methods: We collected two real-world coal samples with low and high reactive pyrite content. When exposed to ambient air, coal containing reactive pyrite undergoes oxidation to form a range of secondary minerals. We monitored the degradation of the coal samples when exposed to warm ambient air and assessed the pH of the liquid exudates that were produced. We also assessed the cytotoxicity (by LDH assay) and inflammatory potential (cytokine production) in A549 (Type II epithelial cell line) cells in response to particle exposure at a range of concentrations (0, 10, 30, 100 and 300 μg/mL).

Results: The sample with the low reactive pyrite content showed limited reactivity and degradation whereas the high reactive pyrite sample degraded rapidly and produced a liquid exudate with a pH of 0.45. Both the low and high reactive pyrite samples caused dose dependent cytoxicity ($p < 0.001$), however the magnitude of the effect was greater in the sample with high reactive pyrite content ($p = 0.03$). Similarly, both the low and high reactive pyrite content samples caused dose-dependent increases in IL-8 production ($p < 0.001$), but the magnitude of the effect was greater in response to the high reactive pyrite particles ($p < 0.001$).

Conclusion: These observations suggest that coal with high reactive pyrite content has the capacity to produce by-products that are likely to cause significant respiratory injury when inhaled. Further studies are required to determine whether this is linked to their fibrogenic potential.

PLEURAL PLAQUES DO NOT INCREASE LUNG CANCER RISK IN ASBESTOS-EXPOSED

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Introduction: Asbestos exposure increases the risk of lung cancer. Pleural plaques (PP) are the most common manifestation of asbestos exposure. There is controversy as to if the presence of PP confers an increased risk for lung cancer.

Aim: To define the relationship between PP and lung cancer risk.

Methods: 1,759 male participants from the Western Australia Asbestos Review Program with occupational exposure to asbestos >3 months cumulative full time exposure (excluding ex-Wittenoom miners and residents) were studied over a 25-year period. All participants were under annual review with chest radiography (CXR) and/or low dose CT (LDCT), with linkage to national cancer and mortality registry data. Subjects were followed up from the date of their latest CXR or LDCT, taken a year or more before the date of death, cancer diagnosis, or end of follow-up. A case was defined as a diagnosis of lung cancer from state cancer registry. Hazard ratios (HR) for lung cancer were estimated by Cox regression, with age as the underlying matching time variable, and tobacco smoking (ever/never smoker and pack-years), asbestos exposure (using the AsbJEM-derived estimated cumulative exposure), International Labour Organisation CXR readings for asbestosis (defined as profusion score $\geq$1/0) or LDCT reading score ≥1, and presence of pleural plaques.

Results: Mean age at follow up was 69.1 years. Asbestosis was present in 705 (40.1%) and PP in 811 (46.1%) subjects. Lung cancer was recorded in 58 (3.3%) cases. 1333 (75.8%) subjects were ever smokers. HRs for risk of lung cancer are presented in Table 1. Tobacco smoke exposure and the presence of asbestosis were associated with increased HR of lung cancer. Time since first asbestos exposure and cumulative asbestos exposure demonstrated non-significant trends of an exposure-response.

Table 1 Hazard ratios for lung cancer from Cox Regression.

		HR	Lower 95% CI	Upper 95% CI	p=
TSFE (yrs)	≤30	1.00	-	-	-
	30-50	1.13	0.25	5.20	0.87
	≥50	1.42	0.28	7.11	0.67
Ever smoker		5.30	1.25	22.4	0.02
Pack years (per 10 pack-years)		1.12	1.05	1.19	<0.01
Asbestosis		2.07	1.20	3.57	<0.01
Asbestos exposure (f/mly)	≤5	1.00	-	-	-
	≥5	1.99	0.99	3.99	0.05
Any pleural plaque		0.63	0.35	1.11	0.11

(TSFE = Time since first asbestos exposure; f/mly = fibres / ml-years; HR = Hazard Ratio; CI = Confidence Interval)

Conclusion: In this population, the presence of pleural plaques did not increase the risk of lung cancer.

Declaration of Interest: We have no conflict of interest to declare.

SARCOID-LIKE GRANULOMATOUS LUNG DISEASE SECONDARY TO OCCUPATIONAL IRON ORE DUST EXPOSURE

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Introduction/Aim: To expand knowledge on sarcoid-like granulomatous lung diseases (SLGLD) secondary to industrial/occupational dust exposure, specifically iron ore (magnetite), through a case report. Occupational lung disease secondary to iron ore dusts have been rarely been documented in the current literature.

Summary of the Case Report: The case report is of a 58 year old man, who was previously healthy and a non-smoker, who presented with a 12 month history of dry cough with a 3 year history of occupational exposure to iron ore dust after working in the blast crew of an iron ore mining industry in Western Australia. Computer tomography of the chest demonstrated nodular ground grass opacities in the apical areas of bilateral upper and lower lobes with sparing of the periphery. Pulmonary function tests demonstrated moderate obstructive lung disease with no bronchodilator response and normal diffusing capacity. Bronchoscopy with washings and lavage was inconclusive. Wedge surgical biopsy of the affected lung regions demonstrated frequently scattered non-necrotising epithelioid granulomas suggestive of SLGLD. He had symptomatic response to sarcoidosis therapy however there was no radiological improvement; a suggestion that sarcoidosis was not the culprit for the granulomatous disease.

Conclusion: Reporting case studies of incidents of occupational exposure-related lung diseases including iron ore dust and management strategies is important given the very sparse knowledge and experience in this field.

THE WITTENOOM LEGACY

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Introduction/Aim: In the fifty years since the Wittenoom crocidolite (blue asbestos) industry ceased operating, the epidemic of asbestos-related diseases in Australia has intensified.

Use of the employment records of the Australian Blue Asbestos Company and records of the Wittenoom township residents has permitted two cohorts of people with virtually exclusive exposure to blue asbestos to be assembled.

Methods: Exposure data have been analysed and follow-up of these two cohorts has been conducted through all available public records including mortality records in all states of Australia and in Italy, cancer registries of Western Australia (WA) and Federal mesothelioma registries.

Results: Although the pattern of occurrence of asbestos-related diseases in the Wittenoom cohorts has changed, there has been an ongoing epidemic of mortality from lung cancer and malignant mesothelioma and also from asbestosis. Benign pleural diseases continue to be seen. Quantitative exposure-response relationships have been established.

Conclusion: The industrial disaster that was Wittenoom has been directly responsible for many deaths as well as ongoing disease and social issues in people who worked in the mine and mill, who lived in the town, were involved in the transport of asbestos or were exposed to the product occupationally, domestically or environmentally subsequently. The legacy continues. It has prompted the establishment of epidemiological, clinical and scientific research groups in order to understand the biology and behaviour of the various asbestos-related diseases and improve their diagnosis and clinical management, thereby contributing significantly to scientific knowledge.

Grant Support

LONGITUDINAL CHANGES IN PROFESSIONAL FIREFIGHTER LUNG FUNCTION: A SYSTEMATIC REVIEW

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Introduction/Aim: Firefighters may be routinely exposed to harmful airborne substances which increase their risk of developing respiratory illness. This systematic review aimed to investigate the rate of change in the forced expiratory volume in one second (FEV_1), often used as a marker of chronic obstructive pulmonary disease risk, in urban professional firefighters.

Methods: A systematic search was conducted in four electronic databases. Articles were included for review if they reported FEV_1 in the same professional firefighters on ≥2 occasions over ≥1 year. Rate of change in FEV_1 was extracted independently by two authors when reported, or manually calculated as the change in FEV_1 from baseline to follow-up divided by the time interval.

Results: Twenty-one studies, published between 1974 and 2016 were included. Fifteen studies reported FEV_1 in firefighters who performed routine firefighting duties, five of which made comparisons to non-firefighter controls. One study showed an improvement in FEV_1 while others reported declines of 27 to 81 mL/yr in never-smokers; typically less than that of smoking firefighters. Studies that compared FEV_1 decline to non-firefighter controls reported conflicting results. A further six studies reported the FEV_1 of firefighters exposed to severe, non-routine levels of smoke or cement dust, observing subsequent FEV_1 declines of 81.2 to 383 mL/yr, over the twelve to eighteen months. Six studies reported the prevalence of 'accelerated' FEV_1 declines at 4.8-50.8 % based on variable definitions.

Conclusion: The large degree of heterogeneity across studies as well as lack of clarity in reporting results makes generalisations difficult. However, healthy, non-smoking firefighters who use respiratory protection, and who are not subjected to a disastrous exposure should expect to have a normal rate of FEV_1 decline.

HYPERSENSITIVITY PNEUMONITIS ASSOCIATED WITH METASTATIC UROTHELIAL CARCINOMA: A PARANEOPLASTIC PHENOMENON?

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Introduction: Peripheral eosinophilia and eosinophilic pleural effusions are known to occur in association with malignancy(1-3). We present a case of metastatic urothelial carcinoma(UC) with concurrent hypersensitivity pneumonitits(HP) in the context of minimal exposure history and in the absence of many classical features of HP.

Case Presentation: A 70 year old man presented with a 3 month history of progressive dyspnoea, lethargy, non-productive cough and weight loss.

He had been an oyster farmer for 50 years. Three days annually were spent preparing wooden frames without respiratory protection; an activity which exposed him to mud dust, tar particulates and tar fumes. He experienced acute inhalational effects of exposure to tar fumes but no prolonged respiratory symptoms.

High resolution CT showed honeycombing and interlobular septal thickening with bilateral apicobasal gradient(Fig 1). Lung biopsy showed extensive lymphatic and vascular invasion by metastatic, poorly differentiated UC(Fig 2). There were also changes consistent with HP, with loose non-necrotising peribronchiolar and interstitial granulomata and mixed infiltrates of lymphocytes, histiocytes and eosinophils.

Blood pathology was normal.

Discussion: While HP associated with lung UC has not previously been reported, paraneoplastic peripheral hyper-eosinophilia is well described(1). There has also been a single previous report of metastatic UC to the lung with peripheral eosinophilia, eosinophilic pleural effusion, and neutrophilic and eosinophilic lung infiltrates(3).

Given our patient had no history of respiratory illness, very infrequent exposure to potential inciting antigens, and no peripheral eosinophilia, it is possible that his HP was induced by local or systemic tumour-related factors.

Conclusion: In the absence of peripheral eosinophilia, which would support a diagnosis of true HP, and in the face of extensive interstitial metastatic UC, it is possible that the findings are a local, tumour-induced immune response or paraneoplastic phenomenon. The authors believe this may be the first report of a UC associated paraneoplastic HP without peripheral blood eosinophilia.

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THE MACROPHAGE INFLAMMATORY RESPONSE TO IRON OXIDE AND SILICA

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Introduction and Aims: Previous studies have focused on the effects of urban PM_{10}, however, little is known about the impacts of geogenic (earth-derived) PM_{10} on respiratory health. in vivo studies suggest that geogenic iron oxide causes inflammation. This study aimed to investigate the in vitro macrophage response to crystalline silica (quartz) and iron oxide (haematite & magnetite).

Methods: The THP-1 human monocyte cell line was differentiated into macrophages prior to exposure to quartz (SiO_2), haematite (Fe_2O_3) or magnetite (Fe_3O_4) at a range of concentrations (0, 10, 25, 50, 75 & 100 μg/mL). To assess the impact of exposure to the particles on the response to bacterial infection, cells were cultured with or without LPS (10 ng/mL). Interleukin (IL)-1β, IL-6 and IL-8 production in the supernatant was measured by ELISA.

Results: IL-8 was significantly increased with exposure to quartz (10, 25, 50, 75 & 100 μg/ml; p<0.001), haematite (25, 50 & 75 μg/mL; p<0.01) and magnetite (50 μg/mL; p=0.01). When stimulated with LPS, IL-8 production was significantly increased by quartz (10, 25 & 50 μg/mL; p<0.05), haematite (25 & 50 μg/mL; p<0.01) and magnetite (50 μg/mL; p<0.01). In the absence of LPS, IL-6 and IL-1β levels were below the limit of detection. With LPS, IL-6 production was increased by quartz (50 & 75 μg/mL; p<0.01), haematite (50 & 100 μg/mL; p<0.01) and magnetite (10, 25 & 75 μg/mL; p<0.05). Similarly, IL-1β increased with exposure to haematite (50, 75 & 100 μg/mL; p<0.001) and magnetite (50 & 100 μg/mL; p<0.05), but not to quartz, in the presence of LPS.

Conclusion: Our data suggests that quartz, haematite and magnetite can induce a pro-inflammatory response and exacerbate the bacterial response in macrophages. Our data suggest that macrophages may play a pivotal role in the inflammatory response to geogenic particles in vivo.

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BACILLUS LICHENIFORMIS IN GEOGENIC DUST INCREASES INFLAMMATORY RESPONSES IN THE RESPIRATORY EPITHELIUM DURING NON-TYPEABLE HAEMOPHILUS INFLUENZAE INFECTION

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Introduction/Aim: The development and progression of chronic lung diseases such as bronchiectasis involves recurrent episodes of severe respiratory bacterial infections. We have recently shown that exposure to environmental geogenic dust PM_{10} (particulate matter <10μm) may exacerbate the response to non-typeable *Haemophilus influenzae* (NTHi) infection in the human airway. The components of geogenic dust that drive these responses are not yet known. Persistent microbial contamination of cultures led us to investigate the bacterial component of geogenic dust.

Methods: Geogenic dust was collected from remote towns in Western Australia, and PM_{10} was extracted. We assessed the microbial component of this community-sampled dust PM_{10} using 16S rRNA sequencing. We exposed immortalized human airway epithelial cells (NuLi-1) to increasing doses of our isolated *Bacillus licheniformis* strain (MOI 0.01, 0.1 and 1:1 bacteria:cells) for 1, 3, or 24 h. *B. licheniformis* and NTHi infection (association and invasion) was assessed using a standard gentamicin survival assay. Epithelial release of IL-6 and IL-8 was assessed using a bead based immunoassay.

Results: We identified the presence of *B. licheniformis,* a spore-forming, environmentally abundant bacteria. *B. licheniformis* was cytotoxic to NuLi-1 cells at 24 h. At 3 h, live and heat-killed *B. licheniformis* produced high IL-6 and IL-8 inflammatory responses. Co-colonisation of *B. licheniformis* with NTHi did not increase NTHi infection, but did evoke significantly greater IL-6 and IL-8 inflammatory responses (p<0.0001 and p<0.0001 respectively) compared with PBS control and NTHi-only challenge.

Conclusion: These findings have important implications for lung health in individuals living in arid environments such as those in the remote regions of Australia, who are exposed to high loads of geogenic dust. Further investigation into the contribution of *B. licheniformis* and the wider dust microbiome to respiratory infection is warranted.

Declaration of Interest: All authors declare no conflicts of interest.

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CEREBRAL ARTERIAL GAS EMBOLISM IN A SCUBA DIVER WITH A PRIMARY LUNG BULLA

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Primary lung bullae have been reported to cause pulmonary barotrauma and lead to cerebral arterial gas embolism (CAGE) in the context of SCUBA diving, however a lack of symptoms and often minimal radiographic findings often preclude a diagnosis of lung bullae prior to undertaking SCUBA diving activity. We present the case of a fit and healthy 27 year old Caucasian male who presented following the second of two introductory resort SCUBA dives. He developed chest discomfort and dyspnoea immediately on surfacing, which was followed by left-sided hemiparesis and paraesthesias as well as expressive aphasia. His neurological symptoms completely resolved after 10 minutes. A chest X-ray showed a large bulla in the right upper zone containing an air-fluid level. A CT chest confirmed the presence of a large thin-walled fluid-containing bulla in the right upper lobe with surrounding alveolar shadowing, likely representing pulmonary haemorrhage. There was a smaller bulla in the left lower lobe. The diagnosis was of pulmonary barotrauma secondary to a primary lung bulla leading to CAGE. A review of the literature identified several isolated case reports of pulmonary barotrauma leading to CAGE secondary to asymptomatic primary lung bullae. This case highlights the clinical sequelae of primary lung bullae in the context of SCUBA diving activity.

PREGNANCY ALTERS THE IMMUNE RESPONSE TO PARTICULATE RESPIRATORY INSULTS

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Introduction/Aim: Air pollution is associated with an increased risk of respiratory morbidity and mortality. Identifying susceptible individuals is key to mitigating the health risk associated with exposure to air pollution. While the *in utero* effect(s) of exposure to inflammatory insults has been studied, there are almost no data on the effect of pregnancy on the respiratory response to air pollution. Therefore, the aim of this study was to determine whether pregnancy alters the inflammatory and immune response to respiratory insults.

Methods: Eight-week-old pregnant C57BL/6J mice were exposed intranasally to saline, iron oxide (Fe_2O_3) particles or house dust mite (HDM) extract at gestational day (E)7.5, E12.5 and E17.5. Non-pregnant controls were exposed at day (D)0, D5 and D10. Mice were euthanased at E18.5 or D11. A bronchoalveolar lavage sample was collected for assessment of inflammatory cell infiltrate and cytokine production. The spleen and thymus were isolated and processed for flow cytometry for assessment of CD4+, CD8+ and CD4+CD25+ T cell populations

Results: Exposure to Fe_2O_3 ($p < 0.001$) and HDM ($p = 0.01$) reduced the %CD4+ T cells and increased the %CD8+ T cells (Fe_2O_3, $p = 0.002$; HDM, $p = 0.006$) in the spleen of non-pregnant mice but not pregnant mice ($p > 0.05$ for all comparisons). Exposure to Fe_2O_3 increased the % CD4+ T cells in the thymus, however this response was not altered by pregnancy ($p = 0.17$). Pregnancy reduced the %CD4+CD25+ T cells in the spleen ($p = 0.007$) and %CD8+ T cells in the thymus, however there was no effect of treatment on these cell populations ($p > 0.05$ for all comparisons).

Conclusion: These results suggest that pregnancy impairs the immune response to particulate respiratory insults. The impact of this on the maternal inflammatory response and fetal immune development is unclear and warrants further investigation.

LUNG HEALTH IN NEW ZEALAND GANG MEMBERS: RESULTS FROM A HEALTH HUI

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Introduction/Aim: Little is known about lung health in New Zealand gang members, their whānau (extended family) and affiliates. The prevalence of smoking, asthma and chronic obstructive pulmonary disease (COPD) are unknown in this group. A better understanding of lung health in this group might inform public health policy and facilitate targeted strategies to improve lung health. We aimed to determine the prevalence of smoking, asthma and COPD in a group of New Zealand gang members, their whānau and affiliates at a health hui (meeting).

Methods: We organised a health hui for the Notorious chapter of the Mongrel Mob in the central North Island of New Zealand. We collected demographics, smoking and respiratory history, height and weight from participants, and we performed spirometry and exhaled nitric oxide tests. A respiratory doctor and nurse were available to offer advice and local health contacts for any known or newly-diagnosed lung disease, and smoking cessation advice was available.

Results: We studied 26 Notorious Mongrel Mob gang members, affiliates and their whānau. 19 participants were current smokers (prevalence 73%), 5 were ex-smokers and 2 had never smoked. Two participants had a known history of asthma and a new diagnosis was made in a third. No COPD diagnoses were noted.

Conclusion: We successfully conducted a community-focused, hard-to-reach gang population study, and were able to obtain first-of-its-kind data on smoking, asthma and COPD in this population. The smoking prevalence of 73% in this group was much higher than the average nationally and for Māori of 16% and 39% respectively.

Pulmonary Physiology & Sleep

SCREENING FOR SLEEP DISORDERED BREATHING IN HAEMODIALYSIS PATIENTS

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Introduction: Previous studies suggest that sleep-disordered breathing (SDB) is common in patients with kidney disease; however this is infrequently assessed in practice. We aim therefore was to evaluate the performance of screening tools and the association of SDB and clinical factors in haemodialysis patients.

Methods: A cross-sectional study recruiting 92 haemodialysis patients was conducted. We examined the presence of SDB using the STOPBANG questionnaire, Epworth Sleepiness Scale (ESS) and nocturnal oximetry. Patients with an oxygen desaturation index (ODI) of ≥5 were classified as having SDB. A STOPBANG score ≥ 3 and or an ESS score ≥ 10 were used as a risk indicator for SDB. Patient characteristics and pre-dialysis blood samples were collected.

Results: The mean±SD age was 67±15.2 years, and 47% were female. Hypertension (67%) and high body mass index (BMI) (65%, mean $28.98k/m^2$) were common. The mean ODI of the 77 patients who completed an overnight oximetry was 15.09±17.34, and 65% had an ODI≥5. STOPBANG was abnormal in 89% of participants, but only 17% had an ESS≥10. ODI and STOPBANG were significantly correlated (r=0.46, p<0.001), as were ODI and BMI (r=0.44, p<0.001), neck circumferences (r=0.47, p<0.001) and dialysis adequacy (Average Kt/v r=-0.38, p=0.0006), but not ESS (r=0.17, p=0.14). Multivariate analysis showed that neck circumference (OR: 1.17, p=0.03), working (OR: 0.02, p=0.02) and haemoglobin (OR: 0.92, p=0.008) were independently associated with the occurrence of SDB.

Conclusion: The prevalence of SDB in patients receiving intermittent haemodialysis is high. Although patients are not presenting with traditional symptoms of daytime tiredness as reflected in the ESS score; other risk factors such as a high STOPBANG score and large neck circumferences were associated with a high ODI score. Diagnostic testing of SDB using polysomnography can be expensive, STOPBANG and neck size may be useful SDB risk screening tools in the haemodialysis population.

Declaration of Interest Statement: Nil

DYSFUNCTIONAL BREATHING IN PATIENTS WITH TREATMENT NAÏVE OBSTRUCTIVE SLEEP APNOEA

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Introduction and Aims: Occasionally patients being evaluated for sleep disordered breathing (SDB) report symptoms of breathlessness that is unexplained by standard cardio-pulmonary evaluation. Dysfunctional breathing (DB) has been reported to result in breathlessness in some patients. A previous study by our group identified DB in 22% of patients referred for sleep studies. The aim of this study was to assess the prevalence of dysfunctional breathing in patients with newly diagnosed obstructive sleep apnoea (OSA).

Methods: We conducted a prospective observation study of patients diagnosed with obstructive sleep apnea (OSA) and had been referred for continuous positive airway pressure (CPAP) therapy. Participants who provided written informed consent were asked to complete the 'Nijmegen' questionnaire, a validated tool to assess the subjective/functional dimension of dyspnoea. Participant demographic, Epworth Sleepiness Score (ESS) and polysomnographic data were also collected.

Results: Forty participants (median age 57, 58% male) have been enrolled so far. Eighteen (45%) had a Nijmegen score of ≥23 (i.e. positive for dysfunctional breathing). Participants with dysfunctional breathing were more likely to have an elevated ESS (median 13 versus 9.5, p<0.001). There was no difference in the apnoea-hypopnoea index, oxygen saturation, sleep latency, body mass index, sex or age between patients with normal and patients with elevated Nijmegen scores.

Conclusion: Our pilot study has identified that dysfunctional breathing is very common in patients with newly diagnosed OSA. Ongoing participant recruitment will allow a larger sample size and will address the question of whether CPAP treatment improves dysfunctional breathing in OSA patients.

APNEALINK® IN THE DIAGNOSIS OF OBSTRUCTIVE SLEEP APNOEA

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Introduction/Aim: A major impediment to the provision of obstructive sleep apnoea (OSA) treatment is the reliance on labour-intensive and costly, sleep physician-led diagnostic laboratory-based polysomnography (PSG).This study investigated if oximetry and nasal flow measurement via the ApneaLink® device (AL) could be used to identify patients with moderate-severe OSA in those referred for PSG to a tertiary Sleep Service.

Methods: New referrals to The Prince Charles Hospital Sleep Disorders Centre were assessed for study suitability. Demographics, anthropometrics, Epworth Sleepiness and OSA50 scores were collected. Exclusion criteria included age <18 years, pregnancy, significant cognitive impairment, poorly controlled psychiatric disorder, domiciliary oxygen and prior OSA treatment. Participants underwent concurrent Level 1 PSG and AL assessments.

Results: The 100 participants had a mean age of 55 (SD 17) and were 49% male. 48 (48%) had moderate-severe OSA on PSG. AL 3% oxygen desaturation index (ODI) ≥16 had receiver operator characteristic area under the curve of 0.86, sensitivity of 88% and specificity of 84% for PSG AHI ≥15. Various composites of AL, anthropometric and questionnaire variables did not improve upon the AUC or sensitivity of 3% ODI ≥16 but did improve specificity. There were 6 false negative AL 3% ODI (AL 3% ODI <16 but PSG AHI ≥15). 7 of the 8 false positives (AL 3% ODI ≥16 but PSG AHI <15) had PSG AHI >5 (mild OSA) and 7 had average PSG SpO_2 <94%.

Conclusion: AL may play a role in the diagnosis of moderate-severe OSA in those referred for PSG to a tertiary Sleep Service. This could lessen the reliance on PSG for OSA diagnosis, shorten time to treatment initiation, improve waiting lists for PSG and provide significant cost savings. False positive results occurred in those with mild sleep apnoea and/or low baseline oxygen saturations.

TEMPORAL METRICS DERIVED FROM ELECTRICAL IMPEDANCE TOMOGRAPHY DEMONSTRATE ABNORMAL REGIONAL VENTILATION DISTRIBUTION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Introduction/Aim: Electrical impedance tomography (EIT) is a non-invasive imaging technique which measures dynamic changes in thoracic electrical impedance during the respiratory cycle, with low spatial but high temporal resolution. We aimed to characterise regional ventilation distribution using temporal metrics derived from EIT in subjects with COPD.

Methods: 6 male COPD subjects (median(range) age 72(50-86) years, mean±SD FEV1 Z-score -3.31±1.49) and 8 healthy male controls (median(range) age 32(23-73) years, mean±SD FEV1 Z-score -0.08±1.24) underwent spirometry and EIT testing (Dräger Pulmovista® 500, 16 electrode belt, frame rate 50 Hz, during 30 s tidal breathing in the upright posture). The tidal variations in impedance (VT) for the global signal and for each of 256 regions of interest (ROIs) were examined offline. ROIs were visualised as heat maps based on the following features: 1) mean expiratory time (TE); 2) mean breath full-width-half-max (FWHM); 3) mean phase shift relative to global VT (PHASE). Regional distribution of ventilation for each feature was determined by: mean, variability of frequency histograms; mean anterior-mean posterior difference (AP); and fractal dimension (FD_{DIST}, slope of the log-log relationship of the SD of differences between ROI pairs as a function of inter-ROI distance).

Results: There were no significant differences between COPD and controls in histogram mean or variability for any feature. PHASE-AP was lower in COPD compared to controls (0.62±2.90 vs 4.30±2.93, p=0.04), indicating less pronounced differences in ventilation phase in the anterior-posterior dimension. PHASE-FD_{DIST} showed expected increasing ventilation phase variability with increasing distance, following a power-law relationship, but was significantly weaker in COPD vs controls (0.12±0.04 vs 0.22±0.06, p=0.004). PHASE-$DIST_{FD}$ was correlated with FEV1 and FEV1/FVC ratio.

Conclusion: Using EIT-derived temporal metrics of respiratory cycle phase differences, the organised regional distribution of ventilation appears to be altered in COPD compared to controls and may relate to the degree of airflow obstruction.

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This abstract has been withdrawn

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PROLONGED RESPIRATORY SUPPORT FOR PATIENTS RECOVERING FROM SEVERE GUILLAIN-BARRE SYNDROME

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Introduction/Aim: Guillain-Barre Syndrome (GBS) is an auto-immune neuropathy which can lead to respiratory failure due to muscle weakness. Recovery can take months to years. In rare cases, it can lead to requirement for prolonged respiratory support. We present the out-comes data from a tertiary referral weaning centre.

Methods: Clinical review of patient records who presented with a diagnosis of GBS between 2006-2016 and were transferred to a 34-bed specialist weaning facility in London, UK. Patient characteristics including age, sex, time to mechanical ventilation and nerve conduction study results were collected. Primary outcome was time to removal of tracheostomy.

Results: 28 patients (21 male) were referred with median age of 60 (range: 18-85). Median time to intubation was 2 days (range: 0-56 days). 9 patients had a demyelinating pattern; 13 with axonal pattern; 6 had equivocal response or results were not available. 19 patients were weaned from mechanical ventilation with a median time of 150 days (range: 50-500); 7 (25%) required long-term non-invasive respiratory support. 1 patient required tracheostomy re-insertion; 1 patient died from hospital acquired pneumonia whilst awaiting placement. Patients with axonal pattern of nerve damage who weaned from invasive ventilation were younger (median: 57 vs. 66) and took longer to wean from mechanical ventilation (median: 183 vs. 137 days).

Conclusion: Guillain-Barre Syndrome can lead to chronic respiratory failure requiring prolonged invasive mechanical ventilation. Our cohort demonstrates that there is potential for long-term recovery and liberation from invasive ventilator support. There is a role for non-invasive ventilation in patients requiring long-term respiratory support allowing them earlier liberation from invasive ventilation.

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COMPARISON OF TWO METHODS OF DETERMINING LUNG DE-RECRUITMENT, USING FOT

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Introduction/Aim: Airway closure has proved to be important in a number of respiratory diseases and may be the primary defect in asthma. Closing volume can be identified using the forced oscillation technique (FOT), by performing a deflation manoeuvre and examining the resultant reactance (Xrs) lung volume relationship. This study aims to determine if a simple slow vital capacity (SVC) manoeuvre during a FOT test can be used to determine closing volume and compare it to existing more complex techniques.

Methods: Three subject groups were included in the study; healthy (n=29), asthmatic (n=18), and COPD (n=10) subjects for a total of 57 subjects. Reactance lung volume curves were generated via FOT recordings during two different breathing manoeuvres (both pre and post bronchodilator). The correlation and agreement between the closing volume (Vol_{crit}) and reactance (Xrs_{crit}) at this volume was analysed. The changes in Vol_{crit} and Xrs_{crit} pre and post bronchodilator were also analysed.

Results: Across all three subject groups the two different measures of Vol_{crit} were shown to be statistically equivalent (P>0.05) and demonstrated a strong fit to the data (R^2 = 0.49, 0.78, 0.59, for asthmatic, COPD and healthy subject groups respectively). A bias was evident between the two measurements of Xrs_{crit} with statistically different means (p<0.05). However the two measurements of Xrs_{crit} displayed the same trends.

Conclusion: In conclusion we have developed a new alternative technique for measuring airway closure from FOT recordings. The technique delivers equivalent and possibly more sensitive results to previous methods while being simple and easily performed by the patient.

A SINGLE CENTRE 6 YEAR AUDIT OF DIAPHRAGM DYSFUNCTION

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Introduction/Aim: Diaphragm dysfunction (DD) results from pathology involving the innervation, contractile properties, or mechanical attachments of the diaphragm. Common causes include cardiac surgery, neuropathy and myopathy. The symptoms and course of DD are highly variable. We examined a cohort of patients in a major tertiary trauma centre (520 beds, 110,000 admissions/year) with high volume heart and lung transplant units to ascertain incidence, aetiology, and clinical significance of DD.

Methods: A retropective medical record audit was performed of patients diagnosed with DD via fluoroscopy or thoracic ultrasound over six years (2011-2017).

Results: Sixty-five patients were identified with DD: 92% unilateral and 8% bilateral. Mean age 56 years, 62% male and mean BMI 24.5. At diagnosis, mean forced vital capacity (FVC) was 2.36 ± 0.84L ($52\% \pm 19\%$) and mean $PaCO_2$ was 45.0 ± 9.7mmHg. Commonest causes of DD were lung transplant (65%), non transplant cardiothoracic surgery (9%), idiopathic (9%) and cardiac transplant (8%). DD was persistent in 38 patients (59%) and complete resolution occurred in 14 patients (22%). Eighteen patients (28%) required treatment with non-invasive ventilation. Baseline $PaCO_2$ was significantly elevated in patients with bilateral compared to unilateral DD with a trend to lower FVC and greater total sleep time with $SpO_2 < 90\%$.

		N	$PaCO_2$ (N=65)	FVC (%) (N=56)	TST $SpO_2 < 90\%$ (N=28)
Laterality	Unilateral	60	46.2 (± 9.5)	2.30 (± 0.85)	19.5 (± 31.2)
	Bilateral	5	55.2 (± 9.5)	1.95 (± 0.58)	29.2 (± 40.8)
	p value		0.0438	0.3513	0.6811
Cause	Post lung transplant	45	47.0 (± 9.6)	2.31 (± 0.84)	13.9 (± 26.3)
	Other cause	20	46.4 (± 10.2)	2.16 (± 0.89)	32.8 (± 37.5)
	p value		0.8066	0.6147	0.1531
Persistence	Persistent	38	46.4 (± 9.1)	2.17 (± 0.76)	16.5 (± 26.0)
	Resolved	21	47.9 (± 10.0)	2.40 (± 0.97)	24.0 (± 39.5)
	p value		0.5703	0.4980	0.3858

Forced vital capacity FVC, total sleep time TST, peripheral capillary oxygen saturation SpO_2

Values are mean (standard deviation)

Conclusion: In a major trauma centre with heart-lung transplant, most cases of DD were caused by lung transplantation. However non-transplant causes accounted for roughly one new diagnosis every three months. Clinicians should be aware of this condition as DD is frequently persistent and over one quarter may require ventilator support.

EFFECT OF ENDOTRACHEAL TUBE RESISTANCE ON OPTIMIZING MECHANICAL VENTILATION

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Introduction/Aim: The endotracheal tube (ETT) serves as the connection between the mechanical ventilator (MV) and the patient. Partial occlusion of ETT is common, and the subsequent increase in ETT resistance (R_{ETT}) theoretically decreases delivered tidal volume (V_T). Although ETT suctioning (removing the blockage) is regularly performed, if MV settings are not adjusted appropriately post-suction the lungs could be subjected to transient or sustained high alveolar pressures (P_{avl}), leading to alveolar injury. Therefore, we aim to develop a model that can quantify the risk of biotrauma (inflammatory response to overstretching) and volutrauma (physical injury by over-distension).

Methods: We present an anatomically-based computational model of ventilation distribution to predict alveolar volume (V_A) and P_{avl}, over the breathing cycle of a MV patient driven by MV pressure (oscillated between 7-25cmH$_2$O). The model was fitted to the patient's flow data, by stiffening alveoli in dependent regions of the lungs, representing a patient with patchy localised atelectasis and/or oedema. A 30cm long and 8mm diameter ETT was assumed to be 1) occluded with a 5cm long and 3.6mm diameter occlusion ($R_{ETT}=10.58$cmH$_2$O/L.s), and 2) un-occluded ($R_{ETT}=5.85$cmH$_2$O/L.s).

Results: In post-suctioning simulations, V_T and average P_{alv} were increased by ~17%(90mL) and ~15%(2cmH$_2$O), respectively, compared with pre-suctioning simulations. The predicted distribution of increased V_A was non-uniform with 16~31% increase in one-third of the lungs and ~1% in the remainder. Volume increase was mainly seen in normal alveoli in dependent regions of the lungs, suggesting that these normally functioning alveoli are most at risk from trauma relating to over-distension.

Conclusion: Prolonged V_A increases of ~30% have been linked to biotrauma, and acute V_A increases >70% to volutrauma. Our model suggests that suctioning without subsequent adjustment of MV settings is unlikely to result in volutrauma but may increase risk of biotrauma in normally functioning regions of the lung.

SMALL AIRWAY FUNCTION IMPROVEMENT WITH MEPOLIZUMAB IN SEVERE EOSINOPHILIC ASTHMA

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Introduction/Aim: Mepolizumab is a monoclonal antibody against interleukin-5 that was recently approved in Australia for severe eosinophilic asthma. In clinical trials, monthly treatment with mepolizumab results in clinically significant reductions in exacerbation rates, coupled with modest improvements in symptom control scores and FEV1. The acute effects of this biologic treatment on small airway function have not been previously described. The aim of this study is to describe changes in ventilation inhomogeneity as a marker of small airway function after the commencement of mepolizumab in adult with severe eosinophilic asthma.

Methods: This is a prospective case series of 5 patients (3 males) commencing mepolizumab for severe eosinophilic asthma according to the Pharmaceutical Benefit Scheme pre-specified criteria. At each monthly visit, patients underwent lung function testing including exhaled nitric oxide (eNO), spirometry and the multiple breath nitrogen washout test to measure functional residual capacity (FRC) and global (Lung Clearance Index, LCI) and regional indices of ventilation inhomogeneity attributed to the acinar (Sacin) and conducting (Scond) airways. Results at baseline and four weeks after the first injection are reported.

Results: Mean (range) age of patients was 61 (41-76) years, BMI 23.6 (23-25) kg/m^2, post bronchodilator FEV1 50 (36-61) %predicted, FEV1/FVC ratio 50 (31-68)% and median (IQR) eNO 42 (32-75) ppb. One month after the first injection, post bronchodilator FEV1 improved variably 56 (27-151) mL. Mean FRC improved from 3.87 to 3.07 L. Measures of ventilation inhomogeneity were abnormal in all 5 patients and improved at one month: LCI 17.6 (13.5-21.6) improving to 12.0 (8.96-19.43), Sacin 0.380 (0.247-0.600) /L improving to 0.256 (0.140-0.399) /L, Scond 0.075 (0.053-0.100) /L improving to 0.061 (0.036-0.105) /L.

Conclusion: Our initial observation suggests an improvement in small airway function, i.e. ventilation inhomogenity, as early as four weeks after the first injection of mepolizumab in patients with severe eosinophilic asthma.

ACT DOMICILIARY OXYGEN & RESPIRATORY SUPPORT SCHEME PORTABLE OXYGEN CONCENTRATOR TRIAL

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Introduction/Aim: Ambulatory oxygen therapy is routinely offered to patients with chronic severe lung disease. Following significant interest from consumers and advocacy groups regarding the portable oxygen concentrator (POC), the ACT Domiciliary Oxygen and Respiratory Support Scheme (DORSS) aimed to evaluate a protocol for prescribing oxygen via a POC and to determine if these devices are a viable alternative to oxygen cylinders for patients using ambulatory oxygen.

Methods: Twelve volunteer oxygen dependent clients from DORSS were first medically assessed by a Respiratory Physician, followed by spirometry and a 6 minute walk test (6MWT) with portable oxygen cylinder to determine POC prescription. 4 participants were excluded from the trial following initial assessment. 6MWT was repeated with a POC and those without significant oxygen desaturation were provided a loan POC for 3 months. A questionnaire about their POC use was sent fortnightly and pre and post POC St George Respiratory Questionnaires (SGRQ) were also completed.

Results: 8 participants completed the trial (median age 76 years). There was no clinically significant difference between pre-trial SGRQ scores (range 23-77, median 54) and post-trial SGRQ scores (range 22-64, median 52). Participants consistently agreed that the POC was easier and more convenient to use. Many felt more confident leaving home and attending social engagements with a POC. However, some found the POC too heavy to carry. There were no reported adverse events while using a POC.

Conclusion: Our study provides evidence that switching from oxygen cylinders to a POC may be done safely with an appropriate scripting process for ambulatory oxygen users. Participants unanimously found the POC superior to oxygen cylinders in terms of size and convenience. However, given our small number of participants, a larger study would be needed to assess safety and impact of the POC on quality of life.

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EXPLORING THE FACTORS ASSOCIATED WITH FAILURE TO ATTEND SLEEP MEDICINE OUT-PATIENT CLINICS

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Introduction/Aim: It is estimated that 10-15% of patients fail to attend (FTA) out-patient sleep medicine clinic appointments. FTA appointments cause considerable disruption to the provision of quality care to patients but the reasons why patients do not attend appointments are poorly understood. The aim of this audit was to evaluate a cohort of patients who FTA sleep medical out-patient clinics in our institution to assess factors associated with non-attendance.

Methods: We identified 100 patients who had FTA a sleep medical appointment during the time period of 2016-2017. Patient demographic and information pertaining to the reason for clinic attendance was gathered from patient electronic medical records.

Results: The mean ($\pm$SD) age of the patients was 53$\pm$16 years. 63% of patients were male. The median (IQR) of distance of patient residential postcode to clinic site was 10 (3-36) kilometres. Of the 100 appointments, 30% were new clinic appointments and 70% were review appointments. The reasons for clinic appointment were: ongoing management of sleep apnea (69%); evaluation of possible sleep apnea (24%); evaluation of narcolepsy (3%); evaluation of possible parasomnias (2%), insomnia (1%) and respiratory failure (1%). In the electronic medical records, there was no documentation of the reason for the fail-to-attend in 93% of patients; 2% of patients had relocated elsewhere; 2% stated that they were unwell and hence could not attend the appointment and 2% stated that they were not interested in attending sleep medical clinics. 27% of patients had previously failed to attend a previous sleep medical out-patient clinic.

Conclusion: In this pilot study we have identified major gaps in knowledge about the process involved in identifying reasons patients' FTA clinics. Considerable research is required to develop innovative approaches to reduce patient clinic FTA rates.

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IMPROVED NON-INVASIVE VENTILATION PRESCRIPTION FORM REDUCES ADMINISTRATION ERRORS: A QUALITY IMPROVEMENT SUCCESS

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Introduction/Aim: Errors in the administration of non-invasive ventilation (NIV) are common. Poor documentation and inappropriate substitution of the values for Positive End Expiratory Pressure (PEEP), Pressure Support (PS), and Inspiratory Positive Airway Pressure (IPAP) contribute to errors. This study aimed to see if implementing a new NIV prescription form would improve prescription documentation and reduce NIV administration errors.

Methods: A multidisciplinary working group designed a new NIV prescription form. Key features allowed clinicians to distinguish between the three pressure values: PEEP, PS, and IPAP. Inpatient NIV episodes were audited pre-intervention (n=62) and post-intervention (n=49) recording 1) absent/incorrect prescription documentation incidence,2) administration error incidence and 3) location of NIV commencement. Staff in ED and ICU received education prior to both audit periods.

Results: The post-intervention administration error rate was 4.1% (n=2/49), a significant (p=0.04) reduction from the pre-intervention error rate of 16% (n=10/62). The administration error rate was highest among patients who commenced NIV in ED without correct prescription documentation. The intervention appeared to reduce both the absent/incorrect documentation rate and the administration error rate only when NIV was initiated in the ED.

	Pre-intervention	Post-intervention	P Value
Overall			
Administration error	16.1% (n=10/62)	4.1% (n=2/49)	0.04
Absent/incorrect documentation	43.5% (n=27/62)	32.7% (n=16/49)	NS
When NIV commenced in ED			
Administration error	25.8% (n=8/31)	6.7% (n=1/15)	0.13
Absent/incorrect documentation	41.9% (n=13/31)	6.7% (n=1/15)	0.02
When NIV commenced as inpatient			
Administration error	6.5% (n=2/31)	2.9% (n=1/34)	NS
Absent/incorrect documentation	45.2% (n=14/31)	44.1% (n=15/34)	NS

Conclusion: Errors in the administration of NIV significantly reduced following the implementation of the new NIV prescription form.

Declaration of Interest Statement: The authors have no competing interests to declare.