

## UPG Phase III efficacy in describing COPD severity

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## COPD

- ▶ Partially reversible obstructive lung disease
- ▶ Umbrella term for a wide range of diseases
  - ▶ Emphysema
  - ▶ Chronic Bronchitis
  - ▶ Chronic Irreversible Asthma
- ▶ Known risk factors
  - ▶ Smoking +++
  - ▶ Pollution
  - ▶ Genetics
  - ▶ Aging



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## COPD

- ▶ Symptoms
  - ▶ Dyspnoea; especially when active
  - ▶ Audible wheeze
  - ▶ Chest tightness
  - ▶ Crackles (due to reopening of collapsed airways)
- ▶ Australian morbidity and mortality
  - ▶ >1.5 million clinically diagnosed
  - ▶ 2 year survival for severe COPD (FEV<sub>1</sub> <50% predicted) - 50%

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## Respiratory Function Tests

- ▶ Spirometry
  - ▶ Reduced FEV<sub>1</sub> and FEV<sub>1</sub>/FVC
  - ▶ Irreversible/Fixed Intrathoracic Obstruction
- ▶ T<sub>1</sub>CO
  - ▶ Reduced T<sub>1</sub>CO and KCO (T<sub>1</sub>CO/V<sub>A</sub>)
- ▶ Lung Volumes (Body Plethysmography)
  - ▶ Increased TLC (Hyperinflation) and Elevated RV (Gas Trapping)

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## COPD Assessment Test (CAT)

- ▶ COPD Assessment test is 8 questions (max score = 40)

CAT score	Interpretation (burden)
31 - 40	Very high
21 - 30	High
10 - 20	Medium
0 - 9	Low

- ▶ Ambiguous
  - ▶ 0 yields (low) burden
  - ▶ 10 is certainly achievable

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## GOLD

- ▶ Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017 update uncoupled FEV<sub>1</sub> from COPD diagnosis
- ▶ Diagnosis is now based upon Symptom experience and Exacerbation rate

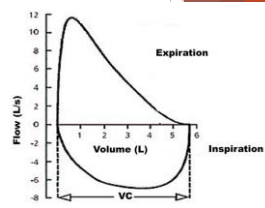
**FEV<sub>1</sub> still serves purpose in describing degree of airflow limitation in the presence of COPD**

C	D	32 (or 33 depending on admission)	Exacerbation (per year)	Airflow limitation	FEV <sub>1</sub> (% predicted)	FEV <sub>1</sub> /FVC
				MILD	≥ 80 %	< 70%
A	B	0-1 (not depending on admission)	MODERATE	50 – 79 %		
			SEVERE	30 – 49 %		
			VERY SEVERE	< 30 % or < 50% with respiratory failure		
GAT4/20 or GAT10/21		GAT5/20 or GAT10/21				
Symptoms						

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## Research opportunity...

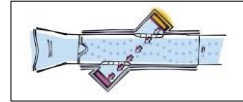
- ▶ Are we best assessing COPD patients?
  - ▶ FEV<sub>1</sub> has been described as a poor indicator for small airway function
    - ▶ COPD is a small airway disease...
- ▶ Is there another test that may detect small airways disease specifically and sensitively?
  - ▶ Proposed for this study - Ultrasonic Pneumography



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## What is Ultrasonic Pneumography??

- ▶ Breath by breath analysis of alveolar emptying
- ▶ Assessment of gas mixing through the lung
- ▶ Uses an ultrasonic spirometer to measure the density and flow of breath



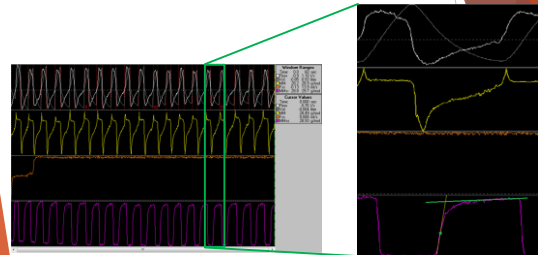
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## Ultrasonic Pneumography

- ▶ Largely novel and sparingly investigated
- ▶ Assessment of ventilation homogeneity...similar to N<sub>2</sub> washout
  - ▶ Research buffs more than clinical sense
- ▶ Side stream analysis of molar mass (CO<sub>2</sub>) during tidal breathing enables detection of flow and expiration of CO<sub>2</sub> from the alveolus recorded at the mouth
- ▶ Inspired and expired breath has different density due to different components
- ▶ Lag exists and must be corrected

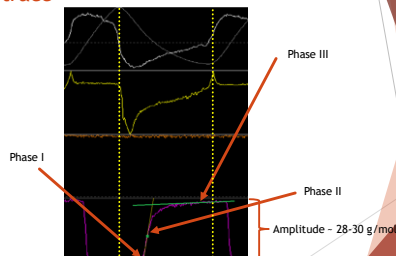
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## UPG trace



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## UPG trace



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## Aims

### Study Question

- ▶ Does UPG align with Spirometry?
- ▶ Does the CAT questionnaire accurately express lung health?

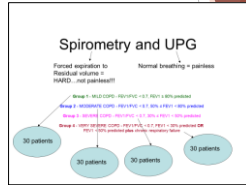
### Study Design

- ▶ Using distinctive classification of airflow limitation based of FEV<sub>1</sub>
- ▶ Do the UPG results classify similar groupings of severity?
- ▶ Up to 30 participants in each group (150 total)
- ▶ Coded according to GROUP and sample number for that group: ie C4

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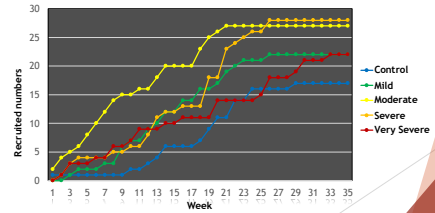
## Proposed Method

- Project a long time in the making...
  - Ethics was granted in 2015...
  - Delayed for "good reason"
- Thesis formed final year of Master of Medical Science programme through Charles Sturt University
  - Graduated August 2019
  - Achieved High Distinction for Research Proposal and final year Dissertation Thesis
  - Dean's Award for School of Biomedical Sciences
- Aiming to publish - Respiriology rejection



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## Recruitment progress



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## Methods

- Cross sectional study
    - 17 (6 male) control participants
    - 22 (11 male) mild (COPD) airflow limitation
    - 27 (12 male) moderate (COPD) airflow limitation
    - 28 (15 male) severe (COPD) airflow limitation
    - 22 (10 male) very severe (COPD) airflow limitation
- 116 participants post screening**

Allocated Group	FEV <sub>1</sub> (GLI 2012 % pred.)	FEV <sub>1</sub> / FVC
Control	≥ 80 %	75 - 85 %
Mild	≥ 80 %	< 70 %
Moderate	50 - 79 %	< 70 %
Severe	30 - 49 %	< 70 %
Very Severe	< 30 %	< 70 %

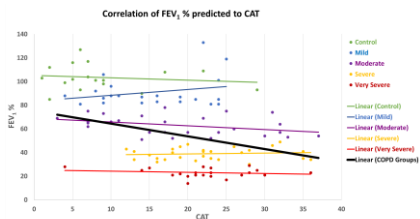
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## Spirometry and CAT

Characteristics	Control	Mild COPD	Moderate COPD	Severe COPD	Very Severe COPD	Total (Control + COPD)
n (male)	17(6)	22(11)	27(12)	28(15)	22(10)	116(56)
BM (Mean ± SD)	73.1 ± 6.6	70.5 ± 5.9	74.1 ± 6.7	77.5 ± 6.0	74.0 ± 5.5	73.1 ± 5.5
Age (Mean ± SD)	58.8 ± 10	64.6 ± 9.5	62.2 ± 10.4	68.0 ± 7.9	64.8 ± 7.5	64.6 ± 8.8
Cigarette history %	12.0 ± 0.1	10.9 ± 0.9	16.4 ± 0.4	22.0 ± 0.5	18.2 ± 0.1	16.4 ± 0.8
Pack Years	11.4 ± 21.2	13.1 ± 24.4	45.6 ± 30.8	43.6 ± 20.1	48.9 ± 22.2	40.9 ± 20.1
FEV <sub>1</sub> (L)	1.08 ± 0.18	1.01 ± 0.17	0.81 ± 0.2	0.61 ± 0.2	0.40 ± 0.1	0.80 ± 0.1
FEV <sub>1</sub> /FVC (Mean ± SD)	81.0 ± 2.4	81.0 ± 4.8	72.1 ± 5.6	58.8 ± 7.4	52.6 ± 7.9	71.5 ± 7.6
CAT (Mean ± SD)	9.0 ± 7.5	15.3 ± 6.7	18.8 ± 9.6	22.5 ± 6.9	22.3 ± 6.5	18.3 ± 8.8
FEV <sub>1</sub> % pred. and CAT	R <sup>2</sup> = 0.1417; p=0.025	R <sup>2</sup> = 0.2322; p<0.001	R <sup>2</sup> = 0.3688; p<0.001	R <sup>2</sup> = 0.1728; p=0.009	R <sup>2</sup> = 0.1728; p=0.009	R <sup>2</sup> = 0.4028; p<0.001
BM and CAT	R <sup>2</sup> = 0.2046; p=0.01	R <sup>2</sup> = 0.2484; p=0.01	R <sup>2</sup> = 0.1512; p=0.03	R <sup>2</sup> = 0.1361; p=0.05	R <sup>2</sup> = 0.1301; p=0.05	R <sup>2</sup> = 0.2070; p=0.001
FEV <sub>1</sub> /FVC and CAT	R <sup>2</sup> = 0.0842; p=0.01	R <sup>2</sup> = 0.1885; p=0.001	R <sup>2</sup> = 0.2388; p=0.001	R <sup>2</sup> = 0.0091; p=0.91	R <sup>2</sup> = 0.0091; p=0.91	R <sup>2</sup> = 0.4028; p<0.001

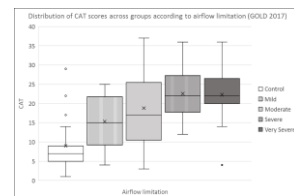
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## Spirometry and CAT

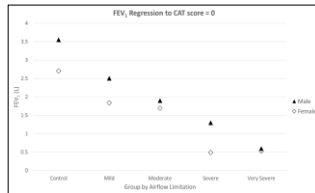


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## CAT distribution

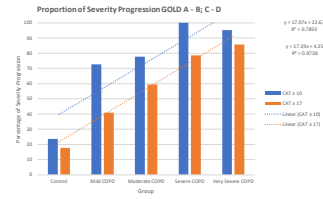


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FEV<sub>1</sub> to achieve CAT = 0

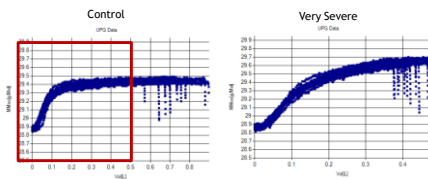
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## CAT cut-off re-evaluation



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## Raw data



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## UPG data

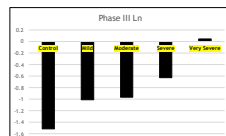
Characteristics	Control	Mild COPD	Moderate COPD	Severe COPD	Very Severe	Total
n (n=100)	110	100	100	100	100	510
Age (Mean ± SD)	55.0 ± 6.9	55.7 ± 6.9	55.7 ± 6.9	55.7 ± 6.9	55.7 ± 6.9	55.7 ± 6.9
Age (Median)	55.0	55.7	55.7	55.7	55.7	55.7
Age Range	45-65	45-65	45-65	45-65	45-65	45-65
FEV <sub>1</sub> % pred. (Mean ± SD)	108.6 ± 11.6	88.9 ± 13.1	62.8 ± 8.0	38.7 ± 11.1	23.1 ± 4.0	62.2 ± 30.5
FEV <sub>1</sub> % pred. (Median)	83.9 ± 1.5	62.7 ± 5.1	52.9 ± 7.3	40.8 ± 8.3	33.4 ± 9.1	53.2 ± 17.3
CAT (Mean ± SD)	4.6 ± 4.4	13.3 ± 7.7	38.5 ± 12.1	23.9 ± 8.0	23.9 ± 7.8	17.7 ± 5.6
Phase II (Mean ± SD)	0.268 ± 0.21	0.405 ± 0.19	0.440 ± 0.21	0.543 ± 0.25	1.000 ± 0.48	0.552 ± 0.36
Phase II (Median)	0.220	0.305	0.385	0.555	1.000	0.465
Phase II (Log)	-0.558	-0.438	-0.42	-0.272	0.034	-0.3979
Phase II (Ln)	-1.144	-1.098	-0.965	-0.625	0.044	-0.9483
CAT and Phase II	R = -0.0227, R <sup>2</sup> = 0.0005, p = 0.9252	R = -0.174, R <sup>2</sup> = 0.0303, p = 0.001	R = -0.174, R <sup>2</sup> = 0.0303, p = 0.001	R = -0.233, R <sup>2</sup> = 0.0546, p = 0.001	R = -0.188, R <sup>2</sup> = 0.035, p = 0.001	R = -0.188, R <sup>2</sup> = 0.035, p = 0.001
FEV <sub>1</sub> % pred. and Phase II	R = -0.107, R <sup>2</sup> = 0.012, p = 0.201	R = -0.107, R <sup>2</sup> = 0.012, p = 0.201	R = -0.107, R <sup>2</sup> = 0.012, p = 0.201	R = -0.107, R <sup>2</sup> = 0.012, p = 0.201	R = -0.107, R <sup>2</sup> = 0.012, p = 0.201	R = -0.107, R <sup>2</sup> = 0.012, p = 0.201

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## Something in the logs??

- Clear difference between Control and COPD
- Progressive change in increased COPD

Logarithm = Exponent  
 $\log_e N = x \Rightarrow N = e^x$   
 (Common Log)  $\log N = x \Rightarrow N = 10^x$   
 (Natural Log)  $\ln N = x \Rightarrow N = e^x$



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## Conclusions

- Highly significant that there was no a lot of correlation across various measures
- UPG revealed some potential for improved diagnosis in early disease using Log/Ln
  - Re-analysis of select breaths that are more consistent may yield better quality data
  - Increasing sample size
  - Data analysis at time of collection for tighter QA

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## Publishing

- ▶ Be on guard - I have discovered a new world of evil...
  - ▶ PREDATORY JOURNALS are out to get you...
- ▶ Listen to intelligent people - librarians are basically know-it-alls

In a good way!!!

Questions???

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