

There is inconsistency in the selection and measurement of outcomes in clinical trials of mechanically ventilated critically ill patients.<sup>1</sup> This presents challenges when comparing trials, and particularly when undertaking meta-analysis of trial data. A core outcome set (COS) is a minimum set of standardised outcomes that should be reported in every trial of a specific intervention. We therefore aimed to develop a COS for use in future trials where the aim of the intervention is to modify the duration of mechanical ventilation. Mixed consensus methods were used to develop this COS. A large, international, online Delphi study was followed by 2 consensus webinars with representatives from the Delphi panel and additional input from a separate patient representative group teleconference. Participants were recruited via international trials groups, critical care societies, charities and associations. Additional researchers were identified through a PubMed search. Participants represented 4 main stakeholder groups; patients, clinicians, researchers and industry. The study was conducted between December 2015 and October 2016. The Delphi ran over 3 rounds; Round 1 included 24 outcomes obtained from a systematic review. During this round a further 23 outcomes were proposed and added by participants. Numbers of participants completing each round were 200, 178 and 161 respectively. A total of 19 outcomes gained consensus through the Delphi process and were discussed at the consensus webinars and the patient teleconference. The outcomes in the final COS were agreed across all 3 meetings and included mortality, health-related quality of life, duration of mechanical ventilation, reintubation, length of stay and successful extubation (Table 1). Using robust consensus methodology this COS has been developed for use in all trials and systematic reviews evaluating interventions that may reduce the duration of mechanical ventilation. Agreement now needs to be reached on how these outcomes should be measured and defined.

## REFERENCE

- Blackwood B, Clarke M, McAuley DF, McGuigan PJ, Marshall JC, Rose L. How outcomes are defined in clinical trials of mechanically ventilated adults and children. *American Journal of Respiratory and Critical Care Medicine* 2014, Apr 15;189(8):886.

**Abstract S133 Table 1** Core outcomes agreed at each consensus meeting and the final COS

Webinar 1	Webinar2	Teleconference	Final COS
Mortality	Mortality	Mortality	Mortality
HRQOL	HRQOL	HRQOL	HRQOL
Duration IMV	Duration IMV	Duration IMV	Duration IMV
Reintubation	Reintubation	Reintubation	Reintubation
Length of Stay	Length of Stay	Length of Stay	Length of Stay
Successful Extubation	Successful Extubation	Successful Extubation	Successful Extubation
	Survival	Survival	Survival
Pulmonary Complications		Pulmonary Complications	Pulmonary Complications

Key: HRQOL, health related quality of life; IMV, invasive mechanical ventilation

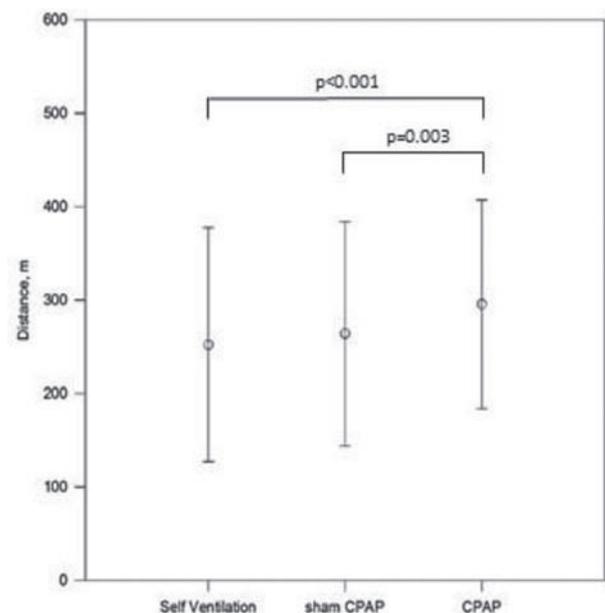
S134

## EFFECT OF CONTINUOUS POSITIVE AIRWAY PRESSURE ON NEURAL RESPIRATORY DRIVE AND FUNCTIONAL CAPACITY IN EXCESSIVE DYNAMIC AIRWAY COLLAPSE PATIENTS

<sup>1</sup>G Kaltsakas, <sup>1</sup>M Patout, <sup>1</sup>G Arbane, <sup>2</sup>L Ahmed, <sup>3</sup>D D'Cruz, <sup>4</sup>M Polkey, <sup>5</sup>J Hull, <sup>1</sup>N Hart, <sup>1</sup>PB Murphy. <sup>1</sup>Lane Fox Respiratory Unit, Guy's and St Thomas' NHS Foundation Trust, London, UK; <sup>2</sup>Department of Thoracic Medicine, Guy's and St Thomas' NHS Foundation Trust, London, UK; <sup>3</sup>Louise Coote Unit, Guy's and St Thomas' NHS Foundation Trust, London, UK; <sup>4</sup>NIHR Respiratory Biomedical Research Unit at the Royal Brompton and Harefield Foundation NHS Trust and Imperial College, London, UK; <sup>5</sup>Department of Respiratory Medicine, Royal Brompton Hospital, London, UK

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Excessive dynamic airway collapse (EDAC) and tracheobronchomalacia (TBM) occur due to weakening of the walls of the central airways leading to airway collapse on expiration. Positive airway pressure provides a pneumatic stent maintaining airway patency. CPAP is used to prevent airway collapse during sleep, but could also facilitate improved exercise capacity in this patient group. The aim of this study was to investigate the effect of ambulatory continuous positive airway pressure (CPAP) on neural respiratory drive and exercise capacity. Patients with CT or bronchoscopic evidence of EDAC or TBM underwent baseline testing and 6 min walk test (6MWT). Physiological testing was performed with patients self-ventilating and on CPAP at 4, 7 and 10 cm H<sub>2</sub>O to identify optimal ambulatory CPAP pressure. Patients then underwent repeat 6MWT on sham or active CPAP in a random order. Neural respiratory drive index (NRDI) was assessed by surface electromyography of the parasternal intercostals (EMG<sub>para</sub> %max  $\chi$  respiratory rate) while self-ventilating and on



**Abstract S134 Figure 1** The 6MWT while on optimal CPAP was increased comparing to self-ventilation and sham CPAP.

CPAP. We studied 20 (9 male), ambulatory adult patients with EDAC and/or TBM: mean  $\pm$ SD age  $60 \pm 13$  years, height  $1.67 \pm 0.86$  m, and BMI  $34.1 \pm 6.6$  kg/m<sup>2</sup>. The NRDI was  $356 \pm 182$  AU while self-ventilating and reduced when CPAP was applied ( $231 \pm 122$  AU;  $p < 0.001$ ). The 6MWT while on optimal CPAP was increased comparing to self-ventilation and sham CPAP ( $296 \pm 112$  m vs  $264 \pm 120$  m vs  $252 \pm 125$  m, respectively;  $p < 0.001$ ) (figure 1). The treatment effect between sham and optimal CPAP was  $31 \pm 39$  m (95% CI: 13 to 50 m). While on optimal CPAP, 12 patients increased their 6MWT more than 30 m compared to self-ventilation (responders). Comparing responders with non-responders, differences were identified for NRDI ( $-167 \pm 110$  AU vs.  $-63 \pm 90$  AU, respectively;  $p = 0.039$ ) and 6MWT while self-ventilating ( $203 \pm 94$  m vs.  $336 \pm 133$  m, respectively;  $p = 0.022$ ).

In conclusion, CPAP reduces neural respiratory drive and increases exercise capacity in patients with EDAC/TBM. Furthermore, the degree of functional limitation and off-loading of the respiratory muscles on CPAP can identify those likely to have a reduction in neural respiratory drive and enhanced exercise tolerance.

### S135 TIMING OF ACIDAEMIA ONSET IN EXACERBATIONS OF COPD REQUIRING ASSISTED VENTILATION AND IN-HOSPITAL MORTALITY

<sup>1</sup>TM Hartley, <sup>1</sup>ND Lane, <sup>1</sup>J Steer, <sup>2</sup>C Echevarria, <sup>1</sup>SC Bourke. <sup>1</sup>Northumbria Healthcare NHS Foundation Trust, North Shields, UK; <sup>2</sup>The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK

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**Introduction** Predicting which patients are likely to benefit from assisted ventilation in exacerbations of COPD (ECOPD) is difficult. Existing prognostic scores did not assess the prognostic value of timing of acidaemia onset relative to admission during development. The 2011 National Chronic Obstructive Pulmonary Disease Resources and Outcomes Project (NCROP) report identified this as a potentially important marker of non-invasive ventilation (NIV) success but further study has been limited. We investigated the relation of timing of respiratory acidaemia to NIV outcomes in ECOPD. Of importance, in both participating hospitals few patients are denied NIV on grounds of assumed futility.

**Methods** A retrospective cohort of consecutive, unique patients, hospitalised with a primary diagnosis of ECOPD were identified from known cohorts, hospital coding records coding and ventilation service records. Other selection criteria included: age 35+ years, smoking history 10+ pack years, air-flow obstruction on spirometry; received assisted ventilation (either NIV or invasive) for acidaemic respiratory failure; and absence of comorbidity expected to limit survival to <12 months (principally metastatic cancer). Population descriptors, ventilation details and outcome data were collected from notes and electronic records.

**Results** 489 consecutive patients were identified between 30/11/08 and 19/5/13; 124 (25.4%) died in-hospital. Median time to ABG prompting ventilation was 2 hour 42 m (IQR 1 hour 2 m – 15 hour 28 m). Most (94.5%) received NIV alone, 5.5% received invasive ventilation (+/-NIV). In patients requiring assisted ventilation within 12 hours of admission, mortality was 18.3% (65/356), compared to 44.3% (59/133) in all those treated after 12 hours ( $p < 0.01$ ).

**Discussion** Our study has several strengths including objective confirmation of COPD, capture of consecutive patients and liberal NIV use. Compared to patients with respiratory acidaemia on or shortly after admission, later development was associated with progressively higher mortality. 12 and 48 hours were identified as clinically useful thresholds. Of note, lower pH, FEV1 and prior LTOT prescription do not account for worse outcome. Older age, greater comorbidity, frailty (eMRC5b: requiring help washing and dressing when recently stable), and a strong trend towards increasing pneumonia are associated with later development of acidaemia. Timing of acidaemia should be considered when deciding whether to initiate NIV.

**Abstract S135 Table 1** Key population descriptors and inpatient mortality grouped by timing of acidaemia onset

Time	Up to 12 hours	12–48 hours	>48 hours
N	356	69	64
Age	71.9 (9.9)	73.8 (10.0)	76 (9.8) *
FEV1%	37.1 (15.6)	42.8 (18.9) *	38.1 (17.4)
BMI	24.9 (7.5)	24.7 (5.9)	22.8 (7.2) †
LTOT	109 (30.6%)	18 (26.1%)	16 (25.0%)
eMRC5	5a (4–5a)	5a (4–5a)	5a (4–5b) †
eMRC5a	120 (33.7%)	25 (36.2%)	19 (29.7%)
eMRC5b	63 (17.7%)	13 (18.8%)	24 (37.5%) *
Charlson Index	1 (1–2)	2 (1–3)	2 (1–3) *
Consolidation at NIV	157 (44.1%)	38 (55.1%)	36 (56.3%)
pH at NIV	7.23 (0.09)	7.26 (0.08) †	7.26 (0.08) †
PCO2 at NIV	10.3 (2.5)	10.0 (2.4)	9.3 (1.8) *
Peak Pressure (IPAP)	20 (18–22)	19 (17–20)	18 (16–20) †
Inpatient Mortality	65 (18.3%)	22 (31.9%) †	37 (57.8%) †

t-test, Mann Whitney U or  $\chi^2$  test for parametric, non-parametric and categorical data respectively.

\* $p < 0.05$ ; † $p < 0.01$ : compared to "Up to 12 hours group"

### S136 LUNG PROTECTIVE MECHANICAL VENTILATION FOR ACUTE RESPIRATORY FAILURE IS NOT BEING IMPLEMENTED IN UK CLINICAL PRACTICE

<sup>1</sup>R Samanta, <sup>1</sup>A Dixit, <sup>2</sup>S Harris, <sup>2</sup>NS MacCallum, <sup>2</sup>DA Brearley, <sup>3</sup>PJ Watkinson, <sup>4</sup>A Jones, <sup>5</sup>S Ashworth, <sup>4</sup>R Beale, <sup>5</sup>SJ Brett, <sup>3</sup>JD Young, <sup>2</sup>M Singer, <sup>1</sup>C Summers, <sup>1</sup>A Ercole. <sup>1</sup>Dept of Medicine, University of Cambridge School of Clinical Medicine, Cambridge, UK; <sup>2</sup>Bloomsbury Institute of Intensive Care Medicine, University College London, London, UK; <sup>3</sup>Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK; <sup>4</sup>Department of Intensive Care, Guy's and St Thomas' NHS Foundation Trust, London, UK; <sup>5</sup>Centre for Perioperative Medicine and Critical Care Research, Imperial College Healthcare NHS Trust, London, UK

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**Introduction** The benefits of lung protective ventilation have been replicated in multiple trials.<sup>1,2</sup> However, we suspected that adherence to this standard of care remained poor. Using the NIHR critical care Health Informatics Collaborative (ccHIC) database, we analysed data from 11 teaching hospital intensive care units (22 524 patient episodes) to investigate real-world clinical practice.

**Methods** 1248 patient episodes, where ventilation was continued for  $\geq 48$  hours, with 232,600 hours of concurrent mechanical ventilation and blood gas data were identified as suitable for analysis. Short gaps in ventilation (<6 hours) were imputed based on the median of nearest known values, and