Supplemental Information

Methods

Study design and intervention (titration of positive airway pressure (PAP) therapy)

The Bi-level PAP group received non-invasive ventilation using a spontaneous timed mode of ventilatory support. Fixed pressure CPAP was used in the CPAP group. Polysomnography was used to facilitate titration of PAP settings at randomization after initial mask fitting and acclimatisation to PAP at the bedside. During this daytime acclimatisation session a range of interfaces were trialled to determine the most suitable for comfort and to minimise leak. During polysomnography CPAP commenced at 5 cmH_2O and was titrated in 1 cmH_2O increments to overcome obstructive events (apnoeas or hyponoeas, snoring or airflow limitation identified by flattening of the inspiratory flow time contour). Where the flow trace normalised but low baseline SpO_2 persisted ($\leq$ 94%) pressure was increased by up to 3cmH_2O. If no improvement in SpO_2 occurred, pressure was reduced to the lowest effective pressure to overcome discrete obstructive events.

In the Bi-level PAP group Bi-level expiratory pressure commenced at 5 cmH_2O and was titrated as per the protocol for CPAP. In addition an increase in expiratory pressure was trialled if there were patient breaths that failed to trigger the ventilator. Inspiratory pressure commenced at 10 cmH_2O (5 cmH_2O of pressure support) and this level of pressure support was maintained until obstructive events were controlled. Pressure support was then titrated in 1 cmH2O increments to overcome nocturnal hypoventilation (assessed by elevated transcutaneous CO_2 (> 45 mmHg, calibrated against $PaCO_2$) or sustained low oxygen saturation ($\leq$ 94%). The inspiratory time was set to be the same as the participants' spontaneous inspiratory time. The ventilator rate was adjusted to two breaths below the awake spontaneous rate initially and finally titrated during sleep to match the participant rate during sleep, aiming to achieve passive ventilation.

Leak was monitored during the night and corrected, including changing the mask if required. If the baseline oxygen saturation remained less than 88% for more than one third of the night, supplemental oxygen was added to maintain $SpO_2 \geq 90\%$.

Outcomes

Pulmonary function and physical activity

Maximal inspiratory and expiratory pressures and physical activity were measured at baseline and 3 months. Inspiratory pressures were measured at functional residual capacity and expiratory pressures at total lung capacity. At least six measurements were taken and the highest three were required to have less than a 20 percent difference. Objective physical activity assessment was undertaken using the SenseWear armband (SWA; BodyMedia, Pittsburgh, USA; professional software version 7.0). Participants were instructed to wear the armband at all times for one week, except for bathing and water-based activities. A minimum of four valid days of data (at least ten hours' wear time per day) were required at each time point, inclusive of at least one weekend day. Time spent sedentary (energy expenditure $\leq 1{\cdot}5$ metabolic equivalents (METs)), time spent in moderate and vigorous physical activity ($\geq$ 3 METs), and number of steps per day were calculated using the proprietary algorithm.

Tables

Supplement Table 1 Sleepiness and Health Related Quality of Life

	Bi-level PAP		CPAP		*p value*
	Baseline	**3 mths**	**Baseline**	**3 mths**	
Sleepiness - ESS	12.10 (1.16)	7.6 (1.22)	11.52 (1.12)	7.26 (1.15)	*Group 0.72, Time <0.01 Interaction 0.86*
Generic Health Related Quality of Life – SF36					
SF36 – SF6D	0.54 (0.027)	0.62 (0.028)	0.59 (0.026)	0.69 (0.026)	*Group 0.25, Time <0.01 Interaction 0.45*
SF36 – Physical Functioning	34.83 (5.15)	42.95 (5.34)	42.10 (4.98)	53.54 (5.02)	*Group 0.31, Time 0.045 Interaction 0.55*
SF36 – Role-Physical	35.13 (5.91)	63.05 (6.25)	36.29 (5.71)	62.21 (5.78)	*Group 0.88, Time <0.01 Interaction 0.81*
SF36 – Bodily Pain	42.24 (5.55)	51.23 (5.84)	46.74 (5.37)	60.65 (5.43)	*Group 0.56, Time 0.10 Interaction 0.51*
SF36 – General Health	38.45 (3.71)	49.91 (3.88)	39.19 (3.58)	53.42 (3.62)	*Group 0.89, Time 0.01 Interaction 0.54*
SF36 – Vitality	32.11 (4.60)	53.40 (4.91)	35.89 (4.45)	54.89 (4.52)	*Group 0.56, Time <0.01 Interaction 0.76*
SF36 – Social Functioning	39.22 (5.71)	60.17 (6.03)	40.73 (5.52)	64.92 (5.58)	*Group 0.85, Time <0.01 Interaction 0.69*
SF36 – Role-Emotional	43.39 (6.41)	66.98 (6.77)	52.69 (6.20)	72.02 (6.27)	*Group 0.30, Time <0.01 Interaction 0.64*
SF36 – Mental Health	51.72 (4.33)	65.35 (4.54)	59.52 (4.19)	69.18 (4.23)	*Group 0.20, Time <0.01 Interaction 0.48*
SF36 – Physical Component Score	33.68 (1.81)	37.96 (1.90)	34.08 (1.75)	40.48 (1.77)	*Group 0.88, Time 0.01 Interaction 0.37*
SF36 – Mental Component Score	34.78 (2.53)	45.68 (2.67)	38.14 (2.45)	47.08 (2.48)	*Group 0.34, Time <0.01 Interaction 0.57*
Respiratory Health Related Quality of Life – SRI					
SRI – Summary Scale	50.63 (3.65)	63.5 (3.74	57.09 (3.53)	67.58 (3.58)	*Group 0.20, Time <0.01 Interaction 0.54*
SRI – Respiratory Complaints	55.64 (4.28)	71.05 (4.41)	58.47 (4.14)	67.01 (4.21)	*Group 0.64, Time <0.01 Interaction 0.16*
SRI – Physical Functioning	49.14 (4.31)	58.14 (4.44)	54.97 (4.16)	65.71 (4.24)	*Group 0.33, Time 0.01 Interaction 0.73*
SRI – Attendant Symptoms & Sleep	40.52 (3.80)	57.05 (3.92)	51.73 (3.67)	61.78 (3.74)	*Group 0.03, Time <0.01 Interaction 0.15*
SRI – Social Relationships	58.48 (4.47)	66.77 (4.58)	69.09 (4.33)	72.53 (4.39)	*Group 0.09, Time 0.01 Interaction 0.29*
SRI – Anxiety	44.48 (5.23)	62.72 (5.42)	47.58 (5.06)	62.86 (5.17)	*Group 0.67, Time <0.01 Interaction 0.66*
SRI – Psychological Well-Being	48.56 (3.93)	59.31 (4.08)	58.06 (3.81)	68.77 (3.89)	*Group 0.08, Time <0.01 Interaction 0.99*
SRI – Social Functioning	57.57 (4.44)	69.01 (4.62)	59.72 (4.30)	75.04 (4.40)	*Group 0.73, Time 0.01 Interaction 0.52*

Mixed model analysis for sleepiness (ESS = Epworth Sleepiness Scale), generic health related quality of life (SF 36 = short form 36) and respiratory health related quality of life (SRI = Severe Respiratory Insufficiency questionnaire), including the subscales for the quality of life measures. Values represent estimated marginal means from the mixed model (standard error) with analysis for the effect of group (Bi-level PAP vs CPAP), time (baseline vs 3 months), and the interaction of group and time.

Supplement Table 2 Relationships to Persistent Ventilatory Failure at 3 Months

Factor		OR (95% CI) †	*P Value*
Age	*****10.13 y (26-74)	1.66 (0.94-2.92)	0.08
Gender	‡ Female cv Male	1.42 (0.49-4.12)	0.52
Presentation	‡ Ambulatory cv acute	0.85 (0.29-2.49)	0.77
Treatment group	‡ CPAP cv Bi-level PAP	1.96 (0.67-5.76)	0.22
BMI	*****11.89 kg/m^2 (35.9-84.5)	0.86 (0.51-1.47)	0.59
Device usage at 3 months	*****2.5 h/night (0-9.42)	0.66 (0.37-1.17)	0.16
Polysomnography			
RDI	*****46.15 events/h (7-218)	0.54 (0.27-1.10)	0.09
Total sleep time SpO2 < 90%	*****31.37% (2.9-100)	1.35 (0.73-2.53)	0.34
ABG at presentation			
pH	*****0.046 (7.21-7.47)	0.60 (0.49-1.07)	0.08
$PaCO_2$	*****13.81 mmHg (46-122)	2.30 (1.09-4.86)	0.03
PaO_2	*****12.43 mmHg (35-107)	1.0 (0.58-1.71)	0.99
HCO_3	*****6.06 mmol (10-59)	2.07 (0.92-4.68)	0.08
Spirometry			
FEV1	*****0.75 L (0.75-4.58)	0.57 (0.31-1.06)	0.08
FEV1 (% predicted)	*****16.56% (32-98)	0.89 (0.51-1.53)	0.67
FVC	*****0.96 L (1.01-5.58)	0.63 (0.34-1.17)	0.14
FVC (% predicted)	*****17.47% (30-98)	0.87 (0.50-1.52)	0.62

† Univariate odds ratio (95% confidence intervals) for risk of persistent ventilatory failure ($PaCO_2$ > 45 mmHg) after three months of treatment for baseline characteristics. Odds ratios represent the change in odds for one standard deviation for continuous variables (* standard deviation (range)) and for binary variables (‡) the odds for the first category listed compared to the second. BMI = body mass index, RDI = respiratory disturbance index, ABG = arterial blood gas, FEV1 = forced expiratory volume in one second and FVC = forced vital capacity.