OHS

Study	Borel 2012[25]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=37)
Countries and setting	Conducted in France; Setting: Grenoble University Hospital sleep department
Line of therapy	Unclear
Duration of study	Intervention + follow up: 1 month
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Severe
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients aged 20 to 75 years with a BMI. 30 kg/m^2 and a Pa co 2 45 mm Hg on daytime blood gas assessment were included unless they declined.

Exclusion criteria	Exclusion criteria: any significant airway obstruction (FEV1 /FVC , 70%), scoliosis, cardiac failure, or progressive neuromuscular disease.
Recruitment/selection of patients	A screening of OHS was proposed to all ambulatory obese patients recruited from advertisements in local newspaper or attending the sleep department referred for diagnosis of sleep disordered breathing
Age, gender and ethnicity	Age - Mean (SD): 56 (7). Gender (M:F): 15/22. Ethnicity: unclear
Further population details	1. BMI: BMI of 30 2 kg/m^2 or more. Co-existing conditions: HTN 3. High risk occupation group: Not stated / Unclear 4. Sleepiness: ESS >9
Indirectness of population	No indirectness
Interventions	(n=19) Intervention 1: Bi-level positive airway pressure/ non-invasive ventilation (NIV) without humidification. NIV treatment was initiated over three to four nights spent in the respiratory ward in individual rooms. Patients were set on bilevel positive pressure ventilation (GoodKnight-425ST; Covidien). After discharge, the patients were asked to use NIV every night. Duration 1 month. Concurrent medication/care: none reported. Indirectness: No indirectness Further details: 1. Precise humidification – : Not stated / Unclear (n=18) Intervention 2: No positive airway pressure device (for OHS and mild OSAHS only) . 1 hour education session, focused on general health risks of OSA and obesity, given dietary and lifestyle counselling by specialist nurse including recommendations for a healthier diet and more exercise. Duration 1 month. Concurrent medication/care: none reported. Indirectness: No indirectness Further details: 1. Precise humidification – : Not applicable
Funding	Study funded by industry

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: BI-LEVEL POSITIVE AIRWAY PRESSURE/ NON-INVASIVE VENTILATION (NIV) WITHOUT HUMIDIFICATION versus NO POSITIVE AIRWAY PRESSURE DEVICE (FOR OHS AND MILD OSAHS

ONLY)

Protocol outcome 1: Sleepiness score at >1 month
- Actual outcome for Severe: ESS change score at 1 month; Group 1: mean -3.4 (SD 5.2284); n=18, Group 2: mean -2.1 (SD 4.6679); n=17
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: difference between groups for age; Group 1 Number missing: 1, Reason: cardiac pacing during FU; Group 2 Number missing: 1, Reason: acute respiratory failure

Protocol outcome 2: AHI/RDI at >1 month
- Actual outcome for Severe: AHI change score at 1 month; Group 1: mean -34.1 (SD 35.3919); n=18, Group 2: mean 6.3 (SD 27.6183); n=17
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: difference between groups for age; Group 1 Number missing: 1, Reason: cardiac pacing during FU; Group 2 Number missing: 1, Reason: acute respiratory failure

Protocol outcome 3: Systolic blood pressure for hypertension at >1 month
- Actual outcome for Severe: systolic BP change score at 1 month; Group 1: mean -1.3 (SD 21.7178); n=18, Group 2: mean -5.4 (SD 10.8917); n=17
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: difference between groups for age; Group 1 Number missing: 1, Reason: cardiac pacing during FU; Group 2 Number missing: 1, Reason: acute respiratory failure

Protocol outcome 4: HbA1c for diabetes at >1 month
- Actual outcome for Severe: HbA1c change score at 1 month; Group 1: mean 0.04 (SD 0.2212); n=18, Group 2: mean -0.12 (SD 0.4668); n=17
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: difference between groups for age; Group 1 Number missing: 1, Reason: cardiac pacing during FU; Group 2 Number missing: 1, Reason: acute respiratory failure

Protocol outcome 5: PaCO2 at >1 month
- Actual outcome for Severe: paco2 change score at 1 month; Group 1: mean -4.9 (SD 3.8207); n=18, Group 2: mean -1.4 (SD 4.2789); n=17
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: difference between groups for age; Group 1 Number missing: 1, Reason: cardiac pacing during FU; Group 2 Number missing: 1, Reason: acute respiratory failure

Protocol outcome 6: Pa02 at >1 month - Actual outcome for Severe: pa02 at 1 month; Group 1: mean 2.4 (SD 10.1663); n=18, Group 2: mean 0.15 (SD 13.9758); n=17 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: difference between groups for age; Group 1 Number missing: 1, Reason: cardiac pacing during FU; Group 2 Number missing: 1, Reason: acute respiratory failure	
Protocol outcomes not reported by the study	Quality of life at >1 month; ODI at >1 month; CO2 control at >1 month; Adverse effects of treatment at >1 month; Adherence in hours of use at >1 month; Mortality at >1 month; Cardiovascular events at >1 month

Study	Howard 2017[95]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=60)
Countries and setting	Conducted in Australia; Setting: the Alfred hospital (Melbourne) and the Royal Prince Alfred hospital (Sydney)
Line of therapy	Unclear
Duration of study	Intervention + follow up: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Undefined severity
Subgroup analysis within study	Not applicable
Inclusion criteria	Participants with a primary diagnosis of OHS (body mass index (BMI) over 30 kg/m^2 and daytime PaCO2 >45 mm Hg) were recruited from the ventilatory failure services at Austin Health, the Alfred Hospital (Melbourne) and The Royal Prince Alfred Hospital (Sydney), Australia.
Exclusion criteria	Potential participants were excluded if they had another condition that may contribute to hypoventilation including neuromuscular disease, chest wall abnormalities, respiratory depressant medications, COPD or an FEV1/FVC ratio <70% after bronchodilators. Participants presented either as a stable outpatient referral or following a hospital admission with an acute respiratory acidosis and initial stabilisation on Bi-level PAP. Arterial blood pH was in the normal range (7.35 –7.45) at randomisation for both groups. Diagnostic polysomnography was not required for diagnosis, but undertaken as clinically indicated outside the protocol. Prior ventilatory support (Bi-level PAP or CPAP) was permitted provided the duration was <1 month in the 3 months prior to enrolment.

Age, gender and ethnicity	Age - Mean (SD): 53 (10). Gender (M:F): 32/28. Ethnicity: unclear
Further population details	1. BMI: BMI of 30 2 kg/m^2 or more. Co-existing conditions: Not stated / Unclear 3. High risk occupation group: Not stated / Unclear 4. Sleepiness: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=29) Intervention 1: Bi-level positive airway pressure/ non-invasive ventilation (NIV) without humidification. The Bi-level PAP group received non-invasive ventilation using a spontaneous timed mode of ventilatory support for 3 months. The protocol included a planned change to Bi-level PAP in the event of treatment failure in the CPAP group. Polysomnography was used to facilitate titration of PAP settings at randomisation. In the Bi-level PAP group, the ventilator rate and pressure support were titrated to overcome nocturnal hypoventilation. Supplemental oxygen was added to maintain SpO2 ≥90%. The devices used were able to deliver both CPAP and Bi-level PAP (VPAP III STA, ResMed, Bella Vista, Australia; Harmony, Philips Respironics, USA). Duration 3 months. Concurrent medication/care: CPAP or Bi-level expiratory pressure was titrated to overcome obstructive events. No formal dietary advice or exercise programme was prescribed. The devices used were able to deliver both CPAP and Bi-level PAP (VPAP III STA, ResMed, Bella Vista, Australia; Harmony, Philips Respironics,USA) Indirectness: No indirectness Further details: 1. Precise humidification – : Not stated / Unclear (n=31) Intervention 2: Fixed pressure CPAP without humidification. Fixed pressure CPAP was used in the CPAP group. The protocol included a planned change to Bi-level PAP in the event of treatment failure in the CPAP group. The devices used were able to deliver both CPAP and Bi-level PAP (VPAP III STA, ResMed, Bella Vista, Australia; Harmony, Philips Respironics, USA) Duration 3 months. Concurrent medication/care: CPAP or Bi-level expiratory pressure was titrated to overcome obstructive events. No formal dietary advice or exercise programme was prescribed. The devices used were able to deliver both CPAP and Bi-level PAP (VPAP III STA, ResMed, Bella Vista, Australia; Harmony, Philips Respironics, USA).

	Indirectness: No indirectness Further details: 1. Precise humidification – : Not stated / Unclear
Funding	Study funded by industry

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: BI-LEVEL POSITIVE AIRWAY PRESSURE/ NON-INVASIVE VENTILATION (NIV) WITHOUT HUMIDIFICATION versus FIXED PRESSURE CPAP WITHOUT HUMIDIFICATION

Protocol outcome 1: Quality of life at >1 month
- Actual outcome for Severe: SF36 physical at 3 months; Group 1: mean 37.96 (SD 8.061); n=27, Group 2: mean 40.48 (SD 7.5095); n=30
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: withdrew; Group 2 Number missing: 1, Reason: withdrew
- Actual outcome for Severe: SF36 mental at 3 months; Group 1: mean 45.68 (SD 11.3279); n=27, Group 2: mean 47.08 (SD 10.5217); n=30
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: withdrew; Group 2 Number missing: 1, Reason: withdrew
- Actual outcome for Severe: SRI at 3 months; Group 1: mean 63.5 (SD 15.8675); n=27, Group 2: mean 67.58 (SD 15.1887); n=30
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: withdrew; Group 2 Number missing: 1, Reason: withdrew

Protocol outcome 2: Sleepiness score at >1 month
- Actual outcome for Severe: ESS at 3 months; Group 1: mean 7.6 (SD 6.5699); n=29, Group 2: mean 7.26 (SD 6.2988); n=30
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: withdrew; Group 2 Number missing: 1, Reason: withdrew

Protocol outcome 3: Adherence in hours of use at >1 month
- Actual outcome for Severe: adherence hours per night at 3 months; Group 1: mean 5.3 (SD 2.63); n=29, Group 2: mean 5 (SD 2.4); n=31
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: withdrew; Group 2 Number missing: 1, Reason: withdrew

Protocol outcome 4: Systolic blood pressure for hypertension at >1 month - Actual outcome for Severe: systolic BP at 3 months; Group 1: mean 137 (SD 17.3948); n=27, Group 2: mean 137 (SD 16.122); n=30 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: withdrew; Group 2 Number missing: 1, Reason: withdrew	
Protocol outcomes not reported by the study	AHI/RDI at >1 month; ODI at >1 month; CO2 control at >1 month; Adverse effects of treatment at >1 month; HbA1c for diabetes at >1 month; Mortality at >1 month; Pa02 at >1 month; PaCO2 at >1 month; Cardiovascular events at >1 month

Study (subsidiary papers)	**Pickwick Project trial: Masa 2015[137], Masa, 2019 [142], Masa 2016[139], Masa 2020 [135]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	3; (2 with severe OSA (n=221)) (1 without severe OSA (n=86)) (1 without severe OSA, n=98)
Countries and setting	Conducted in Spain; Setting: 16 tertiary hospitals in Spain
Line of therapy	Unclear
Duration of study	Intervention + follow up: 2 months,5.44 years and 8.4 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Severe and Mild (Severe and without severe OSA)
Subgroup analysis within study	N/A
Inclusion criteria	Patients with suspected OHS or OSA with substantial experience with NIV and CPAP treatments. OHS was defined as obesity, with a body mass index (BMI) greater than or equal to 30; stable hypercapnic respiratory failure (PaCO2>45 mm Hg, pH>7.35, and no clinical worsening during the 2 previous months). Other inclusion criteria were as follows: (1) severe OSA (apnea–hypopnea index [AHI] >30), (2) an absence of narcolepsy or restless leg syndrome, and (3) a correctly executed 30-minute CPAP/NIV treatment test. Patients without severe OSA were included in the without severe OSA study. For without severe OSA study: (1) nonsevere OSA (apnea-hypopnea index < 30 events/h), (2) an absence of narcolepsy or restless legs syndrome, and (3) a correctly executed 30-min NIV treatment test

Exclusion criteria	The exclusion criteria were as follows: (1) a psychophysical inability to complete questionnaires, (2) severe chronic debilitating illness, (3) severe chronic nasal obstruction, and (4) a lack of informed consent. Patients without severe OSA (AHI<30) were referred to the parallel study protocol. Additional exclusions were; no relevant chronic obstructive pulmonary disease (FEV1>70% predicted when FEV 1/FVC<70) or neuromuscular, chest wall, or metabolic disease.
Recruitment/selection of patients	From May 2009 to March 2013 patients between 15 and 80 years of age who were referred for pulmonary consultations for suspected OHS or OSA at 16 tertiary hospitals in Spain with substantial experience with NIV and CPAP treatments were screened. From April 2013 to December 2014 patients with OHS without severe OSA continued to be included. The study was stopped after 8.4 years of follow-up (May 2009 to November 2017) with the agreement of the 16 clinical centers because of the prespecified criterion of absence of new patient enrollment in the last year.
Age, gender and ethnicity	Age - Mean (SD): 60 (13). Gender (M:F): 97/124. Ethnicity: unclear
Further population details	1. BMI: BMI of 30 2 kg/m^2 or more. Co-existing conditions: HTN 3. High risk occupation group: Not stated / Unclear 4. Sleepiness: ESS >9
Indirectness of population	No indirectness
Interventions	(n=71) severe population Intervention, (n=40 non severe OSA population at 2 months; n=48 non severe population at 3 years) 1: Bi-level positive airway pressure/ non-invasive ventilation (NIV) without humidification. In addition to lifestyle modification and oxygen (if required), patients were instructed to use NIV treatment during the entire sleep period. The ventilator mode was set at bilevel pressure with assured volume. While the patient was awake, the expiratory positive airway pressure (EPAP) was set between 4 and 8 cm H2O, and the inspiratory positive airway pressure (IPAP) was set between 18 and 22 cm H2O (EPAP included). The respiratory rate was adjusted to 12 to 15 breaths/min (close to the spontaneous respiratory rate, if possible), and the target volume was set at between 5 and 6 ml/kg of actual weight, allowing for an increase in the maximum pressure over the previously fixed IPAP, if necessary. Duration 2 months and 3 years. Concurrent medication/care: all patients received lifestyle modification advice and oxygen (if required).

	Indirectness: No indirectness Further details: 1. Precise humidification: Not applicable (n=80) severe population only. Intervention 2: Fixed pressure CPAP without humidification. In addition to lifestyle modification and oxygen (if required), patients were instructed to use at-home fixed CPAP during the entire sleep period before conventional CPAP titration. Duration 2 months. Concurrent medication/care: all patients received lifestyle modification advice and oxygen (if required). Indirectness: No indirectness Further details: 1. Precise humidification: Not stated / Unclear (n=70) severe population, (n=46 non severe population at 2 months; n=48 non severe population at 3 years) Intervention 3: No positive airway pressure device (for OHS and mild OSAHS only). The lifestyle modification consisted of a 1,000-calorie diet and the maintenance of correct sleep hygiene and habits (avoiding the supine decubitus position; maintaining regular sleep habits and exercise; not consuming sedatives, stimulants, or alcohol; not smoking tobacco; and avoiding heavy meals within 4 hours before bedtime). Oxygen therapy was added if the daytime PaO2 was less than 55 mm Hg (18), with the necessary flow to maintain waking arterial oxygen saturation between 88 and 92% or PAO2 greater than or equal to 55 mm Hg for at least 17 h/d. Duration 2 months and 3 years. Concurrent medication/care: all patients received lifestyle modification advice and oxygen (if required). Indirectness: No indirectness Further details: 1. Precise humidification : Not applicable
Funding	Study funded by industry (study had a mix of academic, government and industry funding)
Severe OSA population RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: BI-LEVEL POSITIVE AIRWAY PRESSURE/ NON-INVASIVE VENTILATION (NIV) WITHOUT HUMIDIFICATION versus FIXED PRESSURE CPAP WITHOUT HUMIDIFICATION	

Protocol outcome 1: AHI/RDI at >1 month
- Actual outcome for Severe: change in AHI (severe OSAHS) at 2 months; Group 1: mean -57 (SD 30); n=71, Group 2: mean -60 (SD 31); n=80
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: ODI at >1 month
- Actual outcome for Severe: change in ODI (severe OSAHS) at 2 months; Group 1: mean -46 (SD 30); n=71, Group 2: mean -58 (SD 33); n=80
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 3: Adherence in hours of use at >1 month
- Actual outcome for Severe: adherence (severe OSAHS) at 2 months; Group 1: mean 5.3 hours per night (SD 2.3); n=72, Group 2: mean 5.3 hours per night (SD 2.1); n=80
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: BI-LEVEL POSITIVE AIRWAY PRESSURE/ NON-INVASIVE VENTILATION (NIV) WITHOUT HUMIDIFICATION versus NO POSITIVE AIRWAY PRESSURE DEVICE (FOR OHS AND MILD OSAHS ONLY)

Protocol outcome 1: Quality of life at >1 month
- Actual outcome for Severe: change in SF-36 physical (severe OSAHS) at 2 months; Group 1: mean 1.1 (SD 8.7); n=71, Group 2: mean 0.2 (SD 6.8); n=70
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome for Severe: change in SF-36 mental (severe OSAHS) at 2 months; Group 1: mean 1.7 (SD 14); n=71, Group 2: mean 1.2 (SD 88); n=70
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome for Severe: change in FOSQ (severe OSAHS) at 2 months; Group 1: mean 4.3 (SD 17); n=71, Group 2: mean -1.7 (SD 16); n=70
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Sleepiness score at >1 month
- Actual outcome for Severe: change in ESS (severe OSAHS) at 2 months; Group 1: mean -4.8 (SD 5); n=71, Group 2: mean -1 (SD 4.4); n=70
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 3: AHI/RDI at >1 month
- Actual outcome for Severe: change in AHI (severe OSAHS) at 2 months; Group 1: mean -57 (SD 30); n=71, Group 2: mean -6.8 (SD 30); n=70
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 4: ODI at >1 month
- Actual outcome for Severe: change in ODI (severe OSAHS) at 2 months; Group 1: mean -46 (SD 30); n=71, Group 2: mean -4.7 (SD 26); n=70
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 5: PaCO2 at >1 month
- Actual outcome for Severe: change in PACO2 (severe OSAHS) at 2 months; Group 1: mean -5.5 (SD 7); n=71, Group 2: mean -3.2 (SD 6); n=70
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: FIXED PRESSURE CPAP WITHOUT HUMIDIFICATION versus NO POSITIVE AIRWAY PRESSURE DEVICE (FOR OHS AND MILD OSAHS ONLY)

Protocol outcome 1: Quality of life at >1 month
- Actual outcome for Severe: change in SF36 physical (severe OSAHS) at 2 months; Group 1: mean 1.2 (SD 8.9); n=80, Group 2: mean 0.2 (SD 6.8); n=70
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome for Severe: change in SF36 mental (severe OSAHS) at 2 months; Group 1: mean 4.6 (SD 12); n=80, Group 2: mean 1.2 (SD 8.8); n=70

Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome for Severe: change in FOSQ (severe OSAHS) at 2 months; Group 1: mean 5.1 (SD 16); n=80, Group 2: mean 1.7 (SD 16); n=70
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Sleepiness score at >1 month
- Actual outcome for Severe: change in ESS (severe OSAHS) at 2 months; Group 1: mean -4.3 (SD 4.7); n=80, Group 2: mean -1 (SD 4.4); n=70
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 3: AHI/RDI at >1 month
- Actual outcome for Severe: change in AHI (severe OSAHS) at 2 months; Group 1: mean -60 (SD 31); n=80, Group 2: mean -6.8 (SD 30); n=70
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 4: ODI at >1 month
- Actual outcome for Severe: change in ODI (severe OSAHS) at 2 months; Group 1: mean -58 (SD 33); n=80, Group 2: mean -4.7 (SD 26); n=70
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 5: PaCO2 at >1 month
- Actual outcome for Severe: change in PaCO2 (severe OSAHS) at 2 months; Group 1: mean -3.7 (SD 6.6); n=80, Group 2: mean -3.2 (SD 6); n=70
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Without severe OSA population

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: BI-LEVEL POSITIVE AIRWAY PRESSURE/ NON-INVASIVE VENTILATION (NIV) WITHOUT HUMIDIFICATION versus NO POSITIVE AIRWAY PRESSURE DEVICE/LIFE STYLE MODIFICATION – 2 months follow-up

Protocol outcome 1: Quality of life at >1 month
- Actual outcome for Mild (without severe): change in SF-36 mental (Mild OSAHS) at 2 months; Group 1: mean 4.1 (SD 12.8); n=40, Group 2: mean -0.9 (SD 9.4); n=46
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome for Mild (without severe): change in FOSQ (Mild OSAHS) at 2 months; Group 1: mean 4.4 (SD 19); n=40, Group 2: mean -2.7 (SD 18.2); n=46
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Sleepiness score at >1 month
- Actual outcome for Mild (without severe OSA): change in ESS (Mild OSAHS) at 2 months; Group 1: mean -2.9 (SD 3.8); n=40, Group 2: mean -1.2 (SD 3.4); n=46
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 3: AHI/RDI at >1 month
- Actual outcome for Mild (without Severe): change in AHI (Mild OSAHS) at 2 months; Group 1: mean -11 (SD 12.5); n=40, Group 2: mean 0.1 (SD 9.4); n=46
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 4: ODI at >1 month
- Actual outcome for Mild (without severe) : change in ODI (Mild OSAHS) at 2 months; Group 1: mean -19 (SD 18.8); n=40, Group 2: mean -0.4 (SD 14.1); n=46
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 5: PaCO2 at >1 month

- Actual outcome for Mild (without severe): change in PACO2 (Mild OSAHS) at 2 months; Group 1: mean -6 (SD 5.3); n=40, Group 2: mean -2.8 (SD 5.1); n=46
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 6: Systolic blood pressure for hypertension at >1 month
- Actual outcome for Mild: systolic BP change score (mild) at 1 month; Group 1: mean -4.2 (SD 21.3); n=40, Group 2: mean -4.3 (SD 19.2); n=46
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Without severe OSA population

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: BI-LEVEL POSITIVE AIRWAY PRESSURE/ NON-INVASIVE VENTILATION (NIV) WITHOUT HUMIDIFICATION versus NO POSITIVE AIRWAY PRESSURE DEVICE/LIFE STYLE MODIFICATION – 3 years follow-up

Protocol outcome 1: Hospitalisation
- Actual outcome : mean hospitalization days per year at 3 years; Group 1: mean 2.71 (SD 4.52) ; n=48, Group 2: mean 2.60 (SD 5.31); n=48
Risk of bias: All domain - low, Selection - Low, Blinding - low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Quality of life at >1 month
- Actual outcome : SF-36 physical at 3 years; Group 1: mean 37.31 (SD 13.57); n=48, Group 2: mean 34.96 (SD 14.89); n=48
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 3: Quality of life at >1 month
- Actual outcome : SF-36 mental at 3 years; Group 1: mean 42.82 (SD 17.86); n=48, Group 2: mean 44.29 (SD 19.7); n=48

Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

- Actual outcome : FOSQ at 3 years; Group 1: mean 77.21 (SD 26.5); n=48, Group 2: mean 72.16 (SD 28.5); n=48
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 4: Sleepiness score at >1 month
- Actual outcome: ESS at 3 years; Group 1: mean 4.16 (SD 6.18); n=48, Group 2: mean 7.13 (SD 6.78); n=48
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 5: PaCO2 at >1 month
- Actual outcome : PACO2 at 3 years; Group 1: mean 44.26 (SD 5.97); n= n=48, Group 2: mean 47.54 (SD 5.76); n=48
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 6: Systolic blood pressure for hypertension at >1 month
- Actual outcome for Mild: systolic BP at 3 years; Group 1: mean 135.37 (SD 19.26); n=48, Group 2: mean 132.04 (SD 18.31); n=48
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 7: Diastolic blood pressure for hypertension at >1 month
- Actual outcome : diastolic BP at 3 years; Group 1: mean77.51 (SD 13.52); n=48, Group 2: mean 74.04 (SD 12.88); n=48
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 8: Cardiovascular events
- Actual outcome : cardiovascular events at 3 years; Group 1: 10; n=48, Group 2: 11; n=48
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 9: Mortality
- Actual outcome : Mortality at 3 years; Group 1: 9; n=48, Group 2: 9 n=48

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0	
Narartive results: Oral dryness (3 years)- 3% in NIV group. No other adverse events with NIV at 3 years.	
Protocol outcomes not reported by the study	HbA1c for diabetes at >1 month;

Study	Murphy 2012[168]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=50)
Countries and setting	Conducted in United Kingdom; Setting: respiratory unit in hospitals in UK
Line of therapy	Unclear
Duration of study	Intervention + follow up: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Undefined severity
Subgroup analysis within study	Not applicable
Inclusion criteria	Study inclusion criteria were body mass index >40 kg/m2; daytime stable respiratory failure with PaCO2 >6 kPa and pH >7.35; absence of another identifiable cause of hypoventilation; ratio of forced expiratory volume in 1 s (FEV1) to forced vital capacity (FVC) >0.70; and FVC <70% predicted.
Exclusion criteria	The exclusion criterion was an inability to provide written informed consent.
Recruitment/selection of patients	Patients admitted to the Lane Fox Respiratory Unit, St Thomas' Hospital and to the Sleep and Ventilation Unit, Royal Brompton Hospital for either elective assessment of stable OHS or assessment following an episode of acute decompensated respiratory failure secondary to OHS were screened for study inclusion.
Age, gender and ethnicity	Age - Mean (SD): AVAPS = 53 (9) Fixed level PS = 56 (11). Gender (M:F): 23/27. Ethnicity: unclear

Further population details	1. BMI: BMI of 30 2 kg/m^2 or more. Co-existing conditions: Not stated / Unclear 3. High risk occupation group: Not stated / Unclear 4. Sleepiness: ESS >9
Indirectness of population	No indirectness
Interventions	(n=25) Intervention 1: Bi-level positive airway pressure/ non-invasive ventilation (NIV) without humidification. Volume assured NIV. AVAPS (average volume-assured pressure support) mode, mean Vte 657ml. 2/25 required supplemental oxygen. Duration 3 months. Concurrent medication/care: Both modes were delivered by a BiPAP synchrony device (Philips-Respironics, Murrysville, Pennsylvania, USA). Supplementary oxygen was provided to patients who met the criteria for daytime hypoxaemia (PaO2 <7.3 kPa or <8 kPa with secondary features of hypoxia or right heart failure) at the lowest flow rate that corrected hypoxaemia (PaO2>8 kPa). Indirectness: No indirectness Further details: 1. Precise humidification – : Not stated / Unclear (n=25) Intervention 2: Bi-level positive airway pressure/ non-invasive ventilation (NIV) without humidification. Fixed NIV bi-level PS mean IPAP 25cm H2O, 4/25 required supplemental oxygen. Duration 3 months. Concurrent medication/care: Ventilator set-up done over two days in both groups. Both modes were delivered by a BiPAP synchrony device (Philips-Respironics, Murrysville, Pennsylvania, USA). Supplementary oxygen was provided to patients who met the criteria for daytime hypoxaemia (Po2 <7.3 kPa or <8 kPa with secondary features of hypoxia or right heart failure) at the lowest flow rate that corrected hypoxaemia (PaO2>8 kPa). Indirectness: No indirectness Further details: 1. Precise humidification – : Not stated / Unclear
Funding	Study funded by industry

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: BI-LEVEL POSITIVE AIRWAY PRESSURE/ NON-INVASIVE VENTILATION (NIV) WITHOUT HUMIDIFICATION versus BI-LEVEL POSITIVE AIRWAY PRESSURE/ NON-INVASIVE VENTILATION (NIV)

WITHOUT HUMIDIFICATION Protocol outcome 1: Quality of life at >1 month - Actual outcome for Undefined severity: SRI at 3 months; Group 1: mean 11 (SD 12); n=23, Group 2: mean 7 (SD 13); n=23 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2; Group 2 Number missing: 2 Protocol outcome 2: Sleepiness score at >1 month - Actual outcome for Undefined severity: ESS at 3 months; Group 1: mean -5 (SD 6); n=23, Group 2: mean -6 (SD 6); n=23 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2; Group 2 Number missing: 2 Protocol outcome 3: Adherence in hours of use at >1 month - Actual outcome for Undefined severity: adherence hours per night at 3 months; Group 1: mean 4.2 (SD 2.9); n=23, Group 2: mean 5.1 (SD 2.4); n=23 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2; Group 2 Number missing: 2 Protocol outcome 4: PaCO2 at >1 month - Actual outcome for Undefined severity: PaCO2 at 3 months; Group 1: mean 6.4 (SD 0.8); n=23, Group 2: mean 6.2 (SD 0.8); n=23 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2; Group 2 Number missing: 2 Protocol outcome 5: Pa02 at >1 month - Actual outcome for Undefined severity: PaO2 at 3 months; Group 1: mean 9.1 (SD 1.2); n=23, Group 2: mean 9.3 (SD 1.2); n=23 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2; Group 2 Number missing: 2	
Protocol outcomes not reported by the study	AHI/RDI at >1 month; ODI at >1 month; CO2 control at >1 month; Adverse effects of treatment at >1 month; HbA1c for diabetes at >1 month; Mortality at >1 month; Systolic blood pressure for hypertension at >1 month; Cardiovascular events at >1 month

Study	Piper 2008[206]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=36)
Countries and setting	Conducted in Australia; Setting: Sleep Investigation Unit at Royal Prince Alfred Hospital Australia.
Line of therapy	Unclear
Duration of study	Intervention + follow up: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Undefined severity
Subgroup analysis within study	Not applicable
Inclusion criteria	Inclusion criteria included: (1) obesity with a BMI over 30 kg/m^2; (2) stable awake compensated respiratory failure with arterial carbon dioxide tension (PaCO2) >45 mm Hg and pH>7.34; (3) the absence of any significant respiratory, neuromuscular or other disorder that could account for the hypercapnia; (4) ratio of forced expiratory volume in 1 s/forced vital capacity (FEV1/FVC)>70%; (5) no major psychiatric illness that would affect the patient's ability to participant in the study; and (6) not currently being treated with positive pressure therapy.
Exclusion criteria	Based on clinical consensus and safety concerns, a priori criteria were set so that patients who displayed significant and prolonged desaturation or significant carbon dioxide retention during an

	initial CPAP trial were excluded from the study. These criteria were: (1) oxygen saturation remaining below 80% continuously (10 min) in the absence of frank apnoea; (2) an acute rise in transcutaneous carbon dioxide pressure (TcCO2) (TCM3, Radiometer, Copenhagen, Denmark) during episodes of rapid eye movement (REM) sleep>10 mm Hg; or (3) an increase in afternoon to morning Pa CO2 of >10 mm Hg in those patients with an awake Pa CO2 .55 mm Hg.
Recruitment/selection of patients	Patients with obesity and daytime hypercapnia were recruited from the Sleep Disorders Clinic and Sleep Investigation Unit at Royal Prince Alfred Hospital.
Age, gender and ethnicity	Age - Mean (SD): 50 (15). Gender (M:F): 23/13. Ethnicity: unclear
Further population details	1. BMI: BMI of 30 2 kg/m^2 or more. Co-existing conditions: Not stated / Unclear 3. High risk occupation group: Not stated / Unclear 4. Sleepiness: ESS >9
Indirectness of population	No indirectness
Interventions	(n=18) Intervention 1: Bi-level positive airway pressure/ non-invasive ventilation (NIV) without humidification. Overnight titration of CPAP was performed in all patients in a sleep laboratory using manual titration. Pressure was increased in 1cmH2O increments with the aim of preventing obstruction, flow limitation, desaturation and arousal. Those patients randomised to BVS then underwent a further trial to titrate appropriate bilevel pressure settings. During the bilevel titration, the EPAP was commenced at 2cmH2O below the pressure needed to abolish obstructive events during the CPAP titration or at 5cmH2O, whichever was higher. The EPAP was then increased in 1cmH2O increments if inspiratory efforts did not consistently trigger IPAP. The IPAP was initially set 4cmH2O higher than EPAP, and then increased to eliminate hypopneas and improve saturation. A spontaneous mode of bilevel support was used in all patients. Duration 3 months. Concurrent medication/care: patients were encouraged to contact the clinical service if they were experiencing any problems with therapy, and to return to their local doctor and referring physician for ongoing medical management. All patients received general information and advice about of life style changes including weight loss and diet. The protocol permitted the administration of supplemental home oxygen at 1-2L/min to maintain a SpO2>90% if SpO2 remained <88% in NREM sleep during the patient's allocated home treatment

	study at the maximum pressure that eliminated obstructive apneic or hypopneic events. patients were discharged home for 3 months with Duet LX bilevel devices: Respironics, Murrysville or VPAP II bilevel machines ResMed. Indirectness: No indirectness Further details: 1. Precise humidification – : Not stated / Unclear (n=18) Intervention 2: Fixed pressure (default) CPAP with humidification. A short period of CPAP acclimatisation prior to the titration night was undertaken, which included mask fitting and use of CPAP at a range of pressures from 5-10cmH2O to ensure the patient understood the sensations they were likely to experience when using the therapy overnight. Overnight titration of CPAP was performed in all patients in a sleep laboratory using manual titration. Pressure was increased in 1cmH2O increments with the aim of preventing obstruction, flow limitation, desaturation and arousal. Patients were then discharged home on positive pressure therapy REMstar CPAP. Duration 3 months. Concurrent medication/care: Patients were encouraged to contact the clinical service if they were experiencing any problems with therapy, and to return to their local doctor and referring physician for ongoing medical management. All patients received general information and advice about of life style changes including weight loss and diet. The protocol permitted the administration of supplemental home oxygen at 1-2L/min to maintain a SpO2>90% if SpO2 remained <88% in NREM sleep during the patient's allocated home treatment study at the maximum pressure that eliminated obstructive apneic or hypopneic events. patients were discharged home for 3 months with Duet LX bilevel devices: Respironics, Murrysville or VPAP II bilevel machines ResMed. Indirectness: No indirectness Further details: 1. Precise humidification – : Not stated / Unclear
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: BI-LEVEL POSITIVE AIRWAY PRESSURE/ NON-INVASIVE VENTILATION (NIV) WITHOUT HUMIDIFICATION versus FIXED PRESSURE (DEFAULT) CPAP WITH HUMIDIFICATION

Protocol outcome 1: Sleepiness score at >1 month
- Actual outcome for Undefined severity: ESS change score at 3 months; Group 1: mean -9 (SD 5); n=18, Group 2: mean -6 (SD 8); n=18;

ESS 0-24 Top=High is poor outcome Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 2: Adherence in hours of use at >1 month - Actual outcome for Undefined severity: adherence hours per night at 3 months; Group 1: mean 6.1 hours (SD 2.1); n=18, Group 2: mean 5.8 hours (SD 2.4); n=18 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 3: PaCO2 at >1 month - Actual outcome for Undefined severity: PaCO2 change score at 3 months; Group 1: mean -6.9 (SD 6.7); n=18, Group 2: mean -5.8 (SD 8.4); n=18 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Quality of life at >1 month; AHI/RDI at >1 month; ODI at >1 month; CO2 control at >1 month; Adverse effects of treatment at >1 month; HbA1c for diabetes at >1 month; Mortality at >1 month; Pa02 at >1 month; Systolic blood pressure for hypertension at >1 month; Cardiovascular events at >1 month

Study	**Storre 2006[249]**
Study type	RCT (Patient randomised; Crossover: no details provided)
Number of studies (number of participants)	1 (n=10)

Countries and setting	Conducted in Germany; Setting: university hospital Freiburg Germany
Line of therapy	Unclear
Duration of study	Intervention time: 6 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Undefined severity
Subgroup analysis within study	Not applicable
Inclusion criteria	Clinically stable OHS patients with a BMI over 30 kg/m^2 and daytime hypercapnia (i.e. paco2 >45mmhg) who had failed to respond to CPAP therapy were enrolled.
Exclusion criteria	Excluded if had signs of respiratory infection or acute respiratory failure (eg. RR>30; pH < 7.35) or had any previous ventilatory support or had been intubated in the past 3 months.
Age, gender and ethnicity	Age - Mean (SD): 53.5 (11.7). Gender (M:F): 8/2. Ethnicity: unclear
Further population details	1. BMI: BMI of 30 2 kg/m^2 or more. Co-existing conditions: Not stated / Unclear 3. High risk occupation group: Not stated / Unclear 4. Sleepiness: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=10) Intervention 1: Bi-level positive airway pressure/ non-invasive ventilation (NIV) without humidification. Voume assured (NIV) Bilevel pressure ventilation device with AVAPS (average volume-assured pressure support) enabled. Duration 6 weeks. Concurrent medication/care: no patient received supplemental oxygen. Indirectness: No indirectness Further details: 1. Precise humidification – : Not stated / Unclear

	(n=10) Intervention 2: Bi-level positive airway pressure/ non-invasive ventilation (NIV) without humidification. Fixed NIV Bilevel pressure ventilation device without AVAPS (average volume-assured pressure support) enabled Duration 6 weeks. Concurrent medication/care: no patient received supplemental oxygen. Indirectness: No indirectness Further details: 1. Precise humidification – : Not stated / Unclear
Funding	Study funded by industry

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: BI-LEVEL POSITIVE AIRWAY PRESSURE/ NON-INVASIVE VENTILATION (NIV) WITHOUT HUMIDIFICATION versus BI-LEVEL POSITIVE AIRWAY PRESSURE/ NON-INVASIVE VENTILATION (NIV) WITHOUT HUMIDIFICATION

Protocol outcome 1: Quality of life at >1 month
- Actual outcome for Undefined severity: QOL - SRI at 6 weeks; Group 1: mean 75 (SD 16); n=10,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: AHI/RDI at >1 month
- Actual outcome for Undefined severity: AHI at 6 weeks; Group 1: mean 0 (SD 0); n=10, Group 2: mean 0 (SD 0); n=10
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 3: ODI at >1 month
- Actual outcome for Undefined severity: ODI at 6 weeks; Group 1: mean 33 (SD 17); n=10, Group 2: mean 27 (SD 15); n=10
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 4: PaCO2 at >1 month
- Actual outcome for Undefined severity: PaCO2 at 6 weeks; Group 1: mean 5.6 (SD 0.7); n=10, Group 2: mean 6.1 (SD 0.5); n=10

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Sleepiness score at >1 month; CO2 control at >1 month; Adverse effects of treatment at >1 month; Adherence in hours of use at >1 month; HbA1c for diabetes at >1 month; Mortality at >1 month; Pa02 at >1 month; Systolic blood pressure for hypertension at >1 month; Cardiovascular events at >1 month