Appendix D: Clinical evidence tables

Study	**Askland et al[5]**
Study type	Systematic review
Number of studies (number of participants)	N= 41 studies, 8968 patients Randomised, parallel-controlled trials of any duration.
Countries and setting	Conducted in Multiple countries; Setting: Hospital, community or home based
Line of therapy	Mixed line
Duration of study	Intervention + follow up: 28 days – 2 years
Method of assessment of guideline condition	Yes
Stratum	Severe OSAHS
Subgroup analysis within study	Not applicable
Inclusion criteria	For inclusion in the review, intervention and control groups must have either 1) received the same make of CPAP machine and pressure delivery mode (i.e. fixed, auto-titrating, bi-level, etc.) or 2) receive CPAP machines in a randomly distributed manner, such that machine make remained independent of group assignment. **Intervention group** Any short-term or sustained behavioural intervention aimed at encouraging uptake, acclimation, improvement or maintenance of CPAP adherence among people with a diagnosis of OSA. Examples of modalities that may fall under 'behavioural interventions' include educational, supportive, interactive, group-based, mindfulness-based, cognitive, behavioural, motivational or approaches utilizing a combination of these strategies.

Study	Askland et al[5]
	Control group Participants in the control group may receive instruction that would be used by the study centre in question, provided that the equivalent 'background' level of instruction was also offered and/or delivered to the intervention group.
Exclusion criteria	Trials that explicitly recruited patients with central sleep apnoea were not eligible for inclusion.
Recruitment/selection of patients	Participants had to be randomised in trials assessing one of the following comparisons: 1. Behavioural therapy + CPAP versus control + CPAP 2. Educational interventions + CPAP versus usual care + CPAP 3. Increased practical support and encouragement during follow-up + CPAP versus usual care + CPAP 4. Mixed (SUP/EDU/BEH) Intervention + CPAP versus Usual Care + CPAP
Age, gender and ethnicity	Average age of the study populations was 52.9 years. Patients were of mixed gender predominately male and of different ethnicities.
Further population details	Participants were adults of either sex with a diagnosis of obstructive sleep apnoea (OSA) diagnosed using a recognised sleep diagnostic tool giving an Oxygen Desaturation Index (ODI) of ≥5 per hours or an Apnoea Hypopnea Index (AHI) ≥5 per hour.
Extra comments	Most studies were conducted in the North America and Europe with smaller number of trials conducted in China and Australia. Study population ranged from 12 to 3100 participants.
Indirectness of population	No indirectness
Interventions	Intervention 1 : Behavioural therapy + CPAP versus control + CPAP (n=11 studies; 1139 participants): Duration between 2 months and 12 months

Study	Askland et al[5]
	Indirectness: No indirectness Intervention 2: Educational interventions + CPAP versus usual care + CPAP (n= 11 studies; 2752 participants) Duration between 28 days and 12 months Indirectness: No indirectness Intervention 3: Increased practical support and encouragement during follow-up + CPAP versus usual care + CPAP (n= 14 studies; 1498 participants) Duration 2 months to 6 months. Indirectness: No indirectness Intervention 4: Mixed (SUP/EDU/BEH) Intervention + CPAP versus Usual Care + CPAP (n= 12 studies; 5041 participants) Duration 1 month to 2 years. Indirectness: No indirectness
Funding	The majority of the included studies were funded by industry
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Behavioural therapy + CPAP versus control + CPAP Protocol outcome 1: CPAP device usage (hours/night)	

Study	Askland et al[5]
- Actual outcome: CPAP Device Usage (hours/night) ; MD 1.31 hours/night higher(0.95 higher to 1.66 higher) Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - high, Outcome reporting - high, Measurement - high, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 2: Number of participants who used CPAP therapy > 4 hours per night - Actual outcome: Number of participants who used CPAP therapy > 4 hours per night; RR; 1.33 [95% CI 1.10, 1.61] Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data – High, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 3: Withdrawal - Actual outcome: Withdrawals; RR; 0.70 [95% CI 0.51,0.98] Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - high, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 4: Symptoms (Epworth Sleepiness Scale) - Actual outcome: Epworth sleepiness scale (Endpoint scores); MD; -2.22 (-3.68, -0.75] Risk of bias: All domain - high, Selection –high, Blinding - Low, Incomplete outcome data - High, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: serious indirectness Protocol outcome 5: AHI on treatment - Actual outcome: AHI on treatment (endpoint scores); MD; -0.95 [95% CI -2.25, to 0.35] Risk of bias: All domain - high, Selection - high, Blinding - high, Incomplete outcome data - high, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 6: Quality of life (Functional Outcome of Sleep Questionnaire) - Actual outcome: Quality of life (Functional Outcome of Sleep Questionnaire)Endpoint ; MD 0.01 [95% CI -0.26, 0.29]

Study	Askland et al[5]
Risk of bias: All domain - high, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - high, Measurement - high, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 7: Quality of life (SF-36 PH) - Actual outcome: Quality of life (SF-36 PH); MD -0.07 [95% CI -0.82, 0.67] Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - high, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Educational interventions + CPAP versus usual care + CPAP Protocol outcome 1: CPAP device usage (hours/night) - Actual outcome: CPAP Device Usage (hours/night) ; MD 0.88 hours/night higher (0.40 higher to 1.36 higher) Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - high, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 2: Deemed Adherent (Number of participants who used CPAP therapy > 4 hours/night) - Actual outcome: Number of participants who used CPAP therapy > 4 hours per night; RR; 1.31 [95% CI 1.15, 1.48] Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data – High, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 3: Withdrawals - Actual outcome: Withdrawals; RR 0.73 [0.52, 1.02] Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - high, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 4: Symptoms (Epworth Sleepiness Scale)	

Study	Askland et al[5]
- Actual outcome: Symptoms (Epworth Sleepiness Scale); MD -0.08 [-0.92, 0.76] Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data – high, Outcome reporting – high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Increased practical support and encouragement during follow-up + CPAP versus usual care + CPAP Protocol outcome 1: CPAP Machine usage (hours/night) - Actual outcome: Machine usage (hours/night); MD 0.70 [0.36, 1.05] Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - high, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 2: Deemed Adherent (Number of participants who used CPAP therapy > 4 hours/night) - Actual outcome: Number of participants who used CPAP therapy > 4 hours per night; RR; 1.19 [95% CI 1.03, 1.37] Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - high, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 3: Withdrawals - Actual outcome: Withdrawals; RR 1.22 [0.97, 1.52] Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - high, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 4.1 Symptoms (Epworth Sleepiness Scale) - Actual outcome: Endpoint scores (Epworth Sleepiness Scale); MD 0.03 [-0.59, 0.64] Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data – Low, Outcome reporting – high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 4.2 Symptoms (Epworth Sleepiness Scale) - Actual outcome: Change from baseline (Epworth Sleepiness Scale); MD -0.32 [-1.19, 0.56]	

Study	Askland et al[5]
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data – high, Outcome reporting – Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 5.1: Quality of life (Functional Outcome of Sleep Questionnaire) - Actual outcome: Functional Outcome of Sleep Questionnaire - Endpoint; SMD 0.15 [95% CI -0.23, 0.53] Risk of bias: All domain - high, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - high, Measurement - high, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 5.2: Quality of life (SAQLI) - Actual outcome: SAQLI - Endpoint; SMD 0.22 [95% CI -0.04, 0.47] Risk of bias: All domain - high, Selection - Low, Blinding - Low, Incomplete outcome data - high, Outcome reporting - high, Measurement - low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 5.3: Quality of life (SF-36 PH) - Actual outcome: Quality of life - SF-36 PH - endpoint; SMD 0.13 [95% CI -0.09, 0.34] Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - high, Outcome reporting - low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 6.1: Quality of life (Functional Outcome of Sleep Questionnaire) - Actual outcome: Functional Outcome of Sleep Questionnaire – Change from baseline; SMD 0.24 [95% CI -0.40, 0.87] Risk of bias: All domain - high, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - high, Measurement - high, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 6.2: Quality of life (SF-36 PH) - Actual outcome: Quality of life - SF-36 PH – change from baseline; SMD 0.04 [95% CI -0.40, 0.47] Risk of bias: All domain - high, Selection - low, Blinding - Low, Incomplete outcome data - high, Outcome reporting - low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness	

Study	Askland et al[5]
Protocol outcome 6.3: Quality of life (Functional Outcome of Sleep Questionnaire - 10) - Actual outcome: Functional Outcome of Sleep Questionnaire - 10 – Change from baseline; SMD 0.24 [95% CI 0.00, 0.60] Risk of bias: All domain - high, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - high, Measurement - high, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 7: Anxiety Symptom Rating (HADS-A) - Actual outcome: Anxiety symptom rating (HADS-A) –comparison of values at endpoint; MD -1.10 [95% CI -2.95, 0.75] Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - low, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 8: AHI on treatment - Actual outcome: AHI on treatment –comparison of values at endpoint; MD 0.48 [95% CI -4.23, 5.18] Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - high, Outcome reporting - low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 9.1: HADS - Depression - Actual outcome: HADS Depression –comparison of values at endpoint; SMD -0.43 [95% CI -0.87, 0.01] Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - low, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 9.2: CES - D - Actual outcome: CES – D –comparison of values at endpoint; SMD 0.25 [95% CI 0.02, 0.49] Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - high, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Mixed (SUP/EDU/BEH) Intervention + CPAP versus Usual Care + CPAP Protocol outcome 1: CPAP device usage (hours/night) - Actual outcome: CPAP Device Usage (hours/night) ; MD 0.82 hours/night higher (95% CI 0.20, 1.43)	

Study	Askland et al[5]
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 2: Deemed Adherent (Number of participants who used CPAP therapy > 4 hours/night) - Actual outcome: Number of participants who used CPAP therapy > 4 hours per night; RR; 1.14 [95% CI 1.04, 1.26]	
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data – low, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 3: Withdrawals - Actual outcome: Withdrawals; RR 0.64 [0.32, 1.28]	
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 4.1: Quality of life (Functional Outcome of Sleep Questionnaire - 10) - Actual outcome: Functional Outcome of Sleep Questionnaire - 10 – Change from baseline; SMD 0.25 [95% CI -0.05, 0.54]	
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - high, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 4.2: Quality of life (SF-36 MH) - Actual outcome: Quality of life - SF-36 MH – change from baseline; SMD Not Estimable	
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - low, Outcome reporting - high, Measurement - high, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 4.3: Quality of life (SF-36 PH) - Actual outcome: Quality of life - SF-36 PH – change from baseline; SMD 0.59 [95% CI -0.52, 0.67]	
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - high, Measurement - high, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 5.1: Quality of life (FOSQ - Endpoint) - Actual outcome: QOL: FOSQ - Endpoint; SMD 0.10 [95% CI -0.19, 0.40]	

Study	Askland et al[5]
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness	
Protocol outcome 5.2: Quality of life (SF-36 PH) - Actual outcome: Quality of life - SF-36 PH - endpoint; SMD 0.59 [95% CI -0.01, 1.19]	
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - high, Measurement - high, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness	
Protocol outcome 6.1: Anxiety symptom rating – comparison of values at endpoint - Actual outcome: Anxiety symptom rating - endpoint; SMD -0.19 [95% CI -0.47, 0.09]	
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - high, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness	
Protocol outcome 6.2: DASS - Anxiety - Actual outcome: DASS - Anxiety - endpoint; SMD -0.19 [95% CI -0.47, 0.09]	
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness	
Protocol outcome 6.3: BAI - Anxiety - Actual outcome: BAI – Anxiety - endpoint; SMD -0.15 [95% CI -0.63, 0.34]	
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness	
Protocol outcome 6.4: STAI – State - Actual outcome: STAI – state - Anxiety - endpoint; SMD -0.49 [95% CI -0.92, -0.06]	
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - high, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness	
Protocol outcome 7.1: Depression Symptom rating – endpoint – NO META ANALYSIS PERFORMED - Actual outcome: Depression Symptom rating – endpoint – No totals	

Study	Askland et al[5]
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 7.2: BDI - depression – endpoint – NO META ANALYSIS PERFORMED - Actual outcome: BDI – depression – endpoint – No totals Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 7.3: HADS - depression – endpoint – NO META ANALYSIS PERFORMED - Actual outcome: HADS – depression – endpoint – No totals Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - high, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 7.4: DASS - depression – endpoint – NO META ANALYSIS PERFORMED - Actual outcome: DASS – depression – endpoint – No totals Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 8.1: Epworth sleepiness scale – endpoint scores – NO META ANALYSIS PERFORMED - Actual outcome: Epworth sleepiness scale score – endpoint – No totals Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness Protocol outcome 8.2: Epworth sleepiness scale – change from baseline – NO META ANALYSIS PERFORMED - Actual outcome: Epworth sleepiness scale score – change from baseline – No totals Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	*None*

Study	Berry 2020[12]
Study type	RCT (Patient randomised)
Number of studies (number of participants)	1 (n=250) (Standard care, n= 126, standard care + cloud-based sleep coaches (CBSC), n= 124).
Countries and setting	Conducted in USA; Setting: hospital
Line of therapy	1st line
Duration of study	Intervention + 3 months follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Age 21 to 75 years (men and women) Diagnostic apnea-hypopnea index ≥ 15 events/h (diagnostic polysomnography [PSG], diagnostic portion of split PSG, or home sleep apnea test) Eligible for treatment with automatically adjusting continuous positive airway pressure or bilevel positive airway pressure Residence in area covered by wireless network
Exclusion criteria	· Participation in another interventional research study concerned with sleep disorders within the last 30 days · Major uncontrolled medical condition that would interfere with the demands of the study, adherence to positive airway pressure (PAP), or the ability to commit to follow-up assessment including conditions such as poorly managed or controlled or advanced stages of pulmonary disease, cardiac disease, neurological disease, neuromuscular disease, cancer, and renal disease

Study	Berry 2020[12]
	· Prior PAP use within the previous 12 months · Predominantly central apnoea's (≥ 50% central apnoea's) or Cheyne Stokes respiration (CSR) present during ≥ 20% of total sleep time · Chronic respiratory failure or insufficiency with suspected or known neuromuscular disease, moderate chronic obstructive pulmonary disease, or any condition with an elevation of arterial carbon dioxide levels while awake or the requirement for continuous supplemental oxygen or mechanical ventilation · Surgery involving the upper airway, nose, sinus, eye, teeth, or middle ear within the previous 90 days · PAP therapy is otherwise medically complicated or contraindicated, such as those with a difficult to size or adjust interface (mask) resulting in facial pain, skin irritation or trauma, or excessive air leaks
Recruitment/selection of patients	Participants recruited at PAP set-up
Age, gender and ethnicity	Age: CBSC 54.9 ± 11.5 years; control: 55.2 ± 13.4 years AHI: CBSC 36.6 ± 20.6 events/h; control 36.7 ± 21.1 events/h Gender male %: CBSC 88.7%; control 89.7%
Further population details	Sleepiness: ESS: CBSC 11.2 ± 6.0; control 10.8 ± 6.1
Indirectness of population	No indirectness
Interventions	(n=124) Intervention 1: Cloud-based sleep coach (CBSC) Participants randomised to SC+CBSC follow-up received all elements of standard care and, in addition, interaction/communication from the CBSC service. The participants were informed that they would receive a telephone call from the CBSC system in 3 to 4 days to discuss their experience with therapy. Further contact from the CBSC could be expected if their adherence goals were not reached. All participants received calls on

Study	Berry 2020[12]
	day 3 to 4 and on day 32 after PAP initiation. The participants were also provided with information on, and encouraged to use, the mobile application (PAPapp), allowing them to view their current adherence. (n=126) Intervention 2: standard care Participants attending PAP setup classes were educated about use of their PAP device, including cleaning, ramp option, and humidification. All patients were encouraged to use therapy nightly for as long as they can, preferably for the entire time they sleep. Each participant was fitted with a mask based on physician order, participant preference, and the ability to obtain a good mask seal. The type of PAP device (autoadjusting CPAP or auto-adjusting bilevel PAP) and pressure settings were determined by physician order. Participants practiced putting on their masks and turning on the PAP device. All devices contained wireless modems with information accessed via a cloud-based programme. Device data were uploaded into the database via wireless modems programmed to call in automatically. Device data were associated with the individual participant based upon the serial number of the device and modem entered by the staff. All PAP devices had the ability to deliver heated humidification. At the PAP setup class, participants received information about the PAPapp (written information also supplied with each PAP unit). Participants were provided with telephone numbers for PAP supply replacement and for PAP treatment issues. They were also encouraged to use the secure messaging service “My Healthy Vet” to facilitate communication with the sleep providers. Participants had a 6-week inspection of adherence and efficacy data if ordered by the physician reading the sleep study. Pressure settings could be changed remotely based on physician order. A participant could be scheduled for an individual mask fitting CPAP RT appointment if discomfort or leak issues were significant. A 3-month (90 to 120 days) sleep clinic visit with a sleep provider (physician or physician extender) was scheduled.
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CBSC versus standard care

Protocol outcome 1: adherence
- Actual outcome : Average use (all days) in hours at 3 months; Group 1: CBSC n= 124, (4.4 ± 2.6) ; Group 2: n= 126, (3.7 ± 2.7)
Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: no indirectness

Study	Berry 2020[12]
Protocol outcome 2: adherence - Actual outcome : % Days > 4 hours at 3 months; Group 1: CBSC n= 124, (57.9 ± 35.4) ; Group 2: n= 126, (48.1 ± 36.8) Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: no indirectness Protocol outcome 3: AHI (events/h) - Actual outcome : AHI at 3 months; Group 1: CBSC n= 124, (4.6 ± 4.3); Group 2: n= 126, (4.4 ± 3.9) Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: no indirectness Protocol outcome 4: ESS - Actual outcome: ESS at 3 months; Group 1: CBSC n= 120, (8.9 ± 5.4) ; Group 2: n= 120,(8.3 ± 5.5) Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Quality of life at >1 month; Mortality at >1 month; CO2 control at >1 month; Driving outcomes at >1 month; Neurocognitive outcomes at >1 month; Systolic blood pressure for hypertension at >1 month; HbA1c for diabetes at >1 month

Study	Hanger 2018[34]
Study type	RCT (Patient randomised)
Number of studies (number of participants)	1 (n=56) (standard care, *n*=23); telemedicine (*n*=33).
Countries and setting	Conducted in USA; Setting: hospital
Line of therapy	1st line
Duration of study	Intervention + 3 months follow up

Study	Hanger 2018[34]
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Adults, at least 18 years of age, newly diagnosed with moderate to severe OSA on HSAT or PSG; provision of CPAP device by DME with wireless data transmission capability and English speaking
Exclusion criteria	• Prior PAP use of any kind, including CPAP, APAP, bi-level or adaptive seroventilation • Current use of prescribed supplemental oxygen • Significant co-morbid medical condition(s) that could prevent/interfere with the participant using CPAP on a daily basis • Home location being outside of wireless capability • Sleep environment where the participant does not sleep in the same location on a frequent basis
Recruitment/selection of patients	Participants in the study were adults who had recently been diagnosed with moderate to severe obstructive sleep apnoea through a home sleep apnoea test (HSAT) or in-lab polysomnography (PSG), based on AASM criteria of an apnoea-hypopnea index (AHI) ≥15 as moderate OSA and an AHI of ≥30 as severe OSA. Participants were prescribed treatment with positive airway pressure (PAP) therapy. Participants were recruited into the study from February 21 through June 30, 2018. Data monitoring was completed on October 3, 2018
Age, gender and ethnicity	Age (mean SD): medicine 60.0±14.2 ; control: 51.4±13.8 AHI: telemedicine38.0±21.1; control 37.27±18.8 Gender: female%: telemedicine 42 ; control 42.1
Further population details	Sleepiness: ESS: telemedicine 8.8±4.9 ; control 11.3±5.5

Study	Hanger 2018[34]
Indirectness of population	No indirectness
Interventions	(n=23) Intervention 1: Telemedicine care group (TM). In addition to standard care, participants randomised to the TM group received the intervention, which entailed an initial call to all participants after one week of PAP therapy. CPAP usage data was monitored weekly via a web-based database. Use of CPAP of less than 4 hours per night, on less than 70% of nights (or more than 2 days), in the preceding week of monitoring, was considered non-adherent and triggered a phone call from the research coordinator to provide support and troubleshooting as needed. Participants were seen back in clinic after 6 weeks, per standard care. Data monitoring, as outlined above, continued for the first 3 months of CPAP usage. The study period culminated with a phone call, by the author, to all participants from both study arms, at the end of 3 months, to discuss any questions or concerns and to survey satisfaction of their follow-up care. (n=23) Intervention 2: Standard care Participants in the standard care (SC) group received the standard follow-up regimen currently used by the Sleep Center. Following diagnosis of moderate or severe OSA and the participant was prescribed CPAP therapy. Patients obtained equipment; they were fitted with a mask and given instructions on set up, use and care of the PAP machine. Devices were equipped with wireless data transmission technology. Patients were advised to call for any equipment concerns and the Sleep Center with any other concerns or questions related to PAP use; they were seen back in clinic after 6 weeks to discuss adherence and efficacy, review device data, and to address any issues or questions they may have. If patients were doing well, they were seen back yearly for monitoring, with more frequent follow-up if needed.
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Telemedicine versus standard care

Protocol outcome 1: adherence
- Actual outcome : non-adherence at 3 months; Group 1: n= 25, (2/25) ; Group 2: n=19, 3/19
Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: no indirectness

Study	Hanger 2018[34]
Protocol outcome 2: AHI - Actual outcome :AHI at 3 months; Group 1: n= 25, (4.1±3.0) ; Group 2: n=19, (3.4±3.8) Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: no indirectness Protocol outcome 3: ESS - Actual outcome :ESS at 3 months; Group 1: n= 25, (4.0±2.7); Group 2: n=19, (6.5±4.1) Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: no indirectness Protocol outcome 4: Number of days used >4 hours - Actual outcome : Number of days used >4 hours at 3 months; Group 1: n= 25, (89.9±13.1); Group 2: n=19, (83.5±15.8) Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Quality of life at >1 month; Mortality at >1 month; CO2 control at >1 month; Driving outcomes at >1 month; Neurocognitive outcomes at >1 month; Systolic blood pressure for hypertension at >1 month; HbA1c for diabetes at >1 month

Study	Kotzian 2019[43]
Study type	RCT (Patient randomised)
Number of studies (number of participants)	1 (n=251 recruited; n=70 therapy relevant OSA, n=33 randomised)
Countries and setting	Conducted in Austria; Setting: hospital
Line of therapy	1st line
Duration of study	Intervention + follow up 1year

Study	Kotzian 2019[43]
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Moderate-severe
Subgroup analysis within study	Not applicable
Inclusion criteria	Subacute adult (19-70 years of age) stroke survivors (>1 months to <1 year post stroke) with a completed stroke confirmed by a neurologist based on the history of a sudden onset of a neurological deficit lasting longer than 24 h, the presence of a neurological deficit upon physical examination, and a brain lesion compatible with the neurological deficit in computerised tomography or MRI of the brain were included. For evaluation of OSA, eligible patients underwent in hospital sleep studies. Therapy relevant OSA was defined as showing an AHI >15 per hour of sleep, indicating moderate sleep apnoea.
Exclusion criteria	Patients unable to understand the protocol due to cognitive impairments ;patients with COPD; chronic kidney disease >4; co-existing causes of daytime sleepiness; experiences of major psychiatric or any other acute medical condition; previously established PAP therapy; patients with central sleep apnoea; and patients unable or unwilling to comply with the protocol.
Recruitment/selection of patients	The study was conducted in Vienna, Austria from April 18 2016 to April 18 2018. All people with stroke referred to rehabilitation were initially included in the study.
Age, gender and ethnicity	Age: telemonitoring: 62.9 (5.3 years); control: 61.8 (5.3) years Gender: male: telemonitoring 64.7% : control: 75%
Further population details	1. BMI: telemonitoring: 30.9 kg/m^2 (4.8) : control: 29 kg/m^2 (3.1) 2. AHI: telemonitoring: 37 (14.1): control: 37 (12.8)
Indirectness of population	No indirectness
Interventions	(N=17)Intervention 1: tele medical monitoring system to improve CPAP adherence All patients referred to PAP therapy received a 30 min introductory lesson with nasal or oro-nasal mask fitting, device handling and information about PAP therapy. Patients were provide with an AirSendse 10 Autoset CPAP

Study	Kotzian 2019[43]
	including humidifier and were set to auto-titrate at pressures between 6 and 13 cm H20. Patients were motivated to use the PAP device for at least 4h of sleep/night. The PAP training period lasted at least one week, with bedside coaching in the morning and the evening. During the night the patients were coached by trained nurses. Relatives were also trained in using the humidifier and cleaning the mask and the humidifier chamber. The AHI, oximetry and leakage information were collected every day in coaching sessions with the patient. Pressure limits could be increased or decreased to improve patient comfort. If the patient had problems to tolerate high pressures while falling asleep in the first week, the fixed window was reduced to sub-therapeutic pressures (e.g. 4-8 mbar) for a few nights to enable the patient to get used to therapy. If the Autoset PAP device did not react to obstructive events, titration was too slow or did not decrease; either a fixed CPAP or a narrow Auto CPAP window was attached. Those who tolerated PAP therapy with a median PAP use of >4h/night underwent PSG with PAP. The PAP coordinator at the homecare provider reviewed the downloaded information every morning except on weekends and holidays and contacted the patients if the 90th percentile of pressure was >16 com H20 or mask leakage of the 95th percentile was >24l/min or use was <4h or the AHI was >10 events/h for three consecutive days. (n=16) Intervention 2: Standard PAP treatment. No tele medical monitoring system Both groups: Patients were asked to call their homecare provider if any problems with the device occurred or their physician in case of medical problems. Two days after discharge from return to the hospital they were contacted by their homecare provider and were asked about progress and adherence, as well as about any other problems. They were asked to return to the hospital after 3 months for evaluation therapy including review of PAP pressure, mask leakage, residual respiratory events and compliance.
Funding	This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: telemonitoring system versus no telemonitoring system
Protocol outcome 1: Days PAP used >4 h
- Actual outcome : Days PAP used >4 h [mean SD] at 12 months; Group 1: n=12; 271 (99), Group 2: ; n=11; 282 (55)
Risk of bias: All domain - high, Selection - high,, Blinding - Low, Incomplete outcome data - high,, Outcome reporting - Low, Measurement - Low, Crossover -

Study	Kotzian 2019[43]
Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: serious; Group 1 Number missing: 5 (lost to follow up due to medical reason=1, discontinued intervention due to discomfort device =4), Group 2 Number missing: 5 (Lost to follow up due to medical reason = 2, discontinued intervention due to discomfort with device =3) Protocol outcome 2: AHI - Actual outcome: AHI [mean SD] at 12 months ; Group 1: n=12 : 4.2 (3.9), Group 2 (n=11): 1.6 (1.3) Risk of bias: All domain - high,, Selection - high, Blinding - Low, Incomplete outcome data - high,, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: serious; Group 1 Number missing: 5 (lost to follow up due to medical reason=1, discontinued intervention due to discomfort device =4), Group 2 Number missing: 5 (Lost to follow up due to medical reason = 2, discontinued intervention due to discomfort with device =3) Protocol outcome 3: adherence - Actual outcome : Mean adherence all days (min per day) [mean SD] at 12 months ; Group 1: n=12, 352 (97) Group 2: n=11, 307 (62) Risk of bias: All domain - high, Selection - high,, Blinding - Low, Incomplete outcome data - high, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: serious; Group 1 Number missing: 5 (lost to follow up due to medical reason=1, discontinued intervention due to discomfort device =4), Group 2 Number missing: 5 (Lost to follow up due to medical reason = 2, discontinued intervention due to discomfort with device =3)	
Protocol outcomes not reported by the study	Quality of life at >1 month; Mortality at >1 month; Sleepiness score at >1 month;; CO2 control at >1 month; Driving outcomes at >1 month; self-reported adherence (continuous), mood or anxiety, withdrawals, treatment related withdrawals , oxygen desaturation index , minor adverse effects of treatment Neurocognitive outcomes at >1 month; Systolic blood pressure for hypertension at >1 month; HbA1c for diabetes at >1 month

Study	Murase 2020[57]
Study type	RCT (Patient randomised)
Number of studies (number of participants)	1 (n=508)
Countries and setting	Conducted in Japan; Setting: hospital
Line of therapy	1st line

Study	Murase 2020[57]
Duration of study	Intervention + follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	The criteria for patient inclusion were >18 years old; fulfilled the requirements for CPAP treatment under Japanese governmental health insurance (AHI>20/h by PSG or respiratory event index >40/h by portable monitoring device at OSA diagnosis; CPAP implemented more than 3 months previously; residual AHI under CPAP use<20/h; having clinic visits every month or every 2 months for follow-up of CPAP therapy; recent CPAP adherence data available.
Exclusion criteria	Not stated
Recruitment/selection of patients	Participants were consecutively recruited from patients who were regularly visiting hospitals or clinics for CPAP management.
Age, gender and ethnicity	Age: telemedicine group: 60 (11); control: 60 (13) years AHI: telemedicine: 40.6; control 40.6 Gender: male%: telemedicine 87%; control 86.1%
Further population details	1. BMI: telemedicine: 27.4 kg/m^2 (3.8); control: 27kg/m^2 (5.4) 2. Sleepiness: ESS: telemedicine 5.7 (4.0); 4.9 (2.3)
Indirectness of population	No indirectness
Interventions	(n=161) Intervention 1: telemedicine group Physician checked adherence data utilising the telemonitoring system.

Study	Murase 2020[57]
	Follow-every 3 months. (3 months n= 166; 1 month, n=156) Intervention 2: No telemedicine Follow-up 1 month and 3 months
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: telemonitoring system versus no telemonitoring Protocol outcome 1: adherence - Actual outcome : CPAP use min/night ; Group 1: n= 161, 327(91); Group 2: n=166, 307 (107) Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Quality of life at >1 month; Mortality at >1 month; Sleepiness score at >1 month; AHI/RDI at >1 month; CO2 control at >1 month; Driving outcomes at >1 month; Neurocognitive outcomes at >1 month; Systolic blood pressure for hypertension at >1 month; HbA1c for diabetes at >1 month

Study	Nilius 2019[61]
Study type	RCT (Patient randomised)
Number of studies (number of participants)	1 (n=80)
Countries and setting	Conducted in Germany ; Setting: hospital
Line of therapy	1st line

Study	Nilius 2019[61]
Duration of study	Intervention + follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Moderate severe OSA
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients who had suffered an ischaemic stroke within last 3 months; a moderate to severe baseline OSA with an AHI>15, that had been confirmed in the sleep laboratory; physical capability to operate a PAP device and mask; age<75;CPAP naïve; no COPD; and regular PAP usage (<3h/night) during the inpatient phase.
Exclusion criteria	Not stated
Recruitment/selection of patients	Patients were informed about the study during the first anamnesis upon being admitted to hospital. In case of a positive diagnosis of moderate to severe sleep apnoea (AHI>15/h), the patients received a positive pressure device.
Age, gender and ethnicity	Age: telemedicine 55.4 (10.4) years; control: 58.6 (9.3) years Gender: all females ethnicity: not stated
Further population details	1. BMI: telemedicine 31.7 kg/m^2 (5.4); control 30.1kg/m^2 (6.6) ; Sleepiness ESS: telemedicine 2.4 (3.7); 3.9 (4.9); AHI: 41.2 (19); control: 37.6 (18.4)
Indirectness of population	No indirectness
Interventions	(n=37) Intervention 1: telemedicine Therapy was uniformly initiated in all eligible patients that is after a positive PSG., patients were visited by sleep lab staff, and a training session and mask adjustment followed before the initial therapy PSG. The device used was usually an APAP device set to a pressure 4-18 cm H20.

Study	Nilius 2019[61]
	The online data of the telemedicine group was anonymously transferred to the password protected web server each morning. The data was evaluated for relevant therapy details each week starting 7 days after the individual discharge date of each patient. (n=38) Intervention 2: No intervention – Standard care All patients went home with a PAP device and the sleep lab informed the homecare provider about the therapy settings and equipment. The patients were advised to visit their primary care physician or lung specialist if they experienced any problem. Follow-up 6 months
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: versus

Protocol outcome 1: Usage hours/night
- Actual outcome : ; Group 1: n=37, 4.4 (2.5); Group 2: ; n=38, 2.1 (2.2)
Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: no indirectness .

Protocol outcome 2: ESS
- Actual outcome:; Group 1: n=36, 3.7 (3.2) Group 2: ; n=37, 6.1 (4.1)
Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: no indirectness .

Protocol outcome 3: Systolic blood pressure-
- Actual outcome:; Group 1: n=26, 129.5 (15.2);Group 2: ; n=29, 138.8 (16.1)
Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: no indirectness.

Protocol outcome 4: diastolic blood pressure-
- Actual outcome:; Group 1: n=26, G 78.4 (11.1); group 2: ; n=29, 82.8 (9.2)

Study	Nilius 2019[61]
Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: no indirectness.	
Protocol outcomes not reported by the study	Quality of life at >1 month; Mortality at >1 month; Driving outcomes at >1 month; Neurocognitive outcomes at >1 month; HbA1c for diabetes at >1 month