National Institute for Health and Care Excellence

Final

Obstructive sleep apnoea/hypopnoea syndrome and obesity hypoventilation syndrome in over 16s

Evidence review L: Monitoring

NICE guideline NG202

Intervention evidence review

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Final

Developed by the National Guideline Centre, hosted by the Royal College of Physicians

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1.1 Review question: What is clinically and cost effective strategy for monitoring obstructive sleep apnoea/hypopnoea syndrome (OSAHS)/ obesity hypoventilation syndrome (OHS)/COPD-OSAHS overlap syndrome?

1.2 Introduction

Patients who have been diagnosed with OSAHS/OHS/COPD-OSAHS overlap syndrome can have a significant health burden. The provision of treatment by the health care provider to manage these conditions requires some form of follow-up and monitoring, similar to most conditions. Traditionally patients attend outpatient clinics after first treatment to discuss the care they are receiving, issues that are occurring, titration of the therapy as well as to allow for any further testing or answering clinical questionnaires. The timeliness of a patient's review may impact on a number of factors including compliance and success of treatment. Yet the time to follow-up can vary between various health care providers. Services may see patients within the first two weeks after being set up on therapy, whilst others may not have the ability to review for 3 months. On-going reviews may also be varied from 2 weeks to 6, 12 months or 2 years and longer in some cases.

When a patient is reviewed, the type of monitoring of a patient's treatment is also an area which is not uniform across the health service. There are differences in whether services repeat a sleep study, download patient's device data, take a blood gas or overnight CO2 level. The advent of modems and the capability to use tele-monitoring allows review patient data and even titration of therapy without actually having the patient present. This has opened up further options, to examine what is clinically as well as cost effective in the monitoring of patients' treatment.

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	People with OSAHS/OHS/COPD-OSAHS overlap syndrome Stratified by: • OSAHS vs OHS vs COPD-OSAHS overlap syndrome • stage of treatment (<1 year vs >/= 1 year) • severity (mild vs moderate vs severe, based on AHI)
Interventions	In person outpatient visits Download of data from devices Telephone follow-up Telemonitoring Any of the above at any of the following frequencies: • no routine monitoring • 3 yearly

	• yearly • 6 monthly • 3 monthly • 1 monthly • <1 monthly
Comparisons	Any of the above methods at any frequency vs the same or any other method at any frequency

Outcomes	**Critical**
	• generic or disease specific quality of life measures (continuous)
	• mortality (dichotomous)
	
	Important
	• sleepiness scores (continuous, e.g. Epworth)
	• apnoea-hypopnoea index (continuous)
	• oxygen desaturation index (continuous)
	• CO_2 control (continuous)
	• hours of use (adherence measure, continuous)
	• minor adverse effects of treatment (rates or dichotomous)
	• driving outcomes (continuous)
	• neurocognitive outcomes (continuous)
	• healthcare contacts (rates/dichotomous)
	• impact on co-existing conditions:
	  ○ HbA1c for diabetes (continuous)
	  ○ cardiovascular events for cardiovascular disease (dichotomous)
	  ○ systolic blood pressure for hypertension (continuous)

Study design	• RCTs will be prioritised, if insufficient RCTs are found for guideline decision making, non-randomised studies will be considered if they adjust for key confounders (age, sex, BMI, co-existing conditions) • minimum duration of follow-up 1 month • parallel or crossover studies to be included

1.4 Clinical evidence

1.4.1 Included studies

OSAHS

CPAP

Ten studies were included in this review,[3, 10, 14, 19, 23, 25, 26, 36, 40, 42] these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence table below (Table 3).

Six studies compared telemonitoring and in person follow-up with in-person follow-up. One study compared telemonitoring and phone follow-up with phone follow-up. One study compared multimodal telemonitoring with usual care. Two studies compared telemonitoring and tele visits with in person follow-up. The duration of all included studies was of one year or less.

All studies were in people using fixed level CPAP, except for one study in people using auto CPAP.

All studies included a severe OSAHS population determined by their baseline mean AHI. Studies were stratified based on the AHI/ODI severity of the population. When a mixed severity population was included the severity of the majority of the population was used by taking the mean AHI of the patients included and the study was downgraded for indirectness.

Follow-up of studies ranged from 2 to 12 months. Studies varied in size with the number of participants ranging from 45 in the smallest study to 306 in the largest. Oral devices

No evidence was identified for monitoring of people using oral devices.

Positional modifiers

No evidence was identified for monitoring of people using positional modifiers.

Surgery

No evidence was identified for monitoring of people who have undergone surgery.

OHS

There was no evidence available for people with OHS.

COPD-OSAHS overlap syndrome

There was no evidence available for people with COPD-OSAHS overlap syndrome.

See also the study selection flow chart in appendix C, study evidence tables in appendix D, forest plots in appendix E and GRADE tables in appendix H.

1.4.2 Excluded studies

See the excluded studies list in appendix I.

1.4.3 Summary of clinical studies included in the evidence review

Table 2: Summary of studies included in the evidence review

Study	Intervention and comparison	Population	Outcomes	Comments
Anttalainen 2016[3] RCT Finland	**Telemonitoring and in person follow up:** Wireless telemonitoring system (ResTaxx Online, ResMed Sydney, Australia). The module was attached to the S9 Elite (ResMed, Sydney Australia) CPAP device, which transmitted compliance data every day automatically to ResTaxx Online. The treatment was considered successful when CPAP use was >4h/day, mask <0.4 L/s and AHI <5/h during the last 6 days. Study nurses made the data checkups daily during weekdays and if the criteria for successful CPAP therapy were not achieved during two consecutive nights the nurses adjusted the CPAP remotely and called the patient to give further advice. The patients were encouraged to contact the nurse in case they had any problems. TM group answered the questionnaire at 3 months by email. N=50	OSAHS patients who were commencing CPAP treatment at the department of pulmonary diseases of Turku university hospital. All patients were over 18 years of age. Mean age (SD): Telemonitoring and in person follow up group – 53.9(12.2). In person follow up group – 56.4(11.8) Finland Baseline AHI Telemonitoring group = 34.4 (20.6) Usual care = 34.8 (23.4)	Follow up - 12 months • Quality of life - GHQ12 score • Sleepiness - Epworth scale • AHI • Adherence – CPAP usage h/day	Mixed analysis of mostly randomised and some non-randomised patients in the study Severe OSAHS strata population (strata based on mean AHI)

Study	Intervention and comparison	Population	Outcomes	Comments
	In person follow up: In Person follow up. Usual care group visited the pulmonologist after 3 months leading in a 3 month habituation phase in the UC group. UC group answered the questionnaire at the 3 month visit. CPAP device was used without wireless telemonitoring N=61			
Fox 2012[10] RCT Canada	**Telemonitoring and in person follow up:** Auto-titrating PAP machine that transmitted physiologic information (i.e. adherence, air leak, residual AHI) daily to a website that could be reviewed. N=39 **In person follow up:** Standard care with auto-titrating CPAP. In Person follow up N=36	Patients were recruited from adult (≥ 19 yr. of age) patients with moderate to severe OSAHS (AHI ≥ 15 events/hr by lysomnography (PSG) using the Chicago scoring criteria for the determination of apnoeas and hypopneas, according to the American Academy of Sleep Medicine)10 diagnosed at the Sleep Disorders Program who were seen by one of three respirologists (JF, CFR, NTA) at the University of British Columbia (UBC) between April 8, 2008 to June 1, 2010. Patients with OSAHS who were prescribed PAP therapy by their regular sleep physician and who were willing to accept a trial of therapy were	Follow up 3 months • Epworth sleeping scale • Apnoea-Hypopnea index (AHI) • Adherence • Mean percentage days CPAP used	Severe OSAHS strata population (strata based on mean AHI)

Study	Intervention and comparison	Population	Outcomes	Comments
		potentially eligible for the trial. Mean age (SD): Telemonitoring and in person follow up – 52(10.8) In person follow up – 55.2 (11.5) Canada Baseline AHI Telemedicine group = 44.3 (24.8) Standard = 39.5 (19.6)		
Hoet 2017[14] RCT Belgium	**Telemonitoring and in person follow up:** T4P TM unit was added to the CPAP device of the patient at home. Sleep laboratory technical staff were instructed to connect to the web portal and to analyse individual patient's data each Tuesday and Friday. In case of air leaks >50 L/min, residual AHI >10/h, or CPAP use <3h on 3 consecutive days, they were required to call the patient and to set up a visit with the staff of the sleep laboratory.	Eligible patients were ≥18 years old. They were recently diagnosed with OSAHS with an apnoea-hypopnea index (AHI) ≥20/h according to AASM 2012 scoring rules and sent to our sleep laboratory for initiation of treatment with CPAP therapy. Mean age (SD):	Follow up – 3 months • Adherence – hours of use • Mean percentage nights CPAP use >4 hours	Severe OSAHS strata population (strata based on mean AHI)

Study	Intervention and comparison	Population	Outcomes	Comments
	N=23 **In person follow up:** After CPAP titration night, patients were instructed to use the device each night for the whole night. They received written instructions and were able to contact the sleep unit (with telephone call or visit) as often as needed, during weekdays, in order to resolve any current problem interfering with their CPAP use. a group educational session for CPAP-treated patients was scheduled 1 month after CPAP initiation, and a visit to the pneumologist was scheduled 1.5 and 3 months after CPAP initiation. N=23	Telemonitoring and in person follow up – 59(13) In person follow up – 54(14) Baseline AHI = Telemonitoring and in person follow up – 50(26) In person follow up – 49(24)		
Isetta 2015[19] RCT Spain	**Telemonitoring and televisits:** Patients randomised to the telemedicine group received their follow-up at home supported by a website developed for this study, where they could find information about OSA and CPAP therapy, and a biweekly six-item questionnaire about their status, physical activity, sleep time, CPAP use and treatment side effects. Each centre's staff monitored	All enrolled patients were classified as requiring CPAP treatment after an overnight study Mean age (SD) Telemonitoring and televisits group – 51 (8.9) In person follow up group – 47 (10.9) Spain	Follow up 6 months • Quality of life (E5QD, FOSQ) • Sleepiness Epworth scale • Mean percentage nights CPAP use >4 hours • Adherence	Severe OSAHS strata population (strata based on mean AHI)

Study	Intervention and comparison	Population	Outcomes	Comments
	questionnaire answers and communicated with patients through the website messaging tool to solve treatment-related problems. To participate, patients only required an internet-connected device with a microphone and webcam. Televisits via video conference were undertaken at months 1 and 3. We used Skype due to its availability, ease of use and good performance. Patients automatically received a confirmation email indicating the date and time of their appointment. Extra televisits or hospital visits were scheduled as necessary. N=69 **In person follow up:** Patients randomised to the control group had the same follow-up schedule as the telemedicine group but attended the hospital. Specifically, they received standard face-to-face follow-up with visits at months 1, 3 and 6, and extra visits if needed. N=70	Baseline AHI - median (IQR) = 49 (35-46)		

Study	Intervention and comparison	Population	Outcomes	Comments
Lugo 2019[23] RCT Spain	**Telemonitoring patients and virtual follow up:** Patients treated with a Virtual sleep unit (VSU) were managed exclusively outside of the hospital setting. The diagnostic sleep test consisted of home-based respiratory polygraphy for three consecutive nights, and recorded data were downloaded to a secure server and analysed by a specialised technician. If OSA was diagnosed and CPAP was indicated, patients received CPAP education and along with an automatic CPAP device (Dreamstation, Respironics) at the provider's pick-up point. A technician could remotely adjust CPAP pressure through a website based on data sent by the device. Follow-up visits at 3, 6 and 12 weeks were performed through a custom web application and follow up interviews lasted no more than 15 minutes. Patients could access general information about OSA, CPAP, healthy sleep, and lifestyle, as well as their medical agenda, FAQs, and online clinical questionnaires. An email address to contact professionals and a	Patients with suspected OSA and/or refractory hypertension, age 18–75 years with a basic knowledge of ICTs use (e.g., tablet, smartphone, or computer), and Internet access were considered for inclusion. Consecutive patients with suspected OSA referred to the sleep unit in Barcelona between 2016 and Feb 2017 were randomised if they signed the consent form. Mean age (SD) Telemonitoring group – 50.39 (11.31) In person hospital follow up group – 50.82 (12.15) AHI = 29.12 (25.6)	Follow up at 3 and 6 months EQ5D EQ-VAS ESS Adherence – hours of use Number of healthcare contacts – GP and specialists OSA related	Severe OSAHS strata population for analysis as mean AHI was borderline between both moderate and severe populations (strata based on mean AHI) This study included people with suspected OSHAS and after sleep testing 80.4% of the population had a diagnosis of OSAHS with a mean baseline AHI of 29.12. 19.6% of patients did not have an OSAHS diagnosis, therefore the study was included but downgraded for very serious indirectness.

Study	Intervention and comparison	Population	Outcomes	Comments
	teleconference service to perform the interviews were also available. N=94 **In person hospital follow up:** Sleep tests, medical assessments, and follow-up visits were performed in the Sleep Unit. Based on the patient characteristics, physicians not involved in the trial requested sleep studies (e.g. PSG, or hospital- or home-based respiratory polygraphy). After sleep testing, a sleep physician interviewed patients. If CPAP was indicated, patients received education and training in CPAP use from a specialized nurse or technician in the hospital. CPAP was then titrated in the hospital with manual adjustment by the technician during a sleep study. Once the optimal pressure was determined, patients were provided with a fixed pressure CPAP device to use at home (DreamStation, Respironics). All visits were performed face-to-face in the consultation at 3, 6 and 12 weeks.			

Study	Intervention and comparison	Population	Outcomes	Comments
	N=92			
Mendelson 2014[25] RCT France	**Telemonitoring and in person follow up:** Patients assigned to telemedicine were oriented to CPAP, fitted with a nasal mask, and given an auto titrating machine. Patients received a smartphone with an application designed to transmit clinical information. The patients transmitted self-measured morning and evening BP (3-day measurements), CPAP adherence, and subjective sleepiness weekly through a questionnaire-based application. Quality of life questionnaires were transmitted monthly. Patients received daily pictograms with diet and physical-activity related messages on their smartphones. Patients were contacted after 2 days to ask about adherence, side effects, and any problems encountered with the machine. After 4 weeks of treatment, patients met with their sleep specialist and information was reviewed. After 4 months of treatment, patients consulted their sleep specialist and were re-evaluated. Both groups were asked to continue on their	Patients were eligible for the study if they were between 18 and 85 years old, diagnosed OSA on the diagnostic sleep study with AHI > 15 events/h, BMI of less than 40 kg/m^2, cardiovascular risk SCORE > 5%,20 or being in secondary prevention with a past history of cardiovascular disease (transient ischemic attack, stroke, cerebral haemorrhage, myocardial infarction, angina, coronary revascularization, arteriopathy, aortic aneurism). Mean age (SD): Telemonitoring and in person follow up – 62(9) In person follow up – 63(9) France Baseline AHI = 39.0 (16.7)	Length of follow up – 4 months • Quality of life – Physical composite score and mental composite score • Sleepiness - Epworth score • Adherence	Severe OSAHS strata population (strata based on mean AHI)

Study	Intervention and comparison	Population	Outcomes	Comments
	normal medication regimen. N=54 **In person follow up:** Patients assigned to standard care were evaluated at baseline, fitted with a nasal mask and given an auto titrating machine. Patients were contacted after 2 days to ask about adherence, side effects, and any problems encountered with the machine. After 4 weeks of treatment, patients met with their sleep specialist and information was transferred from their machines (adherence, mask leak, residual respiratory events). After 4 months of treatment, data were downloaded from the machine, and patients saw their sleep specialist and were re-evaluated. N=53			
Munafo 2016[26] RCT USA	**Telemonitoring and phone follow up:** Patients in the telemonitoring group were dispensed a CPAP device on Day 0, along with a pamphlet about U-Sleep, which	Study was conducted by Sleep Data Holdings, LLC, a Joint Commission on Accreditation of Healthcare Organizations-accredited CPAP durable	Length of follow up – 3 months Adherence	Severe OSAHS strata population (strata based on mean AHI)

Study	Intervention and comparison	Population	Outcomes	Comments
	was used to monitor adherence. U-Sleep is a secure, HIPAA-compliant, web-based application that is designed to receive CPAP device data and message patients and providers via text and/or e-mail based on a customisable set of rules. At the time of set up, patients were encouraged to log-in to the U-Sleep website from home so that they could follow their therapy. Sleep Data study staff were trained to set up and use the software, which was provided to patients at no charge. Initial patient contacts were triggered by ≥1 of five intervention points based on metrics (AHI, leak, therapy hours) After initial contact, subsequent contacts were in response to an automated message or based on clinical judgment. All TH patients received a final phone call on day 90. All patients were contacted at day 90 and asked to rate how well the follow-up program had met their expectations (on a scale from1 to 5) N=70	medical equipment provider in Southern California, USA. Mean age (SD): Telemonitoring group – 52.3(10.6) Phone follow up group – 50 (11.7) USA Baseline AHI= Telemonitoring group = 33.4(24.5) Phone follow up group = 27.4 (18.0)		

Study	Intervention and comparison	Population	Outcomes	Comments
	Phone follow up: Telephone follow up: Patients randomised to telephone follow-up were dispensed a CPAP device on Day 0, then contacted via phone on Days 1, 7, 14, 30, and 90 . CPAP usage and efficacy data were tracked via the wireless modem attached to the CPAP machine. Modem data were accessed via ResMed's EasyCare Online (ECO) platform. Sleep Data SOC procedures include frequent phone calls and return clinic visits as necessary N=70			
Pepin 2019[36] RCT France	**Multimodal telemonitoring:** Multimodal telemonitoring included systolic and diastolic HBP and physical activity recorded by connected devices. This assessment of individual risk was associated with CPAP telemonitoring providing adherence, leaks and residual events. Symptoms and quality of life were recorded via electronic questionnaires to be filled by patients. Patients benefited from a demonstration of how to use the remote home telemonitoring equipment and	Eligible patients were aged from 18-75, with severe OSA (apnoea-hypopnea index (AHI)>30events/h) on the basis of respiratory polygraphy or poly somnography. Patients should suffer from at least one cardiovascular disease or exhibit an elevated cardiovascular risk assessed by the 10 year risk of fatal cardiovascular event Systematic Coronary Risk evaluation calculation established specifically for	Length of follow up – 6 months • Quality of life: SF12-physical and SF12 mental • Systolic blood pressure • Sleepiness – Epworth scale • Adherence • Systolic blood pressure	Severe OSAHS strata population (strata based on mean AHI)

Study	Intervention and comparison	Population	Outcomes	Comments
	an explanation of why monitoring psychological variables is relevant for their care. Concerning HBP recommendations, patients had to perform three measurements in the morning and the evening for 3 consecutive days in both groups. one minute was required between each measurement and the patient had to stay sedentary before and during the measurements. N=157 **Usual care:** Not much detail N=149	European countries. Patients with a Systematic Coronary Risk evaluation risk>5% or in secondary prevention were included. Mean age(range): Multimodal telemonitoring group - 60.8(53.8; 66) Usual care group - 61.8 (54.7; 66.1) Baseline AHI - median (IQR)= 46 (35-61)		
Stepnowsky 2007[40] RCT USA	**Telemonitoring and in person follow up:** Telemonitored clinical care group. (Telemonitoring and in person follow up) The essence of the TCC intervention is the ability to telemonitor compliance and efficacy data for each patient on a daily basis from the first day of treatment and to act on those data collaboratively, and in partnership, with the patient. Collaborative management	Diagnosis of moderate-to-severe OSA, defined as an Apnoea-Hypopnea Index (AHI) ≥ 15 events per hour; naive to CPAP therapy; stable sleep environment (operationally defined as a permanent address, requisite for wireless monitoring); and at least 18 years of age. An AHI of ≥15 was chosen in an effort to be consistent with current OSA guidelines and practice parameters.	Length of follow up – 2 months • Functional outcomes of sleep • Sleepiness – Epworth • Apnoea-hypopnea index • Adherence • Mean percentage nights CPAP use >4 hours	Severe OSAHS strata population (strata based on mean AHI)

Study	Intervention and comparison	Population	Outcomes	Comments
	refers to the joint decision making and partnership between provider and patient and is characterized by communication, negotiation, and consideration of important patient factors and preferences. Patients in this group had their objective flow generator data monitored as frequently as needed per specified clinical pathways throughout the active 2-month treatment period. The frequency and nature of the clinical interactions depended on both the objectively measured nightly data values and subjective patient reports. N=24 **In person follow up:** Usual clinical care group. In person follow up. Patients randomised to UCC were treated according to the prevailing standard of care for OSA patients at the VASDHS CPAP Clinic. Usual care consisted of a 1-week telephone call after CPAP initiation and a 1-month in-office follow-up visit by CPAP clinic staff. Patients were encouraged to call the clinic any time they had a problem or	Mean age (SD) Telemonitoring and in person follow up group: 60(10.8) In person follow up group – 58 (13.7) USA Baseline AHI= 39 (16.8)		

Study	Intervention and comparison	Population	Outcomes	Comments
	concern. CPAP compliance and efficacy data were downloaded at the 1-month time point to help direct clinical management. N=21			
Turino 2017[42] RCT Spain	**Telemonitoring and in person follow up:** In the telemonitoring group, patients were also fitted with a mask and given a CPAP device (AirSense 10) and a leaflet explaining how to use it and received the same training sessions from the same personnel as in the standard care arm. Each CPAP device given to patients in this group was equipped with mobile 2G (GSM/GPRS) technology capable of sending daily information on CPAP adherence, CPAP pressures, mask leak and residual respiratory events to the MyOSA–Oxigen Salud web database (www.oxigensalud.com) Automatic alarms for the provider were generated in case of mask leak >30 L·min−1 for >30% of the night or usage of <4 h·night−1 on two consecutive nights. In case of alarm, the pulmonary specialist	Included adult patients (>18 years) with newly diagnosed OSA requiring treatment with CPAP (AHI >15 events·h−1). Assuming an α risk of 0.05 and a β risk of 0.2 in a two-sided test, a sample size of 49 subjects in each group was needed to detect differences ⩾1 h in CPAP treatment compliance. A common standard deviation of 1.75 was assumed. Given the high motivation of both professionals and patients to be involved, no dropouts were anticipated and thus a total of 100 patients were planned to be recruited Mean age (SD): Telemonitoring and in person follow up – 56(13) In person follow up group – 54 (12)	Length of follow up – 3 months • Quality of life – EQ5D • Adherence • Systolic blood pressure	Severe OSAHS strata population (strata based on mean AHI)

Study	Intervention and comparison	Population	Outcomes	Comments
	medical officer of the CPAP provider contacted the patient, providing case-by-case problem solving. This included suggestions about how to minimise symptoms (dry mouth, mask issues, discomfort with the device), specific interventions to improve compliance (mask changing, chin strap, pressure or humidifier settings, saline nasal sprays) and support for the patient in the use of CPAP. N=52 **In person follow up**: Patients randomised to standard care were fitted with a mask and given a CPAP device (AirSense 10; ResMed, Martinsried, Germany) and a leaflet explaining how to use it. A short instruction session on how to use a CPAP device was also given to patients and partners in the sleep unit by a trained nurse with experience in the follow-up of CPAP-treated patients. This included a practical demonstration of how to put on the mask, and the correct management and cleaning of the tubes, masks	Telemonitoring and in person follow up – 52 (25) In person follow up group – 53 (26)		

Study	Intervention and comparison	Population	Outcomes	Comments
	and humidifier. Information on how to turn the CPAP device on and off was provided by the homecare provider at the time of machine delivery. All patients were visited after 1 month of treatment by the specialist nurse at the sleep unit. Information about CPAP pressure, compliance and adherence (use of CPAP for ⩾4 h·day−1), residual respiratory events and leaks were downloaded from the device. CPAP-related side-effects, CPAP machine care and maintenance (changes of mask, tubes and humidifier), and the number of additional visits and calls were recorded by the nurse. N=48			

See appendix D for full evidence tables.

1.4.4 Quality assessment of clinical studies included in the evidence review

Table 3: Clinical evidence summary: Telemonitoring and in person follow up versus in person follow up – severe OSAHS population

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with In person follow up	Risk difference with Telemonitoring + in person follow up (95% CI)
Systolic blood pressure – morning	406 (2 studies) 3-6 months	⨁⨁⊖⊖ LOW1 due to risk of bias,		The mean systolic blood pressure - morning in the control groups was 63.48	The mean systolic blood pressure - morning in the intervention groups was 0.33 higher (3.1 lower to 3.75 higher)
Adherence- h per day Scale from: 0 to 8.	405 (6 studies) 3 - 12 months	⨁⊖⊖⊖ VERY LOW1,2,3,4 due to risk of bias, inconsistency, imprecision, indirectness		The mean adherence- h per day in the control groups was 3.9861	The mean adherence- h per day in the intervention groups was 0.6 higher (0.12 lower to 1.31 higher)
Adherence-on nights PAP used (h per day) Scale from: 0 to 8.	94 (2 studies) 2-3 months	⨁⊖⊖⊖ VERY LOW1,2,4 due to risk of bias, imprecision, indirectness		The mean adherence-on nights pap used (h per day) in the control groups was 3.65	The mean adherence-on nights pap used (h per day) in the intervention groups was 1.22 higher (0.03 lower to 2.48 higher)
Mean % nights CPAP use >4 hours Scale from: 0 to 100 Higher is better	40 (1 study) 2 months	⨁⊖⊖⊖ VERY LOW1,2,4 due to risk of bias, imprecision, indirectness		The mean % nights CPAP use >4 hours in the control groups was 37 %	The mean % nights CPAP use >4 hours in the intervention groups was 15 higher (4.03 lower to 34.03 higher)
Mean % days used Scale from: 0 to 100. Higher is better	54 (1 study) 3 months	⨁⊖⊖⊖ VERY LOW1,2,4 due to risk of bias,		The mean % days used in the control groups was 45.9 %	The mean % days used in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with In person follow up	Risk difference with Telemonitoring + in person follow up (95% CI)
		imprecision, indirectness			10 higher (10.81 lower to 30.81 higher)
Quality of life (Physical composite) difference Scale from: 0 to 100. Higher is better	82 (1 study) 4 months	⨁⊖⊖⊖ VERY LOW1,2,4 due to risk of bias, indirectness, imprecision		The mean quality of life (physical composite) difference in the control groups was 2.9	The mean quality of life (physical composite) difference in the intervention groups was 0.3 higher (3.1 lower to 3.7 higher)
Quality of life (mental) difference Scale from: 0 to 100. Higher is better	82 (1 study) 4 months	⨁⊖⊖⊖ VERY LOW1,2,4 due to risk of bias, imprecision, indirectness		The mean quality of life (mental) difference in the control groups was 1.6	The mean quality of life (mental) difference in the intervention groups was 0 higher (4.15 lower to 4.15 higher)
Quality of life EQ5D Scale from: 0 to 1. Higher is better	100 (1 study) 3 months	⨁⊖⊖⊖ VERY LOW1,2,4 due to risk of bias, indirectness, imprecision		The mean quality of life eq5d in the control groups was 1.6	The mean quality of life eq5d in the intervention groups was 0 higher (0.07 lower to 0.07 higher)
Quality of Life-GHQ12 Scale from: 0 to 12. Higher is better	88 (1 study) 12 months	⨁⊖⊖⊖ VERY LOW1,2,4 due to risk of bias, imprecision, indirectness		The mean quality of life-ghq12 in the control groups was 4.9	The mean quality of life-ghq12 in the intervention groups was 0.2 higher (2.31 lower to 2.71 higher)
Sleepiness Epworth (ESS) Scale from: 0 to 24. Lower is better	264 (4 studies) 2-12 months	⨁⊖⊖⊖ VERY LOW1,4 due to risk of bias, indirectness		The mean sleepiness Epworth (ESS) in the control groups was 3.475	The mean sleepiness Epworth (ESS) in the intervention groups was 0 higher (1 lower to 1 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with In person follow up	Risk difference with Telemonitoring + in person follow up (95% CI)
Apnoea-Hypopnea index (AHI) events/hour Lower is better	182 (3 studies) 3-12 months	⨁⊖⊖⊖ VERY LOW1,2,3,4 due to risk of bias, inconsistency, imprecision, indirectness		The mean apnoea-hypopnea index (ahi) events/hour in the control groups was 4.9333	The mean apnoea-hypopnea index (ahi) events/hour in the intervention groups was 0.44 lower (3.21 lower to 2.33 higher)
Functional outcome of A. sleep questionnaire Higher is better	40 (1 study) 2 months	⨁⊖⊖⊖ VERY LOW1,2,4 due to risk of bias, imprecision, indirectness		The mean functional outcome of sleep a. questionnaire in the control groups was 14.4	The mean functional outcome of sleep a. questionnaire in the intervention groups was 0.8 higher (2.06 lower to 3.66 higher)
Mortality	Outcome not reported				

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs, MID for machine usage (adherence)-1 hour; MID for Systolic and Diastolic BP – 5 mm hg. For mean % of nights that the CPAP was used >4 hours outcome, clinically important difference was considered to be 10 % or 1 hour. Established MIDs for SF-36 physical/mental- 2/3; ESS- 2.5; EQ5D- 0.03; FOSQ- 2. GRADE default MID (0.5XSD) used for all other continuous outcomes.

3 Downgraded by 1 or 2 increments because: The point estimate varies widely across studies, unexplained by subgroup analysis. The confidence intervals across studies show minimal or no overlap, I^2 =50%, unexplained by subgroup analysis. Subgroup analyses were tested for BMI < or >30 kg/m^2, ESS < or >9, coexisting conditions, high risk occupation and type of treatment. Random effects analysis used.

4 Downgraded by 1 or 2 increments because the majority of the evidence included an indirect or very indirect population respectively. The study included a mixed OSHAS severity population based on mean baseline AHI.

Table 4: Clinical evidence summary: Telemonitoring and phone follow-up versus phone follow up – severe OSAHS population

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Phone follow up	Risk difference with Telemonitoring (95% CI)
Adherence hours per day Scale from: 0 to 8.	122 (1 study) 3 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, imprecision, indirectness		The mean adherence hours per day in the control groups was 4.7	The mean adherence hours per day in the intervention groups was 0.4 higher (0.31 lower to 1.11 higher)
Days CPAP used >4 hours, % patients Scale from: 0 to 100. Higher is better	122 (1 study) 3 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, imprecision, indirectness		The mean days CPAP used >4 hours in the control groups was 63.3	The mean days CPAP used >4 hours in the intervention groups was 6.9 higher (2.9 lower to 16.70 higher)
Mortality	No outcome reported				

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs. MID for machine usage (adherence)-1 hour. For mean % of nights that the CPAP was used >4 hours outcome, clinically important difference was considered to be 10 % or 1 hour. GRADE default MID(0.5XSD) used for all other continuous outcomes.

3 Downgraded by 1 or 2 increments because the majority of the evidence included an indirect or very indirect population respectively. The study included a mixed OSHAS severity population based on mean baseline AHI.

Table 5: Clinical evidence summary: Multimodal telemonitoring versus usual care – severe OSAHS population

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual care	Risk difference with Multimodal telemonitoring (95% CI)
Adherence Scale from: 0 to 8. Higher is better	239 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean adherence in the control groups was **4.75**	The mean adherence in the intervention groups was **0.53 higher** (0.07 lower to 1.13 higher)
Sleepiness ESS Scale from: 0 to 24. Lower is better	239 (1 study) 6 months	⨁⨁⊖⊖ LOW1 due to risk of bias		The mean sleepiness (ESS) in the control groups was 6.05	The mean sleepiness (ESS) in the intervention groups was 1.47 lower (2.48 to 0.46 lower)
Quality of life-SF12-Physical Scale from: 0 to 100. Higher is better	239 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life-sf12-physical in the control groups was 44.1	The mean quality of life-sf12-physical in the intervention groups was 1.5 higher (0.14 to 2.86 higher)
Quality of life-SF12 - Mental Scale from: 0 to 100. Higher is better	239 (1 study) 6 months	⨁⨁⊖⊖ LOW1 due to risk of bias		The mean quality of life-sf12 - mental in the control groups was 43.6	The mean quality of life-sf12 - mental in the intervention groups was 0.3 higher (0.88 lower to 1.48 higher)
Systolic blood pressure	239 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean systolic blood pressure in the control group was 130.06	The mean systolic blood pressure in the intervention group was 0.92 higher (3.65 lower to 5.49 higher)
Mortality	No outcome reported				

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs. MID for machine usage (adherence)-1 hour; MID for Systolic and Diastolic BP – 5 mm hg. Established MIDs for SF-36 physical/mental- 2/3; ESS- 2.5. GRADE default MID (0.5XSD)used for all other continuous outcomes.

Table 6: Clinical evidence summary: Telemonitoring and tele-visits versus in person follow up – severe OSAHS population

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with in person follow-up	Risk difference with Telemonitoring+televisits (95% CI)
Adherence h/day	183 (2 studies) 3-6 months	⨁⊖⊖⊖ VERY LOW[1,2] due to risk of bias, and indirectness		The mean adherence h/day in the control groups was 4.92	The mean adherence h/day in the intervention groups was 0.14 higher (0.39 lower to 0.66 higher)
EQ5D[4] Scale from: 0 to 1. Higher is better	282 (2 studies) 3-6 months	⨁⊖⊖⊖ VERY LOW[1,2,3,4] due to risk of bias, indirectness and imprecision		The mean EQ5D in the control groups was 0.87	The mean EQ5D in the intervention groups was 0.03 lower (0.07 lower to 0.01 higher)
FOSQ Scale from: 5 to 20. Higher is better	128 (1 study) 6 months	⨁⨁⊖⊖ LOW[1,2] due to risk of bias and imprecision		The mean FoSQ in the control groups was 18.01	The mean FoSQ in the intervention groups was 1.11 lower (2.32 lower to 0.1 higher)
Sleepiness ESS Scale from: 0 to 24. Lower is better	314 (2 studies) 3-6 months	⨁⊖⊖⊖ VERY LOW[1,2] due to risk of bias, and indirectness		The mean sleepiness (ESS) in the control groups was 6.47	The mean sleepiness (ESS) in the intervention groups was 1.02 higher (0.07 lower to 1.98 higher)
EQ5D- VAS Higher is better	154 (1 study) 3 months	⨁⊖⊖⊖ VERY LOW[1,,3] due to risk of bias, indirectness		The mean EQ5D-VAS in the control groups was 75.09	The mean EQ5D-VAS in the intervention groups was 0.57 higher (4.39 lower to 5.53 higher)
Number of OSA related GP visits	186 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW[1,2,3] due to risk of bias, indirectness and imprecision	RR 0.65 (0.19 to 2.24)	65 per 1000	23 fewer per 1000 (from 53 fewer to 81 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with in person follow-up	Risk difference with Telemonitoring+televisits (95% CI)
Number of OSA related specialist visits	186 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW[1,2,3] due to risk of bias, indirectness and imprecision	RR 1.20 (0.52 to 2.75)	99 per 1000	20 fewer per 1000 (from 47 fewer to 173 more)
Mortality	No outcome reported				

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs. MID for machine usage (adherence)-1 hour; MID for Systolic and Diastolic BP – 5 mm hg. Established MIDs for ESS- 2.5; EQ5D- 0.03; EQ5D VAS- 3.GRADE default MID(0.5XSD) used for all other continuous outcomes.

3 Downgraded by 1 or 2 increments because: The majority of the evidence included an indirect population of moderate to severe severity patients based on the AHI of included population (downgrade by one increment) or a very indirect population (downgrade by two increments)

4 Baseline values differed in the Lugo study for this outcome. Therefore, while the in person follow up group has a higher (better) end score the telemonitoring group had a better change score of 0.04 compared to 0.01 in the in person follow up group.

Narrative results:

Data on machine usage outcomes were measured and reported inconsistently across the studies. Data have been presented narratively for studies where could not be analysed (data were presented as a percentage only). Narrative data was considered alongside the GRADE evidence by the committee when making recommendations. The overall study quality was taken into account as GRADE analysis for each outcome could not be performed.

1. Telemonitoring and in person follow up compared to in person follow up

Hoet 2017 (n=46) (very low quality):

CPAP use of over 4 hours per night %

The study reported a lower rate of CPAP use of over 4 hours per night in the in person follow up group compared to the telemonitoring group (64% versus 82%).

2. Telemonitoring and tele visits compared to in person follow up

Isetta 2015 (n=138) (very low quality): Mean % of nights CPAP used >4 hours

The study reported the mean percentage of nights where CPAP was used for > 4 hours. Results showed this was slightly higher in the telemonitoring plus in person follow up group compared to the in person follow up only group (65% versus 57%, p=0.329).

See appendix F for full GRADE tables.

1.5 Economic evidence

1.5.1 Included studies

Two health economic studies were identified with the relevant comparison and have been included in this review.[19, 42] These are summarised in the health economic evidence profile below (Table 7) and the health economic evidence tables in appendix H.

1.5.2 Excluded studies

One economic study relating to this review question was identified but was excluded due to the availability of more applicable evidence.[2] Reasons for exclusion are given in Appendix I:.

See also the health economic study selection flow chart in appendix G.

1.5.3 Summary of studies included in the economic evidence review

Table 7: Health economic evidence profile: Telemonitoring versus hospital follow-up

Study	Applicability [a]	Limitations	Other comments	Incremental cost [d]	Incremental effects [f]	Cost effectiveness	Uncertainty
Isetta 2015[19] Spain	Partially applicable	Potentially serious limitations [b]	Within trial (RCT) cost-utility analysis, with a 6 month follow up	+£10 Excluding GP visits, outpatient visits and medicines: +£2 [e]	- 0.0012 QALYs (95% CI: -0.0500 to 0.0474)	Hospital follow-up dominates telemonitoring in both costing scenarios	Uncertainty reported in study not relevant [h]
Turino 2017[42] Spain	Partially applicable	Potentially serious limitations [c]	Within trial (RCT) cost-utility analysis, with a 3 month follow up	Saves £45	Scenario 1: -0.003 QALYs Scenario 2: -0.001 QALYs[g]	Scenario 1: Standard care cost £15,000 per extra QALY gained Scenario 2: Standard care cost £60,000 per extra QALY gained	Deterministic sensitivity analysis when there are 25% - 50% cost increases in the CPAP provider costs [i] ICERs in scenario 1: £12,333/£10,000 ICERs in scenario 2: £49,000/£40,000

Abbreviations: ICER= incremental cost-effectiveness ratio; QALY= quality-adjusted life years; RCT= randomised controlled trial

(a) Both these studies have been judged as partially applicable as they are from a Spanish perspective.

(b) There is lack of clarity in the components that have been summed to calculate mean cost per patient (see appendix G).

(c) There is a lack of clarity around the methods used to calculate QALYs (see appendix G).

(d) 2015 and 2013 euros have been converted to UK pounds using the purchasing power parities[30]

(e) There is lack of clarity in the components that have been summed to calculate mean cost per patient (see appendix G).

(f) Both studies used the Euroqol 5 dimensions (EQ-5D) to derive utilities (scale: 0.0 [death] to 1.0 [full health])

(g) There is a lack of clarity around the methods used to calculate QALYs (see appendix G).

(h) The authors have conducted a probabilistic sensitivity analysis (PSA) around the ICER which includes costs from a societal perspective. As the costs have been recalculated to report provider perspective only (thereby conforming to the NICE reference case), this PSA is no longer relevant for the purpose of the guideline.

(i) Scenario 1 reports the QALYs reported in the study which implicitly extrapolates the difference from 3 months to 12 months. Scenario 2 assumes quality of life difference is only for 3 months (see appendix G for more details).

1.5.4 Health economic evidence statements

- One cost-utility analysis found that hospital follow-up dominated telemonitoring for people with OSAHS. This study was assessed as being partially applicable with potentially serious limitations.
- One cost-utility analysis found that hospital follow-up was cost-effective compared with telemonitoring for people with OSAHS, depending on the duration of the quality of life effect (£15,000-£60,000 per QALY gained). This study was assessed as being partially applicable with potentially serious limitations.

1.6 The committee's discussion of the evidence

1.6.1 Interpreting the evidence

1.6.1.1 The outcomes that matter most

The committee considered the outcomes of quality of life and mortality as critical outcomes for decision making. Other important outcomes included sleepiness scores (e.g. Epworth), Apnoea –Hypopnea index (AHI), oxygen desaturation index (ODI), CO_2 control, hours of use (adherence), minor adverse effects of treatment, driving outcomes, neurocognitive outcomes, healthcare contacts, impact on co-existing conditions (HbA1c for diabetes, cardiovascular events for cardiovascular disease, systolic blood pressure for hypertension).

No evidence was identified for the critical outcome mortality in all ten studies.

1.6.1.2 The quality of the evidence

OSAHS (all severities)

CPAP

There was evidence from 10 studies - 6 studies compared telemonitoring (telemonitoring unit added to CPAP device which allows sleep laboratory staff and to connect to web portal to analyse patients data and arrange a visit or phone consultation when necessary) and in person follow-up, 1 study compared telemonitoring and phone follow-up with phone follow-up, 1 study compared multimodal telemonitoring (which included systolic and diastolic blood pressure and physical activity recorded by connected devices) with usual care, 2 studies compared telemonitoring and tele visits (tele visits via video conference (Skype)) with in person follow up.

The duration of all included studies was of one year or less. Studies varied in size with the number of participants ranging from 45 in the smallest study to 306 in the largest.

All studies were in people using fixed level CPAP except for one study in people using auto CPAP.

Studies were stratified based on the AHI/ODI severity of the population. When a mixed severity population was included the severity of the majority of the population was used by taking the mean AHI of the patients included and the study was downgraded for indirectness. The majority of studies included in this review were downgraded for indirectness.

All evidence was in people with severe sleep apnoea (AHI >/=30 severe) determined by their baseline AHI.

The quality of the evidence varied from very low to moderate quality; majority of evidence was downgraded due to risk of bias, imprecision, indirectness and inconsistency. Risk of bias was most commonly due to selection bias, performance bias and incomplete outcome data. Indirectness was present in many of the studies due to the inclusion of mixed severity OSAHS populations, combining people with mild, moderate or severe OSAHS. Imprecision was also present for many outcomes with confidence intervals crossing the MID thresholds. The low quality of evidence, small study sizes and uncertainty around the effect estimate was taken into consideration by the committee when assessing the evidence base for this review.

The committee considered the clinical importance for AHI on a case by case basis, taking into consideration the baseline AHI and the improvement in severity of sleep apnoea.

Oral devices

No evidence was identified for monitoring of people using oral devices.

Positional modifiers

No evidence was identified for monitoring of people using positional modifiers.

Surgery

No evidence was identified for monitoring of people who have undergone surgery.

OHS

There was no evidence identified for people with obesity hypoventilation syndrome

COPD-OSAHS overlap syndrome

There was no evidence identified for people with COPD-OSAHS overlap syndrome.

1.6.1.3 Benefits and harms

OSAHS

CPAP

Telemonitoring and in person follow-up vs in person follow-up - severe OSAHS.

The evidence suggested that adherence measures (nights CPAP used (hours/day), mean % nights CPAP use >4 hours and mean % days used) showed a clinically important benefit of telemonitoring with in person follow-up compared to in person follow-up alone. The committee however were not confident of this outcome as there was some uncertainty around the effect estimate. Additionally, one small study in which results were reported narratively demonstrated a benefit for mean % CPAP used >4 hours in the telemonitoring group compared to in person follow-up alone. This study however was unsuitable for GRADE analysis so was deemed to be very low quality. One of the adherence outcomes – hours that CPAP was used per day showed no clinically important difference.

The evidence suggested that there was no clinically important difference between telemonitoring with in person follow-up and in person follow-up alone for the critical outcomes quality of life measures (SF12 questionnaire - physical and mental composite, quality of life-EQ5D scale, and quality of life – GHQ12 scale).

There was no clinically important difference between telemonitoring and in person follow-up for the outcomes of systolic blood pressure, sleepiness (Epworth), apnoea-hypopnea index, and functional outcome of sleep questionnaire.

Follow-up evidence from the studies was available for 2 – 12 months. The committee agreed that this range of the follow-up in the studies is very wide.

Telemonitoring and phone follow-up vs phone follow-up - severe OSAHS

The evidence from one study suggested that that there was no clinically important difference between telemonitoring and phone follow-up for both adherence outcomes: hours per day used and days CPAP used >4 hours (% of patients). Follow-up evidence was available for 3 months.

Multimodal telemonitoring vs usual care - severe OSAHS

The evidence from one study suggested that there was no difference between multimodal telemonitoring and usual care for critical outcomes of quality of life SF12 physical composite and SF12 mental composite and important outcomes such as adherence (hours used) and systolic blood pressure. Follow-up evidence was available for 6 months.

Telemonitoring and tele visits vs in person follow-up - severe OSAHS

The evidence suggested that there was no difference between telemonitoring and tele visits and in person follow-up for the critical outcomes of quality of life (EQ5D VAS and FoSQ) and important outcomes of adherence (hours/day), sleepiness (Epworth), number of OSA related GP visits and number of OSA related specialist visits. One study in which results were reported narratively and of very low quality also showed no difference between the groups for % of nights CPAP used >4 hours.

There was a clinically important benefit of in person follow-up versus telemonitoring and tele visits for the critical outcome of EQ5D (quality of life measure) however this only just reached the threshold for clinical significance and there was uncertainty around the effect estimate with the confidence interval crossing the MID threshold. All follow-up evidence was available for 3-6 months.

Follow-up for people with OSAHS-the committee's consideration of the evidence

The committee discussed that monitoring of patients on treatment for OSAHS should be used to assess control of symptoms, efficacy of therapy, impact on co-morbidities and adherence to treatment. They noted that follow-up should be tailored to the person's overall treatment plan. This may include lifestyle changes, such as weight management, modifying use of sedative drugs and alcohol, and stopping smoking, and treating underlying lung disease and other comorbidities.

Follow-up for people using CPAP

The committee defined telemonitoring as the use of information and communication technologies to monitor patients remotely and transmit data related to their health. It provides data that can be downloaded including respiratory events, pressure requirements, mask leak and adherence and is used for follow-up with telephone or video consultations.

Overall, the evidence suggested that telemonitoring along with face-to-face or telephone consultations were equally effective as face to face or telephone consultations without telemonitoring. There was some evidence that adherence was improved by telemonitoring in people with severe OSAHS, and the committee discussed its advantages, such as early night-by-night access to data and remote adjustment of CPAP level. There was no evidence to suggest a difference between face-to-face, telephone and video consultations. None of the studies looked at telemonitoring for more than 12 months. The evidence was available for people with severe OSAHS; the committee agreed that the data could be extrapolated to people with mild and moderate OSAHS as well.

The committee discussed that although CPAP is considered the treatment of choice for OSAHS, CPAP adherence is a significant challenge. They agreed that CPAP follow-up through any means (face to face, telephone or video consultation, including review of telemonitoring data where available) would improve adherence and effectiveness of the treatment. The committee agreed that CPAP follow-up should be at less than one month and the subsequent follow-up according to person's clinical needs, until optimal control of symptoms and AHI or ODI is achieved. They discussed that the pattern of CPAP adherence is established within the first week of therapy; therefore, early assessment of progress is helpful for problem-solving and providing support. From their experience the committee believe that greater benefits of CPAP use are associated with longer duration of use; therefore, patients should be encouraged to wear CPAP throughout the whole night, but ideally at least 4 hours/ night. Data from the CPAP machine is important so that CPAP

settings can be adjusted to control residual respiratory events or to detect treatment emergent central sleep apnoea, and problems such as mask leak, rhinitis or poor tolerance to be identified. Some measures of adherence are improved by telemonitoring, and it allows early night-by-night access to data and remote adjustment of CPAP level without the need for patient visits.

The committee based on their experience discussed the advantages of telemonitoring. These include early night-by-night access to data which can lead to early detection of problems such as mask leaks or persistent respiratory events of sleep apnoea, and the ability to monitor that OSAHS so that it continues to be effectively controlled and the individual is adherent to therapy. Telemonitoring makes managing a person's OSAHS more efficient for clinicians as they have ready access to the data should they need it. For example, if contacted by a person with an issue they can use the data to help identify the problem (for example, mask leak or inadequate pressure) and take appropriate action without the need for a scheduled appointment.

The committee agreed that video and telephone consultations along with telemonitoring is also advantageous to people with OSAHS as it can reduce the number of in-person visits needed to the sleep service. This can be particularly beneficial to patients who have difficulty in getting to clinics, for example, people who live in remote places or people with poor mobility, there would be fewer clinic visits in such cases. The reduction in the number of face-to-face consultations will also help reduce the risk of infection during the COVID-19 pandemic. The committee agreed that telemonitoring should be offered alongside CPAP for the first 12 months of treatment, and considered beyond 12 months where optimal control of symptoms and AHI or ODI has not been achieved, or to help with solving problems that people with OSAHS might experience. The committee did not make a research recommendation for long term use of telemonitoring as they believe telemonitoring is already becoming common practice and will remain so in the future. They agreed it is more convenient for CPAP users and clinicians. It also saves time as users do not need to download data and post or take it in to the sleep service.

The committee discussed how often long-term follow-up should happen. Annual and two-yearly follow-up were considered, they agreed that a two-yearly follow-up would probably be too long and interval and decided to make a recommendation to consider annual follow-up. The committee agreed that after CPAP treatment is established, annual follow-up allows continued efficacy of therapy and adherence to be assessed, along with co-morbidities and continuing need of therapy.

In between follow-up appointments the committee agreed that people with OSAHS using CPAP should be offered access to a sleep service for clinical support in case of problems, for provision of advice, and for replacement consumable equipment such as masks, circuitry and filters as needed.

Current practice includes a mixture of face-to-face, telephone, video consultations and telemonitoring. The increasing number of people being offered CPAP means that provision of regular outpatient follow-up is becoming increasingly difficult. Increasing website and app-based access to telemonitoring data will allow patients to access their own results and encourage self-management.

The committee stressed that telemonitoring crucially involves feedback to patients and time should be available for sleep centre staff to review data, act on this and share with the person using CPAP. Current practice already includes ready access to advice and CPAP equipment from sleep centres. Telemonitoring has facilitated remote assessment of patients during the coronavirus pandemic and has become a standard follow-up option in most sleep services. This use is likely to continue long term, because it is convenient for patients, enables them to assess progress themselves and allows access to efficacy and adherence data whenever needed, for example, for problem solving, routine follow-up and to complete DVLA reports. The committee noted that telemonitoring has changed practice for clinicians in

terms of clinic staffing, and for patients in terms of saving time in attending the clinic. The committee also noted that in current practice follow-up is at is 1-3 months and 1 year, hence implementation of these recommendations would not change practice.

Follow-up for people using mandibular advancement splints (MAS) and positional modifiers

As there was no evidence available for monitoring people using MAS or positional modifiers, the committee drew on their clinical experience and agreed that people using mandibular advancement splints or positional modifiers should have follow-up through face to face, video or telephone consultations (including review of downloads from oral device or positional modifiers if available), with early (3 months for both mandibular advancement splints positional modifiers) and subsequent follow-up according to person's clinical needs, until optimal control of symptoms and AHI or ODI is achieved. Adherence to oral devices is less easy to measure objectively. Early face to face follow-up is advisable as further gradual advancement of the mandible by the device may be required. However, the committee agreed that in light of COVID-19 video or telephone consultations may be preferable. Subsequent follow-up should be personalised, with assessment of side effects including impact on dentition and bite.

Objective adherence data can be obtained from positional devices for people with positional OSHAS, but early review allows assessment of symptom control and determination of whether respiratory events are minimised.

Recommendations on monitoring for positional modifiers and mandibular advancement splints are considered to be current practice in many areas and are not expected to lead to major changes in practice.

Follow-up for people who have had surgery

For people who have undergone surgery, initial follow-up consultation within 3 months of the operation should be to assess wound healing, side effects, control of symptoms and include respiratory polygraphy. Any subsequent follow-up is according to the person's clinical needs. There was no evidence available for this population, so recommendations were based on the committee's consensus opinion and clinical experience.

The recommendation on monitoring for surgery is considered to be current practice in many areas and are not expected to lead to major changes in practice.

Follow-up for drivers with excessive sleepiness

The committee agreed that people must not drive if they have excessive sleepiness, having or likely to have an adverse effect on driving, in keeping with DVLA guidance.[8] Driving may resume after satisfactory symptom control, which needs medical confirmation if moderate or severe OSAHS. This is the patient's responsibility, but sleep team professionals will help them assess the likely impact of their symptoms on their safety to drive, by taking a detailed driving history, including distances driven, episodes of drowsy driving, use of alerting mechanisms when driving to avoid falling asleep, or a history of a sleep related accident or near miss. Using a high Epworth Sleepiness Score alone for driving advice is unlikely to be adequate, as it is subjective. Many people can doze off in relaxed situations but retain concentration during specific tasks such as driving. Patients with excessive sleepiness having or likely to have an adverse impact on driving with confirmed moderate or severe obstructive sleep apnoea syndrome must inform the DVLA and their car insurance company of their diagnosis. If patients have excessive sleepiness having or likely to have an adverse impact on driving and a diagnosis of mild OSAHS, they must inform the DVLA of their diagnosis if they have not achieved symptom control in 3 months.[8]

For subsequent licensing, annual review is required by the DVLA for Group 2 licence holders (lorry and bus drivers) and a minimum of 3 yearly review for Group 1 licence holders (cars and motorcycles), to confirm control of OSAHS, improved sleepiness and treatment

adherence.[7] The committee noted that people with OSAHS who do not have symptoms of excessive sleepiness during waking hours will continue to have an annual review which includes assessment of any changes in symptoms.

Even though there was limited evidence on monitoring strategies for CPAP and lack of evidence on monitoring strategies for oral devices, positional modifiers and surgery for people with OSAHS, based on their experience the committee made strong recommendations hence they did not make any research recommendation for monitoring strategies for these treatments.

OHS

The committee noted the lack of evidence for monitoring strategies in OHS and decided to make consensus recommendations based on evidence reviewed for OSAHS, their experience and current practice.

The committee noted that CPAP and non-invasive ventilation are just part of treatment for OHS, and that follow-up should be tailored to the person's overall treatment plan. This should also include lifestyle changes, such as weight management, modifying use of sedative drugs and alcohol, and stopping smoking, and treating underlying lung disease and other comorbidities.

For people with OHS using CPAP or non-invasive ventilation, early follow-up at 1 month is advised to ensure control of symptoms, sleep disordered breathing and adherence. Problem-solving can be achieved by face to face, telephone or video consultations, including review of telemonitoring data where available. The committee agreed that once optimised on CPAP or non-invasive ventilation (with or without oxygen supplementation), 6-monthly to one year follow-up should be considered according to person's clinical needs. The committee agreed that video and telephone consultations with telemonitoring will help reduce the risk of infection during the COVID-19 pandemic.

The committee also agreed that although most studies of telemonitoring are in patients with OSAHS, and that there is not yet the ability to assess hypercapnia through telemonitoring, it is still of value to use for people with OHS.

The committee noted that in current practice follow-up is at is 4 weeks and 1 year, hence implementation of these recommendations would not change practice.

In addition to annual review, people with OSAHS and OHS on CPAP or non-invasive ventilation therapy need to be able to access the sleep service for advice and provision of consumables such as masks, circuitry and filters.

Current practice includes a mixture of face-to-face /telephone/video consultations and telemonitoring. The increasing number of people being offered CPAP means that provision of regular outpatient follow-up has become increasingly difficult. In addition, a more personalised approach enables attention to be focussed on people with problems adapting to therapy. Telemonitoring is included in the overall cost of CPAP devices by some manufacturers for variable periods and is increasingly available for non-invasive ventilators.

The committee discussed that routine use of telemonitoring should reduce the need for face-to-face consultations, and reduce pressure on outpatient clinics, but feedback and discussion with patients is still needed. Increasing website and app-based access to telemonitoring data will allow patients to access their own results to aid self-care.

The committee noted that there has been a significant move to video and telephone consultations to reduce the risk of infection during the COVID-19 pandemic.

<u>Follow-up for drivers with excessive sleepiness</u>

The committee agreed that people must not drive if they have excessive sleepiness, having or likely to have an adverse effect on driving, in keeping with DVLA guidance.[8] Driving may resume after satisfactory symptom control, which needs medical confirmation if moderate or severe OSAHS. This is the patient's responsibility, but sleep team professionals will help them assess the likely impact of their symptoms on their safety to drive, by taking a detailed driving history, including distances driven, episodes of drowsy driving, use of alerting mechanisms when driving to avoid falling asleep, or a history of a sleep related accident or near miss. Using a high Epworth Sleepiness Score alone for driving advice is unlikely to be adequate, as it is subjective. Many people can doze off in relaxed situations but retain concentration during specific tasks such as driving. Patients with excessive sleepiness having or likely to have an adverse impact on driving with confirmed moderate or severe OSAHS with their OHS must inform the DVLA and their car insurance company of their diagnosis. If patients have excessive sleepiness having or likely to have an adverse impact on driving and a diagnosis of mild OSAHS with their OHS, they must inform the DVLA of their diagnosis if they have not achieved symptom control in 3 months.[8]

For subsequent licensing, annual review is required by the DVLA for Group 2 licence holders (lorry and bus drivers) and a minimum of 3 yearly review for Group 1 licence holders (cars and motorcycles), to confirm control of OSAHS, improved sleepiness and treatment adherence.[7] The committee noted that people with OHS who do not have symptoms of excessive sleepiness during waking hours will continue to have an annual review which includes assessment of any changes in symptoms.

Even though there was a lack of evidence on monitoring strategies for people with OHS, based on their experience the committee made strong recommendations hence they did not make any research recommendation for this topic.

COPD-OSAHS overlap syndrome

The committee noted the lack of evidence for monitoring strategies in COPD-OSAHS overlap syndrome and decided to make consensus recommendations based on evidence reviewed for OSAHS, their experience and current practice.

The committee noted that CPAP and non-invasive ventilation are just part of treatment for COPD-OSAHS overlap syndrome, and that follow-up should be tailored to the person's overall treatment plan. This should also include lifestyle changes, such as weight management, modifying use of sedative drugs and alcohol, and stopping smoking, and treating underlying lung disease and other comorbidities. For people with severe COPD, it may also include discussions about care planning (for example COPD exacerbation action plan and advance care planning for those with severe COPD).

The committee agreed that for people with COPD-OSAHS overlap syndrome started on CPAP or non-invasive ventilation early follow-up is advised to ensure control of symptoms, sleep disordered breathing and adherence. Problem-solving can be achieved by face to face consultations, video or telephone consultations, including review of telemonitoring data where available. The committee also agreed that although most studies of telemonitoring are in patients with OSAHS, and that there is not yet the ability to assess hypercapnia through telemonitoring, it is still of value to use for people with COPD-OSAHS overlap syndrome for monitoring OSAHS. The committee agreed that video and telephone consultations with telemonitoring will help reduce the risk of infection during the COVID-19 pandemic.

In addition to their 6-monthly or annual review people with OSAHS and COPD-OSAHS overlap syndrome on therapy need open access to a sleep service for advice, and provision of consumables such as masks, circuitry and filters.

The committee noted that in current practice follow-up is at is 2 weeks and 1 year, hence implementation of these recommendations would not change practice.

Current practice includes a mixture of face-to-face, telephone, video consultations and telemonitoring. The increasing number of people being offered CPAP and non-invasive ventilation means that regular outpatient follow-up becomes increasingly difficult for sleep centres to provide. In addition, a more personalised approach enables attention to be focussed on people with problems adapting to therapy. Telemonitoring is included in the overall cost of CPAP devices by some manufacturers for variable periods. Increasing website and app-based access to telemonitoring data will allow patients to access their own results to aid self-care.

The committee noted that there has been a significant move to video and telephone consultations to reduce the risk of infection during the COVID-19 pandemic.

Follow-up for drivers with excessive sleepiness

The committee agreed that people must not drive if they have excessive sleepiness, having or likely to have an adverse effect on driving, in keeping with DVLA guidance.[8] Driving may resume after satisfactory symptom control, which needs medical confirmation if moderate or severe OSAHS. This is the patient's responsibility, but sleep team professionals will help them assess the likely impact of their symptoms on their safety to drive, by taking a detailed driving history, including distances driven, episodes of drowsy driving, use of alerting mechanisms when driving to avoid falling asleep, or a history of a sleep related accident or near miss. Using a high Epworth Sleepiness Score alone for driving advice is unlikely to be adequate, as it is subjective. Many people can doze off in relaxed situations but retain concentration during specific tasks such as driving. Patients with excessive sleepiness having or likely to have an adverse impact on driving with confirmed moderate or severe obstructive sleep apnoea syndrome must inform the DVLA and their car insurance company of their diagnosis. If patients have excessive sleepiness having or likely to have an adverse impact on driving and a diagnosis of mild OSAHS, they must inform the DVLA of their diagnosis if they have not achieved symptom control in 3 months.[8]

For subsequent licensing, annual review is required by the DVLA for Group 2 licence holders (lorry and bus drivers) and a minimum of 3 yearly review for Group 1 licence holders (cars and motorcycles), to confirm control of OSAHS, improved sleepiness and treatment adherence.[7] The committee noted that people with COPD-OSAHS overlap syndrome who do not have symptoms of excessive sleepiness during waking hours will continue to have an annual review which includes assessment of any changes in symptoms.

Even though there was a lack of evidence on monitoring strategies for people with COPD-OSAHS overlap syndrome, based on their experience the committee made strong recommendations hence they did not make any research recommendation for this topic.

1.6.2 Cost effectiveness and resource use

Since treatments in these conditions are potentially for life it is important for cost effectiveness as well as for patient welfare to monitor whether a treatment is working and then, if necessary, to modify, switch or discontinue treatment.

The clinical evidence was mainly for telemonitoring compared with outpatient follow up for people with OSAHS. There was little difference in the clinical outcomes and so the question of which is less costly is important.

Different manufacturers seem to have different pricing models for telemonitoring.

- Mostly telemonitoring for one year is included in the price of the CPAP machine and a fee is charged for subsequent years

- Sometimes a small fee (e.g. £20) is charged for the modem that will cover the lifespan of the machine when purchased at the same time as the machine.

It might also be possible to turn on and off the modem and transfer it to other patients, thus reducing the price of telemonitoring. This might facilitate the use of telemonitoring to sample one month's data ahead of a follow-up consultation.

Intuitively, there could be cost savings with telemonitoring if it reduces the need for face-to-face consultations (e.g. reduced need for fully equipped outpatient room and reduced staff time as well as reduced risk of transmission of infectious disease) but there are also costs.

Two cost-utility analyses were included, each comparing telemonitoring with hospital clinic follow-up for people with OSAHS. Both were randomised trials in a Spanish setting.

In one study the authors concluded that the telemonitoring strategy was dominated (less effective and more costly) by the hospital follow-up. In this within-trial study, people with OSAHS completed a biweekly six-item questionnaire about the status of their physical activity, sleep time, CPAP use and treatment side effects. Clinicians monitored responses and communicated with patients via the website messaging tool. In this scenario, the committee were of the view that one reason that telemonitoring may not be cost-effective was because clinicians may have been over-using the data, that is respond to all aspects of the remote data. The committee reasoned that the responses to the questionnaire may not be a reliable proxy to identify people with OSAHS who need further follow-up from a clinician because they are still symptomatic or have poor adherence with their CPAP device. Therefore, monitoring responses to this questionnaire may result in clinicians over engaging with participants who may not need this extra attention.

In contrast, the second study found that using an alarm-based system where clinicians only respond if certain events occur (e.g. mask leakage or poor adherence) resulted in standard care being more effective than telemonitoring but not being cost-effective at the £20,000 threshold. However, it should be noted the authors have equated improvements in quality of life measured by the EQ-5D to improvements in QALYs. However, a 0.003 higher EQ-5D at 3 months is not the same as a 0.003 gain in QALYs. Instead, to calculate the correct QALY gains over the three-month period the EQ-5D gains must be multiplied by 0.25 or else an assumption must be stated about how long the difference would be sustained. The results were very sensitive to this assumption.

An original comparative cost analysis was conducted (See Evidence Report F). It found that CPAP with re-titration using auto-CPAP was slightly less costly than CPAP with re-titration using telemonitoring, but this was largely based on assumption rather than evidence. In particular, it only assumed that telemonitoring would reduce the need for follow-up in those patients who needed re-titration.

The committee concluded that there is uncertainty about whether remote follow-up with telemonitoring is less costly than traditional outpatient follow-up and could be affected by local factors including the charges by manufacturers for telemonitoring. However, where telemonitoring for the first year is included in the price of the machine, this is likely to be cost effective. Longer term monitoring could also be cost effective if the price is relatively low. Furthermore, the evidence has not accounted for the need to avoid face-to-face consultations to reduce transmission of infectious disease

All the clinical evidence in the guideline review was for CPAP in the OSAHS population, however the committee used the evidence and their experience to establish principles that cover all interventions and all three guideline populations. The committee recommended that all patients provided with an intervention (CPAP, non-invasive ventilation, oral device or positional modifier), be offered follow-up through face to face, telephone or video consultations within 1 month and telemonitoring then follow-up as required. The provision of face to face appointments was usual practice but recently there has been a big shift to

remote consultations. The committee do not expect there to be an additional resource impact as a result of this recommendation. Also, the number of appointments that people with OSAHS, OHS or OS would be expected to attend is not expected to increase.

1.6.3 Other factors the committee took into account

The committee noted that telemonitoring can be seen as beneficial to patients if it reduces the need for them to attend hospital. They also noted that there has been a significant move to video and telephone consultations to reduce the risk of infection during the COVID-19 pandemic. This change in practice along with telemonitoring has allowed less face to face to appointments while still enabling review of a patient's CPAP data and changing their prescriptions. The committee were of the view that if the cost of modems comes down, then leaving a modem on a device would allow year on year CPAP review without seeing the patient. This can be augmented with telephone consultations where required. Potentially using IT Epworth sleepiness scores could be gained. There could be a lot of options gained from using IT monitoring.

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Appendices

Appendix A: Review protocols

Table 8: Review protocol: monitoring

ID	Field	Content
0.	PROSPERO registration number	Not registered
1.	Review title	Monitoring
2.	Review question	What is the most clinically and cost effective strategy for monitoring OSAHS/OHS/OS (for example based on outpatient visits, download of data from devices or telemonitoring)? What is the optimum frequency of monitoring of OSAHS/OHS/COPD-OSAHS overlap syndrome?
3.	Objective	To determine the most clinically and cost effective strategy for monitoring OSAHS/OHS/OS, encompassing both modes of monitoring and their frequency
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • Epistemonikos Searches will be restricted by: • English language • Human studies • Letters and comments are excluded. Other searches:

		• Inclusion lists of relevant systematic reviews will be checked by the reviewer. The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review.
5.	Condition or domain being studied	Obstructive sleep apnoea/hypopnoea syndrome is the most common form of sleep disordered breathing. The guideline will also cover obesity hypoventilation syndrome and COPD-OSAHS overlap syndrome (the coexistence of obstructive sleep apnoea/hypopnoea syndrome and chronic obstructive pulmonary disease).
6.	Population	People with OSAHS/OHS/COPD-OSAHS overlap syndrome Stratified by: OSAHS vs OHS vs COPD-OSAHS overlap syndrome Stage of treatment (<1 year vs >/= 1 year) Severity (mild vs moderate vs severe, based on AHI) Mild OSAHS: AHI >5 but <15 Moderate OSAHS: AHI >/= 15 but <30 Severe OSAHS: AHI >/= 30
7.	Intervention/Exposure/Test	• In person outpatient visits • Download of data from devices • Telephone follow-up • Telemonitoring Any of the above at any of the following frequencies: • No routine monitoring • 3 yearly

		• Yearly • 6 monthly • 3 monthly • 1 monthly • <1 monthly
8.	Comparator/Reference standard/Confounding factors	Any of the above methods at any frequency vs the same or any other method at any frequency
9.	Types of study to be included	RCTs will be prioritised, if insufficient RCTs are found for guideline decision making, non-randomised studies will be considered if they adjust for key confounders (age, sex, BMI, co-existing conditions) Minimum duration of follow-up 1 month Parallel or crossover studies to be included
10.	Other exclusion criteria	None
11.	Context	N/A
12.	Primary outcomes (critical outcomes)	Generic or disease specific quality of life measures (continuous) Mortality (dichotomous)
13.	Secondary outcomes (important outcomes)	• Sleepiness scores (continuous, e.g. Epworth) • Apnoea-Hypopnoea index (continuous) • Oxygen desaturation index (continuous) • CO2 control (continuous) • Hours of use (adherence measure, continuous) • Minor adverse effects of treatment (rates or dichotomous) • Driving outcomes (continuous)

		• Neurocognitive outcomes (continuous) • Healthcare contacts (rates/dichotomous) • Impact on co-existing conditions: o HbA1c for diabetes (continuous) o Cardiovascular events for cardiovascular disease (dichotomous) o Systolic blood pressure for hypertension (continuous)
14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. EviBASE will be used for data extraction.
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. • Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS) • Randomised Controlled Trial: Cochrane RoB (2.0) 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.
16.	Strategy for data synthesis	• Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). • GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome.

		Publication bias is tested for when there are more than 5 studies for an outcome. The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/ • Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome. • WinBUGS will be used for network meta-analysis, if possible given the data identified. Heterogeneity between the studies in effect measures will be assessed using the I^2 statistic and visually inspected. An I^2 value greater than 50% will be considered indicative of substantial heterogeneity. Sensitivity analyses will be conducted based on pre-specified subgroups using stratified meta-analysis to explore the heterogeneity in effect estimates. If this does not explain the heterogeneity, the results will be presented pooled using random-effects.
17.	Analysis of sub-groups	• High risk occupational groups (for example heavy goods vehicle drivers) vs general population • Sleepiness – Epworth >9 vs Epworth 9 or less • Coexisting conditions – type 2 diabetes vs atrial fibrillation vs hypertension vs none • Type of treatment received – CPAP vs oral devices vs positional modifiers
18.	Type and method of review	☒ Intervention ☐ Diagnostic ☐ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)
19.	Language	English
20.	Country	England
21.	Anticipated or actual start date	
22.	Anticipated completion date	
24.	Named contact	5a. Named contact National Guideline Centre

		5b Named contact e-mail SleepApnoHypo@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and the National Guideline Centre
25.	Review team members	From the National Guideline Centre: Carlos Sharpin, Guideline lead Sharangini Rajesh, Senior systematic reviewer Audrius Stonkus, Systematic reviewer Emtiyaz Chowdhury (until January 2020), Health economist David Wonderling, Head of health economics Agnes Cuyas, Information specialist (till December 2019) Jill Cobb, Information Specialist
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10098
29.	Other registration details	NA – not registered
30.	Reference/URL for published protocol	NA – not registered

31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
32.	Keywords	-
33.	Details of existing review of same topic by same authors	N/A
35..	Additional information	N/A
36.	Details of final publication	www.nice.org.uk

Table 9: Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2003, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[28] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland).

	• Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2003 or later but that depend on unit costs and resource data entirely or predominantly from before 2003 will be rated as 'Not applicable'. • Studies published before 2003 will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B: Literature search strategies

Sleep Apnoea search strategy 5 monitoring

This literature search strategy was used for the following reviews;

- What is the most clinically and cost effective strategy for monitoring OSAHS/OHS/OS (for example based on outpatient visits, download of data from devices or telemonitoring)?
- What is the optimum frequency of monitoring of OSAHS/OHS/OS?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[28]

For more information, please see the Methods Report published as part of the accompanying documents for this guideline.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 10: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 6 July 2020	Exclusions Randomised controlled trials Systematic review studies Observational studies
Embase (OVID)	1974 – 6 July 2020	Exclusions Randomised controlled trials Systematic review studies Observational studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2020 Issue 7 of 12 CENTRAL to 2020 Issue 7 of 12	None
Epistemonikos (Epistemonikos Foundation)	Inception – 29 November 2018	None

Medline (Ovid) search terms

1.	exp Sleep Apnea Syndromes/
2.	(sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab.
3.	(sleep* adj4 disorder* adj4 breath*).ti,ab.
4.	(OSAHS or OSA or OSAS).ti,ab.
5.	(obes* adj3 hypoventil*).ti,ab.
6.	pickwick*.ti,ab.
7.	or/1-6
8.	limit 7 to English language
9.	letter/
10.	editorial/
11.	news/
12.	exp historical article/

13.	Anecdotes as Topic/
14.	comment/
15.	case report/
16.	(letter or comment*).ti.
17.	or/9-16
18.	randomized controlled trial/ or random*.ti,ab.
19.	17 not 18
20.	animals/ not humans/
21.	exp Animals, Laboratory/
22.	exp Animal Experimentation/
23.	exp Models, Animal/
24.	exp Rodentia/
25.	(rat or rats or mouse or mice).ti.
26.	or/19-25
27.	8 not 26
28.	Monitoring, Physiologic/
29.	Patient Outcome Assessment/
30.	monitoring.ti,ab.
31.	((followup or follow-up or check* or evaluat* or appointment* or observation or observations) adj3 (timing* or interval* or year* or annual* or biannual* or month* or periodic* or frequen* or routine*)).ti,ab.
32.	((followup or follow-up or check* or evaluat* or appointment* or monitor*) adj3 (outpatient or out-patient or clinic or telephone or remote or virtual)).ti,ab.
33.	((monitor* or time point* or interval*) adj3 (year* or annual* or biannual* or month* or periodic* or frequen* or routine*)).ti,ab.
34.	(telemonitor* or telemedicine or telehealth or tele monitor* or tele medicine or tele health or download* or smartphone* or smart phone or ipad* or iphone*).ti,ab.
35.	((manage* or monitor*) adj3 (virtual or remote or web* or cloud* or wireless or Internet or wi fi or wifi)).ti,ab.
36.	(monitor* adj3 device*).ti,ab.
37.	Telemedicine/
38.	or/28-37
39.	27 and 38
40.	randomized controlled trial.pt.
41.	controlled clinical trial.pt.
42.	randomi#ed.ti,ab.
43.	placebo.ab.
44.	randomly.ti,ab.
45.	Clinical Trials as topic.sh.
46.	trial.ti.
47.	or/40-46
48.	Meta-Analysis/
49.	exp Meta-Analysis as Topic/
50.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
51.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
52.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.

53.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
54.	(search* adj4 literature).ab.
55.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
56.	cochrane.jw.
57.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
58.	or/48-57
59.	Epidemiologic studies/
60.	Observational study/
61.	exp Cohort studies/
62.	(cohort adj (study or studies or analys* or data)).ti,ab.
63.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
64.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
65.	Controlled Before-After Studies/
66.	Historically Controlled Study/
67.	Interrupted Time Series Analysis/
68.	(before adj2 after adj2 (study or studies or data)).ti,ab.
69.	exp case control studies/
70.	case control*.ti,ab.
71.	Cross-sectional studies/
72.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
73.	or/59-72
74.	39 and (47 or 58 or 73)

Embase (Ovid) search terms

1.	exp Sleep Disordered Breathing/
2.	(sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab.
3.	(sleep* adj4 disorder* adj4 breath*).ti,ab.
4.	(OSAHS or OSA or OSAS).ti,ab.
5.	(obes* adj3 hypoventil*).ti,ab.
6.	pickwick*.ti,ab.
7.	or/1-6
8.	limit 7 to English language
9.	letter.pt. or letter/
10.	note.pt.
11.	editorial.pt.
12.	case report/ or case study/
13.	(letter or comment*).ti.
14.	or/9-13
15.	randomized controlled trial/ or random*.ti,ab.
16.	14 not 15
17.	animal/ not human/
18.	nonhuman/
19.	exp Animal Experiment/

20.	exp Experimental Animal/
21.	animal model/
22.	exp Rodent/
23.	(rat or rats or mouse or mice).ti.
24.	or/16-23
25.	8 not 24
26.	physiologic monitoring/
27.	outcome assessment/
28.	monitoring.ti,ab.
29.	((followup or follow-up or check* or evaluat* or appointment* or observation or observations) adj3 (timing* or interval* or year* or annual* or biannual* or month* or periodic* or frequen* or routine*)).ti,ab.
30.	((followup or follow-up or check* or evaluat* or appointment* or monitor*) adj3 (outpatient or out-patient or clinic or telephone or remote or virtual)).ti,ab.
31.	((monitor* or time point* or interval*) adj3 (year* or annual* or biannual* or month* or periodic* or frequen* or routine*)).ti,ab.
32.	(telemonitor* or telemedicine or telehealth or tele monitor* or tele medicine or tele health or download* or smartphone* or smart phone or ipad* or iphone*).ti,ab.
33.	((manage* or monitor*) adj3 (virtual or remote or web* or cloud* or wireless or Internet or wi fi or wifi)).ti,ab.
34.	(monitor* adj3 device*).ti,ab.
35.	exp telemedicine/
36.	or/26-35
37.	25 and 36
38.	random*.ti,ab.
39.	factorial*.ti,ab.
40.	(crossover* or cross over*).ti,ab.
41.	((doubl* or singl*) adj blind*).ti,ab.
42.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
43.	crossover procedure/
44.	single blind procedure/
45.	randomized controlled trial/
46.	double blind procedure/
47.	or/38-46
48.	systematic review/
49.	meta-analysis/
50.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
51.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
52.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
53.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
54.	(search* adj4 literature).ab.
55.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
56.	cochrane.jw.
57.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
58.	or/48-57

59.	Clinical study/
60.	Observational study/
61.	family study/
62.	longitudinal study/
63.	retrospective study/
64.	prospective study/
65.	cohort analysis/
66.	follow-up/
67.	cohort*.ti,ab.
68.	66 and 67
69.	(cohort adj (study or studies or analys* or data)).ti,ab.
70.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
71.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
72.	(before adj2 after adj2 (study or studies or data)).ti,ab.
73.	or/59-65,68-72
74.	exp case control study/
75.	case control*.ti,ab.
76.	cross-sectional study/
77.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
78.	or/73-77
79.	37 and (47 or 58 or 78)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Sleep Apnea Syndromes] explode all trees
#2.	(sleep* near/4 (apnea* or apnoea* or hypopnea* or hypopnoea*)):ti,ab
#3.	(sleep* near/4 disorder* near/4 breath*):ti,ab
#4.	(OSAHS or OSA or OSAS):ti,ab
#5.	(obes* near/3 hypoventil*):ti,ab
#6.	pickwick*:ti,ab
#7.	(OR #1-#6)
#8.	MeSH descriptor: [Monitoring, Physiologic] this term only
#9.	MeSH descriptor: [Patient Outcome Assessment] this term only
#10.	monitoring:ti,ab
#11.	((followup or follow-up or check* or evaluat* or appointment* or observation or observations) near/3 (timing* or interval* or year* or annual* or biannual* or month* or periodic* or frequen* or routine*)):ti,ab
#12.	((followup or follow-up or check* or evaluat* or appointment* or monitor*) near/3 (outpatient or out-patient or clinic or telephone or remote or virtual)):ti,ab
#13.	((monitor* or time point* or interval*) near/3 (year* or annual* or biannual* or month* or periodic* or frequen* or routine*)):ti,ab
#14.	(telemonitor* or telemedicine or telehealth or download* or smartphone*):ti,ab
#15.	((manage* or monitor*) near/3 (virtual or remote or web* or cloud* or wireless or Internet)):ti,ab
#16.	(monitor* near/3 device*).ti,ab
#17.	MeSH descriptor: [Telemedicine] this term only
#18.	(or #8-#17)

#19.	#7 AND #18

Epistemonikos search terms

1.	((title:((sleep apnea syndromes) OR (sleep* AND (apn?ea* OR hypopn?ea*)) OR (sleep* AND (apn?ea* OR hypopn?ea*)) OR (sleep* AND (disorder* OR breath*)) OR (OSAHS OR OSA OR OSAS) OR (obes* AND hypoventil*) OR pickwick*) OR abstract:((sleep apnea syndromes) OR (sleep* AND (apn?ea* OR hypopn?ea*)) OR (sleep* AND (apn?ea* OR hypopn?ea*)) OR (sleep* AND (disorder* OR breath*)) OR (OSAHS OR OSA OR OSAS) OR (obes* AND hypoventil*) OR pickwick*)))

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to sleep apnoea population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA – this ceased to be updated after March 2018) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics and quality of life studies.

B.2.1 Health economic studies strategy

Table 11: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 6 July 2020	Exclusions Health economics studies
Embase	2014 – 6 July 2020	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

	exp Sleep Apnea Syndromes/
1.	(sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab.
2.	(sleep* adj4 disorder* adj4 breath*).ti,ab.
3.	(OSAHS or OSA or OSAS).ti,ab.
4.	(obes* adj3 hypoventil*).ti,ab.
5.	pickwick*.ti,ab.
6.	or/1-6
7.	limit 7 to English language
8.	letter/
9.	editorial/
10.	news/
11.	exp historical article/
12.	Anecdotes as Topic/
13.	comment/
14.	case report/
15.	(letter or comment*).ti.
16.	or/9-16

17.	randomized controlled trial/ or random*.ti,ab.
18.	17 not 18
19.	animals/ not humans/
20.	exp Animals, Laboratory/
21.	exp Animal Experimentation/
22.	exp Models, Animal/
23.	exp Rodentia/
24.	(rat or rats or mouse or mice).ti.
25.	or/19-25
26.	8 not 26
27.	Economics/
28.	Value of life/
29.	exp "Costs and Cost Analysis"/
30.	exp Economics, Hospital/
31.	exp Economics, Medical/
32.	Economics, Nursing/
33.	Economics, Pharmaceutical/
34.	exp "Fees and Charges"/
35.	exp Budgets/
36.	budget*.ti,ab.
37.	cost*.ti.
38.	(economic* or pharmaco?economic*).ti.
39.	(price* or pricing*).ti,ab.
40.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
41.	(financ* or fee or fees).ti,ab.
42.	(value adj2 (money or monetary)).ti,ab.
43.	or/28-43
44.	27 and 44

Embase (Ovid) search terms

1.	exp Sleep Disordered Breathing/
2.	(sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab.
3.	(sleep* adj4 disorder* adj4 breath*).ti,ab.
4.	(OSAHS or OSA or OSAS).ti,ab.
5.	(obes* adj3 hypoventil*).ti,ab.
6.	pickwick*.ti,ab.
7.	or/1-6
8.	limit 7 to English language
9.	letter.pt. or letter/
10.	note.pt.
11.	editorial.pt.
12.	case report/ or case study/
13.	(letter or comment*).ti.

14.	or/9-13
15.	randomized controlled trial/ or random*.ti,ab.
16.	14 not 15
17.	animal/ not human/
18.	nonhuman/
19.	exp Animal Experiment/
20.	exp Experimental Animal/
21.	animal model/
22.	exp Rodent/
23.	(rat or rats or mouse or mice).ti.
24.	or/16-23
25.	8 not 24
26.	health economics/
27.	exp economic evaluation/
28.	exp health care cost/
29.	exp fee/
30.	budget/
31.	funding/
32.	budget*.ti,ab.
33.	cost*.ti.
34.	(economic* or pharmaco?economic*).ti.
35.	(price* or pricing*).ti,ab.
36.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
37.	(financ* or fee or fees).ti,ab.
38.	(value adj2 (money or monetary)).ti,ab.
39.	or/26-38
40.	25 and 39

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Sleep Apnea Syndromes EXPLODE ALL TREES
#2.	(sleep* adj4 (apn?ea* or hypopn?ea*))
#3.	(sleep* adj4 disorder* adj4 breath*)
#4.	(OSAHS or OSA or OSAS)
#5.	(obes* adj3 hypoventil*)
#6.	(pickwick*)
#7.	#1 OR #2 OR #3 OR #4 OR #5 OR #6

B.2.2 Quality of life studies strategy

Table 12: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	1946 – 26 November 2019	Exclusions Quality of life studies
Embase	1974 – 26 November 2019	Exclusions Quality of life studies

Medline (Ovid) search terms

1.	exp Sleep Apnea Syndromes/
2.	(sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab.
3.	(sleep* adj4 disorder* adj4 breath*).ti,ab.
4.	(OSAHS or OSA or OSAS).ti,ab.
5.	(obes* adj3 hypoventil*).ti,ab.
6.	pickwick*.ti,ab.
7.	or/1-6
8.	limit 7 to English language
9.	letter/
10.	editorial/
11.	news/
12.	exp historical article/
13.	Anecdotes as Topic/
14.	comment/
15.	case report/
16.	(letter or comment*).ti.
17.	or/9-16
18.	randomized controlled trial/ or random*.ti,ab.
19.	17 not 18
20.	animals/ not humans/
21.	exp Animals, Laboratory/
22.	exp Animal Experimentation/
23.	exp Models, Animal/
24.	exp Rodentia/
25.	(rat or rats or mouse or mice).ti.
26.	or/19-25
27.	8 not 26
28.	quality-adjusted life years/
29.	sickness impact profile/
30.	(quality adj2 (wellbeing or well being)).ti,ab.
31.	sickness impact profile.ti,ab.
32.	disability adjusted life.ti,ab.
33.	(qal* or qtime* or qwb* or daly*).ti,ab.
34.	(euroqol* or eq5d* or eq 5*).ti,ab.
35.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
36.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
37.	(hui or hui1 or hui2 or hui3).ti,ab.
38.	(health* year* equivalent* or hye or hyes).ti,ab.
39.	discrete choice*.ti,ab.
40.	rosser.ti,ab.

41.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
42.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
43.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
44.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
45.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
46.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
47.	or/28-46
48.	27 and 47

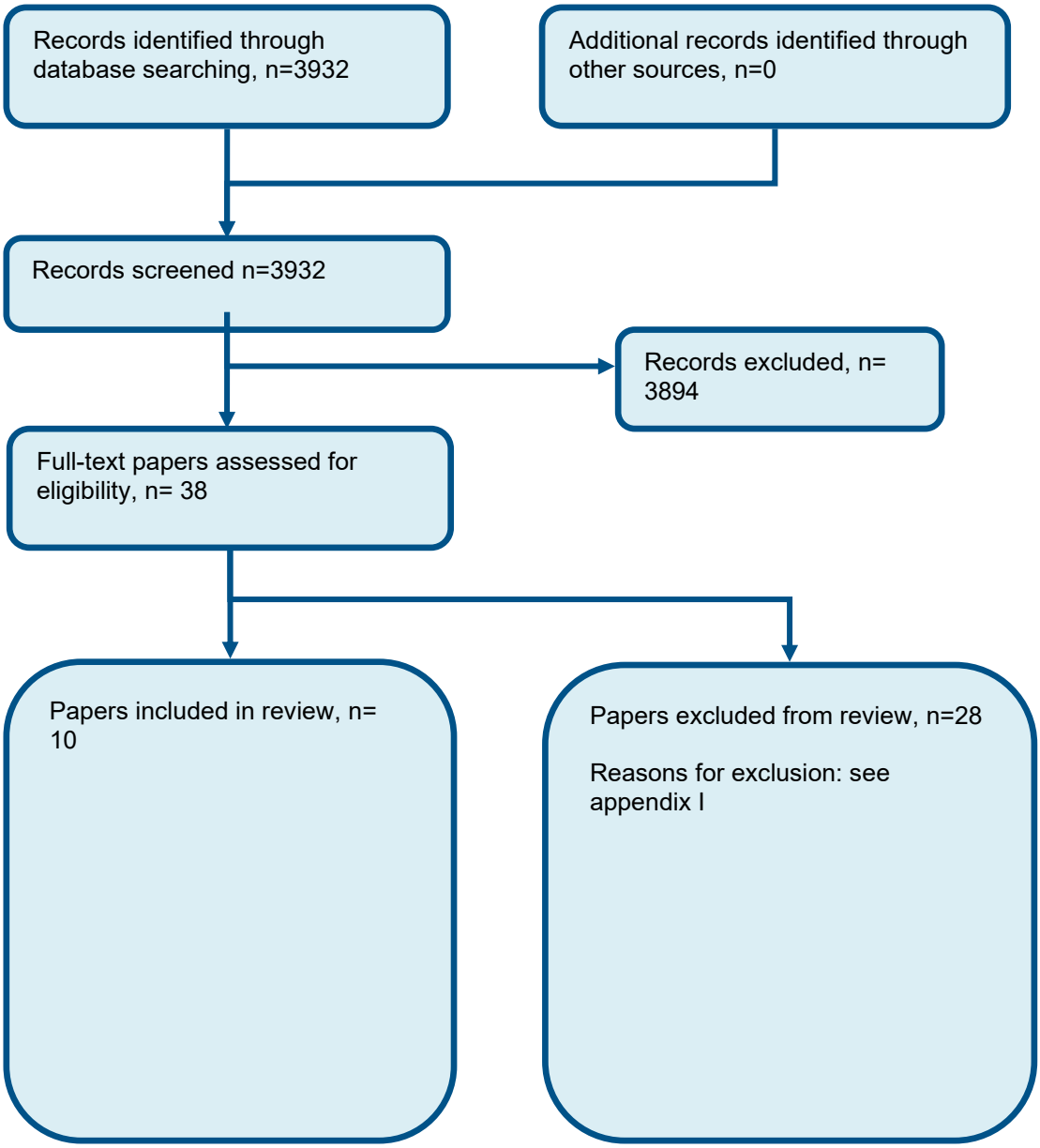
Embase (Ovid) search terms

1.	exp Sleep Disordered Breathing/
2.	(sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab.
3.	(sleep* adj4 disorder* adj4 breath*).ti,ab.
4.	(OSAHS or OSA or OSAS).ti,ab.
5.	(obes* adj3 hypoventil*).ti,ab.
6.	pickwick*.ti,ab.
7.	or/1-6
8.	limit 7 to English language
9.	letter.pt. or letter/
10.	note.pt.
11.	editorial.pt.
12.	case report/ or case study/
13.	(letter or comment*).ti.
14.	or/9-13
15.	randomized controlled trial/ or random*.ti,ab.
16.	14 not 15
17.	animal/ not human/
18.	nonhuman/
19.	exp Animal Experiment/
20.	exp Experimental Animal/
21.	animal model/
22.	exp Rodent/
23.	(rat or rats or mouse or mice).ti.
24.	or/16-23
25.	8 not 24
26.	quality adjusted life year/
27.	"quality of life index"/
28.	short form 12/ or short form 20/ or short form 36/ or short form 8/
29.	sickness impact profile/
30.	(quality adj2 (wellbeing or well being)).ti,ab.
31.	sickness impact profile.ti,ab.
32.	disability adjusted life.ti,ab.
33.	(qal* or qtime* or qwb* or daly*).ti,ab.
34.	(euroqol* or eq5d* or eq 5*).ti,ab.

35.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
36.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
37.	(hui or hui1 or hui2 or hui3).ti,ab.
38.	(health* year* equivalent* or hye or hyes).ti,ab.
39.	discrete choice*.ti,ab.
40.	rosser.ti,ab.
41.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
42.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
43.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
44.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
45.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
46.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
47.	or/26-46
48.	25 and 47

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of position modifiers



Appendix D: Clinical evidence tables

Study	Anttalainen 2016[3]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=111)
Countries and setting	Conducted in Finland; Setting: Department of pulmonary diseases, Turku university hospital, Finland
Line of therapy	Not applicable
Duration of study	Intervention + follow up:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Moderate-severe: n/a
Subgroup analysis within study	Not applicable: n/a
Inclusion criteria	OSAS patients who were commencing CPAP treatment at the department of pulmonary diseases of Turku university hospital. All patients were over 18 years of age.
Exclusion criteria	unclear/ not specified
Recruitment/selection of patients	Consecutive
Age, gender and ethnicity	Age - Mean (SD): Telemonitoring - 53.9(12.2); usual 56.4(11.8). Gender (M:F): Telemonitoring group 36/14; Usual care 43/18. Ethnicity: not stated
Further population details	1. BMI: BMI of 30 kg/m^2 or more (Telemonitoring 34.8(7.6); Usual care 32.9(6.9)). 2. Co-existing conditions: Not stated / Unclear 3. High risk occupation group: Not stated / Unclear 4. Sleepiness: ESS 9 or less (Telemonitoring - 8.2(4.9); Usual care8.2 (4.2)).
Indirectness of population	No indirectness
Interventions	(n=50) Intervention 1: Telemonitoring. Wireless telemonitoring system (ResTaxx Online, ResMed Sydney, Australia). The module was attached to the S9 Elite (ResMed, Sydney Australia) CPAP device, which transmitted compliance data evey day automatically to ResTaxx Online. The treatment was considered successful when CPAP use was >4h/day, mask <0.4 L/s and AHI <5/h during the last 6 days. Study nurses made the data checkups daily during weekdays and if the criteria for successful CPAP therapy was not achieved during two consecutive nights the nurses adjusted the CPAP remotely and called the patient to give further advice. The patients were encouraged to contact the nurse in case they had any problems. TM group

	answered the questionnaire at 3 months by email.. Duration 3 months. Concurrent medication/care: n/a. Indirectness: No indirectness Further details: 1. Intervention type: Electronic (telemonitoring). (n=61) Intervention 2: In person follow-up. In Person follow up. Usual care group visited the pulmonologist after 3 months leading in a 3 month habituation phase in the UC group. UC group answered the questionnaire at the 3 month visit. CPAP device was used without wireless telemonitoring. Duration 3 months. Concurrent medication/care: n/a. Indirectness: No indirectness Further details: 1. Intervention type:
Funding	Equipment / drugs provided by industry (ResTaxx Online System was provided by ResMed)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TELEMONITORING versus IN PERSON FOLLOW-UP

Protocol outcome 1: Quality of life at >1 month
- Actual outcome for Moderate-severe: GHQ-12 score at 12 months; Group 1: mean 5.1 (SD 6.1); n=39, Group 2: mean 4.9 (SD 5.8); n=49
Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Very high, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11; Group 2 Number missing: 12

Protocol outcome 2: Sleepiness score at >1 month
- Actual outcome for Moderate-severe: Sleepiness ESS at 12 months; Group 1: mean 5.4 (SD 3.5); n=39, Group 2: mean 5.4 (SD 3.4); n=49
Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Very high, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11; Group 2 Number missing: 12

Protocol outcome 3: AHI/RDI at >1 month
- Actual outcome for Moderate-severe: Residual AHI at 12 months; Group 1: mean 1.3 (SD 1); n=39, Group 2: mean 3.2 (SD 3.8); n=49
Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Very high, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11; Group 2 Number missing: 12

Protocol outcome 4: Patient preference at >1 month
- Actual outcome for Moderate-severe: Adherence - CPAP usage h/day at 12 months; Group 1: mean 6.4 h/day (SD 2.1); n=39, Group 2: mean 6.1 h/day (SD 1.7); n=49
Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Very high, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11; Group 2 Number missing: 12

Protocol outcomes not reported by the study	Mortality at >1 month; ODI at >1 month; Minor adverse effects of Tx at >1 month; Driving outcomes at >1 month; Neurocognitive outcomes at >1 month; HbA1c at >1 month; CV events at >1 month; Systolic BP at >1 month; Healthcare contacts at >1 month

Study	**Fox 2012[10]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=75)
Countries and setting	Conducted in Canada; Setting: University sleep disorders program in British Columbia, Canada
Line of therapy	Not applicable
Duration of study	Intervention + follow up:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Moderate-severe: n/a
Subgroup analysis within study	Not applicable: n/a
Inclusion criteria	Patients were recruited from adult (≥ 19 yr of age) patients with moderate to severe OSA (AHI ≥ 15 events/hr by polysomnography (PSG) using the Chicago scoring criteria for the determination of apneas and hypopneas, according to the American Academy of Sleep Medicine)10 diagnosed at the Sleep Disorders Program who were seen by one of three respirologists (JF, CFR, NTA) at the University of British Columbia (UBC) between April 8, 2008 to June 1, 2010. Patients with OSA who were prescribed PAP therapy by their regular sleep physician and who were willing to accept a trial of therapy were potentially eligible for the trial
Exclusion criteria	Patients were excluded from participating if they were unable or unwilling to provide informed consent, had active cardiopulmonary or psychiatric disease, had been previously treated for OSA, did not have a telephone line in their bedroom (necessary to transmit information by the modem), or could not return for follow-up visits
Recruitment/selection of patients	n/a
Age, gender and ethnicity	Age - Mean (SD): 52(10.8); 55.2(11.5). Gender (M:F): Telemedicine male - 82%; Standard care - 77.8. Ethnicity: not stated

Further population details	1. BMI: BMI of 30 kg/m^2 or more (Telemedicine - 31.9(5); Standard 32.6(6.2)). 2. Co-existing conditions: Not stated / Unclear 3. High risk occupation group: Not stated / Unclear 4. Sleepiness: ESS >9 (Telemedicine 9.9(5); standard care 9.7(4.7).
Indirectness of population	No indirectness
Interventions	(n=39) Intervention 1: Combined strategies. Auto-titrating PAP machine that transmitted physiologic information information (i.e. adherance, air leak, residual AHI) daily to a website that could be reviewed. . Duration 3 months. Concurrent medication/care: all patients were oriented to CPAP, fitted with a mask, and given an auto-titrating machine. Indirectness: No indirectness Further details: 1. Intervention type: Not applicable (n=36) Intervention 2: In person follow-up. Standard care with auto-titrating CPAP. In Person follow up. Duration 3 months. Concurrent medication/care: all patients were oriented to CPAP, fitted with a mask, and given an auto-titrating machine. Indirectness: No indirectness Further details: 1. Intervention type:
Funding	Study funded by industry (This study was partially supported by a research grant from Phillips Respironics Inc. The authors have indicated no financial conflicts of interest)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINED STRATEGIES versus IN PERSON FOLLOW-UP

Protocol outcome 1: Sleepiness score at >1 month
- Actual outcome for Moderate-severe: Epworth sleeping scale- mean decrease in ESS at 3 months; Group 1: mean 1.6 (SD 5.1); n=28, Group 2: mean 0.7 (SD 5.2); n=26; Comments: p=0.49
Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11; Group 2 Number missing: 10

Protocol outcome 2: AHI/RDI at >1 month
- Actual outcome for Moderate-severe: Apnoea-Hypopnea index (AHI) at 3 months; Group 1: mean 4.7 (SD 3.8); n=28, Group 2: mean 6.6 (SD 4.8); n=26; Comments: p=0.12
Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11; Group 2 Number missing: 10

Protocol outcome 3: Patient preference at >1 month
- Actual outcome for Moderate-severe: Mean adherence (min per day) at 3 months; Group 1: mean 191 minutes (SD 147); n=28, Group 2: mean 105 minutes (SD 118); n=26; Comments: p=0.006

Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11; Group 2 Number missing: 10 - Actual outcome for Moderate-severe: Mean adherence on nights PAP used (min per day) at 3 months; Group 1: mean 321 minutes (SD 80); n=28, Group 2: mean 207 minutes (SD 106); n=26; Comments: <0.0001 Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11; Group 2 Number missing: 10 - Actual outcome for Moderate-severe: mean % days used at 3 months; Group 1: mean 55.9 % (SD 40); n=28, Group 2: mean 45.9 % (SD 38); n=26 Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11; Group 2 Number missing: 10	
Protocol outcomes not reported by the study	Quality of life at >1 month; Mortality at >1 month; ODI at >1 month; Minor adverse effects of Tx at >1 month; Driving outcomes at >1 month; Neurocognitive outcomes at >1 month; HbA1c at >1 month; CV events at >1 month; Systolic BP at >1 month; Healthcare contacts at >1 month

Study	**Hoet 2017[14]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=46)
Countries and setting	Conducted in Belgium; Setting: The study was performed in the sleep unit of the Saint-Pierre University Hospital in Brussels, Belgium.
Line of therapy	Not applicable
Duration of study	Intervention + follow up:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Moderate-severe: n/a
Subgroup analysis within study	Not applicable: n/a
Inclusion criteria	Eligible patients were ≥18 years old. They were recently diagnosed with OSAS with an apnea-hypopnea index (AHI) ≥20/h according to AASM 2012 scoring rules and sent to our sleep laboratory for initiation of treatment with CPAP therapy.
Exclusion criteria	Previous exposure to CPAP therapy, mixed or predominantly central sleep apnea, a planned trip abroad for more than 3 weeks during the first 3 months of follow-up, language barriers, cognitive or psychiatric disorders

	making it difficult to comprehend information regarding CPAP therapy and provide informed consent, and significant comorbidities such as severe chronic obstructive pulmonary disease or hypoventilation syndromes.
Recruitment/selection of patients	n/a
Age, gender and ethnicity	Age - Mean (SD): Telemonitoring group -59(13; Usual care group - 54(14). Gender (M:F): Define. Ethnicity: not stated
Further population details	1. BMI: BMI of 30 kg/m^2 or more (Telemonitoring group - 31(4); usual care group - 32(6)). 2. Co-existing conditions: HTN (TM group - 52%; UC group-52%). 3. High risk occupation group: Not stated / Unclear 4. Sleepiness: ESS >9 (TM group - 10(4); UC group -15(5)).
Extra comments	All patients provided written informed consent to participate in the study
Indirectness of population	No indirectness
Interventions	(n=23) Intervention 1: Telemonitoring. T4P TM unit was added to the CPAP device of the patient at home. Sleep laboratory technical staff were instructed to connect to the web portal and to analyze individual patient's data each Tuesday and Friday. In case of air leaks >50 L/min, residual AHI >10/h, or CPAP use <3h on 3 consecutive days, they were required to call the patient and to set up a visit with the staff of the sleep laboratory. Duration 3 months. Concurrent medication/care: All eligible patients underwent on CPAP titration night with an automated CPAP(APAP) device under fully attended polysomnography (PSG) monitoring. Indirectness: No indirectness Further details: 1. Intervention type: Electronic (CPAP and T4P TM unit). (n=23) Intervention 2: In person follow-up. After CPAP titration night, patients were instructed to use the device each night for the whole night. They received written instructions and were able to contact the sleep unit (with telephone call or visit) as often as needed, during weekdays, in order to resolve any current problem interferring with their CPAP use. a group educational session for CPAP-treated patients was scheduled 1 month after CPAP initiation, and a visit to the pneumologist was scheduled 1.5 and 3 months after CPAP initiation. Duration 3 months. Concurrent medication/care: All eligible patients underwent on CPAP titration night with an automated CPAP(APAP) device under fully attended polysomnography (PSG) monitoring. Indirectness: No indirectness Further details: 1. Intervention type: Physical (CPAP).
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TELEMONITORING versus IN PERSON FOLLOW-UP

Protocol outcome 1: Patient preference at >1 month

- Actual outcome for Severe: Adherence hours of use at 3 months; Group 1: mean 5.7 (SD 1.6); n=21, Group 2: mean 4.2 (SD 1.9); n=20 Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, 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: 3 - Actual outcome for Severe: % nights CPAP use >4 hours at 3 months; Mean; , Comments: Adherent patients (%) CPAP use >4 hours Telemonitoring - 82 %; In person follow up - 64% Mean (range) - hours/night Telemonitoring + in p Follow-up group - 6.2(4-8.1); In person follow up group - 5.2 (4-7.5); Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, 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: 3	
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; ODI at >1 month; Minor adverse effects of Tx at >1 month; Driving outcomes at >1 month; Neurocognitive outcomes at >1 month; HbA1c at >1 month; CV events at >1 month; Systolic BP at >1 month; Healthcare contacts at >1 month

Study	**Isetta 2015[19]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=139)
Countries and setting	Conducted in Spain; Setting: Multicentre randomised trial
Line of therapy	Not applicable
Duration of study	Intervention + follow up:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Severe: n/a
Subgroup analysis within study	Not applicable: n/a
Inclusion criteria	All enrolled patients were classified as requiring CPAP treatment after an overnight study.
Exclusion criteria	Severe sleepiness, severe nasal obstruction, pregnancy, psychiatric disease, dangerous employment, clinical instability and current or previous treatment for OSA. We excluded patients who lacked sufficient internet skills or refused to participate in the study.
Recruitment/selection of patients	n/a

Age, gender and ethnicity	Age - Mean (SD): Telemedicine 51 (8.9); Control - 47(10.9). Gender (M: F): 120/19. Ethnicity: not stated
Further population details	1. BMI: BMI of 30 kg/m^2 or more (Telemedicine - 32.8(7.3); 33.6(8.3)). 2. Co-existing conditions: AF (cardiovascular disease: telemedicine-11; control-7). 3. High risk occupation group: Not applicable 4. Sleepiness: ESS >9 (Telemedicine 10.5(4.6); control 10.8(4.8)).
Indirectness of population	No indirectness
Interventions	(n=69) Intervention 1: Telemonitoring. Telemonitoring +televisits Patients randomised to the telemedicine group received their follow-up at home supported by a website developed for this study, where they could find information about OSA and CPAP therapy, and a biweekly six-item questionnaire about their status, physical activity, sleep time, CPAP use and treatment side effects. Each centre's staff monitored questionnaire answers and communicated with patients through the website messaging tool to solve treatment-related problems. To participate, patients only required an internet-connected device with a microphone and webcam. Televisits via video conference were undertaken at months 1 and 3. We used Skype due to its availability, ease of use and good performance.21 Patients automatically received a confirmation email indicating the date and time of their appointment. Extra televisits or hospital visits were scheduled as necessary. . Duration 6 months. Concurrent medication/care: n/a. Indirectness: No indirectness Further details: 1. Intervention type: Electronic (Telemedicine/Televisits). (n=70) Intervention 2: In person follow-up. Patients randomised to the control group had the same follow-up schedule as the telemedicine group but attended the hospital. Specifically, they received standard face-to-face follow-up with visits at months 1, 3 and 6, and extra visits if needed. . Duration 6 months. Concurrent medication/care: n/a. Indirectness: No indirectness Further details: 1. Intervention type: Physical (In person follow up).
Funding	Equipment / drugs provided by industry (This project was supported by SEPAR/FIS PI14/00416 and ECO2013-47092 (MINECO, Spain).

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TELEMONITORING versus IN PERSON FOLLOW-UP

Protocol outcome 1: Quality of life at >1 month
- Actual outcome for Severe: E5QD at 6 months; Group 1: mean 0.82 (SD 0.19); n=64, Group 2: mean 0.88 (SD 0.2); n=64
Risk of bias: All domain - High, Selection - Low, Blinding - Very high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5; Group 2 Number missing: 6
- Actual outcome for Severe: FOSQ at 6 months; Group 1: mean 16.9 (SD 3.94); n=64, Group 2: mean 18.01 (SD 2.97); n=64
Risk of bias: All domain - High, Selection - Low, Blinding - Very high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5; Group 2 Number missing: 6

Protocol outcome 2: Sleepiness score at >1 month - Actual outcome for Severe: Sleepiness ESS at 6 months; Group 1: mean 6.52 (SD 4.14); n=64, Group 2: mean 5.89 (SD 3.51); n=64 Risk of bias: All domain - High, Selection - Low, Blinding - Very high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5; Group 2 Number missing: 6 Protocol outcome 3: Patient preference at >1 month - Actual outcome for Severe: Adherence h/day at 6 months; Group 1: mean 4.4 (SD 2); n=64, Group 2: mean 4.2 (SD 2); n=64 Risk of bias: All domain - High, Selection - Low, Blinding - Very high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5; Group 2 Number missing: 6 - Actual outcome for Severe: % CPAP use >4 hours at 6 months; Percentage (%) >4 hours/night Telemonitoring + televisits - 65 %; control group - 57%; Risk of bias: All domain - High, Selection - Low, Blinding - Very high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5; Group 2 Number missing: 6	
Protocol outcomes not reported by the study	Mortality at >1 month; AHI/RDI at >1 month; ODI at >1 month; Minor adverse effects of Tx at >1 month; Driving outcomes at >1 month; Neurocognitive outcomes at >1 month; HbA1c at >1 month; CV events at >1 month; Systolic BP at >1 month; Healthcare contacts at >1 month

Study	**Lugo 2019[23]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=186)
Countries and setting	Conducted in Spain; Setting: sleep unit in a hospital clinic Barcelona
Line of therapy	Unclear
Duration of study	Intervention + follow up: 12 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Moderate

Subgroup analysis within study	Not applicable
Inclusion criteria	suspected OSA and/or refractory hypertension, age 18–75 years, basic knowledge of ICTs use (e.g., tablet, smartphone, or computer), and Internet access.
Exclusion criteria	Patients with disabilities that prevented them from completing the questionnaires, invalidating somnolence (medical criteria), unstable disease, previous CPAP use, uvulopalatopharyngoplasty, risk profession or not signing the informed consent form.
Recruitment/selection of patients	Consecutive patients with suspected OSA referred to the sleep unit between 2016 and Feb 2017 were randomised if they signed the consent form
Age, gender and ethnicity	Age - Mean (SD): 50.6 (11.7). Gender (M:F): 127/59. Ethnicity: unclear AHI mean (SD): telemonitoring group 24.7, hospital group 33.6
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	Serious indirectness: patients with mild, moderate and severe OSA were included along with 19.6% of patients with no OSA diagnosis.
Interventions	(n=94) Intervention 1: Telemonitoring. Patients in the Virtual sleep unit (VSU) were managed exclusively outside of the hospital setting. The diagnostic sleep test consisted of home-based respiratory polygraphy for three consecutive nights, using ApneaLink air (ResMed,Spain). Recorded data were downloaded to a secure server and analyzed by a specialized technician. Subsequently, a sleep physician assessed all records and scheduled a video conference visit to inform the results and discuss the therapeutic decision. If OSA was diagnosed and CPAP was indicated, patients received CPAP education and along with an automatic CPAP device (Dreamstation, Respironics) at the providers pick-up point. A technician could remotely adjust CPAP pressure through a website (EncoreAnywhere, Respironics), based on data sent by the device (i.e., pressure, leaks, residual apnoea–hypopnea index, hours of use). Patients were managed remotely and treatment could accurately be controlled. The time of the interview with the physician was similar between the two arms (no more than 15 minute). Follow-up visits at 3, 6 and 12 weeks were performed through a custom web application (https://plataforma.laboratori-virtual-son.com) developed for the study, with separated areas for patients and professionals or phone-calls. Patients could access general information about OSA, CPAP, healthy sleep, and lifestyle, as well as their medical agenda, FAQs, and online clinical questionnaires. An email address to contact professionals and a teleconference service to perform the interviews were also

	available. Professionals could schedule and perform teleconference visits, send messages to patients, and analyze the questionnaire responses. Duration 12 weeks. Concurrent medication/care: Before the HR or VSU diagnostic procedures, patients underwent clinical evaluation of anthropometric data, medical history, OSA symptoms, and treatments received. Patients were or not diagnosed with OSA and, according to the medical opinions, received CPAP treatment and/or sleep hygiene measures and lifestyle recommendations (e.g., diet, exercise, regular sleep hours, sleeping on their side). Patients receiving CPAP treatment were monitored by a specialized nurse at 3, 6 and 12 weeks (face-to-face or videoconference, according to the study group) to assess their general symptoms, CPAP compliance, and side effects. At the final visit, all patients, including those who received sleep hygiene and lifestyle advice, were visited to assess the ESS, QSQ, EuroQol, and their overall satisfaction with the diagnostic and treatment procedure. Indirectness: Serious indirectness; Indirectness comment: patients with mild, moderate and severe OSA were included Further details: 1. Intervention type: Electronic (n=92) Intervention 2: In person follow-up. Sleep tests, medical assessments, and follow-up visits were performed in the Sleep Unit. Based on the patient characteristics, physicians not involved in the trial requested sleep studies (e.g. PSG, or hospital- or home-based respiratory polygraphy). After sleep testing, a sleep physician interviewed patients. If CPAP was indicated, patients received education and training in CPAP use from a specialized nurse or technician in the hospital. CPAP was then titrated in the hospital with manual adjustment by the technician during a sleep study. Once the optimal pressure was determined, patients were provided with a fixed pressure CPAP device to use at home (DreamStation, Respironics). All visits were performed face-to-face in the consultation at 3, 6 and 12 weeks.. Duration 12 weeks. Concurrent medication/care: Before the HR or VSU diagnostic procedures, patients underwent clinical evaluation of anthropometric data, medical history, OSA symptoms, and treatments received. Patients were or not diagnosed with OSA and, according to the medical opinions, received CPAP treatment and/or sleep hygiene measures and lifestyle recommendations (e.g., diet, exercise, regular sleep hours, sleeping on their side). Patients receiving CPAP treatment were monitored by a specialized nurse at 3, 6 and 12 weeks (face-to-face or videoconference, according to the study group) to assess their general symptoms, CPAP compliance, and side effects. At the final visit, all patients, including those who received sleep hygiene and lifestyle advice, were visited to assess the ESS, QSQ, EuroQol, and their overall satisfaction with the diagnostic and treatment procedure.. Indirectness: Serious indirectness; Indirectness comment: patients with mild, moderate and severe OSA were included. Further details: 1. Intervention type: Physical
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TELEMONITORING versus IN PERSON FOLLOW-UP

Protocol outcome 1: Quality of life at >1 month
- Actual outcome for Moderate: EQ5D at 12 weeks ; Group 1: mean 0.84 (SD 0.18); n=80 (baseline value = 0.80, Group 2: mean 0.85 (SD 0.16); n=74 (baseline value = 0.84)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 14, Reason: none provided; Group 2 Number missing: 18, Reason: none provided
- Actual outcome for Moderate: EQ-VAS at 12 weeks ; Group 1: mean 75.66 (SD 13.68); n=80 (baseline value = 70.46), Group 2: mean 75.09 (SD 17.35); n=74 (baseline value = 73.70)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 14, Reason: none provided; Group 2 Number missing: 18, Reason: none provided

Protocol outcome 2: Sleepiness score at >1 month
- Actual outcome for Moderate: ESS at 12 weeks ; Group 1: mean 8.5 (SD 4.44); n=80, Group 2: mean 7.05 (SD 4.31); n=74
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 14, Reason: none provided; Group 2 Number missing: 18, Reason: none provided

Protocol outcome 3: Healthcare contacts at >1 month
- Actual outcome for Moderate: number of OSA related GP visits at 6 months; Group 1: 4/94, Group 2: 6/92
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 14, Reason: none provided; Group 2 Number missing: 18, Reason: none provided
- Actual outcome for Moderate: number of OSA related specialist visits at 6 months; Group 1: 11/94, Group 2: 9/92
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 14, Reason: none provided; Group 2 Number missing: 18, Reason: none provided

Protocol outcomes not reported by the study	Mortality at >1 month; AHI/RDI at >1 month; ODI at >1 month; Minor adverse effects of Tx at >1 month; Driving outcomes at >1 month; Neurocognitive outcomes at >1 month; HbA1c at >1 month; CV events at >1 month; Systolic BP at >1 month; CO2 control at >1 month

Study	Mendelson 2014[25]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=107)
Countries and setting	Conducted in France; Setting: There were 14 recruiting centers in France, with Grenoble as the coordinating center
Line of therapy	Not applicable
Duration of study	Intervention + follow up:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Moderate-severe: n/a
Subgroup analysis within study	Not applicable: n/a
Inclusion criteria	Patients were eligible for the study if they were between 18 and 85 years old, diagnosed OSA on the diagnostic sleep study with AHI > 15 events/h, BMI of less than 40 kg/m^2, cardiovascular risk SCORE > 5%,20 or being in secondary prevention with a past history of cardiovascular disease (transient ischemic attack, stroke, cerebral emorrhage, myocardial infarction, angina, coronary revascularization, arteriopathy, aortic aneurism).
Exclusion criteria	Non-inclusion criteria were the following: central sleep apnea syndrome, cardiovascular score < 5%,20 cardiac failure, history of hypercapnic chronic respiratory failure, incapacitated patients, and pregnancy in accordance with article L 1121-6 of the French public health code, or patients taking part in another clinical trial. All patients provided written informed consent to participate in the study.
Recruitment/selection of patients	n/a
Age, gender and ethnicity	Age - Mean (SD): Total 63(9), Telemedicine - 62(9), Standard care - 63(9). Gender (M:F): Telemedicine male-90.7%; Standard care - 75.5. Ethnicity: not stated
Further population details	1. BMI: BMI of 30 kg/m^2 or more (Total 29.9(4.8), Telemedicine - 29.6 (3.9), Standard care - 30.2 (5.7)). 2. Co-existing conditions: T2DM (Total 36.4 %, Telemedicine - 38.9 %, Standard care - 34.0 %). 3. High risk occupation group: Not stated / Unclear 4. Sleepiness: ESS 9 or less (Total 7.9(4.4), Telemedicine - 8.7(4.5), Standard care - 7.2(4.3)).
Indirectness of population	No indirectness

Interventions	(n=54) Intervention 1: Combined strategies. Patients assigned to telemedicine were oriented to CPAP, fitted with a nasal mask, and given an auto titrating machine. Patients received a smartphone with an application designed to transmit clinical information. The patients transmitted self-measured morning and evening BP (3-day measurements), CPAP adherence, and subjective sleepiness weekly through a questionnaire-based application. Quality of life questionnaires were transmitted monthly. Patients received daily pictograms with diet and physical-activity related messages on their smartphones. Patients were contacted after 2 days to ask about adherence, side effects, and any problems encountered with the machine. After 4 weeks of treatment, patients met with their sleep specialist and information was reviewed. After 4 months of treatment, patients consulted their sleep specialist and were re-evaluated. Both groups were asked to continue on their normal medication regimen Duration 4 months. Concurrent medication/care: n/a. Indirectness: No indirectness Further details: 1. Intervention type: Electronic (TM and In person follow up). (n=53) Intervention 2: In person follow-up. Patients assigned to standard care were evaluated at baseline, fitted with a nasal mask and given an auto titrating machine. Patients were contacted after 2 days to ask about adherence, side effects, and any problems encountered with the machine. After 4 weeks of treatment, patients met with their sleep specialist and information was transferred from their machines (adherence, mask leak, residual respiratory events). After 4 months of treatment, data were downloaded from the machine, and patients saw their sleep specialist and were re-evaluated. Duration 4 month. Concurrent medication/care: n/a. Indirectness: No indirectness Further details: 1. Intervention type: Physical (in person follow up).
Funding	Academic or government funding (This study was supported by a grant from Initiatives pour la Santé Domicile

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINED STRATEGIES versus IN PERSON FOLLOW-UP

Protocol outcome 1:Quality of life at >1 month
- Actual outcome for Moderate-severe: Quality of life (Physical composite score) difference (Visit 1 vs visit 2) at 4 months; Group 1: mean 3.2 (SD 8.6); n=40, Group 2: mean 2.9 (SD 7); n=42
Risk of bias: All domain - Very high, Selection - Low, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 14; Group 2 Number missing: 11
- Actual outcome for Moderate-severe: Quality of life (mental composite score) difference (Visit 1 vs visit 2) at 4 months; Group 1: mean 1.6 (SD 10.9); n=40, Group 2: mean 1.6 (SD 8); n=42
Risk of bias: All domain - Very high, Selection - Low, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 14; Group 2 Number missing: 11

Protocol outcome 2: Sleepiness score at >1 month - Actual outcome for Moderate-severe: Sleepiness score difference(ESS) at 4 months; Group 1: mean -2.3 (SD 4); n=40, Group 2: mean -2.1 (SD 4.1); n=42 Risk of bias: All domain - Very high, Selection - Low, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 14; Group 2 Number missing: 11 Protocol outcome 3: Patient preference at >1 month - Actual outcome for Moderate-severe: Adherence min per day at 4 months; Group 1: mean 187 (SD 178); n=40, Group 2: mean 250 (SD 166); n=42 Risk of bias: All domain - Very high, Selection - Low, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 14; Group 2 Number missing: 11	
Protocol outcomes not reported by the study	Mortality at >1 month; AHI/RDI at >1 month; ODI at >1 month; Minor adverse effects of Tx at >1 month; Driving outcomes at >1 month; Neurocognitive outcomes at >1 month; HbA1c at >1 month; CV events at >1 month; Systolic BP at >1 month; Healthcare contacts at >1 month

Study	**Munafo 2016[26]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=140)
Countries and setting	Conducted in USA; Setting: study was conducted by Sleep Data Holdings, LLC, a Joint Commission on Accreditation of Healthcare Organizations-accredited CPAP durable medical equipment provider in Southern California, USA.
Line of therapy	Not applicable
Duration of study	Intervention + follow up:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Moderate-severe: n/a
Subgroup analysis within study	Not applicable: n/a
Inclusion criteria	Inclusion criteria were age 18–80 years, CPAP-naïve, confirmed OSA (AHI 5–70/h) diagnosis based on polysomnography (PSG) or home sleep test. In addition, patients were required to have access to and be able to utilize, communication technology (text messaging, e-mail)

Exclusion criteria	Exclusion criteria were prominent central apnea (>20 %), claustrophobia, current use of mandibular repositioning device, or other OSA therapy. A simple randomization scheme was used to allocate patients to CPAP treatment plus SOC or TH.
Recruitment/selection of patients	n/a
Age, gender and ethnicity	Age - Mean (SD): TH group - 52.3(10.6); SOC group 50(11.7). Gender (M:F): 45/43. Ethnicity: TH group (Caucasian 72.1%; Hispanic 16.2%; AfricanAmerican-4.4%; Asian 7.4% other-0%); SOC - (Caucasian 82%; Hispanic 6.6%; AfricanAmerican-3.3%; Asian 6.6% other-1.6%)
Further population details	1. BMI: BMI of 30 kg/m^2 or more (TH- 33.5(8.2); SOC-32.9(7.1)). 2. Co-existing conditions: Not stated / Unclear 3. High risk occupation group: Not stated / Unclear 4. Sleepiness: ESS >9 (TH- 10.9(4.7); SOC-10.2(5.7)).
Indirectness of population	No indirectness
Interventions	(n=70) Intervention 1: Telemonitoring. Patients in the TH group were dispensed a CPAP device on Day 0, along with a pamphlet about U-Sleep, which was used to monitor adherence. U-Sleep is a secure, HIPAA-compliant, web-based application that is designed to receive CPAP device data and message patients and providers via text and/or e-mail based on a customizable set of rules. At the time of set up, patients were encouraged to log-in to the U-Sleep website from home so that they could follow their therapy. Sleep Data study staff were trained to set up and use the software, which was provided to patients at no charge. Initial patient contacts were triggered by ≥1 of five intervention points based on metrics (AHI, leak, therapy hours) After initial contact, subsequent contacts were in response to an automated message or based on clinical judgment. All TH patients received a final phone call on day 90. All patients were contacted at day 90 and asked to rate how well the follow-up program had met their expectations (on a scale from1 to 5) Duration 3 months. Concurrent medication/care: At baseline, all patients had a 1-h education session with arespiratory therapist (RRT) about OSA and its consequences, proper use and maintenance of the CPAP device and mask, and therapy expectations. All patients were provided with a fixed or auto CPAP device, heated humidifier, modems, and mask interface (S9 Elite, S9 AutoSet, H5i heated humidifier; ResMed Corp.). Patients saw an RRT at all clinic visits; telephone follow-up was performed by registered PSG technicians (RPSGT). Indirectness: No indirectness Further details: 1. Intervention type: Electronic (Telemonitoring). (n=70) Intervention 2: Telephone follow-up. Patients randomized to SOC were dispensed a CPAP device on Day 0, then contacted via phone on Days 1, 7, 14, 30, and 90 (Fig. 1). CPAP usage and efficacy data were tracked via the wireless modem attached to the CPAP machine. Modem data were accessed via ResMed's

	EasyCare Online (ECO) platform. Sleep Data SOC procedures include frequent phone calls and return clinic visits as necessary Duration 3 months. Concurrent medication/care: At baseline, all patients had a 1-h education session with arespiratory therapist (RRT) about OSA and its consequences, proper use and maintenance of the CPAP device and mask, and therapy expectations. All patients were provided with a fixed or auto CPAP device, heated humidifier, modems, and mask interface (S9 Elite, S9 AutoSet, H5i heated humidifier; ResMed Corp.). Patients saw an RRT at all clinic visits; telephone follow-up was performed by registered PSG technicians (RPSGT). Indirectness: No indirectness Further details: 1. Intervention type: Not applicable (Telephone follow up).
Funding	Other author(s) funded by industry (Medical writing assistance from Nicola Ryan, independent medical writer, was funded by ResMed Corp
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TELEMONITORING versus TELEPHONE FOLLOW-UP Protocol outcome 1: Patient preference at >1 month - Actual outcome for Moderate-severe: Adherence hours of use daily at 3 months; Group 1: mean 5.1 (SD 1.9); n=58, Group 2: mean 4.7 (SD 2.1); n=64 Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 12; Group 2 Number missing: 6	
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; ODI at >1 month; Minor adverse effects of Tx at >1 month; Driving outcomes at >1 month; Neurocognitive outcomes at >1 month; HbA1c at >1 month; CV events at >1 month; Systolic BP at >1 month; Healthcare contacts at >1 month

Study	**Pepin 2019[36]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=306)
Countries and setting	Conducted in France; Setting: Multicetre study. 23 centres were recruited. All centres were sleep sleep units with facilities for diagnosis, treatment and follow up of OSA and had worked with professional home care

	providers trained in CPAP initiating and follow up.
Line of therapy	Not applicable
Duration of study	Intervention + follow up:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Severe: n/a
Subgroup analysis within study	Not applicable: n/a
Inclusion criteria	Eligible patients were aged from 18-75, with severe OSA (apnoea-hypopnea index (AHI)>30events/h) on the basis of respiratory polygraphy or poly somnography. Patients should suffer from at least one cardiovascular disease or exhibit an elevated cardiovascular risk assessed by the 10 year risk of fatal cardiovascular event Systematic Coronary Risk evaluation calculation established specifically for European countries. Patients with a SystematicCoronarry Risk evaluaton risk>5% or in secondary prevention were included.
Exclusion criteria	Patients with central sleep apnea or heart failure with a left ventricular ejection fraction <40% were excluded
Recruitment/selection of patients	n/a
Age, gender and ethnicity	Age - Mean (range): 60.8(53.8; 66); Usual care - 61.8 (54.7; 66.1). Gender (M:F): 226/80. Ethnicity: not stated
Further population details	1. BMI: BMI of 30 kg/m^2 or more (Telemonitoring 32.4(29.6; 36.5); Usual care 31.4 (28.1; 35.2). 2. Co-existing conditions: T2DM (Telemonitoring (20(12.9); Usual care18 (12.2)). 3. High risk occupation group: Not stated / Unclear 4. Sleepiness: ESS >9 (Telemonitoring 9(5;13); Usual care 9(5; 14)).
Indirectness of population	No indirectness
Interventions	(n=157) Intervention 1: Telemonitoring. Multimodal telemonitoring included systolic and diastolic HBP and physical activity recorded by connected devices. This assessment of individual risk was associated with CPAP telemonitoring providing adherence, leaks and residual events. Symptoms and quality of life were recorded via electronic questionnaires to be filled by patients. Patients benefited from a demonstration of how to use the remote home telemonitoring equipment and an explanation of why monitoring psychological variables is relevant for their care. Concerning HBP recommendations, patients had to perform three measurements in the morning and the evening for 3 consecutive days in both groups. One minute was required between each measurement and the patient had to stay sedentary before and during the measurements. Duration 6 months. Concurrent medication/care: The patients were treated by auto-CPAP with a pressure

	window between 6 and 14 cm H2O. Both usual care and remote multimodal telemonitoring arms received the same 1-h CPAP initiating educational program Indirectness: No indirectness Further details: 1. Intervention type: Electronic (multimodal telemonitoring). (n=149) Intervention 2: In person follow-up. In person follow up (not much detail) Duration 6 months. Concurrent medication/care: The patients were treated by auto-CPAP with a pressure window between 6 and 14 cm H2O. Both usual care and remote multimodal telemonitoring arms received the same 1-h CPAP initiating educational program Indirectness: No indirectness Further details: 1. Intervention type: Physical (in person follow up).
Funding	Equipment / drugs provided by industry (The authors have reported to CHEST the following: J.-L.P. and R.T. report grants from Philips, Resmed, Fisher and Paykel, Foundation de la recherche medicale, Direction dela recherche Clinique du CHU De Grenoble, Fond de donation "Agirpour les maladies chroniques"; and personal fees from Perimetre, Philips, Fisher and Paykel RESMED, Astra-Zeneka, SEFAM, Agiradom, ELIA, and Teva, outside the submitted work.

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TELEMONITORING versus IN PERSON FOLLOW-UP

Protocol outcome 1: Quality of life at >1 month
- Actual outcome for Severe: SF12-Physical at 6 months; Group 1: mean 45.3 (SD 5.3); n=117, Group 2: mean 44.1 (SD 5.4); n=122
Risk of bias: All domain - Very high, Selection - Low, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 40; Group 2 Number missing: 27
- Actual outcome for Severe: SF12-Mental at 6 months; Group 1: mean 43.9 (SD 4.4); n=117, Group 2: mean 43.6 (SD 4.9); n=122
Risk of bias: All domain - Very high, Selection - Low, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 40; Group 2 Number missing: 27

Protocol outcome 2: Patient preference at >1 month
- Actual outcome for Severe: adherence at 6 months; Group 1: mean 5.28 (SD 2.23); n=117, Group 2: mean 4.75 (SD 2.5); n=122
Risk of bias: All domain - Very high, Selection - Low, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 40; Group 2 Number missing: 27

Protocol outcome 3: Systolic BP at >1 month - Actual outcome for Severe: Sleepiness ESS (0-24) at 6 months; Group 1: mean 4.58 (SD 3.88); n=117, Group 2: mean 6.05 (SD 4.07); n=122 Risk of bias: All domain - Very high, Selection - Low, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 40; Group 2 Number missing: 27 - Actual outcome for Severe: Systolic blood pressure difference - (6 months and baseline) morning at 6 months; Group 1: mean 130.98 (SD 18.47); n=117, Group 2: mean 130.06 (SD 17.53); n=122 Risk of bias: All domain - Very high, Selection - Low, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 40; Group 2 Number missing: 27	
Protocol outcomes not reported by the study	Mortality at >1 month; Sleepiness score at >1 month; AHI/RDI at >1 month; ODI at >1 month; Minor adverse effects of Tx at >1 month; Driving outcomes at >1 month; Neurocognitive outcomes at >1 month; HbA1c at >1 month; CV events at >1 month; Healthcare contacts at >1 month

Study	**Stepnowsky 2007[40]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=45)
Countries and setting	Conducted in USA; Setting: Participants were patients at the Veterans Affairs San Diego Healthcare System (VASDHS)
Line of therapy	Not applicable
Duration of study	Intervention + follow up:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Moderate-severe: n/a
Subgroup analysis within study	Not applicable: n/a
Inclusion criteria	diagnosis of moderate-to-severe OSA, defined as an Apnea-Hypopnea Index (AHI) ≥ 15 events per hour; naive to CPAP therapy; stable sleep environment (operationally defined as a permanent address, requisite for wireless monitoring); and at least 18 years of age. An AHI of ≥15 was chosen in an effort to be consistent with current OSA guidelines and practice parameters
Exclusion criteria	Patients were excluded from the study if they met any one of the following criteria: allergies or sensitivity to the mask or mask material; previous use of any other PAP device (eg, bi-level PAP, auto-adjusting PAP);

	current use of prescribed supplemental oxygen; or significant comorbid medical conditions that would prevent the patient from completing the protocol. Significant comorbidities were defined as any medical or mental health condition that could interfere with the daily use of CPAP. Additionally, patients were excluded if they lived in a geographically unsuitable region (ie, outside of the wireless network coverage area). A total of 91 patients at the VASDHS Sleep Clinic either signed or gave verbal consent to be contacted so they could learn more about the study. From these 91 patients, 46 were either were not interested in study participation or did not satisfy the inclusion and exclusion criteria
Recruitment/selection of patients	n/a
Age, gender and ethnicity	Age - Mean (SD): TCC - 60(10.8); UCC - 58(13.7). Gender (M:F): overall 98 % male. Ethnicity: not stated
Further population details	1. BMI: BMI of 30 kg/m^2 or more (total- 32.8; TCC - 33.3(4.9); 30.5(5.1)). 2. Co-existing conditions: Not applicable 3. High risk occupation group: Not stated / Unclear 4. Sleepiness: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=24) Intervention 1: Combined strategies. Telemonitored clinical care group. (Telemonitoring and in person follow up) The essence of the TCC intervention is the ability to tele monitor compliance and efficacy data for each patient on a daily basis from the first day of treatment and to act on those data collaboratively, and in partnership, with the patient. Collaborative management refers to the joint decision making and partnership between provider and patient and is characterized by communication, negotiation, and consideration of important patient factors and preferences. Patients in this group had their objective flow generator data monitored as frequently as needed per specified clinical pathways throughout the active 2-month treatment period. The frequency and nature of the clinical interactions depended on both the objectively measured nightly data values and subjective patient reports. Duration 2 months. Concurrent medication/care: Both groups of patients received the monitoring device and were followed for an intervention period of 2 months. Each participant was provided with an AutoSet Spirit flow generator unit (ResMed Corp, Poway, CA) set to fixed-mode pressure, which was equipped with the HumidAire 2i heated humidifier (ResMed Corp, Poway, CA). Each participant was provided a compatible nasal or full-face mask; nasal pillows were not used in this study. Indirectness: No indirectness Further details: 1. Intervention type: Not applicable (Combined - Telemonitoring and in person follow up). (n=21) Intervention 2: In person follow-up. Usual clinical care group. In person follow up. Patients randomized to UCC were treated according to the prevailing standard of care for OSA patients at the VASDHS CPAP

	Clinic. Usual care consisted of a 1-week telephone call after CPAP initiation and a 1-month in-office follow-up visit by CPAP clinic staff. Patients were encouraged to call the clinic any time they had a problem or concern. CPAP compliance and efficacy data were downloaded at the 1-month time point to help direct clinical management. Duration 2 months. Concurrent medication/care: Both groups of patients received the monitoring device and were followed for an intervention period of 2 months. Each participant was provided with an AutoSet Spirit flow generator unit (ResMed Corp, Poway, CA) set to fixed-mode pressure, which was equipped with the HumidAire 2i heated humidifier (ResMed Corp, Poway, CA). Each participant was provided a compatible nasal or full-face mask; nasal pillows were not used in this study. . Indirectness: No indirectness Further details: 1. Intervention type: Physical (In person follow up).
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINED STARTEGIES versus IN PERSON FOLLOW-UP

Protocol outcome 1: Quality of life at >1 month
- Actual outcome for Moderate-severe: Functional outcomes of sleep at 2 months; Group 1: mean 15.2 (SD 5); n=20, Group 2: mean 14.4 (SD 4.2); n=20; Comments: 32 item self report measure. (1poor; 5 excellent)
Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 4; Group 2 Number missing: 1
- Actual outcome for Moderate-severe: Sleepiness- Epworth at 2 months; Group 1: mean 9.2 (SD 6.6); n=20, Group 2: mean 9.9 (SD 5.2); n=20
Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 4; Group 2 Number missing: 1
- Actual outcome for Moderate-severe: Adherence all days at 2 months; Group 1: mean 4.1 (SD 1.8); n=20, Group 2: mean 2.8 (SD 2.2); n=20
Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 4; Group 2 Number missing: 1
- Actual outcome for Moderate-severe: Adherence days used at 2 months; Group 1: mean 5 (SD 1.8); n=20, Group 2: mean 3.8 (SD 2.3); n=20
Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 4; Group 2 Number missing: 1
- Actual outcome for Moderate-severe: % nights with CPAP use >4 hours at 2 months; Group 1: mean 52 percentage (SD 27); n=20, Group 2: mean 37 percentage (SD 24); n=20
Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 4; Group 2 Number missing: 1

Protocol outcome 2: AHI/RDI at >1 month - Actual outcome for Moderate-severe: AHI at 2 months; Group 1: mean 7.9 (SD 4.1); n=20, Group 2: mean 5 (SD 4); n=20 Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 4; Group 2 Number missing: 1 - Actual outcome for Moderate-severe: AHI change at 2 months; Group 1: mean 38.1 (SD 18.4); n=20, Group 2: mean 32.2 (SD 14.8); n=20 Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 4; Group 2 Number missing: 1	
Protocol outcomes not reported by the study	Mortality at >1 month; Sleepiness score at >1 month; ODI at >1 month; Minor adverse effects of Tx at >1 month; Driving outcomes at >1 month; Neurocognitive outcomes at >1 month; Patient preference at >1 month; HbA1c at >1 month; CV events at >1 month; Systolic BP at >1 month; Healthcare contacts at >1 month

Study	**Turino 2017[42]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=100)
Countries and setting	Conducted in Spain; Setting: St Maria Hospital (Lleida, Spain)
Line of therapy	Not applicable
Duration of study	Intervention + follow up:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Moderate-severe: n/a
Subgroup analysis within study	Not applicable: n/a
Inclusion criteria	Included adult patients (>18 years) with newly diagnosed OSA requiring treatment with CPAP (AHI >15 events·h−1). Assuming an α risk of 0.05 and a β risk of 0.2 in a two-sided test, a sample size of 49 subjects in each group was needed to detect differences ⩾1 h in CPAP treatment compliance. A common standard deviation of 1.75 was assumed. Given the high motivation of both professionals and patients to be involved, no dropouts were anticipated and thus a total of 100 patients were planned to be recruited
Exclusion criteria	Patients with impaired lung function (COPD-OSAHS overlap syndrome, obesity hypoventilation and restrictive disorders), severe heart failure, psychiatric disorders, periodic leg movements, pregnancy, other dysomnias or parasomnias, and/or a history of previous CPAP treatment were excluded.

Recruitment/selection of patients	n/a
Age, gender and ethnicity	Age - Mean (SD): Telemedicine 56 (13); Standard care 54(12). Gender (M:F): 77/23. Ethnicity: stated
Further population details	1. BMI: BMI of 30 kg/m^2 or more (Telemedicine 35 (7); Standard care 35 (7)). 2. Co-existing conditions: Not stated / Unclear 3. High risk occupation group: Not stated / Unclear 4. Sleepiness: ESS >9 (Telemedicine 9(5); Standard care 10(4)).
Indirectness of population	No indirectness
Interventions	(n=52) Intervention 1: Combined strategies. In the telemonitoring group, patients were also fitted with a mask and given a CPAP device (AirSense 10) and a leaflet explaining how to use it, and received the same training sessions from the same personnel as in the standard care arm. Each CPAP device given to patients in this group was equipped with mobile 2G (GSM/GPRS) technology capable of sending daily information on CPAP adherence, CPAP pressures, mask leak and residual respiratory events to the MyOSA–Oxigen Salud web database (www.oxigensalud.com) Automatic alarms for the provider were generated in case of mask leak >30 L·min−1 for >30% of the night or usage of <4 h·night−1 on two consecutive nights. In case of alarm, the pulmonary specialist medical officer of the CPAP provider contacted the patient, providing case-by-case problem solving. This included suggestions about how to minimise symptoms (dry mouth, mask issues, discomfort with the device), specific interventions to improve compliance (mask changing, chin strap, pressure or humidifier settings, saline nasal sprays) and support for the patient in the use of CPAP. Duration 3 months. Concurrent medication/care: n/a Indirectness: No indirectness Further details: 1. Intervention type: Electronic (Telemonitoring + in person follow up). (n=48) Intervention 2: In person follow-up. Patients randomised to standard care were fitted with a mask and given a CPAP device (AirSense 10; ResMed, Martinsried, Germany) and a leaflet explaining how to use it. A short instruction session on how to use a CPAP device was also given to patients and partners in the sleep unit by a trained nurse with experience in the follow-up of CPAP-treated patients. This included a practical demonstration of how to put on the mask, and the correct management and cleaning of the tubes, masks and humidifier. Information on how to turn the CPAP device on and off was provided by the homecare provider at the time of machine delivery. All patients were visited after 1 month of treatment by the specialist nurse at the sleep unit. Information about CPAP pressure, compliance and adherence (use of CPAP for ⩾4 h·day−1), residual respiratory events and leaks were downloaded from the device. CPAP-related side-effects, CPAP machine care and maintenance (changes of mask, tubes and humidifier), and the number of additional visits and calls were recorded by the nurse Duration 3 months. Concurrent medication/care: n/a

	. Indirectness: No indirectness Further details: 1. Intervention type:
Funding	Equipment / drugs provided by industry (This study was partially funded by ResMed Spain (Spain) and ALLER (Spain)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINED STRATEGIES versus IN PERSON FOLLOW-UP

Protocol outcome 1: Quality of life at >1 month
- Actual outcome for Moderate-severe: EQ5D change at 3 months; Group 1: mean 0.057 (SD 0.19); n=52, Group 2: mean 0.06 (SD 0.17); n=48
Risk of bias: All domain - Very high, Selection - High, Blinding - Very 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: Patient preference at >1 month
- Actual outcome for Moderate-severe: Adherence h/night at 3 months; Group 1: mean 5.1 (SD 2.1); n=52, Group 2: mean 4.9 (SD 2.2); n=48
Risk of bias: All domain - Very high, Selection - High, Blinding - Very 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: Systolic BP at >1 month
- Actual outcome for Moderate-severe: Systolic blood pressure at 3 months; Group 1: mean -4.3 mmHg (SD 14.8); n=52, Group 2: mean -3.1 mmHg (SD 18); n=48
Risk of bias: All domain - Very high, Selection - High, Blinding - Very 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 outcomes not reported by the study	Mortality at >1 month; Sleepiness score at >1 month; AHI/RDI at >1 month; ODI at >1 month; Minor adverse effects of Tx at >1 month; Driving outcomes at >1 month; Neurocognitive outcomes at >1 month; HbA1c at >1 month; CV events at >1 month; Healthcare contacts at >1 month

Appendix E: Forest plots

E.1 Telemonitoring and in person follow up vs in person follow up – severe OSAHS

Figure 2: Systolic blood pressure – morning

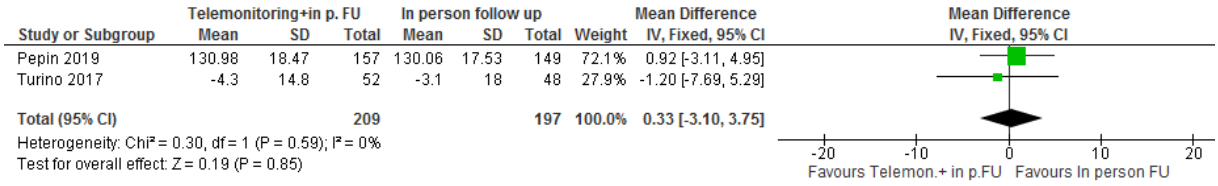


Figure 3: Adherence – hours per day

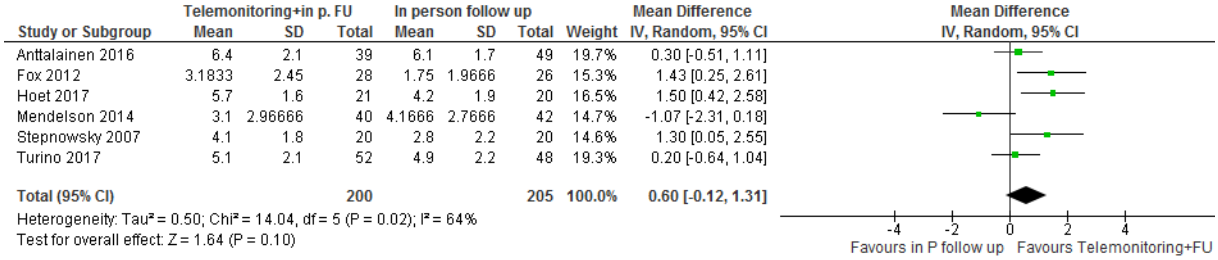


Figure 4: Adherence – on nights PAP used – hours per day

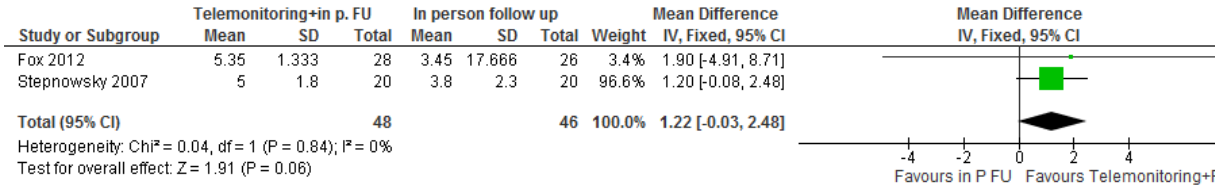


Figure 5: Mean % nights CPAP use >4 hours (adherence)

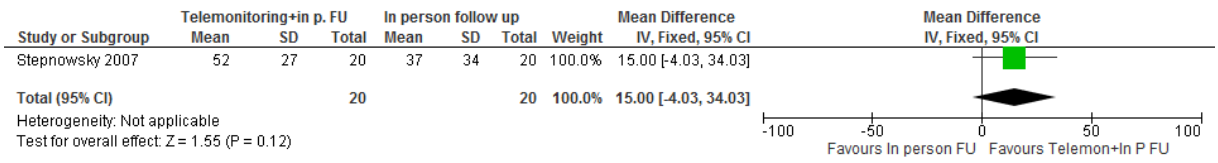


Figure 6: Mean % days CPAP used (adherence)

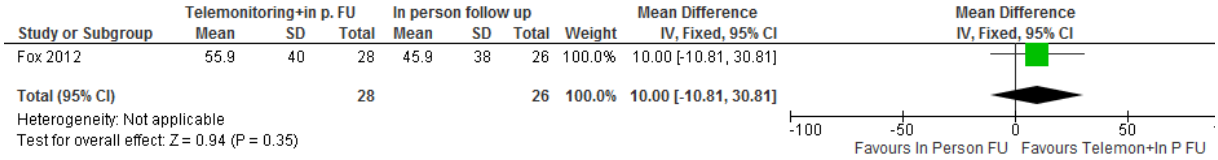


Figure 7: Quality of life – physical composite (change score), 0-100, higher is better

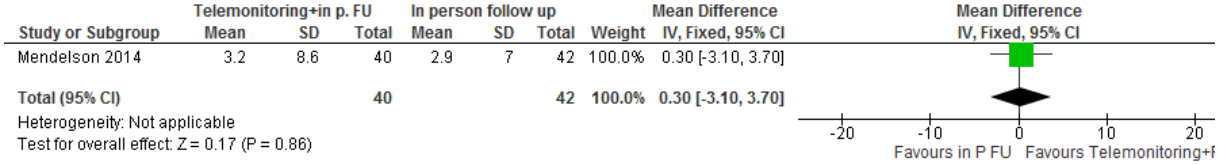


Figure 8: Quality of life – mental composite (change score), 0-100, higher is better

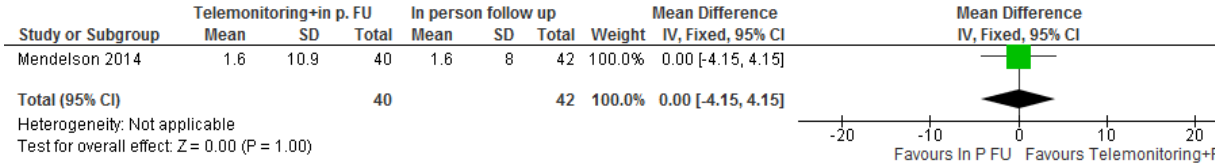


Figure 9: Quality of life – EQ5D, 0-1, higher is better

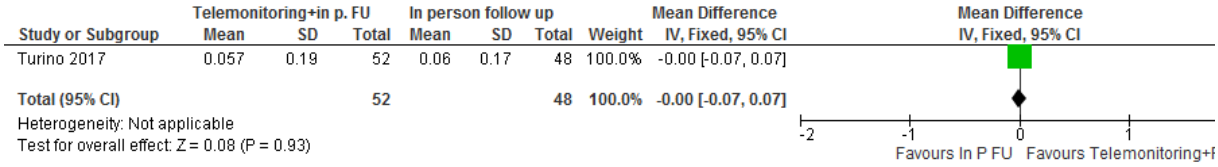


Figure 10: Quality of life – GHQ12, 0-12, higher is worse

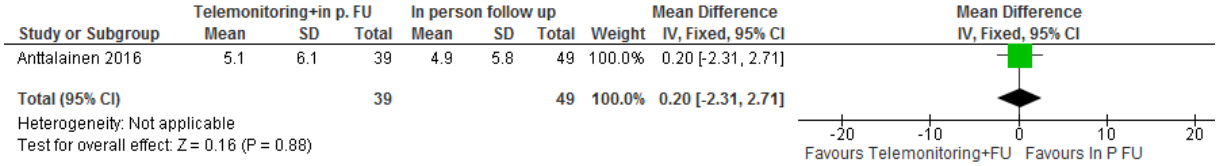


Figure 11: Sleepiness (ESS), 0-24, higher is worse

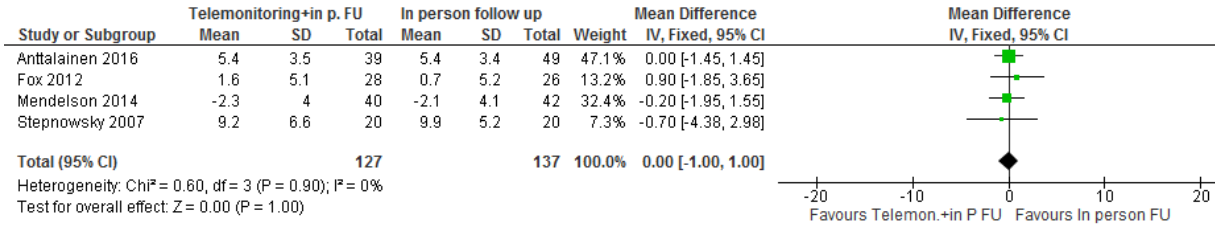


Figure 12: Apnoea-hypopnea index (AHI) events per hour (lower is better)

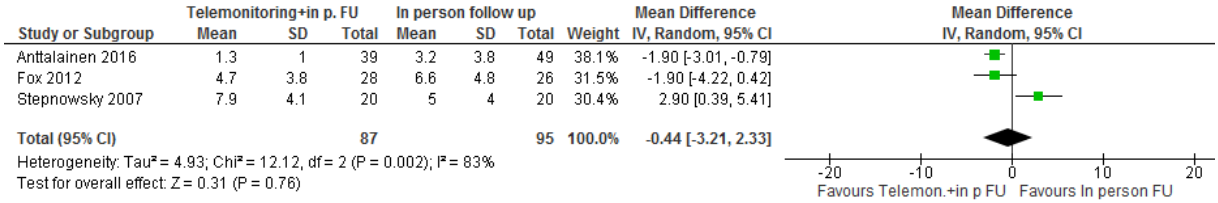
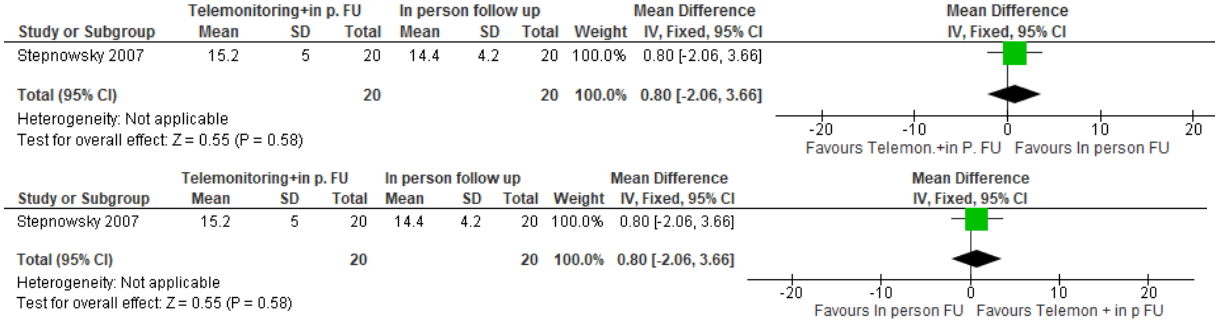


Figure 13: Functional outcome of sleep, 5-20, higher is better



E.2 Telemonitoring and phone follow up vs phone follow up – severe OSAHS

Figure 14: Adherence – hours per day

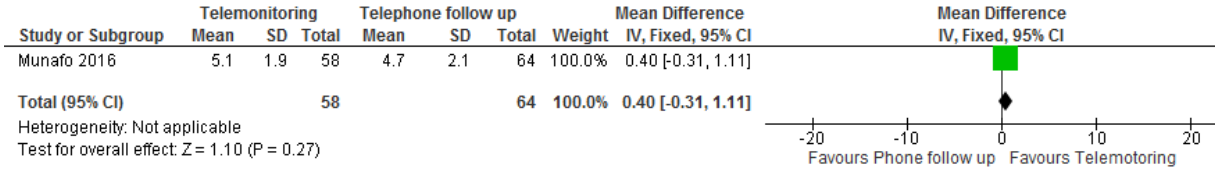
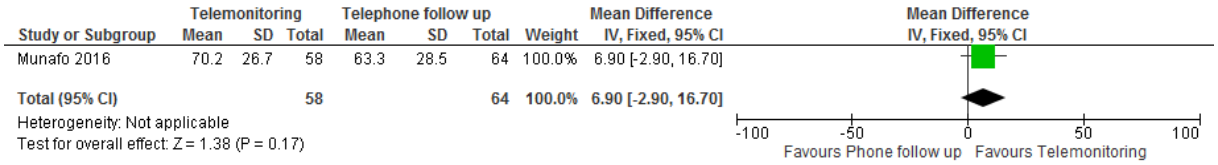


Figure 15: Days CPAP used >4 hours, % patients



E.3 Multimodal telemonitoring vs usual care – severe OSAHS

Figure 16: Adherence (range of scores), 0-8, higher is better

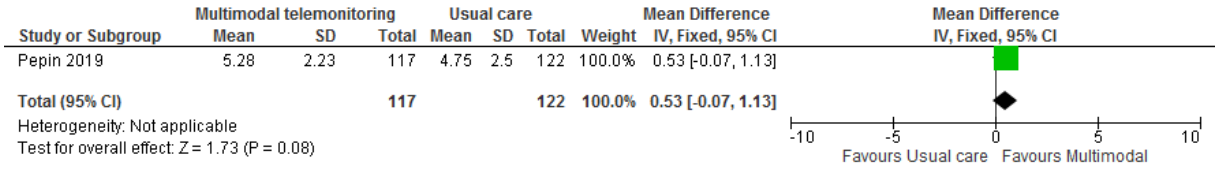


Figure 17: Sleepiness – Epworth scale (ESS), 0-24, higher is worse

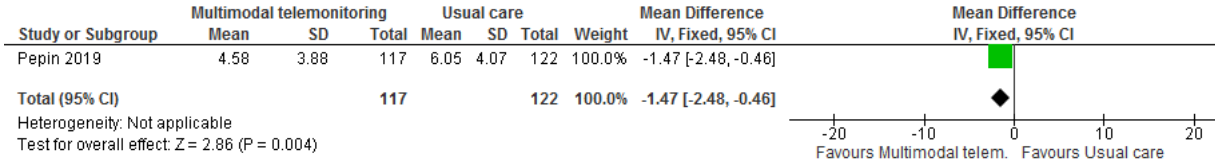


Figure 18: Quality of life –SF 12 Physical, 0-100, higher is better

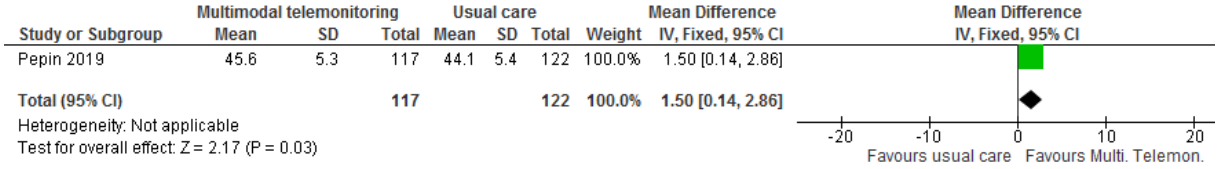


Figure 19: Quality of life – SF 12 mental, 0-100, higher is better

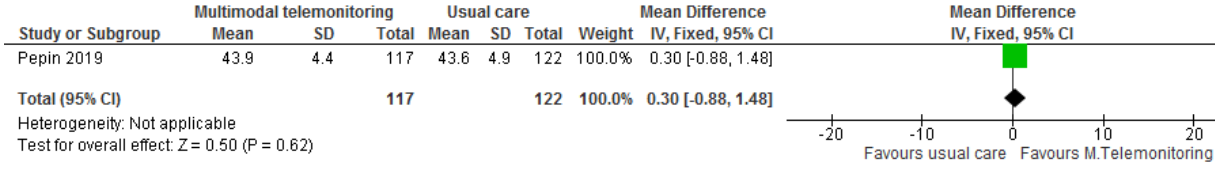
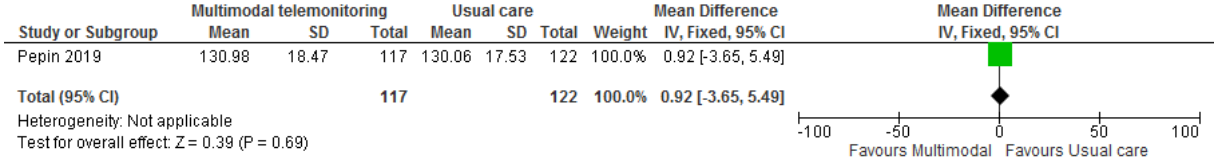


Figure 20: Systolic blood pressure



E.4 Telemonitoring and tele visits vs In person follow up – severe OSAHS

Figure 21: Adherence Hours/day

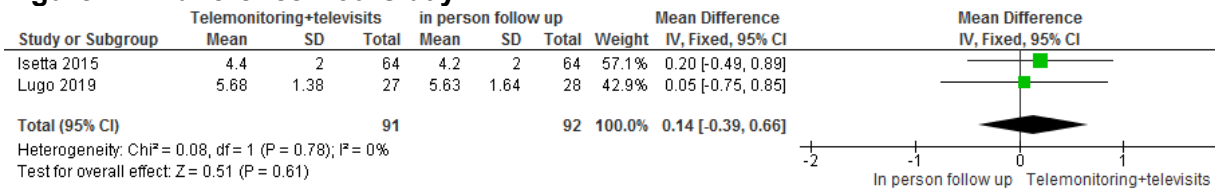
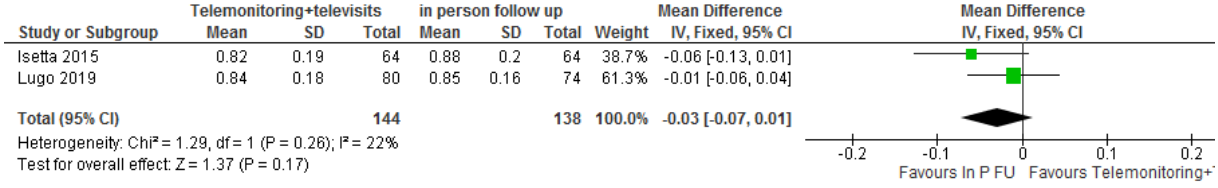


Figure 22: Quality of life – EQ5D [1], 0-1, lower is worse



1. Lugo study reports SD in telemonitoring group as 18, however this appears to be a typo so 0.18 has been used for our analysis

Figure 23: Quality of life – FoSQ 5-20, lower is worse

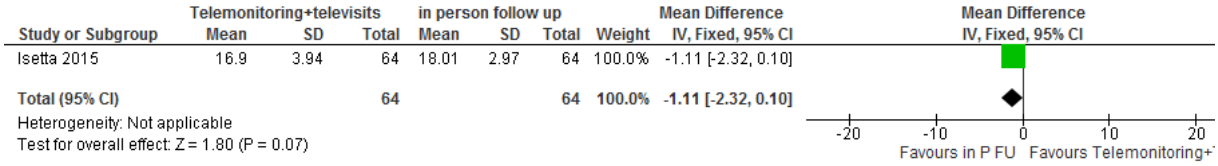


Figure 24: Sleepiness – Epworth scale (ESS), 0-24, higher is worse

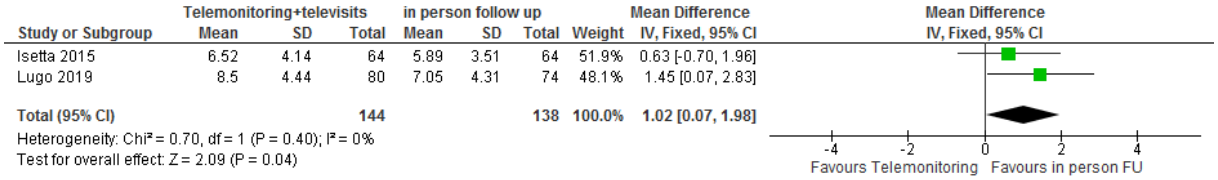


Figure 25: EQ5D – VAS, 0-100, lower is worse

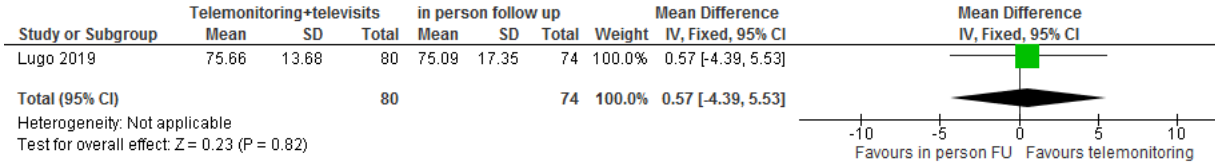


Figure 26: number of OSA related GP visits

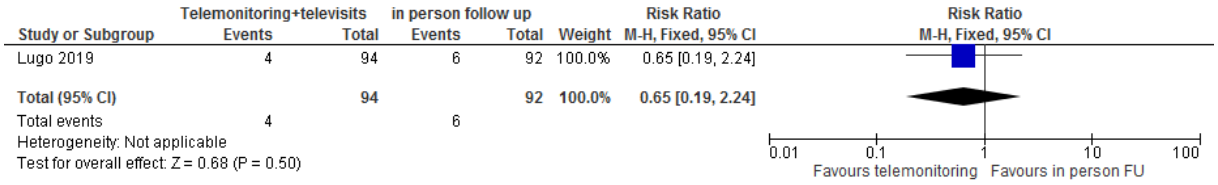
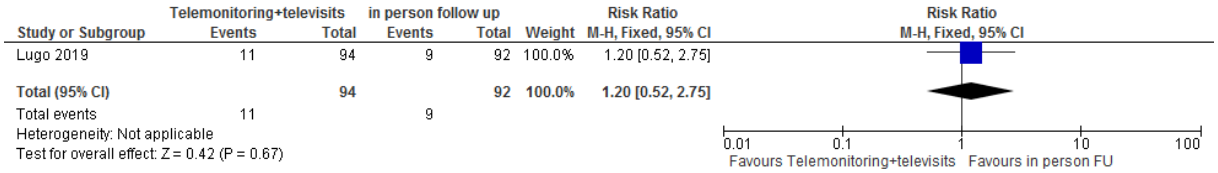


Figure 27: number of OSA related specialist visits



Appendix F: GRADE tables

Table 13: Telemonitoring and in person follow up versus in person follow up – Severe OSAHS

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Telemonitoring + in person follow up	Control	Relative (95% CI)	Absolute		
Systolic blood pressure - morning (follow-up 3-6 months; Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	none	none	209	197	-	MD 0.33 higher (3.1 lower to 3.75 higher)	⊕⊕OO LOW	IMPORTANT
Adherence- h per day (follow-up 3 - 12 months; range of scores: 0-8; Better indicated by higher values)												
6	randomised trials	very serious[1]	very serious[3]	serious indirectness[4]	serious[2]	none	200	205	-	MD 0.6 higher (0.12 lower to 1.31 higher)	⊕OOO VERY LOW	IMPORTANT
Adherence-on nights PAP used(h per day) (follow-up mean 2-3 months; range of scores: 0-8; Better indicated by higher values)												
2	randomised trials	very serious[1]	no serious inconsistency	serious indirectness[4]	serious[2]	none	48	46	-	MD 1.22 higher (0.03 lower to 2.48 higher)	⊕OOO VERY LOW	IMPORTANT
Mean % nights CPAP use >4 hours (follow-up mean 2 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious indirectness[4]	serious[2]	none	20	20	-	MD 15 higher (4.03 lower to 34.03 higher)	⊕OOO VERY LOW	IMPORTANT

Mean % days used (range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[4]	no serious inconsistency	serious indirectness[4]	serious[2]	none	28	26	-	MD 10 higher (10.81 lower to 30.81 higher)	⊕OOO VERY LOW	IMPORTANT
Quality of life (Physical composite)difference (follow-up mean 4 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious indirectness[4]	very serious[2]	none	40	42	-	MD 0.3 higher (3.1 lower to 3.7 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (mental) difference (follow-up mean 4 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious indirectness[4]	very serious[2]	none	40	42	-	MD 0 higher (4.15 lower to 4.15 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life EQ5D (follow-up mean 3 months; range of scores: 0-1; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious indirectness[4]	very serious[2]	none	52	48	-	MD 0 higher (0.07 lower to 0.07 higher)	⊕OOO VERY LOW	CRITICAL
Quality of Life-GHQ12 (follow-up mean 12 months; range of scores: 0-12; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious indirectness[4]	very serious[2]	none	39	49	-	MD 0.2 higher (2.31 lower to 2.71 higher)	⊕OOO VERY LOW	CRITICAL
Sleepiness Epworth (ESS) (follow-up mean 2-12; range of scores: 0-24; Better indicated by lower values)												
4	randomised trials	very serious[1]	no serious inconsistency	serious indirectness[4]	no serious imprecision	none	127	137	-	MD 0 higher (1 lower to 1 higher)	⊕OOO VERY LOW	IMPORTANT
Apnoea Hypopnea index (AHI) events/hour (follow-up mean 3-12 months; Better indicated by lower values)												

3	randomised trials	very serious[1]	very serious[3]	serious indirectness[4]	very serious[2]	none	87	95	-	MD 0.44 lower (3.21 lower to 2.33 higher)	⊕OOO VERY LOW	IMPORTANT
Functional outcome of sleep A. questionnaire (follow-up mean 2 months; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious indirectness[4]	very serious[2]	none	20	20	-	MD 0.8 higher (2.06 lower to 3.66 higher)	⊕OOO VERY LOW	CRITICAL
Mortality												
Not reported												CRITICAL

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs, MID for machine usage (adherence)-1 hour; MID for Systolic and Diastolic BP – 5 mm hg. For mean % of nights that the CPAP was used >4 hours outcome, clinically important difference was considered to be 10 % or 1 hour.. Established MIDs for SF-36 physical/mental- 2/3; ESS- 2.5; EQ5D- 0.03; FOSQ- 2GRADE default MIDs (0.5XSD) used for all other continuous outcomes.

3 Downgraded by 1 or 2 increments because: The point estimate varies widely across studies, unexplained by subgroup analysis. The confidence intervals across studies show minimal or no overlap, I2=50% unexplained by subgroup analysis. Subgroup analyses were tested for BMI < or >30 kg/m^2, ESS < or >9, coexisting conditions, high risk occupation and type of treatment. Random effects analysis used.

4 Downgraded by 1 or 2 increments because the majority of the evidence included an indirect or very indirect population respectively. The study included a mixed OSHAS severity population based on mean baseline AHI.

Table 14: Telemonitoring versus phone follow up – Severe OSAHS

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Telemonitoring**	**Phone follow up**	**Relative (95% CI)**	**Absolute**		
Adherence hours per day (follow-up mean 3 months; range of scores: 0-8; Better indicated by higher values)												

1	randomised trials	very serious[1]	no serious inconsistency	serious indirectness[4]	serious[2]	None	58	64	-	MD 0.4 higher (0.31 lower to 1.11 higher)	⊕OOO VERY LOW	IMPORTANT
Days CPAP used >4 hours (follow-up mean 3 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious indirectness[4]	serious[2]	None	58	64	-	MD 6.9 higher (2.9 lower to 16.70 higher)	⊕OOO VERY LOW	IMPORTANT
Mortality												
Not reported												CRITICAL

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs. MID for machine usage (adherence)-1 hour; MID,For mean % of nights that the CPAP was used >4 hours outcome, clinically important difference was considered to be 10 % or 1 hourGRADE default MID (0.5XSD) used for all other continuous outcomes.

3 Downgraded by 1 or 2 increments because the majority of the evidence included an indirect or very indirect population respectively. The study included a mixed OSHAS severity population based on mean baseline AHI.

Table 15: Multimodal telemonitoring versus usual care – severe OSAHS

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Multimodal telemonitoring**	**Usual care**	**Relative (95% CI)**	**Absolute**		
Adherence (follow-up mean 6 months; range of scores: 0-8; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	None	117	122	-	MD 0.53 higher (0.07 lower to 1.13 higher)	⊕OOO VERY LOW	IMPORTANT
Sleepiness ESS (follow-up mean 6 months; range of scores: 0-24; Better indicated by lower values)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	None	117	122	-	MD 1.47 lower (2.48 to 0.46 lower)	⊕⊕OO LOW	IMPORTANT
Quality of life-SF12-Physical (follow-up mean 6 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	None	117	122	-	MD 1.5 higher (0.14 to 2.86 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life-SF12 - Mental (follow-up mean 6 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	None	117	122	-	MD 0.3 higher (0.88 lower to 1.48 higher)	⊕⊕OO LOW	CRITICAL
Systolic blood pressure (follow-up mean 6 months; Better indicated by lower values)												
	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	None	117	122	-	MD 0.92 higher (3.65 lower to 5.49 higher)	⊕OOO VERY LOW	IMPORTANT
Mortality												
Not reported												CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs; MID for machine usage (adherence)-1 hour; MID for Systolic and Diastolic BP – 5 mm hg. Established MIDs for SF-36 physical/mental- 2/3; ESS- 2.5; GRADE default MID (0.5XSD)used for all other continuous outcomes.

Table 16: Telemonitoring and tele visits versus in person follow up – severe OSAHS

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Telemonitoring+televisits	In person follow-up	Relative (95% CI)	Absolute		
Adherence h/day (follow-up range 3- 6 months; range of scores: 0-8; Better indicated by higher values)												
2	randomised trials	serious[1]	no serious inconsistency	Very Serious[3]	no serious imprecision	none	91	92	-	MD 014 higher (0.39 lower to 0.66 higher)	⊕OOO VERY LOW	IMPORTANT
EQ5D (follow-up range 3- 6 months; range of scores: 0-1; Better indicated by higher values)												
2	randomised trials	very serious[1]	no serious inconsistency	Very Serious[3]	serious[2]	none	144	138	-	MD 0.03 lower (0.7 lower to 0.01 higher)	⊕OOO VERY LOW	CRITICAL
FoSQ (follow-up mean 6 months; range of scores: 5-20; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	64	64	-	MD 1.11 lower (2.32 lower to 0.1 higher)	⊕⊕OO LOW	CRITICAL
Sleepiness ESS (follow-up range 3- 6 months; range of scores: 0-24; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	Very Serious[3]	no serious imprecision	none	144	138	-	MD 1.02 higher (0.07 lower to 1.98 higher)	⊕OOO VERY LOW	IMPORTANT
EQ5D -VAS (follow-up mean 3 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	Very Serious[3]	no serious imprecision	none	80	74		MD 0.57 higher (4.39 lower to 5.53 higher)	⊕OOO VERY LOW	CRITICAL
Number of OSA related GP visits (follow-up mean 3 months; Better indicated by lower values)												

1	randomised trials	very serious[1]	no serious inconsistency	Very Serious[3]	Very serious[2]	none	4/94 (4.3%)	6.5%	RR 0.65 (0.19 to 2.24)	23 fewer per 1000 (from 53 fewer to 81 more)	⊕OOO VERY LOW	IMPORTANT
Number of OSA related specialist visits (follow-up mean 3 months; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	Very Serious[3]	Very serious[2]	none	11/94 (11.7%)	9.86%	RR 1.20 (0.52 to 2.75)	20 more per 1000 (from 47 fewer to 173 more)	⊕OOO VERY LOW	IMPORTANT
Mortality												
Not reported												CRITICAL

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

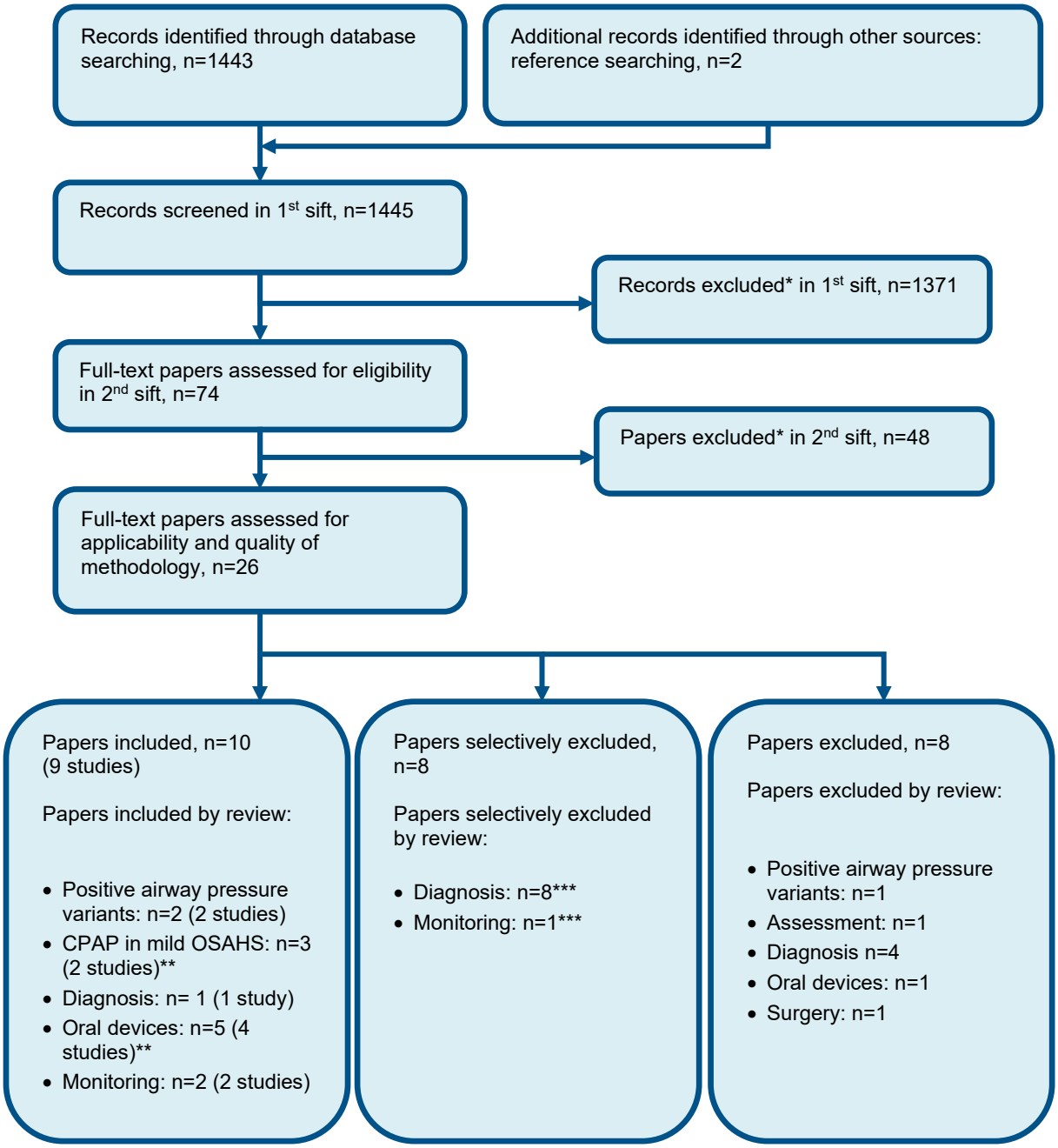
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs. MID for machine usage (adherence)-1 hour.Established MIDs for ESS- 2.5; EQ5D- 0.03; FOSQ- 2. GRADE default MID (0.5XSD)used for all other continous outcomes.

3 Downgraded by 1 or 2 increments because: The majority of the evidence included an indirect population of moderate to severe severity patients based on the AHI of included population (downgrade by one increment) or a very indirect population (downgrade by two increments)

4 Baseline values differed in the Lugo study for this outcome. While the in person follow up has a higher (better) end score the telemonitoring group had a better change score of 0.04 compared to 0.01 in the control group.

Appendix G: Health economic evidence selection

Figure 28: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language
** Two studies (in three papers) were included for two different questions
*** One study was considered for two different questions

Appendix H: Health economic evidence tables

Study	Isetta 2015[19]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: Cost-utility analysis **Study design:** **Approach to analysis:** Within trial analysis (RCT) **Perspective:** Spanish provider perspective [(a)] **Follow-up**: 6 months **Treatment effect duration:**[(b)] 6 months **Discounting:** Costs = NR Outcomes = NR	**Population:** Patients requiring CPAP after an overnight sleep study.[(c)] **Cohort settings:** Mean: 49 N = 139 Drop out: 16 (11.5%) **Intervention 1:** Hospital-based follow-up Received standard face-to-face follow-up with visits at months 1, 3 and 6, and extra visits if needed. **Intervention 2:** Telemedicine-based follow-up Patients received their follow-up at home supported by website which included information about OSA and CPAP. Patients would also complete biweekly six-item questionnaire about their status, physical activity, sleep time, CPAP use and treatment side effects. Staff would monitor responses and	**Scenario 1: Total costs (mean per patient) including GP visits, emergency visits and medication:** Intervention 1: £117 Intervention 2: £127 Incremental (2−1): £10 (95% CI: NR; p=NR) **Scenario 2: Total costs (mean per patient) excluding GP visits, emergency visits and medication:** Intervention 1: £80 Intervention 2: £82 Incremental (2−1): £2 (95% CI: NR; p=NR) **Currency & cost year:** 2013 euros (presented here as 2013 UK pounds [(d)]) **Cost components incorporated:** Scenario 1 includes follow-up visit time (month 1, 3 and 6), mask changes, extra visits by physician or nurse, plus GP visits,	**QALYs (mean per patient):** Intervention 1: 0.0120 Intervention 2: 0.0108 Incremental (2−1): - 0.0012 (95% CI: -0.0500 to 0.0474 NR; p=NR)	**ICER (Intervention 2 versus Intervention 1) [(e)]:** Intervention 2 is dominated by intervention 1 in both costing scenarios.

	communicate with patients through the websites messaging tool. Skype calls were undertaken at months 1 and 3.	emergency visits and medications. Scenario 2 includes follow-up visit time, mask changes and extra visits only.		
Data sources				
Health outcomes: Health-related quality of life (EQ-5D) reported directly from patients **Quality-of-life weights:** EQ-5D tariff used is not explicitly stated, though a reference to the Spanish version of the EQ-5D is made. **Cost sources:** Unit costs calculated by the administrative departments of one of the participating hospitals.				
Comments				
Source of funding: Spanish Society of Pneumology and Thoracic Surgery **Limitations:** Table 4 lists the costing inputs which should sum to the total mean costs (table 5). However, the sum of the costs in table 4 does not equate to the total mean costs reported in the study in table 5 and the difference is too large to be due to rounding. This indicates either a summing error or lack of transparency of other costs which were incurred that have not been reported. The authors have included patient and provider costs, therefore the patient costs were deducted by the NGC to conform to the NICE reference case. Furthermore, the authors have included costs for GP visits, emergency visits and medications without providing clarity as to whether these costs were related to the patient's OSA or another condition. To overcome this limitation two costing scenarios have been reported by the NGC: scenario 1 includes these additional costs, scenario 2 excludes these costs. Another limitation of the study is that the authors state that for hospital-based follow-up visits were arranged at months 1, 3 and 6. For the telemedicine-based follow-up only the appointments at month 1 and 3 are explicitly stated. It is unclear whether a skype meeting also took place at 6 months.				
Overall applicability: Partially Applicable (f) **Overall quality:** Potentially serious limitations (g)				

Abbreviations: 95% CI= 95% confidence interval; CUA= cost–utility analysis; EQ-5D= Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER= incremental cost-effectiveness ratio; NGC=National Guideline Centre; NR= not reported; pa= probabilistic analysis; QALYs= quality-adjusted life years

(a) The study also presented patient costs therefore all costs and ICERs were recalculated to report a provider perspective only.

(b) It is unclear whether the telemedicine-based follow-up lasted for the whole 6 months – see limitations.

(c) It is unclear if the study included participants <18 years.

(d) Converted using 2013 purchasing power parities [30]. The within trial study lasted from 2011 to 2013, as the costs in individual years have not been reported, the UK costs in 2013 has been calculated.

(e) A probabilistic sensitivity analysis (PSA) has been conducted; however the analysis was completed on input parameters which included patient perspective costs. For this reason, the results of the PSA have not been reported here.

(f) Directly applicable / Partially applicable / Not applicable

(g) Minor limitations / Potentially serious limitations / Very serious limitations

Study	Turino 2017[42]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: Cost-utility analysis **Study design:** Within trial analysis (RCT) **Approach to analysis:** Mean costs and mean QALYs compared over the duration of the study period (3 months). **Perspective:** Spanish provider perspective **Follow-up**: 3 months **Treatment effect duration:** 3 months **Discounting:** Costs = NR Outcomes = NR	**Population:** Adult patients (18>) with newly diagnosed OSA (AHI>15events/hr) requiring treatment with CPAP. **Cohort settings:** Mean age: 54 N = 100 Drop out: NR **Intervention 1:** Standard Care (1) Patients are fitted with a mask, given a CPAP device and provided a leaflet on how to use it. A short instruction session is also provided to patients and their partners in the sleep unit by a trained nurse to demonstrate how put on the mask, correct management and cleaning of device. When machine is delivered to patients, advice on how to turn the device on and was given by the homecare provider. (2) All patients visited after 1 month of treatment by the specialist nurse at the sleep unit. Data on: CPAP pressure, compliance and adherence (CPAP use ≥4hrs/day), residual respiratory events and leaks. (3)Additional visits and calls where appropriate. **Intervention 2:** Telemonitoring	**Total costs (mean per patient):** Intervention 1: £170 Intervention 2: £125 Incremental (2−1): saves £45 (95% CI: NR) **Currency & cost year:** 2015 euros (presented here as 2015 UK pounds [(a)]) **Cost components incorporated:** Telemonitoring including 2G (GSM/GPRS) daily data transfer and alarm management, sleep unit visits and consultations, home visits and consultations and costs associated with changes in CPAP device components.	**QALYs (mean per patient) reported in study:** Intervention 1: 0.060 Intervention 2: 0.057 Incremental (2−1): -0.003 (95% CI: NR; p=NR) **QALYs (mean per patient) recalculated[(b)]:** Intervention 1: 0.015 Intervention 2: 0.014 Incremental (2−1): -0.001 (95% CI: NR; p=NR)	**ICER (Intervention 1 versus Intervention 2) using *study* reported QALYs:** £15,000 per QALY gained **ICER (Intervention 1 versus Intervention 2) using *recalculated* QALYs:** £45,000 per QALY gained **Analysis of uncertainty:** A deterministic sensitivity analysis was conducted which explored 25% and 50% increases in the CPAP provider costs. New costs / 25% / 50% 1 / £174 / £178 2 / £137 / £148 ICER (intervention 1 versus intervention 2) when provider costs are increased and *study QALYs* are used: 25% — £12,333 per QALY gained 50% — £10,000 per QALY gained ICER (intervention 1 versus intervention 2) when provider

	(1) Same as (1) in intervention 1. However in this instance, each CPAP device provided to patients was equipped with mobile 2G (GSM/GPRS) technology capable of sending daily information on: CPAP adherence, CPAP pressures, mask leak and residual respiratory events. (2) Data uploaded to a web database. Automatic alarms were generated in case of mask leak (>30L/min for more than 30% of night) or poor compliance (<4hr/night). In cases of alarm, specialist contacted patient to provide case-by-case problem solving.			costs are increased and *recalculated QALYs* are used: 25% £37,000 per QALY gained 50% £30,000 per QALY gained

Data sources

Health outcomes: Health-related quality of life (EQ-5D) reported directly from patients. **Quality-of-life weights:** EQ-5D tariff used not stated. **Cost sources:** Resource use from within RCT; costs reported as the mean costs incurred per patient for the trial duration (January and July 2015) by Catalan Institute of Health.

Comments

Source of funding: Partially funded by ResMed Spain and Associacio Lleidatana de Respiratori (ALLER). **Limitations:** A key limitation of this study is that it has not reported its method for deriving QALYs. Based on the explanations provided, it appears the authors have equated improvements in quality of life measured by the EQ-5D to improvements in QALYs which is methodologically incorrect i.e. a 0.003 higher EQ-5D at 3 months is not the same as a 0.003 gain in QALYs. Instead, to calculate the correct QALY gains over the three month period the EQ-5D gains must be multiplied by 0.25 or else an assumption must be stated about how long the difference would be sustained. Another limitation of the study is the short follow-up and it is unclear whether a longer time horizon would have indicated that the telemonitoring group have greater compliance and therefore improved health outcomes. **Other:** If the QALYs reported in the study are accepted as the true QALYs, standard care would be cost-effective when compared to telemonitoring at the £20,000 threshold. However, if the recalculated QALYs are used, then the new ICER would indicate that standard care is not cost-effective at that threshold.

Overall applicability:(c) Partially Applicable **Overall quality:**(d) Potentially Serious Limitations

Abbreviations: CPAP=Continuous positive airway pressure; EQ-5D= Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER= incremental cost-effectiveness ratio; NR= not reported; pa= probabilistic analysis; QALYs= quality-adjusted life years; RCT = Randomised control trial

(a) Converted using 2014 purchasing power parities [30]

(b) The authors have not clearly described their method of calculating QALYs, and based on their current explanation the authors may have overestimated the QALY gained. Further explanation is provided in the limitation section of the above table.

(c) Directly applicable / Partially applicable / Not applicable

(d) Minor limitations / Potentially serious limitations / Very serious limitations

Appendix I: Excluded studies

I.1 Excluded clinical studies

Table 17: Studies excluded from the clinical review

Study	Exclusion reason
Abreu 2013[1]	Abstract only
Chen 2020[4]	Systematic review- screened for relevant references.
Delanote 2018[5]	Inappropriate intervention
DeMolles 2004[6]	Inappropriate intervention
Fields 2016[9]	Inappropriate intervention
Frasnelli 2016[11]	Inappropriate study design – non randomised study without adequate adjustment for confounders.
Gong 2018[12]	Systematic review references checked
Hanger 2018[13]	Included in adherence review
Hood 2013[15]	Inappropriate intervention -self monitoring or an attention-control (AC) condition.
Hwang 2018[16]	Inappropriate intervention. Study included in the adherence evidence review.
Isetta 2014[18]	Inappropriate intervention
Isetta 2014[17]	Abstract only
Isetta 2017[20]	Inappropriate study design – non comparative study.
Kotzian 2018[22]	Protocol only
Kotzian 2019[21]	Inappropriate intervention- included in adherence review
Mendelson 2013[24]	Abstract only
Murphie 2019[27]	Systematic review references checked
Nilius 2012[29]	Inappropriate intervention – included in adherence review
Palmer 2004[31]	Inappropriate intervention
Parikh 2011[32]	Inappropriate study design – non randomised study without adequate adjustment for confounders.
Peach 2003[34]	Abstract only
Peach 2006[33]	Abstract only
Pengo 2018[35]	Inappropriate intervention.
Pepin 2014[37]	Abstract only
Schoch 2019[38]	Inappropriate intervention- included in adherence review
Sparrow 2010[39]	Inappropriate intervention

Study	Exclusion reason
Taylor 2003[41]	Thesis unavailable
Wozniak 2014[43]	Systematic review references checked

I.2 Excluded health economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2003 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic evaluation protocol for more details.

Table 18: Studies excluded from the health economic review

Reference	Reason for exclusion
Andreu 2012[2]	This study was assessed as partially applicable (cost analysis from Spanish perspective – no health outcomes); however, given that two studies were included, which evaluated both costs and QALYs, this study was selectively excluded.