National Institute for Health and Care Excellence

Draft

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

Economic analyses

NICE guideline <number>

Economic analysis report

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Contents

1 Questions

Modelling was conducted in three areas:

- Comparison of different types of CPAP
- Comparison of different treatments for people with mild OSAHS
- Comparison of different diagnostic pathways for OSAHS.

In this section, we describe these analyses along with some of the key base case assumptions and top-level model parameters. However, a detailed description of methods, data and assumptions is explained in section 2.

1.1 Comparison of different types of CPAP

Review questions	**What is the comparative clinical and cost effectiveness of different types of positive airway pressure devices (for example, fixed-pressure CPAP, variable-pressure CPAP, bi-level positive airway pressure or other modes of non-invasive ventilation) for managing obstructive sleep apnoea/hypopnoea syndrome, obesity hypoventilation syndrome and overlap syndrome?** **What is clinically and cost-effective strategy for monitoring OSAHS/OHS/overlap syndrome?**
Population	Adults with mild OSAHS Adults with moderate OSAHS
Interventions and comparators	A. Fixed-level CPAP with auto-titration B. Fixed-level CPAP with telemonitoring C. Fixed-level CPAP with telemonitoring in first year D. Auto-CPAP E. Auto-CPAP with telemonitoring
Perspective	NHS and personal social services
Outcomes	N/A
Type of analysis	Cost comparison

1.1.1 Overview of methods

- Health outcomes
  - We assumed no difference in patient outcomes between strategies.
- Costs
  - The cost of set-up, 3-month review and annual review costs were assumed to be the same for each strategy and only device costs, telemonitoring and re-titration costs differ between strategies
  - The cost of the CPAP devices and consumables were extracted from the NHS Supply catalogue. The unweighted mean of different devices was used in the model base case - £248 for fixed-level CPAP and £384 for auto-CPAP. Higher and lower costs were used in a sensitivity analysis.
  - The device costs were annuitized using a discount rate of 3.5% and assuming the equipment is replaced after 7 years.

- Telemonitoring costs were from ResMed (£45 for one year or £150 for 5 years).
- Education and set up was costed as a respiratory consultant-led outpatient consultation and follow-up was a non-consultant-led outpatient consultation. The unit costs were 'NHS costs'.

- Re—titration
  - Re-titration using telemonitoring was assumed to take up 20 minutes of a physiologist's time (60 minutes in a sensitivity analysis).
  - Re-titration using auto-titration was assumed to require an auto-CPAP machine over 2 nights and analysis of the results was assumed to take 45 minutes of a physiologist's time (75 minutes in a sensitivity analysis) and 10 minutes of a medical consultant.
  - The unit cost of staff time used in re-titration were standard NHS costs (£47 per hour for a band 6 physiologist and £109 per hour for a medical consultant)
  - It was assumed that 18% of patients using fixed-level CPAP would require re-titration – based on the number of patients having an unplanned contact in one of the included trials.[5] This was increased to 30% in a sensitivity analysis.
- Lifetime costs
  - The lifetime costs were calculated from the main guideline model and include the cost of RTAs and the health care costs associated with treating cardiovascular events. However, these costs were assumed not to vary between strategies. The difference in lifetime cost between strategies is attributable to the differences in device, telemonitoring and re-titration costs.
  - The lifetime costs were based on a cohort of men aged 50. This was calculated separately for men with mild OSAHS and for men with moderate OSAHS. The only difference was that dropout from treatment was greater than for the men with mild OSAHS.

The resulting cost per year of treatment is shown in Table 1.

Table 1: Cost (£) of each strategy per year of treatment

	Device Cost	Staff	Retitration staff time	Tele-monitoring access	Con-sumables	Total
Year 1						
Fixed-level CPAP with auto-titration	39.16	265.57	9.72		120.58	**435.02**
Fixed-level CPAP with telemonitoring	39.16	265.57	2.82	30.00	120.58	**458.12**
Fixed-level CPAP with telemonitoring (yr 1 only)	39.16	265.57	2.82	45.00	120.58	**473.12**
Auto-CPAP only	60.66	265.57			120.58	**446.81**
Auto-CPAP with telemonitoring	60.66	265.57		30.00	120.58	**476.81**
Year 2 onwards						
Fixed-level CPAP with auto-titration	39.16	119.97			120.58	**279.70**
Fixed-level CPAP with telemonitoring	39.16	119.97		30.00	120.58	**309.70**

	Device Cost	Staff	Retitration staff time	Tele-monitoring access	Con-sumables	Total
Fixed-level CPAP with telemonitoring (yr 1 only)	39.16	119.97			120.58	**279.70**
Auto-CPAP only	60.66	119.97			120.58	**301.21**
Auto-CPAP with telemonitoring	60.66	119.97		30.00	120.58	**331.21**

1.2 Comparison of different treatments for people with mild OSAHS

Review questions by scope area	**What is the clinical and cost effectiveness of different types of oral devices for managing obstructive sleep apnoea/hypopnea syndrome (OSAHS), obesity hypoventilation syndrome and overlap syndrome?** **What is the clinical and cost effectiveness of CPAP devices for the treatment of mild OSAHS**
Population	Adults with mild OSAHS
Interventions and comparators	A. Conservative management (Lifestyle advice) B. 'Boil and bite' oral device and lifestyle advice C. Semi-bespoke oral device and lifestyle advice D. Custom-made oral device and lifestyle advice E. CPAP and lifestyle advice
Perspective	NHS and personal social services
Outcomes	Quality-adjusted life-years
Type of analysis	Cost-utility analysis

1.2.1 Overview of methods

Treatment effects

- Each treatment was assumed to have an immediate impact on quality of life (measured in terms of EQ-5D). These were estimated from randomised trials comparing each intervention with conservative management.
- For the base case, the improvement in EQ-5D was 0.012, 0.011 and 0.023 for Boil and bite, semi-bespoke and custom-made MAS respectively. These were from the TOMADO trial in mild and moderate OSAHS. These were recorded at 4 weeks in the trial but were extrapolated for the duration of treatment.
- For CPAP, the difference in ESS change was pooled across all the trials of CPAP in mild OSAHS, giving a reduction of 2.87 compared with conservative management. This was mapped to an EQ-5D improvement of 0.028 using a published mapping equation. Again, this was extrapolated for the whole treatment period.
- Compared with conservative management, all of the treatments were assumed to have the same impact on the incidence of road traffic accidents. A proportion of the

accidents are fatal and so accidents are associated with reduced length of life. Non-fatal accidents are associated with reduced quality of life.

- For treated patients the risk of an RTA was assumed to be the same as the general population. The treatment effect was OR=0.169, which was derived from TA139
- Although cardiovascular events are included in the model, for this mild OSAHS population we assumed that treatment had no impact.
- The rate at which people drop out from using CPAP was differentiated by time and by OSAHS severity. This was taken from a published cohort study. In the absence of additional evidence, the same dropout was assumed for mandibular advancement splints.
- The baseline probability of both cardiovascular events and RTAs were for men aged 50 at the commencement of treatment. The former was estimated using QRISK3 and the latter were from Department of Transport statistics.

Table 2: Summary of base-case cost inputs

Input	Year 1	Year 2
Conservative management	£146	£0
CPAP	£473	£279
Boil and bite mandibular advancement splints	£262	£262
Semi-bespoke mandibular advancement splints	£426	£426
Custom-made mandibular advancement splints	£519	£293

1.3 Comparison of different diagnostic pathways for OSAHS

Review questions	**What are the most clinically and cost effective diagnostic strategies for obstructive sleep apnoea/hypopnea syndrome, obesity hypoventilation syndrome and overlap syndrome, including home- and hospital-based studies, and investigations such as oximetry, capnography, respiratory polygraphy and polysomnography?**
Population	Symptomatic adults being tested for OSAHS
Interventions and comparators	A. Home oximetry (CPAP for all OSAHS) B. Home respiratory polygraphy (CPAP for all OSAHS) C. Hospital respiratory polygraphy (CPAP for all OSAHS) D. Home oximetry screening and then home respiratory polygraphy for those that tested negative (CPAP for all OSAHS) E. Home oximetry (CPAP for moderate and severe OSAHS) F. Home respiratory polygraphy (CPAP for moderate and severe OSAHS) G. Hospital respiratory polygraphy (CPAP for moderate and severe OSAHS)

	H. Home oximetry screening and then home respiratory polygraphy for those that tested negative (CPAP for moderate and severe OSAHS)
Perspective	NHS and personal social services
Outcomes	Quality-adjusted life-years
Type of analysis	Cost-utility analysis

1.3.1 Overview of methods

Diagnostic accuracy

Test threshold	Sensitivity	Specificity
Accuracy at detecting OSAHS (AHI>5 on polysomnography)		
Home Oximetry ODI>5	0.518	0.958
Home RP AHI >5	0.945	0.577
Hospital RP AHI > 5	0.950	0.813
Accuracy at detecting moderate/severe OSAHS (AHI>15 on polysomnography)		
Home Oximetry ODI>15	0.350	0.994
Home RP AHI >15	0.842	0.890
Hospital RP AHI > 15	0.932	0.925

- The table above shows the sensitivities and specificities used in the model. These are the estimates from the guideline review pooled using diagnostic meta-analysis. Where a second test was performed the accuracy of the second test was assumed to be independent of the results of the first test.
- For those people with moderate or severe OSAHS who were misdiagnosed as having no OSAHS after the first test, it was assumed that they would have a second test. This is because they are likely to be markedly symptomatic, which would entail further investigation.

Treatment effects

- CPAP and MAS were assumed to have an immediate impact on quality of life (measured in terms of EQ-5D). These were estimated from randomised trials comparing each intervention with conservative management.
- CPAP was estimated to have an impact on ESS and quality of life (measured in terms of EQ-5D). ESS was estimated from randomised trials comparing CPAP with conservative management and sub-grouped by severity. The ESS improvements were mapped to EQ-5D using a published mapping equation. The resulting EQ-5D improvements used in the base case analysis and were applied to the whole treatment period:

	CPAP vs conservative management	
	ESS	**EQ-5D**
Mild OSAHS	-2.87	0.028
Moderate OSAHS	-2.04	0.020
Severe OSAHS	-3.41	0.033

- For the base case, the improvement in EQ-5D was 0.023 for custom-made MAS. These were from the TOMADO trial in mild and moderate OSAHS. There was assumed to be no benefit for patients with severe OSAHS.
- Compared with conservative management, CPAP was assumed to have the same impact on the incidence of road traffic accidents, regardless of severity. A proportion of the accidents are fatal and these are associated with reduced length of life. Non-fatal accidents are associated with reduced quality of life.
- For treated patients the risk of an RTA was assumed to be the same as the general population. The treatment effect was OR=0.169, which was derived from TA139
- Cardiovascular events were included in the model,
  - For moderate and severe OSAHS there was a modest reduction derived using QRISK from a 1.0mmHg reduction in systolic blood pressure
  - for the mild OSAHS population we assumed that CPAP had no impact
- The rate at which people drop out from using CPAP was differentiated by time and by OSAHS severity. It was assumed that when patients dropped out, their quality of life, RTA risk and CV risk returned to their baseline levels.
- The baseline probability of both cardiovascular events and RTAs were for men aged 50 at the commencement of treatment. The former was estimated using QRISK and the latter were from Department of Transport statistics.

Table 3: Summary of base-case cost inputs

Input	Cost
Diagnostic tests	
Home Oximetry	£47
Home RP	£89
Hospital RP	£636
Treatment	
Conservative management (year 1)	£145
Conservative management (per annum year 2 onwards)	£0
MAS (year 1)	£519
MAS (per annum year 2 onwards)	£293
CPAP (year 1)	£473
CPAP (per annum year 2 onwards)	£280

2 Methods

2.1 Model overview

2.1.1 Time horizon, perspective, discount rate

Costs were from a UK NHS and personal social services perspective and outcomes were from a patient perspective. These analyses adhered to the standard assumptions of the NICE Reference Case, including a lifetime horizon and discount rate of 3.5% per annum for costs and QALYs.

2.1.2 Approach to modelling the diagnostic and treatment pathway

A two-part decision model was constructed to compare the cost-effectiveness of eight diagnostic and treatment strategies. A decision tree was used to divide a starting cohort of patients into 16 distinct subgroups based on the accuracy of each respective diagnostic test and the allocated treatment. Each subgroup then transitioned into one of 16 Markov models to establish the costs and QALYs for that subgroup over a lifetime horizon.

Decision Tree

To estimate the expected costs and QALYs of the different diagnostic strategies it is necessary to differentiate patients according to their true underlying condition (Figure 1). Therefore, the first node of the tree divides patients into those who truly have OSAHS (those with AHI score of ≥5) and those that do not (an AHI score <5). The decision tree then further disaggregates those with OSAHS according to their disease severity.

The subsequent decision nodes utilise sensitivity and specificity of each test at two different thresholds (AHI or ODI ≥5 and ≥15). The diagnostic accuracy of a test at different diagnostic thresholds (where the threshold of the polysomnography reference standard is also the same as the index tests) provides information on the ability of an index test to correctly classify people with OSAHS into the correct disease severity.

In the screening strategy all patients would receive an oximetry test first and all patients who test negative would then receive a retest with a home RP. The choice of the second re-test strategy was decided by the committee based on what would occur in current practice.

For the other strategies, a retest would be provided to those patients who are truly moderate or severe, but the test result was negative. It was assumed that this group would be highly symptomatic and would therefore raise suspicion in the clinician that the results could be a false negative. The second test in the case of home RP and hospital RP is the same as the first. For the oximetry test, the second test is a home RP.

Utilising the diagnostic accuracy data at different thresholds allows the decision tree to disaggregate the initial suspected cohort into one of 12 subgroups. The true state and severity of each of the 12 subgroups assigned by the decision tree is explained in Table 4.

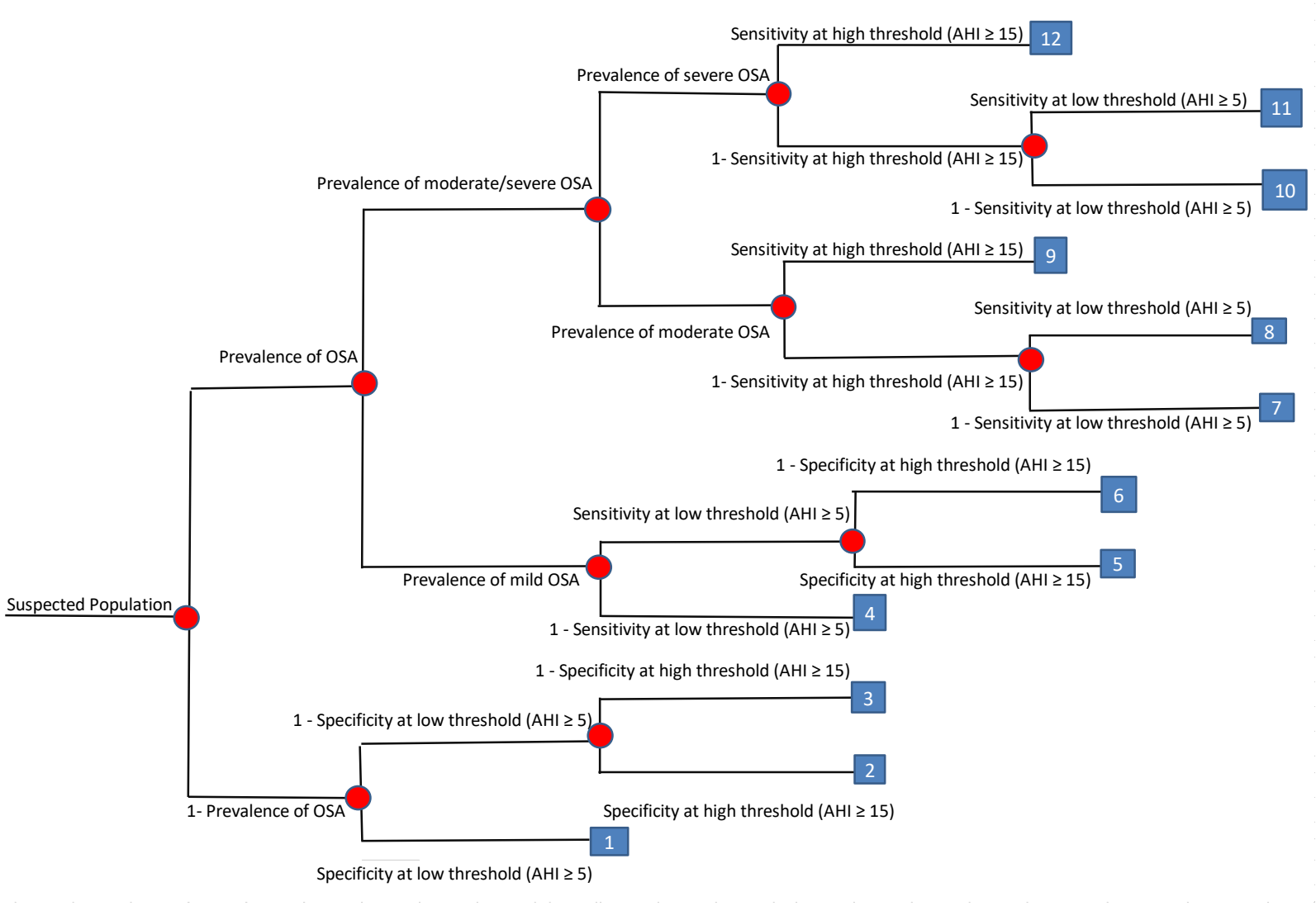


Figure 1: Decision tree for single diagnostic test

Table 4: The 16 subgroups that patients suspected of OSAHS are classified into after proceeding through the diagnostic decision tree

Subgroup	True State and Severity	Treatment	Diagnostic Test Results
1	no OSAHS (AHI/ODI <5)	No treatment	no OSAHS
2		Conservative management	1/3 mild OSAHS
3		Customised mandibular advancement splints	1/3 mild OSAHS
4		CPAP	1/3 mild OSAHS moderate or severe OSAHS
5	mild OSAHS (AHI/ODI ≥5 and ≤15)	No treatment	no OSAHS
6		Conservative management	1/3 mild OSAHS
7		Customised mandibular advancement splints	1/3 mild OSAHS
8		CPAP	1/3 mild OSAHS moderate or severe OSAHS
9	moderate OSAHS (AHI/ODI ≥15 and ≤30)	No treatment	no OSAHS
10		Conservative management	1/3 mild OSAHS
11		Customised mandibular advancement splints	1/3 mild OSAHS
12		CPAP	1/3 mild OSAHS moderate or severe OSAHS
13	severe OSAHS (AHI/ODI ≥ 30)	No treatment	no OSAHS
14		Conservative management	1/3 mild OSAHS
15		Customised mandibular advancement splints	1/3 mild OSAHS
16		CPAP	1/3 mild OSAHS moderate or severe OSAHS

Markov Model

In a Markov model (or state transition model) a set of mutually exclusive health states are defined that describe what can happen to the population of interest over time. Possible transitions are defined between each of the health states. The probability of each transition occurring within a defined period of time (a cycle) is assigned. Some of these probabilities, such as mortality, are time-dependent in the model – they change as the population recovers but also grows older.

From the end of one of 12 branches of the diagnostic decision tree, patients entered one of 16 Markov models according to their underlying diagnosis. Figure 2 shows the model structure and possible transitions between health states.

A cycle length of 12 months was used in the Markov model and there were 64 cycles in total. In subgroup 1, 2, 3 and 4 (see Table 4) where patients truly do not have OSAHS, it is assumed these patients have standard population mortality rates, they therefore do not enter the Markov model structured in Figure 2 and instead are simulated in a Markov model that utilises national lifetables for England and Wales between 2015 and 2017[50]

The need for 9 distinct Markov models is driven by the differences in baseline utility and risks in each subgroup. These differences are discussed more comprehensively in section 2.2 of

this report. All people who enter the Markov model in Figure 2 will do so in the 'OSAHS' health state. Those in this health state can either remain in this state for a lifetime horizon, transition into one of the states where they have OSAHS and a cardiovascular event or they could transition into the Dead state. Transition into the Dead state is possible from all the other states.

- True positives
    - If underlying OSAHS is moderate/severe then they get CPAP regardless of strategy. Consequently, they get improved quality of life and a reduced incidence of road traffic accidents. They also get reduced blood pressure that reduces slightly the incidence of cardiovascular events
    - If they have mild OSAHS and get CPAP or MAS then they get a smaller improvement in quality of life and the same reduction in road traffic accidents. But there is no improvement in blood pressure.
    - If they have mild OSAHS and do not get CPAP then they get conservative management and no benefits.
- False negatives don't get those benefits
- False positives incur the cost of CPAP or MAS but without the benefits. They drop out of treatment in the first year
- True negatives accrue neither cost nor benefits of CPAP or MAS

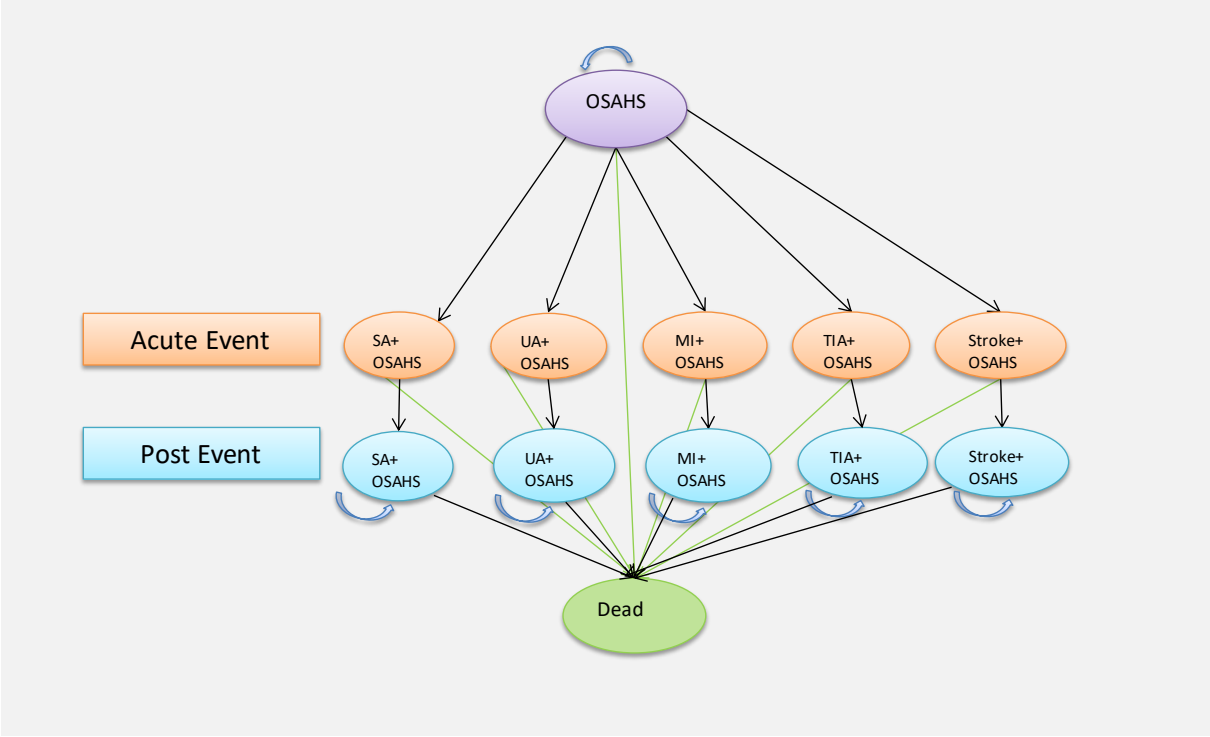


Figure 2: Markov model structure

If the population in the OSAHS health state do have a cardiovascular event, these events are disaggregated into five acute health states. Patients remain in one of these five health states for one cycle:

- Stable Angina (SA)
- Unstable Angina (UA)
- Myocardial Infarction (MI)
- Transient Ischemic Attack (TIA)
- Stroke.

Thereafter, all patients in the acute cardiovascular event state move out of acute states and transition into the post cardiovascular event states in which they remain over a lifetime horizon until they transition into the Dead state. There are five equivalent post-cardiovascular event health states.

The Markov model also captures the impact of road traffic accidents (RTAs) though this is not illustrated in the Markov model diagram. From any of the health states other than the Dead state, patients can have either a slight, serious or fatal RTA. When a patient has a slight or serious RTA there is no change to the transition probabilities of moving into another health state. In the case of a fatal RTA, patients will transition into the Dead state. To simplify the model, an assumption is made that the population cohort will only have one cardiovascular event. The model is run for repeated cycles, and the time spent in the different health states is calculated. By attributing costs and quality of life weights to each of the health states, total costs and QALYs can be calculated for the population.

2.1.3 Uncertainty

The model was built probabilistically to take account of the uncertainty around input parameter point estimates. A probability distribution was defined for each model input parameter. When the model was run, a value for each input was randomly selected simultaneously from its respective probability distribution; mean costs and mean QALYs were calculated using these values. The model was run repeatedly – 10,000 times for the base case – and results were summarised.

To ensure the number of model runs in the probabilistic analysis were sufficient, convergence was checked for in the incremental net monetary benefit. This was done by plotting the number of runs against the mean incremental net monetary benefit at that point (see example in Figure 3) for the base-case analysis. Convergence was assessed visually, and all 7 incremental net monetary benefits had stabilised before 3000 runs.

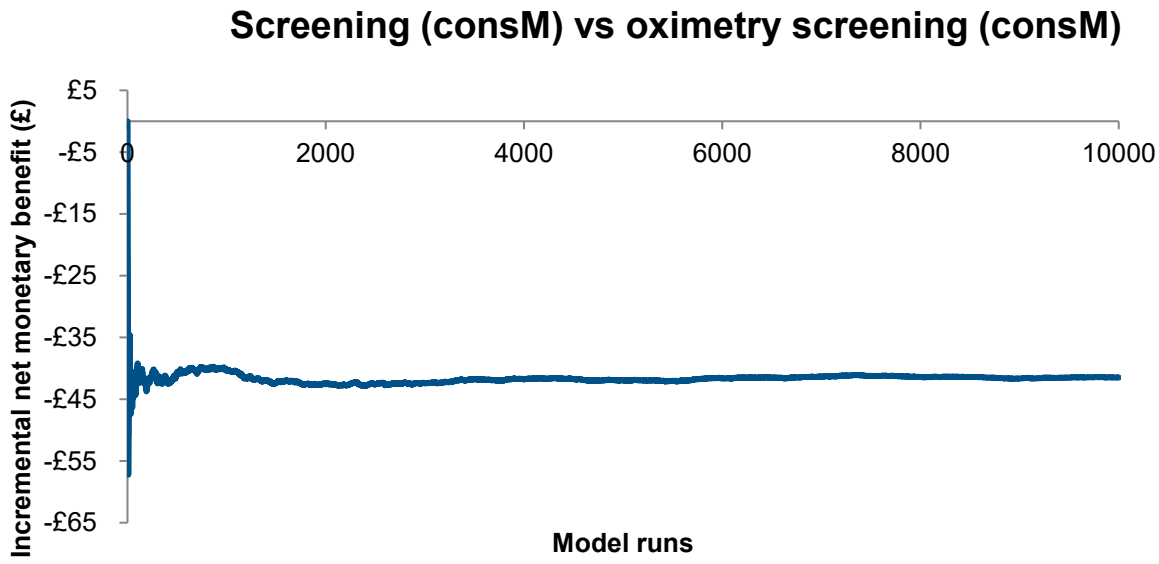


Figure 3: Convergence of incremental net monetary benefit

The way in which distributions are defined reflects the nature of the data, so for example probabilities were given a beta distribution, which is bounded by 0 and 1, reflecting that a probability cannot be outside this range. All the variables that were probabilistic in the model

and their distributional parameters are detailed in Table 5. Probability distributions in the analysis were parameterised using error estimates from data sources.

Table 5: Description of the type and properties of distributions used in the probabilistic sensitivity analysis

Parameter	Type of distribution	Properties of distribution
• Standard mortality ratios (SMRs) • Odds ratio of RTAs	Lognormal	Bounded to positive values. The natural log of the mean was calculated as follows: Mean = ln(mean) − $SE^2/2$ Where the natural log of the standard error was calculated by: SE = [ln(upper 95% CI) − ln(lower 95% CI)]/(1.96×2) $\sqrt{\ln \frac{SE^2 + mean^2}{mean^2}}$
• Prevalence of OSA (mild, moderate and severe) • Population baseline utilities • Utility multipliers of a cardiovascular event	Beta	Bounded between 0 and 1. Derived using mean and standard error, using the method of moments. Alpha and Beta values were calculated as follows: Alpha = $mean^2 / SE^2$ Beta = SE^2 / mean
• Mean difference in QoL score with CPAP	Normal	Unbounded (i.e. can go above and below 0 and 1) so as not to constrain the direction of change.
• Utility decrement; RTA	Gamma	Bounded to positive values and constraints decrements in a particular direction. Derived from mean of total quality of life score and its standard error. Alpha = $mean^2$×[(1−mean)/SE^2]−mean Beta = Alpha×[(1−mean)/mean]

Sensitivity and specificity from WinBUGS

A meta-analysis of sensitivity and specificity of the diagnostic tests (at different thresholds) was conducted in WinBUGS as part of the systematic review for the guideline. The 60,000 paired estimates that form the joint posterior distribution for sensitivity and specificity were extracted from the WinBUGS output. In each run of the probabilistic cost effectiveness analysis a pair of sensitivity and specificity is sampled from this distribution, and this preserves the inverse correlation between them.

Mapping ESS to EQ-5D

McDaid 2009 [35] fitted a simple linear regression model to predict absolute utility scores from absolute ESS, controlling for baseline utility and baseline ESS. To fit this linear regression model, data was sourced from individual patient data from a single trial which measured ESS and EQ-5D profile in the same patients. Two further trials were found that compared ESS and SF-36 profile in the same patients. The results of the regression analysis indicated that an increase in one point in ESS is associated with a 0.01 fall in utility and this is true for both the SF-6D and EQ-5D instruments. Sharples 2014 also identified a similar correlation

between ESS and EQ-5D-3L scores after evaluating patient level data for 404 participants in a single trial[63]

Using the methods described by McDaid 2009 [35], the Cholesky decomposition of the covariance matrix from the regressions was employed to characterise the uncertainty around the estimated coefficients and to reflect the correlation between coefficients in the probabilistic sensitivity analysis.

The following variables were evaluated deterministically (that is, they were not varied in the probabilistic analysis):

- cost-effectiveness threshold
- costs
- distribution of first cardiovascular events

Deterministic sensitivity analyses were undertaken to test the robustness of model assumptions. In these, one or more inputs were changed, and the analysis rerun to evaluate the impact on results and whether conclusions on which intervention should be recommended would change.

2.2 Model inputs

Model inputs were based on clinical evidence identified in the systematic review undertaken for the guideline, supplemented by additional data sources as required. Model inputs were validated with clinical members of the guideline committee.

2.2.1 Patient characteristics

Base case patient cohort characteristics, plus the characteristics of low- and high- risk populations evaluated in sensitivity analysis, are presented in Table 6. Patients entered the model at an age of 50 years old, which was the average age observed in the clinical trials used to inform estimates of diagnostic accuracy. Other clinical characteristics, including smoking status, diabetes, cholesterol ratio, systolic blood pressure and presence of chronic kidney disease were obtained from the report produced by the evidence review group (ERG) for TA139 [35].

Patient cohort characteristics were used to obtain the risk of cardiovascular events from the QRISK®3 risk calculator (section 2.2.7)[29]. The QRISK3 algorithm calculates the average risk of developing a heart attack or stroke over 10 years based on risk factors included in Table 6. It was developed for the UK population and is intended for use in UK medical research.

Table 6. Population cohort characteristics used to define QRISK3 score

	Base case		Low risk		High risk	
	With CPAP	Without CPAP	With CPAP	Without CPAP	With CPAP	Without CPAP
Age	50 years	50 years	50 years	50 years	50 years	50 years
Sex	Male	Male	Female	Female	Male	Male
Smoking status	Non-smoker	Non-smoker	Non-smoker	Non-smoker	Heavy smoker	Heavy smoker
Diabetes	Type 2	Type 2	None	None	Type 2	Type 2
Cholesterol ratio	5.2	5.2	5.2	5.2	5.2	5.2
Systolic blood pressure	129 mmHg	130 mmHg	129 mmHg	130 mmHg	129 mmHg	130 mmHg
Chronic kidney disease	No	No	No	No	Yes	Yes

2.2.2 Prevalence of mild, moderate and severe OSAHS

Two data inputs are required to allocate the cohort to each branch of the decision tree:

- underlying prevalence of mild, moderate, and severe OSAHS
- diagnostic accuracy (test sensitivity and specificity compared with the reference standard)

Prevalence data was extracted from studies that were considered in the guideline's clinical reviews of diagnostic tests and assessment tools. These reviews were chosen because the population of interest in these studies were people in whom OSAHS is suspected and polysomnography was the reference standard. The studies included for analysis are presented in Table 7**Error! Reference source not found.**. Some studies were excluded if the study population was not explicitly being tested for OSAHS.

Table 7 List of studies from which data was extracted

Author (year)	Polysomnography Results			Participants suspected
	AHI ≥ 5	AHI ≥ 15	AHI ≥ 30	
BaHammam 2011[2]	81	59	41	95
Baltzan 2000[3]		39		97
Boynton 2013[6]	169	103	61	219
Claman 2001[9]		22		42
De Oliveira 2009[13]	137			157
Emsellem 1990[20]	39			63
Garg 2014[21]		41		75
Gjevre 2011[22]	32		8	47
Golpe 2002[23]				
Goodrich 2009[25]	39	15	8	48
Gyulay 1993[26]		43		98
Hesselbacher 2012[28]		1577		1900
Masa 2013[33]	313	261		348
Masa 2014[34]	682	577		749
Nakano 2008[37]	89	65	30	100
Ng 2009	48	36		50
Ng 2010[44]	66	41		80
Nigro 2010[49]	51	31	17	66
Nigro (2011)	75	43		90
Nigro 2013[48]	43	28	15	55
Oktay 2011[52]	40			53
Pereira 2013[53]	116	116	116	116
Polese 2013[55]	40	40	40	40
Reichert 2003[58]		20		44
Rofail (2010)	51		18	72
Ryan 1995[61]		32		69
Sangkum 2017[62]	162	100	60	208
Ward 2015[67]	98	75	51	104

Studies were meta-analysed in WinBUGS, the results of this meta-analysis of prevalence is detailed in Table 8

Table 8: Formulae used to establish the prevalence of OSAHS

Prevalence parameter	Extracted data	Mean Estimate (standard error of mean)
People suspected of OSAHS that have an AHI ≥5	$\frac{\#\text{ patients with AHI} \geq 5/\text{hr}}{\#\text{ of patients suspected}}$	0.82 (0.10)
People with mild OSAHS only in a cohort with an AHI ≥5	$\frac{\#\text{ patients with } 5 \geq \text{ AHI} \leq 15/\text{hr}}{\#\text{ of patients with AHI} \geq 5/\text{hr}}$	0.32 (0.12)
People with severe OSAHS only in a cohort with an AHI ≥15	$\frac{\#\text{ patients with AHI} \geq 30/\text{hr}}{\#\text{ of patients with AHI} \geq 15/\text{hr}}$	0.60 (0.07)

2.2.3 Diagnostic accuracy

Table 9 shows the sensitivities and specificities used in the model. These are the estimates from the guideline review pooled using diagnostic meta-analysis in WinBUGS (see Evidence Report D).

Table 9: Accuracy of tests for OSAHS

Test threshold	Sensitivity	Specificity
Accuracy at detecting OSAHS (AHI>5 on polysomnography)		
Home Oximetry ODI>5	0.518	0.958
Home RP AHI >5	0.945	0.577
Hospital RP AHI > 5	0.950	0.813
Accuracy at detecting moderate/severe OSAHS (AHI>15 on polysomnography)		
Home Oximetry ODI>15	0.350	0.994
Home RP AHI >15	0.842	0.890
Hospital RP AHI > 15	0.932	0.925

Each estimate is the median of the posterior distribution. Source Evidence Report D for details.

Misdiagnosed people with moderate or severe OSAHS were assumed to receive a second test because they are likely to remain symptomatic and entail further investigation. If a second test was performed, its accuracy was assumed to be independent of the results of the first test. The impact of 20% and 40% correlation between the results of first and second tests was tested in sensitivity analysis. The diagnostic accuracy of polysomnography was not included in the meta-analysis and was assumed to be 100%.

2.2.4 Mortality

It is assumed that the proportion of the cohort which does not have OSAHS (subgroup 1-3 in Table 4) have general population mortality (age and sex dependent) which is derived from national lifetables for England and Wales[50].

For those that do have OSAHS (subgroup 4-12), non-cardiovascular mortality rates were from national statistics. Cardiovascular mortality was estimated for the cohort population using QRISK3[29] and the ratio of fatal to non-fatal events in Table 17.

Where the patient has had a non-fatal CV event, and they have transitioned to one of the CV health states, the non CVD and non IHD mortality rate calculated earlier is adjusted by multiplying these rates by the standardised mortality ratios (SMRs) in Table 10. The SMRs were sourced from the NICE hypertension guideline 2019[38].

Table 10: Standardised mortality ratios for cardiovascular events

Event Type	Standardised Mortality Ratio Mean (95% CI)	Log mean	Log scale SE	Source
Stable angina	1.95 (1.65-2.31)	0.67	0.09	Rosengren 1998[60]
Unstable angina	2.19 (2.05-2.33)	0.78	0.03	UA/NSTEMI NICE guideline[40]
MI	2.68 (2.48-2.91)	0.99	0.04	Bronnum-Hansen 2001[8]
TIA	1.4 (1.1-1.8)	0.34	0.13	Oxfordshire Community Stroke Project[14]
Stroke	2.72 (2.59-2.85)	1.00	0.02	Bronnum-Hansen 2001[7]

Source: The standardised mortality ratios were taken from the economic model report for the NICE hypertension guideline 2019[38].

2.2.5 Treatment effects – quality of life

2.2.5.1 Baseline utilities

Age- and sex- specific utility values from the general population were used for the people in the model who did not have OSAHS (Ara 2010).[1]

Utility multipliers for people with mild, moderate and severe OSA were calculated by:

1. Mapping mean baseline ESS to EQ-5D values using a published a mapping algorithm (McDaid 2009[35]).[35]
2. Taking from Ara 2010 the utility score for a 50-year old man in the general population, who represented the average base case patient, 0.876
3. The multiplier was the former divided by the latter

These multipliers (Table 11) were then applied to the general population utility scores to give age- and sex-specific utility values for people with mild, moderate and severe OSA.

Table 11: Derivation of OSAHS utility multipliers

	Mean ESS[(a)]	Mean EQ-5D[(a)]	Utility multiplier[(b)]
Mild OSAHS	9	0.805	0.919
Moderate OSAHS	13	0.766	0.875
Severe OSAHS	16	0.737	0.842

(a) Source McDaid 2009[35]
(b) Mean EQ-5D divided by 0.876

2.2.5.2 CPAP effect on Epworth Sleepiness Score

There is a reduction in the ESS when using CPAP, which is correlated with improvement in quality of life. The mean CPAP effects used in the model are shown Table 12.[35]

For CPAP in mild OSAHS, the mean difference from the guideline review was used (Evidence report G). For moderate and severe OSAHS estimates from McDaid 2009 were used. These were calculated by the Evidence Review Group for TA139, although the scores that fed into the base case analysis of the TA model were sub-grouped by ESS severity group rather than AHI.

Table 12: Change in the Epworth Sleepiness Score (CPAP versus placebo) stratified by severity of sleepiness at baseline (AHI)

Severity	Mean difference (95% CI)	Source
Mild (AHI=5-15)	-2.87 (-3.62, -2.11)	Guideline review (Evidence report E)
Moderate (AHI=15-30)	-2.04 (-2.99, -1.09)	McDaid 2009
Severe (AHI>30)	-3.41 (-4.56, -2.26)	McDaid 2009

2.2.5.3 Conservative management effect on Epworth Sleepiness Score

Exploratory analysis was also conducted to identify whether there is any reduction in ESS following conservative management. To do this, a further subgroup analysis was conducted of studies within their respective severities to separate those studies that were comparing CPAP with conservative management from those that were comparing CPAP with sham or placebo. It was hypothesised that the treatment effects (ESS reduction) would be smaller when CPAP was compared with conservative management. However, the results indicated the opposite to be true. This could indicate the presence of a placebo effect, particularly because the patients may demonstrate enthusiasm after receiving a device (even though it was not providing the required pressure levels for it to be clinically effective). The committee explained that it would be unreasonable to assume that as a result of conservative management there would be a quality of life decrement. Instead, it was agreed that there should be no change in the ESS as a result of conservative management. Finally, in those cases where there are false positives and patients received CPAP or conservative management in these cases it was agreed there would be no change in the ESS.

2.2.5.4 CPAP – EQ-5D effect

The treatment effect in the model is the improvement in the ESS as a result of CPAP for the patients who have OSAHS. This has been mapped to the EQ-5D using an algorithm developed by McDaid 2009: Mean difference in ESS × –0.01.

Table 13: CPAP treatment effects

	CPAP vs conservative management	
	ESS	EQ-5D
Mild OSAHS	-2.87	0.028
Moderate OSAHS	-2.04	0.023
Severe OSAHS	-3.41	0.033

2.2.5.5 Oral devices – EQ-5D effect

The quality of life improvement for oral devices was taken from the TOMADO randomised trial of 83 patients.[56]

Table 14: EQ-5D improvement from for mandibular advancement splints compared to no treatment

	Mean	SE
Mild/moderate OSAHS treated with Boil and Bite	0.012	0.01
Mild/moderate OSAHS treated with semi-bespoke	0.011	0.02
Mild/moderate OSAHS treated with custom-made	0.023	0.02

It was assumed that mandibular advancement splints would not give any improvement in quality of life for people with severe OSAHS because there was not trial evidence and because the committee did not think that they would have a sufficient impact on the disease to have a noticeable impact on quality of life.

2.2.6 Treatment effects – road traffic accidents

The age- and sex- specific probabilities of people having a car-driving licence in England were reported by the Department for Transport (DfT) in 2018[15]. The total number of drivers in England was calculated by multiplying these probabilities by the corresponding population in England reported by the Office for National Statistics in 2019.[51]

The number of road traffic driver casualties in England in 2019 was disaggregated according to age, sex and severity of the casualty (slight, serious or fatal[16]).[17] The total number of driver casualties was divided by the number of drivers in each age range and sex category to calculate the probability of slight, serious, and fatal RTAs for males and females over a lifetime (Figure 4 and

Figure 5).

Figure 4: Lifetime probability of road traffic driver injury in males in England

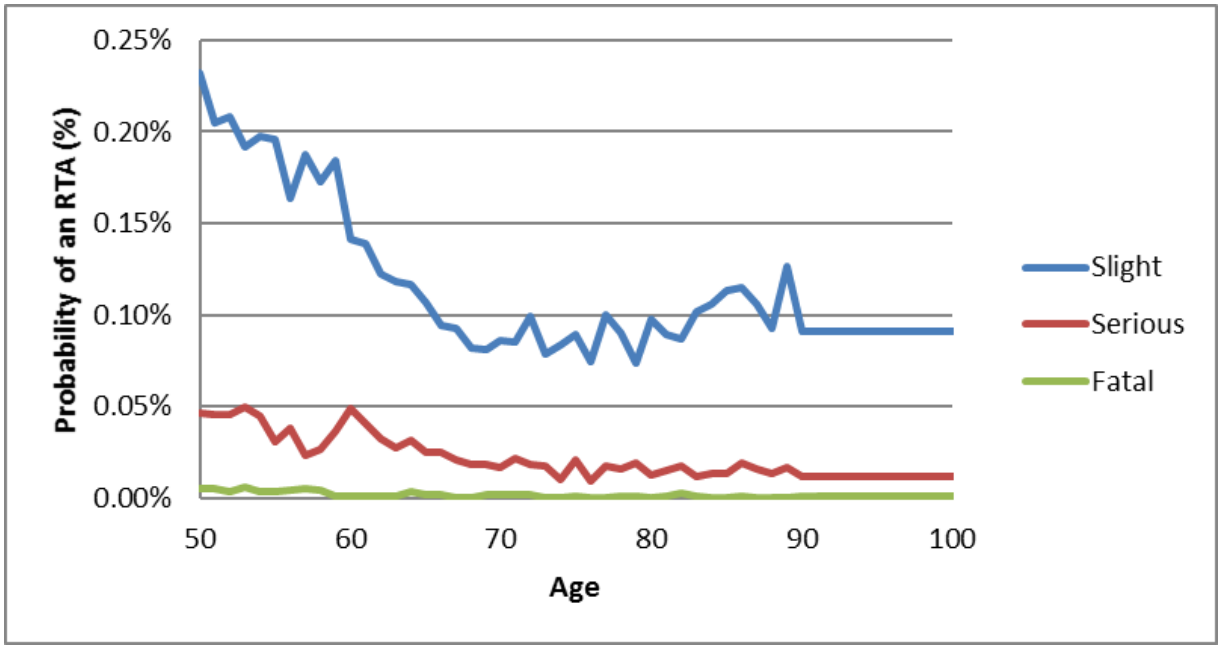
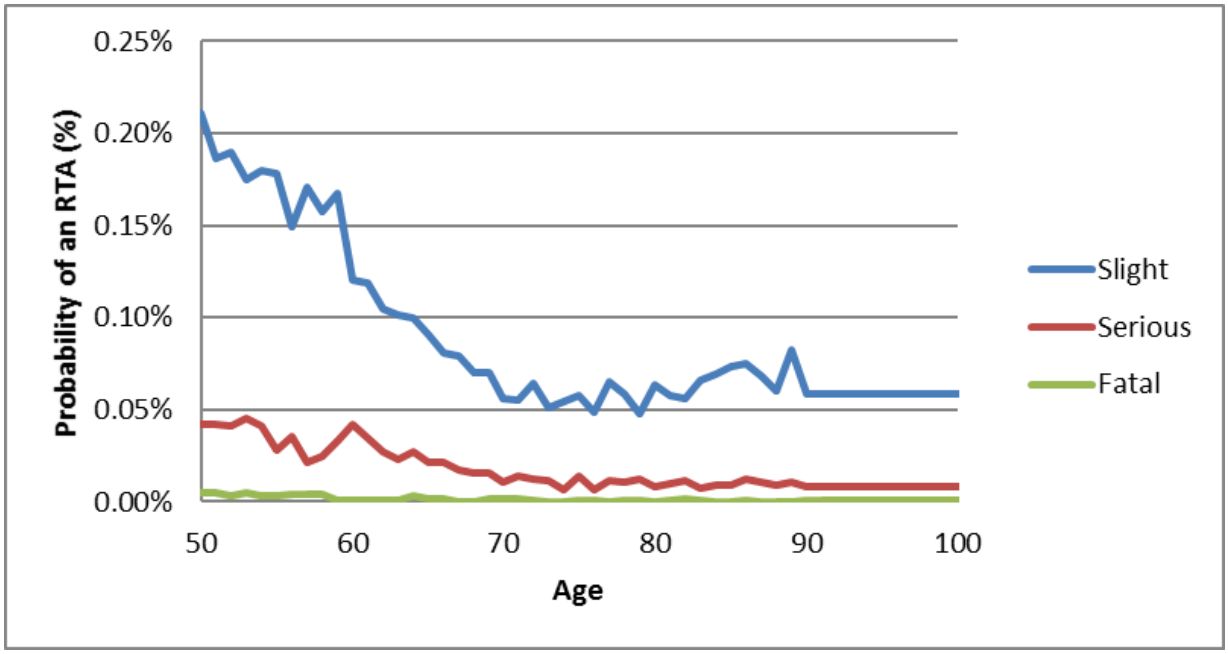


Figure 5: Lifetime probability of road traffic driver injury in females in England



In the OSAHS population, untreated patients or patients who receive an incorrect diagnosis could potentially be at greater risk of being injured in road traffic accidents (as well as causing injuries to others involved in the accident). To calculate the increased risk in this population, McDaid 2009 [35] updated a meta-analysis of the incidence of RTAs before and after CPAP initiation. The odds ratio calculated by McDaid 2009 [35] of RTA rates with CPAP compared to without is 0.168. In order to model the baseline risk of an RTA in the OSAHS population the first assumption that was made was that those patients with OSAHS who receive CPAP would have the same risk of an RTA as the general population. Therefore, to calculate the baseline probability of injuries from RTAs in the untreated OSAHS population, the general population RTA probability (disaggregated according to age, sex and severity) were divided by the proportionate reduction (the odds ratio of RTA rates with CPAP versus without CPAP) in RTA associated with CPAP therapy.

In the base case analysis, we calculate the cost and QALY loss associated with injury to the driver only (the person with OSAHS). But in sensitivity analysis we capture the impact on other casualties. The ratio of all casualties to driver casualties was 1.36 for minor injuries, 1.10 for severe injuries and 1.07 for minor injuries.[16]

In the case of conservative management, if patients with OSAHS were to receive this intervention it was assumed that they will maintain their heightened baseline risk of an RTA.

For oral devices, we assumed the same RTA effect as for CPAP.

The utility associated with experiencing a serious RTA was based on data used by McDaid 2009[35]who sourced EQ-5D measures from the Health Outcomes Data Repository (HODaR)[10]. HODaR recorded EQ-5D data for individuals six weeks after their inpatient episode for injuries experienced from a RTA. There was data available for 56 patients. It was assumed that the quality of life for a patient in the year they experience a serious RTA would reduce to 0.62. It is then assumed that the utilities would recover to the OSAHS baseline in the subsequent year.

Table 15: Impact of road traffic accidents on quality of life

Input	Data	Source
Slight RTA (absolute decrement)	-0.085	Pink 2014[54]
Serious RTA (absolute utility)	0.62	HODaR[10] McDaid 2009 [35]

It was judged that applying a similar decrement in quality of life after a slight RTA would be unreasonable and a more conservative decrement would need to be applied. An estimate was derived for this patient population from an observational study which collected EQ-5D of patients recovering from acute whiplash. There was 12 months data available for 590 patients who experienced whiplash that resulted in no neck pain-related activity restrictions or disabilities[54]. After 12 months there was a utility improvement of 0.0851 in this group. This utility improvement was applied as a one-off utility decrement in the model as a result of experiencing a slight RTA. It was assumed that the patient recovers to their baseline utility in the following year. In order to make this model input probabilistic the standard error had to be calculated from the standard response of the mean (SRM). To do this, first the SRM was converted into a standard deviation which was then converted into a standard error (see formula in Table 16).

Table 16: Formulae to convert standard response of the mean to standard error

$\text{Standard deviation} = \frac{\textbf{\textit{Mean}}}{\textbf{\textit{Standard response of the mean}}}$
$\text{Standard error} = \frac{\textit{Standard deviation}}{\sqrt{\textit{number of participants}}}$

2.2.7 Treatment effects – cardiovascular events

Each year in the Markov model, patients in the 'OSAHS' state can transition to the different acute CV event health states which are SA, UA, MI, TIA or stroke. Annual transition probabilities were calculated for each CV event in the model by converting the 10-year risk of a cardiovascular event as indicated by the QRISK3 calculator into a 1-year probability. The

The QRISK3 calculator provides a 10-year predicted risk of cardiovascular events. From this we calculated an average annual rate. Since this is an average rate, it best reflects the risk in the middle of the 10 year period. We then used the average rate of a 50 year old to determine the probability of an event for a 55 year old, the average rate of a 51 year old to determine the probability for a 56 year old, etc. This way the model matched very closely the 10 year risk estimated by QRISK3.

Then, using distributions published by Ward (2007) [68], the annual probability of a specific cardiovascular events was calculated (Table 17).

Table 17: Relative distribution of cardiovascular events

Distribution of cardiovascular							
Male							
Age	**Stable Angina**	**Unstable Angina**	**MI**	**Fatal CHD**	**TIA**	**Stroke**	**Fatal stroke**
25-34	34	0.307	0.107	0.295	0.071	0.060	0.129
35-44	44	0.307	0.107	0.295	0.071	0.060	0.129

Distribution of cardiovascular							
45-54	54	0.307	0.107	0.295	0.071	0.060	0.129
55-64	64	0.328	0.071	0.172	0.086	0.089	0.206
65-74	74	0.214	0.083	0.173	0.097	0.100	0.270
75-84	84	0.191	0.081	0.161	0.063	0.080	0.343
85+	85	0.214	0.096	0.186	0.053	0.016	0.352
Female							
Age	**Stable Angina**	**Unstable Angina**	**MI**	**Fatal CHD**	**TIA**	**Stroke**	**Fatal stroke**
25-34	34	0.324	0.117	0.080	0.037	0.160	0.229
35-44	44	0.324	0.117	0.080	0.037	0.160	0.229
45-54	54	0.324	0.117	0.080	0.037	0.160	0.229
55-64	64	0.346	0.073	0.092	0.039	0.095	0.288
65-74	74	0.202	0.052	0.121	0.081	0.073	0.382
75-84	84	0.149	0.034	0.102	0.043	0.098	0.464
85+	85	0.136	0.029	0.100	0.030	0.087	0.501

The distributions of events that make up QRISK3 are from sources based on the late 1980s and 1990s. It was accepted that incidence rates in absolute terms have changed over time. However, it is plausible that distribution of events has been relatively stable. This was the assumption that was also made in a model developed for the NICE hypertension guideline (2019) [38] which used similar methods. The British Heart Foundation reports statistics on morbidity and mortality of cardiovascular conditions using a variety of sources. Their 2018 report confirms that the distribution of events relative to each other are approximately correct, for example: CHD is around twice as common as stroke. The report also confirms that the relationship between different types of events for different sexes in the model seemed to have face validity (such as strokes tend to be more common in women compared to other events like MI).

The evidence review group for TA94 used the reduction in systolic blood pressure to link the benefits of CPAP treatments to cardiovascular events. A meta-analysis found that when CPAP was compared with conservative management/sham/placebo there was a -1.06mmHg reduction in systolic blood pressure. As systolic blood pressure is an input parameter in the QRISK3 calculator, patients with OSAHS had their baseline systolic blood pressure reduced from 130mmHg to 129mmHg to calculate their reduced risk of cardiovascular events according to the QRISK3 calculator. It was agreed that conservative management should have no CV treatment benefits.

Quality of life weights associated with cardiovascular events were applied multiplicatively to the baseline population weights. These are summarised in Table 18 and were taken from the economic model developed for the NICE Hypertension Guideline (2019) [38]. When a person has an event in the model, their age and gender related quality of life is using the multiplier associated with the particular event.

Table 18: Cardiovascular event utility multiplier

State	Utility multiplier	Standard error	Alpha	Beta	Source
Well	1				By definition
Stable angina	0.808	0.038	86	20	Melsop 2003 [36]
Post-stable angina	0.808	0.038	86	20	Melsop 2003 [36]

State	Utility multiplier	Standard error	Alpha	Beta	Source
Unstable angina	0.770	0.038	94	28	Goodacre 2004[24] Ward 2007[68]
Post-unstable angina	0.880	0.018	86	20	2008 Lipid modification guideline[39]
MI	0.760	0.018	427	135	Goodacre 2004 [24] Ward 2007[68]
Post-MI	0.880	0.018	286	39	Tsevat 1993 [66]
TIA	0.900	0.025	129	14	Lavender 1998 [32]
Post-TIA	0.900	0.025	129	14	Lavender 1998 [32]
Stroke	0.628	0.040	91	54	Tengs 2003 [65] Youman 2003[69]
Post-stroke	0.628	0.040	91	54	Tengs 2003 [65] Youman 2003[69]

Note: The utility multipliers were taken from the economic model report for the NICE hypertension guideline 2019[38]

2.2.8 Adherence to treatment

The long-term adherence with CPAP has implications for the estimated effectiveness in the target population. Estimates of CPAP adherence was sourced from Kohler (2010)[31] who conducted a large hospital record-based study of 639 patients in England who were provided CPAP for their sleep apnoea. The study includes a Kaplan Meier plot which illustrates the proportion of patients who continue to use CPAP therapy over 10 years disaggregated according to their ODI. These data were used for the CPAP dropout rates in the mild, moderate and severe OSAHS groups, respectively (Table 19).

It was assumed that those using their device after the 10th year would continue to do so over a lifetime horizon. It was also assumed that all of those who receive a false positive diagnosis drop out in the first year after experiencing no benefit from treatment.

Table 19: Points read from a Kaplan-Meier plot of CPAP adherence over 10 years

Year	Points on Kaplan-Meier plot		
	ODI 0-15	ODI 15-30	ODI 30-60
1	0.878	0.900	0.948
2	0.792	0.859	0.922
3	0.756	0.819	0.91
4	0.734	0.792	0.888
5	0.717	0.779	0.879
6	0.703	0.757	0.855
7	0.694	0.748	0.855
8	0.681	0.741	0.835
9	0.621	0.715	0.835
10	0.621	0.714	0.761

Due to lack of evidence, adherence to oral devices was assumed to be the same as for CPAP.

2.2.9 Diagnostic test costs

The component costs of home oximetry were detailed in Table 20. The costs of home RP and hospital RP were directly obtained from NHS reference costs and presented in Table 21.

Home RP was assumed to occur as an outpatient procedure and hospital RP as an elective inpatient procedure. The cost of polysomnography was assumed to be the same as the cost of hospital RP.

Table 20: Cost per oximetry test

Resource use [(a)(b)(c)]	Cost
Oximetry device costs	£561.38
Annuitized cost of oximetry device	£120.13
Annuitized costs per use of oximetry device	£0.92
AAA batteries [(d)]	£0.09
Hospital based band 5 Nurse (30 minutes) [(e)]	£19.00
Hospital based medical consultant (15 minutes) [(f)]	£27.25
Cost per oximetry test	£47.27

(a) Device costs can vary. In this example, the device cost for Nonin pulse oximetry wrist device (FBC331) has been provided with an initial outlay of £561.38. This device costs have been sourced from the NHS supply chain catalogue[45]. Of the available brands and types of oximetry devices, this device was familiar to the committee and had a price point that they thought was reasonable and representative.

(b) Device costs were annuitized to calculate annual equivalent costs of £120.13 for the Nonin device. The formula used to calculate annuitized annual costs was: E = K – [S / (1+r)n] / A(n,r)
Where E = equivalent annual cost; K = Purchase price of the oximetry device; S = resale value; r = discount (interest) rate; n = equipment lifespan; A(n,r) = annuity factor (n years at interest rate r). Assumptions included a resale value of £0, discount rate of 3.5% and equipment lifespan of 5 years, as advised by the committee.

(c) Annuitized costs were divided by 130 to reflect that the device could be used 130 times per year. This assumption was based on committee advice where it was indicated that 48 hours would be required for the patient to do the home oximetry, return the device, and the data download to occur before the same device could be made available again. The device would be provided only Monday – Friday (therefore 5 uses every fortnight).

(d) An average cost for two AAA batteries (as would be required in the Nonin device) was calculated as £0.09 from the following NPC codes from the NHS supply chain – WPA106, WPA146, WPA154 and WPA215. This was then divided by 5 as the batteries would need to be replaced after every fifth patient.

(e) The committee advised that a band 5 nurse could prepare the oximetry device and advise patients how to use the device overnight (15 minutes). The same band of staff would also carry out the data download and initial analysis (15 minutes). The cost per hour of a nurse was £38 from the PSSRU[45] this was then multiplied by the time required for the diagnostic test (30 minutes), for a total of £19.

(f) A consultant would look over the data and prepare the report (15 minutes). The cost per hour of a medical consultant was £109 from the PSSRU. [45]

Table 21: Cost of respiratory polygraphy

Study	Code	Cost per patient
Limited Sleep Study (outpatient)	DZ50Z	£189.28
Limited Sleep Study (inpatient)	DZ50Z	£635.53

Source: NHS reference costs [18, 47]

2.2.10 Treatment costs

2.2.10.1 Conservative management

The cost of a respiratory medicine consultant-led outpatient appointment from National Schedule of NHS Costs 2018/19 (£145.60) was used to represent a one-time cost of conservative management.

2.2.10.2 CPAP costs

Strategies

The following strategies were compared:

- Fixed-level CPAP with auto-titration
- Fixed-level CPAP with telemonitoring
- Fixed-level CPAP with telemonitoring in first year
- Auto-CPAP
- Auto-CPAP with telemonitoring

Device and consumable costs

Table 22: Cost of CPAP devices and consumables

Input	Mean cost	NHS supply chain code[45, 46]	Assumed durability
Fixed-level CPAP device cost	£247.80	FDD2400, FDD5011, FAG1366, FAG2279, FAG4056, FAG4053	7 years in base case (5 years in sensitivity analysis)
Auto-CPAP device cost	£383.90	FAG1365, FAG3369, FAG4059	7 years in base case (5 years in sensitivity analysis)
Mask	£75.66	FAG1196, FAG2256, FAG2258, FAG2264, FAG2267, FAG2492, FAG2496, FAG2498, FAG2629, FAG3857, FAG3897, FAG4271, FDD1467, FDD1989, FDD3739-40, FAG2854, FDD3751-56, FDD4126, FDD752	1 year
Humidifier	£102.47	FAG1392, FAG4728, FAG883, FDD2405, FDD2445, FDF1371, FFT199	3.5 years
Humidifier chamber	£18.58	FAG2812, FAG4756, FAG969, FDE417, FDE427, FDF2251	1 year
Hose	£21.16	FDD2416	1 year
Filters	£2.53	FAG1264, FAG2641, FAG2642, FAG2644, FAG2645, FAG2646, FAG2648, FAG273, FAG4679, FAG4684, FAG4746, FAG4748, FAG4749, FAG4769, FAG4771, FDD2419, FDD2970, FDD3128, FDD4112, FDD4144, FDD4455, FDE532, FDE621, FDE622	6 months
Ultra-fine filters	£2.36	FDD2422, FDE178, FDD2441, FAG277, FDD4109	1 month

All costs were annuitized using a discount rate of 3.5%.

Staff costs

For the initial set-up of the device, the cost of a consultant-led respiratory outpatient appointment was included (£146).[18]

The committee recommended that a CPAP review appointment needs to take place within a month of initiation to assess effectiveness monitor progress, this has been costed as an outpatient non-consultant-led appointment (£120). [18] These review appointments would be expected to occur every 12 months thereafter.

Table 23: Costing CPAP setup

Input		Notes
CPAP device	£247.80	See Table 22
Annuitized CPAP device cost	£39.16	Assuming a life span of seven years
Education and setup	£145.60	Respiratory medicine consultant-led outpatient appointment (WF01A)[18]
3-month review	£119.97	Respiratory medicine non-consultant follow-up (WF01A)[18]
Annual review	£119.97	Respiratory medicine non-consultant follow-up (WF01A)[18]
Mask annual replacement	£75.66	See Table 22
Annuitized mask	£75.66	See Table 22
Humidifier	£102.47	See Table 22
Annuitized humidifier cost	£30.55	Assuming a lifespan of 3.5 years
Humidifier chamber (1/year)	£13.27	See Table 22
Hose	£21.16	See Table 22
Filters pollen (2/year)	£5.07	See Table 22
Ultrafine filters (12/year)	£28.31	See Table 22

Re-titration and telemonitoring

It was assumed that 18% of patients started on fixed-level CPAP would require re-titration. This was based on the rate of unplanned contacts observed in a trial of auto-CPAP vs fixed-level CPAP. [5].

Auto-titration is where a device pressure levels are titrated using auto-CPAP. The strategy requires a patient to collect an auto-CPAP device from the sleep clinic to use overnight. The device is returned the next day and the data is downloaded from the auto-CPAP device which informs the clinician the pressure level that was supplied to the patient throughout the night. The patient's CPAP device is then adjusted to the pressure level that has been informed by usage of the auto-CPAP device. The costs associated with auto-titration are described in Table 24.

Table 24: Costing of auto-titration

Input		Notes
auto-CPAP device	£383.90	See Table 22
Annuitized auto-CPAP device cost	£60.66	$E = K / A(n,r)$ [(a)]
Device cost per titration	£0.58	Device can be used 104 times per year [(b)]
Band 6 physiology auto-CPAP setup and data download (45minutes)	£35.25	PSSRU[45]. Band 6 hospital based physiologist.
Medical Consultant Report (10minutes)	£18.17	PSSRU[45]. Hospital based medical consultant
Total	£54.00	

(a) Where E = equivalent annual cost; K = Purchase price of auto-CPAP device; r = discount (interest) rate=3.5%; n = equipment lifespan=7 years; A(n,r) = annuity factor (n years at interest rate r).

(b) This assumption was based on committee advice where it was indicated that 72 hours would be required for the patient to do the auto-CPAP titration. The device would be provided only Monday – Friday (therefore 2 uses per week).

In the presence of telemonitoring, it was assumed that re-titration would be undertaken remotely requiring 20 minutes of a physiologist's time. The cost of telemonitoring was £45 for one year or £120 for 5 years.

Total cost

The resulting cost per year of treatment is shown in Table 25.

Table 25: Cost (£) of each strategy per year of treatment

	Device Cost	Staff	Re-titration	TM Access	Con-sumables	Total
Year 1						
Fixed-level CPAP with auto-titration	39.16	265.57	9.72		120.58	**435.02**
Fixed-level CPAP with telemonitoring	39.16	265.57	2.82	30.00	120.58	**458.12**
Fixed-level CPAP with telemonitoring (1 year only)	39.16	265.57	2.82	45.00	120.58	**473.12**
Auto-CPAP only	60.66	265.57			120.58	**446.81**
Auto-CPAP with telemonitoring	60.66	265.57		30.00	120.58	**476.81**
Year 2 onwards						
Fixed-level CPAP with auto-titration	39.16	119.97			120.58	**279.70**
Fixed-level CPAP with telemonitoring	39.16	119.97		30.00	120.58	**309.70**
Fixed-level CPAP with telemonitoring (1 year only)	39.16	119.97			120.58	**279.70**
Auto-CPAP only	60.66	119.97			120.58	**301.21**
Auto-CPAP with telemonitoring	60.66	119.97		30.00	120.58	**331.21**

The costs for Fixed-level CPAP with telemonitoring (one year only) were used in:

- The comparison of different treatments for mild OSAHS
- The comparison of diagnostic strategies for OSAHS.

2.2.10.3 Oral device costs

Device costs were obtained from publicly available prices for commonly used devices or were provided by committee members (Table 26).

Table 26: Acquisition cost of oral devices

	Mean price	Products priced	Assumed device life
Boil and bite mandibular advancement splints	£39.14	Sleepro Sleep Tight, Snoreeze oral device,SnoreKit, Tomed SomnoGuard 3, SleepPro Easy Fit, Snorban Mouthpiece, SleepPro 1	4 months
Semi-bespoke mandibular advancement splints	£141.50	Custom SLEEPPRO snoring solution, SleepPro 2	6 months
Custom-made mandibular advancement splints	£355.00	Addenbrooke's, Sleepwell, SomnoMed, Narval	2 years

In the base case, the durability of each device was assumed to be 4 months, 6 months and 2 years respectively. In sensitivity analyses, we assumed a device life of 12-months for boil and bite and semi-bespoke splints and 3 years for custom-made devices. Device costs were annuitized.

For boil and bite and semi-bespoke a respiratory outpatient appointment was assumed for education and set up and for 3 month and annual follow-up (NHS Reference cost £146). For custom-made devices this was done by a dentist (NHS Reference cost £122) and there was a third appointment in year one for fitting.

The total annual costs of each treatment are shown in Table 27.

Table 27: Treatment costs used in the mild OSAHS treatment model

Input	Year 1	Year 2
Conservative management	£146	£0
CPAP	£473	£279
Boil and bite mandibular advancement splints	£262	£262
Semi-bespoke mandibular advancement splints	£426	£426
Custom-made mandibular advancement splints	£519	£293

2.2.11 Event costs

2.2.11.1 Road Traffic Accidents

The Department for Transport have data on the cost of RTAs from a healthcare perspective (Medical and Ambulance) disaggregated according to the severity of the casualty[16] in Table 28.

Table 28: Medical and ambulance cost per road traffic accident casualty

Injury Type	Total Casualties	Total Costs	Cost per casualty (£)
Slight Injury	133,302	£146m	£1,095
Seriously Injured	25,511	£401m	£15,719
Killed	1,784	£11m	£6,166

2.2.11.2 Cardiovascular treatment costs

Table 29: Costs associated with cardiovascular events inflated to 2018/19 prices

State	Cost (annual)	Source
Stroke (initial)	£17,928	Xu et al 2016 – SSNAP project

State	Cost (annual)	Source
Post-stroke	£6,806	Xu et al 2016 – SSNAP project
TIA	£1,807	Danese 2016 [12]
Post-TIA	£608	Danese 2016 [12]
Myocardial infarction	£4,803	Danese 2016 [12]
Post-MI	£795	Danese 2016 [12]
Stable angina	£940	NHS reference costs 2016/17. Total HRGs. EB13. Weighted average of the complication and comorbidity codes. [19]
Post-stable angina	£283	Assumed same as post unstable angina state.
Unstable angina	£2,498	Danese 2016 [12]
Post-unstable angina	£283	Danese 2016 [12]

The costs assigned to the cardiovascular health states in the model are summarised in Table 29. They were taken from the NICE hypertension, which inflated costs to 2016/17 prices using the Hospital & Community Health Services (HCHS) Pay & Prices Index.

Costs of stroke were based on Xu 2016 who undertook a patient level simulation using audit data from the UK Sentinel Stroke National Audit Programme and long-term data from the South London Stroke Registry to generate estimates of the financial burden of Stroke to the NHS and social care services. The estimates of costs attributable to stroke from resulting health and social care provision were estimated up to 5 years after the first stroke. The total of 1-year and 5-year costs were reported with NHS and social care costs being reported separately. Only 50% of the care cost component was counted here, on the basis that the other half would be privately funded[64]. For the event state cost in the model, the 1-year total costs from the study were used. The costs of the post-event state was calculated based on the difference in costs between the 1-year and 5-year period, so as not to double count, and the difference in average life-years between years 1 and 5 in order to derive the cost per-life-year.

Danese 2016[12] aimed to characterise the costs to the UK National Health Service of cardiovascular (CV) events among individuals receiving lipid-modifying therapy. It was a retrospective cohort study that used Clinical Practice Research Datalink records from 2006 to 2012 to identify individuals with their first and second CV-related hospitalisations (first event and second event cohorts). Costs were reported for TIA, unstable angina, MI, and heart failure. The study only included healthcare costs. Costs after each CV event were estimated, and the incremental difference from the period before the first CV event was calculated. The follow-up period was 36 months after the event with costs broken down into the first 6 months, and 7–36 months' time. Costs reported here for the event state are made up of the (first event) 6-month cost plus one fifth of the 7–36-month costs to equate to a crude 12-month cost. Post-event costs are made up of the remainder of the 7–36-month cost, that is, the 13–36-month portion. Although this is for more than a year, these costs were felt to be conservative anyway, as they do not include social care costs or the cost of repeat events.

The cost for the stable angina event state was based on NHS reference costs. The Chest pain of recent onset NICE guideline 2016 (CG95) describes resources that should be involved in diagnosing stable chest pain. These resources include clinical assessment, blood tests, CT angiography, and potentially other non-invasive functional imaging tests such as myocardial perfusion scintigraphy. NHS reference costs reports HRG codes for angina (EB13A-D), taking the weighted average of the complication and comorbidity codes of the total HRGs for these codes equals a cost similar to that of the different components involved in diagnosing stable angina costed separately; therefore, the committee agreed that the NHS reference costs value would be appropriate. Although this would not cover management costs outside of the acute admission in the remainder of the first year of the event, the post-event-state cost was felt to capture the majority of the subsequent management.

For the post-stable angina state, the NICE guideline on Stable angina: management (CG126; 2016) undertook a cost effectiveness analysis comparing coronary artery bypass graft (CABG) with percutaneous coronary intervention (PCI), and reported the resources (and cost) of medical treatment associated with ongoing angina. These costs were discussed with the committee but were felt to be an underestimate because they only include drugs, and the committee felt it was likely that it should also include several consultations. Therefore, the committee agreed that the cost post-stable angina should be assumed to be the same as the post-unstable angina cost.

Cardiovascular event costs were inflated to 2018/19 prices using the NHS Cost Inflation Index (pay and prices).[11]

2.3 Computations

The model was constructed in Microsoft Excel 2010 and was evaluated by cohort simulation. Time dependency was built in by cross referencing the cohorts age as a respective risk factor for mortality, CV events and RTAs. Baseline utility was also time dependent and was conditional on the number of years after entry to the model.

After proceeding through the decision tree, all patients are alive and enter one of 12 Markov models. Three of these Markov models simulate patients with no OSAHS through national lifetables. The other 9 Markov models have distinct characteristics and properties. These are described in Table 30.

Table 30: Properties of each of the Markov models

Markov	True OSAHS severity	Intervention	RTA and CV treatment effect
1	no OSAHS	no further treatment	n/a
2		conservative management	
3		MAS	
4		CPAP	
5	mild OSAHS	no further treatment	Increased CV and increased RTA risk
6		conservative management	Increased CV and increased RTA risk
7		MAS	Increased CV and reduced RTA risk
8		CPAP	Increased CV and reduced RTA risk
9	moderate OSAHS	no further treatment	Increased CV and increased RTA risk
10		conservative management	Increased CV and increased RTA risk
11		MAS	Increased CV and reduced RTA risk
12		CPAP	Reduced CV and reduced RTA risk
13	severe OSAHS	no further treatment	Increased CV and increased RTA risk
14		conservative management	Increased CV and increased RTA risk
15		MAS	Increased CV and increased RTA risk
16		CPAP	Reduced CV and reduced RTA risk

Patients start in cycle 0 in the OSAHS health state. Patients can move to an alternative health state at the end of each cycle and this is defined by the patients' mortality,

cardiovascular and RTA transition probabilities. Costs and Quality-adjusted life-years (QALY) were calculated applying a half cycle correction, to reflect the assumption that people will transition between states on average halfway through a cycle. Costs and QALYs were discounted to reflect time preference (discount rate = 3.5%) using the discounting formula:

Discounting formula:

$$\text{Discounted total} = \frac{\text{Total}}{(1+r)^n}$$

Where:
r=discount rate per annum
n=time (years)

2.4 Model validation

The model was developed in consultation with the committee; model structure, inputs and results were presented to and discussed with the committee for clinical validation and interpretation.

The model was systematically checked by the health economist undertaking the analysis; this included inputting null and extreme values and checking that results were plausible given inputs. The model was peer reviewed by a second experienced health economist from the National Guideline Centre; this included systematic checking of the model calculations.

2.5 Estimation of cost effectiveness

The widely used cost-effectiveness metric is the incremental cost-effectiveness ratio (ICER). This is calculated by dividing the difference in costs associated with 2 alternatives by the difference in QALYs. The decision rule then applied is that if the ICER falls below a given cost per QALY threshold then the result is considered to be cost effective. If both costs are lower and QALYs are higher the option is said to dominate and an ICER is not calculated.

$$ICER = \frac{Costs(B) - Costs(A)}{QALYs(B) - QALYs(A)}$$

Where: Costs(A) = total costs for option A; QALYs(A) = total QALYs for option A

Cost effective if:
- ICER < Threshold

When there are more than 2 comparators, as in this analysis, options must be ranked in order of increasing cost then options ruled out by dominance or extended dominance before calculating ICERs excluding these options. An option is said to be dominated, and ruled out, if another intervention is less costly and more effective. An option is said to be extendedly dominated if a combination of 2 other options would prove to be less costly and more effective.

It is also possible, for a particular cost-effectiveness threshold, to re-express cost-effectiveness results in term of net monetary benefit (NMB). This is calculated by multiplying the total QALYs for a comparator by the threshold cost per QALY value (for example, £20,000) and then subtracting the total costs (formula below). The decision rule then applied is that the comparator with the highest NMB is the cost-effective option at the specified threshold. That is the option that provides the highest number of QALYs at an acceptable cost.

$$Net\ Monetary\ Benefit(X) = (QALYs(X) \times \lambda) - Costs(X)$$

Where: λ = threshold (£20,000 per QALY gained)

Cost effective if:
- Highest net benefit

Both methods of determining cost effectiveness will identify exactly the same optimal strategy. For ease of computation NMB is used in this analysis to identify the optimal strategy.

Results are also presented graphically where total costs and total QALYs for each diagnostic strategy are shown. Comparisons not ruled out by dominance or extended dominance are joined by a line on the graph where the slope represents the incremental cost-effectiveness ratio.

2.6 Interpreting Results

NICE sets out the principles that committees should consider when judging whether an intervention offers good value for money.[41-43] In general, an intervention was considered to be cost effective if either of the following criteria applied (given that the estimate was considered plausible):

- The intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant alternative strategies), or
- The intervention costs less than £20,000 per quality-adjusted life-year (QALY) gained compared with the next best strategy.

As we have several interventions, we use the NMB to rank the strategies on the basis of their relative cost effectiveness. The highest NMB identifies the optimal strategy at a willingness to pay of £20,000 per QALY gained.

3 Results

3.1 Comparison of different types of CPAP

Base case results and sensitivity analyses can be found in Table 31.

The lowest cost type of CPAP for patients with mild and moderate OSAHS was fixed-level CPAP with auto-titration, followed by fixed-level CPAP with telemonitoring for one year, and auto-CPAP. The highest cost strategy for both populations was auto-CPAP with telemonitoring. Per protocol, it was assumed that there was no difference in patient outcomes between CPAP strategies and so QALYs were not included in this analysis.

The difference in lifetime cost between CPAP strategies is attributable to the cost of the device and use of telemonitoring and re-titration. Although the total cost of each CPAP strategy was affected by using higher and lower costs for fixed and auto-CPAP, increasing the proportion of patients requiring re-titration from 18% to 30% for fixed-level CPAP, increasing the time required for a physiologist to re-titrate auto-CPAP from 45 to 75 minutes, or changing all three variables at once, the relative cost ranking for each CPAP strategy in both populations was unchanged (Table 31).

Because resource use was based on expert opinion and QALYs were not included, this analysis was evaluated as being partially applicable to the review question with potentially serious limitations.

Table 31: Lifetime cost per patient for different types of CPAP (deterministic)

	Base case	Sensitivity analyses			
		Low auto-CPAP price and high fixed-level CPAP price	30% require re-titration in year 1	Increased staff time for re-titration	All 3 (least favourable to fixed-level CPAP)
Mild OSAHS					
Fixed-level CPAP with auto-titration	9,968	10,031	9,975	9,973	10,045
Fixed-level CPAP with telemonitoring	10,335	10,398	10,337	10,341	10,409
Fixed-level CPAP with telemonitoring (yr 1 only)	10,007	10,069	10,008	10,012	10,080
Auto-CPAP only	10,227	10,194	10,227	10,227	10,194
Auto-CPAP with telemonitoring	10,600	10,568	10,600	10,600	10,568
Moderate OSASHS					
Fixed-level CPAP with auto-titration	10,280	10,350	10,287	10,284	10,363
Fixed-level CPAP with telemonitoring	10,688	10,758	10,690	10,694	10,769
Fixed-level CPAP with telemonitoring (yr 1 only)	10,318	10,388	10,320	10,324	10,399
Auto-CPAP only	10,568	10,532	10,568	10,568	10,532
Auto-CPAP with telemonitoring	10,983	10,947	10,983	10,983	10,947

3.2 Comparison of different treatments for people with mild OSAHS

The base case results can be found in Table 32, Table 33 and Figure 6.

The lowest cost treatment for people with mild OSAHS was conservative management., despite having the highest cost associated with road traffic accidents.

CPAP resulted in the greatest number of QALYs at a cost of £8,515 per QALY gained compared with conservative management. At a threshold of £20,000 per QALY, CPAP was the most cost-effective treatment for people with mild OSAHS.

Table 32: Base case results – cost breakdown of treatment strategies (£, deterministic)

Cost	Conservative management	Boil and Bite MAS	Semi-Bespoke MAS	Custom-made MAS	CPAP
Intervention	146	3,259	5,308	3,880	3,677
Road traffic accidents	723	292	292	292	292
Cardiovascular events	6,024	6,037	6,037	6,037	6,037
Total	6,892	9,589	11,638	10,210	10,007

Table 33: Base case results - cost-effectiveness of treatment strategies (probabilistic)

	Conservative management	Boil and Bite MAS	Semi-Bespoke MAS	Custom-made MAS	CPAP
Costs (£)	6,894	9,590	11,639	10,211	10,008
QALYs	13.35	13.52	13.52	13.65	13.71
Cost per QALY gained (vs conservative management) (£)		15,162	27,389	10,740	8,515
Incremental net monetary benefit (INMB)* (£)	0	860	-1,280	2,860	4,201
Median Rank of INMB (95% confidence interval)*	3 (2,5)	3 (1,5)	5 (1,5)	2 (1,5)	1 (1,4)
Probability highest rank*	1%	11%	7%	29%	52%

** at a threshold of £20,000 per QALY gained*

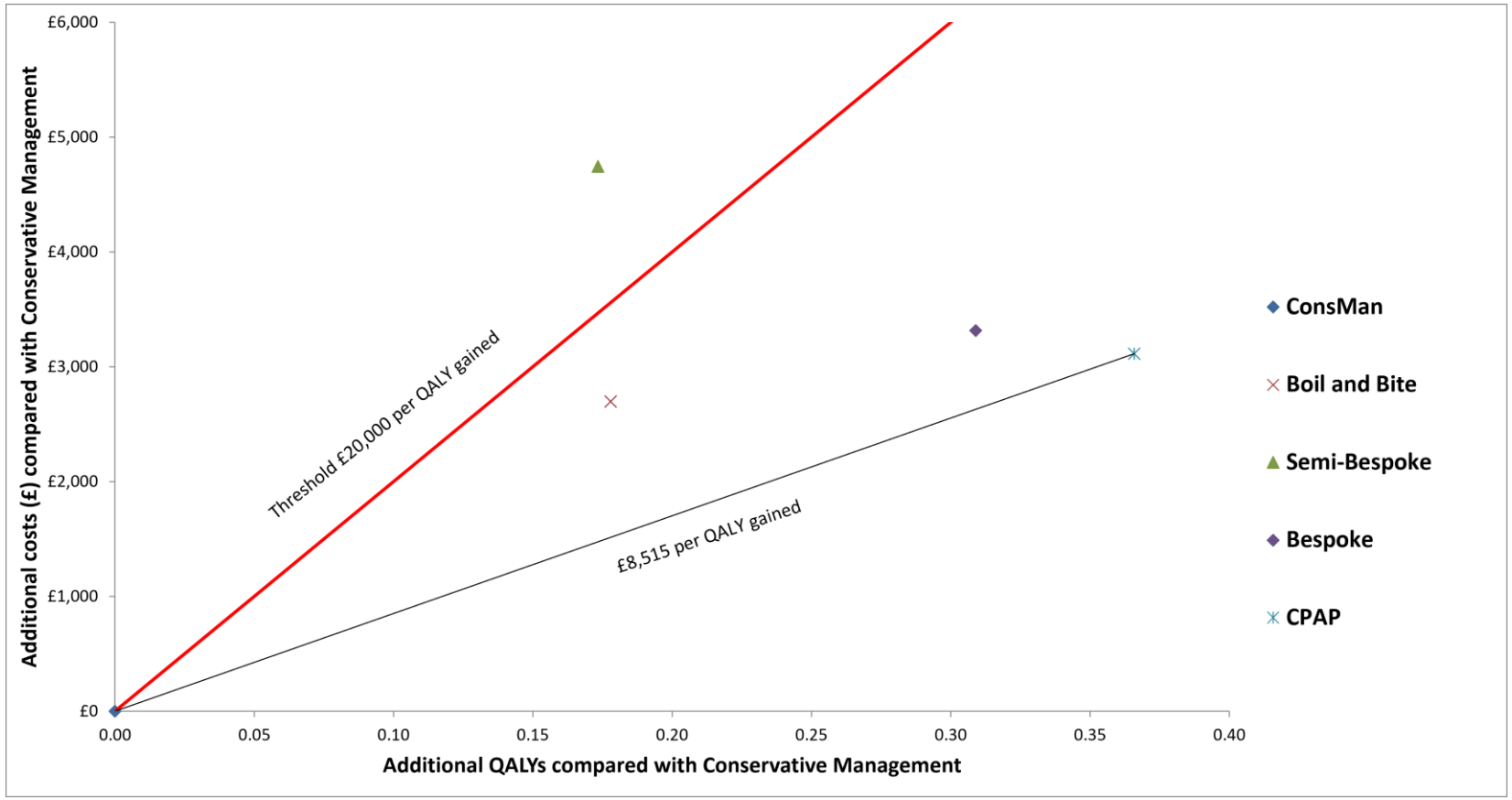


Figure 6: Base case results –cost effectiveness plane (probabilistic)

Compared to conservative management the cost per QALY gained varied between £7,200 and £16,600 for CPAP and between £5,800 and £14,200 for custom-made MAS - Table 34. The ranking of treatments was quite stable across the analyses (Table 35). The only scenario where CPAP was when all the assumptions least favourable to CPAP were used in combination. Semi-bespoke MAS was always the least cost effective intervention but in some scenarios it was cost effective compared to conservative management: when longer durability was assumed or when the quality of life gain was estimated by mapping from the improvements in ESS seen in the trials.

Table 34: Sensitivity analysis - cost per QALY gained compared with conservative management (deterministic)

	Cost per QALY gained (versus Conservative Management)			
Analysis	**Boil and Bite MAS**	**Semi-Bespoke MAS**	**Custom-made MAS**	**CPAP**
Base case results	15,180	28,205	10,787	8,518
CPAP more cost effective				
CV effects apply to CPAP	15,180	28,205	10,787	8,258
CPAP device lower cost	15,180	28,205	10,787	7,846
CPAP device cost and staff costs lower	15,180	28,205	10,787	7,512
All of the above (CPAP more cost effective)	15,180	28,205	10,787	7,271
Oral devices more cost effective				
Longer durability of boil and bite and semi-bespoke oral devices	9,785	17,909	10,787	8,518
Longer durability for bespoke oral devices	15,180	28,205	8,433	8,518
CPAP device durability is 5 years	15,180	28,205	10,787	8,991
High CPAP cost: auto-CPAP with telemonitoring	15,180	28,205	10,787	10,142
High consumable cost for CPAP	15,180	28,205	10,787	11,651
CV treatment effect for oral devices	14,389	26,822	10,787	8,518
Low bespoke oral device cost	15,180	28,205	6,976	8,518
All of the above (oral devices more cost effective)	9,211	16,961	5,849	14,007
Cohort				
Low starting age of 30 years	12,345	23,417	9,224	7,355

Analysis	Cost per QALY gained (versus Conservative Management)			
	Boil and Bite MAS	Semi-Bespoke MAS	Custom-made MAS	CPAP
High starting age of 80 years	17,986	33,716	13,165	10,186
Higher risk profile	15,737	29,276	11,226	8,860
Lower risk profile	15,730	28,925	10,964	8,655
Other				
Reduce treatment dropout rate by 20%	15,328	28,422	10,803	8,533
Increase treatment dropout rate by 20%	15,024	27,979	10,772	8,504
RTAs have larger impact (includes police costs and multiple casualties)	13,569	26,287	9,891	7,781
Treatment has no impact on RTAs	21,197	37,543	13,504	10,556
Quality of life gains for oral devices mapped from ESS rather than direct EQ-5D data	13,037	16,854	10,797	8,518
Sleep study for oral devices	16,245	29,330	11,402	8,518
Least favourable assumptions for intervention	22,488	38,922	14,189	16,554

Table 35: Sensitivity analyses – net monetary benefit rank of treatment strategies (deterministic)

Analysis	Rank of net monetary benefit at £20,000 per QALY gained				
	ConsM	Boil and Bite	Semi-Bespoke	Bespoke	CPAP
Base case results	4	3	5	2	1
CPAP more cost effective					
CV effects apply to CPAP	4	3	5	2	1
CPAP device lower cost	4	3	5	2	1
CPAP device and staff costs lower	4	3	5	2	1
All of the above (CPAP more cost effective)	4	3	5	2	1
Oral devices more cost effective					
Longer durability of boil and bite and semi-bespoke oral devices	5	3	4	2	1

Analysis	Rank of net monetary benefit at £20,000 per QALY gained				
	ConsM	Boil and Bite	Semi-Bespoke	Bespoke	CPAP
Longer durability for bespoke oral devices	4	3	5	2	1
CPAP device durability is 5 years	4	3	5	2	1
Longer durability of boil and bite and semi-bespoke oral devices	4	3	5	2	1
High consumable cost for CPAP	4	3	5	2	1
CV treatment effect for oral devices	4	3	5	2	1
Low bespoke oral device cost	4	3	5	2	1
All of the above (oral devices more cost effective)	5	3	4	1	2
Cohort					
Low starting age of 30 years	4	3	5	2	1
High starting age of 80 years	4	3	5	2	1
Higher risk profile	4	3	5	2	1
Lower risk profile	4	3	5	2	1
Other					
Reduce treatment dropout rate by 20%	4	3	5	2	1
Increase treatment dropout rate by 20%	4	3	5	2	1
RTAs have larger impact (includes police costs and multiple casualties)	4	3	5	2	1
Treatment has no impact on RTAs	3	4	5	2	1
Quality of life gains for oral devices mapped from ESS rather than direct EQ-5D data	5	3	4	2	1
Sleep study for oral devices	4	3	5	2	1
Least favourable assumptions for intervention	3	4	5	1	2

3.3 Comparison of different diagnostic pathways for OSAHS

The base case results can be found in Table 36, Table 37, and Figure 7.

Oximetry with conservative management was the lowest cost diagnostic pathway for symptomatic adults tested for OSAHS, while hospital RP with intervention for mild OSAHS was the highest cost pathway. Most of the difference in lifetime costs between diagnostic pathways was attributable to diagnostic accuracy and the cost of treatment.

Cost effectiveness of tests, if people with mild OSAHS get conservative management

Home respiratory polygraphy was cost effective compared with home oximetry (£10,600 per QALY gained) and compared with screening (£9,400 per QALY gained).

Hospital respiratory polygraphy was not cost effective compared with home respiratory polygraphy (£32,000 per QALY gained) but it was cost effective compared with home oximetry (£15,600 per QALY gained) and compared with screening (£15,000 per QALY gained).

Screening (home oximetry and then re-testing negatives with home respiratory polygraphy) was cost effective at £30,000 per QALY but not at £20,000 per QALY compared with home oximetry alone (£24,200 per QALY gained).

Cost effectiveness of tests, if people with mild OSAHS get intervention

Home respiratory polygraphy was cost effective compared with home oximetry (£9,600 per QALY gained) and compared with screening (£6,700 per QALY gained).

Hospital respiratory polygraphy was not cost effective compared with home respiratory polygraphy (£43,600 per QALY gained) but it was compared with home oximetry (£14,900 per QALY gained) and compared with screening (£16,300 per QALY gained).

Screening was cost effective compared with home oximetry alone (£12,800 per QALY gained).

Most cost-effective pathway overall

At a threshold of £20,000 per QALY, home RP with people with mild OSAHS receiving intervention was the most cost-effective diagnostic pathway.

Although the evidence review found hospital RP to be more sensitive than home RP, the results of our model showed that the increased cost of hospital RP was unlikely to offer value for money compared with home RP.

Table 36: Base case results – Mean cost for diagnostic pathways (deterministic)

	Mean cost (£)					Mean QALYs	Cost per QALY gained (£)[a]	Rank[b]
	Diag-nosis	Treat ment	RTAs	CV events	Total			
Oximetry (ConsM)	80	1,510	423	4,924	6,937	13.359		7
Screening (ConsM)	80	1,510	423	4,924	6,937	13.364	23,909	8
Home RP (ConsM)	135	1,592	416	4,924	7,067	13.422	10,549	4
Hospital RP (ConsM)	190	2,139	350	4,922	7,601	13.440	15,442	6
Oximetry (Interv'n)	637	2,303	330	4,921	8,190	13.429	11,631	5
Screening (Interv'n)	80	2,434	315	4,925	7,753	13.456	11,949	3
Home RP (Interv'n)	135	2,762	281	4,926	8,103	13.488	10,632	1
Hospital RP (Interv'n)	190	2,943	257	4,924	8,314	13.499	13,208	2

ConsM=Conservative management; CPAP=continuous passive airway pressure; CV=cardiovascular; Interv'n=Intervention=1/3 CPAP, 1/3 Mandibular advancement splints, 1/3=conservative management; QALY=quality-adjusted life-year; RP=respiratory polygraphy; RTA=road traffic accidents.
(a) Compared with Oximetry (ConsM)
(b) Rank of net monetary benefit at £20,000 per QALY gained

Table 37: Base case results – cost effectiveness of diagnostic pathways (probabilistic)

N		Mean costs (£)	Mean QALYs	Cost (£) per QALY gained (versus N=1)	INMB (£)* (n versus N=1)	INMB (£)* Rank	Probability highest INMB*	Median Rank of INMB*	95% CI of INMB rank*	
									Lower	Higher
1	Oximetry (ConsM)	6,943	13.526		0	7	8%	7	1	8
2	Screening (ConsM)	7,074	13.531	24,173	-23	8	0%	7	2	8
3	Home RP (ConsM)	7,601	13.587	10,685	573	5	2%	4	2	8
4	Oximetry (Intervention)	7,756	13.595	11,693	577	4	1%	4	2	6
5	Screening (Intervention)	8,107	13.622	12,010	774	3	6%	3	1	6
6	Hospital RP (ConsM)	8,194	13.606	15,612	351	6	0%	6	3	8
7	Home RP (Intervention)	8,316	13.654	10,722	1,188	1	71%	1	1	6
8	Hospital RP (Intervention)	8,793	13.664	13,312	929	2	12%	3	1	8

ConsM=Conservative management, CPAP=continuous passive airway pressure, INMB=Incremental net monetary benefit, QALY=quality-adjusted life-year, RP=respiratory polygraphy.
** at £20,000 per QALY gained*

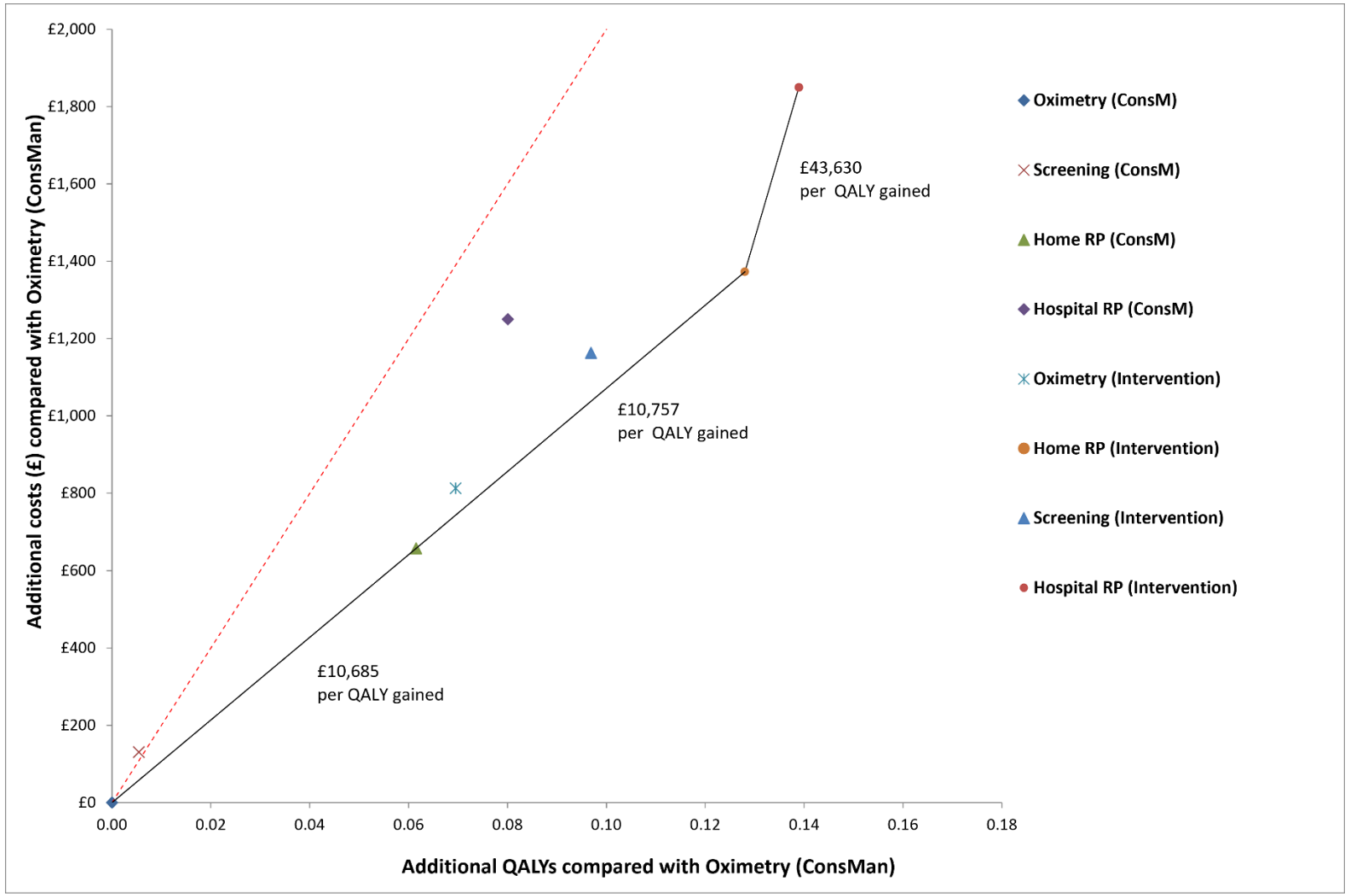


Figure 7: Base case results – incremental cost effectiveness plane for diagnostic pathways (probabilistic)

Sensitivity analyses

The model was robust to a large number of sensitivity analyses, demonstrated by the stability of treatment rank in Table 38 and the cost per QALY gained in Table 39. In every scenario one of the four 'intervention' strategies was ranked first. Only in two scenarios was home respiratory polygraphy not ranked first:

- When it was assumed that all people with mild OSAHS receive CPAP then home oximetry screening was most cost-effective test. We conducted a threshold analysis on the proportion of people that receive CPAP for mild OSAHS to see at which point the most cost-effective strategy switches. If less than 92% of them receive CPAP then home respiratory polygraphy is the most cost-effective test. The reason that it switches is that if we are treating people with mild OSAHS exactly the same as people with moderate OSAHS then the need to differentiate mild OSAHS from moderate OSAHS is not important, whereas far more patients with moderate OSAHS are misdiagnosed as having Mild OSAHS with home oximetry than with home respiratory polygraphy.
- When we relaxed the assumption that that people with moderate/severe OSAHS would be retested due to persistence of symptoms then oximetry screening was the most cost-effective strategy. We conducted a threshold analysis on the proportion of these misdiagnosed people that are retested to see at which point the most cost-effective strategy switches. If 68% or more are re-tested, then home respiratory polygraphy is the most cost-effective test. If it is less than that then the screening strategy, where all patients testing negative are systematically retested yields more QALYs and is more cost effective.

Table 38: Sensitivity analyses – net monetary benefit rank of diagnostic pathways (deterministic)

	Rank of net monetary benefit at £20,000 per QALY gained							
Analysis	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Base case results	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Oximetry (Interv'n)	Home RP (ConsM)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
Diagnostic accuracy of strategies								
Extent of misdiagnosis is constrained (e.g. moderate OSAHS people can only be misdiagnosed as severe or mild OSAHS but not as no OSAHS)	Home RP (Interv'n)	Screening (Interv'n)	Oximetry (Interv'n)	Hospital RP (Interv'n)	Home RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)	Hospital RP (ConsM)
Retest for false negatives with persistent symptoms turned off in model	Screening (Interv'n)	Screening (ConsM)	Home RP (Interv'n)	Hospital RP (Interv'n)	Home RP (ConsM)	Hospital RP (ConsM)	Oximetry (Interv'n)	Oximetry (ConsM)
Retest correlation of 20%	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Hospital RP (ConsM)	Screening (ConsM)	Oximetry (ConsM)

Analysis	Rank of net monetary benefit at £20,000 per QALY gained							
	1	2	3	4	5	6	7	8
Retest correlation of 40%	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Hospital RP (ConsM)	Oximetry (Interv'n)	Screening (ConsM)	Oximetry (ConsM)
Home oximetry diagnostic meta-analysis includes Pataka 2016	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Oximetry (Interv'n)	Home RP (ConsM)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
Diagnostic strategies								
Retest for false negatives with persistent symptoms is Hospital RP	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
1st test in screening strategy home RP	Home RP (Interv'n)	Screening (Interv'n)	Hospital RP (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Screening (ConsM)	Hospital RP (ConsM)	Oximetry (ConsM)
2nd test in screening strategy hospital RP	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
1st test in screening strategy home RP, second test hospital RP	Home RP (Interv'n)	Screening (Interv'n)	Hospital RP (Interv'n)	Oximetry (Interv'n)	Home RP (ConsM)	Screening (ConsM)	Hospital RP (ConsM)	Oximetry (ConsM)
Polysomnography after second test for all False Negatives with underlying moderate/severe disease	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
Polysomnography after first test for all False Negatives with underlying moderate/severe disease	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Oximetry (Interv'n)	Home RP (ConsM)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
Treatment more cost effective								
CPAP ESS effect is based on ESS subgroup (not AHI subgroup)	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Hospital RP (ConsM)	Oximetry (Interv'n)	Oximetry (ConsM)	Screening (ConsM)
Reduce CPAP dropout rate by 20%	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)

Analysis	Rank of net monetary benefit at £20,000 per QALY gained							
	1	2	3	4	5	6	7	8
NHS and police costs	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Oximetry (Interv'n)	Home RP (ConsM)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
CPAP device lower cost	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
CPAP device and staff costs for education and setup are lower	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
All of the above (treatment more cost effective)	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Hospital RP (ConsM)	Oximetry (Interv'n)	Oximetry (ConsM)	Screening (ConsM)
Treatment less cost effective								
Increase CPAP dropout rate by 20%	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
High CPAP cost: auto-CPAP with telemonitoring	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Oximetry (Interv'n)	Home RP (ConsM)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
CPAP lifetime shorter: 5 years	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
Turn off RTA treatment effects	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
Turn off CV treatment effects	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Oximetry (Interv'n)	Home RP (ConsM)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
Turn off CV and RTA treatment effects	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)

Analysis	Rank of net monetary benefit at £20,000 per QALY gained							
	1	2	3	4	5	6	7	8
All of the above (treatment less cost effective)	Home RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Hospital RP (Interv'n)	Oximetry (ConsM)	Screening (ConsM)	Hospital RP (ConsM)
Cohort								
Low starting age of 30 years	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Oximetry (Interv'n)	Home RP (ConsM)	Hospital RP (ConsM)	Screening (ConsM)	Oximetry (ConsM)
High starting age of 80 years	Home RP (Interv'n)	Oximetry (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)	Hospital RP (Interv'n)	Hospital RP (ConsM)
Higher risk profile	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
Lower risk profile	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
Prevalence estimate of OSAHS is lower	Home RP (Interv'n)	Oximetry (Interv'n)	Screening (Interv'n)	Hospital RP (Interv'n)	Home RP (ConsM)	Oximetry (ConsM)	Hospital RP (ConsM)	Screening (ConsM)
Prevalence estimate of OSAHS is higher	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Hospital RP (ConsM)	Screening (ConsM)	Oximetry (ConsM)
Other								
CV treatment effect also applies to mild OSAHS	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
False positives continue with treatment beyond 12 months	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
Patients diagnosed with mild OSAHS: 100% receive CPAP	Screening (Interv'n)	Home RP (Interv'n)	Oximetry (Interv'n)	Hospital RP (Interv'n)	Home RP (ConsM)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)

Analysis	Rank of net monetary benefit at £20,000 per QALY gained							
	1	2	3	4	5	6	7	8
Patients diagnosed with mild OSAHS: 50% receive customised oral devices and 50% CPAP	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Oximetry (Interv'n)	Home RP (ConsM)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
Patients diagnosed with mild OSAHS: 50% receive conservative management and 50% CPAP	Home RP (Interv'n)	Screening (Interv'n)	Hospital RP (Interv'n)	Oximetry (Interv'n)	Home RP (ConsM)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)
Low Home RP costs	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Home RP (ConsM)	Oximetry (Interv'n)	Hospital RP (ConsM)	Screening (ConsM)	Oximetry (ConsM)
High Home RP costs	Home RP (Interv'n)	Hospital RP (Interv'n)	Screening (Interv'n)	Oximetry (Interv'n)	Home RP (ConsM)	Hospital RP (ConsM)	Oximetry (ConsM)	Screening (ConsM)

*ConsM=Conservative management, CPAP=continuous passive airway pressure, INMB=Incremental net monetary benefit, QALY=quality-adjusted life-year, RP=respiratory polygraphy, RTA=road traffic accident, * at £20,000 per QALY gained*

Table 39: Sensitivity analyses - cost per QALY gained for selected comparisons* (probabilistic)

Analysis	Cost per QALY gained		
	Home RP (ConsM) vs Oximetry (ConsM)	Home RP (Interv'n) vs Home RP (Cons M)	Hospital RP (Interv'n) vs Home RP (Interv'n)
Base case results	10,685	10,757	43,630
Diagnostic accuracy of strategies			
Extent of misdiagnosis is constrained (e.g. moderate OSAHS people can only be misdiagnosed as severe or mild OSAHS but not as no OSAHS)	14,552	10,204	751,471
Retest for false negatives with persistent symptoms turned off in model	9,844	10,704	39,684
Retest correlation of 20%	10,178	10,701	43,562
Retest correlation of 40%	9,947	10,677	42,321
Home oximetry diagnostic meta-analysis includes Pataka 2016	10,749	10,711	44,099
Diagnostic strategies			
Retest for false negatives with persistent symptoms is Hospital RP	9,544	10,671	43,930

Analysis	Cost per QALY gained		
	Home RP (ConsM) vs Oximetry (ConsM)	Home RP (Interv'n) vs Home RP (Cons M)	Hospital RP (Interv'n) vs Home RP (Interv'n)
1st test in screening strategy home RP	10,450	10,688	44,053
2nd test in screening strategy hospital RP	10,611	10,782	44,472
1st test in screening strategy home RP, second test hospital RP	10,629	10,743	43,222
Polysomnography after second test for all False Negatives with underlying moderate/severe disease	10,539	10,714	42,589
Polysomnography after first test for all False Negatives with underlying moderate/severe disease	9,540	10,674	44,390
Treatment more cost effective			
CPAP ESS effect is based on ESS subgroup (not AHI subgroup)	8,195	10,011	30,876
Reduce CPAP dropout rate by 20%	10,528	10,713	42,264
NHS and police costs	9,771	9,805	43,423
CPAP device lower cost	9,855	10,283	42,752
CPAP device and staff costs for education and setup are lower	9,567	10,072	42,796
All of the above (treatment more cost effective)	6,869	8,566	28,708
Treatment less cost effective			
Increase CPAP dropout rate by 20%	10,590	10,687	45,342
High CPAP cost: auto-CPAP with telemonitoring	12,116	11,668	45,908
CPAP lifetime shorter: 5 years	10,900	10,946	44,550
Turn off RTA treatment effects	12,532	13,280	46,172
Turn off CV treatment effects	10,742	10,744	45,008
Turn off CV and RTA treatment effects	12,988	13,551	46,636
All of the above (treatment less cost effective)	15,640	15,188	52,916
Cohort			
Low starting age of 30 years	8,880	9,148	34,410
High starting age of 80 years	15,824	13,272	107,579
Higher risk profile	10,921	11,134	47,662

Analysis	Cost per QALY gained		
	Home RP (ConsM) vs Oximetry (ConsM)	Home RP (Interv'n) vs Home RP (Cons M)	Hospital RP (Interv'n) vs Home RP (Interv'n)
Lower risk profile	10,598	10,807	41,201
Prevalence estimate of OSAHS is lower	12,742	11,581	64,530
Prevalence estimate of OSAHS is higher	10,239	10,569	42,177
Other			
CV treatment effect also applies to mild OSAHS	10,543	10,607	43,867
False positives continue with treatment beyond 12 months	10,542	10,728	43,373
Patients diagnosed with mild OSAHS: 100% receive CPAP	10,599	8,622	Dominated
Patients diagnosed with mild OSAHS: 50% receive customised oral devices and 50% CPAP	10,509	10,625	58,403
Patients diagnosed with mild OSAHS: 50% receive conservative management and 50% CPAP	10,415	8,599	55,451
Low Home RP costs	9,362	10,712	52,575
High Home RP costs	11,290	10,718	38,057

ConsM=Conservative management, CPAP=continuous passive airway pressure, INMB=Incremental net monetary benefit, QALY=quality-adjusted life-year, RP=respiratory polygraphy, RTA=road traffic accident
** The comparisons presented are those that were on the cost effectiveness frontier – see Figure 7.*

4 Evidence statements

4.1 Comparison of different types of CPAP

- One original cost comparison found that:
  - Fixed-level CPAP (using auto-CPAP only for re-titration) was the lowest cost strategy
  - Fixed-level CPAP (with telemonitoring) was less costly than auto-CPAP *with* telemonitoring
  - Fixed-level CPAP (with telemonitoring for 1 year) was less costly than auto-CPAP *without* telemonitoring
  - Fixed-level CPAP (with telemonitoring) was *more* costly than auto-CPAP *without* telemonitoring

  This analysis was assessed to be partially applicable with potentially serious limitations.

4.2 Comparison of different treatments for people with mild OSAHS

CPAP compared with conservative management

- One original cost-utility analyses found that CPAP was cost effective compared with conservative management for people with mild OSAHS (£8,500 per QALY gained). This study was assessed as directly applicable with minor limitations.

Oral devices compared with conservative management

- One original cost-utility analysis found that
  - custom-made mandibular advancement splints and boil and bite mandibular advancement splints were cost effective compared with conservative management for people with mild OSAHS (£10,700 and £15,200 per QALY gained).
  - semi-bespoke mandibular advancement splints were not cost effective compared with conservative management for people with mild OSAHS (£27,400 per QALY gained).

  This study was assessed as directly applicable with minor limitations.

CPAP compared with oral devices

- One original cost-utility analysis found that
  - CPAP was cost effective compared with boil and bite mandibular advancement splints for people with mild OSAHS (£2,200 per QALY gained).
  - semi-bespoke mandibular advancement splints and custom-made mandibular advancement splints were dominated by CPAP for people with mild OSAHS.

  This study was assessed as directly applicable with minor limitations.

Comparisons of different oral devices

- One original cost-utility analysis found that
  - custom-made mandibular advancement splints were cost effective compared with boil and bite for people with mild OSAHS (£4,700 per QALY gained).
  - semi-bespoke mandibular advancement splints were dominated by custom-made mandibular advancement splints for people with mild OSAHS.

  This study was assessed as directly applicable with minor limitations.

4.3 Comparison of different diagnostic pathways for OSAHS

- An original cost-utility analysis for symptomatic people suspected of having OSAHS, found that when only moderate and severe OSAHS is treated with CPAP and those with mild OSAHS receive conservative management:
  - home respiratory polygraphy was cost effective compared with home oximetry (£10,600 per QALY gained).
  - hospital respiratory polygraphy was not cost effective compared with home respiratory polygraphy (£32,000 per QALY gained).
  - hospital respiratory polygraphy was cost effective compared with home oximetry (£15,600 per QALY gained).
  - Screening with home oximetry and then re-testing negatives with home respiratory polygraphy was cost effective at £30,000 per QALY but not at £20,000 per QALY compared with home oximetry alone (£24,200 per QALY gained).

  This was assessed as directly applicable with potentially serious limitations.
- An original cost-utility analysis for symptomatic people suspected of having OSAHS found that when 1/3 of people with mild OSAHS receive CPAP, 1/3 receive MAS and the remaining 1/3 receive conservative management:
  - home respiratory polygraphy was cost effective compared with home oximetry (£9,600 per QALY gained).
  - hospital respiratory polygraphy was not cost effective compared with home respiratory polygraphy (£43,600 per QALY gained).
  - hospital respiratory polygraphy was cost effective compared with home oximetry (£14,900 per QALY gained).
  - Screening with home oximetry and then re-testing negatives with home respiratory polygraphy was cost effective compared with home oximetry alone (£12,800 per QALY gained).

  This was assessed as directly applicable with potentially serious limitations..

  These analyses were assessed as having potentially serious limitations because the diagnostic accuracy evidence was very limited (especially for home oximetry).

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