

The cost-effectiveness of nCPAP treatment in patients with moderate-to-severe obstructive sleep apnoea

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The cost-effectiveness of nCPAP treatment in patients with moderate-to-severe obstructive sleep apnoea. J. Mar, J.R. Rueda, J. Durán-Cantolla, C. Schechter, J. Chilcott. ©ERS Journals Ltd 2003.

ABSTRACT: The demand for diagnostic and therapeutic services for obstructive sleep apnoea syndrome (OSAS) showed marked growth during the 1990s. This paper analyses the long-term cost-effectiveness of nasal continuous positive airway pressure (nCPAP) treatment in comparison to conventional null treatment.

A Markov model was used to represent the natural history of OSAS based upon published evidence. Utility values came from a survey of OSAS patients. Data on health costs were collected from hospitals in the Basque Country, Spain.

The incremental cost-effectiveness ratio of nCPAP treatment is <6,000 Euros per quality-adjusted life year. On disaggregated analysis, nCPAP treatment accounts for 86% of incremental costs; 84% of incremental effectiveness is attributable to improved quality of life.

Treatment of obstructive sleep apnoea syndrome with nasal continuous positive airway pressure has a cost-effectiveness that is in line with that of other commonly funded treatments such as antihypertensive drugs. The key clinical benefit of nasal continuous positive airway pressure treatment is improvement in the quality of life of patients with obstructive sleep apnoea syndrome. This benefit is also precisely the one for which the evidence base is strongest. The remaining uncertainties concerning the impact of nasal continuous positive airway pressure on long-term mortality have only a relatively small impact on the economics of treatment.

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Obstructive sleep apnoea syndrome (OSAS) [1] has been associated with increased cardiovascular morbidity and mortality [2–4], traffic accidents [5, 6] and a decline in quality of life [7–9]. Estimates of its prevalence in the adult population range 1–4% in males and 0.5–3% in females [10–12]. Both diagnosis, based on polysomnography, and treatment, with nasal continuous positive airway pressure (nCPAP), carry a potentially high cost [13]. Reflecting the potentially high prevalence, the demand for diagnostic and therapeutic services for OSAS has grown markedly during the 1990s. These two factors, high cost and growing demand, have led to OSAS being defined as a priority disease area for health technology assessment [14, 15]. Prominence has been given to the controversial review of WRIGHT *et al.* [15] questioning the available evidence about the effects of OSAS on cardiovascular morbidity and mortality and the benefit of treatment with nCPAP. Other authors have refuted these arguments, indicating the importance of analysing subgroups defined by severity of OSAS-related functional impairment and acceptance of the improvement in quality of life and risk of traffic accidents that treatment with CPAP provides to patients with severe OSAS [16–20].

Cost-effectiveness studies permit comparison of the benefits and costs of different treatments [21] and have been applied to

OSAS [7, 13, 22]. These studies focused on various diagnostic approaches to OSAS patients. They assume, implicitly, that nCPAP is an efficient treatment compared to other clinical practices and focus analysis on the different diagnostic strategies. Nevertheless, that assessment has not been proved in the literature. There is a lack of information about the impact on effectiveness and cost of introduction of nCPAP in the management of OSAS patients compared to the previous approach based on hygienic measures and follow-up. OSAS knowledge expanded during the 1980s [23]. It is time to determine whether treating it is comparable in cost-effectiveness to widely accepted treatments of other illnesses.

The present article presents an assessment of the cost-effectiveness of nCPAP treatment in patients with OSAS and investigates the relative impact of the potential clinical benefits of treatment.

Methods

Disease treatment pathway model

Each individual OSAS patient lives out a lifetime that consists of moving through different health states over time

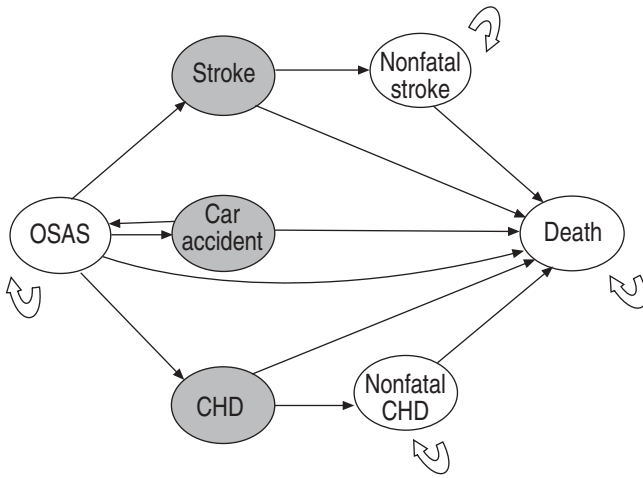


Fig. 1.—Natural history of obstructive sleep apnoea syndrome (OSAS) represented in a Markov-state diagram. Open arrows represent remaining in the same state and solid arrows transition between states (□: Markov state; ■: temporary event). CHD: coronary heart disease.

until death. Treatment with nCPAP changes both the length and quality of life that patients spend in each health state. A Markov model (semi-Markov) [24], implemented in DATA 3.5 (Tree-Age Software, Inc., Boston, MA, USA), was used to represent the natural history of OSAS (fig. 1) and calculate the mean time spent within each state. This figure shows the death risks that are increased in OSAS patients in comparison to the general population and that can be improved with nCPAP treatment: stroke, coronary heart disease (CHD), and car accidents. When the model starts running, all patients are in the state "OSAS". At the end of each cycle (1 yr), they must be in one of the following four states: "OSAS", "nonfatal stroke", "nonfatal CHD" and "death". During a cycle, patients can also experience a "car accident", "stroke" or "CHD" as temporary events. The "death" (absorbing) state is characterised by a zero probability of change. In a Markov model, the distribution of a population among various health states is calculated iteratively: the proportion in each health state at any given time is computed from the proportions in the health states during the preceding time period and known probabilities of changing from one health state to another. These probabilities are called transition probabilities and measure the probability of a patient moving from one state to another one during 1 yr. As the model runs, it calculates the time a patient spends in each state. Since the probabilities, costs and utilities are different, the model is run under the two alternative assumptions (table 1) to calculate the cost and effectiveness associated with each alternative together with the incremental or marginal cost-effectiveness of the novel strategy. The effectiveness measure employed is the quality-adjusted life year (QALY), described in the (Appendix); this measure has the advantage of combining the changes in mortality and morbidity into a single measure. The effectiveness of each alternative under analysis is calculated, by first, multiplying the quality-adjustment weight (utility) for each health state by the time spent in it and, secondly, summing the number of QALYs spent in each state.

The transition probabilities are derived from known epidemiological parameters such as age/sex-specific disease incidence and mortality rate, and vary over time. In the present model, they are based on mortality rates for stroke, CHD, traffic accidents and all causes, by age and sex, in the Basque Country, a region in the North of Spain with 2.3 million inhabitants. The numerator events used to calculate mortality rates for stroke include codes 430–438, and those for CHD codes 410–414, of the Clinical Modification of the ninth

Table 1.—Values of model parameters

	Untreated OSAS	Treated OSAS	[Refs.]
Probabilities[#]			
CHD	1.185	1	[2, 25, 26]
Stroke	1.353	1	[2, 25, 26]
Car accident	8.1	1	[5, 20]
Death after stroke	1.1	1.1	[26]
Death after CHD	1.1	1.1	[26]
Utilities[†]			
OSAS	0.738	0.811	Present study
Nonfatal stroke	0.590	0.649	[27]
Nonfatal CHD	0.664	0.730	[27]
Costs⁺			
Diagnosis	0	1028	[28]
Treatment with nCPAP	0	358	Present study
Stroke hospitalisation	3373	3373	[26]
CHD hospitalisation	3128	3128	[26]

OSAS: obstructive sleep apnoea syndrome; CHD: coronary heart disease; nCPAP: nasal continuous positive airway pressure. [#]: relative risk; [†]: European quality of life 5D scale; ⁺: in Euros.

revision of the International Classification of Diseases. The mortality rates for traffic accidents include codes E810–E819. The transition probabilities from the "OSAS" state to the "death" state were based on mortality rates for all causes except stroke, CHD and car accidents. The Markov cycle duration was 1 yr. Transition probabilities were calculated as $p=1-e^{-rate}$, assuming that the mortality rate is steady throughout each year. Half-cycle correction was applied to improve the accuracy of the results [24]. The general population mortality rates by age and sex were multiplied by the corresponding relative risks, shown in table 1, to calculate the corrected rate applying to each subpopulation (treated and nontreated OSAS patients).

The parameters of the model, including relative risks, utilities and costs, are presented in table 1. The treatment strategy under analysis is the option of diagnosing OSAS and treating it using nCPAP. The conventional alternative consists of letting the natural progression of OSAS continue. Before the introduction of nCPAP, the natural history of OSAS patients could only be improved by treating other cardiovascular risk factors that were associated with it, such as hypertension, or conditions that aggravated its severity, such as obesity. These conditions are also treated when patients use nCPAP. Therefore, it is inappropriate to introduce interventions related to these other risk factors into the model because the measure calculated is the incremental cost-effectiveness ratio specifically related to nCPAP treatment and these interventions are introduced in both of the compared strategies. Effect on blood pressure was introduced because it was assumed that blood pressure returns to pre-OSAS levels as a consequence of the reduction in apnoea/hypopnoea index (AHI) by nCPAP, thereby improving stroke and CHD relative risks. Given uncertainty regarding this assumption [25], it was evaluated through sensitivity analysis, in which the benefit was allowed to range 100–25%.

OSAS is a recognised risk factor for arterial hypertension [2], and relative risks for stroke and CHD [29] have been introduced into the model. The methodology and validation of this element of the model are presented in MAR and RODRIGUEZ-ARTALEJO [26]. The key assumption in assessment of cardiovascular risk is that, for OSAS patients with an AHI of >30, there is an increase in diastolic arterial pressure of 3.6 mmHg [2]. The well-known meta-analysis of MACMAHON *et al.* [29] showed that increases in blood pressure are linearly correlated with the natural logarithm of the risk of stroke and

CHD. By applying this relationship to the 3.6 mmHg increase in diastolic pressure, the natural logarithms of the risks were obtained in order to calculate relative risks for both diseases. As is usual in cardiovascular epidemiology, it was assumed that the relative risk for stroke and CHD remain constant at a given blood pressure [30] and that absolute risk is best estimated by applying this relative risk to the baseline absolute risk for patient age and sex. This condition is introduced in the model by means of rates tables.

The base case is defined as a 50-yr-old male patient with moderate-to-severe OSAS, defined by an AHI of >30 and daytime sleepiness (Epworth scale score of >10), typical of the patients served by the Sleep Unit of Txagorritxu Hospital, Vitoria-Gasteiz, Spain. The parameters (mean \pm SD) describing the last 5,000 patients referred for suspected OSAS are: 81% male, body mass index (BMI) 29.8 ± 5.7 kg·m⁻², patients with a BMI of >30 kg·m⁻² 51.2%, AHI 25.7 ± 25.3 , number of desaturations of $>3\%$ per hour of sleep 24.5 ± 22.0 , and percentage of sleep with an arterial oxygen saturation of $<90\%$ 18.4 ± 27.8 . Primary care physicians refer such patients to the Sleep Unit and, after clinical assessment, they undergo validated cardiorespiratory polygraphy, previously described elsewhere [31]. They are considered to have a low probability of OSAS if a respiratory disturbance index (RDI) of <10 according to cardiorespiratory polygraphy results. This occurs in over one-third of the patients (36%), and another 29% are not considered candidates for treatment with nCPAP because they have only moderate or mild OSAS (RDI <30 and/or absence of symptoms). The remaining 35% undergo split-time polysomnography to confirm the diagnosis of OSAS and for nCPAP titration. Of these, 10% abandon the treatment during the first year and, presumably, accrue no benefit. This equates to 3.2 patients undergoing diagnostic evaluation for every patient ultimately treated with nCPAP or a prevalence of 31.25% in the referred population.

Based on evidence regarding the long-term effectiveness of nCPAP [32, 33], the analytical time horizon used should be 5 yrs. However, sleep units are still treating patients who were diagnosed in the 1980s. In order to take both circumstances into account, the analysis was carried out using two time horizons: 5 yrs and the lifespan of the patient. Patient lifespan is the usual time horizon in the cost-effectiveness literature [21]. It was deemed preferable to calculate the cost-effectiveness of both extreme options rather than employ an intermediate value based upon arbitrary assumptions. Costs and health effects occurring in the future are discounted at 3% per annum [21].

Costs

The cost analysis was undertaken from the perspective of the healthcare system. The direct costs of diagnosis and treatment of OSAS and costs attributable to cardiovascular morbidity were considered. The cost of diagnosis was estimated using data from the year 2000 and included the complete process followed by a patient with treated OSAS, as well as that of patients studied but not treated. The diagnostic protocol includes consultations with conventional testing (111 Euros (€)), cardiorespiratory polygraphy (€98) and polysomnography (€243). The diagnostic costs incurred in the population in order to treat one patient with nCPAP are €1,028. This figure includes the 10% drop-out rate from treatment. All costs were converted using exchange rates and prices current in 2000.

The cost of treatment was calculated based on the price paid for the equipment in 2000 and the cost of its maintenance during the life of the patient. The annual cost (€358) was calculated assuming a device life of 5 yrs and includes follow-up costs. The reference device was the CPAP S VI Plus

(ResMed, Sydney, Australia). Its price in 2001, with all supplies for 5 yrs, was €1,256. Assuming that its residual value after 5 yrs is null, the annual cost is €251. Other costs associated with nCPAP treatment are in-home technical maintenance twice a year (€82) and medical follow-up once a year (€25). Costs of treatment for cardiovascular events have been estimated using 1998 figures from all public hospitals in the Basque Country, adjusted to prices in 2000.

Patients with OSAS consume more healthcare services than the general population [34]. However, the effect of CPAP on this has not been measured; therefore, it was decided not to include it in the model.

Utilities

A survey was undertaken to obtain utility values using the European quality of life (EuroQoL) 5D instrument [35, 36]. EuroQuol 5D is a preference-based health status and multi-attribute utility scale that produces a single index score for each state of health. This score ranges 0–1, where 1 is equivalent to full health and 0 to death. EuroQuol 5D was employed, although it is a generic questionnaire and other instruments, such as Functional Outcomes of Sleep Questionnaire [37] and the Epworth Sleepiness Scale [38], are specifically adapted to measure changes in quality of life in OSAS patients. The reason for this was that, in EuroQuol 5D, the weights used to score utilities were obtained using a preference elicitation technique such as time trade-off [36]. The OSAS-specific instruments are not adapted to economic evaluation because they are not preference-based and cannot be made to correspond to utilities. EuroQuol 5D and the Health Utilities Index [39], developed in Europe and Canada respectively, are highly respected examples of preference-based utility scales. EuroQuol 5D was selected because it has been validated in the Spanish population.

The literature regarding utility values in OSAS patients reveals widely varying figures. The mean utility gain obtained using nCPAP ranges 0.24–0.05 [7, 9]. Consequently, the authors decided to obtain their own data. Patients were recruited consecutively from the Sleep Unit of Txagorritxu Hospital and interviewed twice. The first interview was carried out before the beginning of treatment, and the second when the patient had used nCPAP for 3 months. There was no control group because the aim was to assess usual clinical practice in sleep units, which is focused on treatment of severe OSAS patients. Use of a control group would have required excluding the most severe cases. At the current level of knowledge of OSAS, it would have been unethical to delay treatment for 3 months.

The quality of life of patients with stroke and CHD is worse than that of the general population, but there is no information regarding quality of life in OSAS patients with stroke and CHD. This was modelled by assigning to these states quality-adjustment factors of 0.8 and 0.9 respectively [27] in relation to standard OSAS patient utilities.

Sensitivity analysis

The impact of age at diagnosis (30–60 yrs) and sex on the cost-effectiveness of treatment was explored. The impact of the improvements in quality of life due to nCPAP estimated by TOUSIGNANT *et al.* [7] and in the Trent study [40] is presented. In these analyses, the pretreatment patient utility value was used throughout and the utility gain, or effect size, of the treatment [41] was allowed to vary because the main driving force in the economic assessment is the difference

Table 2. – Cost, effectiveness and incremental cost-effectiveness ratio (ICER) for the base case and two time horizons in males

Horizon	Cost €		Effectiveness QALY		ICER €·QALY ⁻¹
	No treatment	nCPAP	No treatment	nCPAP	
5 yrs	55	2719	3.39	3.73	7861
Lifespan	591	7902	12.90	14.38	4938

Data are means. €: Euro; QALY: quality-adjusted life year; nCPAP: nasal continuous positive airway pressure.

between the values before and after treatment. The range tested was the 95% confidence interval of each survey utility gain.

It has been suggested that, in addition to hypertension, the risk of stroke could be related to independent factors [42]. Accordingly, a further analysis was carried out, in which it was assumed that these factors have the same impact as hypertension.

Another sensitivity analysis was performed to explore the impact of different diagnostic approaches. The diagnostic cost was adjusted as a function of OSAS prevalence and diagnostic protocol applied since these parameters determine cost directly. In this new scenario, the prevalence in referred patients was halved (16%) and a more expensive diagnostic protocol introduced. In the second protocol, cardiorespiratory polygraphy (€98) was substituted for polysomnography (€243) in the initial screening and the second polysomnographic procedure was maintained for nCPAP titration. The consequence is an increase in diagnostic cost from €1,028 to €2,700, with intermediate diagnostic cost when only one parameter is changed.

The discount rate (1–5%), proportion of patients who drop out from treatment (10–50%) and nCPAP cost were also varied to complete the one-way sensitivity analysis. As, in some countries, nCPAP devices are not bought but rented at greater annual cost (€622) [43], the analysis was repeated using this figure. An approach based on separate discounts for costs (6%) and effectiveness (1.5%) was also checked, as recommended by the National Institute for Clinical Excellence and UK Treasury (both London, UK) [40].

In order to measure the separate impact of the three therapeutic effects of nCPAP (disaggregated analysis) [21], additional analyses were performed for the baseline case, in which the effects of traffic accidents, cardiovascular risk and improvement in quality of life (utility) were evaluated separately. In order to calculate the incremental effectiveness of each therapeutic effect, the model was repeatedly computed, each time changing the relevant parameters in both alternatives (treatment and no treatment) and maintaining constant the parameters related to the other two effects. The treatment cost calculation was made computing the model only with nCPAP treatment cost and without taking into account stroke and CHD costs.

Results

Fifty-one patients completed the EuroQoL 5D questionnaire between October 1999–July 2000. One patient refused to take part in the study and four patients were not interviewed a second time. Thus, data were obtained from 46 patients, of whom 87% were male. The mean±SD age was 53±12 yrs, AHI 41.3±14.6, Epworth score 13.8±5.8 and BMI 39.7±13.6. The mean (95% confidence interval) EuroQoL 5D score obtained was 0.738 (0.646–0.829) before beginning nCPAP. The mean gain 3 months later was 0.073 (0.015–0.131).

The incremental cost-effectiveness ratio for the base case is €7,861·QALY⁻¹ if the time horizon is limited to 5 yrs and €4,938·QALY⁻¹ when the model is computed using the lifespan of the patient (table 2).

Table 3 shows the results of the sensitivity analysis by sex, age, treatment drop-out rate, discount rate, nCPAP cost, stroke relative risk and utility gain. The incremental cost-effectiveness ratio is very stable and remains in the region €5,000–10,000·QALY⁻¹ under these alternative assumptions. The results of the analysis are only shown by age and female sex. The other sensitivity analyses are limited to males because the results were similar for both sexes. The incremental cost-effectiveness ratio of nCPAP treatment is only >€20,000·QALY⁻¹ for the worst scenario evaluated (*i.e.* the lower limit of the authors survey's confidence interval and the 5-yr time horizon). The stroke relative risk, the discount rate, the treatment drop-out rate and the beneficial effect of nCPAP on blood pressure have very little influence on the cost-effectiveness ratio. Conversely, the cost-effectiveness ratio clearly grows with nCPAP cost. As expected, separate analysis of increased cost and reduced

Table 3. – Sensitivity analysis by time horizon

Parameter	Sensitivity analysis Range tested	ICER €·QALY ⁻¹	
		5 yrs	Lifespan
Age yrs			
Males	30–60	7896–7789	5035–4853
Females	30–60	7879–7473	4734–4180
RR stroke (untreated)	1.353–1.706	7861–7823	4938–4634
Utility gain			
Present study	0.013–0.126	42235–4573	17544–3021
Ref. [7]	0.112–0.367	5142–1576	3366–1092
Ref. [36]	0.09–0.16	6388–3606	4103–2418
Benefit of nCPAP on blood pressure %	100–25	7861–7916	4938–5381
Drop-out rate	0.1–0.5	7861–9381	4938–5286
Cost of nCPAP €	358–622	7861–11444	4938–8114
Discount rate	0.01–0.05	7723–8001	4603–4938
Separate discount	Cost 0.06; effectiveness 0.015	3653	3008

ICER: incremental cost-effectiveness ratio; €: Euro; QALY: quality-adjusted life year; RR: relative risk; nCPAP: nasal continuous positive airway pressure.

Table 4. – Incremental cost-effectiveness ratio (ICER) of obstructive sleep apnoea syndrome (OSAS) treatment by time horizon and diagnostic scenario in population studied

OSAS prevalence	Diagnostic protocol	Diagnostic cost per patient €	ICER €·QALY ⁻¹	
			5 yrs	Lifespan
0.32	Present study	1028	7861	4938
0.16	Present study	1818	10193	5472
0.32	Two PSG	1468	9160	5235
0.16	Two PSG	2700	12796	6607

€: Euro; QALY: quality-adjusted life year; PSG: polysomnography.

Table 5. – Dissaggregated incremental effectiveness in 50-yr-old males treated with nasal continuous positive airway pressure (nCPAP) for two time horizons

	Car accidents		Cardiovascular risk		Utility effect	
	Treated	Untreated	Treated	Untreated	Treated	Untreated
RR car accidents	1	8.1	1	1	1	1
RR CHD	1	1	1	1.185	1	1
RR stroke	1	1	1	1.353	1	1
Utility	1	1	1	1	0.738	0.811
5-yr time horizon						
Effectiveness	4.596	4.595	4.596	4.593	3.728	3.392
Incremental effectiveness [#]	0.001 (0.3)		0.003 (0.9)		0.336 (98.8)	
Lifespan time horizon						
Effectiveness	17.729	17.691	17.729	17.513	14.378	13.084
Incremental effectiveness [#]	0.038 (2.4)		0.216 (14.0)		1.294 (83.6)	

Incremental effectiveness data are presented as disaggregated incremental effectiveness (percentage of total incremental effectiveness); RR: relative risk; CHD: coronary heart disease. [#]: difference between the effectiveness estimated with and without treatment for each scenario analysed.

effectiveness yields a decreased cost-effectiveness ratio. Table 4 shows the influence of diagnostic costs on cost-effectiveness. Tables 2–6 also show the relationship between cost-effectiveness and efficacy duration, expressed in terms of time horizon.

The relative contributions of the main factors affecting the incremental costs and effectiveness for the base case are shown in tables 5 and 6. These results are very sensitive to time horizon. Over the whole life of the patient, improvements in quality of life account for 84% of the incremental effectiveness of nCPAP and the purchase and maintenance costs of nCPAP are responsible for 86% of the overall incremental cost. Reducing the time horizon to 5 yrs changes these figures to 98 and 61%, respectively.

Discussion

There is no clear consensus in the health economics literature regarding the value of incremental cost-effectiveness ratio below which a treatment should be regarded as efficient. A controversial study, published in a Canadian context, stated that it lies in the range 20,000–100,000 Canadian dollars·QALY⁻¹ [44]. TENGS *et al.* [45], in a very extensive review of the cost-effectiveness of 500 life-saving interventions, found that the median cost per life year saved was US\$19,000 in the health sector. An assessment of the cost-effectiveness of cardiovascular prevention programmes in Spain showed figures ranging US\$3,000–>100,000 [46]. The present results are centred around €5,000·QALY⁻¹ and only in the least favourable scenario rise above €20,000·QALY⁻¹. Therefore, it can confidently be stated that treatment of OSAS with nCPAP has a cost-effectiveness in line with that of other widely used interventions.

In Txagorritxu Hospital Sleep Unit, following the recommendations of the Spanish Respiratory Society [47], patients with OSAS are treated when they have an AHI of >30 and exhibit symptoms of drowsiness. This decision was made taking into account the fact that nCPAP is not effective in patients with an AHI of >30 but without daytime sleepiness [48]. Consequently, the conclusions of the present study cannot be applied to less severe patients. In the literature on OSAS, definitions, epidemiology and natural history are considered together because there is a continuum between normality and severe OSAS [49]. In the same way, the current authors are in agreement with the comment of FLEETHAM [16] that understanding of the natural history of OSAS and nCPAP is at a stage similar to that of hypertension and

hypercholesterolaemia in the 1970s. As with hypertensive patients, it is clear that severe patients should be treated, and the best recommendation for the mildest cases is simply monitoring. The problem is knowing what combination of AHI and symptomatology separates these groups.

Obesity is a big health problem and its strong association with OSAS is likely to be causal [50]. It functions as a confounding factor in epidemiological studies measuring cardiovascular risk in OSAS patients. The multivariate models obtained in the Sleep Heart Health Study [51] suggest that the degree of obesity associated with the degree of sleep-disordered breathing, along with age and sex, explains most of the elevation in the other cardiovascular risk factors, with the exception of hypertension in males. Acknowledging this, obesity has been introduced into the present model only as a consequence of the blood pressure rise associated with an AHI of 30. The figures used were drawn from the population-based study of YOUNG *et al.* [2] since it established the linear relationship between blood pressure and AHI adjusted for BMI. In the clinical approach to OSAS, obesity is a key factor that must be intensively assessed when present. In the cost-effectiveness of OSAS treatment, the effect of obesity and its treatment on the natural history are excluded. OSAS can be a consequence of obesity but nCPAP does not produce weight changes. Conversely, if the cost-effectiveness of weight loss interventions were being estimated, OSAS should be introduced into the model to take into account their effect on sleep-disordered breathing.

As observed in table 5, the improvement in quality of life with nCPAP is the main driving force behind its clinical effectiveness measured in quality-adjusted life years. Its impact is seven times greater than that of reduced cardiovascular mortality, and this, in turn, is seven times greater than that of decreased numbers of traffic accidents. Other authors have reached the same conclusion; the available

Table 6. – Dissaggregated incremental cost in 50-yr-old males treated with nasal continuous positive airway pressure (nCPAP) for two time horizons

Horizon	Diagnostic cost		Treatment cost	
	€	%	€	%
5 yrs	1028	39	1636	61
Lifespan	1028	14	6238	86

€: Euro.

evidence indicates that improved daytime alertness and quality of life represent the most important clinical end points of therapy since there is, as yet, insufficient evidence to justify prescribing nCPAP with the goal of reducing cardiovascular morbidity and mortality [52]. The present study has confirmed this assessment by quantifying the impact of each factor.

The utility values employed in the base case come from a survey performed using the EuroQoL 5D instrument. The difference in quality of life is similar to that obtained by JENKINSON *et al.* [9] using the EuroQoL 5D questionnaire (0.78–0.83). The improvement found by JENKINSON *et al.* [9] was much greater than that found employing other instruments, such as the 36-item short-form health survey and Patient-Generated Index. Similarly both TOUSIGNANT *et al.* [7] and the Trent study [40] found a larger improvement in quality of life before and after treatment, ranging 0.112–0.367 [7] and 0.09–0.16 [36], respectively. In spite of having used the most conservative estimates of effectiveness, the long-term incremental cost-effectiveness ratio remains $<€18,000 \cdot QALY^{-1}$ in both males and females. From a clinical point of view, use of the EuroQoL 5D questionnaire could be seen as an odd decision because there are other questionnaires better adapted to OSAS. In the measurement of quality of life, the instrument used depends on the purpose and perspective of the study. The present study was designed to consider nCPAP in the context of overall resource allocation. The present authors would not employ the EuroQoL 5D questionnaire to assess the progression of the quality of life of an OSAS patient. Nevertheless, its property of being a preference-based health status scale and wide use help in the comparison of results with other treatment assessments [53].

The lack of a control group is a limitation of not only the present study but also all the literature regarding measurement of utility values in OSAS patients [7, 9, 40]. The increased utility calculated could be an overestimation since a placebo effect and regression to the mean could cause some of the improvement seen. Uncertainty about this parameter would be resolved if a study with a control group resolving ethical and technical constraints were carried out.

The relation of OSAS to car accidents has little effect on the cost-effectiveness of nCPAP treatment when analysis is undertaken, as here, at the population level. Consequently, a differential approach should be used to assess groups prone to having car accidents, such as taxi drivers, or with great responsibility, such as coach drivers or aeroplane pilots.

Authors have paid much attention to different diagnostic approaches to OSAS [13, 14, 22, 28]. There are two elements that affect the efficiency of diagnosis, the prevalence of OSAS in the studied population and the diagnostic protocol employed. The cost of diagnosis per patient identified for nCPAP treatment increases as OSAS prevalence decreases. The diagnostic protocols employed depend on the use of polysomnography and cardiorespiratory polygraphy. In the least efficient scenario (table 5), prevalence is halved and polysomnography is used in the initial screening. Nevertheless, its impact on the economic efficiency of treatment of OSAS is quite low. In this context, the efficiency of use of nCPAP is reduced, although the cost-effectiveness remains $>€7,000 \cdot QALY^{-1}$. The reason for this is that the key factor in the overall cost is the cost of the nCPAP device.

It is well known that the cost of nCPAP differs greatly from one country to another, depending mainly on whether the device is bought or rented. Strictly speaking, what varies is not cost but charges. The cost is the aggregate value of the resources needed to provide a health or clinical intervention [21]. nCPAP device prices are similar across Europe. The main charge difference among countries appears because some National Health Services rent the devices, usually at higher charges. In

Spain, for instance, the nCPAP service to a patient is provided for €622 per year [43]. The decision regarding how to provide the service is made by policy makers. If that decision is not as efficient as it should be, responsibility for population-level nCPAP costs must not be assigned at the clinical level. The present authors are confident that the figure of €358 reflects the true cost of nCPAP treatment. There is no issue of statistical uncertainty in this parameter of the model.

Efficacy duration has quite an important impact on cost-effectiveness ratios. The 5-yr time horizon is based on the available empirical evidence on efficacy duration but at the same time means that nCPAP becomes totally ineffective after that time. This assumption clearly contradicts general clinical practice in sleep units, which maintain the treatment beyond 5 or 10 yrs. Nonetheless, the decrease in efficiency, related to the 5-yr time horizon, does not change any of the main conclusions of the analysis. The cost-effectiveness ratios increase, but still remain within an efficient range.

In conclusion, treatment of obstructive sleep apnoea syndrome with nasal continuous positive airway pressure has a cost-effectiveness that is in line with that of other commonly funded healthcare interventions such as antihypertensive drugs and other cardiovascular risk factor treatments. There has been much controversy in the literature concerning the quality of the evidence regarding the link between treatment with nasal continuous positive airway pressure and cardiovascular mortality and road traffic accidents. This study puts that controversy into perspective: the key clinical benefit of nasal continuous positive airway pressure treatment is the improvement in the quality of life of patients with obstructive sleep apnoea syndrome. This is also precisely the benefit for which the evidence base is strongest. The remaining uncertainties concerning the impact of nasal continuous positive airway pressure on long-term mortality have only relatively little impact on the clinical and economic efficiency of treatment.

Appendix: glossary

The following definitions are taken from a report of the American Panel on Cost-Effectiveness in Health and Medicine [21].

Cost-effectiveness analysis. An analytical tool in which the costs and effects of a programme and at least one alternative are calculated and presented as the ratio of incremental cost to incremental effect.

Semi-Markov model. A type of Markov model that allows for systematic changes in transition probabilities as a function of simulated time rather than having constant transition probabilities. Also called time-varying Markov models.

Utility. A concept in economics, psychology and decision analysis referring to the preference for, or desirability of, a particular outcome.

Quality-adjusted life year. A measure of health outcome which assigns to each period of time a weight, ranging 0–1, corresponding to the health-related quality of life during that period, where 1 corresponds to optimal health and 0 to a health state judged equivalent to death.

Discount rate. The interest rate used to compute present value or discount future sums.

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