

Cost-effectiveness of Continuous Positive Airway Pressure Therapy for Moderate to Severe Obstructive Sleep Apnea/Hypopnea

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Background: Obstructive sleep apnea/hypopnea (OSAH) is a common disorder characterized by recurrent collapse of the upper airway during sleep, and is associated with an increased risk of motor vehicle crashes (MVCs). Common first-line therapy for OSAH is continuous positive airway pressure (CPAP). We assessed the cost-effectiveness of CPAP therapy vs none for the treatment of OSAH.

Methods: We used a 5-year Markov model that considers the costs and quality-of-life improvements of CPAP therapy, accounting for the gains from reduced MVC rates. Utility values were obtained from published studies. The MVC rates under the CPAP and no-CPAP scenarios were calculated from National Highway Traffic Safety Administration data and a systematic review of published studies. Costs of MVCs, equipment, and physicians were obtained from US Medicare and the National Highway Traffic Safety Administration. The target population included male and female patients aged 25 to 54 years and newly diagnosed as having moderate to severe OSAH. We ex-

amined the findings from the perspectives of a third-party payer and society.

Results: From a third-party payer or a societal perspective, CPAP therapy was more effective but more costly than no CPAP, with incremental cost-effectiveness ratios of \$3354 or \$314 per quality-adjusted life-year gained, respectively. The incremental cost-effectiveness ratio estimate was most dependent on viewpoint (varying more than 10-fold between societal and third-party payer perspectives) and choice of utility measurement method (varying more than 5-fold between the use of standard gamble and EuroQol 5D utility assessment values).

Conclusion: When quality of life, costs of therapy, and MVC outcomes are considered, CPAP therapy for patients with OSAH is economically attractive.

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OBSTRUCTIVE SLEEP APNEA/hypopnea (OSAH) is a common disorder¹ characterized by recurrent collapse of the upper airway during sleep. This leads to sleep fragmentation, daytime sleepiness, reduced quality of life,² and an increased rate of motor vehicle crashes (MVCs).³

The primary therapy for OSAH is continuous positive airway pressure (CPAP), which is delivered with a device that consists of a mask, or a mask alternative, worn on the face and connected with plastic tubing to a flow generator. By preventing upper airway collapse during sleep, CPAP relieves daytime sleepiness, improves quality of life,^{4,5} and reduces the risks of MVCs.⁶

Despite these benefits, it is unclear whether CPAP is a cost-effective use of limited health care resources. The cost-effectiveness of medical therapies is usually assessed by the incremental cost-effectiveness ratio (ICER), the ratio of the incremental cost and the incremental

change in quality-adjusted life-years (QALYs), which follow from the adoption of one treatment vs another strategy (eg, no treatment). An ICER of less than \$50 000 per QALY gained is generally considered cost-effective, but some evidence suggests this value should be higher.^{7,8}

The purpose of this study was to assess the cost-effectiveness of CPAP therapy, compared with no CPAP, in patients with moderate-to-severe OSAH.

METHODS

DECISION MODEL STRUCTURE

The base-case analysis considered US drivers (aged 25-55 years) with newly diagnosed moderate-to-severe OSAH. A state-transition Markov model compared the costs and outcomes of OSAH treated with CPAP with no therapy for 5 years (Markov cycle length, 1 year) (**Figure 1** and **Figure 2**).

With each year in the model, patients could have an MVC resulting in property damage, in-

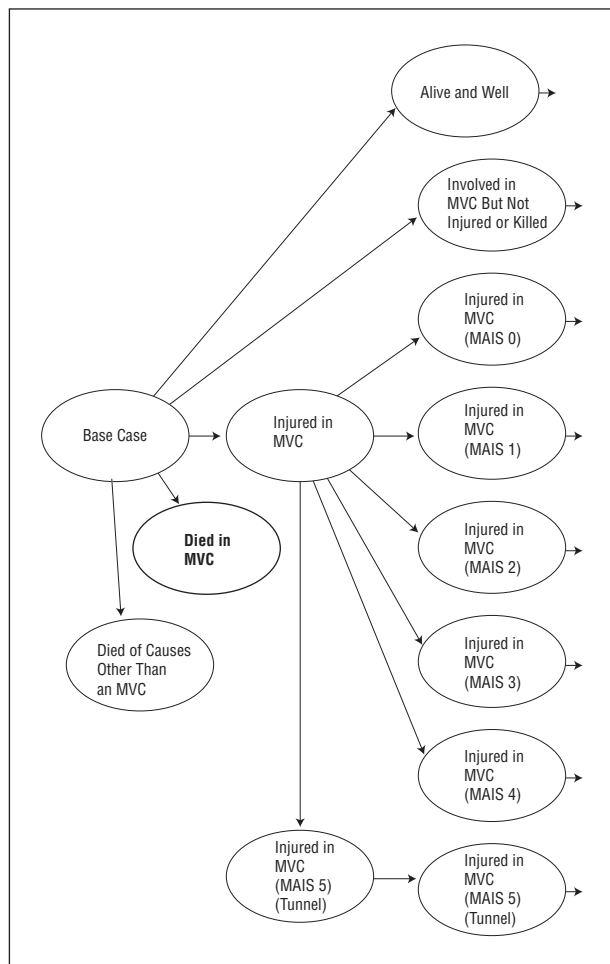


Figure 1. Markov model of patients not prescribed continuous positive airway pressure therapy. MAIS indicates Modified Abbreviated Injury Scale; MVC, motor vehicle crash. MAIS scores are described in the "Decision Model Structure" subsection of the "Methods" section.

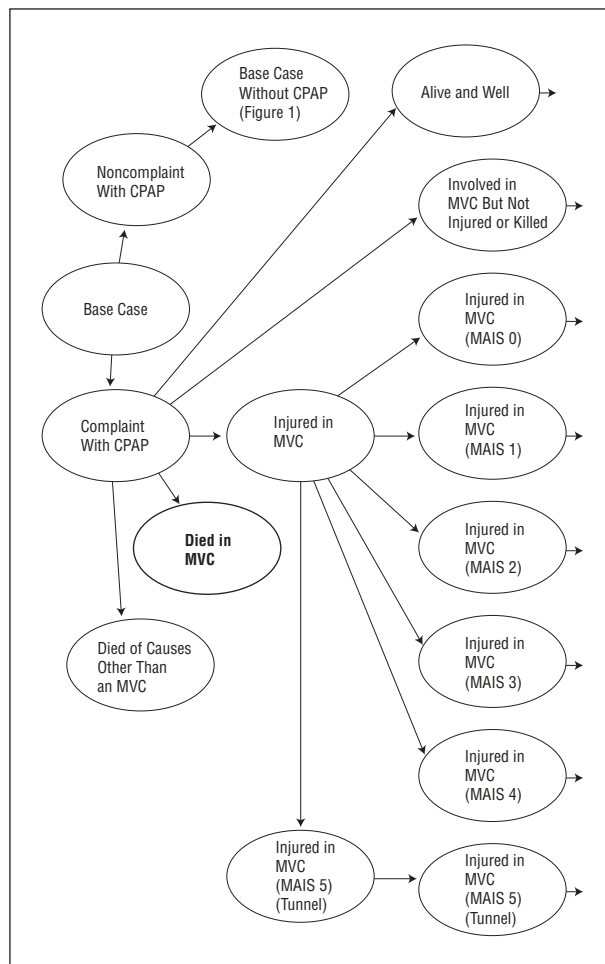


Figure 2. Markov model of patients prescribed continuous positive airway pressure (CPAP) therapy. MAIS indicates Modified Abbreviated Injury Scale; MVC, motor vehicle crash. MAIS scores are described in the "Decision Model Structure" subsection of the "Methods" section.

jury, or death; could die of natural causes; or could survive incident free. Injuries were subclassified into severity categories according to the Maximum Abbreviated Injury Scale (MAIS), with scores ranging from 1 (minimal injury) to 5 (most severely injured). The MVC survivors with the most severe injuries were assumed to be unable to drive afterward and were at no risk of a subsequent MVC (ie, they were confined to a tunnel state). All other survivors were at risk of a subsequent MVC. Transition probabilities depended on whether patients were effectively treated with CPAP. Decision analyses were performed with Data Pro for HealthCare software (TreeAge Software Inc, Williamston, Mass); statistical analyses were performed with SAS software (version 8; SAS Institute Inc, Cary, NC).

CLINICAL DATA INPUTS

Proportion of Patients in Each Sex/Age Group

This analysis may be thought of as a weighted average of the findings for 6 patient groups defined by age (25-34, 35-44, and 45-54 years) and sex. The weights used in this calculation (**Table 1**) were obtained from the primary referral center for OSAH in Vancouver, British Columbia. Data from patients diagnosed as having moderate-to-severe OSAH (apnea-hypopnea index, ≥ 15 events per hour) from 2003 to 2004 were

used (n=99 patients). The distribution is comparable to that in the United States.^{20,21}

Rates of MVCs

The annual MVC probability in individuals without OSAH was determined using MVC data for 2003 (115 million licensed motorists aged 25-55 years) from the National Highway Traffic Safety Administration.²² Probabilities of MVC were stratified by the relevant patient groups and further classified by the following MVC types: property damage only, injury related, or fatal. Severity of MVC injury was assumed to have the following distribution: 85.6% for MAIS 1, 10.5% for MAIS 2, 3.3% for MAIS 3, 0.4% for MAIS 4, and 0.2% for MAIS 5.²³

Impact of CPAP on MVC Rates

To determine the impact of CPAP on rates of MVC, we performed a meta-analysis of all studies that examined MVC rates in patients with OSAH before and after CPAP. A comprehensive search of MEDLINE (1966 to March 2005) using Ovid was conducted using the following exploded MESH terms: *sleep apnea syndromes* AND *positive pressure respiration* OR *continuous positive airway pressure* AND *automobile driving* OR *accident*. A total of 38 studies were identified. Studies were included if they compared rates of MVC (by self-report or by more objec-

Table 1. Key Model Assumptions

Variable	Point Estimate	Description (Source)
Study population proportions		
Male subjects, age range, %		No distribution assigned (Sleep Disorders Program, Vancouver Acute Hospitals, Vancouver, British Columbia)
25-34 y	14	
35-44 y	5	
45-54 y	34	
Female subjects, age range, %		
25-34 y	5	
35-44 y	34	
45-54 y	8	
Total, %	100	
Utilities*		
No CPAP	0.32	Beta distribution, $\alpha = 2.4$; $\beta = 5.1$ (Chakravorty et al, ⁹ 2002)
Incremental gain from CPAP	0.23	Beta distribution, $\alpha = 5.0$; $\beta = 16.8$ (Chakravorty et al, ⁹ 2002)
Functional Capacity Index		
MAIS 1†	0.93	Beta distribution, $\alpha = 7.5$; $\beta = 0.6$ (Graham et al, ¹⁰ 1997)
MAIS 2†	0.89	Beta distribution, $\alpha = 10.8$; $\beta = 1.3$ (Graham et al, ¹⁰ 1997)
MAIS 3†	0.84	Beta distribution, $\alpha = 13.9$; $\beta = 2.7$ (Graham et al, ¹⁰ 1997)
MAIS 4†	0.93	Beta distribution, $\alpha = 7.5$; $\beta = 0.6$ (Graham et al, ¹⁰ 1997)
MAIS 5†	0.19	Beta distribution, $\alpha = 11.7$; $\beta = 50$ (Graham et al, ¹⁰ 1997)
Discount rate, %	3	No distribution assigned (Gold et al, ¹¹ 1996)
Compliance, %	70	No distribution assigned (McArdle et al, ¹² 1999)
Time horizon, y	5	No distribution assigned (assumption)
Scaling factor for converting lifetime MVC costs to match 5-y Markov time frame	0.125	No distribution assigned (based on the assumptions of a uniform lifetime distribution of MVC costs and a 40-y future life span for all drivers)
Reduction of MVC with CPAP therapy	0.15	Log-normal distribution (95% CI, 0.10-0.22) (meta-analysis of George, ⁶ Findley et al, ¹³ Krieger et al, ¹⁴ Engleman et al, ¹⁵ Horstmann et al, ¹⁶ Cassel et al, ¹⁷ Yamamoto et al, ¹⁸ and Suratt and Findley ¹⁹)
All costs		Triangular distribution defined by $\pm 25\%$ end points (assumption)

Abbreviations: CI, confidence interval; CPAP, continuous positive airway pressure; MAIS, Maximum Abbreviated Injury Scale; MVC, motor vehicle crash.

*Utility values for patients with obstructive sleep apnea/hypopnea injured in an MVC were calculated by multiplying utility values by Functional Capacity Index values.

†Described in the "Decision Model Structure" subsection of the "Methods" section.

Table 2. Studies With Rates of MVC With and Without CPAP Therapy

Source	Country	No. of Patients	Mean AHI*	Mean Age, y	Definition of Crash	Rate of MVC	
						CPAP	No CPAP
George ⁶	Canada	210	54	52	From provincial insurance database	0.06/y	0.18/y
Findley et al ¹³	United States	50	37	56	State DMV (injury or property damage >\$500)	0/y	0.07/y
Krieger et al ¹⁴	France	547	59.8	56.6	Self-reports	0.0256/y	0.084/y
Engleman et al ¹⁵	Scotland	215	47	53	Self-reports (major incidents)	0.001 per 16 000 km driven	0.005 per 16 000 km driven
Horstmann et al ¹⁶	Switzerland	85	NA	NA	Self-reports	2.7 per 1 000 000 km driven	10.6 per 1 000 000 km driven
Suratt and Findley ¹⁹	United States	22	NA	NA		0.023/y	0.30/y
Cassel et al ¹⁷	Germany	59	38.9	49	Self-reports	0.14 per 100 000 km	0.8 per 100 000 km
Yamamoto et al ¹⁸	Japan	39	55.7	48	Self-reports	0.17/y	0/y

Abbreviations: AHI, apnea hypopnea index; CPAP, continuous positive airway pressure; DMV, department of motor vehicles; MVC, motor vehicle crash; NA, not available.

*Calculated as number of events per hour.

tive measures such as insurance databases) in patients with OSAH before and after the initiation of CPAP therapy. Review articles and studies that reported changes in driving performance by simulator rather than actual MVC rates were excluded. The remaining studies were reviewed by one of us (N.T.A.), and 7 were appropriate for the meta-analysis.^{6,13-18} After review of bibliographies and consultation with experts, we

identified an additional study published in abstract form.¹⁹ These 8 studies examined a total of 1227 patients^{6,13-19} (**Table 2**). To calculate the pooled reduction in MVC risk with CPAP, we used random-effects meta-analysis using the inverse variance of the logarithm of the odds ratio.

We assumed that the MVC crash rate in patients with OSAH receiving CPAP treatment equaled that in the general popula-

Table 3. Cost Estimates

Variable	Base-Case Cost Estimate, US \$
CPAP-related costs	
Mask	117.64
Tubing	41.02
Headgear	37.16
CPAP rental per month	96.99
Heated humidifier per month	30.11
Initial office visit (45 min)	151.92
Follow-up office visit (15 min)	59.62
Lifetime direct medical costs*	
MAIS 0†	24
MAIS 1†	2477
MAIS 2†	16740
MAIS 3†	49536
MAIS 4†	139672
MAIS 5†	352318
Lifetime nonmedical costs*	
MAIS 0†	
Insurance	85
Legal	0
Productivity	71
MAIS 1†	
Insurance	787
Legal	159
Productivity	5173
MAIS 2†	
Insurance	7303
Legal	5265
Productivity	36248
MAIS 3†	
Insurance	19970
Legal	16710
Productivity	102315
MAIS 4†	
Insurance	34179
Legal	35606
Productivity	147082
MAIS 5†	
Insurance	39237
Legal	84410
Productivity	630206

Abbreviations: CPAP, continuous positive airway pressure; MAIS, Maximum Abbreviated Injury Scale

*Costs of motor vehicle crashes (MVCs) entered (as 1-time payoffs) into the 5-year Markov model were 5 years/40 years = 1/8 of lifetime MVC cost values.

†Described in the "Decision Model Structure" subsection of the "Methods" section.

tion,⁶ as reported in annual data from the US Federal Highway Administration. The MVC rates in patients without CPAP were obtained by dividing MVC rates by the percentage reduction in MVCs associated with CPAP therapy.

Mortality Rates

Transition probability to death was calculated by adding the yearly, sex-specific probability of death in an MVC to the rate of death due to natural causes as obtained from US life tables.²⁴

Utility Values

Quality-adjusted life-years are the sum of the durations of health states multiplied by the mean utility of each of the health states.¹¹ The base-case analysis used utility results obtained by the stan-

dard gamble, which is often considered the standard.^{25,26} We used data from a prospective study that demonstrated an increase in utility value from 0.32 to 0.55 (difference, 0.23) in those receiving CPAP⁹; this is an increase similar to that documented in a retrospective study by Tousignant et al.²⁷

Utilities have also been assessed by the EuroQol 5D (EQ-5D). In 1 study,²⁸ utility values assessed by the EQ-5D before and after CPAP were 0.738 and 0.811, respectively (increase, 0.073). Jenkinson and coworkers²⁹ used the EQ-5D and found an improvement in utility of 0.05 with CPAP (from 0.78 to 0.83). The EQ-5D figures were used in subsequent sensitivity analyses to determine their impact on the ICER.

Quality weights for the various MAIS injury levels were obtained from the literature using the Functional Capacity Index (FCI).³⁰ The FCI weights represent rating scale preferences elicited from a sample of people who have sustained injuries that resulted in functional limitations for longer than 1 year. These FCI weights were applied using methods similar to those of other investigators.¹⁰

Costs

The base-case analysis used the third-party payer perspective and only considered direct medical costs. In the first year of the model, the total cost of using CPAP was derived from the 2004 US Medicare fee schedule. Cost components included the CPAP device, mask, tubing, headgear, and heated humidifier. In keeping with Medicare guidelines, after 15 months of rental fees, patients incurred a rental fee equivalent to 1 month's rent every 6 months. Additional first-year costs included 1 specialist consultation and 2 physician follow-up visits. We assumed that a standard CPAP machine would last 5 years. For years 2 through 5, ongoing annual CPAP cost components included 1 mask, tubing, headgear, CPAP rental, and 2 physician visits (**Table 3**).

Direct medical and indirect costs of MVC stratified by the MAIS were obtained from a technical report from the National Highway Traffic Safety Administration.²³ This comprehensive report used American public sources to attach lifetime costs to MVC outcomes and services (Table 3). All costs were updated to the year 2003 using the medical component of the US Consumer Price Index and prorated to suit the 5-year time frame of the analysis under the conservative assumption that all MVC-related costs would be (in present-value terms) uniformly distributed over a future of 40 years for all patient groups. The MVC costs consist of direct medical costs (medical and emergency services), indirect costs (losses in household and market productivity and associated workplace costs), legal costs, and insurance administration costs. Market productivity was valued in terms of lost wages and benefits. Lost household activity was valued at the market price for hiring a person to accomplish the same tasks.

CPAP Compliance

We assumed a compliance rate of 70% as reported in the literature.¹² Noncompliant patients were assumed to use the CPAP machine for 3 months, incurring rental costs of the machine and humidifier and costs associated with the mask, tubing, headgear, and 1 physician visit. Patients were assumed not to benefit from CPAP for this period of 3 months.

PROBABILISTIC COST-EFFECTIVENESS ANALYSIS

We performed a probabilistic cost-effectiveness analysis using second-order Monte Carlo simulations. We specified distributions for model variables to represent the uncertainty in these

Table 4. Results of the Univariate Sensitivity Analysis on the ICER

Variable (Base Case)	Range Varied	ICER Estimates (95% CI), US \$*	
		Third-Party Payer Perspective	Societal Perspective
Reference category		3354 (1062-9715)†	314 (CS-6114)
EQ-5D utility values, mean ± SD (standard gamble utilities)	CPAP, 0.77 ± 0.18; no CPAP, 0.73 ± 0.18	17 250 (3125-259 547)‡	1615 (CS-121 054)§
Discount rate (3%)	0%	3250 (763-9445)	191 (CS-5182)
	5%	3445 (1031-10 341)	399 (CS-6136)
	7%	3540 (1253-9447)	485 (CS-6542)
Compliance rate (70%)	50%	3437 (916-10 260)	395 (CS-7014)
	90%	3328 (1187-9230)	271 (CS-5269)
Time horizon (5 y)	3 y	3490 (814-10 587)	424 (CS-5756)
	7 y	3245 (1050-9088)	46 (CS-6222)
Scaling factor for converting lifetime costs to fit 5-y Markov time frame (0.125)	0.25	3078 (587-9091)	CS (CS-7674)
	0.75	1976 (CS-8029)	CS (CS-15 068)
	1.00	1425 (CS-7515)	CS (CS-17 263)
Reduction of MVC with CPAP therapy (0.15)			
Upper CI	0.10	3065 (519-8911)	CS (CS-5498)
Lower CI	0.22	3530 (1188-10 105)	745 (CS-6289)

Abbreviations: CI, confidence interval; CPAP, continuous positive airway pressure; CS, cost saving; EQ-5D, EuroQol 5D; ICER, incremental cost-effectiveness ratio; MVC, motor vehicle crashes.

*Calculated as the incremental cost divided by the incremental quality-adjusted life-years.

†Indicates base-case scenario.

‡Indicates 76% of simulations supported the cost-effectiveness of CPAP therapy.

§Indicates 91% of simulations supported the cost-effectiveness of CPAP therapy.

||Indicates the odds ratio of an MVC in those treated with CPAP vs no CPAP.

estimates. Beta distributions were given to all conditional probabilities (eg, the probability of a severe injury with a MAIS score of 5, given the occurrence of an MVC injury) and utilities generated by the standard gamble and FCI. For costs, triangular distributions were used, with upper and lower limits determined by adding and subtracting 25% from the point estimates. A log-normal distribution was given to the odds ratio associated with an MVC in patients with OSAH who were receiving CPAP treatment vs no CPAP (Table 1). We randomly sampled from these distributions in second-order Monte Carlo simulations to generate 1000 incremental cost and effectiveness pairs.

SENSITIVITY ANALYSES

To assess the robustness of our model, we performed deterministic sensitivity analyses. Analyses were repeated after modifying a number of variables to assess their impact on the ICER (Table 4). Variables of interest were the probability of compliance with CPAP, utility values, the discount rate for costs and QALYs, the cost-scaling factor for adjusting lifetime costs to the 5-year time horizon, and the reduction in the rates of MVC according to the 95% confidence limits determined in the meta-analysis.

RESULTS

EFFECTIVENESS OF CPAP IN REDUCING MVC

Results of the meta-analysis are shown in Table 2. The mean apnea-hypopnea index of the patients in the studies ranged from 37 to 60 events per hour. There was no significant heterogeneity among the studies ($Q_6=4.34$; $P=.50$). Treatment with CPAP reduced the rate of MVC by a factor of approximately 7 (odds ratio of MVC with

CPAP compared with no CPAP, 0.15 [95% confidence interval (CI), 0.10-0.22]).

COST-EFFECTIVENESS ANALYSIS

A CPAP strategy was more effective but more costly than the no-CPAP strategy from the perspective of a third-party payer. Specifically, the CPAP strategy, compared with the no-CPAP strategy, was associated with a mean gain of 0.75 QALY (2.22 QALYs [95% CI, 0.86-3.89] vs 1.47 QALYs [95% CI, 0.28-3.08] in the CPAP and no-CPAP groups, respectively). The incremental cost for the CPAP strategy was \$2519 (\$4177 [95% CI, \$2804-\$6057] vs \$1659 [95% CI, \$283-\$3936] in the CPAP and no-CPAP groups, respectively) resulting in an ICER of \$3354 per QALY (95% CI, \$1062 per QALY to \$9715 per QALY). From the perspective of society, the CPAP strategy was more costly (\$7123 [95% CI, \$4324-\$11 906] vs \$6887 [95% CI, \$3113-\$14 843] for the no-CPAP strategy) as well as more effective, implying an incremental cost-effectiveness of \$314 (95% CI, cost saving to \$6114).

Results of the probabilistic analysis from the third-party payer and societal perspectives can be viewed as a joint distribution of cost differences and QALY differences (Figure 3). Adopting the commonly cited value of society's willingness to pay for a QALY of \$50 000, 100% of the Monte Carlo simulations favored the cost-effectiveness of CPAP therapy. This is reflected by the points in the upper and lower right quadrants of Figure 3 falling below the line with the slope of \$50 000 per QALY gained. The probability that CPAP is cost-effective, measurable as the proportion of Monte Carlo simulations that favor the therapy's cost-effectiveness, can be plotted as a function of

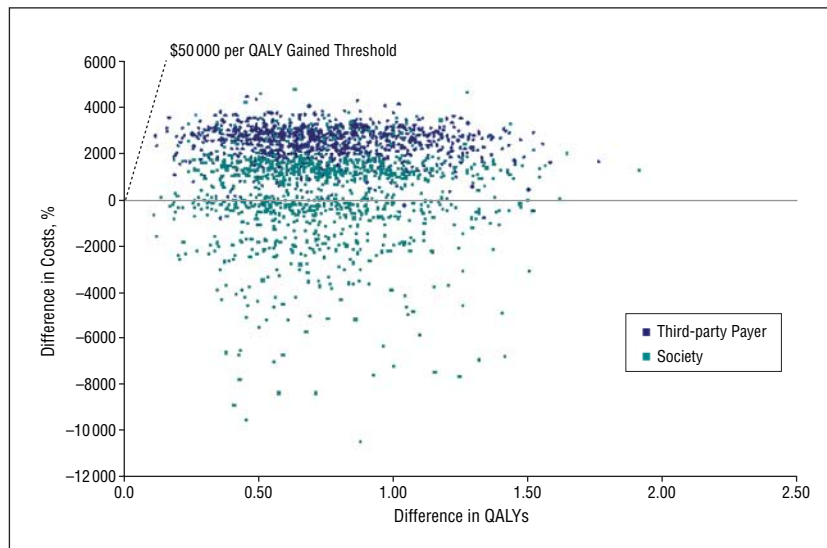


Figure 3. Scatterplot displaying, on the incremental cost-effectiveness plane, the incremental cost and effectiveness pairs resulting from 1000 iterations of the model comparing continuous positive airway pressure (CPAP) with no CPAP. The slope of the line drawn from each point to the origin is the incremental cost-effectiveness ratio of CPAP to no CPAP as estimated from 1 iteration of the model. Points in the right upper quadrant represent iterations for which CPAP was more costly and more effective than no CPAP, whereas points in the right lower quadrant represent simulations where CPAP was the dominant strategy (ie, more effective but less costly). QALYs indicates quality-adjusted life-years.

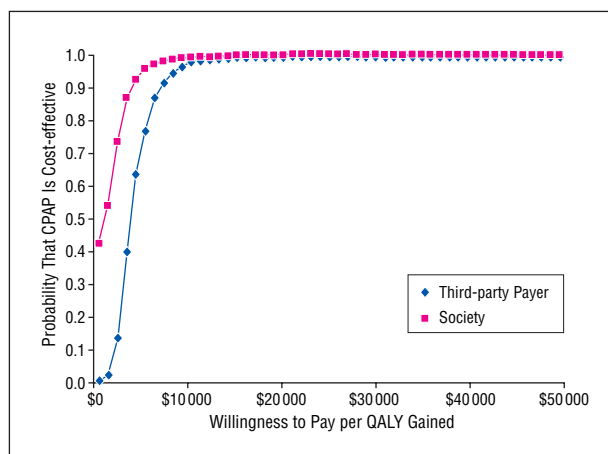


Figure 4. The cost-effectiveness acceptability curve plots the estimated probability that continuous positive airway pressure (CPAP) is cost-effective vs society's willingness to pay for a quality-adjusted life-year (QALY). The probability of cost-effectiveness is calculated as the proportion of Monte Carlo simulations indicating that either CPAP therapy leads to greater health outcomes at a price that is acceptable to society or (in the present context, only a theoretical possibility) that no CPAP therapy leads to improved health outcomes but at a price that is too high.

the willingness to pay per QALY gained, generating a cost-effectiveness acceptability curve (**Figure 4**). From the societal perspective, 42% of the ICERs from the simulations fell within the lower right quadrant, indicating that CPAP was dominant (more effective and less costly).

SENSITIVITY ANALYSES

One-way sensitivity analyses showed that the ICER estimates were robust to many alternative assumptions pertaining to discount rate, compliance rate, time horizon, lifetime distribution of costs, and strength of association between OSAH and MVC incidence. The most influential factor was analytical perspective (ie, third-party payer vs societal), leading to a more than 10-fold difference in ICER estimates. The second most influential factor was choice of utilities values. When EQ-5D utili-

ties were used instead of standard gamble utilities, the ICER estimate increased more than 5 times (Table 4).

COMMENT

Continuous positive airway pressure therapy for OSAH is an efficient use of health care resources. When both indirect and direct costs were considered (under the societal perspective), CPAP was cost-effective with an ICER of \$314 per QALY gained. When the third-party payer perspective was used, CPAP therapy was still cost-effective, with an ICER of \$3354 per QALY. These values compare very favorably with other publicly funded therapies such as primary prevention of cardiovascular events using cholesterol-lowering therapy (\$54 000 per QALY to \$1 400 000 per QALY gained)³¹ and biological agents for the treatment of rheumatoid arthritis (\$30 500 per QALY).³² They are substantially less than the ICER of lung volume reduction surgery in the treatment of chronic obstructive pulmonary disease (\$190 000 per QALY).³³

Our results are conservative, and the benefits of CPAP are likely greater, as we did not include a number of potential benefits in our model. These include improvements in work productivity,³⁴ reduction in occupational injuries,³⁵ reduced use of antihypertensive medications,³⁶ and improvements in bed-partner quality of life.³⁷

In particular, although there is growing evidence that CPAP may lead to a reduction in cardiovascular disease such as hypertension, strokes, and heart attacks, there is considerable controversy surrounding this issue.^{38,39} Long-term studies describing potential reductions in cardiovascular events with CPAP have been observational in nature^{40,41} and thus are subject to confounding by indication/compliance. Others have used surrogate short-term (usually ≤ 1 month) end points such as endothelial function,⁴² C-reactive protein level,⁴³ or blood pressure.⁴⁴ Some of these studies conflict, with one study that demonstrated a reduction in C-reactive protein level with CPAP⁴³ and another that demonstrated no signifi-

cant effect.⁴⁵ Some studies have also shown no significant effect of CPAP on blood pressure.³⁹ Although we suspect that CPAP may reduce rates of cardiovascular disease, we did not feel comfortable putting this in the model because the data concerning this issue are not robust. We thus made the conservative decision not to include potential cardiovascular benefits in our analysis. Even with our conservative model, CPAP was still cost-effective.

Our data confirm and extend the findings of previous investigators. Other studies have demonstrated that CPAP offers excellent value for money.⁴⁶ Tousseignant and colleagues²⁷ reported ICERs of \$3400 per QALY to \$9800 per QALY (in Canadian dollars). Because these values were based only on quality-of-life data and did not assess the impact of CPAP on MVC, these values were higher than what we found.

Similarly, Mar and coworkers²⁸ reported a cost-effectiveness analysis of CPAP therapy in patients with moderate-to-severe OSAH in Spain. Although the ICER was well within the range of what would be considered cost-effective (€7861 per QALY saved), it was greater than our base-case ICER estimate. The impact of MVC was included in the study by Mar et al,²⁸ but only fatalities were considered. Other costs associated with these MVC costs were not. Therefore, we believe our model more accurately represents the costs and benefits of CPAP therapy with respect to MVC.

We acknowledge that our study has limitations. First, much of the benefit that we have attributed to CPAP therapy is based on its effectiveness in reducing rates of MVC and its improvement in quality of life. We have based our estimate of the reduction in MVC rates on 8 studies. A major limitation of these studies is their reliance on a before-after design (ie, rates of crashes before and after CPAP therapy were compared). It is thus possible that some patients may have been sent for assessment of suspected sleep-disordered breathing because of an MVC (referral bias), falsely inflating rates prior to using CPAP. However, we doubt this is a significant factor because, when the odds ratio was decreased to the lower end of the confidence interval, the ICER was still close to \$3530 per QALY.

Second, much of the data used to construct the transition probabilities were based on studies of patients with severe OSAH. Our analysis was also limited to patients aged 25 to 55 years. Therefore, our model may not be applicable to mild-to-moderate OSAH or to older and younger patients.

Finally, utilities in our base-case analysis were based on the standard gamble given directly to patients. Thus, these values represent patient preferences and not those of society. We tested the impact of using societal preferences (as captured through the EQ-5D) and found that the incremental cost-effectiveness ratio was still within the range of what is considered cost-effective. It is not clear whether there is a difference in responsiveness between the standard gamble and the EQ-5D in this disease state or a difference between societal and patient preferences.

In conclusion, previous studies^{4,6} have demonstrated that CPAP is effective in improving daytime sleepiness and reducing rates of MVC in patients with OSAH. We have shown that, when quality of life and costs of therapy

and MVCs are considered, CPAP therapy in patients with OSAH is an excellent use of health care resources.

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