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 examined 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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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-

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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-

![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.](#)
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 patients6,13-19 (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-
The base-case analysis used utility results obtained by the stan-

1. Utility values obtained by dividing MVC rates by the percentage reduction in MVCs associated with CPAP therapy.

2. 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

3. 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

Table 3. Cost Estimates

<table>
<thead>
<tr>
<th>Variable</th>
<th>Base-Case Cost Estimate, US $</th>
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</thead>
<tbody>
<tr>
<td>CPAP-related costs</td>
<td></td>
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<tr>
<td>Mask</td>
<td>117.64</td>
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<tr>
<td>Tubing</td>
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<td>Headgear</td>
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<td>CPAP rental per month</td>
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<td>Heated humidifier per month</td>
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<td>Lifetime nonmedical costs*</td>
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<tr>
<td>Productivity</td>
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</tr>
</tbody>
</table>

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.

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.25 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

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 CPAP,6 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.30
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 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 (Q₉ = 4.34; P = 0.50). 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 QALYs (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
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 utilities were used instead of standard gamble utilities, the ICER estimate increased more than 5 times (Table 4).

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) and biological agents for the treatment of rheumatoid arthritis ($30 500 per QALY). They are substantially less than the ICER of lung volume reduction surgery in the treatment of chronic obstructive pulmonary disease ($190 000 per QALY).

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, reduction in occupational injuries, reduced use of antihypertensive medications, and improvements in bed-partner quality of life.

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. Long-term studies describing potential reductions in cardiovascular events with CPAP have been observational in nature and thus are subject to confounding by indication/compliance. Others have used surrogate short-term (usually ≤1 month) end points such as endothelial function and C-reactive protein level or blood pressure. Some of these studies conflict, with one study that demonstrated a reduction in C-reactive protein level with CPAP and another that demonstrated no signifi-
cant effect. Some studies have also shown no significant effect of CPAP on blood pressure. 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. Tousignant and colleagues 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 coworkers 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., 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 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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