Cost-effectiveness of continuous positive airway pressure therapy in patients with obstructive sleep apnea-hypopnea in British Columbia

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BACKGROUND: Obstructive sleep apnea-hypopnea (OSAH) is a common disorder characterized by recurrent collapse of the upper airway during sleep. Patients experience a reduced quality of life and an increased risk of motor vehicle crashes (MVCs). Continuous positive airway pressure (CPAP), which is the first-line therapy for OSAH, improves sleepiness, vigilance and quality of life.

OBJECTIVE: To assess the cost-effectiveness of CPAP therapy versus no treatment for OSAH patients who are drivers.

METHODS: A Markov decision analytical model with a five-year time horizon was used. The study population consisted of male and female patients, between 30 and 59 years of age, who were newly diagnosed with moderate to severe OSAH. The model evaluated the cost-effectiveness of CPAP therapy in reducing rates of MVCs and improving quality of life. Utility values were obtained from previously published studies. Rates of MVCs under the CPAP and no CPAP scenarios were calculated from Insurance Corporation of British Columbia data and a systematic review of published studies. MVCs, equipment and physician costs were obtained from the British Columbia Medical Association, published cost-of-illness studies and the price lists of established vendors of CPAP equipment in British Columbia. Findings were examined from the perspectives of a third-party payer and society.

RESULTS: From the third-party payer perspective, CPAP therapy was more effective but more costly than no CPAP (incremental cost-effectiveness ratio [ICER] of $3,626 per quality-adjusted life year). From the societal perspective, the ICER was similar ($2,979 per quality-adjusted life year). The ICER was most dependent on preference elicitation method used to obtain utility values, varying almost sixfold under alternative assumptions from the base-case analysis.

CONCLUSION: After considering costs and impact on quality of life, as well as the risk of MVCs in individuals with OSAH, CPAP therapy for OSAH patients is a highly efficient use of health care resources. Provincial governments who do not provide funding for CPAP therapy should reconsider.

Key Words: Cost-effectiveness; CPAP; Obstructive sleep apnea

Patients with obstructive sleep apnea-hypopnea (OSAH) experience recurrent collapse of the upper airway during sleep. OSAH is a common disorder (1) that has many adverse consequences, including sleep fragmentation, daytime sleepiness and reduced quality of life (2). Presumably due to reduced vigilance associated with OSAH, patients have an increased...
risk of motor vehicle crashes (MVCs) (3). Continuous positive airway pressure (CPAP) is the first-line therapy for OSAH, which is delivered with a device that consists of a mask worn on the face and connected by plastic tubing to a flow generator. Treatment leads to improved daytime sleepiness, increased vigilance, improved quality of life and a reduced MVC rate (4-6). Despite these benefits, it is unclear whether CPAP is a cost-effective use of health care resources, especially when health care resources are limited and health care demands are vast. A common measure of the cost-effectiveness of a medical intervention is the incremental cost-effectiveness ratio (ICER), which is the incremental cost divided by the incremental change in quality-adjusted life years (QALYs) associated with one strategy (course of action) versus another (7,8).

We previously published a cost-effectiveness analysis of CPAP therapy in the United States (9). The study found that CPAP therapy was a cost-effective intervention. However, cost-effectiveness results are known to vary by jurisdiction due to differences in health care treatments, resource use and costs (10). Thus, the purpose of the present study was to evaluate the cost-effectiveness of CPAP therapy, versus no CPAP, for OSAH patients in a Canadian context.

METHODS

A state-transition Markov model was used to compare the costs and health outcomes of OSAH treated with CPAP therapy versus no CPAP therapy. A hypothetical cohort of British Columbia drivers (between 30 and 59 years of age) with newly diagnosed moderate-to-severe OSAH was considered (Figures 1 and 2). The time horizon was five years (Markov cycle length, one year).

**Figure 1** Markov model of patients not prescribed continuous positive airway pressure therapy. Starting node is shown in bold. Tunnel refers to patients fixed in a specified state until death. MAIS Modified Abbreviated Injury Scale; MVC Motor vehicle crash

**Figure 2** Markov model of patients prescribed continuous positive airway pressure (CPAP) therapy. Starting node is shown in bold. Tunnel refers to patients fixed in a specified state until death. MAIS Modified Abbreviated Injury Scale; MVC Motor vehicle crash

**Decision model structure**

In each year of the model, patients could have an MVC resulting in property damage, injury or death; die of natural causes; or survive incident-free. Injuries were subclassified into severity categories according to the Maximum Abbreviated Injury Scale (MAIS) 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 (ie, they were fixed in a tunnel state) and thus were no longer at risk of an MVC. All other survivors were at risk of a subsequent MVC. The CPAP treatment strategy, versus no CPAP, differed in transition probabilities and upfront costs. All monetary values were adjusted to the value of Canadian dollars in 2005. The decision analysis was performed with Data Pro for HealthCare software (TreeAge Software Inc, USA). The statistical analysis was performed with SAS version 8 (SAS Institute Inc, USA).

**Clinical data inputs**

Proportion of patients in each sex and age group: The analysis was structured as a weighted average of six patient groups.
Rates of MVCs: The annual MVC probability in individuals without OSAH was determined using data for 1997 (1.6 million motorists aged 30 to 60 years) from the Insurance Corporation of British Columbia – the insurer for all licensed motorists in the province. MVC probabilities were stratified by patient group and by the following MVC types: property damage only, injury related or fatal. MVC injury severity was assumed to have the distribution of 85.6% MAIS 1, 10.5% MAIS 2, 3.3% MAIS 3, 0.4% MAIS 4 and 0.2% MAIS 5 (11). Because the proportion of OSAH in the general population is relatively small, these values were assumed to apply to a population without OSAH.

Impact of CPAP on MVC rates: To assess the impact of CPAP on MVC rates, a meta-analysis was performed. The search strategy and results were reported previously (9). Briefly, a search of MEDLINE (1966 to March 2005) identified eight studies (Table 2) that compared rates of MVCs before and after CPAP therapy in patients predominantly with severe disease (mean apnea-hypopnea index values ranging from 37 events/h to 60 events/h) (6,12-18). CPAP therapy reduced the MVC rate by approximately sevenfold (OR of MVCs with CPAP compared with no CPAP, 0.148; 95% CI 0.097 to 0.224).

The MVC rate in OSAH patients treated with CPAP was assumed to be comparable with that in the general population (6). Hence, annual MVC probabilities for patients treated with CPAP were obtained from British Columbia traffic collision statistics. MVC probabilities for patients with untreated OSAH were calculated by dividing the MVC rate for British Columbia by the percentage reduction in MVCs associated with CPAP therapy.

Mortality rates: Mortality was calculated by adding the yearly, sex-specific probability of death in an MVC to stratified all-cause mortality estimates obtained from Canadian life tables (19).

Utility values: QALYs were calculated as the sum of the time spent in health states multiplied by the mean utility associated with each of the health states. In the base-case analysis, utility results were obtained by the standard gamble method, which is often considered the gold standard technique in health status measurement (21,22). Evaluation of the increase in utility due to CPAP was based on a prospective study that demonstrated an increment in utility from 0.32 to 0.55 (difference of 0.23) (23). A retrospective study by Tousignant et al (24) found a similar improvement in utility.

Utilities were also assessed using the EuroQol 5D (EQ-5D). One study (25) showed an EQ-5D improvement from 0.738 to 0.811 (increase of 0.073) due to CPAP. Another study (26) reported an EQ-5D improvement in utility of 0.05 (from 0.78 to 0.83). The robustness of ICER estimates to different utility values stratified by injury level using methods similar to those of other investigators (28).

Costs: The base-case analysis, which adopted a third-party payer perspective, considered only direct costs. In the first year of the Markov simulation, the total cost of CPAP was based on the standard of care provided to patients at our referral centre for OSAH in Vancouver, and pricing information from two established CPAP equipment vendors in the locality. CPAP treatment costs included the costs for the CPAP device, mask, tubing, headgear and heated humidifier. The costs of one specialist consultation and two physician follow-up visits, which were also included in the first year, were obtained from the

**TABLE 1**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Point estimate</th>
<th>Description or comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study population proportions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male subjects, age group, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39 years</td>
<td>15.0</td>
<td>No distribution assigned.</td>
</tr>
<tr>
<td>40–49 years</td>
<td>25.8</td>
<td>Source: Sleep Disorders</td>
</tr>
<tr>
<td>50–59 years</td>
<td>35.7</td>
<td>Program, Vancouver Acute</td>
</tr>
<tr>
<td>Female subjects, age group, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39 years</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>40–49 years</td>
<td>8.4</td>
<td></td>
</tr>
<tr>
<td>50–59 years</td>
<td>13.6</td>
<td></td>
</tr>
<tr>
<td>Total, %</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Utilities

- No CPAP: 0.32; Beta distribution (alpha = 2.4, beta = 5.1). Source: (23)
- Incremental gain from CPAP: 0.23; Beta distribution (alpha = 5.0, beta = 16.8). Source: (23)
- Functional capacity index, by MAIS (SD in parentheses): MAIS = 1: 0.83; Beta distribution. Source: for all values: (11) and the assumption of a SD of 0.09 for each of the point estimates. MAIS = 2: 0.89; MAIS = 3: 0.93; MAIS = 4: 0.93; MAIS = 5: 0.19; Source: (23)
- Discount rate, %: 3; No distribution assigned. Source: (20)
- Compliance, %: 70; No distribution assigned. Source: (33)
- Time horizon, years: 5; No distribution assigned. Source: Assumption
- Scaling factor for converting lifetime MVC costs to match five-year Markov timeframe: 0.125; No distribution assigned. Source: Based on the assumptions of a uniform lifetime distribution of MVC costs, and a 40-year future lifespan for all drivers
- Reduction of MVC with CPAP therapy (SD in parentheses): 0.15; Log-normal distribution (95% CI: 0.10 to 0.22). Source: Meta-analysis. (6,12-18)
- All costs: Triangular distribution defined by a +/- 25% end points. Source: Assumption

CPAP Continuous positive airway pressure; MAIS Modified Abbreviated Injury Scale; MVC Motor vehicle crash

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TABLE 2
Studies with rates of motor vehicle crashes (MVCs) with and without continuous positive airway pressure (CPAP) therapy

<table>
<thead>
<tr>
<th>Source</th>
<th>Country</th>
<th>Number of patients</th>
<th>Mean AHI, events/h</th>
<th>Mean age, years</th>
<th>Definition of crash</th>
<th>CPAP</th>
<th>No CPAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>George (6)</td>
<td>Canada</td>
<td>210</td>
<td>54.0</td>
<td>52.0</td>
<td>From provincial insurance database</td>
<td>0.06/year</td>
<td>0.18/year</td>
</tr>
<tr>
<td>Findley et al (12)</td>
<td>United States</td>
<td>50</td>
<td>37.0</td>
<td>56.0</td>
<td>State DMV (injury or property damage more than $500)</td>
<td>0.06/year</td>
<td>0.07/year</td>
</tr>
<tr>
<td>Krieger et al (13)</td>
<td>France</td>
<td>547</td>
<td>59.8</td>
<td>56.6</td>
<td>Self-reports</td>
<td>0.0256/year</td>
<td>0.084/year</td>
</tr>
<tr>
<td>Engleman et al (14)</td>
<td>Scotland</td>
<td>215</td>
<td>47.0</td>
<td>53.0</td>
<td>Self-reports (major incidents)</td>
<td>0.001/10,000 miles</td>
<td>0.005/10,000 miles driven</td>
</tr>
<tr>
<td>Horstmann et al (15)</td>
<td>Switzerland</td>
<td>85</td>
<td>N/A</td>
<td>N/A</td>
<td>Self-reports</td>
<td>2.7/1,000,000 km</td>
<td>10.6/1,000,000 km driven</td>
</tr>
<tr>
<td>Suratt and Findley (18)</td>
<td>United States</td>
<td>22</td>
<td>N/A</td>
<td>N/A</td>
<td>Self-reports</td>
<td>0.023/year</td>
<td>0.30/year</td>
</tr>
<tr>
<td>Cassel et al (16)</td>
<td>Germany</td>
<td>59</td>
<td>38.9</td>
<td>49.0</td>
<td>Self-reports</td>
<td>0.14/100,000 km</td>
<td>0.8/100,000 km</td>
</tr>
<tr>
<td>Yamamoto et al (17)</td>
<td>Japan</td>
<td>39</td>
<td>55.7</td>
<td>48.0</td>
<td>Self-reports</td>
<td>0.17/year</td>
<td>0/year</td>
</tr>
</tbody>
</table>

AHI: Apnea-hypopnea index; DMV: Department of motor vehicles; N/A: Not available

TABLE 3
Cost estimates

<table>
<thead>
<tr>
<th>Variable</th>
<th>Base-case cost estimate, $*</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPAP-related costs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headgear and mask</td>
<td>222.50</td>
<td>Average of prices charged by three homecare companies</td>
</tr>
<tr>
<td>Tubing</td>
<td>30.00</td>
<td></td>
</tr>
<tr>
<td>CPAP machine</td>
<td>1,536.25</td>
<td>in British Columbia</td>
</tr>
<tr>
<td>Heated humidifier</td>
<td>350.00</td>
<td></td>
</tr>
<tr>
<td>Initial office visit (45 min)</td>
<td>141.11</td>
<td>BCMA 2005 Medical Services Plan Physician Fee schedule (29)</td>
</tr>
<tr>
<td>Follow-up office visit (15 min)</td>
<td>41.07</td>
<td>BCMA 2005 Medical Services Plan Physician Fee schedule (29)</td>
</tr>
<tr>
<td>Lifetime direct costs (average for all injuries, including fatalities)</td>
<td>345.00</td>
<td>Economic Burden of Unintentional Injuries in Canada¹ (30)</td>
</tr>
<tr>
<td>Lifetime direct costs (average for all PDO motor vehicle crashes)</td>
<td>229.00</td>
<td>1997 ICBC actuarial report (32)</td>
</tr>
<tr>
<td>Lifetime societal costs² (average for all injuries, including fatalities)</td>
<td>1,538.00</td>
<td>Economic Burden of Unintentional Injuries in Canada¹ (30)</td>
</tr>
<tr>
<td>Lifetime societal costs² (PDO average)</td>
<td>1,053.00</td>
<td>1994 Ontario study (31)</td>
</tr>
</tbody>
</table>

*Values are adjusted to Canadian dollars in 2005; ¹Incidence data on motor vehicle collisions in Canada, required to convert the global cost estimates of the Economic Burden of Unintentional Injuries in Canada to a per injury basis, was obtained from Transport Canada; ²Cost of lost productivity associated with mortality was $7723, or 47% of the societal cost. BCMA British Columbia Medical Association; CPAP Continuous positive airway pressure; ICBC Insurance Corporation of British Columbia; PDO Property damage only

CPAP compliance: A compliance rate of 70% was assumed as reported in the literature (33). Noncompliant patients were also assumed to use the CPAP machine for three months, incurring the prorated cost of the machine and humidifier, as well as the costs associated with the mask, tubing, headgear and one physician visit. Patients were assumed not to benefit from CPAP for this period of three months.

Probabilistic cost-effectiveness analysis
To account for uncertainty in our model, a probabilistic cost-effectiveness analysis with second-order Monte Carlo simulations was conducted. This analysis involved assigning probabilistic distributions to key model parameters. Beta distributions were given to conditional transition probabilities (eg, the probability of a minor injury with a MAIS score of 1, given the occurrence of an MVC injury), and to standard gamble utilities and FCI values. Costs were assigned triangular distributions to key model parameters. Beta distributions were given to conditional transition probabilities (eg, the probability of a minor injury with a MAIS score of 1, given the occurrence of an MVC injury), and to standard gamble utilities and FCI values. Costs were assigned triangular distributions to key model parameters. Beta distributions were given to conditional transition probabilities (eg, the probability of a minor injury with a MAIS score of 1, given the occurrence of an MVC injury), and to standard gamble utilities and FCI values. Costs were assigned triangular distributions to key model parameters.
The analysis was re-run, varying parameter values for the probability of compliance with CPAP, utilities, the future discount rate, the cost scaling factor for adjusting lifetime costs to a five-year time horizon, and the reduction in MVC rate from CPAP therapy.

RESULTS

Cost-effectiveness analysis

From a third-party payer perspective, CPAP therapy was more effective but more costly than no CPAP. Specifically, the CPAP strategy, compared with the no CPAP strategy, had a mean gain of 0.75 QALYs (2.22 QALYs [95% CI 0.90 to 3.87] versus 1.45 QALYs [95% CI 0.29 to 3.03] in the CPAP and no CPAP groups, respectively). The incremental cost of CPAP was $2,716 ($2,983 [95% CI $2,587 to $3,369] versus $266 [95% CI $206 to $330] in the CPAP and no CPAP groups, respectively) resulting in an ICER of $3,626 per QALY gained (95% CI $1,911 to $9,175). From a societal perspective, the CPAP strategy had a lower incremental cost of $2,230 ($3,448 [95% CI $3,078 to $3,839] versus $1,218 [95% CI $947 to $1,516] for the no CPAP strategy), and the same incremental effectiveness. The ICER was $2,979 per QALY gained (95% CI $1,597 to $8,078).

Sensitivity analyses

One-way sensitivity analysis results are presented in Table 4.

DISCUSSION

Our analysis showed that CPAP therapy for OSAH is a cost-effective use of resources. From a third-party perspective, CPAP therapy for OSAH is a cost-effective use of resources.

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CPAP cost $3,356 per additional QALY (from a societal perspective, $2,979 per QALY gained) when compared with no CPAP therapy. This cost compares very favourably with publicly funded therapies, such as the treatment of end-stage renal disease with hemodialysis ($96,283 to $139,665 per QALY gained in 2005 Canadian dollars) and a recent recommendation in favour of a WTP threshold greater than US$100,000 (CDN$114,000) per QALY gained (7,8). A review of studies that took into consideration WTP values (eg, from wage premiums earned by workers in dangerous occupations) found a median WTP value of $353,457 per QALY gained (34).

A previous Canadian economic evaluation of CPAP therapy by Tousignant et al (35) found an ICER of $4,214 to $12,146 per QALY. However, these values were based only on quality of life data and excluded the impact of CPAP on MVCs. This helps to explain our lower ICER estimate. Our results were very similar to those we had previously published in a study of the United States, in which the ICER for CPAP was $3,811 per QALY gained in the base-case analysis (assuming US$1 is equal to CDN$1.14). Many of the country-specific differences between the two studies likely counterbalanced themselves. For instance, the MVC risk in patients on CPAP was greater in the Canadian analysis (by 1% to 3%), but the probability of an injury in the event of a crash was higher in the American study (by 13% to 18%).

Furthermore, we believe our model is very conservative and does not include many other potential CPAP benefits. These may include improvements in work performance (36), prevention of work-related injuries (37), reduction in cardiovascular disease (38-40), reduced use of antihypertensive medications (41) and improvements in spousal quality of life (42). Although data are accumulating in these fields, they are not as robust as the MVC and quality of life data. Nevertheless, even with the exclusion of these potential benefits, CPAP is still a cost-effective use of resources. Despite clear data demonstrating the potential benefits of CPAP, the majority of provinces, excluding Ontario, Saskatchewan and Manitoba, do not provide funding for CPAP.

There are a number of limitations in the present study. First, much of the data used to determine the transition probabilities originated from studies of patients with severe OSAH. Our analysis was also limited to patients 30 to 59 years of age. Hence, our model may not be applicable to patients with mild-moderate OSAH, or to younger and older patients.

Second, our model was largely based on the effectiveness of CPAP in reducing MVC rates and improving quality of life. We had derived our reduction estimate from studies with a before and after design (ie, a comparison of MVC rates before and after CPAP therapy). Some patients in these studies may have been sent for assessment of suspected sleep-disordered breathing because of a previous MVC. Thus, rates might be falsely inflated before using CPAP (referral bias). However, we doubt this significantly influenced our overall findings. When the MVC OR was decreased to the lower end of its 95% CI, the ICER was still close to $3,660 per QALY.

Third, our model was based on costs and MVC rates in British Columbia. Our results may not be applicable to other provinces because of the cost differences in physicians, CPAP therapy and MVC. Nevertheless, we suspect these differences are minor and unlikely to affect our results substantially. Finally, our base-case analysis used utilities measured by the standard gamble method administered directly to patients. These utilities represent the health state preferences of patients and not society. When we used EQ-5D utilities, however, which do reflect societal preferences, we found a modest change in the ICER estimate. CPAP seemed slightly less appealing. Nonetheless, even with the use of the EQ-5D, our ICER estimates fell within a generally considered cost-effective range. The difference in ICER results may be due to differences between the responsiveness of the preference elicitation instruments, or between the preferences of patients and society.

CPAP has previously been shown to be an effective therapy in improving OSAH symptoms (2,4). Our results show that in British Columbia CPAP also appears to be a cost-effective use of health care resources. Despite this finding, most provinces in Canada do not provide funding for CPAP therapy. Further work in educating health care decision makers of the importance of sleep apnea and the clear benefits of treatment is recommended.

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REFERENCES

Cost-effectiveness analysis of CPAP in Canada
