

ANESTHESIOLOGY

Cost-effectiveness Analysis of Preoperative Screening Strategies for Obstructive Sleep Apnea among Patients Undergoing Elective Inpatient Surgery

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Obstructive sleep apnea is common, frequently undiagnosed, and associated with increased risk of postoperative complications.
- This risk may be mitigated if obstructive sleep apnea is identified preoperatively.
- Several screening modalities are available. Polysomnography is the gold standard but expensive. The STOP-Bang questionnaire and portable monitors are cheaper but less accurate alternatives.

What This Article Tells Us That Is New

- In a Canadian single healthcare payer model, the cost-effectiveness of preoperative obstructive sleep apnea screening differs depending on time horizon.
- Preoperative screening with STOP-Bang followed by immediate confirmatory testing with polysomnography is cost-effective on the lifetime horizon but not the perioperative horizon.

Obstructive sleep apnea is a common sleep-related breathing disorder receiving increased attention in perioperative medicine because of recognized challenges in

ABSTRACT

Background: Obstructive sleep apnea is underdiagnosed in surgical patients. The cost-effectiveness of obstructive sleep apnea screening is unknown. This study's objective was to evaluate the cost-effectiveness of preoperative obstructive sleep apnea screening (1) perioperatively and (2) including patients' remaining lifespans.

Methods: An individual-level Markov model was constructed to simulate the perioperative period and lifespan of patients undergoing inpatient elective surgery. Costs (2016 Canadian dollars) were calculated from the hospital perspective in a single-payer health system. Remaining model parameters were derived from a structured literature search. Candidate strategies included: (1) no screening; (2) STOP-Bang questionnaire alone; (3) STOP-Bang followed by polysomnography (STOP-Bang + polysomnography); and (4) STOP-Bang followed by portable monitor (STOP-Bang + portable monitor). Screen-positive patients (based on STOP-Bang cutoff of at least 3) received postoperative treatment modifications and expedited definitive testing. Effectiveness was expressed as quality-adjusted life month in the perioperative analyses and quality-adjusted life years in the lifetime analyses. The primary outcome was the incremental cost-effectiveness ratio.

Results: In perioperative and lifetime analyses, no screening was least costly and least effective. STOP-Bang + polysomnography was the most effective strategy and was more cost-effective than both STOP-Bang + portable monitor and STOP-Bang alone in both analyses. In perioperative analyses, STOP-Bang + polysomnography was not cost-effective compared to no screening at the \$4,167/quality-adjusted life month threshold (incremental cost-effectiveness ratio \$52,888/quality-adjusted life month). No screening was favored in more than 90% of iterations in probabilistic sensitivity analyses. In contrast, in lifetime analyses, STOP-Bang + polysomnography was favored compared to no screening at the \$50,000/quality-adjusted life year threshold (incremental cost-effectiveness ratio \$2,044/quality-adjusted life year). STOP-Bang + polysomnography was favored in most iterations at thresholds above \$2,000/quality-adjusted life year in probabilistic sensitivity analyses.

Conclusions: The cost-effectiveness of preoperative obstructive sleep apnea screening differs depending on time horizon. Preoperative screening with STOP-Bang followed by immediate confirmatory testing with polysomnography is cost-effective on the lifetime horizon but not the perioperative horizon. The integration of preoperative screening based on STOP-Bang and polysomnography is a cost-effective means of mitigating the long-term disease burden of obstructive sleep apnea.

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its diagnosis and management.¹ The estimated prevalence of obstructive sleep apnea in surgical populations is nearly 20%, of whom a large proportion are undiagnosed.^{2,3} Obstructive

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sleep apnea is associated with increased risk of perioperative complications including respiratory failure and long-term complications such as myocardial infarction and stroke.⁴⁻⁸ Preoperative diagnosis and treatment of obstructive sleep apnea including judicious use of sedating medications, postoperative monitoring, and treatment with continuous positive airway pressure may mitigate these risks.^{9,10} As a result of its high prevalence and the potential for risk mitigation with readily available treatments, screening for obstructive sleep apnea in the preoperative period is recommended.¹¹⁻¹³

Screening can be performed using various modalities.¹⁴ The diagnostic gold standard is polysomnography, an overnight laboratory test where obstructive sleep apnea diagnosis and severity are defined based on the apnea-hypopnea index. Although assessment with polysomnography is comprehensive, constraints on healthcare funding and conflict with surgical timing limit its use in the preoperative period.¹⁵ To this end, screening questionnaires for obstructive sleep apnea have been developed and validated.¹⁶ The STOP-Bang questionnaire is most commonly used and includes eight items, including four questions related to snoring, tiredness, observed apneas, and hypertension and four demographic queries.¹⁷ Positive responses are summed to generate the STOP-Bang score with high scores associated with increased probability of obstructive sleep apnea.¹⁸ Although STOP-Bang can be completed as part of preoperative patient evaluation at minimal added cost, it has low specificity resulting in added costs if relied on exclusively for assigning treatment.¹⁹ Level 3 portable monitors are a sensitive screening modality developed as a less-expensive and more-accessible alternative to polysomnography.^{14,20} Polysomnography or portable monitors can be combined with STOP-Bang to improve specificity. The comparative effectiveness of screening strategies for obstructive sleep apnea in the preoperative period has not been studied, and examining the complex trade-offs between cost and effectiveness prospectively is resource-intensive.

The objective of this study was to model the cost-effectiveness of the following preoperative screening strategies: (1) no screening; (2) STOP-Bang alone; (3) STOP-Bang and confirmation with polysomnography if STOP-Bang positive (STOP-Bang + polysomnography); and (4) STOP-Bang and confirmation with portable monitor if STOP-Bang positive (STOP-Bang + portable monitor). Cost-effectiveness was assessed in two separate analyses (1) over the perioperative period alone and (2) over the lifetime horizon among adults with no prior obstructive sleep apnea diagnosis undergoing elective inpatient noncardiac surgery.

Materials and Methods

A cost-effectiveness analysis was conducted using individual-level Markov modeling to simulate costs and consequences of adopting different preoperative screening strategies for patients undergoing inpatient elective noncardiac surgery. Two time horizons were explored: (1) the

perioperative time horizon, encompassing preoperative evaluation, surgical procedure, and 30-day postoperative course, and (2) the lifetime horizon, which extended the first analysis to include the remaining lifespan of simulated patients. The methods and results are reported in accordance with the Consolidated Health Economic Evaluation Reporting Standards statement for the design and reporting of cost-effectiveness studies.²¹ All analyses were performed using TreeAge Pro Healthcare (version 2020 R1.1, USA).

Model Population and Setting

The characteristics of each patient entering the simulation were randomly drawn from distributions modeling a previously published cohort of 26,068 consecutive patients who underwent elective inpatient noncardiac surgery at a quaternary care hospital network (University Health Network, Toronto, Ontario, Canada) between 2011 and 2016 (table 1).²² Aggregate estimates were used from the published study, and this study was therefore exempt from institutional research ethics review. This cohort of 50.5% male patients had a mean age of 59.5 yr (95% CI, 59.2 to 59.7) and a mean body mass index of 28 kg/m² (95% CI, 27.6 to 27.8). Other patient characteristics used to determine STOP-Bang score, including presence of snoring, daytime sleepiness, and hypertension, were prospectively collected for each patient in the cohort and modeled accordingly. In each simulation, screening strategies were applied in the preoperative clinic before one of six common major elective surgical procedures in Ontario, including total hip arthroplasty, total knee arthroplasty, prostatectomy, hysterectomy, thyroidectomy, or bowel resection.²³

Model Structure

Simulated patients were assigned to one of four preoperative obstructive sleep apnea screening strategies: (1) no screening; (2) STOP-Bang alone, where “screen positive” was defined by score greater than or equal to 3¹⁹; (3) STOP-Bang followed by immediate confirmatory testing with polysomnography if STOP-Bang screen positive (STOP-Bang + polysomnography); and (4) STOP-Bang followed by immediate confirmatory testing with level 3 portable monitor if STOP-Bang screen positive (STOP-Bang + portable monitor; fig. 1). Relevant screening costs were applied for each patient. Screen-positive patients incurred the cost of a 12-h level 2 intensive care unit stay as part of an enhanced monitoring protocol. The effectiveness of this protocol, which included adjunctive measures such as judicious use of opioids and sedating medications and continuous positive airway pressure as needed, was assumed to be equal to long-term obstructive sleep apnea treatment.²⁴ Based on the diagnostic accuracy of each screening modality, we determined the probability of true positive, false positive, true negative, and false negative screening, and each patient entered a corresponding Markov model (fig. 2).

Table 1. Model Inputs: Patient Characteristics

Parameter	Estimate	95% CI	Distribution	Reference
Mean age, yr	59.5	59.2–59.7	Normal (SD = 14.94)	21
Proportion male, %	50.5	49.7–51.4	β ($\alpha = 7043.12$, $\beta = 6895.37$)	
Mean body mass index, kg/m ²	27.7	27.6–27.8	γ ($\alpha = 21.90$, $\lambda = 0.79$)	
Proportion snoring, %	24.7	24.0–25.4	β ($\alpha = 3606.31$, $\beta = 10982.32$)	
Proportion daytime tiredness, %	19.0	18.3–19.6	β ($\alpha = 2571.42$, $\beta = 10983.77$)	
Proportion observed apneas, %	11.0	10.5–11.5	β ($\alpha = 1462.63$, $\beta = 11882.52$)	
Proportion hypertension, %	37.8	36.9–38.6	β ($\alpha = 5328.38$, $\beta = 8779.06$)	
Proportion large neck, %	19.6	18.9–20.3	β ($\alpha = 2638.27$, $\beta = 10836.05$)	

Parameter estimates and corresponding CI were used to derive distributions, which were independently sampled for individuals entering the model.

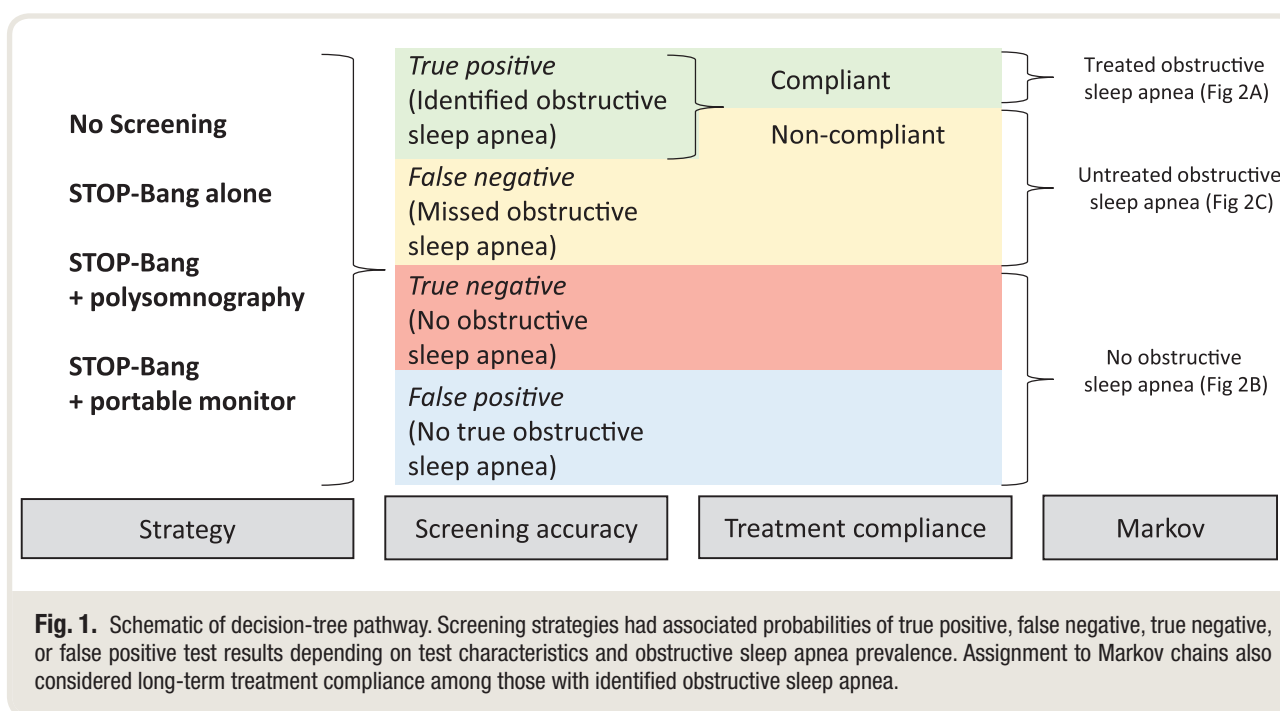


Fig. 1. Schematic of decision-tree pathway. Screening strategies had associated probabilities of true positive, false negative, true negative, or false positive test results depending on test characteristics and obstructive sleep apnea prevalence. Assignment to Markov chains also considered long-term treatment compliance among those with identified obstructive sleep apnea.

A Markov model estimates the amount of time an individual spends in various health states by considering the current health state and the probability of transitioning to alternate health states.²⁵ All individuals began in the postoperative state for the first 30-day cycle where they incurred volume-weighted mean procedure cost, the disutility of postoperative recovery, and the disutility of treated or untreated obstructive sleep apnea as appropriate.^{26–30} During the first 30 days, patients were at risk for postoperative complications and mortality and incurred their relevant costs and disutilities. Modeled postoperative complications included respiratory failure requiring reintubation, pneumonia, arrhythmia, myocardial infarction, cardiac arrest, and pulmonary embolus. The probability of each event varied according to obstructive sleep apnea and treatment status.⁹ Screening strategies were evaluated for cost-effectiveness at postoperative day 30 for the first perioperative analysis.

Survivors of the perioperative state transitioned to one of three long-term states: treated obstructive sleep apnea, untreated obstructive sleep apnea, or no obstructive sleep apnea. Those with untreated obstructive sleep apnea could eventually receive diagnosis and treatment for obstructive sleep apnea; the time to definitive diagnosis was modeled with an exponential decay function according to screening status.³¹ Screen-positive patients underwent sleep physician consultation and definitive diagnosis in a median time frame consistent with that of an individual with suspected obstructive sleep apnea, whereas screen-negative patients had a median time to diagnosis consistent with the overall undiagnosed population.³¹ After diagnosis, treatment with continuous positive airway pressure was modeled factoring in long-term compliance with therapy.³² The risk of long-term cardiovascular complications of obstructive sleep apnea including myocardial infarction and stroke were modeled according to obstructive sleep

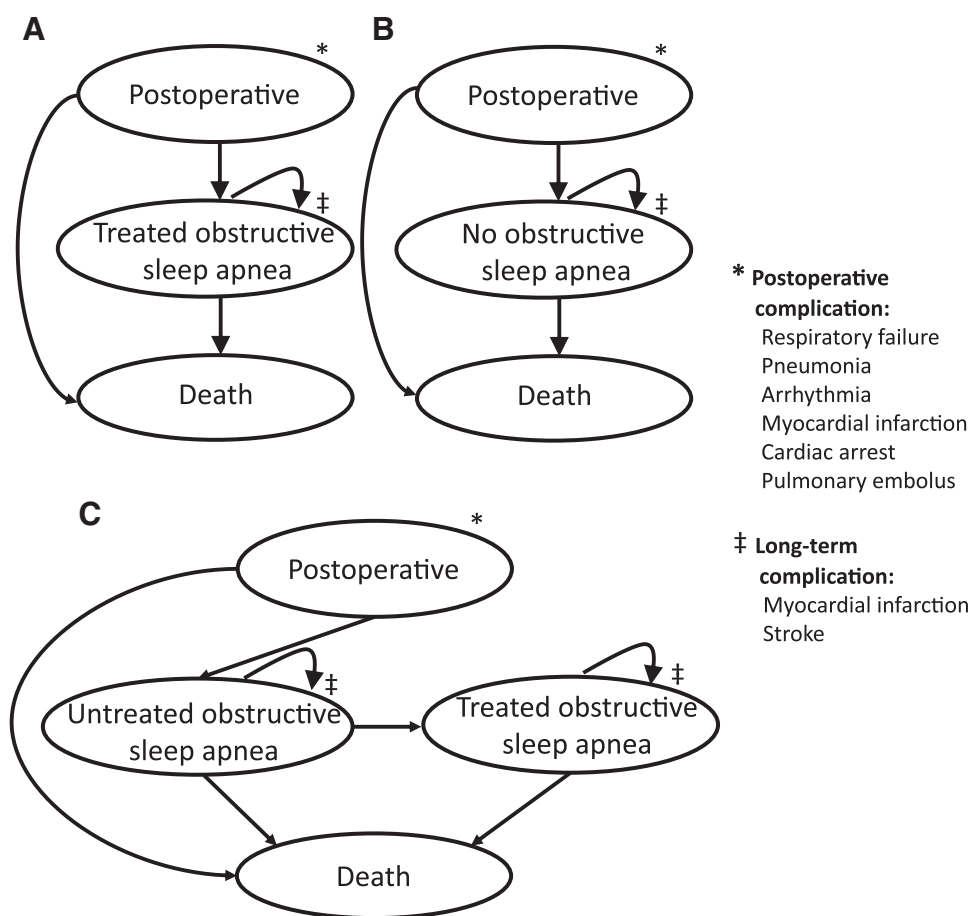


Fig. 2. Schematic of Markov chains. Simulated patients assigned to the Markov model of treated obstructive sleep apnea (A) had been diagnosed with obstructive sleep apnea and determined to be compliant with long-term treatment. These patients began in the postoperative state for one cycle where they were at risk of experiencing postoperative complications and death; they subsequently transitioned to the treated obstructive sleep apnea long-term state, where they were at risk of long-term complications. They continued to cycle in the treated obstructive sleep apnea long-term state until they reached the terminal death state. Simulated patients without obstructive sleep apnea entered the Markov model of no obstructive sleep apnea (B) regardless of screening strategy but incurred the cost of screening and perioperative treatment if they falsely screened positive. These patients also began in the postoperative state for one cycle where they were at risk of experiencing postoperative complications and death; they subsequently transitioned to the no obstructive sleep apnea long-term state, where they were at risk of long-term complications. They continued to cycle in the no obstructive sleep apnea long-term state until they reached the terminal death state. Patients with untreated obstructive sleep apnea (C) could eventually receive obstructive sleep apnea diagnosis and treatment. These patients also began in the postoperative state and subsequently transitioned to the untreated obstructive sleep apnea long-term state. From this state, they could either remain in the untreated obstructive sleep apnea long-term state or transition to the treated obstructive sleep apnea long-term state if they received obstructive sleep apnea diagnosis and were compliant with treatment. From either the untreated or treated obstructive sleep apnea long-term states, they could experience long-term complications or enter the terminal death state. Risks of postoperative (*) and long-term (†) complications in all chains were assigned according to obstructive sleep apnea and treatment status.

apnea and treatment status. The additional model assumptions are summarized in table 2.^{32,33} In the second lifetime horizon analysis, we considered the cost-effectiveness of screening strategies over the lifespan of simulated patients.

Model Inputs

The perioperative course and lifespan of 100,000 patients was simulated. Model inputs, including screening accuracy,

probabilities, utilities, and costs were derived from a structured literature search, favoring results of systematic reviews and meta-analyses where available. If systematic reviews were not available for a given parameter, the values and ranges included in primary analyses were verified independently by two authors from a minimum of two published sources and content experts (M.S. and S.G.M.). The model inputs, distribution parameters for

sensitivity analyses, and literature references are detailed in table 3.^{2,3,17,20,26–33}

Probabilities. State transition probabilities are summarized in table 4.^{9,34–36} The prevalence of undiagnosed obstructive sleep apnea was obtained from cohorts of patients undergoing inpatient elective noncardiac surgery in academic centers in North America.³ The median time to definitive obstructive sleep apnea diagnosis if screened positive or negative were 4.4 and 84 months, respectively.³¹ The probabilities of postoperative outcomes were obtained from a prospective cohort of patients undergoing major surgery (table 4).³⁴ Postoperative and long-term complications were obtained from studies that compared outcomes between no obstructive sleep apnea, untreated obstructive sleep apnea, and treated obstructive sleep apnea groups.^{35,36} Age- and sex-dependent background risk of myocardial infarction and stroke were derived from longitudinal studies, and these risks were modified based on obstructive sleep apnea and treatment status by applying hazard ratios derived from published Cox proportional hazards models (table 4).³⁷ Where more than one hazard ratio applied to a simulated patient, a multiplicative function was applied.³⁸

Utilities. Utilities for the conditions examined were obtained from the Tufts Cost-Effectiveness Analysis Registry (table 3).²⁷ Where multiple utility sources were available, preference was given to those derived from the EuroQol-5D utility instrument.²⁷ Observed longitudinal changes in utility after each complication were modeled.^{26–30} The well state was assigned utility of 1.

Costs. Costs were considered from the hospital perspective (table 3). The costs of surgery, diagnosis, and treatment for obstructive sleep apnea and complications were sourced from the Ontario Case Costing Analysis Tool of the Canadian Institute of Health Information. This tool tracks and summarizes costs of inpatient, ambulatory, and surgical care for participating hospitals in Ontario, Canada, and is used for hospital-level budgeting.³³ All costs in this study were imputed as 2016 Canadian Dollars.³³

Model Outputs

The effectiveness of each screening strategy was measured by their effect on health-related quality of life of simulated

patients. The time that each simulated patient spent in a particular health state was multiplied by that health state's utility, a modifier representing health-related quality of life on a scale anchored at 1 (perfect health) and 0 (dead). The cumulative quality-adjusted time accrued by simulated patients was the reported measure of effectiveness. In the perioperative analyses, the 30-day perioperative period was simulated, and quality-adjusted life months were reported. In the lifetime analyses, simulated patients' life expectancy was adjusted for quality of life, and quality-adjusted life years were reported.

Cost-effectiveness was expressed as the cost spent to accrue each quality-adjusted life month or quality-adjusted life year. Strategies that were more costly and less effective were said to be “absolutely dominated” by other strategies. Strategies were said to be “dominated by extension” if any other strategy was more effective and more cost-effective, regardless of cost. Remaining strategies were compared based on the incremental cost needed to pay for incremental effectiveness, a value termed the incremental cost-effectiveness ratio.

We used global 1.5% discounting for costs and outcomes, in accordance with Canadian Agency for Drugs and Technologies in Health guidelines and explored alternative discounting rates in sensitivity analyses.³⁹ Where analysis required the submission of a willingness-to-pay threshold, which reflects the acceptable cost per increment in quality-adjusted life year, the \$50,000/quality-adjusted life year threshold was applied.³⁹ When interpreting the perioperative analysis, this threshold is equal to \$4,167/quality-adjusted life month.

Sensitivity Analyses

Uncertainty in model outputs was explored using both deterministic and probabilistic sensitivity analyses. Each sensitivity analysis was performed with 10,000 simulated patients. In deterministic sensitivity analyses, model parameters are varied over a prespecified range. The upper and lower limits of parameters are defined by 95% CI where available.

In probabilistic sensitivity analyses, all model parameters are simultaneously varied. Each parameter was randomly

Table 2. Major Model Assumptions

1. Individuals with no obstructive sleep apnea never developed obstructive sleep apnea.
2. STOP-Bang characteristics had no impact on mortality outside of the obstructive sleep apnea effect.
3. All patients who screen positive for obstructive sleep apnea (in STOP-Bang alone, STOP-Bang + polysomnography, STOP-Bang + portable monitor) received perioperative treatment modifications taking obstructive sleep apnea into account.
4. Patients who screened positive but did not have a true obstructive sleep apnea diagnosis incurred a one-time consultation cost to reverse the diagnosis.
5. Those with undiagnosed obstructive sleep apnea eventually received diagnosis and treatment; the duration to definitive diagnosis was impacted by screening status.
6. Patients with diagnosed obstructive sleep apnea were assigned to treatment-compliant or non-treatment-compliant status in proportions consistent with previous cohort studies of obstructive sleep apnea treatment compliance.³² In our study, patients remained in the same compliance status indefinitely.
7. Patients experienced only one postoperative and one long-term complication.
8. Postoperative complications did not impact risk of long-term complications except *via* increased hazard of mortality.
9. Major cardiovascular events (myocardial infarction and stroke) were the only long-term obstructive sleep apnea-related complications.
10. Obstructive sleep apnea and complication-related utilities and hazard ratios were multiplicative.³⁸

Table 3. Model Inputs: Probabilities, Utilities, and Costs

	Estimate	Range	Distribution	Reference
Probabilities				
Prevalence of undiagnosed obstructive sleep apnea among patients undergoing major surgery, %	19	10–50	γ ($\alpha = 86.68$, $\lambda = 456.19$)	2,3
Months to obstructive sleep apnea diagnosis, median				
Clinical suspicion (screen positive)	4.4	2–36	γ ($\alpha = 1.00$, $\lambda = 0.23$)	31
No clinical suspicion	84	1–120	γ ($\alpha = 1.00$, $\lambda = 0.01$)	
STOP-Bang				
Sensitivity	0.88	0.79–0.95	β ($\alpha = 74.98$, $\beta = 10.22$)	17
Specificity	0.3	0.22–0.40	β ($\alpha = 24.90$, $\beta = 58.10$)	
Portable monitor				
Probability of screening positive if STOP-Bang positive, %	49	31–55	β ($\alpha = 135.57$, $\beta = 141.10$)	
Sensitivity	0.79	0.71–0.86	β ($\alpha = 106.20$, $\beta = 28.23$)	20
Specificity	0.79	0.63–0.89	β ($\alpha = 51.63$, $\beta = 13.73$)	
Long-term continuous positive airway pressure therapy compliance	0.59	SD 0.23	β ($\alpha = 3.10$, $\beta = 2.15$)	32
Utilities (duration applied)				
Untreated obstructive sleep apnea (lifetime)	0.84	0.80–0.93	β ($\alpha = 270.22$, $\beta = 51.47$)	
Treated obstructive sleep apnea (lifetime)	0.93	0.84–0.98	β ($\alpha = 92.10$, $\beta = 6.93$)	
Major surgery recovery (1 month)	0.70	0.65–0.95	β ($\alpha = 8.34$, $\beta = 3.57$)	
Pneumonia (1 month)	0.85	0.79–0.92	β ($\alpha = 84.11$, $\beta = 14.84$)	
Respiratory failure (lifetime)	0.73	0.60–0.88	β ($\alpha = 280.36$, $\beta = 57.42$)	
Arrhythmia (lifetime)	0.95	0.95–0.98	β ($\alpha = 16.39$, $\beta = 0.86$)	26–30
Cardiac arrest (1 month, then myocardial infarction utilities)	0.72	0.68–0.78	β ($\alpha = 154.17$, $\beta = 59.96$)	
Myocardial infarction (first year)	0.76	0.65–0.94	β ($\alpha = 43.25$, $\beta = 13.66$)	
Myocardial infarction (lifetime)	0.88	0.67–0.94	β ($\alpha = 4.22$, $\beta = 0.58$)	
Stroke (lifetime)	0.65	0.26–0.92	β ($\alpha = 3.08$, $\beta = 1.66$)	
Pulmonary embolus (1 month, then arrhythmia utility for lifetime)	0.75	0.65–0.94	β ($\alpha = 14.21$, $\beta = 4.74$)	
Costs (2016 Canadian dollars)				
Obstructive sleep apnea				
Portable monitor	141.26	47.09	γ ($\alpha = 9.00$, $\lambda = 0.06$)	33
Polysomnography	548.64	274.32	γ ($\alpha = 9.00$, $\lambda = 0.02$)	
Perioperative treatment	1,796.00	898.00	γ ($\alpha = 4.00$, $\lambda = 0.00$)	
Ongoing treatment	202.00	331.00	γ ($\alpha = 0.37$, $\lambda = 0.02$)	
Acute complication				
Myocardial infarction	8,119.15	12,622.56	γ ($\alpha = 0.4$, $\lambda = 5.096$)	
Respiratory failure	30,850.64	55,613.37	γ ($\alpha = 0.31$, $\lambda = 9.98$)	
Pneumonia	5,631.55	10,070.60	γ ($\alpha = 0.31$, $\lambda = 5.55$)	
Cardiac arrest	17,520.26	19,532.67	γ ($\alpha = 0.81$, $\lambda = 4.59$)	
Arrhythmia	4,962.93	7,891.71	γ ($\alpha = 0.39$, $\lambda = 7.97$)	
Stroke	8,277.00	15,487.00	γ ($\alpha = 0.29$, $\lambda = 3.45$)	
Pulmonary embolus	5,749.60	9,864.16	γ ($\alpha = 0.34$, $\lambda = 5.91$)	
Long-term complication (annual)				
Myocardial infarction	1,589.00	1,399.00	γ ($\alpha = 1.29$, $\lambda = 0.01$)	33
Arrhythmia	472.00	1,060.00	γ ($\alpha = 0.20$, $\lambda = 0.01$)	
Stroke	507.00	1,069.00	γ ($\alpha = 0.22$, $\lambda = 0.01$)	

Parameter estimates and corresponding ranges were used to derive distributions, which were independently sampled for individuals entering the model.

selected from a distribution that models its value in the population. Functions defining distributions were derived using published summary statistics. Distribution types were selected based on characteristics of the model parameter of interest. For example, health state utilities were modeled using β distributions, which are continuous probability distributions defined on the interval [0,1]. Model parameters in these analyses were assumed to be independent. To generate 10,000 iterations of the model, 10,000 sets of model parameters were drawn. For each model iteration, the perioperative course and lifespan of 10,000 patients was simulated. The outputs of probabilistic sensitivity analyses

were cost-effectiveness acceptability curves, which depict the proportion of iterations in which each screening strategy was favored at a given willingness-to-pay threshold.

Model Validation

The model was assessed for face and content validity by clinical experts including an anesthesiologist, a sleep medicine specialist, and a head-and-neck surgeon. Construct validity was assessed by graphically comparing predicted survival from the model to empirical survival rates of historical cohorts of patients with obstructive sleep apnea and

Table 4. Model Inputs: Complication Probabilities and Associated Hazards

	No Obstructive Sleep Apnea	Untreated Obstructive Sleep Apnea	Treated Obstructive Sleep Apnea	Reference
Probability of perioperative outcomes, %				
Mortality (95% CI)	1.9 (1.7–2.1)	1.9 (1.7–2.1)	1.9 (1.7–2.1)	9,34
Arrhythmia (SD)	1.5 (0.005)	1.6 (0.005)	1.4 (0.005)	
Myocardial infarction (SD)	0.6 (0.002)	1.4 (0.005)	0.6 (0.002)	
Reintubation/respiratory failure (SD)	1.8 (0.006)	2.7 (0.009)	1.4 (0.005)	
Pneumonia (SD)	1.7 (0.006)	1.9 (0.006)	1.6 (0.005)	
Pulmonary embolus (SD)	1.0 (0.005)	1.3 (0.004)	1.4 (0.003)	
Cardiac arrest (SD)	0.6 (0.002)	0.9 (0.003)	0.4 (0.001)	
Hazard ratio for long-term complications (95% CI)				
Mortality	Reference	2.28 (1.50–3.00)	1.08 (0.95–1.14)	35,36
Myocardial infarction	Reference	1.28 (1.18–1.39)	0.99 (0.85–1.15)	
Stroke	Reference	1.23 (1.11–1.36)	0.99 (0.82–1.19)	

Parameter estimates and corresponding CI were used to derive distributions, which were independently sampled for individuals entering the model.

to other models of the mortality of patients without treatment for obstructive sleep apnea.

Results

Model Validation

There was unanimous agreement by clinical experts on adequacy of content validity including modeling of screening strategies; included probabilities, utilities, and costs; and Markov models. Graphical comparison of our model with three longitudinal population studies and a model of patients with obstructive sleep apnea revealed comparable estimated survival probabilities (fig. 3).^{35,40–43}

Analysis 1: Perioperative Time Horizon

Base Case Analysis. The cost and effectiveness of each screening strategy over the perioperative time horizon is presented in table 5. Over 100,000 simulated patient encounters, no screening was the least costly and least effective strategy. STOP-Bang alone was the costliest strategy, but it was not the most effective. STOP-Bang + polysomnography was both less costly and more effective than STOP-Bang alone, and STOP-Bang alone was therefore dominated. STOP-Bang + polysomnography was both more effective and more cost-effective than STOP-Bang + portable monitor, which was therefore dominated by extension. The incremental cost-effectiveness ratio of STOP-Bang + polysomnography compared to no screening was \$52,888/quality-adjusted life month. This exceeded the predetermined willingness-to-pay threshold of \$4,166.67/quality-adjusted life month, and no screening was therefore the favored strategy over the perioperative time horizon.

Deterministic Sensitivity Analysis. One-way deterministic sensitivity analyses were performed to explore the influence of varying model parameters on incremental cost-effectiveness ratios comparing undominated strategies (fig. 4).

The conclusion that no screening was the favored strategy over STOP-Bang + polysomnography was robust to variation in all but one of the explored model parameters. When the hazard ratio for perioperative complications among untreated *versus* treated obstructive sleep apnea exceeded 5.6, STOP-Bang + polysomnography became the favored strategy.

Probabilistic Sensitivity Analysis. No screening was the favored strategy in more than 90% of model iterations at all examined willingness-to-pay thresholds (fig. 5).

Analysis 2: Lifetime Horizon

Base Case Analysis. As in the perioperative time horizon, no screening was the least costly and least effective strategy. STOP-Bang alone was again the costliest but not the most effective strategy and was therefore dominated (table 6). STOP-Bang + polysomnography was both more effective and more cost-effective compared to STOP-Bang + portable monitor, which was again dominated by extension. Similar to the perioperative analysis, no screening and STOP-Bang + polysomnography were the only undominated strategies. Contrary to findings in the perioperative analysis, STOP-Bang + polysomnography compared with no screening had an incremental cost-effectiveness ratio of \$2,044/quality-adjusted life year, which was *below* the willingness-to-pay threshold (\$50,000/quality-adjusted life year). STOP-Bang + polysomnography was therefore the favored strategy over a lifetime horizon.

Deterministic Sensitivity Analysis. The conclusion that STOP-Bang + polysomnography was the favored strategy over no screening was robust to variation in all explored model parameters (fig. 4).

Probabilistic Sensitivity Analysis. At a willingness-to-pay threshold of \$50,000/quality-adjusted life year, STOP-Bang + polysomnography was the favored strategy in 63.8% of model iterations (fig. 4). STOP-Bang + polysomnography

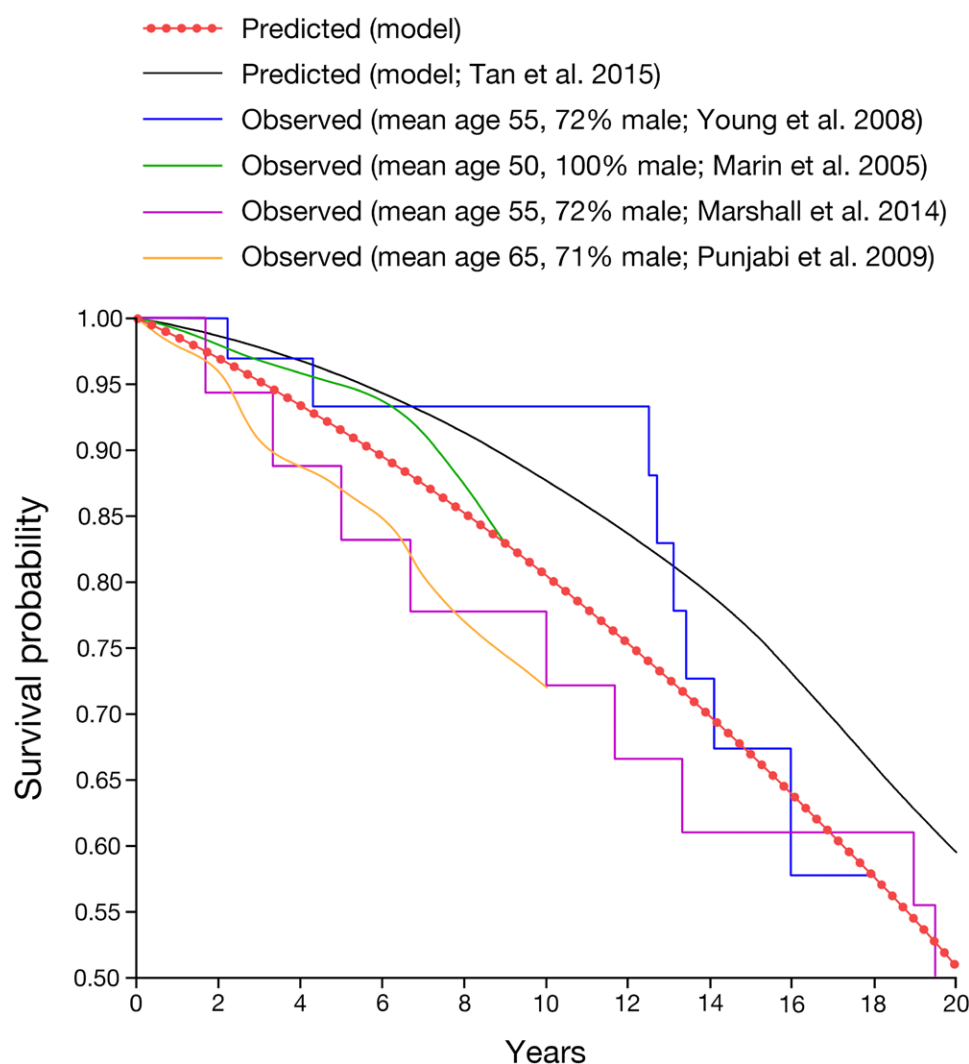


Fig. 3. Plotted survival probabilities for untreated obstructive sleep apnea according to duration of follow up for our model (*red dots*), another model of obstructive sleep apnea survival, and four observed longitudinal cohorts. The survival of our base case (mean age, 59 yr; 51% male) approximates the survival in observed cohorts and the other published model (figure reproduced with edits with permission from Tan *et al.*⁴³).

was the favored strategy in a majority of model iterations at all willingness-to-pay thresholds above \$2,000/quality-adjusted life year.

Discussion

The cost-effectiveness of preoperative obstructive sleep apnea screening strategies were evaluated over the perioperative time horizon and over a lifetime horizon. In the perioperative time horizon, no screening was favored; the added effectiveness of any screening strategy was cost-prohibitive. Favorability of screening strategies changed when the remaining lifespan of the patient was also considered. Over the lifetime horizon, the favored strategy is to administer the STOP-Bang questionnaire and confirm

the diagnosis preoperatively with polysomnography for screen-positive patients.

The conclusions regarding favored strategy in both perioperative and lifetime analyses were robust in sensitivity analyses. When only the perioperative period is considered, screening is cost-effective only if the benefit of identifying and treating patients with obstructive sleep apnea is exaggerated. For any screening strategy to be favored perioperatively, the hazard ratio for perioperative complications for untreated compared with treated obstructive sleep apnea would need to exceed 5.6, a value three-fold higher than published estimates.⁴⁴ Variation in the remaining explored parameters including costs, utilities and complication probabilities did not impact model conclusions.

Table 5. Results from Base Case Analysis over 100,000 Microsimulations: Perioperative Analysis

Strategy	Cost, 2016 Canadian Dollars	Effectiveness, Quality-adjusted Life Month	Incremental Cost-effectiveness Ratio, \$/Quality-adjusted Life Month
No screening	6,176	0.653	
STOP-Bang + portable monitor	6,607	0.659	Dominated by extension
STOP-Bang + polysomnography	6,652	0.662	52,888
STOP-Bang alone	7,027	0.658	Absolutely dominated

Screening with STOP-Bang + polysomnography was favored over a lifetime horizon, indicating that the benefit of screening is derived from mitigating the long-term risk of obstructive sleep apnea-related complications. The preoperative assessment is therefore an opportunity to diagnose obstructive sleep apnea and offer a lifetime of treatment.

However, obtaining polysomnography with preoperative assessment may be practically challenging, particularly in the context of urgent surgical procedures. If STOP-Bang + polysomnography is eliminated as a potential screening strategy, the favorability of other strategies is affected. Specifically, in lifetime horizon analyses, STOP-Bang alone would no longer be dominated and would become the favored strategy. Given that the benefit of preoperative screening is derived from reduced long-term complication risk, the favorability of STOP-Bang alone in this scenario is driven by shortened time to definitive diagnosis and treatment. Timely and reliable follow-up for identified high-risk patients is therefore important if polysomnography cannot be completed preoperatively and must be accounted for in budgetary forecasts.¹⁵

Level 3 portable monitors have been touted as a cost-saving alternative to polysomnography for the diagnosis of obstructive sleep apnea.²⁰ In our model, a screening strategy including portable monitors in place of polysomnography was indeed less expensive, but these cost-savings were insufficient to overcome its reduced effectiveness because of lower specificity (79%; 95% CI, 63 to 89%).²⁰ Effective screening strategies combine a sensitive screening test with a specific confirmatory test.⁴⁵ STOP-Bang followed by polysomnography exemplifies such an approach, and it is therefore unsurprising that this strategy is favored over a lifetime horizon.

Our model parameters were derived from the best available evidence. Estimates from some well designed studies did not meet criteria for parameterization of our model due to our requirement for comparative risk estimates for untreated, treated, and no obstructive sleep apnea groups.^{9,35,36} For example, a recent prospective cohort study of patients at risk of obstructive sleep apnea undergoing major noncardiac surgery reported that unrecognized severe obstructive sleep apnea is associated with postoperative cardiovascular complications.⁴⁴ The risks of postoperative cardiovascular complications observed in this cohort were

similar to the risks in our model. For example, myocardial injury occurred at an unadjusted hazard ratio of 2.1 (95% CI, 1.4 to 3.2) in the severe obstructive sleep apnea group compared to the group with no obstructive sleep apnea in the cohort; we modeled myocardial infarction at a hazard ratio of 2.5 in the untreated group *versus* the no obstructive sleep apnea group and explored hazard ratios of 1.5 to 3 in sensitivity analyses. As such, the results of this study support the validity of our model. Similarly, given the best existing evidence, we modeled a STOP-Bang score of greater than or equal to 3 as being screen positive. Emerging evidence supports a higher STOP-Bang threshold score (*e.g.* score higher than 5) or addition of other parameters such as serum bicarbonate to increase the specificity of STOP-Bang.^{17,46} It is unclear whether the added specificity and costs of these proposed changes would affect the cost-effectiveness of STOP-Bang alone.

Modeling studies are subject to limitations. Uncertainty of model parameter estimates is an important consideration. Whether uncertainty in model parameters changes the conclusions drawn from our model is analyzed using sensitivity analyses. The favored strategy in both perioperative and lifetime analyses were robust in probabilistic sensitivity analyses, where all model parameters were simultaneously varied. In the perioperative time horizon, no screening was favored; one threshold was identified in deterministic sensitivity analyses: the hazard of perioperative complications of untreated compared with treated obstructive sleep apnea groups. Beyond a threshold hazard of 5.6, STOP-Bang + polysomnography became favored perioperatively. Although the true value of comparative risk for perioperative complications for patients with untreated compared with treated obstructive sleep apnea is uncertain, previous evidence dictates that the likelihood that this value exceeds 5.6 is extremely low. For example, one recent estimate of the hazard ratio for perioperative cardiovascular complications among patients with untreated severe obstructive sleep apnea compared with no obstructive sleep apnea is 2.23 (95% CI, 1.49 to 3.34).⁴⁴ It is unlikely that the hazard comparing untreated moderate-to-severe obstructive sleep apnea with treated moderate-to-severe obstructive sleep apnea exceeds this comparison of severe obstructive sleep apnea *versus* no obstructive sleep apnea patients.

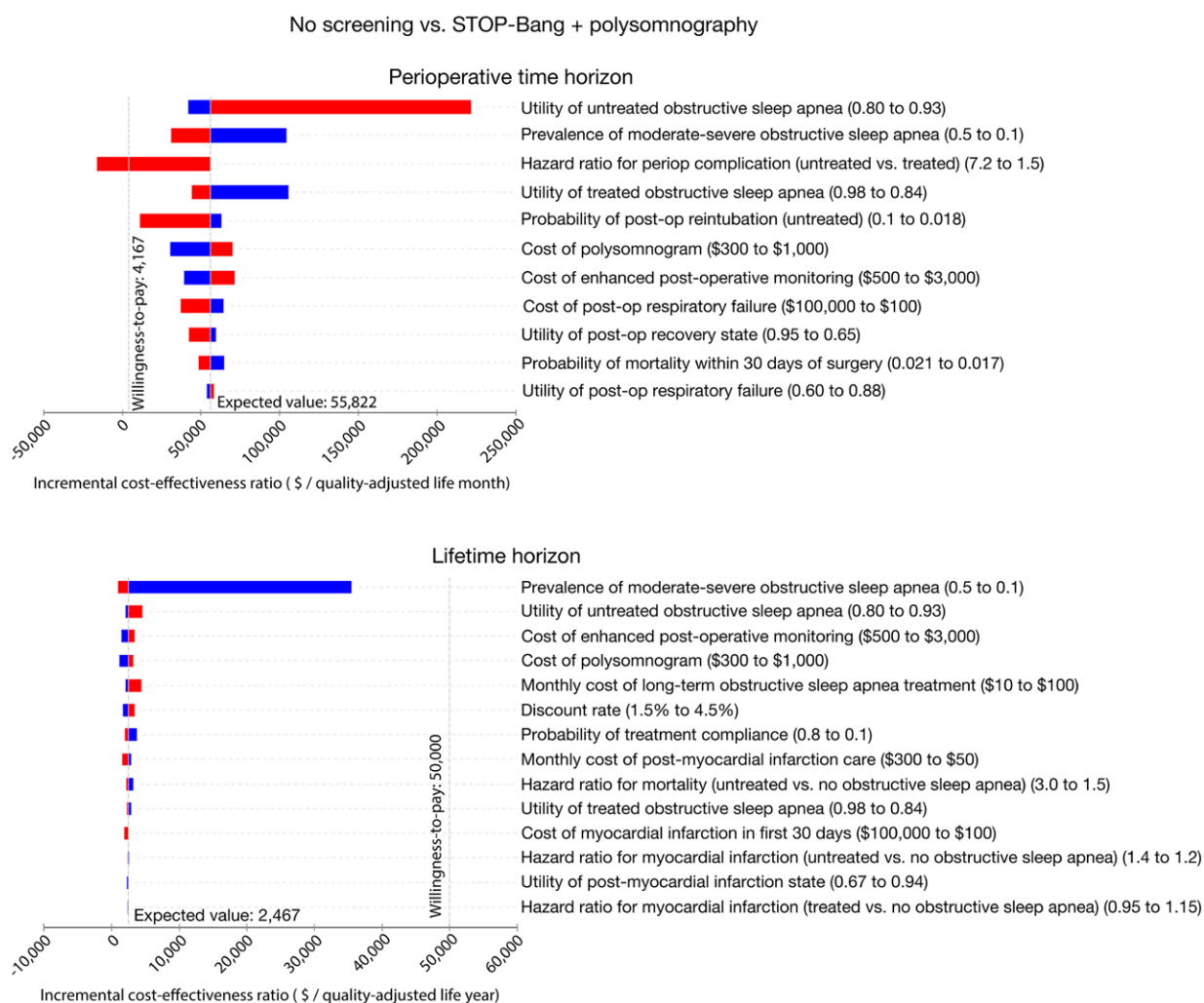


Fig. 4. Deterministic one-way sensitivity analysis for no screening *versus* STOP-Bang + polysomnography. Influential parameters were varied along ranges indicated in *parentheses*, and their effects on incremental cost-effectiveness ratios are presented. The expected value is the incremental cost-effectiveness ratio observed with a simulation that used base case parameters. The willingness-to-pay threshold for the perioperative time horizon was \$4,167/quality-adjusted life month; this is equivalent to the willingness-to-pay threshold for the lifetime horizon of \$50,000/quality-adjusted life year. The incremental cost-effectiveness ratio is represented by *blue bars* when the parameter estimate is at the low end of the explored range and by *red bars* at the high end. For example, in the perioperative time horizon analysis where the utility of untreated obstructive sleep apnea is varied, the *blue bar* indicates the incremental cost-effectiveness ratio at the low end of the explored range (0.80), and the *red bar* indicates the same at the high end of the explored range (0.93). Where *bars* cross the willingness-to-pay threshold, a change in preferred strategy is indicated. post-op, postoperative.

Modeling necessitates a simplification of reality. A valid model accounts for the most influential determinants of cost and effectiveness. For example, we modeled a simplified natural history of obstructive sleep apnea accounting only for long-term cardiovascular complications. This is justified by the observation that cardiovascular complications are primarily responsible for obstructive sleep apnea-related mortality risk, which in turn is the most important determinant of outcome quality-adjusted life years.^{44–46} This is supported by comparable survival estimates generated by our

model as compared to international cohorts. Uncertainty associated with model simplification may be accounted for in sensitivity analyses of included model parameters. For example, individuals referred for screening may be lost to follow-up, and this scenario was not explicitly modeled. This loss to follow-up would conceivably have a similar effect on model outputs as treatment noncompliance, a factor that was explored in sensitivity analyses. Similarly, all screen-positive patients were offered enhanced monitoring and treatment strategies in our model. Further refinement

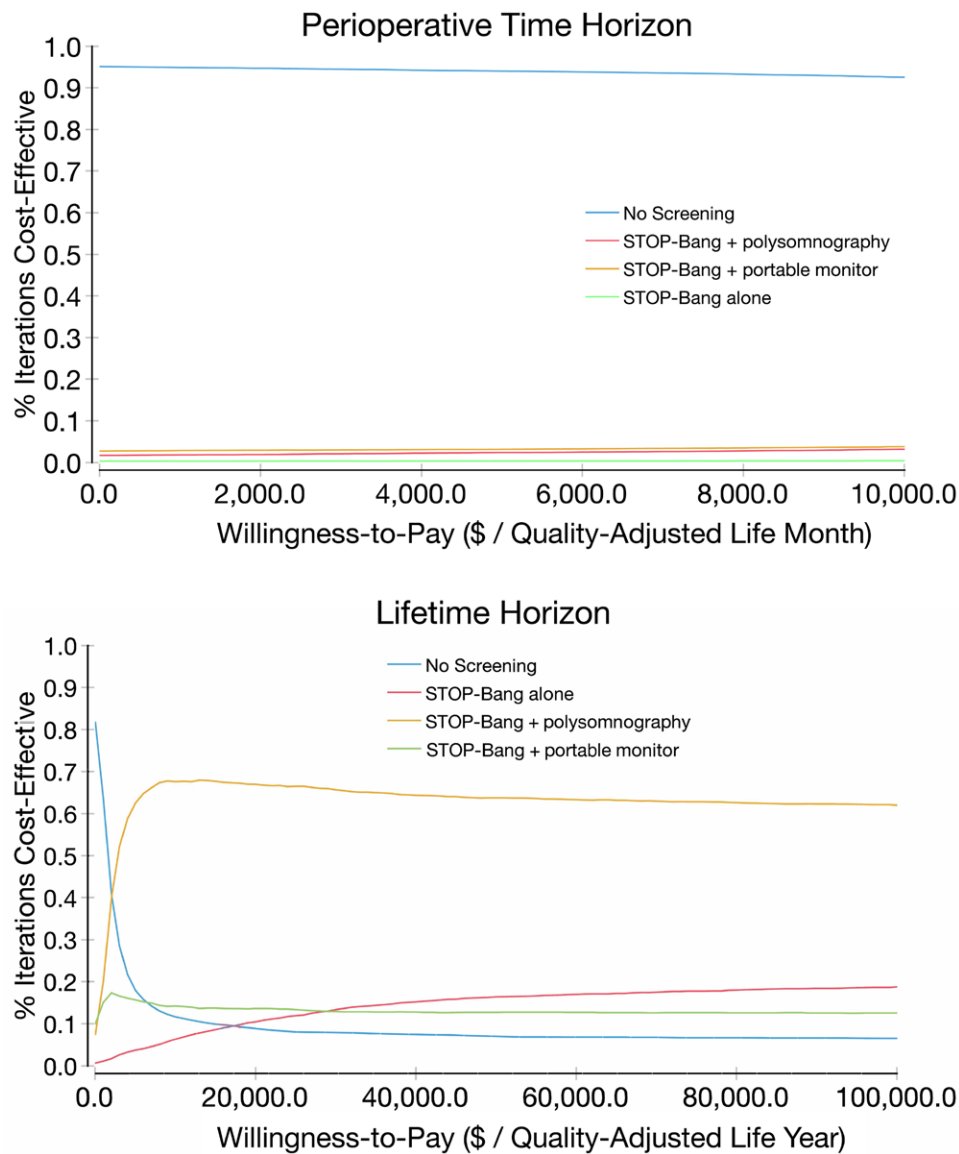


Fig. 5. Cost-effectiveness acceptability curve illustrating the results of the probabilistic sensitivity analysis. The percentage of simulated iterations in which each strategy was favored is plotted over a range of willingness-to-pay thresholds.

of postoperative strategies such as judicious assignment of postoperative treatment strategies directed at patients exhibiting recurrent postoperative events could be another consideration for future studies.⁴⁷

Models are constructed to a specified perspective and setting. Our model setting is a Canadian universal single-payer system in which healthcare is funded publicly but administered by privately run hospitals.⁴⁸ Therefore, findings are applicable to healthcare systems within similar settings. Costs were considered from the hospital perspective, because preoperative screening interventions are applied at the institutional level. It is known that disparities in health coverage exist in both Canadian and American

settings.⁴⁹ However, similarities can be drawn between the Canadian healthcare context and universal coverage within Medicare and Medicaid plans.⁵⁰ The Veterans Affairs health system is similar to the Canadian context, where remuneration for perioperative patient care is evolving to bundled payment models to hospitals that reflect the cost of surgical procedures and their associated complications.^{51,52} Furthermore, under private health insurance (individual or employer-sponsored) and health maintenance organizations, a single payer is responsible for covering costs of short-term as well as long-term complications across hospitals; the payer perspective is comparable to a hospital perspective, and the findings of this study apply. On the other

Table 6. Results from Base Case Analysis over 100,000 Microsimulations: Lifetime Analysis

Strategy	Cost, 2016 Canadian Dollars	Effectiveness, Quality-adjusted Life Year	Incremental Cost-effectiveness Ratio, \$/Quality-adjusted Life Year
No screening	9,792	15.080	
STOP-Bang + portable monitor	10,187	15.199	Dominated by extension
STOP-Bang + polysomnography	10,258	15.308	2,044
STOP-Bang alone	10,709	15.291	Absolutely dominated

hand, other healthcare payment structures such as the care of uninsured patients and supplemental coverage plans may differ from our model setting, and future work is needed to establish generalizability to these settings. Generalizability was also addressed during model validation; the lifetime survival of simulated patients in our study was comparable to previous cohorts of patients around the world.^{36,40–43}

The cost and cost-effectiveness also have implications on generalizability of study findings. Costs in our model were derived from a single valid source: the Ontario Case Costing Analysis Tool;³³ included costs had large variance, necessitating broad ranges in sensitivity analyses. The findings of our study were robust to variation in costs, indicating that the model findings are generalizable to alternate health systems with differing costs. Furthermore, we considered a willingness-to-pay threshold of \$50,000/quality-adjusted life year for cost-effectiveness in our analyses. The threshold of US\$50,000/quality-adjusted life year has been a resilient threshold, and its consideration facilitates interpretation of cost-effectiveness.⁵³ Other cost-effectiveness thresholds have been proposed. For example, in the United Kingdom, the National Institute for Health and Care Excellence guidelines indicate a willingness-to-pay threshold of £20,000 to 30,000/quality-adjusted life year.⁵⁴ Our finding of lifetime cost-effectiveness of STOP-Bang and polysomnography at thresholds as low as \$2,000/quality-adjusted life year suggest that its cost-effectiveness is unlikely to change in other contexts.

Conclusions

The cost-effectiveness of strategies for preoperative screening for obstructive sleep apnea differed based on the time horizon considered. Based on available evidence, when only the perioperative period is considered, it is not cost-effective to screen patients for obstructive sleep apnea. However, if preoperative assessment is considered an opportunity to screen for and offer lifetime treatment for obstructive sleep apnea, administering the STOP-Bang questionnaire and confirming the diagnosis with polysomnography for screen-positive patients is the favored strategy. The integration of preoperative screening based on STOP-Bang and polysomnography into clinical care pathways is a cost-effective means of mitigating the long-term disease burden of obstructive sleep apnea.

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Competing Interests

Dr. Singh serves on the medical advisory board of the Hypersomnia Foundation (Atlanta, Georgia) on a voluntary basis. Dr. Memtsoudis has provided consultations in the past for Teikoku Pharma (San Jose, California) and Sandoz (Princeton, New Jersey). The other authors declare no competing interests.

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