



ScienceDirect

Contents lists available at sciencedirect.com
Journal homepage: www.elsevier.com/locate/jval

Economic Evaluation

Cost-Effectiveness of Propofol (Diprivan) Versus Inhalational Anesthetics to Maintain General Anesthesia in Noncardiac Surgery in the United States



Tim Kampmeier, MD, PhD, Sebastian Rehberg, MD, PhD, Abdul Jabbar Omar Alsaleh, PharmD, MA, Stefan Schraag, MD, PhD, Jenny Pham, MSc, Martin Westphal, MD, PhD

ABSTRACT

Objectives: It is not known whether using propofol total intravenous anaesthesia (TIVA) to reduce incidence of postoperative nausea and vomiting (PONV) is cost-effective. We assessed the economic impact of propofol TIVA versus inhalational anesthesia in adult patients for ambulatory and inpatient procedures relevant to the US healthcare system.

Methods: Two models simulate individual patient pathways through inpatient and ambulatory surgery with propofol TIVA or inhalational anesthesia with economic inputs from studies on adult surgical US patients. Efficacy inputs were obtained from a meta-analysis of randomized controlled trials. Probabilistic and deterministic sensitivity analyses assessed the robustness of the model estimates.

Results: Lower PONV rate, shorter stay in the post-anesthesia care unit, and reduced need for rescue antiemetics offset the higher costs for anesthetics, analgesics, and muscle relaxants with propofol TIVA and reduced cost by 11.41 ± 10.73 USD per patient in the inpatient model and 11.25 ± 9.81 USD in the ambulatory patient model. Sensitivity analyses demonstrated strong robustness of the results.

Conclusions: Maintenance of general anesthesia with propofol was cost-saving compared to inhalational anesthesia in both inpatient and ambulatory surgical settings in the United States. These economic results support current guideline recommendations, which endorse propofol TIVA to reduce PONV risk and enhance postoperative recovery.

Keywords: cost-effectiveness, Diprivan, intravenous anesthesia, inhalation anesthesia, PONV, propofol.

VALUE HEALTH. 2021; 24(7):939–947

Introduction

In most of the 321.5 million surgical procedures conducted worldwide each year,¹ patients receive total intravenous anaesthesia (TIVA) with propofol or inhalational anesthesia with volatile anesthetics. The choice between TIVA and inhalational anesthesia is often based on regional and institutional preferences, even though in recent years, the environmental impact of inhalational anesthesia has received increasing recognition.² However, this may not reflect best practice,³ because evidence shows that the anesthetic agent may actually influence patient outcomes, such as postoperative pain,⁴ postoperative cognitive dysfunction,⁵ emergence agitation,⁶ and postoperative nausea and vomiting (PONV).⁷ In fact, the most comprehensive meta-analysis investigating patient-relevant postoperative outcomes with propofol and inhalational agents to date reported a 39% lower relative risk for PONV, lower pain scores after extubation, and shorter time spent in the postanesthesia care unit (PACU) associated with propofol-based TIVA.⁷

PONV is one of the most unpleasant but still most common events patients may experience during the postoperative period and frequently complicates recovery from surgery.⁸ Independent predictors for PONV are female gender, history of PONV or motion sickness, nonsmoking status, younger age, duration of anesthesia with volatile anesthetics, and postoperative opioids.⁹ Its overall incidence is estimated to be about 20% to 30% and may be as high as 70% in high-risk patients.¹⁰ Surgical patients prefer to suffer pain rather than PONV¹¹ and would be willing to pay considerable amounts of money to avoid this unpleasant experience.¹² Together with postoperative pain, PONV is not only a major determinant of patient dissatisfaction,^{13,14} it also leads to prolonged PACU stay and use of antiemetics for PONV rescue such as droperidol, metoclopramide, or promethazine.¹⁵ Accordingly, requirements for postoperative care and associated healthcare costs are higher in patients who experience PONV.¹⁶ However, it is unclear to date if using an anesthetic agent that reduces the incidence of PONV is also cost-effective. In fact, a recent systematic review on cost-effectiveness research in anesthesiology concluded that there

is a lack of cost-effectiveness literature, particularly relating to intraoperative interventions, and a need for more cost-effectiveness analyses in many areas of anesthesiology.¹⁷

Therefore, we conducted this cost-effectiveness analysis assessing the economic impact of maintaining general anesthesia with propofol versus inhalational anesthetics in a simulated model with adult patients undergoing ambulatory or inpatient procedures relevant to the US healthcare system.

Methods

This cost-effectiveness analysis compares propofol with inhalational anesthetics (sevoflurane, desflurane, and isoflurane) for maintenance of general anesthesia in adult patients undergoing ambulatory or inpatient noncardiac surgeries. Cost-effectiveness analyses combine the incremental cost of an intervention with the benefit it provides. This cost-effectiveness analysis measures the benefit in a natural unit as the number of avoided PONV episodes. The main outcome measure, the incremental cost-effectiveness ratio (ICER), is therefore cost per averted PONV. The ICER allows comparison of the cost-effectiveness of treatments across disease areas and is the preferred outcome measure of health technology assessment bodies, such as the National Institute for Health and Care Excellence (NICE, UK). The cost-effectiveness of propofol was analyzed over a short time-horizon (OR block). As for the short time-horizon of the analysis, no discounting was applied. The analysis was conducted from the perspective of a hospital in the United States.

Model Structure

We developed 2 decision models using Microsoft Excel and Visual Basic for Applications for Microsoft Excel based on a patient-level, probabilistic, discrete event simulation technique¹⁸: 1 for inpatient surgery and 1 for ambulatory surgery. In each model, 2 treatment arms were simulated: 1 for general anesthesia with inhalational anesthetics and 1 for general anesthesia with propofol TIVA, as shown in Appendix Figure 1 in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2021.01.008>. Each simulated patient concurrently passed through the inhalational-based and propofol-based anesthesia arm, so that the 2 alternatives were simulated in the same patient cohort. Both models considered PACU stay, PONV episodes, and consumption of anesthetics, analgesics, muscle relaxants, and antiemetics as outcomes. Discharge from the PACU determined the end of the patient pathway.

Identification of Economic Inputs and Baseline Efficacy

Economic inputs to feed the models were extracted from studies reporting data on adult American surgical patient outcomes as shown in Appendix Table 1 in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2021.01.008>. The

consumption inputs were derived from studies reporting propofol requirements for induction¹⁹ and requirements of propofol,²⁰ sevoflurane,²¹ desflurane,²¹ isoflurane,²¹ fentanyl,²² and rocuronium²³ during maintenance. The cost of anesthesia with propofol was split into cost of induction and cost of maintenance to ensure a realistic measure of the number of vials required. Details are shown in Appendix Table 2 in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2021.01.008>. Where appropriate, treatment groups were combined using the formula suggested in the *Cochrane Handbook for Systematic Reviews of Interventions* version 6.0 (Table 6.5a).²⁴ The algorithm for antiemetic rescue was calculated from the percentage of patients with PONV who received the 1st, 2nd, and 3rd rescue agent in Habib et al¹⁶ and is shown in Appendix Table 3 in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2021.01.008>. PACU costs per minute were derived from Habib et al,¹⁶ and unit costs for drug acquisition and services were defined according to the pharmaceutical prices schedule of the Veterans Affairs National Acquisition Center as shown in Appendix Table 4 in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2021.01.008>.²⁵

The baseline efficacy inputs used in the model were obtained from a meta-analysis of 229 randomized, controlled trials with 20 991 patients investigating general anesthesia maintenance with propofol or inhalational anesthetics for ambulatory and inpatient surgery. The search strategy for the studies is described in detail there.⁷ The authors reported a reduced incidence of PONV, shorter PACU stay, and lower pain score after extubation with propofol. However, propofol was also associated with increased analgesic and muscle relaxant requirements compared to inhalational anesthetics. They also reported that time to respiratory recovery and tracheal extubation was longer with propofol, although this difference was not considered clinically relevant. In our analysis, respiratory recovery time has been accounted for by the PACU time, which covers recovery time. The efficacy inputs are shown in Table 1.

Inhalational Anesthetic Data Input

The proportional usage of inhalational anesthetics was 62% sevoflurane, 22% isoflurane, and 16% desflurane. Proportions were estimated from total units sold as reported in an analysis of the US inhalation anesthesia market.²⁶ Details are shown in Appendix Table 5 in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2021.01.008>. Patients in the inhaled anesthetics group could receive 1 of the 3 agents (sevoflurane, desflurane, or isoflurane) in the maintenance phase; the probability of selecting each agent was based on the current market shares of the 3 agents in the US market.²⁶

The cost of anesthetics in the inhaled anesthesia group was based on retrieved information on the mean consumption of each agent per minute of maintaining anesthesia (ml/min) for each patient multiplied by the simulated duration of anesthesia. It was

Table 1. Clinical efficacy of propofol TIVA based on the results in Schraag et al 2018.⁷

Propofol efficacy				
	Pooled estimate	SEM	Source	Description
RR PONV	0.61	0.04	Schraag et al 2018 ⁷	Pooled risk ratio
Δ PACU stay (min)	−2.91	1.31		Pooled mean difference
Δ Analgesic consumption	0.20	0.09		Pooled, standardized mean difference
Δ Muscle relaxant usage	0.18	0.07		Pooled, standardized mean difference

RR indicates relative risk; SEM, standard error of means; PACU, post-anesthesia care unit; PONV, postoperative nausea and vomiting.

simulated by drawing anesthesia minutes from the assigned probability distribution to the retrieved mean duration of anesthesia in each pathway. Finally, the consumed volume in milliliters of each agent was multiplied by the mean cost/ml of the corresponding agent. The cost is also adjusted according to the inflation rate data from the US Labor Department.

Simulation and Discount Rate

The simulation was run over 10 000 iterations, each representing one patient journey. Since all parameter values were drawn from their probability distributions, the probabilistic analysis was included. No discount rate was applied to outcomes and costs due to the short timeframe of the simulation, which ranged from anesthesia induction to discharge from PACU.

Sensitivity Analyses

To assess the robustness of the model-derived estimates, we conducted both probabilistic and deterministic sensitivity analyses for the model parameters.

Probabilistic sensitivity analysis

In the probabilistic sensitivity analysis, input parameter values were simultaneously drawn from their probability distributions to create 1000 sets of unique parameter combinations. When reliable data on uncertainty was missing, we used a standard deviation of 10% of the mean value and chose normal distribution for continuous data and Dirichlet distribution for categorical data.

Deterministic sensitivity analysis

In the deterministic sensitivity analysis, all input parameters were varied individually within the lower and upper limit of the confidence interval, while the remaining parameter values were kept constant. If the confidence interval was unavailable, a variation of $\pm 20\%$ was used to assess the sensitivity of the cost estimates to the underlying model assumptions.

Results

Inpatient Model Simulation Results

Lower PONV rate, shorter PACU stay, and reduced need for rescue antiemetics with propofol-based TIVA resulted in a cost reduction of 11.41 ± 10.73 USD per patient compared to inhalational anesthesia. In the patient-level simulation, the propofol arm showed a lower PONV incidence (-10.59% absolute difference) and 2.91 minutes shorter PACU stay, reducing the PACU costs by 18.39 USD on average and offsetting the 6.83 ± 10.69 USD higher mean anesthetic costs with propofol. Cost differences due to higher analgesic (0.03 ± 0.11 USD) and muscle relaxant consumption (0.20 ± 0.70 USD) and lower antiemetic requirements with propofol (0.09 ± 0.32 USD) did not contribute significantly to the total costs. The ICER was estimated at USD -107.5 per PONV averted, which means every PONV episode avoided with propofol was associated with a reduction in the cost of anesthesia of USD 107.5 per patient. Detailed cost-effectiveness results of the inpatient model are shown in Table 2.

Probabilistic Sensitivity Analysis

The probabilistic sensitivity analysis demonstrated stability and robustness to changes in the parameters of all results. The sampling variation associated with the estimate of the incremental cost-effectiveness ratio (ICER) in the inpatient model demonstrated that propofol was cost-saving compared to

inhalational anesthesia in 88% of the simulations, with cost savings of about 11 USD per patient on average (Fig. 1A).

Deterministic Sensitivity Analysis

The results of the deterministic sensitivity analysis are displayed as a tornado diagram in Figure 1B and show the influence of variations in each parameter on costs per patient. The parameter with the strongest effect was the reduction in PACU stay with propofol, resulting in cost differences within the confidence interval ranging from -27.58 USD to 4.77 USD to per patient versus inhalational anesthetics. Further influential parameters were the cost and consumption of propofol and the cost of sevoflurane. With the cost per PACU minute used in the base-case analysis, propofol use needs to reduce PACU stay by at least 40 seconds to reduce overall costs significantly (threshold analysis not shown).

Ambulatory Patient Model Simulation Results

In analogy to the inpatient results, reduced PONV rate and shorter PACU stay with propofol resulted in a cost reduction of 12.29 ± 5.78 USD compared to inhalational anesthetics in ambulatory patients. The patient-level simulation showed a lower PONV incidence (12.6% absolute difference) and 2.91 minutes shorter PACU stay in patients undergoing propofol anesthesia, resulting in 18.39 USD lower PACU costs on average and offsetting the 6 ± 5.74 USD higher mean anesthesia costs with propofol. The ICER was estimated at USD -97.5 per PONV averted, which means every PONV episode avoided with propofol was associated with a reduction in the cost of anesthesia of USD 97.5 per patient. The cost-effectiveness results of the outpatient model are shown in Table 2.

Probabilistic Sensitivity Analysis

The sampling variation associated with an estimate of the ICER in the ambulatory patient model shows that propofol was cost-saving compared to inhalational anesthesia in 91% of the simulations, demonstrating stability and robustness of the results to changes in the input parameters. Cost savings were about 12 USD per patient on average (Fig. 2A).

Deterministic Sensitivity Analysis

The most influential parameters in the ambulatory patient model were the reduction in the PACU stay with propofol, the cost and consumption per minute of propofol, and the cost of sevoflurane as shown in the tornado diagram in Figure 2B. Cost differences between propofol and inhalational anesthetics within the confidence interval owing to the variation in PACU stay ranged from -28.46 USD to 3.89 USD per patient. With the cost per PACU minute used in the base-case analysis, propofol requires at least 22 seconds shorter PACU time to be cost-saving (threshold analysis not shown).

Discussion

This cost-effectiveness analysis was based on 2 models simulating individual patient pathways through inpatient and ambulatory surgery with propofol TIVA or inhalational anesthesia. There is a paucity of recent cost-effectiveness analyses in the literature regarding the choice of anesthetics during surgery.¹⁷ Previous cost-effectiveness studies comparing propofol and inhalational anesthetics were often based on a small number of patients in specific surgical settings. A Hungarian study from 2018 compared sevoflurane or propofol with and without additional monitoring for anesthesia maintenance in ear-nose-throat

Table 2. Cost-effectiveness results of the inpatient model and the outpatient model.

	Propofol-based anesthesia	Inhalation-based anesthesia	Difference
Inpatient model			
Effectiveness outcomes			
PONV incidence (%)	15.91 %	26.50 %	-10.59 %
PACU stay (min)	63.97 ± 6.06	66.88 ± 6.06	-2.91 ± 0
Analgesic (mg)	433.71 ± 351.64	414.05 ± 335.70	19.66 ± 15.94
Muscle relaxant (mg)	75.83 ± 22.84	71.75 ± 21.61	4.08 ± 1.23
Costs (USD)			
Anesthetics	25.59 ± 11.95	18.76 ± 12.6	6.83 ± 10.69
Analgesics	0.88 ± 0.53	0.85 ± 0.51	0.03 ± 0.11
Muscle relaxants	5.27 ± 1.35	5.07 ± 1.32	0.20 ± 0.70
PACU stay	404.17 ± 38.30	422.55 ± 38.30	-18.39 ± 0
Antiemetics	0.13 ± 0.36	0.21 ± 0.46	-0.09 ± 0.32
Total cost per patient	436.03 ± 40.36	447.44 ± 40.39	-11.41 ± 10.73
Outpatient model			
Effectiveness outcomes			
PONV incidence (%)	18.87 %	31.47 %	-12.60 %
PACU stay (min)	82.19 ± 27.73	85.1 ± 27.73	-2.91 ± 0
Analgesic (mg)	247.9 ± 153.02	236.66 ± 146.08	11.24 ± 6.94
Muscle relaxant (mg)	73.01 ± 17.03	69.08 ± 16.11	3.93 ± 0.92
Costs (USD)			
Anesthetics	19.45 ± 5.23	13.45 ± 6.55	6 ± 5.74
Analgesics	0.59 ± 0.25	0.58 ± 0.24	0.02 ± 0.09
Muscle relaxants	5.18 ± 0.99	5.01 ± 0.98	0.16 ± 0.63
PACU stay	519.31 ± 175.20	537.70 ± 175.20	-18.39 ± 0
Antiemetics	0.12 ± 0.32	0.20 ± 0.39	-0.08 ± 0.27
Total cost per patient	544.65 ± 175.27	556.94 ± 175.29	-12.29 ± 5.78

Results are based on the 10 000 patient-level simulations in the base-case scenario.

PACU indicates post-anesthesia care unit; PONV, postoperative nausea and vomiting.

surgery. The authors reported that the bispectral index and train-of-four monitoring reduced drug requirements, but the additional disposable costs associated with bispectral index monitoring increased the overall costs compared to the groups without additional monitoring for both anesthetic regimes. Drug costs for propofol and sevoflurane were similar.²⁷ Older studies in different surgical settings reported mixed results,^{28,29} and propofol was considered cost-effective when costs for PACU and associated medical personnel were included into the analyses.^{30,31} However, the studies were based on older propofol prices, which have declined in the United States by approximately 25.5% since then.³² This aspect should be taken into account when considering the applicability of the results from older analyses to present clinical circumstances. Other cost-effectiveness analyses on interventions in anesthesia and perioperative medicine published in the last decade investigated hemodynamic therapy,³³⁻³⁵ delirium prevention,³⁶ spinal anesthesia,³⁷ and perioperative infection reduction.^{38,39}

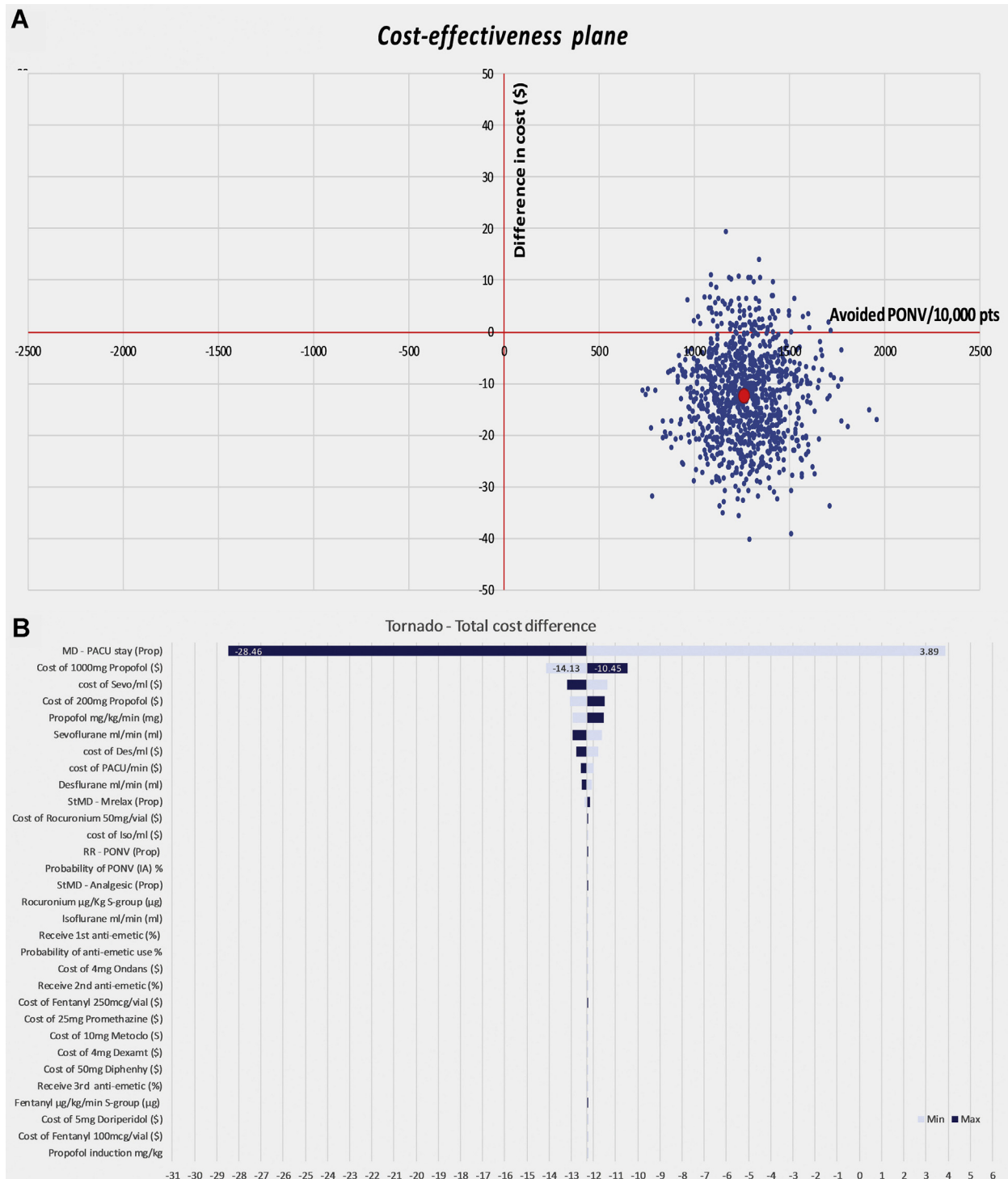
PONV prevention is a central element in protocols for enhanced recovery after surgery. Single-center studies, multi-center observational studies, and meta-analyses have reported that the application of protocols for enhanced recovery after surgery is associated with improvements in postoperative outcomes,

including reductions in postoperative complications and length of stay,⁴⁰ by up to 30%-40%.⁴¹

The current recommendations in enhanced recovery programs advocate the use of predictive risk scores and multimodal anti-emetic prophylaxis to reduce the frequency and impact of this complication. For high-risk patients, the combination of 2-3 antiemetics in addition to propofol TIVA is recommended, because it is most effective in reducing PONV.¹⁰ Furthermore, the current guideline for the management of PONV recommends using propofol for induction and maintenance of anesthesia, and avoiding inhalational anesthetics, to reduce the baseline risk of PONV.⁴² The present results corroborate these recommendations, showing that reducing the risk of PONV with propofol TIVA is, in fact, cost-effective, because it reduces PONV at lower costs for the healthcare system. The lower incidence of PONV is likely to be a major reason for the shorter PACU stay after propofol TIVA, because the time until discharge from PACU has been reported about 20% longer for patients with PONV and more than 50% longer for patients with emesis.¹⁵

Stability and robustness of the results to uncertainties in input parameters was demonstrated by the probabilistic sensitivity analyses in both the inpatient and the ambulatory patient models, where propofol was cost-saving compared to

Figure 1. (A) The incremental cost-effectiveness ratio (ICER) distribution of the probabilistic sensitivity analysis simulation for propofol TIVA versus inhalational anesthesia in surgery in the inpatient model. Propofol was cost-saving compared to inhalational anesthesia in 93% of the simulations, and cost-savings were about 14 USD per case on average. (B) Tornado plot of the deterministic sensitivity results in the inpatient model. The plot shows the influence of variations in each individual parameter within its probability distribution on costs per patient. The mean difference (MD) in PACU stay was the most influential parameter.

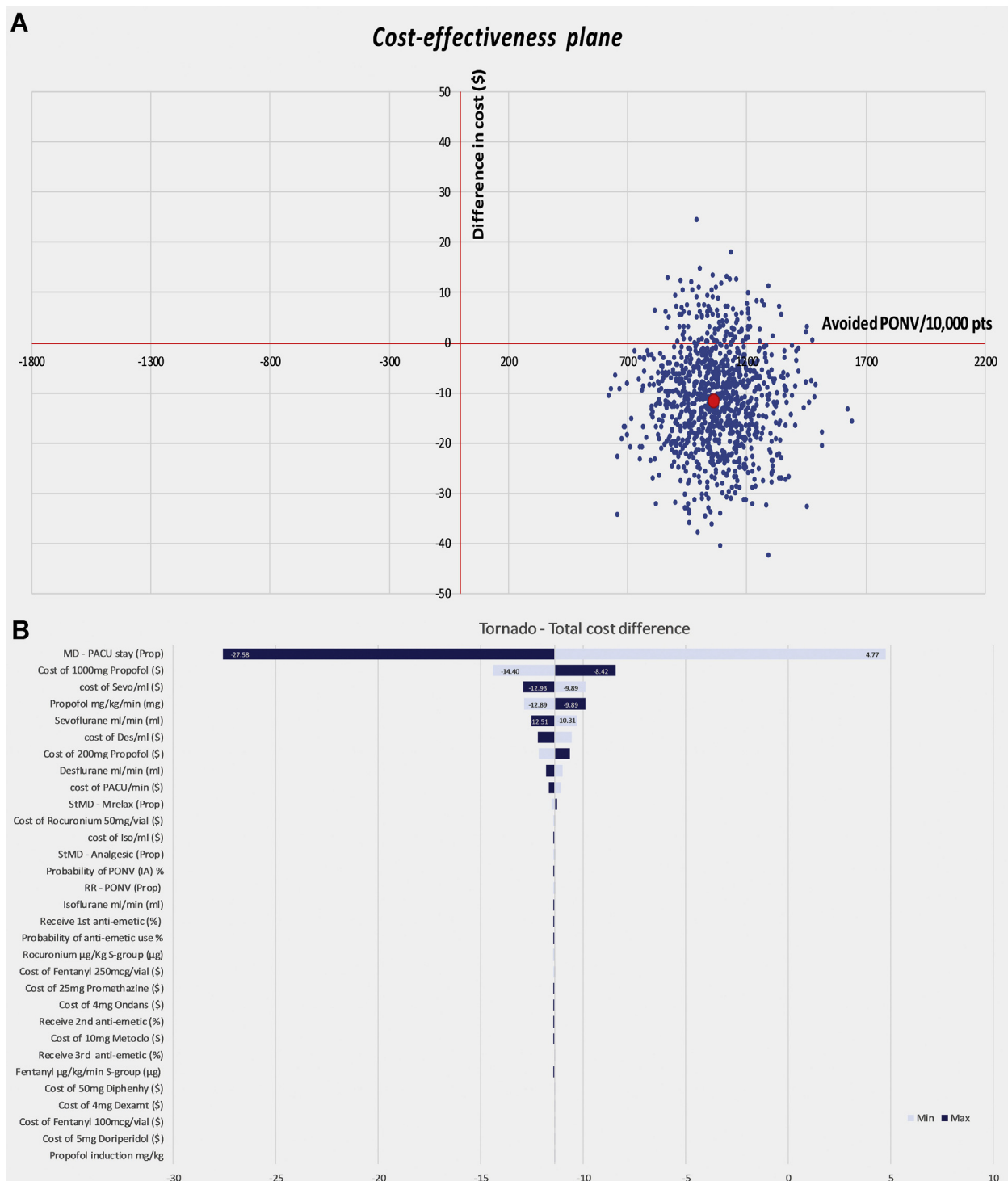


inhalational anesthetics in 88% and 91% of the simulations, respectively.

The tornado diagrams in Figure 1b and 2b demonstrate that the mean difference in PACU stay was the only parameter in which

variations could have changed the results of the cost-effectiveness analyses. As this parameter was derived from the comprehensive study by Schraag et al,⁷ in which the mean difference in PACU stay was calculated from a meta-analysis of 21 randomized, controlled

Figure 2. (A) The incremental cost-effectiveness ratio (ICER) distribution of the probabilistic sensitivity analysis simulation for propofol TIVA versus inhalational anesthesia in 96% of the simulations, and cost savings were about 16 USD per case on average. (B) Tornado plot of the deterministic sensitivity results in the ambulatory patient model. The plot shows the influences of variations in each individual parameter within its probability distribution on costs per patient. The mean difference (MD) in PACU stay was the most influential parameter.



trials with 2653 patients, it is supported by the highest level of evidence. Of note, the second most influential parameter in the deterministic sensitivity analyses was the cost of propofol.

Therefore, the cost savings may be even higher in healthcare systems with lower costs for propofol relative to inhalational anesthetics than for those in the United States.

The systematic review and meta-analysis by Schraag et al⁷ reported shorter PACU stay, lower PONV rates, reduced pain scores after extubation, and higher patient satisfaction with propofol compared to inhalational agents. Conversely, time to respiratory recovery and tracheal extubation were marginally longer with propofol compared to inhalational agents (0.82 and 0.70 minutes, respectively).

This analysis focuses on early PONV up to discharge from the PACU, but nausea and emesis after anesthesia may be delayed up to 24 hours after surgery. The recent guidelines on PONV prevention⁴² state that the effect of volatile anesthetics is most prominent until 2 to 6 hours after surgery. Furthermore, Apfel et al identified inhalational anesthetics as the primary cause of early PONV 0 to 2 hours after surgery.⁴³ Therefore, both the antiemetic effect of propofol and the pro-emetic effect of inhalational anesthetics seem to be limited to the early postoperative period.

Nevertheless, PONV continues to be frequent even after the first 24 hours postsurgery, despite high compliance to antiemetic recommendations. McLoughlin et al 2019 showed that PONV during day 2 after colorectal surgery negatively affects the nutritional postoperative recovery and independently prolonged the hospital stay by up to 2 days. In addition to opioid administration, early PONV on day 0 after the surgery was identified as a risk factor of developing delayed nausea and vomiting.⁴⁴ Therefore, anesthesia with propofol TIVA may be an appropriate choice to prevent nausea and vomiting in the immediate postoperative period and consequently enhance patient recovery until discharge.

Patient-reported outcomes in clinical trials are important for healthcare providers to improve the quality of care and can enrich our understanding of the patients' experience of the perioperative journey.⁴⁵ As PONV and postoperative pain are major determinants of patient dissatisfaction,^{13,14} propofol TIVA has the potential to improve patients' perception of the quality of postoperative recovery. In fact, studies investigating the quality of recovery reported better outcomes for propofol TIVA compared to desflurane,^{46,47} isoflurane,⁴⁸ and sevoflurane.^{49,50} Schraag et al confirmed these results in a meta-analysis of 10 trials with 924 patients.⁷

The strengths of our analysis include the high evidence level of the effectiveness inputs, which were derived from a comprehensive meta-analysis.⁷ Furthermore, drug acquisition inputs were taken from the 2020 US Department of Veteran Affairs federal supply schedule and are therefore both current and relevant to the US healthcare system.²⁵ In addition, PACU costs per minute were derived from a retrospective database analysis investigating resource utilization and duration of PACU stay due to PONV in a US teaching hospital published in 2006, and they have been adjusted for inflation.¹⁶ The calculated PACU cost of 6.32 USD per minute was similar to other studies, for example, 6.37 USD per minute in 2014 in a US pediatric hospital.⁵¹

The main limitation of this analysis is that it is based on historic data from the studies included in the meta-analysis by Schraag et al⁷ and not on a prospective data collection of real-world data. Some of the studies were published before 2001 and may no longer be representative of current scientific consensus and clinical practice. However, more than 80% of the studies included data from 2001 onward, and 40% were published between 2011 and 2016. Furthermore, the algorithm for antiemetic rescue has been developed in 2006.¹⁶ Yet the agents in the algorithm, ondansetron, dexamethasone, and promethazine are still recommended for treating PONV in the current guideline.⁴² Therefore, the results of this analysis are relevant for contemporary practice. Another point of potential concern is the missing fixed cost data for anesthesia equipment. This holds true for TIVA

(eg, for infusion pumps) as well as for inhalational anesthesia (eg, exhaust devices, supply lines for gases, or waste gases during standby). However, these costs are difficult to assess. Other cost types have assumed comparable equipment cost for different types of anesthesia or have not mentioned that aspect at all.⁵²⁻⁵⁴

In addition, the longer time to respiratory recovery and tracheal extubation reported by Schraag et al⁷ were not included as a separate parameter in the model since respiratory recovery and tracheal extubation are covered in our model by PACU time as an overall indicator of the post-anesthesia phase in US hospitals. As a final limitation, the economic inputs of our models were based on the US market, which limits the applicability of the results to other regions. Developments since, however, including lower propofol acquisition costs, have likely shifted the benefits further toward propofol-based techniques as the preferred option.

In conclusion, maintenance of general anesthesia with propofol is cost-saving compared to inhalational anesthesia in both inpatient and ambulatory noncardiac surgical settings in the United States, as it was associated with a reduction in PONV cases, less time spent in the PACU, and a concurrent decrease in mean costs. These results corroborate current guideline recommendations, which endorse postoperative TIVA to reduce the baseline risk of PONV and enhance postoperative recovery. This intervention is clinically superior as well as cost-efficient and thus an economically dominant strategy.

Conclusions

Propofol TIVA was the dominant strategy to maintain general anesthesia in both inpatient and ambulatory surgical settings in the United States, as it was associated with a reduction in PONV cases, less time spent in the PACU, and a concurrent decrease in mean costs. When an intervention is both clinically superior and cost-saving, it is referred to as an economically "dominant" strategy. The cost difference in both models was largely attributable to the shorter duration of PACU stay with propofol, which most likely resulted from the lower PONV rate associated with propofol.

Supplemental Material

Supplementary data associated with this article can be found in the online version at <https://doi.org/10.1016/j.jval.2021.01.008>.

Article and Author Information

Accepted for Publication: January 7, 2021

Published Online: April 1, 2021

doi: <https://doi.org/10.1016/j.jval.2021.01.008>

Author Affiliations: Department of Anesthesiology, Intensive Care and Pain Medicine, University Hospital of Muenster, Muenster, Germany (Kampmeier); Department of Anesthesiology, Intensive Care, Emergency Medicine, Transfusion Medicine, and Pain Therapy, Protestant Hospital of the Bethel Foundation, University Hospital OWL, Campus Bielefeld-Bethel, Bielefeld, Germany (Rehberg); Department of Economics, University of Bologna, Bologna, Italy (Omar Alsaleh); Department of Perioperative Medicine, Golden Jubilee National Hospital, Clydebank, Scotland, UK (Schraag); Medical, Clinical, and Regulatory Affairs, Fresenius Kabi AG, Bad Homburg, Germany (Pham); Department of Anesthesiology, Intensive Care and Pain Medicine, University of Muenster, Muenster, Germany and Fresenius Kabi AG, Bad Homburg, Germany (Westphal).

Correspondence: Tim Kampmeier, MD, PhD, Department of Anesthesiology, Intensive Care and Pain Medicine, Albert-Schweitzer-Campus 1, Gebäude A1, 48149 Münster, Germany. Email: kampmeier@uni-muenster.de

Author Contributions: *Concept and design:* Rehberg, Omar Alsaleh, Westphal

Acquisition of data: Omar Alsaleh

Analysis and interpretation of data: Kampmeier, Rehberg, Omar Alsaleh, Schraag, Pham, Westphal

Drafting of the manuscript: Kampmeier, Omar Alsaleh

Critical revision of the paper for important intellectual content: Kampmeier, Rehberg, Omar Alsaleh, Schraag, Pham, Westphal

Statistical analysis: Omar Alsaleh, Schraag, Pham

Administrative, technical, or logistic support: Kampmeier, Pham, Westphal

Supervision: Kampmeier, Rehberg, Schraag

Conflict of Interest Disclosures: Dr Kampmeier reported receiving personal fees from Fresenius Kabi Germany outside the submitted work. Dr Rehberg reported receiving personal fees from Fresenius Kabi Germany, CSL Behring, and Amomed Pharma outside the submitted work. Dr Schraag reported receiving personal fees from Fresenius Kabi during the conduct of the study; personal fees and nonfinancial support from Medasense outside the submitted work; and personal fees from Medtronic outside the submitted work. Drs Pham and Westphal are employees of Fresenius Kabi.

Funding/Support: This work has been supported by Fresenius Kabi.

Role of the Funder/Sponsor: The 2 authors with a company background have participated in the joint discussions of the setup and execution of the study, provided logistic support, and commented on the manuscript, but the final decision about the contents and submission lay with the academic group members.

Acknowledgment: We thank Dr Lorenzo Pradelli, AdRes-Health Economics and Outcome Research, Torino, Italy for support with the analysis and valuable comments on the manuscript and Dr Mario Pahl, DBM Wissen schafft GmbH, Wiesloch, Germany for expert medical writing support. Tim Kampmeier and Sebastian Rehberg contributed equally to this work.

REFERENCES

- Rose J, Weiser TG, Hider P, Wilson L, Gruen RL, Bickler SW. Estimated need for surgery worldwide based on prevalence of diseases: a modelling strategy for the WHO Global Health Estimate. *Lancet Glob Health*. 2015;3:13–20.
- Health Care Without Harm Europe. Reducing the carbon footprint of anaesthetic gasses. <https://noharm-europe.org/issues/europe/reducing-carbon-footprint-anaesthetic-gasses>. Accessed October 9, 2020.
- Irwin MG, Chung CKE, Ip KY, Wiles MD. Influence of propofol-based total intravenous anaesthesia on peri-operative outcome measures: a narrative review. *Anaesthesia*. 2020;75(Suppl 1):e90–e100.
- Peng K, Liu H, Wu S, Liu H, Zhang Z, Ji F. Does propofol anesthesia lead to less postoperative pain compared with inhalational anesthesia? a systematic review and meta-analysis. *Anesth Analg*. 2016;123(4):846–858.
- Miller D, Lewis SR, Pritchard MW, et al. Intravenous versus inhalational maintenance of anaesthesia for postoperative cognitive outcomes in elderly people undergoing non-cardiac surgery. *Cochrane Database Syst Rev*. 2018;8:CD012317.
- Costi D, Cyna AM, Ahmed S, et al. Effects of sevoflurane versus other general anaesthesia on emergence agitation in children. *Cochrane Database Syst Rev*. 2014;9:CD007084.
- Schraag S, Pradelli L, Alsaleh Abdul Jabbar Omar, et al. Propofol vs. inhalational agents to maintain general anaesthesia in ambulatory and in-patient surgery: a systematic review and meta-analysis. *BMC Anesthesiol*. 2018;18(1):162.
- Gan TJ. Postoperative nausea and vomiting—can it be eliminated? *JAMA*. 2002;287(10):1233.
- Apfel CC, Heidrich FM, Jukar-Rao S, et al. Evidence-based analysis of risk factors for postoperative nausea and vomiting. *Br J Anaesth*. 2012;109(5):742–753.
- Feldheiser A, Aziz O, Baldini G, et al. Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 2: consensus statement for anaesthesia practice. *Acta Anaesthesiol Scand*. 2016;60(3):289–334.
- van Wijk MG, Smalhout B. A postoperative analysis of the patient's view of anaesthesia in a Netherlands teaching hospital. *Anaesthesia*. 1990;45(8):679–682.
- Gan T, Sloan F, Dear G de L, El-Moalem HE, Lubarsky DA. How much are patients willing to pay to avoid postoperative nausea and vomiting? *Anesth Analg*. 2001;92(2):393–400.
- Myles PS, Weitkamp B, Jones K, Melick J, Hensen S. Validity and reliability of a postoperative quality of recovery score: the QoR-40. *Br J Anaesth*. 2000;84(1):11–15.
- Royce CF, Chung F, Newman S, Stygall J, Wilkinson DJ. Predictors of patient satisfaction with anaesthesia and surgery care: a cohort study using the Postoperative Quality of Recovery Scale. *Eur J Anaesthesiol*. 2013;30(3):106–110.
- Darkow T, Gora-Harper ML, Goulson DT, Record KE. Impact of antiemetic selection on postoperative nausea and vomiting and patient satisfaction. *Pharmacotherapy*. 2001;21(5):540–548.
- Habib AS, Chen Y, Taguchi A, Hu XH, Gan TJ. Postoperative nausea and vomiting following inpatient surgeries in a teaching hospital: a retrospective database analysis. *Curr Med Res Opin*. 2006;22(6):1093–1099.
- Teja BJ, Sutherland TN, Barnett SR, Talmor DS. Cost-effectiveness research in anesthesiology. *Anesth Analg*. 2018;127(5):1196–1201.
- Caro JJ. Pharmacoeconomic analyses using discrete event simulation. *Pharmacoeconomics*. 2005;4(23):323–332.
- Dongare DH, Kale JV, Naphade RW. Comparison of vital capacity induction with sevoflurane to intravenous induction with propofol in adult patients. *Anesth Essays Res*. 2014;8(3):319–323.
- Luginbühl M, Wüthrich S, Petersen-Felix S, Zbinden AM, Schnider TW. Different benefit of bispectral index (BIS) in desflurane and propofol anaesthesia. *Acta Anaesthesiol Scand*. 2003;47(2):165–173.
- Epstein RH, Dexter F, Maguire DP, Agarwalla NK, Gratch DM. Economic and environmental considerations during low fresh gas flow volatile agent administration after change to a nonreactive carbon dioxide absorbent. *Anesth Analg*. 2016;122(4):996–1006.
- Banevičius G, Rugytė D, Macas A, Tamašauskas A, Stankevičius E. The effects of sevoflurane and propofol on cerebral hemodynamics during intracranial tumors surgery under monitoring the depth of anaesthesia. *Medicina (Kaunas)*. 2010;46(11):743–752.
- Kim KS, Cheong MA, Lee HJ, Lee JM. Tactile assessment for the reversibility of rocuronium-induced neuromuscular blockade during propofol or sevoflurane anaesthesia. *Anesth Analg*. 2004;99(4):1080–1085.
- Higgins J, Thomas J, Chandler J, et al. *Cochrane Handbook for Systematic Reviews of Interventions* version 6.0. Table 6.5.a. <https://training.cochrane.org/handbook/current/chapter-06>.
- US Department of Veterans Affairs. Pharmaceutical prices. Office of Procurement, Acquisition, and Logistics (OPAL) website. <https://www.va.gov/opal/nac/fss/pharmPrices.asp>. Accessed October 12, 2020.
- Grand View Research Inc, USA. Inhalation Anesthesia Market Size Share and Trends Analysis Report by Application (Induction, Maintenance), by Product (Sevoflurane, Isoflurane, Desflurane), by Region, and Segment Forecasts, 2019–2025. <https://www.grandviewresearch.com/industry-analysis/inhalation-anaesthesia-market>. Accessed October 12, 2020.
- Bocskai T, Loibl C, Vamos Z, et al. Cost-effectiveness of anaesthesia maintained with sevoflurane or propofol with and without additional monitoring: a prospective, randomized controlled trial. *BMC Anesthesiol*. 2018;18(1):100.
- Luntz SP, Janitz E, Motsch J, Bach A, Martin E, Böttiger BW. Cost-effectiveness and high patient satisfaction in the elderly: sevoflurane versus propofol anaesthesia. *Eur J Anaesthesiol*. 2004;21(2):115–122.
- Singh Y, Singh AP, Jain G, Yadav G, Singh DK. Comparative evaluation of cost effectiveness and recovery profile between propofol and sevoflurane in laparoscopic cholecystectomy. *Anesth Essays Res*. 2015;9(2):155–160.
- Brady WJ, Meenan DR, Shankar TR, Balon JA, Mennett DR. Use of a remifentanyl and propofol combination in outpatients to facilitate rapid discharge home. *AANA J*. 2005;73(3):207–210.
- Elliott RA, Payne K, Moore JK, et al. Clinical and economic choices in anaesthesia for day surgery: a prospective randomised controlled trial. *Anaesthesia*. 2003;58(5):412–421.
- Fresenius Kabi. *Internal analysis of propofol prices using IQVIA (IMS) 2006–2019 US data*. Updated 2020.
- Bartha E, Davidson T, Hommel A, Thorngren K, Carlsson P, Kalman S. Cost-effectiveness analysis of goal-directed hemodynamic treatment of elderly hip fracture patients: before clinical research starts. *Anesthesiology*. 2012;117(3):519–530.
- Ebm C, Cecconi M, Sutton L, Rhodes A. A cost-effectiveness analysis of postoperative goal-directed therapy for high-risk surgical patients. *Crit Care Med*. 2014;42(5):1194–1203.
- Cuthbertson BH, Campbell MK, Stott SA, et al. A pragmatic multi-centre randomised controlled trial of fluid loading in high-risk surgical patients undergoing major elective surgery: the FOCUS study. *Crit Care*. 2011;15(6):R296.
- Akunne A, Davis S, Westby M, Young J. The cost-effectiveness of multi-component interventions to prevent delirium in older people undergoing surgical repair of hip fracture. *Eur J Orthop Surg Traumatol*. 2014;24(2):187–195.
- Borendal Wodlin N, Nilsson L, Carlsson P, Kjølhede P. Cost-effectiveness of general anesthesia vs spinal anesthesia in fast-track abdominal benign hysterectomy. *Am J Obstet Gynecol*. 2011;205(4):326.e1–326.e7.
- Courville XF, Tomek IM, Kirkland KB, et al. Cost-effectiveness of preoperative nasal mupirocin treatment in preventing surgical site infection in patients undergoing total hip and knee arthroplasty: a cost-effectiveness analysis. *Infect Control Hosp Epidemiol*. 2012;33(2):152–159.

39. Lee BY, Wiringa AE, Bailey RR, et al. The economic effect of screening orthopedic surgery patients preoperatively for methicillin-resistant *Staphylococcus aureus*. *Infect Control Hosp Epidemiol*. 2010;31(11):1130–1138.
40. Ripollés-Melchor J, Ramírez-Rodríguez JM, Casans-Francés R, et al. Association between use of enhanced recovery after surgery protocol and postoperative complications in colorectal surgery: the Postoperative Outcomes Within Enhanced Recovery After Surgery Protocol (POWER) Study. *JAMA Surg*. 2019;154(8):725–736.
41. Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: a review. *JAMA Surg*. 2017;152(3):292–298.
42. Gan TJ, Belani KG, Bergese S, et al. Fourth consensus guidelines for the management of postoperative nausea and vomiting. *Anesth Analg*. 2020.
43. Apfel CC, Kranke P, Katz MH, et al. Volatile anaesthetics may be the main cause of early but not delayed postoperative vomiting: a randomized controlled trial of factorial design. *Br J Anaesth*. 2002;88(5):659–668.
44. McLoughlin S, Terrasa SA, Ljungqvist O, Sanchez G, Garcia Fornari G, Alvarez AO. Nausea and vomiting in a colorectal ERAS program: impact on nutritional recovery and the length of hospital stay. *Clin Nutr ESPEN*. 2019;34:73–80.
45. Mercieca-Bebber R, King MT, Calvert MJ, Stockler MR, Friedlander M. The importance of patient-reported outcomes in clinical trials and strategies for future optimization. *Patient Relat Outcome Meas*. 2018;9:353–367.
46. Na SH, Jeong KH, Eum D, Park JH, Kim M. Patient quality of recovery on the day of surgery after propofol total intravenous anesthesia for vitrectomy: a randomized controlled trial. *Medicine*. 2018;97(40):e12699.
47. Lee W, Kim M, Kang S, Kim S, Lee J. Type of anaesthesia and patient quality of recovery: a randomized trial comparing propofol-remifentanyl total i.v. anaesthesia with desflurane anaesthesia. *Br J Anaesth*. 2015;114(4):663–668.
48. Gecaj-Gashi A, Hashimi M, Sada F, et al. Propofol vs isoflurane anaesthesia-incidence of PONV in patients at maxillofacial surgery. *Adv Med Sci*. 2010;55(2):308–312.
49. Tang J, Chen L, White PF, et al. Recovery profile, costs, and patient satisfaction with propofol and sevoflurane for fast-track office-based anaesthesia. *Anesthesiology*. 1999;91(1):253–261.
50. Hofer CK. Patient well-being after general anaesthesia: a prospective, randomized, controlled multi-centre trial comparing intravenous and inhalation anaesthesia. *Br J Anaesth*. 2003;91(5):631–637.
51. Subramanyam R, Varughese A, Kurth CD, Eckman MH. Cost-effectiveness of intravenous acetaminophen for pediatric tonsillectomy. *Paediatr Anaesth*. 2014;24(5):467–475.
52. Kendall J, Wildsmith JAW, Gray IG. Costing anaesthetic practice. *Anaesthesia*. 2000;55(11):1106–1113.
53. Ryksen E, Diedericks BJ. Calculation of comparative utilisation and cost: a South African perspective on intravenous vs. inhalational anaesthesia for procedures of differing duration. *South Afr J Anaesth Analg*. 2014;18(6):310–317.
54. Hu J, He Z. Cost of general anaesthesia during radical gastrectomy using different specifications of propofol: cost-minimization analyses. *Int J Clin Exp Med*. 2015;8(11):21266–21278.