A time-motion economic analysis of postoperative nausea and vomiting in ambulatory surgery

Une analyse économique des temps et mouvements pour les nausées et vomissements postopératoires en chirurgie d'un jour

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Abstract

Background One-third of surgical outpatients experience postoperative nausea and vomiting (PONV) during their hospital stay or post-discharge nausea and vomiting (PDNV) after hospitalization. We determined the incremental costs of PONV/PDNV in ambulatory patients with this time-and-motion study.

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Methods In 100 ambulatory surgery patients, we evaluated the incidence of PONV, time staff spent with patients, use of PONV-related supplies, recovery duration, PONV rescue treatments, and quality-of-life through to the third postoperative morning. Patients with and without PONV/PDNV were compared in relation to PONV-related cost after adjusting for age, American Society of Anesthesiologists status, body mass index, and duration and complexity of surgery.

Results Thirty-seven percent of the patients experienced PONV during hospitalization; this increased to 42% by the first postoperative morning and increased further to 49% by the third postoperative morning. Patients with PONV spent one hour longer in the postanesthesia care unit than patients without PONV (median [interquartile range] 234 [188–287] min vs 171 [144–212] min, respectively; $P = 0.001$). The amount of nursing time required for patients with PONV was significantly greater than that required for patients without PONV (82 [63–106] min vs 68 [57–79] min, respectively; $P = 0.02$). The total cost of postoperative recovery was significantly greater for patients with PONV/PDNV than for those without (US\$730 vs \$640, respectively; $P = 0.006$). Postoperative nausea and vomiting/PDNV was associated with an adjusted incremental total cost of \$75 (95% confidence interval \$67 to \$86). Postoperative nausea and vomiting was also associated with worsened postoperative quality of life (49% of patients with PONV/PDNV rated quality high in four domains vs 94% of patients without PONV/PDNV; $P < 0.001$).

Conclusion Postoperative nausea and vomiting/PDNV were common; they impaired quality of life and imposed an incremental cost of \$75 per patient. This incremental cost is comparable with the cost patients are willing to pay to avoid PONV.

Résumé

Contexte Un tiers des patients de chirurgie éprouvent des nausées et vomissements postopératoires (PONV) au cours de leur hospitalisation ou des nausées et vomissements post congé (PDNV) après une hospitalisation. Nous avons déterminé les coûts additionnels des PONV/PDNV chez les patients ambulatoires dans cette étude temps-mouvement.

Méthodes Nous avons évalué, chez 100 patients de chirurgie d'un jour: l'incidence des PONV, le temps passé par le personnel avec les patients, l'utilisation de fournitures liées aux PONV, les traitements de secours contre les PONV et la qualité de vie jusqu'au troisième matin postopératoire. Les patients avec et sans PONV/PDNV ont été comparés en termes de coûts liés aux PONV après ajustement pour l'âge, le statut selon l'American Society of Anesthesiologists, l'indice de masse corporelle, la durée et la complexité de l'intervention chirurgicale.

Résultats Trente-sept pour cent des patients ont éprouvé des nausées et vomissements postopératoires (PONV) au cours de leur hospitalisation; ce chiffre a augmenté à 42 % au premier matin postopératoire et a augmenté encore jusqu'à 49 % au troisième matin postopératoire. Les patients présentant des PONV ont passé une heure de plus en salle de réveil que les patients sans PONV (médiane [écart interquartile]: 234 [188-287] minutes contre 171 [144-212] minutes; $P = 0,001$). La durée des soins infirmiers nécessités par les patients ayant des PONV a été significativement supérieure à celle nécessitée par les patients sans PONV (respectivement: 82 [63-106] minutes contre 68 [57-79] minutes; $P = 0,02$). Le coût total de la récupération postopératoire a été significativement plus élevée pour les patients avec PONV/PDNV que pour ceux n'ayant pas eu de nausées et vomissements post opératoires (730 \$US contre 640 \$US; $P = 0,006$). Les PONV/PDNV ont été associés à un coût total supplémentaire ajusté de 75 \$ (intervalle de confiance à 95 %: 67 \$ - 86 \$). Les nausées et vomissements postopératoires ont également été associés à une moins bonne qualité de vie postopératoire (49 % des patients ayant des PONV/PDNV ont donné une évaluation élevée dans quatre domaines contre 94 % des patients sans PONV/PDNV; $P = 0,001$).

Conclusion Les PONV/PDNV sont fréquents; ils ont altéré la qualité de vie et ont imposé un coût supplémentaire de 75 \$ par patient. Ce coût supplémentaire est comparable au prix que les patients sont prêts à payer pour éviter les PONV.

and economic impact, and it is associated with high levels of patient discomfort and dissatisfaction.¹ To many patients, PONV is a distressing adverse event which patients fear almost as much as postoperative pain.²

Postoperative nausea and vomiting alone or combined with pain is one of the leading causes for delayed discharge and unplanned hospital admission following outpatient surgery.³⁻⁵ The overall incidence of PONV is estimated to be 25-30%, and it can be as high as 80% among high-risk patients⁶ (e.g., a female non-smoker with a history of PONV who requires postoperative opioids).⁷ With most surgeries now performed on an outpatient basis, PONV may also occur after hospital discharge, which is generally referred to as post-discharge nausea and vomiting (PDNV). More than 35% of surgical outpatients experience PONV following discharge, many of whom had not experienced nausea and vomiting while in the recovery room. Carroll *et al.* reported that 17% of patients experience PDNV for < 48 hr, and 9% experience PDNV for > 48 hr.⁵

The cost of PONV is believed to be high, but cost estimates differ, possibly because of variations in methodological approaches, populations, and healthcare systems.⁸⁻¹¹ Furthermore, most studies evaluate PONV for only 24 hr. There is increasing evidence that PONV extends well beyond the first postoperative morning. We thus sought to determine the incremental costs of PONV in ambulatory patients over the initial three postoperative days (PODs) within a large healthcare institution in Cleveland, Ohio, USA. Our purpose was to provide a basis for estimating the incremental costs associated with the use of various antiemetic, prophylactic, and treatment strategies, a cost that could then be applied to results from studies where the methodology necessary to estimate cost with greater accuracy was not included. We thus conducted a time-and-motion study of patients undergoing ambulatory surgery at our institution. A time-and-motion study involves a continuous observation of patients by a trained researcher who records all the events and their duration during a period of time.

Methods

With approval of the Cleveland Clinic Institutional Review Board and written consent, we enrolled American Society of Anesthesiologists (ASA) physical status I to III adults scheduled for ambulatory surgery which was expected to last at least one hour. All patients received general endotracheal anesthesia, and all had at least two of the four major risk factors for PONV for adults undergoing inhalational anesthesia: 1) female sex, 2) history of PONV and/or currently prone to motion sickness, 3) non-smoking status, and 4) anticipated postoperative opioid therapy.⁷

Postoperative nausea and vomiting (PONV) is a frequent side effect of general anesthesia with considerable medical

Our goal was to enroll a population where about half would experience PONV.

Exclusion criteria included patients deemed unable to understand and cooperate with study procedures, those with a body mass index $> 40 \text{ kg}\cdot\text{m}^{-2}$, or those who experienced PONV or used antiemetic medications within 24 hr before surgery. The following medications were considered antiemetics: 5-HT₃ antagonists, phenothiazines, butyrophenones, hydroxyzine, cannabinoids, scopolamine, benzamides, corticosteroids, and dimenhydrinate.

Volatile endotracheal anesthesia was provided per clinician preference. Nitrous oxide was permitted. A single antiemetic dose was permitted, either ondansetron 4 mg or dexamethasone 4 mg, per preference of the attending anesthesiologist. Premedication and use of opioids were not restricted.

Rescue medication for treatment of PONV was allowed at the discretion of the attending anesthesiologist. Rescue medications were defined as any drug taken for nausea or vomiting symptoms from the end of surgery to the third postoperative morning. Antiemetic medications included:

- 5-HT₃ receptor antagonists (ondansetron, dolasetron, granisetron),
- benzamides (metoclopramide),
- phenothiazine antiemetics (e.g., promethazine),
- scopolamine,
- dimenhydrinate,
- corticosteroids, excluding topical or inhaled preparations, and
- over-the-counter antiemetics.

Patients were discharged home using their score on a modification of the Aldrete scale as a basis for postanesthesia care unit (PACU) discharge (Table 1).¹² A minimum score of 7/10 was required for discharge. Patients were moved to a Phase II PACU before discharge to home; we thus defined “PACU duration” as all time from the end of surgery until patients left the hospital.

Measurements

Demographic and morphometric characteristics were recorded along with anesthetic and surgical details. An investigator remained with each patient throughout hospitalization and asked patients about nausea and emetic episodes until hospital discharge and then daily via phone call until the third postoperative morning. Patients were asked to rate the worst nausea they experienced within the preceding time interval as “none,” “mild,” “moderate,” or “severe”. Emetic episodes were periods of vomiting or retching separated by a distinct period with neither. Patients were considered to be in the PONV group when they experienced any nausea and/or vomiting or retching at

Table 1 Modified Aldrete Scale for PACU discharge

ACTIVITY

Able to move 4 extremities = 2

Able to move 2 extremities = 1

Able to move 0 extremities = 0

OXYGEN SATURATION

O₂ Saturation $> 92\%$ on room air = 2

O₂ Saturation $> 90\%$ with oxygen = 1

O₂ Saturation $< 90\%$ with oxygen = 0

CONSCIOUS LEVEL

Fully = 2

Arousable = 1

Unresponsive = 0

CIRCULATION

(From preoperative BP)

BP ± 20 mmHg = 2

BP ± 21 -50 mmHg = 1

BP > 50 mmHg = 0

VENTILATION

Deep Breath + Cough Freely = 2

Dyspnea or Limited Breathing = 1

Apnea = 0

BP = blood pressure; O₂ = oxygen; PACU = postanesthesia care unit

any time from the end of surgery until the third postoperative morning.

The cumulative time nurses spent with each patient was measured from PACU admission to PACU discharge. Physician time was similarly recorded, and the number of nursing calls to physicians was recorded. All supplies related to PONV (i.e., emesis basins, new sheets) were quantified. Time and effort were tracked, and the duration of recovery was considered to be the number of minutes elapsed from the end of anesthesia until patients left the hospital.

Patients were contacted by phone and asked whether they had taken any analgesics or medications for treatment of nausea and vomiting since the last evaluation. Drug types and doses were documented. Visits to a physician's office, an emergency department, and readmissions were also recorded.

The effect of nausea and vomiting symptoms on patients' quality of life (QOL) was evaluated with a modified Osoba Nausea and Emesis Module each of the first three postoperative mornings.¹³ The module we used included four questions which asked the extent to which nausea and/or vomiting in the previous 24 hr 1) interfered with appetite, 2) affected sleep, 3) interfered with physical activities (including self care), and 4) interfered with social activities. There were four possible responses to each question, ranging from “not at all” to “very much.”

Overall QOL (utility) was also evaluated with a Standard Gamble questionnaire which determines patients' feelings about their surgical experience. Specifically, the Standard Gamble asks how much risk patients are willing to accept in exchange for a chance of perfect health, and since it involves uncertainty, it is considered a robust utility measure.¹⁴ The Standard Gamble was administered according to the questionnaire's original design by an investigator during a telephone encounter. A one-page paper version was also designed to help administration produce comparable results.^{15,16} Patients were instructed to consider their entire surgical experience when responding to the Standard Gamble questionnaire administered by phone on the first postoperative morning.^{17,18}

Data analysis

Our cost analysis was conducted using two time horizons. The first time period was from the end of anesthesia until hospital discharge. Healthcare costs were measured during this period using time-and-motion methods. The second time period was from hospital discharge until the third postoperative morning. Healthcare costs were estimated during this period with information obtained from daily calls to patients.

The cost data included primarily the direct healthcare cost for patients with or without PONV. Direct costs included labour and supplies from the end of surgery until hospital discharge as well as costs of unplanned hospital admissions, emergency department visits, laboratory tests, and prescribed medications during the follow-up period from hospital discharge to the third POD. We also considered indirect costs, including loss of work. Summing the direct and indirect costs provided the total cost from a societal perspective.

During recovery and until discharge, we observed and recorded the time that nurses and physicians spent with each patient (irrespective of the specific activity) for each visit, the use of supplies related to emetic episodes, and the use of analgesic and antiemetic medications. The cost of nursing and physician efforts was determined based on the time spent with the patient and the mean hourly wages for nurses and physicians in the Cleveland area. The General Services Administration contract price list was used to cost supplies, e.g., emesis basins. The medication name and total dose were collected for each prescribed antiemetic. National drug codes were used to estimate the cost of prescriptions based on the average wholesale price reported in the 2009 Drug Topics Red Book.¹⁹

The direct cost during the follow-up to the third POD included the use of healthcare resources, such as outpatient care, physician visits, laboratory tests, prophylaxis medications, and unanticipated hospital readmission. Current

procedural terminology codes were determined based on the individual healthcare resources used, and a standard cost value was assigned based on Medicare reimbursement for the corresponding procedural code.

Among patients with regular employment, we recorded the number of days lost to work, excluding the day of surgery. The mean hourly wage in the Cleveland area was used to infer the monetary value of loss of work due to the disease treatment. Hill *et al.*⁹ estimated that the cost of an extra hour of PACU time (PACU delay), independent of direct nursing interventions, was \$34.75/hr in 1998; we thus used this value in our analysis after inflating it to 2009 dollars (\$45.74/hr).

Per standard practice, total health-related costs included the cost of using all healthcare resources so as to avoid any bias due to the arbitrary judgement between PONV-related and non-PONV-related costs. The outcome of interest was the total cost difference between patients who experienced PONV and those who did not experience PONV. Since this study was conducted in 2009, all costs are reported in 2009 United States dollars. A secondary outcome was the difference in quality adjusted days between patients who experienced PONV and those who did not experience PONV.

Our primary outcome was total postoperative recovery cost over the period from the end of anesthesia until the third morning after planned ambulatory surgery. The study focus was mean cost because it can be extrapolated to the population for budgeting or economic evaluation purposes. However, due to the skewed distribution of the total cost, we applied a generalized linear model with a gamma distribution and a log-link function to compare the cost of patients with PONV/PDNU *vs* those without. To account for possible confounding, even if minimal, we included age, ASA status, body mass index, and duration of surgery as linear terms and complexity of surgery (Table 2) as factors in the model. Furthermore, the mean difference in the total cost (i.e., average of the individual marginal effects of PONV/PDNU) with the corresponding 95% confidence interval was estimated by using the recycled prediction method.²⁰ This was accomplished by holding all controlled variables in the model at their actual values for each subject, for example, the cost outcome was predicted while varying only the value shown for each patient with or without PONV/PDNU. These costs were then averaged over the whole sample to provide the results.

Paper Standard Gamble questionnaire

With a one-page Standard Gamble questionnaire, patients were asked to estimate the largest risk they would be willing to accept for the chance to achieve perfect health. The state of health is described by a series of 18 Standard

Table 2 Summary of type of surgery by the complexity

Complexity	Description of surgery	Frequency
Small	Bilateral laparoscopic tubal ligation, dilatation and curettage.	1
	Bilateral tubal cautery laparoscopically,	1
	Dilatation and curettage, hysteroscopy, laparoscopic tubal sterilization with Filshie spring clip mechanism	1
	Diagnostic laparoscopy	8
	Diagnostic laparoscopy and right ovarian cystectomy	1
	Diagnostic laparoscopy, fulguration of endometriosis implants	1
	Diagnostic laparoscopy, irrigation of cul-de-sac	1
	Failed hysteroscopy and a diagnostic laparoscopy	1
	Hysterectomy, dilatation and curettage, ablation, 1 x tubal cauterization,	1
	hysteroscopy, dilatation and curettage, laparoscopic tubal sterilization with Filshie spring clip mechanism	1
	Hysteroscopy, dilatation and curettage, NovaSure® ablation and laparoscopic tubal cauterization	1
	Hysteroscopy, dilatation and curettage, aspiration of pelvis, drain left ovarian cyst	1
	Laparoscopic bilateral tubal fulguration	1
	Laparoscopic bilateral tubal ligation with Filshie clips	7
	Laparoscopy, bilateral tubal ligation with Falope rings	2
	Laparoscopic tubal banding	2
	Laparoscopic tubal ligation	4
	Laparoscopic tubal ligation with Falope rings	4
	Laparoscopic tubal ligation with Filshie clips	3
	Laparoscopic tubal ligation with Filshie clips, endometrial ablation with NovaSure	3
	Laparoscopic tubal sterilization with application of Filshie spring clip mechanism	2
	Laparoscopy and cul-de-sac aspiration of fluid.	1
	Laparoscopy, aspiration of cul-de-sac, removal of small peritoneal cyst	1
	Laparoscopy ovarian cyst	1
	Laparoscopic tubal ligation	1
	Laparoscopic tubal ligation, endometrial ablation	1
	Nasal/sinus SCOPE and biopsy	1
	Laparoscopic left ovarian cystectomy and diagnostic laparoscopy	1
	Diagnostic laparoscopy, left ovarian cystectomy, and chromotubation	1
	NovaSure ablation, dilatation and curettage, hysterectomy	1
Medium	Bilateral laparoscopic tubal cauterization, incision and drainage of right ovarian cyst	1
	Diagnostic laparoscopy and cystoscopy	1
	Laparoscopic bilateral salpingectomy	1
Large	Laparoscopic left ovarian cystectomy with lysis of adhesions	1
	Bilateral ovarian cystectomy, extensive lysis of adhesions	1
	Extended abdominoplasty	1
	Laparoscopic cholecystectomy, excision lipoma - left chest wall	1
	Laparoscopic bilateral salpingo-oophorectomy	1
	Laparoscopic bilateral salpingo-oophorectomy and lysis of adhesions	1
	Laparoscopic cholecystectomy	13
	Laparoscopic cholecystectomy with cholangiogram.	2
	Laparoscopic cholecystectomy with intraoperative cholangiogram	10
	Laparoscopic cholecystectomy with operative cholangiography	7
	Right salpingo-oophorectomy including right paratubal cyst	1

Gamble tradeoffs in descending order (“walk down”) from 100% chance of cure (utility = 1.0) to 10% chance of cure (utility = 0.0). Standard Gamble utility was estimated as

the midpoint between the chance of cure the patient would accept and the next chance. We assessed the association between Standard Gamble utility and PONV using the

Wilcoxon rank-sum test as well as analysis of variance by ranks adjusting for the same potential confounders as above.

Finally, we assessed possible interference of nausea and vomiting on QOL using the Friedman two-way analysis of variance by ranks, adjusting for assessment time (POD one to three) and the potential confounders.

Based on a previous study, we assumed an average standard deviation (SD) cost of \$450 (\$100) for patients without PONV and a PONV incidence of 50%.²¹ A total of 100 patients would provide 80% power for detecting differences in per patient costs of $\geq$ \$57. We similarly had 90% power to detect a difference of \$66, or 15% of the expected average baseline cost. The study was thus planned for 100 patients without an interim analysis. SAS® software version 9.2 for Windows (SAS Institute, Cary, NC, USA) was used for all statistical analyses.

Results

One hundred patients were enrolled at the Cleveland Clinic (138 patients were screened, and 114 patients met the eligibility criteria). Two patients who experienced PONV during recovery were lost to follow-up after discharge; two others were lost on days two and three without experiencing PONV before discharge. All four were excluded from evaluation of our primary hypothesis (i.e., comparing the total cost for patients with PONV/PDNDV vs the cost for patients without PONV/PDNDV); thus, the costs for 96 patients were analyzed. For the secondary analyses, 98 patients with a completed paper Standard Gamble questionnaire and a QOL survey for at least one day were analyzed.

Thirty-seven percent of the patients experienced PONV during hospitalization, a figure which increased to 42% by the first postoperative morning and then increased to 49% by the third postoperative morning. From the first to the third postoperative mornings, 19 patients (19%) experienced PONV, seven of whom did not experience PONV before the first postoperative morning. Thus, the incidence of new-onset late PDNDV was 7% of the entire population and 14% among those who experienced PONV at any time. The two patients who were lost to follow-up on postoperative days two and three were assumed not to have experienced PONV/PDNDV based on assessments at earlier times. There were no clinically important differences in baseline, demographic, or morphometric characteristics between patients who did and did not experience PONV/PDNDV (Table 3).

The duration of anesthesia (mean difference 2 min; 95% confidence interval [CI] −10 to 13 min) and the duration of surgery (mean difference −1 min; 95% CI −11 to 10 min)

Table 3 Baseline and intraoperative patient characteristics

Variable	PONV (n = 49)	No PONV (n = 51)
Age, yr	41 (10)	39 (9)
Male Sex, n (%)	1 (2)	0 (0)
Race, n (%) ¹		
White	37 (77)	38 (75)
African-American	9 (19)	12 (24)
Asian	2 (4)	1 (2)
Height, cm	164 (5)	165 (7)
Weight, kg	68 [62–80]	74 [62–94]
BMI, kg·m ^{−2}	26 (5)	28 (7)
Heart rate, beats·min ^{−1}	75 (11)	75 (12)
BP systolic, mmHg	121 (15)	121 (17)
BP diastolic, mmHg	73 [67–80]	73 [67–79]
ASA physical status, n (%)		
I	9 (19)	11 (22)
II	33 (67)	38 (75)
III	7 (15)	1 (2)
IV	0 (0)	1 (2)
Complexity of surgery, n (%)		
Small	27 (55)	30 (59)
Medium	0	5 (10)
Large	22 (45)	16 (31)
Duration of anesthesia, min	86 (26)	83 (29)
Duration of surgery, min	45 (22)	45 (28)

Results presented as means (standard deviations), medians [interquartile range], or n (%)

¹ One patient in the PONV group had missing value

ASA = American Society of Anesthesiologists; BMI = body mass index; BP = blood pressure; PONV = postoperative nausea and vomiting

were similar in patients with and without PONV/PDNDV. However, the duration of recovery and the amount of nursing effort were significantly longer in those who experienced PONV/PDNDV (median difference 14 min; 95% CI 4 to 25 min). In contrast, there were no differences in physician effort (median difference 0; 95% CI −1 to 1 min), the number of physician calls (median difference 0; 95% CI 0 to 0) or physician visits (median difference 0; 95% CI 0 to 0). One patient required readmission because of uncontrolled PONV (Table 4). As shown in Table 5, the consumption of medication during recovery was generally similar in patients with and without PONV/PDNDV. Seven patients who experienced PONV/PDNDV used emesis basins.

The observed mean (SD) total cost of postoperative recovery was \$730 (\$198) for patients with PONV/PDNDV (n = 47) and \$640 (\$98) for patients without (n = 49), i.e., the unadjusted mean difference was \$90 (95% CI \$27 to \$153). The total cost was significantly greater in the patients with PONV/PDNDV than those without (P = 0.006) after

Table 4 Summary of cost-related outcomes

Outcome	PONV (n = 49)	No PONV (n = 51)
<i>Recovery</i>	<i>Medians [interquartile range] or n (%)</i>	
Duration recovery (min) ¹	234 [188-287]	171 [141-212]
Nausea (worst rating)		
None	12 (24)	51 (100)
Mild	15 (31)	0 (0)
Moderate	13 (27)	0 (0)
Severe	9 (18)	0 (0)
Emetic episodes		
0	41 (84)	51 (100)
1	4 (8)	0 (0)
3	2 (4)	0 (0)
≥ 4	2 (4)	0 (0)
Nursing effort (min)	82 [63-106]	68 [57-79]
Physician effort (min)	2 [0-4]	2 [0-3]
Number of calls by nurses to physicians		
0	20 (41)	19 (37)
1	24 (49)	25 (49)
2	5 (10)	6 (12)
3	0 (0)	1 (2)
<i>Post-discharge</i> ²		
Nausea (worst rating)		
None	22 (47)	49 (100)
Mild	11 (23)	0 (0)
Moderate	8 (17)	0 (0)
Severe	6 (13)	0 (0)
Emetic episodes		
0	36 (77)	49 (100)
1	9 (19)	0 (0)
2	2 (4)	0 (0)
Hospital readmissions	1 (2)	0 (0)
Physician visits		
0	45 (96)	48 (98)
1	0 (0)	1 (2)
2	2 (4)	0 (0)
Lost work (days)		
1	1 (2)	1 (2)
2	5 (11)	8 (16)
3	41 (87)	40 (82)

Duration of recovery was considered to be the interval from the end of anesthesia to actual hospital discharge. Lost work (days) does not include the days of surgery

¹ One patient in the PONV group had missing value

² Two patients in each group had missing values due to lost follow-up after hospital discharge

PONV = postoperative nausea and vomiting

adjusting for covariates; PONV/PDNDV was associated with an incremental total cost of \$75 (95% CI \$67 to \$86). The difference in total cost was due largely to the difference in

Table 5 Summary of medication consumption during recovery

Medication	Unit	PONV (n = 49)		No PONV (n = 51)	
		n	Total Dose	n	Total Dose
Acetaminophen	mg			4	1,425
Diphenhydramine	mg			1	25
Prochlorperazine	mg	3	30		
Propoxyphene/Acetaminophen	tab	4	5	3	4
Meperidine	mg	20	988	28	1,488
Hydromorphone	mg	11	9.9	3	3.4
Fentanyl	µg	37	3,550	34	3,200
Ibuprofen	mg			2	1,200
Morphine	mg	6	42	7	56
Naproxen	mg	1	500		
Oxycodone/Acetaminophen	tab	11	15	18	22
Promethazine	mg	23	150	24	150
Scopolamine Patch	patch	3	1.5		
Ketorolac	mg	14	345	11	270
Codeine/Acetaminophen	mg			3	90
Hydrocodone/Acetaminophen	tab	2	2	5	6
Ondansetron	mg	17	80		

PONV = postoperative nausea and vomiting

the PACU stay. Table 6 provides a summary of cost by categories.

The Standard Gamble utility was not associated with postoperative PONV/PDNDV experience ($P = 0.67$); the estimated mean difference was -0.02 (95% CI -0.04 to 0.01). Quality adjusted days for PONV/PDNDV patients were 2.9 days and for non-PONV/PDNDV patients were 2.95 days (mean difference -0.05 ; 95% CI -0.11 to 0.02 days). The multivariable model adjusting for covariates gave similar results ($P = 0.98$).

Experiencing PONV/PDNDV was associated with worse postoperative QOL scores ($P < 0.001$, Friedman's test, both with and without adjusting for the same confounders). Forty-nine percent (23/47) of patients with PONV/PDNDV and 94% (48/51) of patients without PONV/PDNDV gave the best score (1 = not at all) for all four QOL questions through POD one to three.

Discussion

The mean cost (SD) of postoperative recovery in patients who experienced PONV/PDNDV was \$730 (\$198) vs \$640 (\$98) in those who did not experience PONV/PDNDV. After controlling for age, ASA status, body mass index, duration of surgery, and complexity of surgery, PONV/PDNDV was thus associated with an incremental ambulatory care cost of

Table 6 Summary of costs by categories

Cost (U.S. dollars)	PONV (<i>n</i> = 47)		No PONV (<i>n</i> = 49)	
	Mean (SD)	Median [IQR]	Mean (SD)	Median [IQR]
Recovery				
PACU stay	191 (72)	179 [143-221]	148 (56)	133 [112-162]
Nurse effort	44 (16)	41 [32-53]	36 (11)	35 [29.5-39.5]
Physician effort	3 (3)	2.2 [0-4.5]	3 (4)	2.2 [0-3.4]
Supplies	0 (0)	0 [0-0]	0 (0)	0 [0-0]
Medications	4 (5)	3.3 [2.1-4.1]	3 (1)	2.8 [1.4-3.6]
†Recovery total	243 (87)	227 [194-274]	190 (64)	166 [149-207]
Post-discharge				
Readmissions	23 (158)	0 [0-0]	0 (0)	0 [0-0]
Physician visits	6 (32)	0 [0-0]	1 (9)	0 [0-0]
Medications for nausea	0 (2)	0 [0-0]	0 (0)	0 [0-0]
Loss of work	458 (67)	482 [482-482]	449 (73)	482 [482-482]
‡Post-discharge total	488 (178)	482 [482-482]	451 (74)	482 [482-482]
	730 (198)	707 [646-778]	640 (98)	638 [621-668]

PACU = postanesthesia care unit; PONV = postoperative nausea and vomiting; SD = standard deviation; IQR = interquartile range

† The total cost during recovery was significantly higher in patients with PONV than in those without PONV (mean \$48; 95% confidence interval (CI) \$39 to \$59; $P < 0.001$) after adjusting for age, ASA status, body mass index, duration of surgery, and complexity of surgery

‡ The total post-discharge cost was not significantly different (mean \$25; 95% CI \$23 to \$29; $P = 0.30$) with the same covariable adjustment

\$75 (95% CI \$67 to \$86). Coincidentally, this cost is comparable with the amount patients are willing to pay to avoid PONV.^{8,22,23}

The cost differential was not driven by physician expense. Postoperative physician visits were rarely required, and the number was similar between the two groups. Postoperative antiemetic use was higher in the PONV group, but these medications contributed little to overall cost because most antiemetics are inexpensive. The major total societal cost of the study was caused by lost employment income, especially since most patients lost three full days of work. However, the indirect cost attributed to lost work was virtually identical between the two groups.

Direct nursing effort was 14 min longer in patients with PONV, but by far the major factor differentiating cost was the duration of recovery, which was a full hour longer in patients who experienced PONV. Consequently, duration of recovery contributed \$50 to the \$75 total cost difference (covariate-adjusted estimates) between patients who presented PONV/PDNV and patients who did not. Our results are consistent with those reported by Habib *et al.*²¹ They also found that the cost of PONV was influenced mainly by duration of PACU stay, with the difference in their patients being 25 min, which corresponded to a \$52 difference in cost. Hill *et al.*⁹ concluded that PACU personnel constitutes the major portion of recovery costs, and they suggested that decreasing the peak number of patients in the PACU can be accomplished by arranging the operating

room schedule to optimize PACU admission rates.²⁴ Our study extends previous work by including costs accrued over three postoperative days and by presenting a detailed accounting of cost categories, each contributing to the total incremental cost of PONV and PDNV.

Nearly 60% of the patients who experienced PONV at any time did so after hospital discharge. However, only about 25% of the patients first experienced PONV after discharge. Thus, PDNV was relatively common but occurred mostly in patients who had already manifested symptoms in the PACU. While no doubt disturbing to patients, the costs attributable to post-discharge PONV were low and therefore of little financial consequence.

Only 49% of patients with PONV/PDNV gave the best score (1 = not at all) for all four QOL questions through POD one to three, whereas 94% of patients without PONV/PDNV gave the best score, nearly a two-factor difference. In contrast, utility measured by the paper Standard Gamble showed that patients were not willing to accept any risk of death to improve their perioperative experience. Postoperative nausea and vomiting thus worsened QOL but not utility for which patients would be willing to risk life. We noticed, though, that seven patients developed PDNV on the second or third POD and thus may have responded differently to the Standard Gamble had it been administered later in the postoperative course.

A limitation of our study is that it was largely conducted at a single suburban medical centre. Our recovery duration well exceeded the 67 (2) min average for the patients who

did not experience PONV (2006 National Survey of Ambulatory Surgery).²⁵ However, to the extent that the duration of recovery among patients without PONV is shorter in other centres, the relative increment imposed by PONV may be even greater.

Our patients were not randomly selected even within the Cleveland Clinic surgical population, much less from across the United States. Instead, we targeted a 50% incidence of PONV/PDND (the actual incidence was 49%) with the goal of enhancing the comparison between patients with and without PONV. The female dominance (99%) in our sample — as in so many PONV studies — predictably resulted from our requirement that participants have at least two risk factors. The cost of PONV in men might differ from women, but a substantial divergence seems unlikely. Depending on subject selection and anesthetic management, e.g., use of volatile anesthetics and postoperative opioids, the incidence of PONV will differ in other contexts. However, the costs associated with PONV were estimated using United States values and thus can reasonably be generalized to the country as a whole. Of course, costs will vary substantially in other healthcare environments,²⁶ but local costs can be estimated from local drug and labour costs.

Our study well characterized most costs associated with PONV and PDND. However, we did not have enough patients to identify significant differences in readmission rates for PONV. Only one of our patients was readmitted for PONV (2%), which is similar to the 1% incidence reported in a previous large study.⁹ Thus, while an overnight hospital admission is expensive, roughly \$1,000, readmissions are so rare that they contribute little (i.e., \$10) to the average cost of PONV.

Many studies have evaluated the cost-effectiveness of different medications in the treatment of PONV. Chang *et al.* concluded that prochlorperazine was more cost-effective than ondansetron (\$32 vs \$275, respectively).²⁷ Additionally, Hill *et al.* found that droperidol was more cost-effective than ondansetron or placebo (\$104, \$112, and \$164, respectively).⁹ Finally, Tang *et al.* conducted two studies, first comparing droperidol, ondansetron, and placebo. The first study showed that droperidol was the most cost-effective medication in the treatment of PONV (\$7) followed by ondansetron (\$28) and placebo (\$35).⁸ Ondansetron is now generic, however, and hence contributes almost nothing to the cost of PONV management. The second study of Tang *et al.* was a comparison of different doses of ondansetron given at different points (pre-induction and end of surgery) and placebo. They concluded that administering ondansetron before the end of surgery was more cost-effective (\$36) than giving it with induction (\$46), administering half with induction and half before the end of surgery (\$64), and providing placebo only (\$53).¹⁰

In summary, patients who manifest PONV in the PACU frequently continued to experience nausea and vomiting after hospital discharge. New-onset PDND also occurred, but it was much less common. Postoperative nausea and vomiting/PDND reduced QOL and imposed an incremental cost of \$75 per patient over the initial three PODs. This increment was driven mainly by the increased PACU stay in patients who presented with PONV, and it resulted from the high hourly cost of PACU care.^{9,21} This estimate may reasonably be used to estimate cost reductions associated with various antiemetic strategies, even when cost *per se* is not evaluated in particular studies.

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Conflicts of interest None declared.

References

1. Gan TJ, Meyer TA, Apfel CC, *et al.* Society for Ambulatory Anesthesia guidelines for the management of postoperative nausea and vomiting. *Anesth Analg* 2007; 105: 1615-28.
2. Macario A, Weinger M, Carney S, Kim A. Which clinical anesthesia outcomes are important to avoid? The perspective of patients. *Anesth Analg* 1999; 89: 652-8.
3. Junger A, Klasen J, Benson M, *et al.* Factors determining length of stay of surgical day-case patients. *Eur J Anaesthesiol* 2001; 18: 314-21.
4. Hedayati B, Fear S. Hospital admission after day-case gynaecological laparoscopy. *Br J Anaesth* 1999; 83: 776-9.
5. Carroll NV, Miederhoff P, Cox FM, Hirsch JD. Postoperative nausea and vomiting after discharge from outpatient surgery centers. *Anesth Analg* 1995; 80: 903-9.
6. Kovac AL. Prevention and treatment of postoperative nausea and vomiting. *Drugs* 2000; 59: 213-43.
7. Apfel CC, Laara E, Koivuranta M, Greim CA, Roewer N. A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. *Anesthesiology* 1999; 91: 693-700.
8. Tang J, Watcha MF, White PF. A comparison of costs and efficacy of ondansetron and droperidol as prophylactic antiemetic therapy for elective outpatient gynecologic procedures. *Anesth Analg* 1996; 83: 304-13.
9. Hill RP, Lubarsky DA, Phillips-Bute B, *et al.* Cost-effectiveness of prophylactic antiemetic therapy with ondansetron, droperidol, or placebo. *Anesthesiology* 2000; 92: 958-67.
10. Tang J, Wang B, White PF, Watcha MF, Qi J, Wender RH. The effect of timing of ondansetron administration on its efficacy, cost-effectiveness, and cost-benefit as a prophylactic antiemetic in the ambulatory setting. *Anesth Analg* 1998; 86: 274-82.
11. Lachaine J. Therapeutic options for the prevention and treatment of postoperative nausea and vomiting: a pharmacoeconomic review. *Pharmacoeconomics* 2006; 24: 955-70.

12. Aldrete JA. The post-anesthesia recovery score revisited. *J Clin Anesth* 1995; 7: 89-91.
13. Martin CG, Rubenstein EB, Elting LS, Kim YJ, Osoba D. Measuring chemotherapy-induced nausea and emesis. *Cancer* 2003; 98: 645-55.
14. Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. Cost-utility analysis. In: Drummond MF, editor. *Methods for the Economic Evaluation of Health Care Programmes*. 3rd ed. Oxford: Oxford University Press; 2005. p. 137-209.
15. Littenberg B, Partilo S, Licata A, Kattan MW. Paper Standard Gamble: the reliability of a paper questionnaire to assess utility. *Med Decis Making* 2003; 23: 480-8.
16. Ross PL, Littenberg B, Fearn P, Scardino PT, Karakiewicz PI, Kattan MW. Paper standard gamble: a paper-based measure of standard gamble utility for current health. *Int J Technol Assess Health Care* 2003; 19: 135-47.
17. Lin MR, Hwang HF, Chung KP, Huang C, Chen CY. Rating scale, standard gamble, and time trade-off for people with traumatic spinal cord injuries. *Phys Ther* 2006; 86: 337-44.
18. van Wijck EE, Bosch JL, Hunink MG. Time-tradeoff values and standard-gamble utilities assessed during telephone interviews versus face-to-face interviews. *Med Decis Making* 1998; 18: 400-5.
19. Red Book 2009: Pharmacy's Fundamental Reference (Red Book Drug Topics). Montvale, NJ: Physicians' Desk Reference Inc., 2009: 1-1032.
20. Altman DG, Machin D, Bryant T, Gardner S. *Statistics with Confidence: Confidence Intervals and Statistical Guidelines*. 2nd ed. London: BMJ Books; 2000.
21. Habib AS, Chen YT, 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: 1093-9.
22. Gan TJ, Sloan F, de L Dear G, El-Moalem HE, Lubarsky DA (2001) How much are patients willing to pay to avoid postoperative nausea and vomiting? *Anesth Analg* 92: 393-400.
23. Kerger H, Turan A, Kredel M, et al. Patients' willingness to pay for anti-emetic treatment. *Acta Anaesthesiol Scand* 2007; 51: 38-43.
24. Dexter F, Tinker JH. Analysis of strategies to decrease postanesthesia care unit costs. *Anesthesiology* 1995; 82: 94-101.
25. Cullen KA, Hall MJ, Golosinskiy A. Ambulatory Surgery in the United States, 2006. *National Health Statistics Reports* 2009; 11: 1-28. Available from URL: <http://www.cdc.gov/nchs/data/nhsr/nhsr011.pdf> (accessed November 2011).
26. Frighetto L, Loewen PS, Dolman J, Marra CA. Cost-effectiveness of prophylactic dolasetron or droperidol vs rescue therapy in the prevention of PONV in ambulatory gynecologic surgery. *Can J Anesth* 1999; 46: 536-43.
27. Chang P, Okamoto M, Chen J, Frame D. Cost-effectiveness analysis of ondansetron and prochlorperazine for the prevention of postoperative nausea and vomiting. *J Manag Care Pharm* 2005; 11: 317-21.