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Cost-effectiveness of Prophylactic Antiemetic Therapy with Ondansetron, Droperidol, or Placebo

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Background: **In an era of growing economic constraints on healthcare delivery, anesthesiologists are increasingly expected to understand cost analysis and evaluate clinical practices. Postoperative nausea and vomiting (PONV) are distressing for patients and may increase costs in an ambulatory surgical unit. The authors compared the cost-effectiveness of four prophylactic intravenous regimens for PONV: 4 mg ondansetron, 0.625 mg droperidol, 1.25 mg droperidol, and placebo.**

Methods: **Adult surgical outpatients at high risk for PONV were studied. Study drugs were administered intravenously within 20 min of induction of nitrous oxide–isoflurane or enflurane anesthesia. A decision-tree analysis was used to group patients into 12 mutually exclusive subgroups based on treatment and outcome. Costs were calculated for the prevention and treatment of PONV. Cost-effectiveness analysis was performed for each group.**

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Results: **Two thousand sixty-one patients were enrolled. Efficacy data for study drugs have been previously reported, and the database from that study was used for pharmacoeconomic analysis. The mean–median total cost per patient who received prophylactic treatment with 4 mg ondansetron, 0.625 mg droperidol, 1.25 mg droperidol, and placebo were $112 or $16.44, $109 or $0.63, $104 or $0.51, and $164 or $51.20, respectively ($P = 0.001$, active treatment groups *vs.* placebo). The use of a prophylactic antiemetic agent significantly increased patient satisfaction ($P < 0.05$). Personnel costs in managing PONV and unexpected hospital admission constitute major cost components in our analysis. Exclusion of nursing labor costs from the calculation did not alter the overall conclusions regarding the relative costs of antiemetic therapy.**

Conclusion: **The use of prophylactic antiemetic therapy in high-risk ambulatory surgical patients was more effective in preventing PONV and achieved greater patient satisfaction at a lower cost compared with placebo. The use of 1.25 mg droperidol intravenously was associated with greater effectiveness, lower costs, and similar patient satisfaction compared with 0.625 mg droperidol intravenously and 4 mg ondansetron intravenously. (Key words: Ambulatory; anesthesia; emesis; nausea; postoperative.)**

IN the United States, more than 60% of surgical procedures are performed on an ambulatory basis.[1] One of the major limiting factors in early discharge of ambulatory surgery patients is the presence of postoperative nausea and vomiting (PONV).[2] PONV is also a major cause of unanticipated hospital admission.[2] With the increasing national attention on health care and healthcare costs, anesthesiologists, and other medical specialists, must apply therapy in a rational manner. In this era of limited resources, the cost-effectiveness of antiemetic therapy will be closely scrutinized. Although newer and more expensive drugs such as the 5HT-3 antagonists have been shown to be effective, it is unclear what constitutes the best strategy for the prevention of PONV. Confining attention to drug acquisition costs without considering all direct and indirect costs ultimately may lead to an inefficient use of resources.[3] The database of a multicenter study[4] comparing prophylactic use of 4 mg ondansetron, 0.625 mg droperidol, 1.25 mg droperidol,

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and placebo was used to calculate the incremental cost-effectiveness of antiemetic agents for the prevention of PONV in adult day surgery patients at high risk for PONV.

Methods

A randomized, double-blind, placebo control, multicenter study was conducted at 50 institutions in North America. Patients classified as American Society of Anesthesiologists physical status I or II between the ages of 18 and 65 yr scheduled for general anesthesia outpatient procedures planned to last no more than 2 h were included in the study. Eligible patients had a history of motion sickness or PONV. In addition, patients were limited to those undergoing procedures considered to have high emetogenic potential (*i.e.,* laparoscopic procedures, genitourinary procedures, lower extremity orthopedic procedures, umbilical or ventral herniorrhaphies, or partial mastectomies or lumpectomies). All patients provided written, informed consent, and the study was approved by the Institutional Review Board at each study site.

The patients were randomized to one of four intravenous treatments: 4 mg ondansetron, 0.625 mg droperidol, 1.25 mg droperidol, or placebo (normal saline). All drugs were mixed with 0.9% saline to a final volume of 10 ml by a pharmacy and administered in a double-blind fashion within 20 min of induction of anesthesia. After study drug administration, patients were allowed, but not required, to receive up to 2 mg midazolam, fentanyl, or alfentanil (dose at anesthesiologist's discretion) as a premedicant. Anesthetic induction was accomplished with thiamylal, methohexital, or sodium thiopental. After laryngoscopy and tracheal intubation, anesthesia was maintained with a combination of oxygen, nitrous oxide, and isoflurane or enflurane. Patients were allowed to receive either fentanyl or alfentanil for analgesic supplementation. The use and choice of neuromuscular blocking agent and antagonist were at the discretion of the anesthesiologist.

The initial study period began in the postoperative anesthesia care unit (PACU) immediately after the patients were sufficiently coherent to complete a verbal nausea assessment and continued for the next 2 h. Patient nausea assessments were repeated every 30 min during the study period. Independent study personnel recorded episodes of nausea, vomiting, and adverse events. Patients were administered fentanyl intravenously as needed for pain relief in the primary (phase I) PACU and oral analgesics as needed in the secondary (phase II) PACU. Rescue medications for nausea or vomiting were given if nausea was intractable and lasted for at least 15 min, if three emetic episodes occurred within 15 min, or at any time at the patient's request. The choice of rescue antiemetic was at the discretion of the attending anesthesiologist. Time to "street readiness" (times when institutional discharge criteria for outpatients were met) were recorded by study personnel. At discharge from the hospital, patients were asked to keep a diary for the next 24 h.

Efficacy data of the study medications have been previously reported.[4] Using the database from the study, we evaluated the financial impact of using 4 mg ondansetron, 0.625 mg droperidol, 1.25 mg droperidol, or placebo as a prophylactic antiemetic in this patient population. The perspective used was that of the chief financial officer of an ambulatory surgical facility that employed an anesthesiologist who worked in a managed care environment. Each treatment group was partitioned into subsets based on a decision-tree analysis (fig. 1) initially described by Watcha and Smith.[3] The criteria for partitioning were based on the following: (1) presence of PONV after prophylactic therapy, (2) need for additional rescue antiemetic therapy despite prophylaxis, (3) success of rescue antiemetic therapy, (4) occurrence of side effects, and (5) treatment of side effects. All patients could be assigned to 1 of 12 mutually exclusive subgroups, and the probability of a patient after a specific path was calculated.

Costs for reaching 1 of the 12 defined end points in the decision analysis tree were calculated (table 1). The product of the costs for this outcome and the probability of a patient reaching this end point provided the weighted cost for a specific outcome. The sum of these costs provided the weighted total costs associated with the use of a given antiemetic drug (fig. 1). For example, the costs for the "No PONV" path were TP1 + TP2 + TP3. The basis for assigning costs to each end point necessitated data for direct and indirect costs.[5] These costs included the acquisition cost for prophylactic drugs, and the incremental costs for personnel time, drugs, and materials used to manage emesis. Costs for the management of emesis included material costs (*i.e.,* gowns, linens, basins, and paper towels for "emesis clean up"), rescue antiemetic therapy, and management of side effects of the prophylactic antiemetic therapy. The costs associated with delay in leaving the PACU

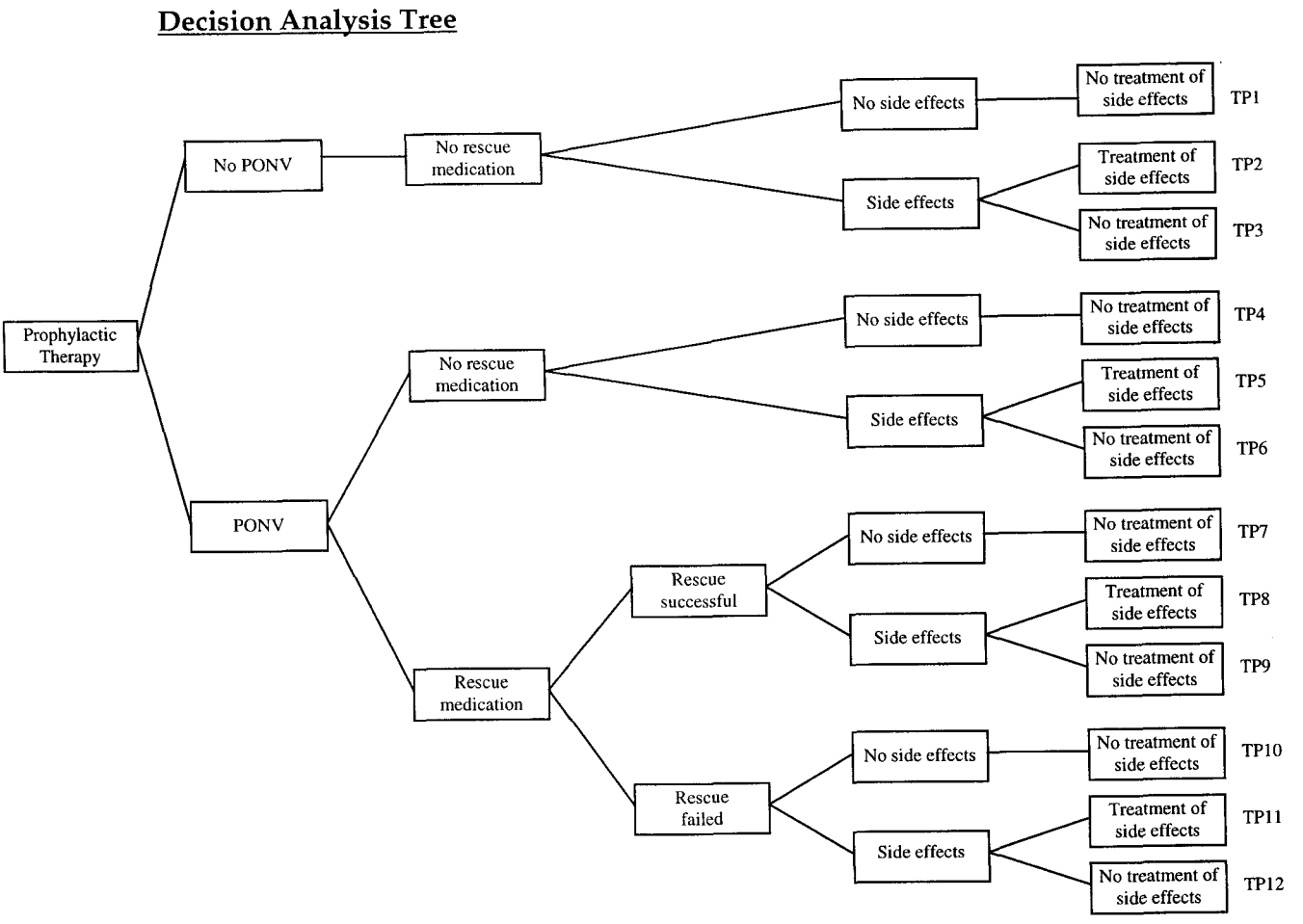

Fig. 1. Decision tree analysis. The cost for reaching a specific outcome was calculated. For example, the cost of following the "No PONV" path is TP1 + TP2 + TP3. TP = end point on the decision analysis tree. (Reproduced with permission).

and unplanned hospital admission were included in our calculations.

Costs used for the cost analysis are shown table 2. The drug acquisition costs and prorated hourly nursing, nursing aids, nurse anesthetists, and anesthesiologists' salaries and benefits costs were provided by the hospital administration at Duke University, and the nurse:patient ratios in the phase I PACU and phase II recovery area were in keeping with the guidelines of the American Society of Postanesthesia Nurses. The time spent by the nurses and nursing aids in (1) providing, emptying, and cleaning emesis basins, suction tubing, and Yankauer suckers; (2) providing mouth wash, comforting the patient, and changing patient linen and bed clothes after emesis; and (3) calling a physician, administering antiemetic drugs, and recording these events in the chart were recorded. The additional time spent by the anesthesia care team in directly managing PONV in the PACU was also recorded. The hospital cost for an unexpected hospital admission varied from $900 to $1,500/day depending on the type of hospital; but for our calculations, we used a recently published estimated average daily hospital cost of $1,053/day.[6] We were unable to use hospital admission costs from Duke because this information is confidential because of managed care contractual negotiations.

After discharge from the ambulatory surgical center, the patients were asked to complete a diary for 24 h about the incidence and severity of PONV, adverse events, and the use of medications, including rescue antiemetics. Costs for managing emesis after discharge were limited to the costs of drugs used at home and any admission to hospital. Because the cost analysis was performed from the perspective of the institution, indi-

Table 1. Mean Costs ($) of Outcomes TP1–TP12 and the Probabilities of Patients Having that Outcome

	Ondansetron 4 mg			Droperidol 0.625 mg			Droperidol 1.25 mg			Placebo (Saline)		
End Point	Cost per Patient	Weighted Cost	% in Subgroup	Cost per Patient	Weighted Cost	% in Subgroup	Cost per Patient	Weighted Cost	% in Subgroup	Cost per Patient	Weighted Cost	% in Subgroup
TP1	18.82	3.95	21	0.74	0.18	24	2.84	0.80	28	0.03	0.01	17
TP2	16.93	1.69	10	3.91	0.35	9	0.58	0.06	10	0.39	0.02	6
TP3	16.96	1.53	9	0.55	0.06	11	1.86	0.24	13	0.01	0.00	6
TP4	64.74	7.77	12	39.04	5.07	13	31.67	3.48	11	70.5	8.46	12
TP5	60.14	3.61	6	111.21	4.45	4	86.01	4.30	5	98.03	4.90	5
TP6	50.59	4.05	8	39.64	2.77	7	78.23	5.48	7	67.99	5.44	8
TP7	174.53	13.96	8	188.85	10.69	9	185.52	16.70	9	196.65	19.67	10
TP8	224.57	11.23	5	145.04	5.80	4	283.06	5.66	2	280.48	16.83	6
TP9	195.62	13.69	7	144.87	10.14	7	255.48	10.22	4	258.61	28.45	11
TP10	356.44	14.26	4	299.41	11.98	4	573.93	17.22	3	321.24	22.49	7
TP11	629.93	25.20	4	917.41	27.52	3	766.39	30.65	4	615.20	24.61	4
TP12	300.42	18.03	6	462.81	23.1	5	303.27	12.13	4	421.71	33.74	8
Total weighted costs		$118.97			$102.11			$104.94			$164.62	

Weighted cost = % in subgroup × cost per patient; weighted total cost = sum of weighted costs (TP1–TP12).

Table 2. Costs Used in the Cost-effectiveness Analysis

Resource	Cost (US$)
Material (per item of basin, glove, paper, linen and gown)	1.51
Hospital	
PACU delay (per hour)	34.75
admission (one day)	1,053.00
Personnel (per hour)	
MD	125.00
RN	21.00
Aid	12.00
CRNA	42.40
LPN	14.00
Treatment drug (per dose)	
Ondansetron	16.44
Droperidol	0.51

CRNA = certified nurse anesthetist; LPN = licensed practice nurse; MD = anesthesiologist; PACU = postanesthesia care unit; RN = registered nurse.

rect costs of a companion caretaker, lost wages, and cost of travel to a pharmacy, physician, or hospital were not included in the calculations.

The total cost per PONV-free patient was calculated using the number of successful outcomes (no PONV) as the denominator and the total group cost as the numerator. The cost per patient with no PONV or side effects was calculated the same way, but with the number of successful outcomes (no PONV or side effects) as the denominator. Incremental cost-effectiveness ratios were used to determine the most cost-effective therapy for various outcomes. The incremental cost-effectiveness ratio was calculated by dividing the difference in costs among treatment groups by the difference in success rates among these groups. A calculation was also performed to determine how much it would cost to gain one additional PONV-free patient with each of the prophylactic drugs compared with placebo. This was determined by dividing the cost of treating the patients by the percentage of PONV-free patients gained. The result is the cost to gain one additional PONV-free patient. Similar calculations were performed for no PONV, side effect-free, and emesis-free patients. The Wilcoxon rank sum test was used to compare the cost per patient among the three drug treatment groups (the placebo group was not included in this analysis), and $P < 0.05$ was considered statistically significant.

Results

Two thousand sixty-one patients from 50 institutions in North America (Appendix) completed the study. There were 515, 518, 510, and 518 patients in the 4 mg ondansetron, 0.625 mg droperidol, 1.25 mg droperidol, and placebo groups, respectively. There were no significant differences in demographics among the groups.

The mean cost per patient in each path of the decision tree and the probability of being in that path for each of the four groups are presented in table 1. The total incremental mean and median costs associated with the prophylactic use of 4 mg ondansetron, 0.625 mg droperidol, 1.25 mg droperidol, and placebo were $112 and $16.44, $109 and $0.63, $104 and $0.51, and $164 and $51.20

Table 3. Total Incremental and Component Costs per Patient

	Ondansetron 4 mg	Droperidol 0.625 mg	Droperidol 1.25 mg	Placebo (Saline)
Prophylactic antiemetic				
Mean and median	16.44	0.51	0.51	0
Rescue antiemetic				
Mean (SD)	3.6 (9.7)	2.8 (7.0)	2.8 (7.1)	4.5 (9.1)
Median (10th–90th percentile)	0 (0–10)	0 (0–10)	0 (0–10)	0 (0–17)
Material cost				
Mean (SD)	0.1 (0.4)	0.2 (0.4)	0.1 (0.3)	0.2 (0.7)
Median (10th–90th percentile)	0.2 (0–0.4)	0 (0–0)	0.20 (0–0.4)	0 (0–0.63)
Personnel				
MD/CRNA				
Mean (SD)	3.8 (51.2)	1.8 (35.2)	6.6 (88.7)	10.4 (109.0)
Median (10th–90th percentile)	0 (0–0)	0 (0–0)	0 (0–0)	129.2 (200.9)
PACU nurses				
Mean (SD)	79.6 (156.5)	84.6 (202.6)	75.3 (187.8)	0 (0–0)
Median (10th–90th percentile)	0 (0–315)	0 (0–252)	0 (0–215)	0 (0–357)
PACU delay				
Mean (SD)	3.3 (18.6)	7.1 (60.0)	4.2 (37.5)	5.4 (45.4)
Median (10th–90th percentile)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Hospital admission				
Mean (SD)	6.1 (103.7)	12.2 (112.9)	14.4 (139.3)	14.2 (121.8)
Median (10th–90th percentile)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Total cost				
Mean (SD)	112.3 (235.0)	109.2 (260.5)	104.0 (284.1)	164.1 (287.7)*
Median (10th–90th percentile)	16.44 (16.44–332)	0.63 (0.51–317)	0.51 (0.51–316)	51.2 (0–421)*

CRNA = certified nurse anesthetist; MD = anesthesiologist; PACU = postanesthesia care unit.

* $P = 0.001$, statistically significant between active treatment groups *versus* placebo.

Total costs do not exactly equal the sum of the components because of rounding of figures.

per patient, respectively (table 3). Placebo patients incurred significantly higher mean and median costs compared with active treatment groups ($P = 0.001$), although there were no statistically significant differences among the active treatment groups. The individual component costs that composed the total costs are presented in table 3. When personnel costs were excluded from the calculations, the total incremental median costs were \$16.44, \$0.51, \$0.51, and \$20.41, respectively. Total incremental mean costs for a PONV-free patient and a PONV- and side effect-free patient are presented in table 4.

The efficacy data and cost per patient to gain one additional PONV-free, PONV and side effect-free, and emesis-free patient were calculated for the 4-mg prophylactic ondansetron, 0.625-mg droperidol, or 1.25-mg droperidol groups compared with the placebo group and are shown in table 5. Costs in both droperidol-treated groups are significantly cheaper than in the ondansetron-treated group in each of the three scenarios ($P < 0.0001$). The incremental cost-effectiveness ratio of antiemetics comparing mean costs and outcome success are presented in table 6. Droperidol 1.25 mg was the most cost-effective in achieving a PONV-free, PONV and side effect-free, and emesis-free patient (table 6).

Table 4. Total Incremental Mean Costs per PONV-free Patient and per PONV- and Side Effect–free Patient

Therapy	Per PONV-free Patient	Per PONV- and Side effect–free Patient
Ondansetron	286	551
Droperidol 0.625 mg	251	457
Droperidol 1.25 mg	206	375
Placebo	575*	960*

Numbers are US \$.

PONV = postoperative nausea and vomiting.

* $P < 0.01$, active treatment group *versus* placebo.

Although there was no statistically significant differences in the time to home readiness among the groups, patients in the placebo group required more materials (*i.e.,* basin, gloves, gown, linen, tissue paper) for management of PONV ($P = 0.001$) and more healthcare personnel (*i.e.,* nursing, nurse anesthetists, anesthesiologist) time ($P = 0.001$). Patients who received a prophy-

Table 5. Efficacy Data and Costs To Gain an Additional PONV-free, PONV- and Side Effect–free, and Emesis-free Patient as a Result of Prophylaxis

	Ondansetron 4 mg	Droperidol 0.625 mg	Droperidol 1.25 mg
PONV-free (%)	39	43	50
Increase over placebo (%)	11	15	22
Cost to gain additional PONV-free patient	$149*	$3.4	$2.3
PONV- and side effect–free (%)	20	24	28
Increase over placebo (%)	3	7	11
Cost to gain additional PONV- and side effect–free patient	$548*	$7.3	$4.6
Emesis-free (%)	62	63	69
Increase over placebo (%)	16	17	23
Cost to gain additional emesis-free patient	$102*	$3.0	$2.3

* $P < 0.0001$, ondansteron *versus* the two droperidol groups.
PONV = postoperative nausea and vomiting.

lactic antiemetic were significantly more satisfied than patients in the placebo group ($P < 0.05$); however, there was no difference in satisfaction scores among the antiemetic treatment groups.[4]

The cost for treating patients with a vomiting episode was higher than that for those who had nausea only; the mean costs per patient were $303 and $82, and the median costs per patient were $194 and $0.63, respectively ($P = 0.0001$). Table 7 presents the component costs that composed the totals. Twenty-four patients were admitted to the hospital overnight because of persistent postoperative vomiting: Ondansetron 4 mg (three patients; 0.6%), 0.625 mg droperidol (seven patients; 1.4%), 1.25 mg droperidol (seven patients; 1.4%), and placebo (seven patients; 1.4%). The number of patients admitted to the hospital in each group was not statistically different. There was no significant difference in the number of adverse events reported by patients in the treatment groups. The incidence of hypotension, sedation, agitation, or anxiety was not significantly different among the groups; however, the incidence of headache was significantly lower in the droperidol groups (0.625 mg droperidol, 11%; 1.25 mg droperidol, 11%) compared with the ondansetron group (17%).[4]

Discussion

This study showed that the administration of a prophylactic antiemetic in day surgery patients at high risk for PONV was associated with greater effectiveness and increased patient satisfaction, which were achieved with a lower overall cost compared with placebo. PONV is one of the most common complications after anesthesia, with an incidence of 20–80%.[7–10] The symptoms are distressing for patients and may cause dehydration, electrolyte disturbances, pain, and wound dehiscence. It is a major limiting factor in early discharge of patients and is a leading cause of unanticipated hospital admission after outpatient surgery (0.1–2%).[2,11–15]

In an era of diminished resources, the choice of one antiemetic drug *versus* another is based not only on the comparative safety and effectiveness profiles but also on an economic appraisal of the consequences of a particular choice.[16] Cost-effectiveness analysis can be used to determine the net cost and benefits of individual drugs. The incremental cost-effectiveness ratio can be applied to create a rank-order list to prioritize drug spending and maximize the net health benefit from a fixed amount of scarce resources (table 6). Although the costs for drugs used by anesthesiologists account for a large share of total hospital drug expenditures, drug costs alone form a minor proportion of total patient costs.[17] Therefore, it is important to assess the overall costs rather than concentrate on the costs of antiemetic drugs alone.

In this analysis, we evaluated the economic consequences of various strategies and outcomes in the management of PONV using a decision analysis tree.[18,19] We calculated the direct and indirect costs involved with the prophylaxis and management of PONV and the probability of a patient after a given path to reach a specific and mutually exclusive end point. Previous studies with fewer patients have tried to calculate the probability of reaching specific end points from multiple data sources and assumptions and were therefore subject to errors.[3] In our analysis, we had a large number of patients (2,061); therefore, we were able to reduce errors in our calculations by using actual numbers of patients at each end point to calculate the probability. Because estimates of costs involved vary among institutions, we used Duke University–derived actual costs instead of charges to reduce the errors in our calculations.[20] These costs are representative of other tertiary care institutions in North America.[21]

Some of the direct and indirect costs may be fixed costs and independent of the volume of activity (*e.g.*, hospital admission costs) or the costs may be variable and depend on the activity volume (*e.g.*, cost of emesis clean up materials). The direct variable costs included the acquisition cost of the prophylactic antiemetic drug and the materials used for its administration, the cost of materials and personnel time spent in the management

Table 6. Incremental Cost-effectiveness Ratio of Antiemetics Comparing Mean Costs and Outcome Success for PONV-free Patients, PONV- and Side Effect–free Patients, and Emesis-free Patients*

	Treatment A			
	Ondansetron 4 mg	Droperidol 0.625 mg	Droperidol 1.25 mg	Placebo
Treatment B				
Ondansetron 4 mg		Droperidol 0.625 mg	Droperidol 1.25 mg	Ondansetron 4 mg
Droperidol 0.625 mg			Droperidol 1.25 mg	Droperidol 0.625 mg
Droperidol 1.25 mg				Droperidol 1.25 mg

The analysis assumes all side effects are equal, *i.e.*, dysphoria or sedation from droperidol is equal to headache from ondansetron. Incremental cost-effectiveness ratio = (cost of treatment A − cost of treatment B)/(success of treatment A − success of treatment B).

* For example: when comparing ondansetron 4 mg and droperidol 0.625 mg for all the three outcomes, droperidol 0.625 mg is superior to ondansetron 4 mg. Superior = lower cost and more efficacious.

Table 7. Mean (SD) and Median (10th–90th percentile) Management Cost per Patient for an Episode of Postoperative Nausea or Vomiting

	Emesis (n = 641)	Nausea (n = 593)
Antiemetic cost		
Mean (SD)	6.9 (9.7)	2.4 (5.5)
Median (10th–90th)	0.86 (0–18.7)	0 (0–9)
Material cost		
Mean (SD)	0.5 (0.7)	0.04 (0.1)
Median (10th–90th)	0.3 (0.1–11.5)	0 (0–0.1)
Personnel		
MD/CRNA		
Mean (SD)	15 (113.2)	3.2 (57.5)
Median (10th–90th)	0 (0–0)	0 (0–0)
PACU nurses		
Mean (SD)	238.1 (241.7)	63.1 (121.8)
Median (10th–90th)	168 (42–525)	0 (0–210)
PACU delay		
Mean (SD)	10.9 (52.8)	5.8 (55.8)
Median (10th–90th)	0 (0–32)	0 (0–0)
Hospital admission		
Mean (SD)	31.3 (197.5)	7.1 (86.4)
Median (10th–90th)	0 (0–0)	0 (0–0)
Total cost		
Mean (SD)	304.6 (384.3)*	82.2 (185.2)
Median (10th–90th)	194 (42–637)*	0.6 (0–222)

* $P = 0.0001$, nausea *versus* emesis episode.

CRNA = certified nurse anesthetist; MD = anesthesiologist; PACU = post-anesthesia care unit.

of emesis, and the costs of rescue antiemetic drugs and management of side effects from the prophylactic antiemetics. Direct and indirect costs were included in the cost of unanticipated hospital stay. Some indirect costs were harder to quantify, such as the opportunity costs occurring as a result of nurses having less time available to spend with other patients while treating patients with PONV.[3]

Intangible costs of pain or suffering associated with PONV are difficult to quantify and were not considered in this analysis. Previous studies suggest that patients place a high value in avoiding PONV and are willing to accept some side effects from antiemetics, including dysphoria, pain, and decreased mental acuity.[22] The willingness of a patient to pay for an antiemetic may be used to assign a cost benefit in avoiding PONV. However, there is often a lack of consistency in what patients are willing to pay for prevention of PONV because this depends on severity and duration of the PONV, previous experience of PONV, and socioeconomic factors. Recently, Diez[23] surveyed parents of children who underwent previous surgery regarding their willingness to pay for an antiemetic and found that the median willingness to pay for a reduction in postoperative emesis to be approximately $80. In an analysis of cost-benefit ratio for prophylactic antiemetic therapy, Gan *et al.*[24] showed that patients are willing to pay $60–$104 for an effective antiemetic, depending on the presence or absence of PONV on the day of survey. Furthermore, the increase in patient satisfaction associated with the use of a prophylactic antiemetic, as shown in the current study, was not taken into account. Thus, the willingness to pay such amounts may actually underestimate the value of prophylactic treatment.

In our analysis, the cost-effectiveness ratio of droperidol and ondansetron when used as antiemetic prophylaxis in patients at high risk of PONV is as follows: 1.25 mg droperidol > 0.625 mg droperidol > 4 mg ondansetron. The overall costs depend on the various cost components of the ondansetron and droperidol groups (table 3). Nursing personnel costs constitute the major portion of the overall costs in all four groups. There is a wide distribution of total costs per patient within each group. Although the costs to most patients were small, a few

patients experienced severe PONV necessitating significantly more nursing care. Patients who required unanticipated hospital admission greatly increased the overall total cost in each group; however, there were no differences in the admission rates and costs of hospital stay among the four groups. The median costs for each group are lower than mean costs, suggesting that the data were skewed, which is not surprising. However, it did not change the conclusions of the study; namely, that prophylactic antiemetic reduces overall PONV-related costs in this population. Interestingly, we found mean and median costs of treating a patient with vomiting are at least three times as high the cost of treating nausea.

Personnel costs in the PACU constitute the major portion of recovery costs. PACU care necessitates a sufficient number of nurses to be present at any time to care for all the patients. The number of personnel necessary depends on the peak number of patients in the PACU and must be sufficient to prevent a "bottleneck" in patient flow. Previous studies have suggested that more efficacious antiemetics would not decrease time to discharge sufficiently to decrease the peak number of patients in the PACU.[25] For example, because personnel costs are semifixed, attending to the care of several patients with PONV or adding a few minutes to a patient's PACU time may not necessarily increase salary costs, just more fully use the existing nurses.[26] Conversely, increasing the use of perioperative resources may eventually necessitate the need to employ more nurses in the PACU and increase expenditure in discrete steps. Time spent by nurses caring for patients with PONV may result in fewer nurses available for other nursing tasks. This is based on the concept of opportunity costs, in which it is assumed that nurses treating patients with PONV have less time available to spend with other patients and that this work would have to be done by additional personnel hired for this purpose. However, personnel costs may be variable if personnel are paid extra money for working additional hours in the PACU. Many anesthesia studies still treat PACU nursing personnel costs as simple variable costs and calculate "cost savings" as minutes of reduced PACU stay multiplied by nursing costs per hour.[27,28] Many factors affect personnel costs; for example, the way the operating room and PACU are scheduled, how nurses are paid, salaries, and the number of patients an ambulatory surgical center cares for in a day.[29] Therefore, we calculated costs with and without labor costs included. It is important to note that the overall cost is higher in the placebo group compared with the treatment groups even when labor costs were excluded from the analysis.

Time to home readiness was used rather than the time of discharge from the ambulatory surgery center because the time of actual discharge from the hospital is dependent on many factors that are not related to the medical condition of the patient.[30] These include the completion of paperwork, time waiting for discharge medication, and availability of transportation home. The current study found no significant difference in the mean time to home readiness between the ondansetron, droperidol, and placebo groups. However, other studies produced conflicting results. Splinter *et al.*[31] demonstrated that patients receiving ondansetron had a shorter hospital stay compared with those receiving placebo. Grond *et al.*[32] found that 2.5 mg droperidol was associated with a delay in recovery room discharge, whereas other studies reported no significant difference between 1.25 mg droperidol intravenously and 4 mg ondansetron intravenously.

The side effects of antiemetics may limit their usefulness in the ambulatory unit. Increased drowsiness, delayed discharge, and postdischarge restlessness have been reported with high doses of droperidol, and headaches have been associated with the administration of ondansetron.[33,34] The associated side effects may be reduced by decreasing the dose of the antiemetic. In this study, approximately one half of the patients in each treatment group reported adverse events. Most were minor and generally did not delay hospital discharge. The low doses of droperidol used in this study may explain why there was no difference in sedation among the droperidol, ondansetron, and placebo groups.

We did not collect data to enable analysis of cost-effectiveness ratio from the societal perspective. However, Tang *et al.*[30] found that costs from the societal perspective were very similar to costs from the hospital perspective. Additional societal costs include costs of a caretaker, lost wages, and cost of travel to a pharmacy, physician, or hospital. The cost of rescue antiemetic drugs administered after discharge and the cost of materials used for emesis clean up at home constitute only a minor proportion of overall costs.

The cost-effectiveness of antiemetics depends on the effectiveness and cost of the drug, frequency and severity of PONV, and whether the antiemetic is used as prophylactic or rescue medication. As the frequency of PONV decreases, it becomes less cost-effective to use prophylactic antiemetics. Tang *et al.*[30] calculated the frequency of PONV for this crossover point as 30% for

ondansetron and 13% for droperidol. However, a recent study suggests that there is no benefit with the prophylactic use of antiemetics because there was no clinically important difference in patient outcomes and satisfaction between the use of prophylactic antiemetics and the use of rescue antiemetics when PONV developed in patients.[35] The authors considered all patients, regardless of the risk of developing PONV. Indeed, in a subgroup analysis, patients with a history of PONV who were undergoing emetogenic surgery achieved greater satisfaction with PONV management when a prophylactic antiemetic was used. This is in agreement with the findings of the current study, and we have shown that it is also less costly to provide a prophylactic antiemetic in this high-risk group.

The preferences of the patient should also be taken into consideration. PONV is the most common reason for poor patient satisfaction during the perioperative period.[36] Moreover, patients do not consider early discharge from the surgical ambulatory unit as important as prevention of PONV.[37] Finally, analysis of patient "willingness to pay" suggests that the prevention of PONV is important and highly valued by patients.[23,24]

Prophylactic antiemetics are cost-effective in preventing PONV in ambulatory patients at high risk for PONV. Their use is also associated with an increase in patient satisfaction. In this analysis, 1.25 mg droperidol was the most cost-effective prophylactic antiemetic, followed in order by 0.625 mg droperidol and 4 mg ondansetron. These conclusions were not altered by excluding nursing labor costs in the analysis.

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Appendix: PONV Ondansetron *versus* Droperidol Participating Centers

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