



Tong J. Gan, MD* - **Tricia Meyer, MS, FASHP†** - **Christian C. Apfel, MD‡** - **Frances Chung - FRCPC§** - **Peter J. Davis - MD** - **Steve Eubanks - MD¶** - **Anthony Kovac, MD#** - **Beverly K. Philip - MD**** - **Daniel I. Sessler - MD††** - **James Temo, CRNA – MSN - MBA‡‡** - **Martin R. Tramer - MD - DPhil§§** - and **Mehernoor Watcha - MD** - Departments of *Anesthesiology and ¶Surgery - Duke University Medical Center - Durham, North Carolina - †Departments of Pharmacy and Anesthesiology - Scott and White Memorial Hospital - Texas A&M University System HSC College of Medicine – Temple - Texas - ‡Outcomes Research™ Group and Department of Anesthesiology, - University of Wuerzburg, Wuerzburg – Germany - §Department of Anesthesia, University of Toronto, Toronto, Canada - Departments of Anesthesiology and Pediatrics, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; #Department of Anesthesiology, University of Kansas Medical Center, Kansas City, Kansas - **Department of Anaesthesia, Harvard Medical School, Boston, Massachusetts - ††Outcomes Research™ Institute and Departments of Anesthesiology and Pharmacology, University of Louisville, Louisville, Kentucky - ‡‡Duke University Nurse Anesthetist Program, Durham, North Carolina - §§Division of Anaesthesiology, Geneva University Hospital, Geneva, Switzerland - and Department of Anesthesia, Children’s Hospital of Philadelphia, Philadelphia, Pennsylvania

Postoperative nausea and vomiting (PONV) continues to be a common complication of surgery. It is a limiting factor in the early discharge of ambulatory surgery patients and is a leading cause of unanticipated hospital admission [1,2](#). PONV can lead to increased recovery room time, expanded nursing care, and potential hospital admission—all factors that may increase total health care costs. Equally important are the high levels of patient discomfort and dissatisfaction associated with PONV. Patients report that avoidance of PONV is of greater concern than avoidance of postoperative pain [3](#) and are willing to spend up to US\$100 out of pocket for an effective antiemetic [4](#), yet more than a quarter of patients continue to experience PONV within 24 h of surgery [5,6](#). Among high-risk patients, the incidence of PONV can be as frequent as 70% to 80% [7](#).

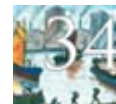
Published evidence suggests that universal PONV prophylaxis is not cost-effective. Although some advocate prophylactic antiemetic therapy for high-risk patients and rescue antiemetic treatment for episodes of PONV, the optimal approach to PONV management remains unclear to many clinicians. Guidelines for prevention and treatment of PONV based on data from systematic reviews of randomized trials have been published [8, 9](#). However, these guidelines did not consider evidence from sources other than systematic reviews.

Evidence from single studies or data from logistic regression (aiming to identify risk factors for PONV) were not included. These guidelines also need to be updated with new evidence on the control of PONV.

Establishment of Expert Guidelines

A multidisciplinary panel of experts convened to review the medical literature on PONV (up to February 2002) and to produce guidelines for its management that were valid, reliable, clinically applicable, flexible, and clear. In establishing the guidelines, the panel based their recommendations on available evidence regarding the prevention or minimization of PONV with prophylactic and/or rescue therapy.

Members of the panel were assigned specific topics to review before the meeting. Evidence was then presented and discussed at the meeting before a consensus was reached. When full agreement could not be obtained, the majority view was presented, and the lack of full agreement was stated.



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Goals of Guidelines

The panel defined the following goals for the guidelines: 1) identify the primary risk factors for PONV in adults and children, 2) reduce the baseline risks for PONV, 3) identify the optimal approach to PONV prevention and therapy in various patient populations, 4) determine the optimal choice and timing of antiemetic administration, and 5) identify the most effective antiemetic monotherapy and combination therapy regimens.

Strength of Evidence

The panel consulted the medical literature for level of evidence rating scales that were pertinent and widely used and then adapted them to the body of scientific literature relating to PONV 10, 11. In the absence of published data, recommendations were made on the basis of expert opinion.

The scales used in rating the guidelines are shown in Table 1. The aim of the evidence rating scale was to present information on both the design and the source of the data (I to V) independent of the validity of those data. The quality of the data was judged by the panel, which determined whether the recommendation was good, fair, or insufficient. For instance, a logistic regression analysis that aims to identify risk factors for PONV would be in Level IV, because such trials are not randomized. However, information emerging from that study may be judged as “A” by the panel.

Consensus Guidelines

The panel agreed that recommendations for PONV prophylaxis and treatment must consider the following factors: the patient’s level of PONV risk; potential morbidity associated with PONV, including suture dehiscence 12, esophageal rupture 13,14, hematoma formation, and aspiration pneumonitis 15; potential adverse events associated with the various antiemetics, in particular the recent Food and Drug Administration (FDA) warning about QT prolongation and fatal arrhythmias associated with droperidol; efficacy of antiemetics; costs of antiemetic therapy; and increased health care costs associated with PONV. The panel agreed that not all patients should receive PONV prophylaxis. In general, patients at small risk for PONV are unlikely to benefit from prophylaxis and would be put at unnecessary risk from



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the potential side effects of antiemetics. Thus, prophylaxis should be reserved for those patients at moderate to high risk for PONV. In developing these guidelines, the panel deliberately chose, for several reasons, not to quantify the percentage of patients who would be in the low-, moderate-, and high-risk categories.

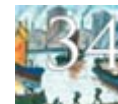
The sensitivity and specificity of the various risk scoring systems are not 100% (only approximately 70%) and hence have a degree of uncertainty 16-18. Even if health care providers knew with confidence the true underlying risk, their and the patient’s perception of this risk and, thus, the need for prophylaxis, would not be universally accepted.

The decision was made, instead, to allow the health care professionals who use the guidelines to determine the level of risk according to their own local and institutional norms. For instance, although a 20% incidence of PONV may constitute a small risk in some institutions, it may be considered a moderate risk in others because of institutional variations in rates of ambulatory surgery, types of surgery, and patient populations. In addition, the decision to give antiemetic prophylaxis should be reached by both the care provider and the patient on the basis of the best available evidence.

Throughout the guidelines, antiemetic efficacy was expressed as number needed to treat (NNT) whenever this information was available from the literature. In this context, a NNT indicates the number of patients with a high baseline risk (corresponding to a control- or placebo-event rate of 40%– 80% in a randomized, controlled trial) and who needed to receive a particular antiemetic intervention to prevent one emetic event that would have occurred had the patient not received the intervention 19.

When a dose range is presented, the smallest dose is recommended. Risk of adverse drug reactions is expressed as number needed to harm whenever this information was available from the literature.

Table 1. Evidence Rating Scale	
Level of evidence based on study design	
I.	Large randomized, controlled trial, n > 100 per group
II.	Systematic review
III.	Small randomized, controlled trial, n > 100 per group
IV.	Nonrandomized, controlled trial or case report
V.	Expert opinion
Strength of recommendation based on expert opinion	
A.	Good evidence to support the recommendation
B.	Fair evidence to support the recommendation
C.	Insufficient evidence to recommend for or against



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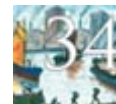
Table 2. Risk Factors for Postoperative Nausea and Vomiting (PONV) in Adults
<p>Patient-specific risk factors (7,16,17)</p> <ul style="list-style-type: none"> • Female sex (IA) • Nonsmoking status (IVA) • History of PONV/motion sickness (IVA) <p>Anesthetic risk factors</p> <ul style="list-style-type: none"> • Use of volatile anesthetics within 0 to 2 h (IA) (20) • Nitrous oxide (IIA) (21) • Use of intraoperative (IIA) and postoperative (IVA) opioids (7,18,21–23) <p>Surgical risk factors</p> <ul style="list-style-type: none"> • Duration of surgery (each 30-min increase in duration increases PONV risk by 60%, so that a baseline risk of 10% is increased by 16% after 30 min) (IVA) (16) • Type of surgery (laparoscopy, ear-nose-throat, neurosurgery, breast, strabismus, laparotomy, plastic surgery) (IVB)(16,24,25)

Guideline 1: Identify Adults at High Risk for PONV

Risk factors for PONV in adults are shown in Table 2. The identification of individuals at high risk for PONV can narrow the pool of potential candidates for prophylactic antiemetic therapy, indicating those most likely to benefit and reducing antiemetic side effects and costs for patients unlikely to benefit. Apfel et al. 7 created a simplified risk factor chart identifying four primary risk factors for PONV in patients receiving balanced inhaled anesthesia: female sex, nonsmoking status, history of PONV, and opioid use.

The incidence of PONV with the presence of none, one, two, three, or all four of these risk factors was approximately 10%, 20%, 40%, 60%, and 80%, respectively. This simplified risk score was recently validated in inpatients 18,26.

The panel did not reach full agreement about the association between type surgery and increased PONV risk; thus, type of surgery was given a strength of evidence rating of B. Apfel et al. 7 found that type of surgery was not an independent risk factor for PONV.



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When other risk factors, such as type of anesthetic and duration of operation, were considered, a causal effect on PONV by type of operation could not be established in this study. The panel noted that these data were based on inpatient surgical cases. In addition to the abovementioned risk factors by Apfel et al., a large study of 18,000 ambulatory patients showed an increased risk for PONV (15%) among patients undergoing breast augmentation, dental surgery, orthopedic shoulder procedures, gynecologic laparoscopy (for sterilization), varicose vein stripping, and strabismus repair 16.

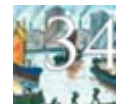
Guideline 2: Identify Children at High Risk for Postoperative Vomiting

Risk factors for postoperative vomiting (POV) in children are shown in Table 3. The panel recommended identification of children at high risk for POV as candidates for prophylactic antiemetic therapy. Because of the difficulty in diagnosing nausea in younger children, only vomiting is studied and treated in this population.

POV is problematic in children. It is one of the leading postoperative complaints from parents and the leading cause of readmission 28. Most risk factors for POV in children are the same as those in adults, with several important differences. POV increases as children age. It is rare in children younger than 2 yr old. However, children aged 3 yr have an average vomiting incidence of 40%—almost twice as frequent as the rate in adults 5. The increased vomiting incidence tapers when children reach puberty. Sex differences in risk of vomiting are not seen in children before puberty 27.

Operations associated with an increased incidence of vomiting in children include adenotonsillectomy, strabismus repair, hernia repair, orchiopexy, and penile surgery 5.

Table 3. Risk Factors For Postoperative Vomiting (POV) in Children
<ul style="list-style-type: none"> • Risk factors for children are similar to those in adults, with the following differences: • Studies in children are often limited to data on vomiting only and not nausea • Vomiting incidence is twice as frequent among children as among adults 5 • Risk increases as children age, decreasing after puberty • Sex differences are not seen before puberty 27 • Risk increases more consistently with specific operations 5



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Table 4. Strategies to Reduce Baseline Risk
<ul style="list-style-type: none"> • Use of regional anesthesia (IIIA) 16 • Use of propofol for induction and maintenance of anesthesia (IA) 29 • Use of intraoperative supplemental oxygen (IIIB) 30,31 • Use of hydration (IIIA) 32 • Avoidance of nitrous oxide (IIA) 19,33 • Avoidance of volatile anesthetics (IA) 18,20 • Minimization of intraoperative (IIA) and postoperative (IVA) opioids 7,18,21–23 • Minimization of neostigmine (IIA) 34

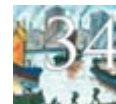
Guideline 3: Reduce Baseline Risk Factors for PONV

Approaches for decreasing baseline risk factors are presented in Table 4. A reduction in baseline risk factors can significantly decrease the incidence of PONV (8,9). The panel thus recommended reducing baseline risk when clinically practical. Sinclair et al. 16 found that patients receiving general anesthesia had an 11-fold increased risk for PONV compared with those receiving regional anesthesia. Propofol, administered for the induction and maintenance of anesthesia, effectively reduced early PONV incidence (0–6 h) 29.

The NNT with propofol to reduce PONV. Duration of surgery (each 30-min increase in duration increases PONV risk by 60%, so that a baseline risk of 10% is increased by 16% after 30 min) (IVA) 16 Type of surgery (laparoscopy, ear-nose-throat, neurosurgery, breast, strabismus, laparotomy, plastic surgery) (IVB) 16,24,25 is approximately 5, compared with not using propofol.

Among patients undergoing colon resection, use of supplemental oxygen (80% oxygen) reduced PONV by half when it was administered perioperatively and for 2 h after surgery 30. Oxygen supplementation restricted to the intraoperative period also halved the risk of PONV 31. Hydration reduced the incidence of PONV 32.

Avoiding nitrous oxide and volatile inhaled anesthetics and minimizing intraoperative and postoperative opioid use reduced the incidence of PONV 7,18-23,33. To achieve satisfactory analgesia without opioids, alternate modalities of pain management may be used. For instance, in patients undergoing



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tonsillectomy, nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids are equianalgesic, but NSAIDs are less emetogenic; the NNT to prevent PONV with a NSAID during surgery compared with an opioid is approximately 9 ²². Neostigmine, used at the end of surgery, is associated with increased PONV, especially when used in large doses (μ 2.5 mg) ³⁴.

Minimizing large doses of this drug can reduce PONV. Many of the aforementioned strategies to reduce baseline PONV risk have been incorporated into a multimodal approach to minimize PONV ³⁵. Scuderi et al. ³⁶ tested the efficacy of a multimodal approach to reducing PONV. Their multimodal approach consisted of preoperative anxiolysis and aggressive hydration; oxygen; prophylactic antiemetics (droperidol and dexamethasone at the induction and ondansetron at the end of surgery); total IV anesthesia with propofol and remifentanyl; and ketorolac.

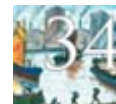
No nitrous oxide or neuromuscular blockade was used. Patients who received multimodal therapy had a 98% complete response rate, compared with a 76% response rate among patients receiving antiemetic monotherapy and a 59% response rate among those receiving routine anesthetic plus saline placebo.

Guideline 4: Antiemetic Therapy for PONV Prophylaxis in Adults

Prophylactic doses and timing for the administration of antiemetics in adults are shown in Table 5. Serotonin Receptor Antagonists. The panel agreed that there is no evidence of any difference in the efficacy and safety profiles of the serotonin (5-HT₃) receptor antagonists—ondansetron, dolasetron, granisetron, and tropisetron—in the prophylaxis of PONV. These drugs are most effective when given at the end of surgery ^{38,39}.

Most research on the 5-HT₃ receptor antagonists has been performed with ondansetron, which has greater antiemetic than antinausea effects ³⁷. Ondansetron 4 mg has a NNT of approximately 7 in the prevention of nausea compared with placebo (0–24 h); the 8-mg dose has a NNT of approximately 6 ³⁷.

For the prevention of vomiting (0–24 h), ondansetron 4 mg has a NNT of approximately 6; the 8-mg dose has a NNT of approximately 5 ³⁷.



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Dolasetron has shown efficacy for the prophylaxis of PONV at a dose of 12.5 mg. In a study of 635 high-risk patients, Graczyk et al. [39](#) found a statistically significant increase in complete responders, a decreased need for rescue antiemetic, less nausea, and more patient satisfaction with dolasetron versus placebo. Granisetron 0.35–1 mg and tropisetron 5 mg are also used for PONV prophylaxis and treatment [40-43](#). Smaller doses of granisetron (0.1 mg) are effective when used for treatment [83](#). When a dose range is presented, the smallest dose is recommended.

The 5-HT₃ antagonists have a favorable side effect profile and are considered equally safe. The number needed to harm with a single dose of ondansetron is 36 for headache, 31 for increased liver enzymes, and 23 for constipation; this means, for example, that 36 patients would need to be treated with a single dose of this drug for one to develop headache who would not have done so had they all received a placebo [37](#). Dexamethasone. Dexamethasone, administered at a prophylactic dose of 8–10 mg IV, effectively prevents nausea and vomiting with a NNT of approximately 4 [44](#).

More recently, smaller doses (2.5–5 mg) have been found to be as effective [45,46](#). Dexamethasone appears to be most effective when administered before the induction of anesthesia rather than at the end [47](#). Side effects with long-term administration of corticosteroids can include wound infection and adrenal suppression, among others, but adverse events have not been noted after a single bolus dose of dexamethasone (44). Droperidol. Prophylactic doses of droperidol (well below 1 mg) are effective for the prevention of PONV [48–50](#).

The efficacy of droperidol is equivalent to that of ondansetron for PONV prophylaxis, with a NNT of approximately 5 for prevention of nausea and vomiting (0–24 h) [8](#). Droperidol is most effective when administered at the end of surgery [50](#). It is also effective when given concomitantly with patient-controlled analgesia devices that deliver morphine, with a NNT of approximately 3 [57](#). Recently, the FDA issued a “black box” warning about droperidol [58](#). The warning states that droperidol may cause death or life-threatening events associated with QT prolongation and torsades de pointes.

This warning is based on 10 reported cases (1.25 mg or below) in association with droperidol use over the approximately 30 yr that it has been available on the market [84](#). It is interesting to note that there has not been a single case report in a peer-reviewed journal in which droperidol in doses used for the management of PONV has been associated with QTc prolongation, arrhythmias, or cardiac arrest [35](#).



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Likewise, in Europe and elsewhere, there has been no such report. The panel expressed considerable concerns about the quality and quantity of evidence and the validity of the FDA conclusion. If it were not for the “black-box” warning, droperidol would have been the panel’s overwhelming first choice for PONV prophylaxis.

Other Antiemetics. Most of the older antiemetics (for instance, promethazine, haloperidol, and prochlorperazine) have been tested in single studies. Their role in the control of PONV is still poorly understood. Dimenhydrinate, an antihistaminic, has been reviewed systematically [51](#).

Its degree of efficacy seems to be similar to that of the 5-HT₃ receptor antagonists and droperidol. Transdermal scopolamine has also been reviewed systematically [55](#).

Transdermal scopolamine applied the evening before surgery or 4 h before the end of anesthesia has an antiemetic effect. Its limitations are a 2- to 4-honset of effect, as well as its medical contraindications and age-related considerations [56](#).

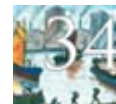
Promethazine 12.5– 25 mg IV and prochlorperazine 5–10 mg IV, administered at the end of surgery, have been shown to be effective [53,54](#). However, use of phenothiazines is limited in the ambulatory setting because of the resulting sedation. All three of these drugs may cause dizziness, dry mouth, and sedation. IM ephedrine is another antiemetic that has shown efficacy for inpatient and outpatient surgery [52](#).

Nonpharmacological Techniques. Nonpharmacologic techniques, including acupuncture, transcutaneous electrical nerve stimulation, acupoint stimulation, and acupressure, have shown antiemetic efficacy when used before surgery.

The NNT for PONV prophylaxis (6 h after surgery) is approximately 5 for these techniques [59](#).

Hypnosis has been found to be effective when compared with placebo [60](#). Lack of Evidence of Effect. Metoclopramide, when used in standard clinical doses (10 mg IV), is ineffective for PONV prophylaxis [61](#).

Even in larger doses, metoclopramide does not appear to be an effective antiemetic [20](#). However, one study showed that metoclopramide 20 mg was comparable to 8 mg of ondansetron when administered at the end of laparoscopic cholecystectomy [62](#).



Tong J. Gan, MD* - **Tricia Meyer, MS, FASHP†** - **Christian C. Apfel, MD‡** - **Frances Chung - FRCPC§** - **Peter J. Davis - MD** - **Steve Eubanks - MD¶** - **Anthony Kovac, MD#** - **Beverly K. Philip - MD**** - **Daniel I. Sessler - MD††** - **James Temo, CRNA – MSN - MBA‡‡** - **Martin R. Tramer - MD - DPhil§§** - and **Mehernoor Watcha - MD** - Departments of *Anesthesiology and ¶Surgery - Duke University Medical Center - Durham, North Carolina - †Departments of Pharmacy and Anesthesiology - Scott and White Memorial Hospital - Texas A&M University System HSC College of Medicine – Temple - Texas - ‡Outcomes Research™ Group and Department of Anesthesiology, - University of Wuerzburg, Wuerzburg – Germany - §Department of Anesthesia, University of Toronto, Toronto, Canada - Departments of Anesthesiology and Pediatrics, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; #Department of Anesthesiology, University of Kansas Medical Center, Kansas City, Kansas - **Department of Anaesthesia, Harvard Medical School, Boston, Massachusetts - ††Outcomes Research™ Institute and Departments of Anesthesiology and Pharmacology, University of Louisville, Louisville, Kentucky - ‡‡Duke University Nurse Anesthetist Program, Durham, North Carolina - §§Division of Anaesthesiology, Geneva University Hospital, Geneva, Switzerland - and Department of Anesthesia, Children’s Hospital of Philadelphia, Philadelphia, Pennsylvania

Although most members of the panel agreed that metoclopramide could not be recommended as an antiemetic, agreement was not unanimous. Ginger root, a pharmacologic alternative to medical therapy, has not been found to be effective for PONV prophylaxis [63](#).

Cannabinoids (nabilone and tetrahydrocannabinol), although promising in the control of chemotherapy-induced sickness [64](#), have not shown antiemetic efficacy in the PONV setting [65](#). Cost-Effectiveness.

The cost-effectiveness of the various antiemetics is a determinant in their use. Hill et al [66](#) found that prophylactic PONV therapy in high-risk patients was more cost-effective than placebo because of the increased costs associated with nausea and vomiting.

They determined that the additional costs associated with PONV in placebo patients were up to 100 times more expensive compared with prophylaxis with a generic antiemetic. The cost of treating vomiting was three times more than the cost of treating nausea. The panel estimated that each episode of emesis delays discharge from the recovery room by approximately 20 min [67](#).

Similarly, a study evaluating dolasetron, droperidol, or no prophylaxis in high-risk patients found that prophylaxis with either of the two antiemetics was more cost-effective than no prophylaxis and subsequent rescue therapy [68](#). It has been suggested that PONV prophylaxis is cost-effective with the older, less expensive drugs.

Guideline 5: Antiemetic Therapy for POV Prophylaxis in Children

The prophylactic antiemetic doses recommended for children at risk for POV are shown in Table 6. The POV rate in children can be twice as frequent as the rate in adults [5](#). Thus, more children than adults may be candidates for POV prophylaxis. Ondansetron has been studied extensively for POV prophylaxis in children at a dose range of 50 to 100 g/kg. Compared with placebo, the NNT to prevent early (0 – 6 h) and late (0 –24 h) vomiting is between 2 and 3 [37](#). The optimal dose for POV prophylaxis with dolasetron, as suggested by the manufacturer, is 350 g/kg (71). Because the 5-HT₃ antagonists as a group have greater efficacy in the prevention of vomiting than nausea, they are the drugs of first choice for prophylaxis in children. When dexamethasone was used in children at a dose of 150 g/kg, the NNT to prevent early and late vomiting was approximately 4 [44](#).



Tong J. Gan, MD* - Tricia Meyer, MS, FASHP† - Christian C. Apfel, MD‡ - Frances Chung - FRCPC§ - Peter J. Davis - MD - Steve Eubanks - MD¶ - Anthony Kovac, MD# - Beverly K. Philip - MD** - Daniel I. Sessler - MD†† - James Temo, CRNA – MSN - MBA‡‡ - Martin R. Tramer - MD - DPhil§§ - and Mehernoor Watcha - MD - Departments of *Anesthesiology and ¶Surgery - Duke University Medical Center - Durham, North Carolina - †Departments of Pharmacy and Anesthesiology - Scott and White Memorial Hospital - Texas A&M University System HSC College of Medicine – Temple - Texas - ‡Outcomes Research™ Group and Department of Anesthesiology, - University of Wuerzburg, Wuerzburg – Germany - §Department of Anesthesia, University of Toronto, Toronto, Canada - Departments of Anesthesiology and Pediatrics, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; #Department of Anesthesiology, University of Kansas Medical Center, Kansas City, Kansas - **Department of Anaesthesia, Harvard Medical School, Boston, Massachusetts - ††Outcomes Research™ Institute and Departments of Anesthesiology and Pharmacology, University of Louisville, Louisville, Kentucky - ‡‡Duke University Nurse Anesthetist Program, Durham, North Carolina - §§Division of Anaesthesiology, Geneva University Hospital, Geneva, Switzerland - and Department of Anesthesia, Children’s Hospital of Philadelphia, Philadelphia, Pennsylvania

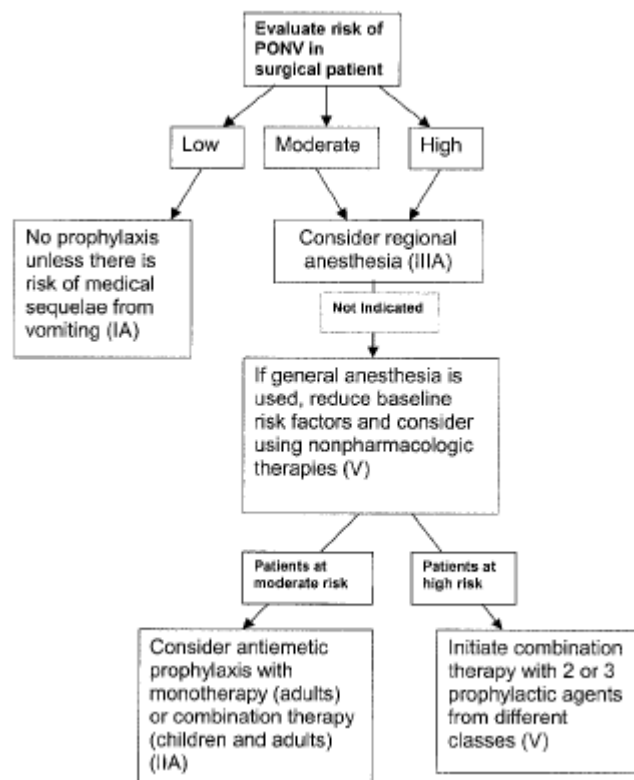
Droperidol can also be used for the prophylaxis of POV and is administered in a dose range of 50 to 75 g/kg. The NNT for prevention of early vomiting is approximately 5; for prevention of late vomiting, the NNT is between 4 and 5 50. Because of the increased risk for extrapyramidal symptoms and high levels of sedation found with droperidol, the panel recommended that this drug be reserved for patients who have failed all other therapies and are being admitted to the hospital.

Drug	Dose	Evidence	Timing	Evidence
Ondansetron	4–8 mg IV 37	IA	At end of surgery 38	IIIA
Dolasetron	12.5 mg IV 39	IA	At end of surgery 39	IIIA
Granisetron	0.35–1 mg IV 40–42	IA	At end of surgery 40,42	IIIA
Tropisetron	5 mg IV 43	IA	At end of surgery	VA
Dexamethasone	5–10 mg IV 44–46	IIA	Before induction 47	IIIA
Droperidol	0.625–1.25 mg IV 48,49	IA	At end of surgery 50	IIA
Dimenhydrinate	1–2 mg/kg IV 51	IIA		IIIB
Ephedrine	0.5 mg/kg IM 52	IIIB		IIIB
Prochlorperazine	5–10 mg IV 53	IIIA	At end of surgery 53	IIB
Promethazine	12.5–25 mg IV 54	IIIB	At end of surgery 54	
Scopolamine	Transdermal patch 55,56	IIB	Applied prior evening or 4 h before end of surgery 56	

Drug	Dose	Evidence
Ondansetron	50–100 µg/kg up to 4 mg 37	IIA
Dolasetron	350 µg/kg up to 12.5 mg 71	V
Dexamethasone	150 µg/kg up to 8 mg 44	IIA
Droperidol	50–75 µg/kg up to 1.25 mg 50	IIA
Dimenhydrinate	0.5 mg/kg 51	IIA
Perphenazine	70 µg/kg 72,73	IA

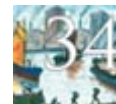
Tong J. Gan, MD* - Tricia Meyer, MS, FASHP† - Christian C. Apfel, MD‡ - Frances Chung - FRCPC§ - Peter J. Davis - MD - Steve Eubanks - MD¶ - Anthony Kovac, MD# - Beverly K. Philip - MD** - Daniel I. Sessler - MD†† - James Temo, CRNA – MSN - MBA‡‡ - Martin R. Tramer - MD - DPhil§§ - and Mehernoor Watcha - MD - Departments of *Anesthesiology and ¶Surgery - Duke University Medical Center - Durham, North Carolina - †Departments of Pharmacy and Anesthesiology - Scott and White Memorial Hospital - Texas A&M University System HSC College of Medicine – Temple - Texas - ‡Outcomes Research™ Group and Department of Anesthesiology, - University of Wuerzburg, Wuerzburg – Germany - §Department of Anesthesia, University of Toronto, Toronto, Canada - Departments of Anesthesiology and Pediatrics, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; #Department of Anesthesiology, University of Kansas Medical Center, Kansas City, Kansas - **Department of Anaesthesia, Harvard Medical School, Boston, Massachusetts - ††Outcomes Research™ Institute and Departments of Anesthesiology and Pharmacology, University of Louisville, Louisville, Kentucky - ‡‡Duke University Nurse Anesthetist Program, Durham, North Carolina - §§Division of Anaesthesiology, Geneva University Hospital, Geneva, Switzerland - and Department of Anesthesia, Children’s Hospital of Philadelphia, Philadelphia, Pennsylvania

Figure 1. Algorithm for management of postoperative nausea and vomiting (PONV).



Guideline 6: Use Prophylaxis in Patients at High Risk for PONV and Consider Prophylaxis in Patients at Moderate Risk for PONV

Figure 1 illustrates a possible algorithm for PONV prophylaxis. Prophylaxis is likely to be useful only for patients at moderate to high risk for PONV. Patients at low risk for PONV are usually not given PONV prophylaxis unless they are at risk for medical sequelae from vomiting (i.e., patients with wired jaws or increased intracranial pressure or who are having fundoplication surgery).



Tong J. Gan, MD* - Tricia Meyer, MS, FASHP† - Christian C. Apfel, MD‡ - Frances Chung - FRCPC§ - Peter J. Davis - MD - Steve Eubanks - MD¶ - Anthony Kovac, MD# - Beverly K. Philip - MD** - Daniel I. Sessler - MD†† - James Temo, CRNA – MSN - MBA‡‡ - Martin R. Tramer - MD - DPhil§§ - and Mehernoor Watcha - MD - Departments of *Anesthesiology and ¶Surgery - Duke University Medical Center - Durham, North Carolina - †Departments of Pharmacy and Anesthesiology - Scott and White Memorial Hospital - Texas A&M University System HSC College of Medicine – Temple - Texas - ‡Outcomes Research™ Group and Department of Anesthesiology, - University of Wuerzburg, Wuerzburg – Germany - §Department of Anesthesia, University of Toronto, Toronto, Canada - Departments of Anesthesiology and Pediatrics, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; #Department of Anesthesiology, University of Kansas Medical Center, Kansas City, Kansas - **Department of Anaesthesia, Harvard Medical School, Boston, Massachusetts - ††Outcomes Research™ Institute and Departments of Anesthesiology and Pharmacology, University of Louisville, Louisville, Kentucky - ‡‡Duke University Nurse Anesthetist Program, Durham, North Carolina - §§Division of Anaesthesiology, Geneva University Hospital, Geneva, Switzerland - and Department of Anesthesia, Children’s Hospital of Philadelphia, Philadelphia, Pennsylvania

Among patients at moderate and high risk for PONV, regional anesthesia should be considered. If general anesthesia is used, the panel recommended reduction of baseline risk factors when possible (Guideline 3).

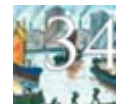
Nonpharmacologic therapies, such as acupuncture, acupressure, transcutaneous electrical nerve stimulation, or acupoint stimulation, should be considered. Antiemetics recommended for prophylaxis in adults and children are shown in Tables 5 and 6. Adults and children who are at moderate or high risk for PONV should receive combination therapy with two or three prophylactic drugs from different classes. In general, combination therapy is superior to monotherapy for PONV prophylaxis [74,75](#). Drugs with different mechanisms of action should be used in combination to optimize efficacy. The 5-HT₃ antagonists, which have better antiemetic than antinausea efficacy, yet are associated with headache, can be used in combination with droperidol, which has greater antinausea efficacy and a protective effect against headache [9](#).

The 5-HT₃ antagonists can also be effectively combined with dexamethasone [44](#). The combination of a 5-HT₃ antagonist and promethazine significantly reduces both the frequency and severity of nausea and vomiting [54](#).

Optimal antiemetic dosing with combination therapy needs to be established. It has been suggested that, with combination therapy, dexamethasone doses should not exceed 10 mg IV (150 µg/kg in children) and droperidol doses should not exceed 1 mg IV (50 µg/kg in children) (9). When used in combination with another drug, ondansetron doses in adults typically do not exceed 4 mg and can be much smaller (50 µg/kg in both children and adults) (9).

Guideline 7: Provide Antiemetic Treatment to Patients with PONV Who Did Not Receive Prophylaxis or in Whom Prophylaxis Failed

The recommended treatment regimens for PONV are shown in Table 7. When persistent nausea and vomiting occur after the patient has left the postanesthesia care unit, the first response should be a bedside examination to exclude an inciting medication or mechanical factor. Contributing factors might include morphine patient-controlled analgesia, blood draining down the throat, or an abdominal obstruction.



Tong J. Gan, MD* - **Tricia Meyer, MS, FASHP†** - **Christian C. Apfel, MD‡** - **Frances Chung - FRCPC§** - **Peter J. Davis - MD** - **Steve Eubanks - MD¶** - **Anthony Kovac, MD#** - **Beverly K. Philip - MD**** - **Daniel I. Sessler - MD††** - **James Temo, CRNA – MSN - MBA‡‡** - **Martin R. Tramer - MD - DPhil§§** - and **Mehernoor Watcha - MD** - Departments of *Anesthesiology and ¶Surgery - Duke University Medical Center - Durham, North Carolina - †Departments of Pharmacy and Anesthesiology - Scott and White Memorial Hospital - Texas A&M University System HSC College of Medicine – Temple - Texas - ‡Outcomes Research™ Group and Department of Anesthesiology, - University of Wuerzburg, Wuerzburg – Germany - §Department of Anesthesia, University of Toronto, Toronto, Canada - Departments of Anesthesiology and Pediatrics, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; #Department of Anesthesiology, University of Kansas Medical Center, Kansas City, Kansas - **Department of Anaesthesia, Harvard Medical School, Boston, Massachusetts - ††Outcomes Research™ Institute and Departments of Anesthesiology and Pharmacology, University of Louisville, Louisville, Kentucky - ‡‡Duke University Nurse Anesthetist Program, Durham, North Carolina - §§Division of Anaesthesiology, Geneva University Hospital, Geneva, Switzerland - and Department of Anesthesia, Children’s Hospital of Philadelphia, Philadelphia, Pennsylvania

Once medication and mechanical factors are excluded, rescue antiemetic therapy can be initiated. If a patient has received no prophylaxis, therapy with small-dose 5-HT₃ receptor antagonists should be initiated on the first signs of PONV [76](#). In general, treatment doses of the 5-HT₃ antagonists are about a quarter of those used for prophylaxis [77](#). Small-dose therapy includes ondansetron 1.0 mg, dolasetron 12.5 mg, granisetron 0.1 mg, and tropisetron 0.5 mg. NNTs to prevent further PONV within 24 h are between 4 and 5 [76](#). For all the other antiemetics, data on their therapeutic efficacy are sparse, and optimal doses are unknown. One study found that promethazine was as effective as PONV treatment in the general surgical population [78](#). Droperidol was not different from ondansetron as therapy for established PONV [77](#).

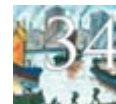
When prophylaxis with dexamethasone fails to prevent PONV, treatment with a small-dose 5-HT₃ receptor antagonist has been recommended [79](#). When prophylaxis with a 5-HT₃ antagonist is inadequate to prevent PONV, a 5-HT₃ antagonist should not be initiated as rescue therapy within the first 6 h after surgery because it confers no additional benefit [80](#). Similarly, the failure of prophylaxis with a 5-HT₃ antagonist plus dexamethasone should be treated with a drug from another class: for instance, droperidol or promethazine [78](#).

A triple-therapy dosing regimen (for instance, a 5-HT₃ antagonist, droperidol, and dexamethasone) has never been tested. If the patient experiences PONV symptoms despite triple prophylaxis, the triple regimen should not be repeated within the first 6 h of administration, and alternative antiemetics should be administered.

Propofol, 20 mg as needed, can be considered for rescue therapy in patients still in the postanesthesia care unit [81,82](#). The antiemetic effect with small doses of propofol is probably brief.

When PONV occurs more than 6 h after surgery, repeat dosing of 5-HT₃ antagonists and droperidol can be considered. The optimal doses and interval for readministration of these two antiemetics remain unknown.

The panel recommended that dexamethasone administration not be repeated more often than every 8 h.



Tong J. Gan, MD* - Tricia Meyer, MS, FASHP† - Christian C. Apfel, MD‡ - Frances Chung - FRCPC§ - Peter J. Davis - MD - Steve Eubanks - MD¶ - Anthony Kovac, MD# - Beverly K. Philip - MD** - Daniel I. Sessler - MD†† - James Temo, CRNA – MSN - MBA‡‡ - Martin R. Tramer - MD - DPhil§§ - and Mehernoor Watcha - MD - Departments of *Anesthesiology and ¶Surgery - Duke University Medical Center - Durham, North Carolina - †Departments of Pharmacy and Anesthesiology - Scott and White Memorial Hospital - Texas A&M University System HSC College of Medicine – Temple - Texas - ‡Outcomes Research™ Group and Department of Anesthesiology, - University of Wuerzburg, Wuerzburg – Germany - §Department of Anesthesia, University of Toronto, Toronto, Canada - Departments of Anesthesiology and Pediatrics, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; #Department of Anesthesiology, University of Kansas Medical Center, Kansas City, Kansas - **Department of Anaesthesia, Harvard Medical School, Boston, Massachusetts - ††Outcomes Research™ Institute and Departments of Anesthesiology and Pharmacology, University of Louisville, Louisville, Kentucky - ‡‡Duke University Nurse Anesthetist Program, Durham, North Carolina - §§Division of Anaesthesiology, Geneva University Hospital, Geneva, Switzerland - and Department of Anesthesia, Children’s Hospital of Philadelphia, Philadelphia, Pennsylvania

Table 7. Antiemetic Treatment for Patients with Postoperative Nausea and Vomiting (PONV) Who Did Not Receive Prophylaxis or in Whom Prophylaxis Failed—Exclude Inciting Medication or Mechanical Causes of PONV (V)	
Initial Therapy	Failed Prophylaxis
No prophylaxis or dexamethasone	Administer small-dose 5-HT3 antagonista (IIA)
5-HT3 antagonista plus second agent ^b	Use drug from different class (V)
Triple therapy with 5-HT3 antagonista plus two other agents ^b when PONV occurs _6 h after surgery (V)	Do not repeat initial therapy (IIIA)
	Use drug from different class (V) or propofol, 20 mg as needed in postanesthesia care unit (adults) (IIIB)
Triple therapy with 5-HT3 antagonista plus two other agents ^b when PONV occurs _6 h after surgery (V)	Repeat 5-HT3 antagonista and droperidol (not dexamethasone or transdermal scopolamine)
	Use drug from different class (V)

5-HT3 serotonin.

a Small-dose 5-HT antagonist dosing: ondansetron 1.0 mg, dolasetron 12.5 mg, granisetron 0.1 mg, and tropisetron 0.5 mg.

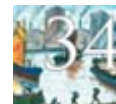
b Alternative therapies for rescue: droperidol 0.625 mg IV, dexamethasone (2–4 mg IV), and promethazine 12.5 mg IV.

Guideline 7: Provide Antiemetic Treatment to Patients with PONV Who Did Not Receive Prophylaxis or in Whom Prophylaxis Failed

The recommended treatment regimens for PONV are shown in Table 7. When persistent nausea and vomiting occur after the patient has left the postanesthesia care unit, the first response should be a bedside examination to exclude an inciting medication or mechanical factor.

Contributing factors might include morphine patient-controlled analgesia, blood draining down the throat, or an abdominal obstruction. Once medication and mechanical factors are excluded, rescue antiemetic therapy can be initiated. If a patient has received no prophylaxis, therapy with small-dose 5-HT3 receptor antagonists should be initiated on the first signs of PONV [76](#).

In general, treatment doses of the 5-HT3 antagonists are about a quarter of those used for prophylaxis [77](#). Small-dose therapy includes ondansetron 1.0 mg, dolasetron 12.5 mg, granisetron 0.1 mg, and ropisetron 0.5 mg. NNTs to prevent further PONV within 24 h are between 4 and 5 [76](#). For all the other antiemetics,



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data on their therapeutic efficacy are sparse, and optimal doses are unknown. One study found that promethazine was as effective as PONV treatment in the general surgical population [78](#).

Droperidol was not different from ondansetron as therapy for established PONV [77](#). When prophylaxis with dexamethasone fails to prevent PONV, treatment with a small-dose 5-HT3 receptor antagonist has been recommended [79](#). When prophylaxis with a 5-HT3 antagonist is inadequate to prevent PONV, a 5-HT3 antagonist should not be initiated as rescue therapy within the first 6 h after surgery because it confers no additional benefit [80](#). Similarly, the failure of prophylaxis with a 5-HT3 antagonist plus dexamethasone should be treated with a drug from another class: for instance, droperidol or promethazine [78](#).

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The panel recommended that dexamethasone administration not be repeated more often than every 8 h.

Conclusion

These guidelines provide a comprehensive, evidencebased reference tool for the management of patients at risk for PONV. Not all surgical patients will benefit from antiemetic prophylaxis; thus, identification of patients who are at increased risk is imperative.

The first step in reducing PONV risk is to reduce baseline risk factors among patients at risk. Drugs for PONV prophylaxis for adults should be considered for use as monotherapy or in combination for patients at moderate risk for PONV. There is increasing evidence that the combination of several potentially beneficial factors (multimodal approach) may lead to an improved outcome. Double and triple antiemetic

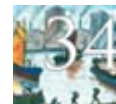


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combinations are recommended for patients at high risk for PONV. All prophylaxis in children at moderate or high risk for POV should be with combination therapy using a 5-HT3 antagonist and a second drug. Antiemetic rescue therapy should be administered to patients who have an emetic episode after surgery. If PONV occurs within 6 h after surgery, patients should not receive a repeat dose of the prophylactic antiemetic. An emetic episode more than 6 h after surgery can be treated with any of the drugs used for prophylaxis except dexamethasone and transdermal scopolamine.

References

1. Gold BS, Kitz DS, Lecky JH, Neuhaus JM. Unanticipated admission to the hospital following ambulatory surgery. *JAMA* 1989; 262:3008–10.
2. Fortier J, Chung F, Su J. Unanticipated admission after ambulatory surgery: a prospective study. *Can J Anaesth* 1998;45: 612–9.
3. Macario A, Weinger M, Carney S, Kim A. Which clinical anesthesia outcomes are important to avoid? *Anesth Analg* 1999;89: 652–8.
4. Gan T, Sloan F, Dear G, et al. How much are patients willing to pay to avoid postoperative nausea and vomiting? *Anesth Analg* 2001;92:393–400.
5. Lerman J. Surgical and patient factors involved in postoperative nausea and vomiting. *Br J Anaesth* 1992;69(Suppl 1):S24–32.
6. Cohen MM, Duncan PG, DeBoer DP, Tweed WA. The postoperative interview: assessing risk factors for nausea and vomiting. *Anesth Analg* 1994;78:7–16.
7. Apfel CC, Laara E, Koivuranta M, et al. A simplified risk score for predicting postoperative nausea and vomiting. *Anesthesiology* 1999;91:693–700.
8. Tramer`r MR. A rational approach to the control of postoperative nausea and vomiting: evidence from systemic reviews. I. Efficacy and harm of antiemetic interventions, and methodological issues. *Acta Anaesthesiol Scand* 2001;45:4–13.
9. Tramer`r MR. A rational approach to the control of postoperative nausea and vomiting: evidence from systemic reviews. II. Recommendations for prevention and treatment and research agenda. *Acta Anaesthesiol Scand* 2001;45:14–9.
10. Grimes DA. An overview of clinical research: the lay of the land. *Lancet* 2002;359:57–61.
11. Harbour R, Miller J. A new system [Scottish Intercollegiate Guidelines Network (SIGN)] for grading recommendations in evidence based guidelines. *BMJ* 2001;323:334–6.



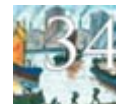
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12. Col C, Soran A, Col M. Can postoperative abdominal wound dehiscence be predicted? *Tokai J Exp Clin Med* 1998;23:123–7.
13. Temes R, Feteiha M, Mapel D, et al. Esophageal rupture after regional anesthesia: report of two cases. *J Clin Gastroenterol* 1999;28:360–3.
14. Ferri L, Mulder D. Soft-tissue case 40: Boerhaave’s syndrome—postemetic esophageal rupture. *Can J Surg* 2001;44: 259, 306.
15. Nanji GM, Maltby JR. Vomiting and aspiration pneumonitis with the laryngeal mask airway. *Can J Anaesth* 1992;39:69–70
16. Sinclair DR, Chung F, Mezei G. Can postoperative nausea and vomiting be predicted? *Anesthesiology* 1999;91:109–18.
17. Koivuranta M, Laara E, Snare L, Alahuhta S. A survey of postoperative nausea and vomiting. *Anaesthesia* 1997;52:443–9.
18. Apfel CC, Kranke P, Eberhart LH, et al. Comparison of predictive models for postoperative nausea and vomiting. *Br J Anaesth* 2002;88:234–40.
19. Tramer M, Moore A, McQuay H. Meta-analytic comparison of prophylactic antiemetic efficacy for postoperative nausea and vomiting: propofol anaesthesia vs. omitting nitrous oxide vs. total i.v. anaesthesia with propofol. *Br J Anaesth* 1997;78:256–9.
20. Apfel CC, Katz MH, Kranke P, 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;88:659–68.
21. Sukhani R, Vazquez J, Pappas AL, et al. Recovery after propofol with and without intraoperative fentanyl in patients undergoing ambulatory gynecologic laparoscopy. *Anesth Analg* 1996; 83:975–81.
22. Møiniche S, Rømsing J, Dahl JB, Tramer MR. Nonsteroidal antiinflammatory drugs and the risk of operative site bleeding after tonsillectomy: a quantitative systematic review. *Anesth Analg* 2003;96:68–77.
23. Polati E, Verlato G, Finco G, et al. Ondansetron versus metoclopramide in the treatment of postoperative nausea and vomiting. *Anesth Analg* 1997;85: 395–9.
24. Fabling JM, Gan TJ, El-Moalem HE, et al. A randomized, double-blinded comparison of ondansetron, droperidol, and placebo for prevention of postoperative nausea and vomiting after supratentorial craniotomy. *Anesth Analg* 2000;91:358–61.
25. Gan TJ, Ginsberg B, Grant AP, Glass PS. Double-blind, randomized comparison of ondansetron and intraoperative propofol to prevent postoperative nausea and vomiting. *Anesthesiology* 1996;85:1036–42.
26. Pierre S, Benais H, Pouymayou J. Apfel’s simplified score may favourably predict the risk of postoperative nausea and vomiting. *Can J Anaesth* 2002;49:237–42.
27. Rowley MP, Brown TCK. Postoperative vomiting in children. *Anaesth Intensive Care* 1982;10:309–13.



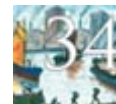
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28. Derrico C, Voepel-Lewis TD, Siewert M, Malviya S. Prolonged recovery stay and unplanned admission of the pediatric surgical outpatient: an observational study. *J Clin Anesth* 1998;10:482–7.
29. Visser K, Hassink EA, Bonsel GJ, et al. Randomized controlled trial of total intravenous anesthesia with propofol versus inhalation anesthesia with isoflurane-nitrous oxide: postoperative nausea with vomiting and economic analysis. *Anesthesiology* 2001;95:616–26.
30. Greif R, Lacity S, Rapf B, et al. Supplemental oxygen reduces the incidence of postoperative nausea and vomiting. *Anesthesiology* 1999;91:1246–52.
31. Goll V, Ozan A, Greif R, et al. Ondansetron is no more effective than supplemental intraoperative oxygen for prevention of postoperative nausea and vomiting. *Anesth Analg* 2001;92: 112–7.
32. Yogendran S, Asokumar B, Cheng DC, Chung F. A prospective randomized double-blinded study of the effect of intravenous fluid therapy on adverse outcomes on outpatient surgery. *Anesth Analg* 1995;80:682–6.
33. Tramer`r M, Moore A, McQuay H. Omitting nitrous oxide in general anaesthesia: meta-analysis of intraoperative awareness and postoperative emesis in randomized controlled trials. *Br J Anaesth* 1996;76:186–93.
34. Tramer`r MR, Fuchs-Buder T. Omitting reversal of neuromuscular blockade: effect on postoperative nausea and vomiting and risk of residual paralysis: a systemic review. *Br J Anaesth* 1999; 82:379–86.
35. Gan TJ. Postoperative nausea and vomiting: can it be eliminated? *JAMA* 2002;287:1233–6.
36. Scuderi PE, James RL, Harris L, Mims GR. Multimodal antiemetic management prevents early postoperative vomiting after outpatient laparoscopy. *Anesth Analg* 2000;91:1408–14. ANESTH ANALG SPECIAL ARTICLE GAN ET AL. 69 2003;97:62–71 CONSENSUS GUIDELINES FOR MANAGING POSTOPERATIVE NAUSEA AND VOMITING
37. Tramer`r MR, Reynolds DJM, Moore RA, McQuay HJ. Efficacy, dose-response, and safety of ondansetron in prevention of postoperative nausea and vomiting: a qualitative systematic review of randomized placebo-controlled trials. *Anesthesiology* 1997; 87:1277–89.
38. Sun R, Klein KW, White PF. The effect of timing of ondansetron administration in outpatients undergoing otolaryngologic surgery. *Anesth Analg* 1997;84:331–6.
39. Graczyk SG, McKenzie R, Kallar S, et al. Intravenous dolasetron for the prevention of postoperative nausea and vomiting after outpatient laparoscopic gynecologic surgery. *Anesth Analg* 1997;84:325–30.
40. Wilson AJ, Diemunsch P, Lindeque BG, et al. Single-dose i.v. granisetron in the prevention of postoperative nausea and vomiting. *Br J Anaesth* 1996;76:515–8.
41. Cieslak GD, Watcha MF, Phillips MB, Pennant JH. The doseresponse relation and cost-effectiveness of granisetron for the prophylaxis of pediatric postoperative emesis. *Anesthesiology* 1996;85:1076–85.
42. Mikawa K, Takao Y, Nishina K, et al. Optimal dose of granisetron for prophylaxis against postoperative emesis after gynaecological surgery. *Anesth Analg* 1997;85:652–6.



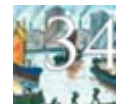
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43. DiBrijn KM. Tropisetron. *Drugs* 1992;43(Suppl 3):11–22.
44. Henzi I, Walder B, Tramer`r MR. Dexamethasone for the prevention of postoperative nausea and vomiting: a quantitative systematic review. *Anesth Analg* 2000;90:186–94.
45. Liu K, Hsu CC, Chia YY. The effective dose of dexamethasone for antiemesis after major gynecological surgery. *Anesth Analg* 1999;89:1316–8.
46. Wang JJ, Ho ST, Lee SC, et al. The use of dexamethasone for preventing postoperative nausea and vomiting in females undergoing thyroidectomy: a dose-ranging study. *Anesth Analg* 2000;91:1404–7.
47. Wang JJ, Ho ST, Tzeng JI, Tang CS. The effect of timing of dexamethasone administration on its efficacy as a prophylactic antiemetic for postoperative nausea and vomiting. *Anesth Analg* 2000;91:136–9.
48. Domino KB, Anderson EA, Polissar NL, Posner KL. Comparative efficacy and safety of ondansetron, droperidol, and metoclopramide for preventing postoperative nausea and vomiting: a meta-analysis. *Anesth Analg* 1999;88:1370–9.
49. Fortney JT, Gan TJ, Graczyk S, et al. A comparison of the efficacy, safety, and patient satisfaction of ondansetron versus droperidol as antiemetics for elective outpatient surgical procedures: S3A-409 and S3A-410 Study Groups. *Anesth Analg* 1998;86:731–8.
50. Henzi I, Sonderegger J, Tramer`r MR. Efficacy, dose response, and adverse effects of droperidol for prevention of postoperative nausea and vomiting. *Can J Anaesth* 2000;47:537–51.
51. Kranke P, Morin AM, Roewer N, Eberhart LH. Dimenhydrinate for prophylaxis of postoperative nausea and vomiting: a metaanalysis of randomized controlled trials. *Acta Anaesthesiol Scand* 2002;46:238–44.
52. Hagemann E, Halvorsen A, Holgerson O, et al. Intramuscular ephedrine reduces emesis during the first three hours after abdominal hysterectomy. *Acta Anaesthesiol Scand* 2000;44: 107–11.
53. Chen JJ, Frame DG, White TJ. Efficacy of ondansetron and prochlorperazine for the prevention of postoperative nausea and vomiting after total hip replacement or total knee replacement procedures: a randomized, double-blind, comparative trial [published erratum appears in *Arch Intern Med* 1999;159: 615]. *Arch Intern Med* 1998;158:2124–8.
54. Khalil S, Philbrook L, Rabb M, et al. Ondansetron/ promethazine combination or promethazine alone reduces nausea and vomiting after middle ear surgery. *J Clin Anesth* 1999; 11:596–600.
55. Kranke P, Morin AM, Roewer N, et al. The efficacy and safety of transdermal scopolamine for the prevention of postoperative nausea and vomiting: a quantitative systematic review. *Anesth Analg* 2002;95:133–43.
56. Bailey PL, Streisand JB, Pace NL, et al. Transdermal scopolamine reduces nausea and vomiting after outpatient laparoscopy. *Anesthesiology* 1990;72:977–80.
57. Tramer`r MR, Walder B. Efficacy and adverse effects of prophylactic antiemetics during PCA therapy: a quantitative systematic review. *Anesth Analg* 1999;88:1354–61.



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58. FDA strengthens warnings for droperidol. Available at <http://www.fda.gov/bbs/topics/ANSWERS/2001/ANS01123.html>.
59. Lee A, Done ML. The use of nonpharmacologic techniques to prevent postoperative nausea and vomiting: a meta-analysis. *Anesth Analg* 1999;88:1362–9.
60. Enqvist B, Bjorklund C, Englman M, Jakobsson J. Preoperative hypnosis reduces postoperative vomiting after surgery of the breasts: a prospective, randomized and blinded study. *Acta Anaesthesiol Scand* 1997;41:1028–32.
61. Henzi J, Walder B, Tramer`r MR. Metoclopramide in the prevention of postoperative nausea and vomiting: a quantitative systematic review of randomized placebo-controlled studies. *Br J Anaesth* 1999;83:761–71.
62. Quaynor H, Raeder JC. Incidence and severity of postoperative nausea and vomiting are similar after metoclopramide 20 mg and ondansetron 8 mg given by the end of laparoscopic cholecystectomies. *Acta Anaesthesiol Scand* 2002;46:109–13.
63. Ernst E, Pittler MH. Efficacy of ginger for nausea and vomiting: a systematic review of randomized clinical trials. *Br J Anaesth* 2000;84:367–71.
64. Tramer`r MR, Carroll D, Campbell FA, et al. Cannabinoids for control of chemotherapy-induced nausea and vomiting: quantitative systemic review. *BMJ* 2001;323:16–21.
65. Lewis IH, Campbell DN, Barrowcliffe MP. Effect of nabilone on nausea and vomiting after total abdominal hysterectomy. *Br J Anaesth* 1994;73:244–6.
66. 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.
67. Carroll NV, Miederhoff PA, Cox FM, Hirsch JD. Costs incurred by outpatient surgical centers in managing postoperative nausea and vomiting. *J Clin Anesth* 1994;6:364–9.
68. 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 Anaesth* 1999;46:536–43.
69. Watcha MF, Smith I. Cost-effectiveness analysis of antiemetic therapy for ambulatory surgery. *J Clin Anesth* 1994;6:370–7.
70. Tramer`r MR, Philips C, Reynolds DJM, et al. Cost-effectiveness of ondansetron for postoperative nausea and vomiting. *Anaesthesia* 1999;54:226–35.
71. Anzemet® (dolasetron) [package insert]. Bridgewater, NJ: Aventis Pharmaceuticals, 2003.
72. Splinter WM, Rhine EJ. Prophylaxis for vomiting by children after tonsillectomy: ondansetron compared with perphenazine. *Br J Anaesth* 1998;80:155–8.
73. Splinter W, Roberts DJ. Prophylaxis for vomiting by children after tonsillectomy: dexamethasone versus perphenazine. *Anesth Analg* 1997;85:534–7.



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74. Habib AS, Gan TJ. Combination therapy for postoperative nausea and vomiting: a more effective prophylaxis? *Ambulatory Surg* 2001;9:59–71.
75. Eberhart LH, Morin AM, Bothner U, Georgieff M. Droperidol and 5-HT₃-receptor antagonists, alone or in combination, for prophylaxis of postoperative nausea and vomiting: a metaanalysis of randomized controlled trials. *Acta Anaesthesiol Scand* 2000;44:1252–7.
76. Kazemi-Kjellberg F, Henzi I, Trame`r MR. Treatment of established postoperative nausea and vomiting: a quantitative systemic review. *BMC Anesthesiol* 2001;1:2.
77. Trame`r M, Moore RA, Reynolds DJM, McQuay HJ. A quantitative systemic review of ondansetron in treatment of established postoperative nausea and vomiting. *BMJ* 1997;314:1088–92.
78. Kreisler NS, Spiekermann BF, Ascari CM, et al. Small-dose droperidol effectively reduces nausea in a general surgical adult patient population. *Anesth Analg* 2000;91:1256–61.
79. Scuderi PE, James RL, Harris L, Mims GR. Antiemetic prophylaxis does not improve outcomes after outpatient surgery when compared to symptomatic treatment. *Anesthesiology* 1999;90: 360–71.
80. Kovac AL, O’Connor TA, Pearman MH, et al. Efficacy of repeat intravenous dosing of ondansetron in controlling postoperative nausea and vomiting: a randomized, double-blind, placebocontrolled multicenter trial. *J Clin Anesth* 1999;11:453–9.
81. Gan TJ, El-Molem H, Ray J, Glass PSA. Patient-controlled antiemesis. *Anesthesiology* 1999;90:1564–70.
82. Gan TJ, Glass PSA, Howell ST, et al. Determination of plasma concentrations of propofol associated with 50% reduction in postoperative nausea. *Anesthesiology* 1997;87:779–84.
83. Taylor AM, Rosen M, Diemunsch PA, et al. A double-blind, parallel-group, placebo-controlled, dose-ranging, multicenter study of intravenous granisetron in the treatment of postoperative nausea and vomiting in patients undergoing surgery with general anesthesia. *J Clin Anesth* 1997;9:658–63.
84. Habib AS, Gan TJ. Food and drug administration black box warning on the perioperative use of droperidol: a review of the cases. *Anesth Analg* 2003;96:1377–9.