REVIEW ARTICLE

Risk Factors for Postoperative Nausea and Vomiting

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Knowledge of postoperative nausea and vomiting (PONV) risk factors allows anesthesiologists to optimize the use of prophylactic regimens. Modern PONV risk research began in the 1990s with publication of studies using logistic regression analysis to simultaneously identify multiple independent PONV predictors and publication of meta-analyses and systematic reviews. This literature shows that female gender post-puberty, nonsmoking status, history of PONV or motion sickness, childhood after infancy and younger adulthood, increasing duration of surgery, and use of volatile anesthetics, nitrous oxide, large-dose neostigmine, or intraoperative or postoperative opioids are well established PONV risk factors. Possible risk factors include history of migraine, history of PONV or motion sickness in a child's parent or sibling, better ASA physical status, intense preoperative anxiety, certain ethnicities or surgery types, decreased perioperative fluids, crystalloid versus colloid administration, increasing duration of anesthesia, general versus regional anesthesia or sedation, balanced versus total IV anesthesia, and use of longer-acting versus shorter-acting opioids. Early-phase menstruation, obesity and lack of supplemental oxygen are disproved risk factors. Current risk scoring systems have ~55%–80% accuracy in predicting which patient groups will suffer PONV. Further research examining genetic and under-investigated clinical patient characteristics as potential risk factors, and involving outpatients and children, should improve predictive systems.

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Postoperative nausea and vomiting (PONV) is the most frequent side effect after anesthesia (1), occurring in ~30% of unselected inpatients and up to 70% of "high-risk" inpatients during the 24 h after emergence (2). Its incidence may be less frequent in ambulatory surgery than in inpatient surgery, but PONV may be under-recognized in the outpatient setting, where patients quickly leave direct medical oversight (2,3). Although PONV is almost always self-limiting and non-fatal (4), it can cause significant morbidity, including dehydration, electrolyte imbalance, suture tension and dehiscence, venous hypertension and bleeding, esophageal rupture, and life-threatening airway compromise, although the more severe complications are rare (5,6). Each vomiting episode delays discharge from the recovery room by ~20 min (7).

In a preoperative survey, patients ranked emesis as the most undesirable and nausea as the fourth most undesirable of 10 negative postoperative outcomes; postoperative pain ranked third in this study (8). In another study, patients were, on average, willing to pay $56 out-of-pocket to avoid PONV; the figure increased to $73 and $100 in patients who had experienced postoperative nausea or postoperative vomiting, respectively (9). Because patients find PONV so highly unpleasant, it has been proposed that PONV management, similar to pain management, could be considered an end unto itself (6).

However, interventions to prevent PONV are not needed in the majority of the general patient population who, even without prophylaxis, will not suffer these symptoms. In addition, current interventions may cause side effects and may entail substantial effort or expense (7,10). Moreover, current interventions lack universal efficacy, especially as monotherapy (11).

Therefore, it is important to direct interventions to the patients most likely to experience PONV (7,10), especially in the case of combination therapy or "multimodal management," which are the most effective management strategies now available but which are also more costly and can have added side effects. Knowledge of PONV risk factors is essential to this process.

However, current understanding of risk factors for PONV is incomplete, in part because much remains to be elucidated about the pathophysiology of these

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symptoms, particularly their molecular biology. Obtaining understanding of PONV risk factors and pathophysiology is complicated by the multifactorial nature of PONV because of the involvement of multiple receptors and stimuli (12,13). At least 7 neurotransmitter types are documented, or believed to be implicated, in PONV, namely serotonin, dopamine, muscarine, acetylcholine, neurokinin-1, histamine, and opioids. Stimulation of the vestibular-cochlear, glossopharyngeal, or vagus nerves also may be involved.

Nonetheless, understanding of PONV risk factors has dramatically improved since the advent in the early 1990s of clinical studies that used more sophisticated multivariable statistical analyses and stratification. The wider use of meta-analyses and systematic reviews also has added knowledge. In addition, the development and validation of predictive scoring systems based on the results of the aforementioned clinical studies, and the publication of trials using the scoring systems to allocate and tailor prophylaxis, provide guidance for the application of risk factors to everyday practice.

The aim of this qualitative review is to summarize the findings of the past decade and a half of research on PONV risk factors in both adults and children. The review focuses on key prospective clinical studies (based on author opinion) involving consecutive adult or pediatric patients or both, published in peer-reviewed journals, that controlled for multiple variables, i.e., patient characteristics and types of anesthesia or surgery, and in most cases, did not report having given anti-PONV prophylaxis. Important meta-analyses and systematic reviews also are discussed. These publications were identified based on searches of the PubMed® and Medline® databases for the period January 1990–June 2005 under the keywords "postoperative nausea and vomiting" or "postoperative nausea" or "postoperative vomiting" and "risk factors." Additional publications were identified based on citations in papers found in the database searches and from the author's knowledge. The present review also seeks to present the clinical implications of the recent PONV research and to suggest avenues for further investigation. The review begins by explaining key PONV terminology and classifications.

Definition and Classification of PONV

PONV encompasses three main symptoms that may occur separately or in combination after surgery. *Nausea* is the subjective sensation of an urge to vomit, in the absence of expulsive muscular movements; when severe, it is associated with increased salivary secretion, vasomotor disturbances, and sweating (14). *Vomiting* or *emesis* is the forcible expulsion through the mouth of the gastric contents. Vomiting results from coordinated activity of the abdominal, intercostal, laryngeal, and pharyngeal muscles, including retrograde giant contraction of the intestines, relaxation of the gastric fundus, closure of the glottis, and elevation of the soft palate. This activity is associated with increased heart rate and breathing and with sweating (15). *Retching* is an unproductive effort to vomit (14). Retching and vomiting are collectively termed *emetic episodes*.

PONV may take place in single or multiple episodes, which may last minutes, hours, or even days (6). It is classified as early, occurring up to 2 to 6 h after surgery, or late, occurring up to 24 or 48 h after surgery, with the exact cut-off times depending upon the individual investigator's definition. As may be inferred from this lack of a standard cut-off time, the delineation is somewhat arbitrary and is related to the patient's location at the time of evaluation for the symptoms, e.g., the postanesthesia care unit, surgical or other ward, or home. However, there are suggestions that early and late PONV may differ at least somewhat in their pathogenesis. The use of volatile anesthetics may be a main cause of early PONV (5,6). Opioid-induced symptoms and motion sickness caused by transportation from the PACU to the ward or from the hospital to the home may account for much of late PONV (16–19). However, for the most part, PONV research has focused on identifying risk factors themselves rather than their time of activity.

Risk Factors for PONV

Overview. PONV risk factors have been described in the literature since the late 1800s (20). Traditionally, investigation focused on a single potential factor at a time, with little to no attempt to control for other variables, i.e., to account for the possible independent effects of additional factors (21,22). In studies with these drawbacks, the true influence of the investigated risk factor remained unclear.

The modern era in PONV risk factor research began in the early 1990s, with publication of the first studies that attempted to simultaneously identify multiple risk factors and, in so doing, used regression models to control for a wide variety of variables (21,22). At least 20 key multivariable studies have been published in English; they are summarized in Table 1. Nearly all these studies were prospective and relied on logistic regression analysis (23). Logistic regression analysis uses modeling in which a binary or dichotomous dependent variable, that is, an outcome comprising two possible categories (e.g., PONV: yes or no), is described as a function of one or more independent variables. Logistic regression analyses generate an odds ratio (OR) for each factor examined. The OR is the ratio of the likelihood of an outcome in a group

Table 1. Characteristics of Key Multivariable PONV Risk Factor Studies

Study, year of Publication	N*	Patient and other study characteristics	Outcome(s) measured	Data collection methods	PONV incidence	Comments
Junger et al. (34), 2001	27,626	Patients: inpatients and outpatients (mean age ~42 y, 43% F) Surgery: varied (trauma, 20%, OPHTH, 16%, EN 15%) Study duration: 3 yrs Setting: PACU at 1 German center Prophylactic antiemetic use: some patients (no 5-HT_3 antagonists)	Recorded antiemetic (given for all queried† or observed PONV) use in PACU within ~90 min‡	Computerized chart review	7.8% within ~90 min	Retrospective analysis of data from an anesthesia information management system.
Sinclair et al. (17), 1999	17,638	Patients: predominantly adult (92% age ≥21 y) outpatients (67% F) Surgery: 8 main classes of ambulatory surgery (OPHTH, 36%, GYN, 34%, ORTHO, 18%) Study duration: 3 yr Setting: 1 Canadian center Prophylactic antiemetic use: all patients (dimenhydrinate)	PONV within 24 h: observed or volunteered N, V§; (observed V: only that treated with rescue antiemetics)	Observation in ASU and PACU, 24-h phone interviews with 30% of patients	4.6% in PACU or ASU, 9.1% within 24 h (interviewees only)	Developed risk scoring system; only study to focus on outpatients.
Cohen et al. (22), 1994	15,992	Patients: adult inpatients Surgery: varied Study duration: 3 y Setting: 4 Canadian teaching hospitals Prophylactic antiemetic use: not reported	Quaried PO N or V, presumably within 72 h	Face-to-face patient interview within 72 h	72% N, 17% V, presumably within 72 h	Provides risk factor data for N or V, but detailed data only for N for 1 hospital
Apfel et al. (29), 1999	2722	Patients: adult (18+ yr) inpatients Surgery: 4 main classes (ENT, 34%, OPHTH, 14%) under general anesthesia with volatile anesthetics Study duration: ~4 mo (Finnish center) or ~1 y (German center) Setting: 1 Finnish center (n = 520) and 1 German (n = 2202) center Prophylactic antiemetic use: not reported (Finnish center) or none (German center)	Queried PONV within 24 h	Patient interviews: by nurse at 2 h, physician at 24 h	35.9% overall, 55.6% in Finnish center, 31.3% in German center, within 24 h	Developed simplified risk scoring systems. All patients previously reported in (27) or (30) or (19).
Apfel et al. (28, 80), 2002; Apfel et al. (28, 80), 2004	1566	Patients: adult inpatients Surgery: 4 main classes (ORTHO, 57%) under balanced anesthesia Study duration: not reported Setting: 2 German centers Prophylactic antiemetic use: none	Aueried PONV within 24 h	Patient inverviews, by nurses or anesthesiologists: at 6+ h and 24+ h	38.3% within 24 h	Initial study (28) sought to compare various risk scoring systems; later study (80) sought to compare use of site of surgery or history of PONV as single factors versus simplified risk factor scoring system (29).
Van den Bosch et al. (26, 81), 2005, (26, 81), 2005	1388	Patients: adult inpatients Surgery: superficial (74%) or other procedures Study duration: 1.75 y Setting: 1 Dutch center Prophylactic antiemetic use: none	Queried PONV within 24 h	Patient interviews every 15 min (4 times) in the PACU, then hourly in the ward	48%	One study (81) sought to validata Apfel et al. (29) and Koivuranta et al. (19) simplified risk scoring systems in a distinct population. Using the same population, the other study (26) sought to assess the value of preoperative anxiety as a risk factor, and developed a new scoring system. The study population was enrolled in a trial comparing impact on PONV total IV anesthesia with propofol versus inhaled anesthesia (88).
Eberhart et al. (36), 2004	1257	Patients: pediatric (age ≤14 yr) inpatients or outpatients (63% M) Surgery: single (93%) or multiple ENT (~34%), urologic (~24%), OPHTH (~14%), abdominal (~13%) or other Study duration: 22 mo Setting: 2 university hospitals, 1 community children's hospital, and 1 outpatient surgical center in Germany Prophylactic antiemetic use: not reported	Aueried or observed PO V (including retching) in the PACU	Interviews of patients and/or their parents at 24 h; medical record review	Not reported	Only study published to develop and validata a simplified risk scoring system in children.
Apfel et al. (5) 2001; Kranke et al. (44), 2002	1180	Patients: adult (~50%) or pediatric (~50%) inpatients, with a ≥20% risk for PONV Surgery: elective ENT (75%) or strabismus Study duration: 2 yr Setting: 1 German center Prophylactic antiemetic use: ~80% of patients	Queried PO V (all patients), PO N, PONV (adults only) within 24 h	Patient interviews at 1, 2, 6 and 24 h after end of anesthesia	30.1% PV (34.7% in children) 43.6% PONV (n = 587 adults),	Study used 5-way factorial design to identify anesthetic and surgical independent risk factors.

Continued

Table 1. Continued

Study, year of Publication	N*	Patient and other study characteristics	Outcome(s) measured	Data collection methods	PONV incidence	Comments
Apfel et al. 927), 1998	1137	Patients: adult inpatients Surgery: ENT Study duration: ~13 mo Setting: at 1 German center Prophylactic antiemetic use: none	Queried PO N, V within 24 h; PO V main outcome	Patient interviews by nurse in PACU, by anesthesiologist at 24+ h	21.5% PV within 24 h	Developed scoring system. Patients also reported in (29).
Koivuranta et al. (19), 1997	1107	Patients: adult (~96%) and pediatric inpatients (66% F) Surgery: 4 main classes (59% general, 22% GYN) under general (74%) or regional anesthesia Study duration: ~4 mo Setting: 1 Finnish hospital Prophylactic antiemetic use: not reported	Recorded and queried PO N, V within 0–2, 2–24, 24 h	Medical record review, patient interviews by anesthesiologist at 24 h	18% N, 5% V during 0–2 h, 49% N, 24% V during 2–24 h, 52% N, 25% V from 0–24 h	Developed scoring system. Some patients (n = 520) also reported in (29).
Apfel et al. (30), 1998	1091	Patients: adult inpatients Surgery: elective general (~83%) or OPHTH under general anesthesia Study duration: ~13 mo Setting: 1 German center Prophylactic antiemetic use: none	Observed and queried PO N, V within 24 h; PV within 24 h was main outcome	Observed, patient interview by anesthesiologist at 24+ h	25.5% PV within 24 h	Tested scoring system. Patients also reported in (29). Droperidol used in IV pain drip.
Eberhart et al. (48), 2004	983	Patients: pediatric (age ≤12 yr) inpatients or outpatients (64% M) Surgery: single (92%) or multiple ENT (~42%), urologic (~24%), OPHTH (~16%), abdominal (~10%) or other Study duration: 22 mo Setting: 2 university hospitals, 1 community children's hospital, and 1 outpatient surgical center in Germany Prophylactic antiemetic use: not reported	Queried or observed PO V (including retching) in the PACU	Patients and/or their parents interviews at 24 h, medical record review and querying of nurses	33.2% PV within 24 h	Only published study to seek to validate in children risk scoring systems developed in adults (17,19,21,27,29). Unclear if population also was included in earlier study by Eberhart et al. (36).
Stadler et al. (18), 2003	671	Patients: adults (age ≥15 yr) inpatients Surgery: 8 main classes under general (72%) or regional anesthesia Study duration: 3 mo Setting: 1 Belgian center Prophylactic antiemetic use: none	Observed and queried PO N, V (included R)	Observation, patient interview by nurse every 2 hrs from 0–4 h. every 4 h from 4 to 72 h, except if patient asleep	N 19%, V, 10%, PONV 19% within 72 h	Used bivariate Dale modeling, sought to assess whether there were differences in independent risk favors for PO N and PO V.
Pierce et al. (31), 2002	428	Patients: adult inpatients (90% F) Surgery: 3 main classes (breast, 68%, ENT, 24%) Study duration: ~7 mo Setting: 1 French center Prophylactic antiemetic use: not reported	Observed, recorded and queried PO N, V within 24 h	Observation, record review, and patient interview by nurses and in some cases, anesthesiologists at 1, 2, 4, 6 h and every 4 h from 6–24 h	49.5% PONV at 24 h	Validated the Apfel et al. simplified risk scoring system (29).
Toner et al. (32), 1996	400	Patients: adult inpatients (69% F) Surgery: 6 main classes (35% GYN, 29% general surgery) Study duration: not reported Setting: 1 British medical center Prophylactic antiemetic use: not reported	Observed and queried PONv within 24 h	Observation, patient interview at 24 h	36% PONV at 24 h	Validated the Palazzo and Evans risk scoring system (21).
Fabling et al. (33), 1997	199	Patients; adult (ages 18–70) inpatients Surgery: elective craniotomies Study duration: 18 mo Setting: 1 American center Prophylactic antiemetic use: intraoperative antiemetics in 7% of patients	Recorded PO N, V within 48 h	Chart review	16% PO N, 15% PO V, 15% PO antiemetics within 48 hrs	Retrospective study.
Palazzo and Evans (21), 1993	147	Patients: adult inpatients Surgery: minor peripheral ORTHO Study duration: 3 yr Setting: 1 British center Prophylactic antiemetic use: not reported	Observed, volunteered, queried PO N, V with 24 h	Observation and questioning by nurses	27.2% PONV at 24 h	First study to use multivariable analysis to identify independent risk factors for PONV.

ASU = ambulatory surgery unit; ENT = ear, nose and throat; F = female; GYN = gynecology; M = male; N = nausea; OPHTH = ophthalmology or ophthalmological; ORTH = orthopedic; PACU = postanesthesia care unit; PO = postoperative; PONV = postoperative nausea and vomiting; V = vomiting.

Table includes key prospective clinical studies (based on author opinion) involving consecutive adult or pediatric patients or both, published in peer-reviewed journals, that controlled for multiple variables, i.e., patient, anesthesia or surgical characteristics.

* Evaluable patients.

†Queried symptoms were identified based on patient response to questioning. Studies that measured queried symptoms presumably also included (the likely few) observed but not queried symptoms; ‡All times are postsurgery unless otherwise noted; §V was defined to include retching unless otherwise noted.

Table 2. Key PONV Risk Factor Findings In Adults and Children

Well-established risk actors (References)	Possible risk factors (References)	Disproved risk factors (References)
Patient-Related		
Female gender from puberty* (5,17–19,21,22,26–34)	Better ASA physical status (19,22)	Early stage of the menstrual cycle (40)
Nonsmoking status (5,17–19,21,22,26–30,32,34,89,90)	History of migraine [nausea only] (18,19)	Obesity (Body Mass Index) (44)
History of PONV or motion sickness (5,17,19,21,26–32,34,36,48)	History of PONV or motion sickness in a parent or sibing (children only) (36)	
Childhood after infancy and younger adulthood† (5, 17,22,26,27,30–36,48)	Preoperative anxiety (26) Ethnicity (Dutch/English versus Scandinavian) (42)	
Surgery-Related		
Increasing duration of surgical procedures‡ (17,19, 29,34,36)	Certain surgery types: · intraabdominal (5,11,17–19,22,25,26, 28,30,33,36,45–48) · hernia repair [children] (46) · laparoscopic (5,11,17–19,22,25,26,28, 30,33,36,45–48) (46) · orthopedic (5,11,17–19,22,25,26,28, 30,33,36,45–48) · major GYN (5,11,17–19,22,25,26,28, 30,33,36,45–48) · ENT [including adenotonsillectomy in children] (5,11,17–19,22,25,26,28, 30,33,36,45–48) · thyroid (28) · strabismus [children] (5,11,17–19,22, 25,26,28,30,33,36,45–48) · neurosurgery (5,11,17–19,22,25,26, 28,30,33,36,45–48) · breast surgery (5,11,17–19,22,25,26, 28,30,33,36,45–48) · plastic surgery (5,11,17–19,22,25,26, 28,30,33,36,45–48) · orchiopexy [children] (46) · penile surgery [children] (5,11,17–19,22,25,26,28,30,33,36,45–48) Less pre- or intraoperative fluid administration (49, 50) Introperative crystalloid versus colloid administration (51)	
Anesthesia-Related		
Volatile anesthetics (5,11,26,52)	Increasing duration of anesthesia (5, 17, 22, 27, 48)	Standard (30%) versus supplemental (50% or 80%) oxygen (11,67–69)
Nitrous oxide (11,26,34,53)	General versus other forms of anesthesia (17, 18, 66)	
Balanced versus total IV anesthesia (11,34,52,54)	Use of longer- versus shorter-acting opioids (64)	
Large-dose (≥2.5 mg) neostigmine (55)		
Intraoperative opioids (34,56)		
Postoperative opioids (5,18,19,21,22,28,29,31,32,57,58)		
Larger doses of perioperative (59) or postoperative (61,63) opioids		

ASA = American Society of Anesthesiologists, ENT ear, nose and throat; GYN = gynecological; PONV = postoperative nausea and vomiting.
* No significant gender differences are seen in prepubescent pediatric patients (35,36); †Children have twice the vomiting incidence as adults (5,25); ‡Each 30 min increase in duration of surgery increases baseline PONV risk by 60% (17).

with the given risk factor to the likelihood of the outcome in a group lacking that factor. The statistical significance of each OR is also assessed. In addition, the 95% confidence interval (CI) of the OR, i.e., that is, the range of values that is 95% likely to include the true OR in the study population, is calculated. When the lower limit of the 95% CI of its OR exceeds 1.00, there is little doubt that a given factor increases PONV risk. For a more detailed statistical explanation of logistic regression and the related terminology, readers may refer to several published references (23,24).

The potential risk factors studied thus far (Tables 2 and 3) may be classified as patient-, surgery-, or anesthesia-related and as fixed or variable, that is, amenable to change by the patient's caregivers

Table 3. PONV Risk Factors: Other Potential Factors Examined in Multivariable Studies and Candidates for Future Investigation

Other potential risk factors examined [specific variables examined] (Reference[s])*	Candidate potential risk factors† for future investigation (Reference[s])
Patient-Related	
History of morning sickness (21, 32)	Expression and activity of P450 (CYP) hepatocellular enzymes (74,77)
Preoperative anxiety (26, 28)	Alcohol consumption [presurgery and chronic] 74,77)
History of starvation nausea (32) (i.e., nausea when fasting)	Ethnicity (43, 74)
History of sickness in presence of pain (21)	Prescription medication use (e.g., P450 enzyme inducers/ suppressors such as cimetidine, erythromycin, terfenadine) (74)
History of sickness after alcohol consumption (21)	Hepatitis C infection (91)
History of vertigo (32)	Clinical depression (92)
Presence of heartburn (21)	Anxiety disorder (93)
Allergies (32)	Specific foods consumed before surgery [e.g., vegetables containing P450 enzyme inducers/suppressors, such as cabbage, brussels sprouts, cauliflower, red pappers] (74)
Height (34)	
Preoperative medical conditions (22,32)	
Preoperative medications (32)	
Diagnosis leading to surgery (34)	
Hospital where patient is treated (22,32)	
Surgery-Related	
Duration of surgery (5,17–19,31,32,34,36,48,81)	
Prior diagnostic procedures [number] (34)	
Admission status [inpatient vs. outpatient] (34)	
Nonsurgical therapeutic or anxiliary methods (34)	
Month of surgery (34)	
Duration of preoperative fast (21, 32)	
Surgery performing the operation (32)	
IV fluid use (32)	
Anesthesia-Related	
Type of additional regional anesthesia used (e.g., caudal block, infiltration/field block) (36,48)	
Induction regimen [drug, midazolam] (31,32,36,48)	
Maintenance anesthetic used (5,36,48)	
Anesthetic route [difficult vs. easy tracheal intubation, use of intubation vs. other techniques] (22,27,30,32,34,36,48)	
Preinduction anxiety (21)	
Preinduction nausea (21)	
Preinduction thirst (21)	
Preinduction hunger (21)	
Intraoperative hypotension (34)	
Intraoperative bradycardia (34)	
Intraoperative systolic arterial blood pressure (32)	
Intraoperative SaO_2 (32)	
Itnraoperative E_CO_2 (32)	
Intermittent positive pressure ventilation/spontaneous ventilation (32)	
Anesthesiologist performing the anesthesia (32,94)	
Presence of anesthesia resident (94)	
Airway device used (36,48)	
Gastric tube use (34)	
Antiemetic use [drug presence or absence, timing] (5,32–34)	
Barbiturate use (27,30)	
IV hypnotic use (34)	
Muscle relaxant use [drug, category] (27,30,32,34,36,48)	
IV analgesic use (30)	
Non-opioid analgesia use [drug PACU] (34)	
Class of postoperative analgesics (18)	
Postoperative pain level (18)	
Time to first oral intake (18)	
Duration of PACU stay (34)	

ASA = American Society of Anesthesiologists; PACU = postanesthesia care unit; PONV = postoperative nausea and vomitting.

* Listed potential risk factors have been examined in various permutations, depending upon the study; specific variables given in brackets represent examples of the permutations. In the author's opinion, current evidence suggests that they are unlikely to be true risk factors, and probably do not merit further investigation. The list of references in this table is not exhaustive, but includes the key multivariable studies summarized in Table 1. Not all studies report all risk factors that they investigated, or describe all investigated risk factors clearly. Where the nature of a risk factor was unclear, the study or risk factor, as applicable, was omitted from this table.

†Based on author opinion.

Table 4. Overview of Risk Factors Use in Risk Scoring Systems

Risk Factor*	Adults, simplified or semisimplified systems			Adults, nonsimplified systems				Children, simplified system	Number of systems in which risk factor is used
	Apfel et al. (29)	Koivuranta et al. (19)	Van den Bosch et al. (26)	Apfel et al. (27)	Koivuranta et al. (19)	Palazzo and Evans (21)	Sinclair et al. (17)	Eberhart et al. (36)	
Patient-related									
Female	X	X	X	X	X	X	X		7/8
History of PONV or motion sickness	X	X	X	X	X	X	X	X	8/8
Nonsmoker	X	X	X	X	X		X		6/8
Age		X	X					X	3/8
Surgery-related									
Duration of surgery		X			X		X	X	4/8
Type of surgery			X				X	X	3/8
Anesthesia-related									
Duration of anesthesia				X					1/8
Anesthetic technique			X				X		2/8
Postoperative opioids	X					X			2/8
Number of each type of risk factors	3 PR, 1 AR	4 PR, 1 SR	4 PR, 1 SR, 1 AR	4 PR, 1 AR	4 PR, 1 SR	3 PR, 1 AR	3 PR, 8 SR, 1 AR	2 PR, 2 SR	
Number of risk factors	4	5	6	5	5	4	12	4	

AR = anesthesia-related; D&C = dilation and curettage; ENT = ear nose and throat; GYN = gynecologic; OPHTH = ophthalmologic; ORTHO = orthopedic; PONV = postoperative nausea and vomiting; PR = patient-related; SR = surgery-related, X = used in the particular risk scoring system.

* For specific permutations of these risk factors in the different scoring systems, the reader is referred to Appendix, Table A1.

† Simplified scoring systems omit constants and coefficients derived from logistic reression modeling in favor of binary, yes/no scoring for each item in the system. The semi-simplified system of Van den Bosch et al. (26) also omits constants and coefficients. However, instead of using binary scoring for its items, the Van den Bosch system assigns different point values to particular alternative variables for each, so that a nomogram is required to use the system.

(16,21,25). Most patient and surgical technique-related factors are fixed; some other surgery-related factors and some anesthesia-related factors are variable.

Key Risk Factor Findings to Date. Table 2 summarizes key findings of modern risk factor studies. To facilitate application of these findings to everyday practice, Table 2 classifies risk factors as "well-established," "possible," or "disproved" (according to expert consensus and author opinion) as well as by relationship to the patient, surgery, or anesthesia.

Patient-Related Factors Probably the strongest risk factor identified is female gender from puberty on: all adult studies listed in Table 1 (5,17–19,21,22,26–34) concurred in identifying female gender as a risk factor, and no study has contradicted this finding. All adult risk scoring systems include this factor (Table 4). In most studies, ORs for this predictor have ranged from 2.0–4.0, reflecting a twofold to fourfold increased PONV risk for adolescent and adult females (18,21,22,27–29,31,32,34). That prepubescent girls apparently lack increased likelihood of PONV (35,36) could imply that the risk relates to hormonal factors. However, although initial studies (37,38) reported increased susceptibility to PONV during the first week of the menstrual cycle, early stage of the menstrual cycle has been disproved as a risk factor by a subsequent study (39) and in a systematic review (40).

Nonsmoking status has been identified as an independent PONV risk factor in numerous adult studies (17–19,22,27–29,34) as has history of PONV and/or motion sickness (5,17,19,21,27–32); intriguingly, a recent study in children also found history of PONV in a parent or sibling to be a risk factor (36). There have been few contradictory reports (21,31,32). Nonsmoking status is included in all but one adult risk scoring system, and history of PONV or motion sickness in all risk scoring systems (Table 4). Most studies have found ORs of ~1.5–2.5 for nonsmoking status and of ~1.8–3.1 for history of PONV, motion sickness, or both.

A number of investigators also have identified childhood after infancy and younger adulthood as independent PONV risk factors (5, 17, 22, 26, 27, 30, 31, 33–36). For example, 2 reports noted a >10% decreased risk for every decade of age in adults (17,31). A study in children age ≤14 yr found a sharp increase in PONV risk around age 3, with a 0.2%–0.8% per year increase in risk thereafter, depending on the presence of other risk factors (36). However, age is included in only a minority of risk scoring systems (Table 4).

Possible PONV risk factors include better ASA physical status (19,22) and a history of migraine (postoperative nausea only) (18,19). A recent adult study found higher scores on the Spielberger State-Trait Anxiety Inventory anxiety scale or on the Amsterdam Preoperative Anxiety and Information Scale anxiety section to be weak PONV risk factors (OR, 1.01; 95% CI, 1.00–1.02; $P = 0.04$ and OR, 1.04; 95% CI, 1.02–1.05; $P = 0.02$, respectively); their inclusion in the investigators' risk scoring system did not improve its discriminating power (26). In contrast, a pediatric study found preoperative anxiety to not be a significant PONV risk factor (41). A meta-analysis of PONV after gynecological surgery (42) and studies in the laboratory-induced motion sickness setting (43) suggest that ethnicity (Dutch or English versus Scandinavian and Chinese or Asian-American versus Caucasian- or African-American, respectively) could be a PONV risk factor. However, two studies using multivariable analyses do not support a role for this characteristic (26,32).

Besides early stage of the menstrual cycle, obesity has been disproved as a patient-related PONV risk factor (44). Interestingly, the systematic review that did so found that the belief in increased body mass index as a risk factor apparently largely stemmed from a "chain reaction" of 14 review articles misquoting or misinterpreting 4 original studies.

Surgery-Related Factors Increasing duration of surgery has been shown to be an independent PONV risk factor by a few well-conducted studies in adults (17,19,29,34) or children (36). An outpatient study found that each 30-min increase in surgery duration increased baseline PONV risk by 60% (17). However, although type of surgery has been identified as a risk factor in numerous reports (5,17–19,22,25,28,30,33,45–47), its status as such is still somewhat controversial; the specific procedures implicated as particularly emetogenic sometimes vary among studies. Types of procedures that may be viewed as possible risk factors include intraabdominal (5,11,17–19,22,25,26,28, 30,33,36,45–48), laparoscopic (5,11,17–19,22,25,26, 28,30,33,36,45–48), orthopedic, major gynecological (5,11,17–19, 22, 25, 26, 28, 30, 33, 36, 45–48), ear, nose and throat (ENT) (5,11,17–19,22,25,26,28,30,33,36,45–48), thyroid (28), breast (5,11,17–19,22,25,26,28,30, 33,36,45–48) and plastic surgery (5,11,17–19,22,25,26,28, 30,33,36,45–48), as well as neurosurgery (5,11,17–19,22,25,26,28,30,33,36,45–48), and, in children, hernia repair (46), adenotonsillectomy (46), strabismus (5,11,17–19, 22, 25, 26, 28, 30, 33, 36, 45–48), or penile surgery (5,11,17–19, 22, 25, 26, 28, 30, 33, 36, 45–48), and orchiopexy (46). Half of risk scoring systems include duration of surgery, and several incorporate one or more types of surgery (Appendix). Other possible surgery-related PONV risk factors include less preoperative or intraoperative fluid administration (49,50) or intraoperative colloid versus crystalloid administration (51), when a large volume of crystalloid in a prolonged surgery may result in gastrointestinal tissue edema leading to an increased incidence of PONV.

Anesthesia-Related Factors Numerous anesthesia-related variables have been well established as PONV risk factors, including use of volatile anesthetics (5,11,34,52), nitrous oxide (11,26,34,53), balanced inhaled versus total IV anesthesia (11,34,52,54), and large-dose (≥2.5 mg) neostigmine (55). The choice of volatile anesthetic, e.g., isoflurane versus sevoflurane versus enflurane, appears not to affect the risk of PONV (5,11). Use of intraoperative (34,56) or postoperative (18,19,21,22,28,29,31,32,57,58) opioids and larger perioperative (59) and postoperative doses of these drugs also have been implicated as associated with PONV (60–63). However, some contradictory findings have been reported with respect to postoperative opioid use in adults (26), intraoperative or postoperative opioid use in children (36), or intraoperative opioid use in a mixed adult and pediatric population (5). Interestingly, despite the relatively large number of anesthesia-related variables identified as risk factors, most risk scoring systems do not include any, and the remainder of the systems include only a few (Table 4).

Administration of a long-acting rather than a short-acting opioid is, at best, a possible PONV risk factor. Although a small recent study observed an association between use of fentanyl versus remifentanil as an adjunct to propofol maintenance (64) and PONV, another similarly sized study found no association of alfentanil versus remifentanil use and PONV (65). Moreover, a 5199-patient multinational multifactorial designed study of anti-PONV interventions (11) failed to find fentanyl versus remifentanil as a PONV risk factor.

Far more likely, but not yet well established, anesthesia-related PONV risk factors include longer duration of anesthesia (5,17,22,27,48) or general versus other forms of anesthesia, e.g., regional or sedation (17,18,66). Together with postoperative opioid or isoflurane use, they comprise the anesthesia-related risk factors used by current risk scoring systems (Table 4). Use of standard (30%) rather than supplemental (50% or 80%) oxygen seems to have been disproved as a risk factor (11,67–69), despite early evidence of its validity as such (70,71).

Limitations of Modern Research and Suggestions for Future Investigation. Although recent studies have vastly improved knowledge of PONV risk factors, identification of such factors remains imperfect (72,73). Five limitations of research published thus far should be borne in mind.

First, there are substantial gaps in the list of potential risk factors investigated (Table 3). Studies continue to pursue an essentially epidemiological approach,

focusing on readily discernible clinical factors. However, genetic and other molecular biological patient characteristics have not been extensively examined, and even certain clinical characteristics remain underinvestigated (Table 3).

For example, in a thought-provoking editorial (74), Sweeney highlights as potential PONV risk factors the degree of expression and activity of selected cytochrome P (CYP) 450 hepatocellular enzymes. CYP450 enzymes metabolize many drugs, including widely used anesthetic and analgesic drugs and antiemetics (75,76). The greater the expression and activity of a CYP450 enzyme, the more rapid the metabolism of its substrate drug(s). Based on those characteristics, individuals may be classified as "poor," "intermediate," "extensive," or "ultrarapid" metabolizers of the drug(s) (77).

In addition, CYP450 enzyme synthesis may be stimulated or suppressed by environmental influences. Sweeney has speculated that the protective effect of smoking against PONV might relate to the induction of CYP450 enzymes by polycyclic aromatic hydrocarbons. These hydrocarbons are components of the "tar" portion of cigarette smoke. Other clinical characteristics that affect CYP450 enzyme expression, for example, the consumption of alcohol, of commonly prescribed medications such as cimetidine, erythromycin, or terfenadine, or of vegetables including cabbage, Brussels sprouts, cauliflower, or red pepper, should be investigated as potential PONV risk factors. Further, gender and racial differences have been documented in CYP450 enzyme expression. Other suggestions that ethnicity merits further study as a potential PONV risk factor come from a meta-analysis of PONV after gynecological surgery (42) and from motion sickness studies, in which Chinese or Asian-American subjects were significantly more susceptible to symptoms induced by a standardized drum rotation procedure than were European- or African-American subjects (43).

A second limitation of PONV risk factor research is the difficulty of controlling for subtle clinical factors, particularly in smaller or single-center studies. For example, unusual proficiency of particular anesthesiologists or surgeons might mask the nature of a procedure that would be emetogenic in less skilled hands (13).

A third limitation of recent PONV risk factor research is variation in outcomes and data collection methods. Some studies have considered nausea or emetic events as separate outcomes, some as a combined outcome. Although there is an obvious, intuitive relationship between nausea and emetic events, there are important pathophysiological differences between the two. Nausea is a subjective feeling and a conscious cortical activity; emetic episodes are an autonomic reflex and as such, directed by the brainstem (14). The symptoms are not inevitably linked: in a single-center, 671-patient study, Stadler et al. (18) observed nausea or vomiting alone in 11% and 2% of patients, respectively, and together in 8%. In another study, involving 587 adults (5), 18% of patients suffered only nausea, 4%, only vomiting, and 22% both.

The Stadler et al. study identified overlapping but not identical risk factors for nausea or vomiting. Female gender, nonsmoking status, use of postoperative morphine analgesia, general versus regional anesthesia, and urological versus ENT procedures were independent predictors of both symptoms, but abdominal or gynecological versus ENT procedures and history of migraine were significant or near-significant predictors only for nausea (18). On the other hand, some argue that the rarity of postoperative vomiting in the absence of nausea suggests that postoperative nausea should be viewed as a symptom for potential vomiting. Further research is required to clarify the relationship between the two symptoms.

Moreover, some studies have defined PONV as recorded or volunteered symptoms, whereas many others have included in the definition symptoms reported in response to a specific query. One study (34) used administration of rescue antiemetics as its sole criterion for presence of PONV. Most studies have collected data by asking patients about specific symptoms but a few have relied on chart reviews. In a large multicenter risk factor study that examined the issue, patients reported PONV far more often than was shown in their charts (22), and it is believed that direct and specific questioning captures a larger percentage of actual PONV incidence than does spontaneous patient report (22,78). Furthermore, a heavy nursing or anesthesiologist workload may lead to underobservation of emetic episodes (17). The nature and severity of the PONV noted in a study obviously may affect the accuracy or applicability of its independent risk factor findings.

Gaps in the patient populations studied are a fourth limitation of PONV risk factor research. Only a single major multivariable study has focused on outpatients (17), and only two have focused on children (36,48). This deficiency raises at least some questions about the general applicability of findings that derive from adult inpatients.

One further limitation of current PONV risk factor research is the difficulty in separating "true" from "surrogate" risk factors (21,79). This difficulty relates to deficiencies in knowledge of PONV pathophysiology and to the peril in epidemiological research of confusing association and causality. For example, certain types of surgery, e.g., gynecological procedures, might be surrogate risk factors for the true risk factor of female gender. Postoperative opioid use might be a surrogate for pain level, or *vice versa*, and certain types of surgery, e.g., orthopedic shoulder procedures, also

might be a surrogate for opioid use or pain level. Duration of surgery might be a surrogate for duration of anesthesia or *vice versa*. Thus, even if multivariable analysis identifies an independent PONV predictor, factors potentially underlying that predictor must be considered when applying the finding in clinical practice (79).

Clinical Application of Risk Factor Findings

Scoring Systems. A number of groups have sought not only to identify independent PONV risk factors (Table 1) but to develop formulas quantifying a given patient's likelihood of suffering nausea, emetic events, or both (17,19,21,27,29,36). They have introduced 8 major PONV risk scoring systems (Table 4 and Appendix). With 2 exceptions (17,36), these formulas preponderantly include patient-related factors and only 2 formulas include both surgery-related and anesthesia-related factors (17,26) (Table 4).

Seven of the 8 systems have been validated in additional populations, centers, or both, from those in which the formulas originally were developed. In the original studies devising 4 of the scoring systems, the overall patient populations were randomly divided into an "evaluation" subgroup, in whom the risk factors were first identified and incorporated into a formula, and a "validation" subgroup in whom the significance of the risk factors and accuracy of the scoring system were then tested (17,27,29,36). In addition, 6 of the 8 scoring systems have been validated in separate populations by the original (11,28–30,32,80) and, in some cases, also other investigators (1,31,48,81).

The accuracy of PONV scoring systems, that is, their ability to correctly discriminate between patients who will or will not suffer PONV, has most commonly been tested through calculation of the area under a given system's receiver operating characteristic (ROC) curve. This curve plots the scoring system's true-positive rate (sensitivity) against its false-positive rate (1 − specificity). The area under the curve is expressed as a value between 0 and 1. An area under the ROC curve of 0.50 denotes that a scoring system is correct half of the time, i.e., is no better than guessing. An area of 1.0 denotes that the scoring system is correct 100% of the time.

Given the previously discussed limitations of PONV risk factor research, as well as the limited statistical strength of predictors identified thus far (ORs generally 1.5–3.0) (79), it is not surprising that scoring systems have shown only poor to moderate accuracy, i.e., areas under the ROC curve ranging from 0.56–0.785 (Appendix). In other words, these scoring systems achieve a 12%–57% relative improvement over guesswork.

Despite the limitations in accuracy of PONV risk scoring systems, their use to better tailor antiemetic interventions has been shown to significantly reduce the incidence of PONV in general and particularly in high-risk patient populations, while avoiding the expense and potential side effects of prophylactic antiemetics in lower-risk individuals. For example, in a recent study ($n = 162$) involving adult inpatients undergoing surgery under general anesthesia in several departments, the overall incidence of PONV in the 24 h after surgery was reduced from an expected 47% historically to 36%, a 23% relative decrease (82). Another study in a similar population ($n = 428$) achieved a significant reduction in the overall PONV rate in the 24 h after surgery from 49.5% historically to 14.3% ($P < 0.001$), a 71% relative decrease (83). Moreover, the use of a scoring system (combination of risk factors) has been shown to have a greater discriminating power than the use of a single risk factor (80). The Apfel et al. (29) simplified scoring system predicted PONV significantly more accurately than did the single risk factors of the surgical site or a history of PONV or motion sickness: the area under the ROC curve was 0.68 (95% CI, 0.66–0.71) for the simplified scoring system versus 0.53 (0.50–0.56) for surgical site and 0.58 (0.56–0.61) ($P < 0.001$) for history of PONV or motion sickness.

No scoring system yet has emerged as a "gold standard" based on accuracy. The main improvements in scoring systems have consisted of simplification and, hence, increased user-friendliness, rather than performance enhancement. Koivuranta et al. (19), Apfel et al. (29), and Eberhart et al. (36) found that omission of the constants and coefficients derived from logistic regression modeling only minimally, if at all, diminishes scoring system accuracy. In addition, Koivuranta et al. and Apfel et al. came to the counter-intuitive conclusion that inclusion of more than a few risk factors attains little to no improvement in accuracy. Apfel et al. speculate that the latter observation may be attributable to the limited number of predictive factors identified that are applicable across populations (28).

Thus for adults, Apfel et al. (29) and Koivuranta et al. (19) have been able to create simplified scoring systems removing weighting of predictors and incorporating only 4 and 5 risk factors, respectively (Table 4, Appendix). More recently, Eberhart et al. (48) created a 4-item simplified scoring system for children. Van den Bosch et al. (26) have taken a somewhat different approach that could be characterized as "semi-simplification." Their scoring system also omits constants or coefficients, and it contains only 5 items. However, rather than scoring each item 0 or 1 ("no" or "yes"), the system assigns different point values to particular alternative variables for each item, so that a nomogram is required to use the system (Appendix). Eberhart et al. (48) and Van den Bosch et al. (81) devised their new scoring systems because they found

what they judged to be relatively limited discriminating power of existing formulas in pediatric patients (0.56–0.65) or in their adult patients undergoing a wide range of procedures (0.63–0.66), respectively (Appendix).

The simplified scoring systems obviate laborious calculations and may reduce the scope of required detailed history-taking but have demonstrated equivalent or superior discriminating power compared with more complex formulas (1,28,31). This has been seen in published scoring system comparisons, although these are limited in number. The comparisons also have suggested some differences in accuracy among the various systems. In adults, the Koivuranta et al. (19) simplified system has been shown to have a statistically higher predictive value than the Palazzo and Evans nonsimplified system (21) (0.71 versus 0.68 for postoperative nausea; $P = 0.007$ and 0.70 versus 0.64 for postoperative vomiting; $P < 0.05$) (28) and a numerically greater area under the ROC curve (0.66 versus 0.63) than does the Apfel et al. simplified system (29). In children, the Koivuranta et al. simplified system had a significantly larger area under the ROC curve (0.61) than did the Palazzo and Evans system (0.56; $P < 0.001$) or the Apfel et al. simplified (0.58) or nonsimplified (0.59) systems ($P < 0.003$ for both Apfel et al. systems) (48). In adults, the Apfel et al. simplified (28) or original (1) systems exhibited significantly greater accuracy than did the Palazzo and Evans formula (0.68 versus 0.64, $P < 0.05$ for PONV and 0.73 versus 0.68 for postoperative vomiting, $P = 0.005$, respectively). The Apfel et al. simplified system also showed significantly greater accuracy than the Sinclair et al. (17) nonsimplified formula in one adult study (0.71 versus 0.64; $P = 0.008$), but the Sinclair et al. system had a significantly larger area under the ROC curve than did either of the Apfel et al. systems in a pediatric study (0.65 versus 0.59 or 0.58; $P < 0.003$) (48). In that pediatric study, the Sinclair et al. system also had significantly greater discriminating power than did the Palazzo and Evans formula (0.65 versus 0.56; $P < 0.001$). In judging these comparisons, it should be kept in mind that unlike the other systems, the Sinclair et al. formula was developed in outpatients but all comparisons were in inpatients.

Taken as a whole, the comparisons suggest that for inpatients, the Koivuranta et al. simplified system (19) is perhaps the most accurate, but not vastly more accurate than the Apfel et al. simplified (29) or original (27) or the Sinclair et al. (17) systems. All four of these systems do seem superior to the Palazzo and Evans formula (21), however. The comparisons also suggest that the use of different scoring systems for adult versus pediatric inpatients may increase accuracy.

In conclusion, I believe that their accuracy, and, most importantly, simplicity relative to the other scoring systems make the Koivuranta et al. (19) or Apfel et al. (28) simplified scoring systems the current preferred choice for use in adults, especially inpatients, and the Eberhart et al. (36) simplified system the current preferred choice for use in children, especially inpatients. However, it should be noted that these scoring systems are only moderately accurate in predictive ability.

Clinical and Research Implications. Modern multivariable risk factor studies have strengthened the belief in the multifactorial nature of PONV and led to the development of a so-called "multimodal approach" to better address this issue (52,84). The innovative feature of the multimodal approach is its reliance on risk factor reduction, e.g., avoidance of volatile anesthetics, in addition to prophylaxis with antiemetics.

Insofar as applying risk factor findings to PONV management, a "decision-tree" approach has been advocated in which patients are divided into "low," "moderate," "high," or "extremely high-risk" populations based on the number or nature of their risk factors or their score on a formula (2,85,86). Consensus is emerging that antiemetic prophylaxis is not cost-effective in low-risk patients (<10% or <20% expected risk) and is appropriate in other patients. Consensus also is emerging that antiemetic prophylaxis may be best accomplished in moderate, high-risk, or extremely high-risk patients with combinations of drugs from different antiemetic classes or of pharmacological plus nonpharmacological interventions (e.g., acupuncture), with multimodal management, or with both (7,11,87) [(88–94)].

Conclusions

Knowledge of independent PONV risk factors is crucial for the optimal use of antiemetic prophylaxis and multimodal management strategies. Modern multivariable studies, meta-analyses, and systematic reviews have greatly increased such knowledge. Independent risk factors identified by modern research, such as female gender from puberty, nonsmoking status, history of PONV or motion sickness, childhood after infancy or younger adulthood, lengthy or emetogenic surgery, or administration of nitrous oxide, volatile anesthetics, or postoperative opioids, may be used in combination to predict, with moderate accuracy, the likelihood of PONV in a given patient. Further PONV research examining patient genetic characteristics and under-investigated potential clinical risk factors and involving outpatients and children should lead to predictive systems with improved discriminating power and applicability. This development, in turn, will enable anesthesiologists to better identify at-risk patients, further reduce the incidence of PONV, and increase the safety and cost-effectiveness of PONV prophylaxis.

Appendix. PONV Risk Scoring Systems

Scoring system (reference[s])	Formula	Accuracy: area under the receiver operating characteristic curve [95% CI] (reference[s])*	Comments
Simplified (Unweighted) Scoring Systems			
Apfel et al. (29)	(gender: male = 0, female = 1) + (history of PONV or motion sickness: no = 0, yes = 1) + (smoking status: no = 0, yes = 1) + anticipated use of postoperative opioids: no = 0, yes = 1)	0.58 [0.54–0.62] in children (48) 0.63 [0.60–0.66] (81) 0.679 [0.634–0.724] (20) 0.68 [0.66–0.72] (28) 0.71 [not reported] (31)	Range of possible scores: 0–4. Risk of PONV by score (29): 0, 10% 1, 21% 2, 39% 3, 61% 4, 79%
Eberhart et al. (36)	(duration of surgery ≥30 min: no = 0, yes = 1) + (age ≥3 yr: no = 0, yes = 1) + (strabismus surgery: no = 0, yes = 1) + (history of PV in child or of PV/PONV in a parent or sibling: no = 0, yes = 1)	0.72 (0.68–0.77) (36)	Range of possible scores: 0–4. Only scoring system developed for children. Developed for vomiting only. Risk of PV by score (36): 0, 9% 1, 10% 2, 30% 3, 55% 4, 70%
Koivuranta et al. (19)	(gender: male = 0, female = 1) + (history of PONV: no = 0, yes = 1) + (duration of surgery >60 min: no = 0, yes = 1) + (smoking: no = 0, yes = 1) + (history of motion sickness: no = 0, yes = 1)	0.61 [0.58–0.65] in children (48) 0.66 [0.63–0.69] for PONV, 0.66 [0.63–0.69] for nausea, 0.65 [0.62–0.68] for vomiting (81) 0.692 [0.648–0.736] (29) 0.71 [0.69–0.73] (1) 0.719 for nausea, 0.695 for vomiting [95% CIs not reported] (19)	Range of possible scores: 0–5 Risk of PO nausea, vomiting, respectively, by score (19): 0, 17%, 7% 1, 18%, 7% 2, 42%, 17% 3, 54%, 25% 4, 47%, 38% 5, 87%, 61%
"Semi-Simplified Scoring System": requiring a nomogram			
Van den Bosch et al. (26)	= sex (male = 0, female = 6) + history of PONV or motion sickness (no = 0, yes = 10) +smoking status (no = 8, yes = 0) +surgery type (lower abdominal or middle ear = 8, other = 0) +anesthetic technique (propofol = 0, isoflurane = 9) +age (15–19 yr = 20, 20–24 yrs = 19, 25–29 yr = 17, 30–34 yr = 16, 35–39 yr = 14, 40–44 yr = 13, 45–49 yr = 11, 50–54 yr = 10, 55–59 yr = 9, 60–64 yr = 7, 65–69 yr = 6, 70–74 yr = 4, 75–79 yr = 3, 80–84 yr = 1, ≥85 yr = 0)	0.72 [0.70–0.74] (26) 0.70 [0.68–0.72] (predicted for other inpatient populations) (26)‡	Range of possible scores: 0–61. Risk of PONV by point score: 2, 10% 12, 20% 19, 30% 25, 40% 31, 50% 31, 50% 36, 60% 42, 70% 49, 80% 59, 90%
Weighted Scoring Systems: predicted risk = $e/1\text{-}e^{z}$ when:			
Apfel et al. (27)	−0.92 +1.28 x (gender: male = 0, female 1) −0.029 x (age in yr) −0.74 x (smoking status: no = 0, yes = 1) +0.63 x (history of PONV or motion sickness: no = 0, yes = 1) +0.26 x (duration of anesthesia in hours)	0.59 [0.56–0.63] for vomiting in children (48) 0.62 [not reportd] (81) 0.698 [0654–0.742] (29) 0.70 [0.67–0.72] (1) 0.77 [not reported] for vomiting (27)	Developed for vomiting only.
Koivuranta et al. (19)	−2.21† +0.93 x (gender: male = 0, female = 1) +0.82 x (history of PONV: no = 0, yes = 1) +0.75 x (duration of surgery >60 min: no = 0, yes = 1) +0.61 x (smoking status: no = 1, yes = 0) + 0.59 x (history of motion sickness: no = 0, yes = 1) −0.92	0.689 [0.645–0.733] (29) 0.66 [not reported] (81) 0.695 for vomiting, 0.719 for nausea [95% CI is not reported] (19)	

(Continued)

Appendix. Continued

Scoring system (reference[s])	Formula	Accuracy: area under the receiver operating characteristic curve [95% CI] (reference[s])*	Comments
Palazzo and Evans (21)	−5.03 +2.34 x (postoperative opioids: no = 0, yes = 1) +3.97 x (history of PONV: no = 0, yes = 1) +2.4 x (gender: male = 0, female = 1) +078 x (history of motion sickness: no = 0, yes = 1) −3.2 (female with previous PONV: no = 0, yes = 1)	0.56 [0.52–0.60] in children (48) 0.62 for vomiting, 0.682 for nausea [95% CIs not reported] (19) 0.64 [0.62–0.67] (28) 0.68 [0.65–0.70] (1) 71% [not reported] § (32)	
Sinclair et al. (17)	−5.97 −0.14 x (age in yr/10) −1.03 x gender (gender: female = 0, male = 1) −0.42 x (smoking status: no = 0, yes = 1) +1.14 x (history of PONV: no = 0, yes = 1) +0.46 x (duration of surgery in 30-min increments) +2.36 x (general anesthesia; no = 0, yes = 1) +1.48 x (ENT surgery: no = 0, yes = 1) 1.77 x (ophthalmological surgery: no = 0, yes = 1) +1.90 x (plastic surgery: no = 0, yes = 1) +1.2 x (gynecological surgery except dilatation and curettage: no = 0, yes = 1) +1.04 x (orthopedic surgery on knee: no = 0, yes = 1) +1.78 x (orthopedic surgery on shoulder: no = 0, yes = 1) +094 x (orthopedic surgery elsewhere: no = 0, yes = 1)	0.65 [0.61–0.69] in children (48) 0.64 [not reported in inpatients (31) 0.68 [0.66–0.71[in inpatients (28) 0.785 [0.774–0.796] in original outpatient population (17)	Only scoring system developed in outpatients.

CI = confidence interval; ENT = ear, nose and throat; PO = postoperative; PONV = postoperative nausea and vomiting; PV = postoperative vomiting.
*All values are for PONV in adults unless indicated otherwise; †Published in (26); ‡Estimated by using bootstrapping techniques, adjusted for over-optimism (26); § This figure represents the overall correct prediction rate of the Palazzo and Evans scoring system in a second patient population rather than the area under the receiver-operating characteristics curve.

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