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Effect of Postoperative Experiences on Willingness to Pay to Avoid Postoperative Pain, Nausea, and Vomiting

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Background: **The authors assessed the willingness to pay (WTP) for "perfect" prophylactic antiemetics and analgesics in patients who were scheduled to undergo surgery during general anesthesia. Furthermore, they determined whether postoperative experiences of pain and nausea and vomiting (PONV) changed patients' WTP.**

Methods: **Data were collected alongside a randomized clinical trial that investigated the incidence of PONV in patients anesthetized with either inhalation anesthesia or total intravenous anesthesia. A subset of 808 consecutive patients participating in the trial completed WTP questionnaires 1 day before and 2 weeks after surgery. The outcome measure was the maximum amount of money that patients were willing to pay for "perfect" antiemetics and analgesics. Preoperative WTP and individual WTP changes after surgery were analyzed in relation to baseline characteristics and postoperative pain and PONV experiences.**

Results: **Prevention of postoperative pain was valued higher than prevention of PONV. The median preoperative WTP for analgesics was US $35 (interquartile range, $7–69) *vs.* US $17 (interquartile range, $7–69) for antiemetics. Individual WTP changes for antiemetics were not related to PONV experience, whereas severe postoperative pain (numerical rating score ≥ 8) was associated with an increase in the WTP for analgesics.**

Conclusions: **Severe postoperative pain experiences increased patients' WTP for analgesics, but PONV did not increase WTP for antiemetics. The elicited WTP values were lower than those reported in previous studies, which is possibly related to differences in market culture or patients' attitudes toward postoperative pain, nausea, and vomiting.**

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Additional material related to this article can be found on the ANESTHESIOLOGY Web site. Go to http://www.anesthesiology.org, click on Enhancements Index, and then scroll down to find the appropriate article and link. Supplementary material can also be accessed on the Web by clicking on the "ArticlePlus" link either in the Table of Contents or at the top of the Abstract or HTML version of the article.

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DESPITE advances in anesthetic practice, postoperative pain and postoperative nausea and vomiting (PONV) remain prevalent, unpleasant side effects of anesthesia and surgery.[1–5] Possible strategies to reduce the incidence of PONV include risk-based prophylactic administration of antiemetics[6–12] and the use of newer anesthetic drugs (propofol instead of volatile anesthetics, substitution of nitrogen for nitrous oxide).[7,13,14] Postoperative pain management may be improved by use of an "acute pain service"[15] and perhaps by preoperative identification of patients at high risk of severe pain.[16]

It is difficult to evaluate these interventions using a cost–utility analysis,[17] because there is no universally accepted method of assigning monetary value to transient disutility such as postoperative pain or PONV. A possible alternative is to use the "stated preference approach." This approach establishes how patients value a certain healthcare outcome by asking them how much they are willing to pay (WTP) for an intervention that yields this outcome.[18] The elicited WTP values may be used as input in cost–benefit analyses of strategies for avoiding PONV and postoperative pain. When the costs of a strategy do not exceed the values that patients attach to its effects, one might decide to implement the strategy.

Several WTP studies have been performed in relation to PONV.[9,19–22] However, these studies involved children[19] or were performed with small[20–22] or restricted[9,20] study populations, and WTP was measured after surgery only. So far, only one small study addressed patients' WTP for avoiding postoperative pain.[22]

The current study assessed the WTP for a hypothetical, "perfect" antiemetic or analgesic, both 1 day before and 2 weeks after surgery, in a large, unselected mix of adult inpatients and outpatients scheduled to undergo surgery during general anesthesia. Furthermore, we identified factors that determined patients' preoperative WTP and investigated whether postoperative pain and PONV experiences changed an individual's WTP.

Materials and Methods

Patients

Patients were recruited from a single-center, patient-blinded, observer-blinded, randomized trial that com-

pared the incidence of PONV after inhalation anesthesia with isoflurane–nitrous oxide *versus* intravenous anesthesia with propofol. The design of this trial was approved by the institutional review board of the Academic Medical Center of the University of Amsterdam, Amsterdam, The Netherlands, and is described elsewhere.[14] In short, this trial included inpatients and outpatients who were aged 18–80 yr and were scheduled to undergo various surgical procedures (with the exception of cardiac surgery or intracranial neurosurgery) during general anesthesia. All patients gave written informed consent before being included in the study. Exclusion criteria were: American Society of Anesthesiologists physical status greater than III, use of antiemetic or proemetic medication in the 2 weeks before surgery, or insufficient command of the Dutch language.

Blinded trained research nurses recorded baseline characteristics such as sex, age, patient status (outpatient *vs.* inpatient), previous surgery, previous PONV, history of motion sickness, anxiety state and trait as measured with the Spielberger State-Trait Anxiety Inventory (STAI),[23] net household income, and type of scheduled surgery.

Patients' postoperative experiences of PONV (*i.e.*, nausea or retching or vomiting or a combination of these symptoms) and severe pain (measured as an 11-point numerical rating score [NRS], where 0 indicates no pain at all and 10 indicates the most severe pain imaginable) were recorded every 15 min until discharge from the postanesthesia care unit (PACU). Severe pain was defined as a NRS of 8 or greater.

WTP Questionnaire

The WTP questionnaire was presented to the last 852 participants in the trial. The WTP questionnaire was piloted for comprehensibility and self-report suitability. Identical self-administered WTP questionnaires were used preoperatively and postoperatively. The questionnaire that patients filled out postoperatively was returned by mail.

The WTP questionnaire contained three questions. First, the patient was requested to indicate for a series of predefined amounts of money (US $7, 17, 35, 69, 173, and 346; see also Analysis section) whether he or she would be willing to pay each of these amounts out of pocket for a hypothetical, "perfect" antiemetic ("cumulative bidding technique"). This question was presented as follows: "Suppose a pill exists that completely prevents the occurrence of nausea and vomiting after surgery. This pill will not be reimbursed by your medical insurance company. You have to go and buy this pill yourself at the pharmacy before the operation. How much would you be willing to pay for this pill? Fill out for each amount of money whether you would buy, would doubt to buy, or would not buy the pill" (appendix, question 1). A similar scenario was presented for a hypothetical pill that completely avoids postoperative pain (appendix, question 2). A third question was added to measure patients' preferences for PONV *versus* pain prevention (appendix, question 3). Here, the patient was asked to choose one out of five possible "combination pills" with different treatment efficacy for PONV and pain, varying from almost perfect treatment of PONV, but minimal effect on pain, to almost perfect treatment of pain, but minimal effect on PONV. This pill was stated to be free of charge. This question served as a check on the questionnaire's convergent validity. This means that preferences for either PONV or pain prevention should be consistent with possible differences in WTP for PONV and pain.

Analysis

The outcome on the individual level was the patient's maximal accepted bid (MAB), *i.e.*, the maximum amount of money that a patient was willing to pay for a "perfect" antiemetic or analgesic. The MAB of a patient who did not want to pay the lowest amount of money (US $7) was set to US $0.

It should be noted that the original WTP values were measured in Dutch guilders. These values were converted to US dollar values after a correction for price changes in the period from 1998 (year of data collection) to 2003 (most recent price index available), using a price index of 115.2. This index was calculated by the Dutch Central Bureau of Statistics, Voorburg, The Netherlands.

No formal sample size calculation was performed, but in view of previous studies a sample size in excess of 800 was regarded as sufficient to detect changes under a wide range of assumptions.

The following characteristics were considered as possible covariates for preoperative WTP: sex, age, previous surgery, previous PONV, history of motion sickness, net household income (up to 1,382 US$; 1,382 $<$ US$ $\leq$ 2,281; 2,281 $<$ US$ $\leq$ 3,318; more than 3,318 US$), patient status (inpatient or outpatient), and STAI anxiety state and trait. Individual WTP changes after surgery were tested for postoperative experiences of PONV and pain, in addition to anesthetic technique and the mentioned baseline characteristics.

Univariate and multivariate analyses for preoperative WTP dependence on baseline characteristics were performed with ordinal logistic regression. Before these analyses, the proportional odds assumption was tested with the score test.[24,25] The proportional odds assumption was justified for pain (without any measures). The assumption was also justified for PONV, but only after the variable for preoperative WTP was recoded (the categories US $173 and $346 were collapsed to one category) and age was excluded from the multivariate analysis.

Univariate and multivariate analyses for dependence of individual WTP changes on PONV and pain experiences,

income, and other baseline characteristics were performed with linear regression. Here, the change of WTP (in bids) was considered as a continuous variable with range −6 to +6 bids, in case a patient who was willing to pay US $346 before surgery changed his or her MAB to US $0 after surgery or *vice versa*.

Variables were included in the multivariate analysis if the *P* value in the univariate analysis was 0.15 or less. All analyses were performed with SPSS for Windows 10.1.0 (SPSS Inc., Chicago IL). The proportional odds assumptions were tested with SAS 8.2 (TS2MO; SAS Institute Inc. Cary, NC).

Results

Response and Baseline Characteristics of Respondents

Of the 852 participants, 808 (95%) responded to the WTP questionnaire. Preoperative WTP data were obtained from 803 patients (94%) for antiemetics and 808 patients (95%) for analgesics. Postoperative WTP data were obtained from 681 patients (80%) for both antiemetics and analgesics. Complete preoperative and postoperative WTP data for antiemetics and analgesics were obtained from 681 (80%) patients.

Of the 808 respondents, 57% were women and 74% were inpatients, with a median age of 42 yr (interquartile range [IQR], 32–54 yr). Eighty-three percent of the respondents had undergone previous surgery, of whom 32% reported to have experienced PONV. Motion sickness was reported in 19% of the respondents. The median preoperative STAI anxiety state score was 40 points (IQR, 33–49 points), and the STAI anxiety trait score was 37 points (IQR, 31–45 points). The net median household income per month was US $2,074 ($1,382–3,110); 37% of the respondents declined to reveal their net monthly household income (table 1). Baseline characteristics of nonrespondents were similar to those of respondents.

Table 1. Characteristics of the Respondents

Characteristic	% of Respondents
Female sex	57
Inpatient status	74
Age, yr*	42 (32–54)
Previous surgery	83
History of PONV in patients with previous surgery	32
History of Motion sickness	19
STAI† anxiety state score*	40 (33–49)
STAI† anxiety state score > 50 points	20
STAI† anxiety trait score*	37 (31–45)
STAI† anxiety trait score > 50 points	12
Net household income per month§	
Quartile‡ 1: ≤ 1,382 US$	16
Quartile‡ 2: 1,382 < US$ ≤ 2,281	20
Quartile‡ 3: 2,281 < US$ ≤ 3,318	15
Quartile‡ 4: > 3,318 US$	13
Unwilling to provide income data	18
Missing	19
Type of surgery§	
Superficial	75
Lower abdominal	4
Upper abdominal	4
Laparoscopy	10
Strabismus	1
Middle ear	5

Data are presented as percentages unless stated otherwise.

* Median (interquartile range). † Using Spielberger's State-Trait Anxiety Inventory (STAI), the patient's anxiety state and trait are both scored on a continuous scale from 20 to 80 points. Patients scoring more than 50 points are considered to be very anxious or to have a strong anxiety trait, respectively. ‡ Income quartiles for the population in The Netherlands as defined by the Dutch Central Bureau of Statistics in 1996. § Total percentage is not equal to 100% due to rounding error.

PONV = postoperative nausea and vomiting.

Pill Preference and WTP for "Perfect" Antiemetics and Analgesics

The distribution of the respondents' pill preferences and maximal accepted bids for "perfect" antiemetics and analgesics is shown in figure 1.

For antiemetics, the median WTP was US $17 (IQR, $7–69) before surgery. Two weeks after surgery, the median WTP for antiemetics was US $17 (IQR, $7–35) (table 2). After surgery, 47% of the respondents were willing to pay the same amount of money for preventing PONV as before surgery, whereas 32% decreased their bid and 21% increased their bid.

For analgesics, the median WTP was US $35 (IQR, $7–69) before and after surgery (table 2). After surgery, 48% of the respondents were willing to pay the same amount of money for preventing pain, 27% decreased their bid, and 25% increased their bid.

The higher WTP for analgesics compared with antiemetics was also reflected by the responses to the pill preference question. Respondents generally favored a pill that was more effective against pain than against PONV: 56% preferred pill A or B, whereas 27% preferred pill D or E. Sixteen percent of the respondents showed no preference for either pain or PONV prevention (pill C) (fig. 1C).

Preoperative WTP in Relation to Baseline Characteristics

According to univariate ordinal regression analysis, previous surgery was negatively related ($P = 0.025$) to preoperative WTP for antiemetics, whereas STAI preoperative anxiety state score ($P = 0.12$) and net household income ($P < 0.001$) had a positive association with this outcome. A multivariate regression analysis showed that preoperative WTP for antiemetics was increased if patients were more anxious ($P = 0.023$) or had a higher net household income ($P < 0.001$). Additional information regarding this is available on the ANESTHESIOLOGY Web site at http://www.anesthesiology.org (Web table 1).

According to univariate ordinal regression analysis, fe-

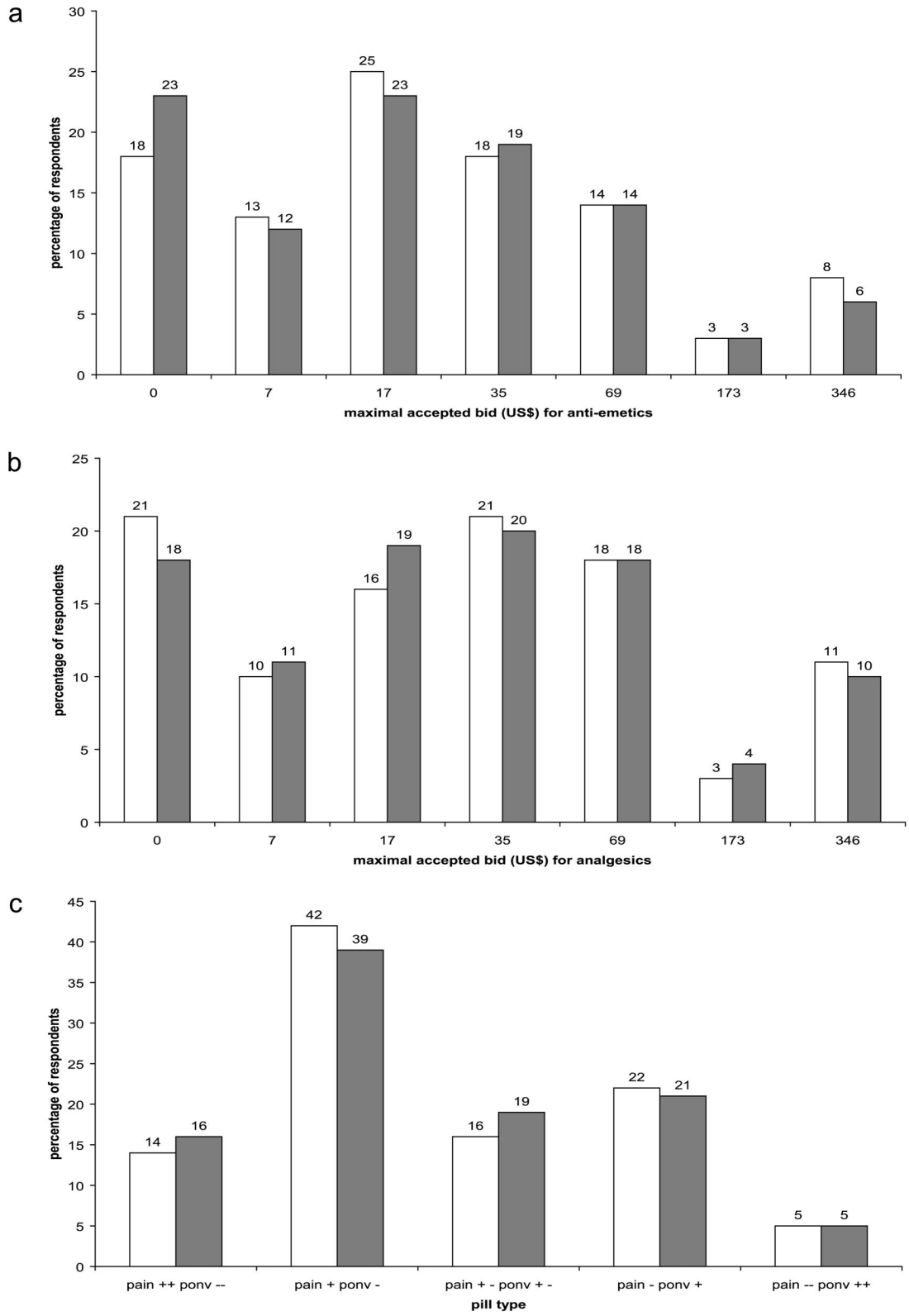

Fig. 1. Maximal accepted bids and pill preferences before (*white bars*) and 2 weeks after (*shaded bars*) surgery. *A* shows the distribution of respondents' maximal accepted bids for "perfect" antiemetics. *B* shows the distribution of respondents' maximal accepted bids for "perfect" analgesics. *C* shows the distribution of respondents' pill preferences. PONV = postoperative nausea and vomiting.

male sex ($P = 0.101$) and age ($P = 0.029$) were negatively related to preoperative WTP for analgesics, whereas inpatient status ($P = 0.021$), STAI preoperative anxiety state score greater than 50 points ($P = 0.006$), and net household income ($P < 0.001$) had a positive association with this outcome. Multivariate analysis

Table 2. Absolute WTP before and 2 Weeks after Surgery and Individual Change of WTP (in Number of Bids Change)

	Absolute WTP		
	Preoperative WTP	Postoperative WTP	Individual WTP Change
PONV	17 (7–69)	17 (7–35)	0 (−1; 0)
No PONV	17 (7–69)	17 (0–35)	0 (−1; 0)
Any PONV	17 (7–69)	17 (7–69)	0 (0; 1)
Nausea (moderate or severe)	17 (7–69)	17 (17–69)	0 (−1; 0.5)
Retching or vomiting	17 (7–69)	35 (17–69)	0 (0; 0.75)
Pain	35 (7–69)	35 (7–69)	0 (−1; 0)
NRS > 4	35 (7–69)	35 (7–69)	0 (−1; 1)
NRS ≥ 7	35 (7–69)	35 (7–69)	0 (0; 1)
NRS ≥ 8	35 (7–69)	35 (7–69)	0 (0; 1)

Data are presented as median (interquartile range).

NRS = numerical rating score; PONV = postoperative nausea and vomiting; WTP = willingness to pay.

showed that preoperative WTP for analgesics was higher if patients had an inpatient status ($P = 0.004$), were more anxious (*i.e.*, STAI state score > 50 points) ($P = 0.028$), or had a higher net household income ($P < 0.001$). Additional information regarding this is available on the ANESTHESIOLOGY Web site at http://www.anesthesiology.org (Web table 1).

Individual WTP Changes in Relation to Postoperative Experiences of Pain and PONV in the PACU

In the PACU, 75% of all respondents were free of PONV, 13% were moderately or severely nauseated, and 13% experienced at least one episode of retching or vomiting. Moderate pain (NRS > 4) was experienced by 63% of patients, whereas 39% (NRS ≥ 7) and 23% (NRS ≥ 8) experienced severe pain in the PACU (table 3).

According to univariate linear regression analysis, experience of any PONV in the PACU was positively related ($P = 0.054$) to a postoperative change (increase) of the MAB for antiemetics. Other factors that were associated with an increase of the MAB were female sex ($P = 0.076$), STAI preoperative anxiety state score ($P = 0.025$), STAI anxiety trait score ($P = 0.017$), and isoflurane–nitrous oxide anesthesia ($P = 0.005$). Older respondents ($P = 0.083$) and respondents with higher incomes, however, were more inclined to decrease their MAB ($P = 0.028$). The income effect was confirmed in the multivariate analysis ($P = 0.043$), but the influence of the other factors including experience of any PONV in the PACU could not be demonstrated. Additional information regarding this is available on the ANESTHESIOLOGY Web site at http://www.anesthesiology.org (Web table 2).

Table 3. PONV and Pain Experiences in the Postanesthesia Care Unit

Postoperative Experience	% of Respondents
PONV	
No PONV	75
Any PONV	25
Nausea (moderate or severe)	13
Retching or vomiting	13
Pain	
NRS > 4	63
NRS ≥ 7	39
NRS ≥ 8	23

Data are presented as percentages.

NRS = numerical rating score; PONV = postoperative nausea and vomiting.

According to univariate linear regression analysis, experience of severe pain (NRS ≥ 8) in the PACU was associated ($P = 0.016$) with a postoperative increase of the MAB for analgesics, and so was female sex ($P = 0.142$), whereas respondents with a STAI anxiety trait score greater than 50 points ($P = 0.011$) tended to decrease their bids. These associations were also evident from the multivariate analysis (P value of 0.006 for STAI anxiety trait score > 50 points and 0.015 for NRS ≥ 8), although the effect of female sex could not be confirmed. Additional information regarding this is available on the ANESTHESIOLOGY Web site at http://www.anesthesiology.org (Web table 2).

Discussion

We measured surgical patients' WTP for "perfect" antiemetics and analgesics before and 2 weeks after surgery and investigated which factors altered patients' WTP after surgery. We also assessed whether patients preferred prevention of PONV over avoidance of pain or *vice versa*.

Patients generally preferred avoidance of pain over prevention of PONV. Before surgery, half of our respondents were willing to pay US $35 or more out of pocket to avoid postoperative pain *versus* US $17 or more to prevent PONV. Also, after surgery, the MAB was more often decreased for PONV than for pain, whereas the percentage of patients who were willing to pay the same amount of money as before surgery was about the same (48%).

We expected that patients who experienced PONV or pain would increase their bid 2 weeks after surgery. After surgery, however, the WTP for pain was not changed, irrespective of the severity of early postoperative pain experience (table 2). Although the WTP for PONV was increased for patients who experienced retching or vomiting, it increased only slightly for patients who experienced moderate or severe nausea (table 2). Despite these variations in WTP between subgroups with different postoperative PONV experiences, multivariate analyses showed that only income determined whether individual patients would change their WTP for PONV after the operation. In contrast, individual changes in WTP for pain were not income depen-

dent, but evoked by severe postoperative pain (NRS ≥ 8) and related to a patient's preoperative anxiety trait.

Higher preoperative anxiety levels also increased patients' willingness to pay for PONV and pain prevention before surgery. Other factors that were positively related to preoperative WTP were income (antiemetics and analgesics) and inpatient status (analgesics). Although our results confirm the relation between income and WTP that was evident from previous studies,[19,21] the influence of previous PONV experience on WTP[21] could not be confirmed.

When interpreting our results, it should be noted that 83% of our patients underwent surgery on a previous occasion. On average, these patients had lower preoperative MABs for PONV (US $17) than inexperienced surgical patients (US $35). The preoperative MABs for pain were the same as in patients who had never undergone surgery before (US $35).

Five previous studies have investigated the WTP for PONV prevention in surgical patients. One study assessed how much parents (n = 162) whose child had undergone surgery within the previous 2 yr were willing to pay to reduce the chance that their child would experience PONV from 1 in 3 to less than a 1 in 10 chance, in case the child had to undergo a hypothetical simple surgical procedure requiring general anesthesia.[19] The median WTP in this study was UK £50 (95% confidence interval, £20–80). Another study assessed the WTP for preventing PONV in 164 women scheduled to undergo outpatient laparoscopic surgery. The study focused on a hypothetical situation in which the patient had to undergo the same laparoscopic operation in the future.[20] The mean (SD) WTP out of pocket in this population was US $117 ($82). In a third study, 80 elective surgical outpatients were asked (after recovery in the PACU) how much they were willing to pay to receive a hypothetical new drug, which would eliminate PONV, instead of the routine antiemetic, which would still allow a chance of PONV.[21] The median WTP out of pocket in this patient sample was US $56 (IQR, $26–97). The WTP ranged from US $40 (IQR, $20–95) in patients who did not develop PONV to US $100 (IQR, $61–200) in patients who experienced emesis. The fourth study measured WTP in a group of female patients admitted for gynecologic and breast surgery, of which 108 at high risk of PONV received multimodal antiemetic treatment, and a control group of 71 women at a lower risk of PONV did not receive antiemetics.[9] The WTP for receiving the same anesthetic technique in the future was high in patients who received multimodal prophylaxis, UK £84 (IQR, £33–184), compared with UK £14 (IQR, £4–30) for patients in the control group. Finally, in a study of 66 generally young white patients, patients were willing to pay US $162 and $230 to avoid nausea and vomiting, respectively. The same patients were willing to pay US $267 to prevent pain.[22]

Remarkably, the WTP for avoiding PONV and postoperative pain in these previous studies was much higher than that observed in our study (US $17 for PONV and $35 for pain; table 2). Although we used a bidding range with preset monetary values, which is vulnerable to starting point bias, the lower WTP values found in our study can not be explained by the choice of the bidding range, because the highest value in our bidding range (US $7–346) is even larger than the maximum values of the bidding ranges used in previous studies (US $0–190 or > $190,[19] and $0–250 or other[20]). Alternatively, the differences in WTP values may be related to differences in sample size and patient selection (previous study populations were approximately 5 times smaller and consisted of female patients with an increased risk of PONV, or parents who may be inclined to pay more to prevent PONV in their children). The fact that the median WTP in the outpatient study and in the subsample of patients who did not experience PONV was much closer to the WTP values we found also seems to point in this direction. Differences in (market) culture or patients' attitudes toward postoperative pain, nausea, and vomiting may also play a role. It remains to be defined whether this is actually so and whether this has a substantial influence on WTP values, when corrected for the influence of other factors. If cultural differences play a role, these may limit the generalizability of the results, but this effect may be counterbalanced by the fact that our study is the first study that assessed the WTP in a nonselected group of patients.

If we accept the WTP values for "perfect" antiemetics and analgesics elicited in this study, we may use them as input in cost–benefit analyses of strategies for avoiding PONV and postoperative pain. When the costs of a strategy do not exceed the values that patients attach to its effects, one might decide to implement the strategy. Alternatively, one might decide to ask for a modest copayment for improved drugs, knowing that both the preoperative and postoperative WTP values for antiemetics and analgesics were in the magnitude of existing copayments currently used for some medications in The Netherlands.

In conclusion, severe postoperative pain experiences increased patients' WTP for analgesics, but PONV did not increase WTP for antiemetics. The elicited WTP values were lower than reported in previous studies, which is possibly related to differences in market culture or patients' attitudes toward postoperative pain, nausea, and vomiting.

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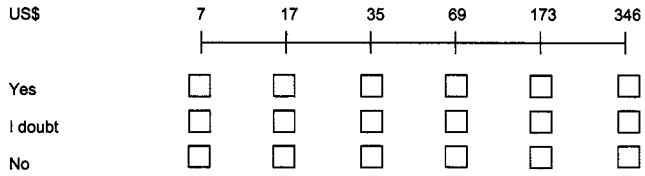
Appendix: Willingness-to-pay Questionnaire

Question 1: Willingness to Pay for "Perfect" Antiemetics

Suppose a pill exists that completely prevents the occurrence of *nausea and vomiting* after surgery. This pill will not be reimbursed by your medical insurance company. You have to go and buy this pill at the pharmacy before the operation. How much would you be willing to pay for this pill? Fill out for each amount of money whether you would buy, would doubt to buy, or would not buy the pill.



Question 2: Willingness to Pay for "Perfect" Analgesics

Suppose a pill exists that completely prevents *pain* after surgery. This pill will not be reimbursed by your medical insurance company. You have to go and buy this pill at the pharmacy before the operation. How much are you willing to pay for this pill? Fill out for each amount of money whether you would buy, would doubt to buy, or would not buy the pill (see above).

Question 3: Pill Preference

Unfortunately, a pill that completely prevents both nausea/vomiting and pain does not exist. Suppose we can offer you one of the following pills for free. You do not have to pay for it. Which pill would you choose to make you feel as comfortable as possible after the operation?

- Pill A: Relieves pain almost completely; hardly relieves nausea and vomiting
- Pill B: Relieves pain well; relieves nausea and vomiting a little
- Pill C: Relieves both pain and nausea and vomiting fairly well
- Pill D: Relieves pain a little; relieves nausea and vomiting well
- Pill E: Hardly relieves pain; relieves nausea and vomiting almost completely