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Sedation *versus* No Sedation in the Performance of Diagnostic Upper Gastrointestinal Endoscopy: A Canadian Randomized Controlled Cost-Outcome Study

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BACKGROUND: Sedation is not required to perform a technically adequate gastroscopy (EGDE), but does improve patient satisfaction, comfort, and willingness to repeat particularly in the elderly and those with decreased pharyngeal sensitivity. The comparative cost-efficacy of sedation *versus* no sedation remains poorly characterized.

AIM: To compare the cost-efficacy of diagnostic EGDE with and without sedation in an adult ambulatory Canadian population.

METHODS: A double-blind randomized controlled trial assigned patients to sedation *versus* placebo. "Successful endoscopy" was considered an EGDE rated 4/4 in technical adequacy (1 = inadequate to 4 = totally adequate), and 1–2/5 in patient self-reported comfort (1 = acceptable to 5 = unacceptable). Secondary outcomes included recovery room time, patient satisfaction alone, and willingness to repeat the procedure. Cost data were obtained using a published, institutional activity-based costing methodology. Analysis was intention to treat using standard univariate and multivariate methods.

RESULTS: 419 patients (mean age 54.5, 48% male) were randomized (N = 210 active *vs* N = 209 placebo). Among patients randomized to active medication 76% of procedures were "successful" (placebo 46%), 79% were satisfied with their level of comfort (placebo 47%), and willingness to repeat was 81% (placebo 65%). We observed a 10% crossover rate from placebo to active medications. The use of sedation was the major determinant of successful endoscopy (OR = 3.8; 95% CI: 2.5–5.7), but contributed to an increased recovery room time (29 *vs* 15 min; $p < 0.0001$). The expected cost of an additional successful endoscopy using sedation was $90.06 (CDN). In a planned subgroup analysis, among the elderly (>75; N = 53) unsedated endoscopy became the dominant approach. Indeed, in this population, a trend was observed favoring the effectiveness of placebo (63%) *versus* active medication (57%) (OR = 0.75; 95% CI: 0.25–2.3) and was less costly resulting in $450 savings/unsedated EGDE.

CONCLUSIONS: In the average Canadian ambulatory adult population, sedated diagnostic EGDE is more costly but remains an efficacious strategy by increasing the rate of successful endoscopies, patient satisfaction, and willingness to repeat. However, among the elderly (>75 yr), an unsedated strategy may be more cost-efficacious.

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INTRODUCTION

Diagnostic upper gastrointestinal esophagogastroduodenal endoscopy (EGDE) is carried out for a multitude of clinical indications (1). It is the most commonly performed endoscopic procedure with an incidence of about 8.6 per thousand population (2), and in Canada represents 51–65% of all gastrointestinal (GI) endoscopic procedures performed in teaching hospitals (3).

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The use of conscious sedation has resulted in the widespread diffusion and acceptance of this technology among physicians and patients alike (4). Improved patient tolerance and satisfaction afforded by parenteral sedation must be weighed against the risk of adverse cardiopulmonary events and the unit cost. It is estimated that sedation and related issues are responsible for up to 40% of total endoscopic cost including overhead costs and indirect costs (5).

We have previously shown that the use of routine parenteral sedation is not required to ensure a successful endoscopy in all adult ambulatory patients (6). In this prospective observational study of unsedated EGDE, 60% of EGDE were successful (technically feasible with a patient who remained comfortable) with 61% of patients reporting satisfaction with comfort and 80% of patients willing to repeat their procedure under the same test conditions. In this pilot study, patients with advancing age and decreased pharyngeal sensitivity were most likely to have a successful unsedated endoscopy. Given these pilot study results, an adequately powered double-blinded randomized controlled trial was necessary to compare cost-efficacy of routine sedation *versus* no sedation.

METHODS

Patient Population

This study was a double-blind placebo-controlled randomized trial that enrolled patients from 1999 to 2002 at two participating sites of the McGill University Health Center (Montreal General and Royal Victoria Hospitals). The primary base from which this study population was drawn is a racially and ethnically diverse outpatient population from a large metropolitan Canadian city (over 4,500,000 in population). The overall number of EGDE performed by each of the co-investigators at this university center totals about 500–600/yr of which approximately 80% are done on outpatients for diagnostic purposes.

Potential patients were identified from the outpatient endoscopy list, and those scheduled for a diagnostic EGDE were approached by the research coordinators in a consecutive fashion and invited to participate in the trial. Written institutional consent, approved by the Ethics Review Committee, was obtained in all cases.

All consenting ambulatory adult patients (>16 yr of age) deemed fit and scheduled for a diagnostic EGDE (*i.e.*, without a planned therapeutic component) with one of the participating endoscopists at one of the two participating sites were eligible to participate. The following inclusion criteria were fulfilled by all potential subjects: patients of legal age were able to consent, no other significant cardiorespiratory or medical comorbidities precluding their participation (*i.e.*, deemed able to tolerate routine sedation), nor any known documented allergy to lidocaine anesthetic spray, no anticipated need for antibiotic coverage or therapeutic endoscopic intervention. Exclusion criteria included: low baseline oxygen saturation (<85% on room air), significant preexisting respiratory comorbidity, emergency procedures, patients with an American Society of Anesthesiologist physical status classification (ASA score) greater than 4 (suggesting severe systemic disease) (7), and patients with a documented drug dependence or a documented oropharyngeal swallowing disorder.

Study Intervention

PRIMARY INTERVENTION. In the intervention group, all patients were administered titrated intravenous doses of meperidine and/or midazolam according to the patient's tolerance and clinical status. The dose administered was determined by the individual endoscopist and recorded for each patient. In the control group, all patients received an equivalent titrated dose of normal saline placebo. If the subsequent gastroscopy was unsuccessful due to patient intolerance in the opinion of the blinded operator, patients were given titrated doses of sedation in an open label fashion, without breaking the blinding. These patients were designated as "crossovers" when they in fact had been randomized to placebo administration.

ENDOSCOPIC INTERVENTION. All EGDE procedures were performed by a member of the attending staff or an appropriately supervised GI fellow using a regular sized 9.8-mm endoscope (Olympus America Inc., Melville, NY). An endoscopy nurse and research assistant were present for each examination.

Randomization and Blinding Procedure

Patients were randomized in blocks of 20 by a computer generated randomization list produced centrally by an independent biostatistician. The investigators, subjects, study statistician, and research nurses involved with the recruitment and assessment of the patient were blinded to randomization group.

An endoscopy nurse who was not participating in the measurement of study outcomes prepared the solution to be administered (active sedation or placebo) as per the randomization list. Concealment of allocation was respected by the preparation of the study medications by this nurse outside the procedure room, and by the labeling of the syringes of medication or placebo as "D" (meperidine or placebo) or "V" (midazolam or placebo). Both the active medication and normal saline have a transparent appearance in the syringe, thus limiting as best possible unblinding of the individual who administered the drugs.

STUDY OUTCOMES

The main outcome was "successful endoscopy," a measure of clinical efficacy. "Successful endoscopy" was defined as a composite score of patient satisfaction with the procedure as well as quality of the examination (technical adequacy) as assessed by the operator. These were determined by the administration of standardized Likert scales as previously

published by Abraham *et al.* (6) and Walmsley *et al.* (8), and described below.

Secondary outcomes included patient satisfaction alone, recovery room time (defined as "the time following completion of the procedure/arrival in the recovery room to discharge from the recovery room area"), technical adequacy of the procedure, the time spent by the patient in a monitored recovery room, and patients' willingness to repeat the procedure under similar test conditions. Also planned was a subgroup analysis of sedation *versus* no sedation in the elderly.

Immediately following the EGDE, the endoscopist scored the technical adequacy of the examination. Each anatomic area (esophagus, stomach, duodenum up to the second stage, and proximal stomach viewed via retroflexion) that was adequately viewed received a score of 1 *versus* 0 if inadequately viewed, for a maximum score (4/4) if all four main anatomic areas of the examination were well visualized.

Similarly, at the completion of their examination prior to being told the results of their procedure and prior to discharge from the recovery room, patients were asked to rate their level of satisfaction from 1 = acceptable to 5 = unacceptable. The composite outcome of "successful endoscopy" was both technically adequate (*i.e.*, 4/4 as rated by the endoscopist) and comfortable for the patient (1 or 2 on the 5 point scale of satisfaction as rated by the patient). Willingness to repeat was assessed by the administration of a telephone verbal rating scale (yes/no) 24 h following the procedure.

Confounders considered: Clinical factors assessed to insure equal distribution between study groups included: demographic characteristics (gender, age, level of education, and cultural background), life style (smoking, alcohol use), prior experience with endoscopy, expectations of endoscopy, and pharyngeal sensitivity of the patient as observed by the endoscopist during the application of topical anesthetic spray and the administration of open-labeled active medication.

In order to eliminate the use of pharyngeal anesthesia as a potential confounder of successful endoscopy, all patients received pharyngeal anesthesia with titrated doses of xylocaine spray in a standardized fashion to emulate a "real-life clinical setting," as previously described by Abraham *et al.* (6). Also as previously described (6), an *a priori* definition of gag reflex was used to standardize assessment of pharyngeal sensitivity.

As well, as it was recognized that some endoscopists might be able to predict whether or not their patient had received active medication, the endoscopist's impression of sedation status was recorded at the end of the procedure prior to unblinding such that it could be also measured as a potential confounder.

Costing Data

We obtained cost data for sedated and unsedated EGDE from the published activity-based approach by Crott *et al.* (9), a study that was run concurrently with this RCT. In this microcosting time-motion study, the EGDE procedure was broken down into tasks to which resources were allocated at the department level (labor, equipment, and materials). Included in these cost estimates were capital expenses for equipment (annualized over their economic lifespan), repair, and maintenance costs. Also included were hospital overhead costs grouped by: administrative activities, clinical medical support activities, and technical repair and maintenance activities. Not included in these cost estimates are the physician reimbursement fees for biopsy analysis and the professional fee for the endoscopist that are billed directly to the Ministry of Health. Given that these fees would be identical in both groups, it would not alter conclusions of the current analysis. Indirect costs attributable to time away from work for the patient or the accompanying person were not included.

Analytic Methods

SAMPLE SIZE AND POWER. Given the pilot study results (6), we hypothesized that technical adequacy would not be affected by sedation status. Thus, the estimates of patient self-reported comfort or tolerance alone were used to generate sample size and power calculations. The sample size calculation was calculated to have sufficient power to detect the smallest possible difference in main outcome (successful endoscopy) between both groups, using 10% as the smallest clinically relevant difference. Accordingly, we predicted that a sample size of 419 patients would permit us to detect a difference as small as 10% in patient satisfaction with a type 1 error of 0.05 and a power of 85%.

STATISTICAL ANALYSIS. All statistical analyses were carried out using the Statistical Analysis System (version 8.0; SAS Institute Inc, Carey, NC) under an intention-to-treat principle. Standard descriptive analyses were performed to compare baseline characteristics of the cohort and to ensure adequacy of the randomization process. Clinically significant variables that were not equally distributed were noted as possible confounders as were Mantel-Haenszel odds ratio (OR) estimates that varied by >10% from the crude estimate. The effect of sedation on each outcome was assessed with logistic regression analysis, while adjusting for possible confounders listed previously, using BIC criteria (Bayesian Information Criterion) (10) and Schwartz Criteria, a multivariate technique that adjusts for both the number of covariates and the sample size.

RESULTS

Four hundred and nineteen patients were randomized (N = 210 active *vs* N = 209 placebo, Fig. 1) with a mean age of 54.5 yr (standard deviation [SD]: 16 yr). There was an equal gender distribution (52% female), and the majority was Caucasian (86%). Forty-nine percent had a prior history of EGDE experience and 74% had positive expectations of their upcoming endoscopic examination. Ninety-four percent of the procedures were performed with a standard 9.8-mm endoscope and biopsies were taken in 80%. Overall, the baseline characteristics were similar between both treatment arms, suggesting

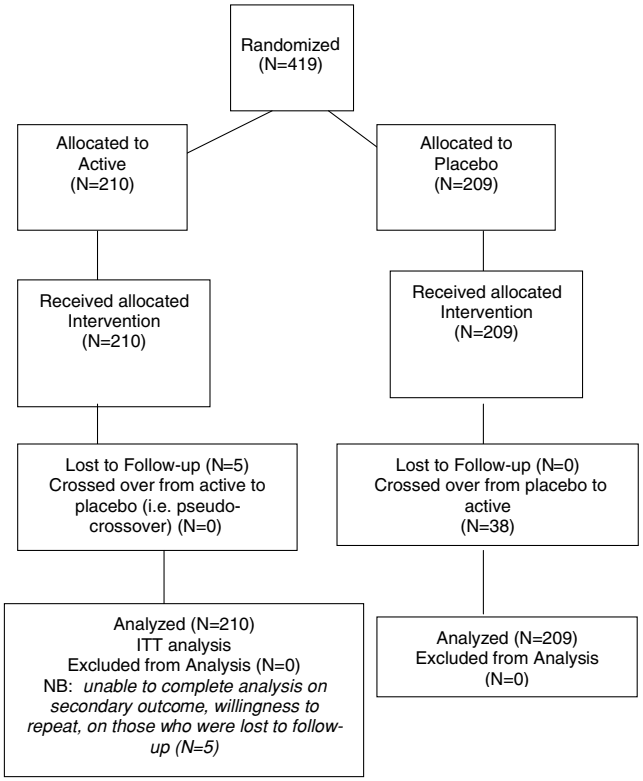

Figure 1. Patient flow diagram of all randomised patients.

integrity of the randomization process (Table 1). There were no adverse events reported during the trial.

Primary Outcome

Overall, 61% of EGDE were successful (76% active *vs* 46% placebo; (unadjusted OR 3.77; 95% CI: 2.5–5.7). Ninety percent of patients randomized to placebo were able to complete their examinations under these test conditions. There was a 10% cross over rate from placebo to active medication. No patients randomized to sedation required additional active medication in an open label fashion.

Univariate analysis suggested that randomization to active medication (OR = 3.8; 95% CI: 2.5–5.7), and positive expectations of the procedure (OR = 1.67; 95% CI: 1.1–2.6) may be predictive of successful endoscopy. The presence of pharyngeal sensitivity decreased the odds of a successful endoscopy (OR = 0.66; 95% CI: 0.44–1.08). Multivariate analysis confirmed that randomization to active medication was the strongest predictor of a successful endoscopy (OR = 6.69; 95% CI: 2.8–15.8) when adjusted for patient expectations of the procedure (OR 2.69; 95% CI: 1.36–5.34) and crossovers from placebo to active medication (OR 0.32; 95% CI: 0.15–0.67). When the subgroup of patients >75 yr was examined (N = 53), the proportion of patients with a successful endoscopy in the unsedated arm (N = 30) was greater than the sedated arm (N = 23) (57% active *vs* 63% placebo; OR 0.75; 95% CI: 0.25–2.29), however, this result was not statistically significant as demonstrated by the 95% CI. The limited sample size prohibited multivariate analysis in this subgroup.

Table 1. Baseline Demographic and Clinical Characteristics of Patients (N = 419) Randomized to Sedation (N = 210) or No Sedation (N = 209)

Characteristic	Sedated (N = 210)	Nonsedated (N = 209)
Female	109 (52%)	107 (51%)
Caucasian	179 (86%)	174 (84%)
Education: University	67 (32%)	66 (32%)
Smoker	37 (17%)	28 (14%)
Anxious	87 (42%)	98 (47%)
Tx anxiety disorder	23 (9%)	21 (10%)
Indication: dyspepsia	55 (26%)	58 (28%)
Indication: GERD	30 (14%)	44 (21%)
Prior EGDE	98 (47%)	106 (51%)
Positive expectations	154 (74%)	151 (74%)
Sensitive pharynx	45 (22%)	53 (26%)
Regular 9.8-mm scope	197 (97%)	191 (94%)
Biopsy taken	168 (81%)	166 (79%)

Anxious = self-reported anxiety; Tx anxiety disorder = treatment for an anxiety disorder; GERD = gastroesophageal reflux disease; EGDE = esophagogastroduodenal endoscopy.

Secondary Outcomes

TECHNICAL ADEQUACY. There was no significant difference between the objective assessment of technical adequacy by the endoscopist between both treatment arms. Ninety-seven percent of EGDE were technically adequate overall (score of 4/4 with good visualization of esophagus, stomach, duodenum, and retroflexion) *versus* 96% among the placebo group (OR = 1.4; 95% CI: 0.4–4.6).

PATIENT SATISFACTION ALONE. Sixty-three percent of patients rated their level of comfort during their procedure as "satisfactory." However, the proportion of patient satisfaction was greater in the sedated arm, 79% active *versus* 47% placebo (OR = 4.2; 95% CI: 2.7–6.5). Among patients aged >65 yr (N = 124), satisfaction was rated 73% in the sedated arm *versus* 54% in the unsedated arm (OR 2.20; 95% CI: 1.07–4.9). However, among patients >75 yr (N = 53), satisfaction was rated 67% in the sedated arm *versus* 63% in the unsedated arm (OR 1.16; 95% CI: 0.36–3.7) (Fig. 2).

WILLINGNESS TO REPEAT. Patients randomized to sedation were more likely to agree to repeat their procedure under similar test conditions (81% active *vs* 65% placebo; OR = 2.4; 95% CI: 1.5–3.8).

RECOVERY ROOM TIME. Those patients who had received active medication spent significantly ($p < 0.001$) more time in the recovery room (28.9 min SD: 16.0 min) when compared to those who had undergone an unsedated procedure (14.5 min SD: 13.7 min), prior to receiving their test results from the physician and being discharged from the endoscopy unit.

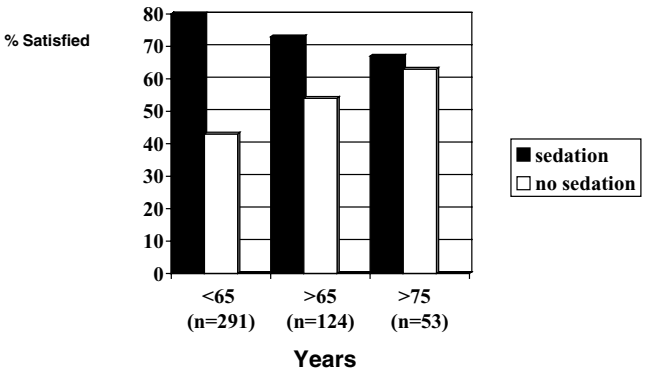

Figure 2. Assessment of patient satisfaction alone; stratified by age in 419 patients randomised to sedation *vs*. placebo.

INCREMENTAL COST-EFFICACY. Using the microcosting methodology of Crott *et al.* (14), the total cost/unsedated endoscopy was $103.09 (CDN) compared to $130.11 (CDN) for a sedated procedure. The incremental cost-efficacy ratios (ICER) for the primary and secondary outcomes are listed in Table 2. The cost-effectiveness ratio for each group was calculated by dividing the cost of the procedure by the percentage of successful endoscopy (active-placebo). For every additional successful endoscopy with sedation, one must spend $90.06 (95% CI: $69.03 to $126.38; $CDN), given an incremental cost-efficacy ratio of 27.02/0.30. However, in patients >75 yr, the unsedated strategy became the dominant strategy due to improved efficacy among the placebo group (57% active *vs* 63% placebo). Thus, for each additional unsedated procedure performed, there occurred a cost savings of $450.00 (95% CI: −$80.85 to $136.53; $CDN).

When patient satisfaction alone is used as the efficacy outcome of interest, for each additional satisfied patient scoped under sedated conditions, you must spend $84.44 (95% CI: $66.37 to $116.42; $CDN). When stratified by age, the cost of an additional sedated procedure increases with advancing age to $142.21/additional sedated procedure in patients >65 yr (95% CI: $76.37 to $1,211.66; $CDN) and $675.50/additional sedated procedure in patients >75 yr (95% CI: −$116.47 to $90.49; $CDN). Finally, the cost to ensure an additional patient is willing to repeat their procedure under sedated test conditions is $168.88 in all comers (95% CI: $106.04 to $335.65; $CDN), $168.88 in patients >65 yr (95% CI: −$6,928.21 to $84.73; $CDN) and $300.22 in patients >75 yr (95% CI: −$143.95 to $72.83; $CDN).

SENSITIVITY ANALYSIS. A one-way probabilistic sensitivity analysis was conducted with the clinical probabilities of successful endoscopy and total direct medical costs for patients in each randomized arm (active medication *vs* placebo). In keeping with a cost-outcome study, the total change in percentage of successful endoscopy (active-placebo) was varied over a range of ± 10% from the base case estimate (successful endoscopy = 30%), while assuming no variance in the cost, to provide the range of the sensitivity analysis (*i.e.*, successful endoscopy = 20–40%). These results are reported in Table 3. This showed that the cost of an additional successful endoscopy performed with sedation decreased as a greater discrepancy in successful endoscopy (*i.e.*, 40% difference between both arms) was noted between the active and the placebo group. Conversely, as the two strategies came closer to equivalence (*i.e.*, 20% difference between both arms), the cost of an additional successful endoscopy performed under sedated conditions increased.

DISCUSSION

The standard use of sedation to facilitate the performance of EGDE was initially established with the use of rigid and semirigid endoscopes. This trend has continued despite the evolution of flexible endoscopy, such that now in the United States, "it is the expectation of most patients in the United States that sedation and analgesia are provided for endoscopic

Table 2. Incremental Cost-Outcome Ratios of Primary and Secondary Clinical Outcomes Stratified by Age, in a Randomized Placebo-Controlled Trial of Sedation *versus* No Sedation in 419 Adult Patients

Clinical Outcome	Efficacy* (95%CI)	Cost Difference (CDN$)**	ICER^ (95% CI)
Successful endoscopy			
All patients	30% (21 to 39)	27.02	$90.06 ($69.03 to $126.38)
>65 yr	16% (−0.78 to 33)	27.02	$168.88 ($–3,464.10 to $82.30)
>75 yr	−7% (−33 to 20)	27.02	$−450.00 ($−80.85 to $ 136.53)
Patient satisfaction alone			
All patients	32% (23 to 41)	27.02	$84.44 ($66.37 to $116.42)
>65 yr	19% (2 to 35)	27.02	$142.21 ($76.37 to $1,211.66)
>75 yr	4% (−23 to 30)	27.02	$ 675.50 ($−116.47 to $90.49)
Willingness to repeat alone			
All patients	16% (8 to 25)	27.02	$168.88 ($106.04 to $335.65)
>65 yr	16% (−0.4 to 32)	27.02	$168.88 ($−6,928.21 to $84.73)
>75 yr	9% (−19 to 37)	27.02	$ 300.22 ($−143.95 to $72.83)

*Efficacy = outcome (active) − outcome (placebo).
**Cost Difference (CDN$) = cost (active) − cost (placebo).
^ICER = $ per additional successful endoscopy performed with sedation.

procedures" (11). A Canadian consensus conference (12) and an American survey (13) report that the majority of North American gastroenterologists choose routine parenteral sedation when performing diagnostic EGDE.

We now have data from Canada (6), Scandinavia (4, 13), Britain (14), and Iraq (15) confirming that in some subsets of the adult ambulatory population, it is possible to perform a comfortable and technically adequate unsedated diagnostic EGDE. This is supported by a recently published retrospective study from the UK that demonstrates a 54% decline in the use of parenteral sedation for diagnostic EGDE, over a 10-yr period from 1989 to 1998 (16).

This study has some important strengths that distinguish it from the existing literature. It was a large prospective RCT, in which 98.5% of enrolled patients were successfully contacted for follow-up. Randomization was performed to address the risk of potential unknown confounders. Gender was not found to be an important predictor of successful endoscopy or patient satisfaction with the test conditions under which they had their EGDE.

All potential patients were approached during the specified time frame for inclusion in this study. There were very few exclusion criteria. Independent observers were responsible for data collection and patients themselves rated their satisfaction as opposed to the use of a physician surrogate assessment (15, 17). The postprocedure patient centered outcomes were assessed following recovery from sedation, prior to disclosure of randomization group and test results. Thus, we minimized confounding by reassurance or anxiety evoked by the information of the test results or sedation status, allowing similar patient conditions for pre- and postprocedural patient outcomes. Based on our previous published work, we also believe our findings are clinically generalizable to the population from which study patients were recruited (18).

Several limitations are also noteworthy. We were unable to guarantee blinding of the endoscopist to randomization group in all cases, in that some endoscopists could perhaps predict which patient had been sedated by the patient's behavior. However, when the study population was stratified by the endoscopist's impression of randomization group, the potential lack of physician blinding did not prove to be a confounding variable. Indeed, surprisingly, in 20% of procedures the physicians' impression of patients' sedation status was not correct. Secondly, our study was conducted at an academic tertiary center. This may influence the generalizability of our findings to nontertiary settings. As well, cultural and societal influences are likely an important (though difficult to measure) modifier of a patient's satisfaction and willingness to undergo an unsedated endoscopy. Waye recently noted the prevalent use of sedation in North America and South America (72%) as compared to Europe (56%) and Asia (44%) (19).

Finally, we were limited in our ability to assess patient satisfaction with endoscopy. Some tools are available including the modified Group Health Association of America-9 (GHAA-9) patient satisfaction survey (20). When Yacovone *et al.* administered this scale to 559 patients with prior endoscopic experience to identify and prioritize the elements inherent in the prediction of patient satisfaction they found that the patients' perceived satisfaction with their comfort during the procedure was an important predictor of patient satisfaction. Unfortunately, an accurate assessment of patient satisfaction with their self-perceived comfort is not addressed by any of the 15 items included in the modified GHAA-9 scale (20). In the absence of an accepted biometric tool, we chose to use a constructed variable based on a 5-point Likert Scale as previously published (6, 8) with demonstrated face validity and sensitivity to change. However, we remain cognizant of the risk of possible ceiling and floor effects inherent in our Likert scale, which may limit its discriminant ability (20).

Consistent with our previous clinical observations (6), age was an important predictor of successful endoscopy. The presence of pharyngeal sensitivity decreased the odds of a successful endoscopy (OR = 0.66; 95% CI: 0.44–1.08), however, this observation was limited by a small number of patients with significant pharyngeal sensitivity (N = 98). The high technical adequacy rate (98%) showed no compromise by the absence of sedation, as we have previously suggested (6).

It remains unclear why the elderly appear to better tolerate the unsedated EGDE. Several investigators (21–24), including our group (6), have noted the importance of advancing age in predicting successful unsedated endoscopy. It has been postulated that the improved ability of the elderly to tolerate unsedated gastroscopy reflects a physiologic difference in pharyngeal sensory function (25) or may correspond to an age-dependent decline in the integrity of the efferent pathway of the gag reflex, which occurs as an isolated abnormality of the neurological examination among elderly without overt functional impairment (26).

Table 3. One-Way Probabilistic Sensitivity Analysis, where the Total Change in Percentage of Successful Endoscopy (Active-Placebo) Was Varied over a Range of ± 10% from the Base Case Estimate (Successful Endoscopy = 30%), while Assuming No Variance in the Cost

Clinical Outcome	Efficacy* (95%CI)	Cost Difference (CDN$)**	ICER^ (95% CI)
Successful endoscopy			
	20% (11–29%)	27.02	$133.37 ($91.94–$241.25)
	30% (29–31%)	27.02	$90.06 ($87.16–$93.17)
	40% (31–49%)	27.02	$67.11 ($55.40–$85.10)

*Efficacy = outcome (active) – outcome (placebo).
**Cost difference (CDN$) = cost (active) – cost (placebo).
^ICER = $ per additional successful endoscopy performed with sedation.

In the present study, with advancing age came improved unsedated successful endoscopy. At age > 75 yr, successful endoscopy was more likely in the unsedated group, yet the difference did not achieve statistical significance. The study is underpowered to fully assess this secondary outcome due to limited sample size but is concordant with previous work by our group (6) and adds support to the hypothesis suggested by other investigators (21–24).

Our current study adds to this literature by examining the economic impact of age on successful endoscopy. To our knowledge, the present study is the first in which conventional pharmacoeconomic methods are used to analyze the relative cost-outcome of conventional parenteral sedation *versus* no sedation in the performance of upper gastrointestinal endoscopy. We may have underestimated the true value of unsedated endoscopy by assessing clinical outcomes related to direct endoscopic costs only. One of the advantages of unsedated endoscopy may be potential indirect cost-savings associated with minimization of time away from work, as well as in the loss of productivity of the individual who must accompany the sedated patient as an escort following discharge.

Our evaluation of the incremental cost-efficacy (ICER) ratios for the two treatment strategies show the true cost-benefit ratio of "purchasing" patient self-reported comfort with parenteral sedation. As demonstrated, every additional successful EGDE performed with sedation comes at an additional cost of CDN $90.06 in the Canadian setting. The costs of medication and the nursing time for patient preparation and surveillance in the recovery room were the drivers in the time-motion cost study.

Given the equivalent technical adequacy in both arms, the true determinant of successful endoscopy appears to be a patient's satisfaction with their self-perceived level of comfort during the procedure. The proportion of patients who were satisfied with their comfort during unsedated endoscopy increased with age. Consequently, the cost of patient satisfaction (per additional sedated procedure) increases with advancing age to $142.20/additional sedated procedure in patients >65 yr and $675.50/additional sedated procedure in patients >75 yr.

With our current results, there still remains the suggestion that the elderly appear to be the subgroup in which the cost-benefit ratio for unsedated EGDE may be most favorable. In fact the unsedated approach may be the dominant strategy in these individual because of its improved efficacy (increased proportion of successful endoscopy) and decreased cost. Furthermore, a clinical observation towards increasing cost-efficacy (ICER) was noted for all secondary outcomes as age advanced.

The observation that advancing age may be an important modifier of successful endoscopy is particularly important when you consider that it is among the elderly that the risks of cardiorespiratory complications from the sedated gastroscopy, although very low, become most clinically relevant (27). Our study was not adequately powered to conclusively answer this question among elderly subgroups, however, the observation was consistent among all secondary outcomes, and at the least, these exploratory results justify further work to assess the use of unsedated gastroscopy in this elderly population.

In conclusion, for the primary outcome of successful endoscopy, although sedated diagnostic EGDE is more costly, it remains the most efficacious strategy by increasing clinical efficacy. The conclusion may differ for elderly patients in whom an unsedated strategy may dominate. This is an important area that merits future research with larger numbers of elderly patients required to confirm these exploratory results.

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