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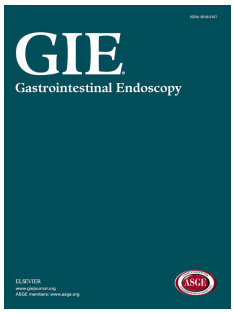

Patient safety during Sedation by Anesthesia Professionals during Routine Upper Endoscopy and Colonoscopy: An Analysis of 1.38 Million Procedures

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Abstract

Background and Aims: Sedation directed by anesthesia professionals (ADS) for GI endoscopy is used with the intent to improve throughput and patient satisfaction. However, data on its safety are sparse due to the lack of adequately powered randomized controlled trials comparing it with endoscopist directed sedation (EDS). This study was intended to determine whether ADS provides a safety advantage when compared with EDS for esophagogastroduodenoscopy (EGD) and colonoscopy.

Methods: Retrospective, nonrandomized, observational cohort study using the Clinical Outcomes Research Initiative (CORI) National Endoscopic Database, a network of 84 sites in the United States comprised of academic, community, health maintenance organization, military and Veterans Affairs practices. Serious adverse events (SAE) were defined as any event requiring administration of cardiopulmonary resuscitation (CPR), hospital or emergency department admission, administration of rescue / reversal medication, emergency surgery, procedure termination due to an adverse event, intra-procedural adverse events requiring intervention, or blood transfusion.

Results: A total of 1,388,235 patients were included in this study including 880,182 colonoscopy procedures (21% ADS) and 508,053 EGD procedures (23% ADS) between 2002 and 2013. When compared with EDS, the propensity adjusted SAE risk for patients receiving ADS was similar for colonoscopy (OR, 0.93; 95% CI, 0.82 - 1.06) but higher for EGD (OR, 1.33; 95% CI, 1.18 - 1.50). Additionally, with further stratification by ASA class, the use of ADS was associated with a higher SAE risk for ASA I/II and ASA III subjects undergoing EGD and showed no difference for either group undergoing colonoscopy. The sample size was not sufficient to make a conclusion regarding ASA IV/V patients.

Conclusions: Within the confines of the SAE definitions used, use of anesthesia professionals does not appear to bring a safety benefit to patients receiving a colonoscopy and is associated with an increased SAE risk for ASA I, II and III patients undergoing EGD.

Introduction

Sedation is an integral part of the majority of GI endoscopic procedures performed in the United States. The goals of sedation are to improve the patient experience by reducing pain and anxiety, ultimately leading to better adherence to recommended screenings and follow-up[1]. Options for sedation are primarily endoscopists targeting minimal to moderate sedation (endoscopist directed sedation - EDS) or anesthesia professionals that typically target deep sedation or general anesthesia (anesthesia-directed sedation [ADS]). Anesthesia professionals have become increasingly involved in sedation for screening colonoscopies, rising from 11% in 2001 to 53.4% in 2015[2,3]. This increase is likely due to a perceived increase in satisfaction and throughput with propofol sedation compared with a narcotic/benzodiazepine based sedation[4]. This practice is increasing overall procedural costs by approximately 20%[2].

The Centers for Medicare and Medicaid Services (CMS) recently released a ruling that will ensure coverage of anesthesia services for screening colonoscopies instead of placing the burden upon the patient[5]. The costs for involving anesthesia professionals are substantial[3]. An important inquiry therefore is what benefit is brought to the patient by using anesthesia professionals in regards to patient safety and the quality of the procedure[2,6]. The aim of better health care at a reduced cost has become a driving initiative that forces the health care system to ask this question[7].

Background

With regard to colonoscopy, there have been several studies addressing the method of sedation used and the effect on adenoma detection rates, a measure of quality of the procedure. One study showed there was no difference in the detection of polyps using moderate or deep sedation[8]. Similarly, other studies comparing propofol delivered by an anesthesiologist and endoscopist-directed

midazolam/fentanyl based sedation, found no differences in the number of patients who had adenomatous polyps detected[9,10].

Without a clear benefit in the quality of the colonoscopic examination, the increased cost for the use of ADS could potentially be justified by improved safety. As an appropriately powered randomized prospective controlled trial would be impractical due to the rarity of significant events, a few investigators have conducted retrospective studies. An increased rate of perforations during colonoscopies under propofol sedation and an increased risk of aspiration pneumonia with sedation delivered by anesthesia professionals have been observed[11–13]. With this landscape in mind, we examined the National Endoscopic Database (NED) created by the Clinical Outcomes Research Initiative (CORI) over the years of 2002 to 2013 to understand what role ADS may have in improving patient safety.

Methods

The data for this study came from the National Endoscopic Database (NED), a database of gastrointestinal endoscopy procedure reports. The database is created and maintained by CORI, a large multicenter consortium of gastroenterology practices. From 2002-2013, 84 practice sites, including university medical centers, Veteran Affairs Health Care Systems and gastrointestinal private practices, contributed procedure reports to the database. Demographics, provider, and procedure data were collected in patients 18 years of age and older for all EGDs and colonoscopies over this time period. Participating sites agree to use a structured computerized report generator to produce all endoscopic reports and comply with quality-control requirements. Each site's data files are transmitted electronically to a central data repository, the NED. The data that are transmitted from the local site to the NED do not contain most patient identifiers and qualifies as a Limited Data Set under 45 C.F.R.

Section 164.514(e). The NED is reviewed by the institutional review board of the Oregon Health & Science University (eIRB no. 7331), and most recently approved in September 2014. This study used a limited dataset and was therefore exempted from further institutional review board review.

Primary Outcome Variable

The primary outcome variable was defined as a serious adverse event (SAE) requiring intervention. This was defined as any event requiring administration of cardiopulmonary resuscitation (CPR), hospital or ER admission, administration of rescue / reversal medication, emergency surgery, procedure termination due to an adverse event, intra-procedural adverse events requiring intervention, or blood transfusion.

Independent Variable of Interest

The independent variable of interest was the specialty of health care provider who was directly responsible for the administration of procedural sedation, as documented in the CORI procedure report. This was defined as an anesthesia professional (anesthesia-directed sedation [ADS]) (anesthesiologist or nurse anesthetist) or a non-anesthesia professional (endoscopist-directed sedation [EDS]), specifically the endoscopist or other non-anesthesiologist procedure staff. Those sedation providers with ambiguous status (eg, “physician,” “resident,” and “technician”) were considered to be unknown, and were excluded from the analysis.

Statistical analysis

Data were analyzed using both multivariate logistic regression modeling and propensity score analyses. Analyses involving propensity scores included adjusting for propensity. All analyses were performed using SAS version 9.4 software (SAS Institute, Cary, NC).

Multivariate logistic regression model

Separate multivariate logistic regression models were created for colonoscopies and EGDs, modeling the likelihood of SAEs. Both models adjusted for patient age, gender, ASA classification, narcotic medication administered (yes/no), was a sedative administered (yes/no), sedation provider status (ADS vs EDS), involvement of fellow or other trainee in the procedure, practice type (community/health maintenance organization, academic or Veterans Affairs/military), and a select group of procedure indications. The procedure indications for colonoscopy are screening, surveillance, positive FOBT and undefined. For EGD the indications are Barrett's screening/surveillance, gastric polyps/ulcer, *H pylori*, and varices.

Propensity score analyses

Because this is a retrospective review of observational data, there is a risk of inherent bias on selection of whether an anesthesia professional (ADS) or endoscopist (EDS) provides sedation. To help manage this bias, propensity scores were calculated. A propensity score is the probability of a treatment being assigned to a patient, based on observed characteristics (collected covariates). For this analysis, that treatment was if an ADS was used. When using a propensity score, it is possible to mimic some, but clearly not all, of the benefits when doing a randomized controlled trial[14]. This score can be used to adjust for the likelihood of being in the ADS (treatment) or EDS (non-treatment) groups, helping to ensure that both groups are comparable for all observed variables[15].

For each colonoscopy and EGD in the cohort, a propensity score was calculated. In this study, we calculated propensity scores measuring the likelihood that a given procedure would use ADS versus EDS, regardless of the actual sedation provider status. A score was calculated using separate multivariate logistic regression models, for colonoscopy and EGD. The output from each procedure was assessed as a likelihood from 0% to 100% for having used ADS, and this value was used in the logistic regression

analysis as a continuous predictor. Covariates included in the model include all those used in the standard multivariate logistic regression models, as well as bowel prep results, depth of sedation intended, and all documented procedure indications. Multivariate logistic regression analyses were performed to estimate the association between sedation provider and risk of SAEs, adjusting for the propensity to have used ADS.

Results

Patient demographics

The demographics of the 1,388,235 procedures evaluated are shown in Table 1. There were 880,182 colonoscopies and 508,053 EGDs. Mean patient age was 60.1 (12.5) years for colonoscopy and 58.4 (15.9) years for EGD. Most patients were ASA physical classification I/II (84% colonoscopy, 74% EGD), outpatients, and received their procedures at a community, HMO, or private practice. 182,694 (21%) of the colonoscopy procedures and 115,320 (23%) of the EGD procedures used ADS respectively. Among EDS procedures, the prevalence of propofol use was low at 2.9% for colonoscopies and 2.5% EGDs.

Significant adverse events

As stated above, an SAE was defined as any event requiring administration of cardiopulmonary resuscitation (CPR), hospital or ER admission, administration of rescue / reversal medication, emergency surgery, procedure termination due to an adverse event, intra-procedural adverse events requiring intervention, or blood transfusion. Table 2 shows a descriptive breakdown of the SAE events. Overall, for colonoscopy, EDS had a numerically higher SAE rate (0.28%) compared with ADS (0.20%). This increase is primarily due to an increased use of rescue medications and reversal agents, where ADS used only 0.07% compared with 0.16% compared with EDS. For EGD, ADS had a numerically higher SAE rate (0.39%) compared with EDS (0.32%). As with colonoscopy, there was a similar rate of rescue medications

/ reversal agents used in both groups with EDS having an increased use (ADS 0.07%, EDS 0.16%). Unlike colonoscopy, for EGD there was a significant increase in airway management related SAEs for ADS (0.14%) compared with EDS (0.02%).

The SAE risk stratified by procedure indication is shown in Table 3. Although procedure indication was taken into account in the multivariate logistic regression analysis, the raw SAE rates were still assessed to determine what influence it may have on the rates. For colonoscopy patients indicated with a positive FOBT (0.39%) or hematochezia / melena / anemia (0.33%) the SAE rate was higher compared with the other procedure indications (0.22% - 0.26%). For EGD patients indicated with a therapeutic intervention (0.95%), bleeding / varices / anemia (0.59%) had a higher SAE rate compared with the other indications (0.13%-0.39%).

Risk Factors for SAEs: Multivariate Logistic Regression Analysis

The results of the multivariate logistic regression analysis are shown in Table 4. The most significant predictor of SAE risk was the ASA classification with an odds ratio (OR , 95% Confidence Interval (CI)) of 5.85 (95% CI, 4.24 - 8.06) for colonoscopy and an OR of 7.01 (95% CI, 5.82 - 8.46) for EGD respectively in ASA IV/V patients when compared with their ASA I/II counterparts. Increasing age (≥75 years of age) was also a significant risk factor with an OR of 3.53 (95% CI, 2.96 - 4.19) for colonoscopy and 2.06 (95% CI, 1.78 - 2.39) for EGD versus patients less than 50. Narcotic administration resulted in an increased risk of SAEs, as well as sedative administration for colonoscopy procedures. Compared with community/HMO facilities, procedures performed at academic (colonoscopy and EGD) and VA/military (colonoscopy only) facilities had an increased risk of SAEs.

A trainee being present also increased the risk of SAEs for EGD procedures. Table 5 provides the SAEs for EGD and colonoscopy stratified by the presence of a trainee, the sedation provider and the site type. Consistent with the increased risk of SAEs, for EGD procedures the presence of a trainee was associated with a higher rate of SAEs at all three site types and both sedation providers. SAEs were more prevalent with ADS in both the Trainee Present and Trainee Not Present groups. The most significant difference was seen at the community / HMO sites (EDS: trainee present 0.92%, trainee not present 0.22% and ADS: trainee present 1.08%, not present 0.29%). For colonoscopy, there were no differences seen across all three site types and both sedation provider, except for the VA/military sites with ADS which had the highest observed rate (trainee present 1.27%, trainee not present 0.38%).

Sedation Provider and Risk of SAE: Regression Analysis Adjusted for Propensity Score

In multivariate logistic regression analysis, the use of ADS was associated an increased risk for SAEs when compared with EDS for EGD (OR, 1.34; 95% CI, 1.13, - 1.58), as shown in Table 4. There was no statistical difference for colonoscopy, with an OR of 1.18 (95% CI, 0.99 - 1.39] for colonoscopy. To better assess this result of whether ADS is associated with an increased SAE risk, a propensity-adjusted risk assessment for SAEs was performed, with the results shown in Table 6. For colonoscopy, after adjusting for the likelihood (propensity) of using ADS, the risk of a SAE was still not significantly different between ADS and EDS, with an OR of 0.93 (95% CI, 0.82 - 1.06). For EGD, after adjusting for the likelihood (propensity) of seeing an anesthesia professional, the risk of SAEs was greater when sedation was provided by an anesthesia professional, with an OR of 1.33 (95% CI, 1.18 - 1.50).

Sedation Provider and Risk of SAE: Stratified by ASA Classification

To further evaluate the association between ADS and the risk of SAEs for EGD, multivariate logistic regression analysis was used on data stratified by ASA I/II and ASA III to see if there is difference in SAE

risk for these two populations. The results are shown in Table 6, for both all patients and then stratified by ASA I/II and ASA III. There were an insufficient number of ASA IV/V patients (less than 10,000) to include that stratification. For colonoscopy neither group had an increased risk of an SAE if ADS was used (ASA I/II with an OR of 0.91 [95% CI, 0.77 - 1.06] and ASA III with an OR of 0.90 [95% CI, 0.69 - 1.16]). For EGD both groups had an increased risk of an SAE if ADS was used (ASA I/II with an OR of 1.26 [95% CI, 1.03 - 1.54] and ASA III with an OR of 1.38 [95% CI, 1.14 - 1.67]).

Mortality

The mortality results are shown in Table 7. Ten patient deaths occurred in the 1,388,235 patient population (1/138,824 patients). Three deaths occurred during a colonoscopy, 7 during an EGD. Only 1 of the colonoscopy deaths was potentially related to over-sedation (patient 3), resulting in a rate of 1 out of 880,182 for colonoscopy. Stratifying by sedation provider, the rates are similar at 1 out of 697,488 for EDS and 0 out of 182,694 for ADS.

Five deaths in the EGD group were potentially due to over-sedation (patients 5, 6, 8, 9, and 10), resulting in a rate of 5 of 508,053 (approximately 1/101,611). Stratifying by sedation provider, the rates are similar for EDS (~1/98,183) and ADS (1/115,320).

Discussion

There has been a substantial increase in the utilization of anesthesia professionals providing sedation for routine endoscopic procedures, with rates regionally exceeding 50%[2–4]. This results in increased costs of endoscopic procedures, at a time when the cost of health care is putting a severe strain on the system. Additionally in certain areas of the United States there is a shortage of anesthesia providers so special consideration must be taken to ensure the proper allocation of limited health care resources[16]. In light

of CMS's decision on paying for anesthesia services for all screening colonoscopies, the potential safety and quality benefits need to be critically defined, especially given that the majority of the increase in anesthesia services has been seen in low-risk patients[5,16,17].

This study of 1.38 million procedures from 84 practice sites, including university medical centers, Veteran Affairs Health Care Systems and gastroenterology private practices, addresses the safety aspect of that question. The sample size of 1.38 million procedures using propensity score analysis allows for a large number of covariates to be accounted for, providing greater confidence in the results. A prospective study of sufficient size will not be conducted given the logistical complexity and costs. Therefore, CORI-NED's large database allows a robust analysis of safety outcomes as a function of the sedation provider. We found that the propensity adjusted SAE risk for pooled ASA physical classification patients undergoing ADS was similar to EDS for colonoscopy but higher for EGD procedures. Additionally, with further stratification into ASA class I/II and III, the use of ADS was associated with higher odds for an SAE for ASA I/II/III subjects undergoing upper endoscopy. When dichotomized into ASA I/II and ASA III for patients undergoing colonoscopy, the SAE risk for ADS and EDS were similar.

Several other risk factors were significantly associated with an increased risk of SAE beyond ASA and the sedation provider. These included patient age, the presence of a trainee and Academic or Military/VA site type. Certain indications for colonoscopy or EGD had higher raw rates as well. It is not surprising that patient factors (age, comorbidity), procedures with a higher likelihood of therapeutic interventions or the presence of less trained endoscopists would be associated with SAEs. There is a possibility that there is a synergy between risk factors that played a role, as table 5 suggests. However, controlling for these factors in multivariate logistic and propensity adjusted analyses did not eliminate the significant association between ADS and SAEs in EGD procedures.

The fact that the raw SAE rate for colonoscopy of 0.20% for ADS compared with 0.28% for EDS failed to reach significance whereas for EGD 0.39% for ADS compared with 0.32% for EDS did reach statistical significance warrants some discussion. It is important to note that these are raw incidence rates and do not account for confounding variables. When age, gender, ASA classification, narcotic use, sedative status, trainee present, site type and indication are taken into account, no significant association is found between sedation provider and colonoscopy. Therefore, although EDS does have a higher rate when not including confounding factors, once confounding factors are taken into account there is no longer an increase seen in the SAE rate for colonoscopy. A trend seen in the EDS group for colonoscopy and EGD alike was an increase in the use of rescue and reversal medications compared with ADS. This may in part be due to the fact that EDS is done with traditional benzodiazepine/narcotic based sedation where a reversal medication is available, compared with ADS which predominantly uses propofol based sedation, where a reversal agent is not available. Of note, for EGD procedures, ADS had significantly more airway management SAEs.

A potential weakness of this study is the retrospective design. The data collected in the NED database does not contain all potential demographic and procedural data, such as body mass index and Mallampati score. One of the key procedural data points missing from the database is the type of sedation given by the provider (the targeted level of sedation and if the patient was intubated or not). In addition to demographic and procedural data, we also cannot be assured that all events identified in this study as an SAE were captured, especially less significant events such as the use of a nasal or oral airway. The propensity score analysis, although superior to a simple regression analysis, still will have some hidden biases in the match results, factors that were not observed that can influence the scores. Although it mimics some of the benefits of a randomized controlled trial, it should not be confused as

being equivalent to a randomized controlled trial. It must be emphasized that to our knowledge, this is the first time that this methodology has been applied to the question of endoscopic sedation and SAEs, representing a robust attempt to remove bias in addition to the traditional multivariate analysis with adjustment.

As previously mentioned, there has been no study published showing a quality benefit based on the method of sedation (polyp detection or adenoma detection rate)[8,9,18,19]. A benefit has been seen with anesthesia professionals using propofol is patient satisfaction. In a meta-analysis of 36 moderate sedation studies, propofol sedation provided slightly more patient satisfaction when compared with midazolam plus narcotics[20]. It is unclear if the increase in patient satisfaction is due to the presence of an anesthesia professional or the use of propofol.

For safety, a smaller retrospective study of 118,004 colonoscopies, compared propofol and non-propofol administration (fentanyl, midazolam, meperidine, and/or diazepam), showing a 2.5 increased rate in colonoscopic perforations for therapeutic colonoscopies (6.9 vs 2.7 per 10,000; p=0.0015) in the propofol administration group (administered by anesthesia professionals)[11,13]. Another study of 165,527 colonoscopies in 100,359 patients found an increased risk of aspiration pneumonia when sedation was delivered by an anesthesia professional[12]. Most recently, a claims data analysis of more than 3 million colonoscopies found a 13% increase in 30-day adverse events when anesthesia was used[21]. Though an increased risk of an SAE with colonoscopy was not seen in this study, it cannot be excluded that there is an association for SAEs that might present or be diagnosed in a delayed fashion.

This study addresses the question of safety with a comprehensive view of patient risk, assessed by the SAE rate, a significantly greater size compared with most other retrospective studies, particularly those

using endoscopic reports or patient medical records. It accounts for many covariates both in the logistic regression analysis and the propensity score analysis. The majority of the data was ASA I/II/III patients. In reviewing the data, pooled and stratified by ASA classification I/II and III, it appears there is no clinical safety benefit with ADS. In fact, in the case of EGD, ADS is associated with an increased risk of SAEs for ASA I, II, and III patients. It is clear from the data and the confines of our SAE definition set that anesthesia professional utilization does not reduce the risk of an SAE when compared with endoscopist directed sedation.

It is unclear why there was no benefit in using an anesthesia professional in reducing the SAE incidence, including ASA III patients, who are more likely to experience an SAE. There are several potential reasons that ADS sedation may not bring a benefit. The most likely possibility is the level of sedation. Anesthesia professionals are trained to provide deep sedation and general anesthesia, levels of sedation that have increased risks of an SAE. Additionally, the level of sedation may not be aligned with the procedure, resulting in extended periods of over-sedation, especially during reduced stimulus. EGD patients, where an increase in SAE risk was seen, deeper levels of sedation likely blunted protective reflexes, perhaps contributing to the increase in the risk for cardiopulmonary unplanned events. The collected data does not allow us to determine if the increased risk for EGD is due to aspiration or respiratory depression. Future studies would be useful to understand the reason and provide clinical insight on how to reduce this risk. There are other reasons that could account for this, including drug selection (eg. propofol), poly-pharmacy, and other un-measured patient and procedure variability.

Given the small sample size of ASA IV/V patients in the database, no conclusions can be drawn for these patients from this analysis, especially given the fact that very few did not use an anesthesia professional. The database appears to reflect actual colonoscopy / EGD procedures where the majority of procedures

are outpatient compared with inpatient. In this study an ASA classification of IV/V was the most significant predictor for risk of an SAE. For those patients with an ASA classification IV or V, or have other complicating factors, it is clinically appropriate that these patients have an ADS provide the sedation for the procedure, as recommended per the American Society of Anesthesia guidelines[22].

Based on this analysis of over 1.38 million endoscopic procedures, the use of anesthesia professionals to provide sedation did not reduce the rate of the measured significant adverse events in ASA I, II, and III patients receiving a colonoscopy or EGD. In fact, the findings of this study suggest that ADS for EGD increases the risk of SAEs. The findings do not exclude a likely safety benefit for higher risk patients (ASA IV/V) with high comorbidity where the airway management and cardiovascular support skills of the anesthesia professional are necessary. For most patients undergoing standard upper and lower endoscopic procedures, it is difficult to justify the use of anesthesia professional services based on reasons of safety.

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Table 1. Demographics

	Colonoscopy	**EGD**
N	880,182	508,053
Age (mean) (SD)	60.1 (12.5)	58.4 (15.9)
ASA Classification - N(%)		
Unknown	61,046 (6.9)	37,112 (7.3)
I	179,866 (20.4)	80,920 (15.9)
II	561,670 (63.8)	295,028 (58.1)
III	75,255 (8.5)	88,046 (17.3)
IV	2,312 (0.3)	6,812 (1.3)
V	33 (0.0)	135 (0.03)
Gender - N(%)		
Female	410,122 (46.6)	245,097 (48.2)
Male	470,060 (53.4)	262,956 (51.8)
Race - N(%)		
Black	52,659 (6.0)	35,428 (7.0)
White	793,539 (90.2)	448,945 (88.4)
Other	33,984 (3.9)	23,680 (4.7)
Location - N(%)		
Outpatient	800,187 (90.9)	413,941 (81.5)
Inpatient	25,260 (2.9)	52,378 (10.3)
Unknown	54,735 (6.2)	41,734 (8.2)
GI Trainee - N(%)		
Present	106,806 (12.1)	99,680 (19.6)
Not Present	773,376 (87.9)	408,373 (80.4)
Site - N(%)		
Academic	89,060 (10.1)	84,630 (16.7)
VA/Military	148,818 (16.9)	87,912 (17.3)
Community/HMO/Private Practice	642,304 (73.0)	335,511 (66.0)
Sedation Provider - N(%)		
Anesthesia Professional	182,694 (20.8)	115,320 (22.7)
Non-Anesthesia Professional	697,488 (79.2)	392,733 (77.3)

Abbreviations: ASA, American Society of Anesthesiologists; SD, Standard Deviation; VA, Veterans Affairs; HMO, Health Maintenance Organization; FOBT, Fecal Occult Blood Test

Table 2. SAE Descriptive Data

	ADS		EDS	
Colonoscopy				
N	182,694		697,488	
Total SAE Rate	370	(0.20%)	1952	(0.28%)
Medication/Sedation Reversal	128	(0.07%)	1143	(0.16%)
Procedure Stopped	71	(0.04%)	309	(0.04%)
Intra-Procedural AEs Requiring Intervention	46	(0.03%)	256	(0.04%)
Admit ER / Hospital	51	(0.03%)	130	(0.02%)
Airway Management	51	(0.03%)	81	(0.01%)
Surgery	15	(0.01%)	37	(0.01%)
Adverse Physiology with No Documented Treatment	14	(0.01%)	37	(0.01%)
Cardiovascular Rescue - No Drug	1	(0.00%)	28	(0.00%)
Code 99 / CPR	3	(0.00%)	19	(0.00%)
Blood Transfusion	1	(0.00%)	11	(0.00%)
Other Intervention	47	(0.03%)	158	(0.02%)
EGD				
N	115,320		392,732	
Total SAE Rate	447	(0.39%)	1247	(0.32%)
Medication/Sedation Reversal	75	(0.07%)	609	(0.16%)
Procedure Stopped	119	(0.10%)	267	(0.07%)
Intra-Procedural AEs Requiring Intervention	30	(0.03%)	171	(0.04%)
Admit ER / Hospital	45	(0.04%)	112	(0.03%)
Airway Management	164	(0.14%)	67	(0.02%)
Surgery	6	(0.01%)	15	(0.00%)
Adverse Physiology with No Documented Treatment	5	(0.00%)	14	(0.00%)
Cardiovascular Rescue - No Drug	4	(0.00%)	11	(0.00%)
Code 99 / CPR	10	(0.01%)	23	(0.01%)
Blood Transfusion	13	(0.01%)	54	(0.01%)
Other Intervention	30	(0.03%)	84	(0.02%)

[a]Other includes Trendelenburg positioning, chin tilt w/suctioning and other advanced airway maneuvers

Table 3. SAE Risk Stratified by Procedure Indication

	n	SAE %
Colonoscopy		
Screening	358,867	0.22%
Surveillance	188,625	0.26%
Positive FOBT	40,691	0.39%
Hematochezia / Melena / Anemia	137,368	0.33%
Other non-bleed	154,631	0.26%
EGD		
Barrett's Esophagus Evaluation/Screening/Surveillance	27,423	0.19%
Bleeding / Varices/ Anemia	107,535	0.59%
Dysphagia	87,303	0.34%
Chest Pain / Dyspepsia	98,800	0.13%
GERD	75,306	0.14%
Nausea / Vomiting	21,568	0.23%
Therapeutic Intervention	13,566	0.95%
Other	76,552	0.39%
Abbreviations: SAE, Significant Adverse Event		

Table 4. SAE Risk Multivariate Logistic Regression[a]

	Colonoscopy - OR [95% CI]	**EGD - OR [95% CI]**
Age (Reference: <50 years)		
50-64 years	1.66 [1.41 - 1.96]	1.29 [1.12, 1.48]
65-74 years	2.59 [2.19 - 3.07]	1.43 [1.23, 1.67]
≥ 75 years	3.53 [2.96, 4.19]	2.06 [1.78, 2.39]
Gender (Reference: Female)		
Male	1.05 [0.96, 1.15]	1.07 [0.96, 1.19]
ASA Classification (Reference: I/II)		
III	1.79 [1.59, 2.01]	2.52 [2.25, 2.82]
IV/V	5.85 [4.24, 8.06]	7.01 [5.82, 8.46]
Unknown	0.95 [0.78, 1.16]	1.48 [1.21, 1.80]
Narcotic Administered (Reference: No)		
Yes	1.53 [1.29, 1.82]	1.26 [1.07, 1.48]
Unknown	1.26 [0.82, 1.94]	1.21 [0.80, 1.83]
Sedative Administered (Reference: No)		
Yes	1.50 [1.01, 2.23]	1.22 [0.83, 1.81]
Trainee Present (Reference: No)		
Yes	1.07 [0.95, 1.21]	2.06 [1.82, 2.34]
Site Type (Reference: Community / HMO)		
Academic	1.52 [1.34, 1.73]	1.17 [1.02, 1.35]
VA / Military	1.56 [1.38, 1.76]	0.94 [0.81, 1.10]
Sedation Provider (Reference: EDS)		
ADS	1.18 [0.99, 1.39]	1.34 [1.13, 1.58]

Abbreviations: OR, Odds Ratio; ASA, American Society of Anesthesiologists; ADS, Anesthesia-Directed Sedation; EDS, Endoscopist-Directed Sedation; SAE, Significant Adverse Event

[a]Adjusted for Age, Gender, ASA Classification, Narcotic Administration, Sedative Administration, Trainee Present, Site Type, Sedation Provider, and Indication (Colonoscopy: Screening vs. Surveillance vs. Positive FOBT vs. Other; EGD: Barrett's Screening/Surveillance, Gastric Polyps/Ulcer, H. Pylori, Varices).

Table 5. SAE Risk Stratified by Site Type and Presence of a Trainee

SEDATION Provider	**Colonoscopy % of Group with SAE**		**EGD % of Group with SAE**	
Community / HMO	EDS	ADS	EDS	ADS
Trainee Present	0.32%	0.00%	0.92%	1.08%
Trainee Not Present	0.22%	0.19%	0.22%	0.29%
Academic				
Trainee Present	0.39%	0.29%	0.55%	0.93%
Trainee Not Present	0.36%	0.45%	0.32%	0.74%
VA / Military				
Trainee Present	0.43%	1.27%	0.54%	0.91%
Trainee Not Present	0.37%	0.38%	0.25%	0.48%

Abbreviations: ADS, Anesthesia-Directed Sedation; EDS, Endoscopist-Directed Sedation; SAE, Significant Adverse Event

Table 6. SAE Risk EDS versus ADS Multivariate Logistic Regression Adjusted for Propensity Score[a]

	Colonoscopy - OR [95% CI]	**EGD - OR [95% CI]**
All ASA Classes [95% CI]		
Sedation Provider (Reference: EDS)		
ADS	0.93 [0.82 - 1.06]	1.33 [1.18 - 1.50]
ASA I/II [95% CI] n=741,536 (1,797 events)		
Sedation Provider (Reference: EDS)		
ADS	0.91 [0.77, 1.06]	1.26 [1.03, 1.54]
ASA III [95% CI] n=72,255 (412 events)		
Sedation Provider (Reference: EDS)		
ADS	0.90 [0.69, 1.16]	1.38 [1.14, 1.67]
Abbreviations: ASA, American Society of Anesthesiologists; ADS, Anesthesia-directed sedation		
[a]Adjusted for Age, Gender, ASA Classification, Narcotic Administration, Sedative Administration, Trainee Present, Site Type, Sedation Provider, and Indication (Colonoscopy: Screening vs. Surveillance vs. Positive FOBT vs. Other; EGD: Barrett's Screening/Surveillance, Gastric Polyps/Ulcer, H. Pylori, Varices).		

Table 7. Mortality

	Incidence	Mean Age (SD)	ASA Class (n)	AP Sedation (n)
Colonoscopy	3	59.0 (16.3)	I (1), III(2)	0
Patient 1	vasovagal reaction; arrhythmia, bradycardia, and hypotension			
Patient 2	collapsed 1 hour at home; brought to hospital, refractory ventricular fibrillation			
Patient 3	hypoxemia during the procedure			
EGD	7	64.0 (15.2)	II (1), III (5), IV(1)	1
Patient 4	vasovagal reaction; arrhythmia, bradycardia, and hypotension			
Patient 5	sinus tachycardia, then idioventricular rhythm (rate in 30s and 40s), hypotension			
Patient 6	intra-procedural bradycardia			
Patient 7	bleed resulting in hypotension			
Patient 8	prolonged hypoxia resulting in cardiopulmonary arrest			
Patient 9	transferred to ER, died from hypotension 2 days later			
Patient 10	unresponsive with normal vitals, unable to palpate a pulse			

Abbreviations: ASA, American Society of Anesthesiologists; AP, Anesthesia Professional

Acronyms

Acronym	Definition
ADS	Anesthesia Directed Sedation
AP	Anesthesia Professional
ASA	American Society of Anesthesiologist
CMS	Centers for Medicare and Medicaid Services
CORI	Clinical Outcomes Research Initiative
CPR	CardioPulmonary Resuscitation
EDS	Endoscopist Directed Sedation
EGD	EsophaGogastroDuodenoscopy
ER	Emergency Room
FOBT	Fecal Occult Blood Test
HMO	Health Maintenance Organization
NED	National Endoscopic Database
OR	Odds Ratio
SAE	Serious Adverse Event
VA	Veterans Affairs