TITLE: DESIGNING OPTIMAL PREVENTION AND MANAGEMENT OF POSTOPERATIVE NAUSEA AND EMESIS FOR PATIENTS UNDERGOING LAPAROSCOPIC SLEEVE GASTRECTOMY.

PRINCIPAL INVESTIGATOR: Konstantinos Spaniolas, MD

Co-investigator: Dr. Pryor Aurora, Dr. Daryn Moller

I. SUMMARY

Bariatric surgery remains the most effective therapy for obesity and the metabolic syndrome. Postoperative nausea and vomiting (PONV) are commonly reported following bariatric surgery; our preliminary results suggest that 90.8% of patients report PONV during their index hospital stay, and 30.4% of readmitted patients report PONV as the reason for re-hospitalization. Importantly, we have previously found that 49% of patients are unable to be discharged on time due to oral intake intolerance attributed to PONV. Multiple small studies have attempted to introduce single-level intervention to decrease PONV with limited success in this patient population. The proposed study focuses on the most common bariatric procedure performed, laparoscopic sleeve gastrectomy (LSG), and aims to assess the effect of a PONV-specific intervention using a multimodal contemporary approach. We hypothesize that the PONV-intervention group will experience a more than 50% relative risk reduction of PONV-related prolonged hospital stay and significantly improve patient-reported quality of recovery from surgery and quality of life. To test this hypothesis, subjects undergoing LSG will be prospectively randomized to two groups: control (physician driven prophylaxis) vs PONV-intervention group (two anti-emetic agents prior to surgery, total intravenous anesthesia, two additional anti-emetic agents during surgery, and sugammadex as reversal agent). The primary end-point will be PONV-related prolonged hospital length of stay, using postoperative day 1 as the target for hospital discharge as per clinical pathway. Serial assessments of PONV, quality of life and quality of recovery, will allow us to identify an effect of the PONV-intervention on PONV incidence and severity. Importantly, we will evaluate for an impact in patient-reported measures of quality of life. Our proposal is extremely innovative, because it addresses a high impact topic, evaluates the effect of PONV-intervention in all phases of recovery, and includes instruments to measure self-reported patient experience with surgery.

II. SPECIFIC AIMS

PONV is associated with delayed hospital discharge and readmissions following LSG. The impact of PONV on patient experience, self-reported outcomes, and overall recovery is unknown for this patient population. *The proposed study aims to assess the effect of a PONV-specific intervention using a multimodal contemporary approach in subjects undergoing LSG*. The PONV intervention will include specific steps using total intravenous anesthesia and staged anti-emetic medications, in the pre-, intra- and post-operative phase of care. We hypothesize that a comprehensive multi-level PONV intervention will decrease the incidence and severity of PONV, increase successful patient hospital discharge on postoperative day (POD) 1, facilitate late phase postoperative recovery and positive patient experience.

Specific Aim 1: Evaluate the impact of a PONV-specific intervention on PONV-related prolonged length of hospital stay following LSG surgery. Subjects will be serially assessed for the presence and scale of nausea and emesis during their early, intermediate and late phases of recovery, measured with a PONV-specific survey. Time from completion of the index procedure until patient hospital discharge will be assessed; subjects who remain in the hospital past POD 1 due to PONV will be considered as having a prolonged length of stay, which is the primary endpoint for this aim. We will also assess the effect of a PONV-specific intervention on post-discharge PONV-related resource utilization following LSG. Patients will be followed to capture hospital readmissions, emergency department visits and outpatient intravenous hydration for PONV. We hypothesize that the PONV-intervention group will experience a higher rate of successful POD 1 discharge, and a decrease in incidence and severity of both nausea and emesis.

Specific Aim 2: Assess the effect of a PONV-specific intervention on patient reported outcomes (PRO). Patient-reported outcome measures will be collected to evaluate recovery from surgery and health-related quality of life at 2- and 4-weeks following LSG. We hypothesize that a PONV-specific intervention will allow patients to have improved self-assessed recovery and quality of life during the first 30-days following surgery.

III. SIGNIFICANCE

Bariatric surgery is the most effective method to treat obesity and associated diseases. Currently, the LSG is the most common bariatric procedure performed [1]. In this patient population, however, PONV occurs commonly. Published studies suggest a 59-87% incidence of PONV during the hospital stay following LSG [2, 3].

The burden of PONV in the bariatric population, and specifically after LSG, is particularly high. We have previously demonstrated that PONV is the most common cause for hospital readmission following LSG, with 30.4% of readmitted LSG patients reporting PONV and oral intake intolerance as their primary reason for readmission [4]. This is markedly different in gastric bypass patients, where only 18% of readmitted patients reported PONV as their primary complaint. Additionally, our preliminary data suggest that half of LSG patients experience a delay in pathway-expected hospital discharge due to PONV (see Preliminary Data section under Approach). With the drive to minimize hospital length of stay, PONV control is paramount to achieve safe early hospital discharge.

The impact on PONV on PRO is unclear. One third of patients who received double PONV prophylaxis and routine anti-emetics for the first two days at home following ambulatory laparoscopic surgery reported that nausea had a negative effect on their quality of life, during self-assessment on POD 5 [5]. Following ambulatory surgery, the incidence of PONV increases over time; 16.1% of patients experience PONV in early recovery, and 31.2% of patients report PONV on POD 5, during late recovery at home [6]. These rates are almost double for patients undergoing ambulatory laparoscopic surgery, suggesting that PROs after discharge are of high value for the assessment of a PONV-related effect. Importantly, PONV at home significantly impairs the ability to perform activities of daily living, which is an important goal of recovery for patients [7]. Since PONV is reported commonly in LSG patients, we anticipate that improvement in PONV will affect PROs and overall experience during the intermediate (from post-anesthesia care unit until hospital discharge) and late (from hospital discharge to return to usual activity) phases of recovery.

Although the benefit of a multimodal approach to PONV prevention has been well established [8], evidence in the bariatric, and specifically the LSG population is not clear. A study evaluating a triple-agent protocol in 96 LSG patients, using ondansetron, dexamethasone and haloperidol, demonstrated improvement in PONV incidence, but no effect on hospital length of stay [3]. The lack of effect on hospital discharge may be related to the use of short half-life preventive agents, the lack of aggressive postoperative anti-PONV management or the implementation of a post-care pathway with less emphasis in early hospital discharge. This would possibly underline the value of longer lasting antiemetic agents, as prevention. The only study to date evaluating the use of aprepitant, an agent with half-life exceeding 12 hours, in bariatric surgery demonstrated significant decrease in the rate of emesis compared to controls (3.1% vs 15%, $p=0.021$), but is limited by the non-inclusion of LSG patients, and the lack of triple prophylaxis as control [9]. Furthermore, the use of sugammadex has emerged as a modality to decrease pain and PONV. A randomized study of 88 bariatric surgery patients assigned to this agent vs neostigmine demonstrated a significant decrease in the early incidence of PONV (6.8% vs 18.2%, $p<0.05$)[10]. Studies evaluating the longer-term effect of this reversal approach to PONV in this patient population are not available.

Recently published recommendations from European societies for the enhanced recovery of bariatric surgery include multimodal PONV prevention, but the evidence, as also noted in the article, is lacking [11]. Despite the significant impact of PONV in this patient population, there is no consensus on the optimal approach in PONV prevention. Given the proportion of LSG procedures performed, the effect of PONV in this patient population and the paucity of high quality data, the proposed study will allow us to advance science in bariatric surgery, change the standard of care and improve patient experience. A standardized anti-PONV intervention with proven efficacy could minimize length of stay and readmissions after LSG, minimizing costs and improving patient experience.

IV. INNOVATION

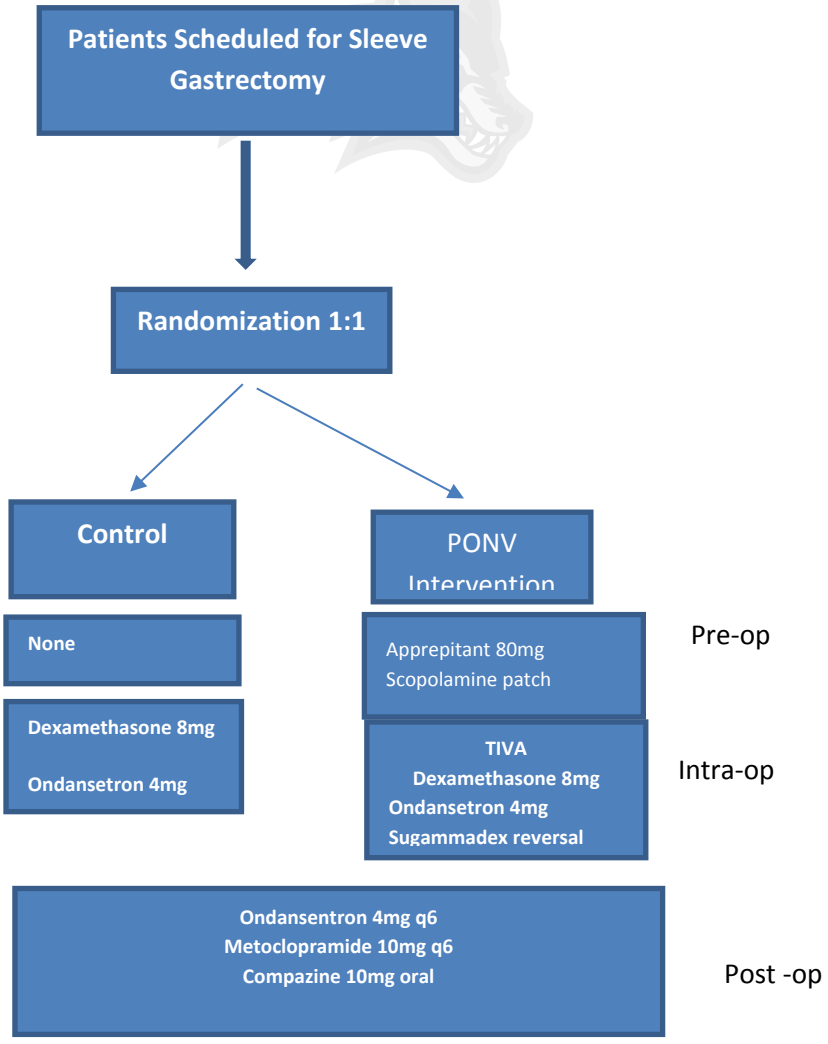
Multiple studies suggest that PONV is a significant postoperative problem for bariatric surgery patients [4]. Despite this, no studies have addressed PONV in this patient population in a systematic fashion, or using a multilevel approach. Furthermore, PONV is this patient population has likely different pathophysiology compared to similar symptoms in colectomy and other gastrointestinal patients. Development of a program specific to bariatric surgery for the prevention and management of PONV using interventions before, during and following surgery is a novel approach to this clinical problem. Furthermore, the current proposal is innovative in a three-fold way:

a. Evaluation of PONV during the ***late phase of recovery*** from surgery for patients undergoing LSG hasn't been previously reported. The proposed study will try to fill this knowledge gap, which is especially important given that PONV is the most common cause for hospital readmission in this group.

b. Although PONV has a significant ***impact on patient experience*** during recovery from surgery, this hasn't been explored, especially in patients undergoing LSG, despite the high incidence of PONV in this setting. Using standardized questionnaires, patients following LSG will be able to provide PROs on quality of life and quality of recovery. The use of PROs, including instruments of quality of life assessment, for the evaluation of PONV is novel, and will afford us the ability to assess if a PONV-specific intervention can have a patient-centered impact.

V. APPROACH

Overall design: We will conduct a randomized controlled trial to evaluate the effect of a multi-level PONV-specific intervention (pre-, intra- and post-operative) for patients undergoing LSG. Patients will be followed for 30 days to assess the benefit of this intervention on all phases of postoperative recovery (early, intermediate and late).



Human Subjects: Adult patients (18 years and older) undergoing LSG will be assessed for eligibility to participate in this study. Subjects will be recruited at the Stony Brook University Bariatric and Metabolic Weight Loss Center by study personnel. Patients with documented allergy to the study medications, history of chronic nausea and emesis requiring medication, poorly controlled diabetes (HgA1c>9 mg/dl), or history of previous bariatric or gastro-esophageal surgery will be excluded from this study.

Study Groups: Eligible subjects for this study will be randomized to two groups using an online random number generator. Randomization will occur during the last outpatient visit prior to undergoing LSG. Subjects will be assigned to two groups: control vs PONV-intervention (Figure).

Intervention: A) *Pre-operatively*: The experimental group will undergo treatment with aprepitant 80 mg orally and scopolamine transdermal patch one hour prior to scheduled surgery (figure 1).

B) *Intra-operatively*: Anesthetic parameters: Induction of anesthesia will be performed with propofol (1-2.5 mg/Kg IV) and succinylcholine (1-1.5 mg/Kg IV) or rocuronium (0.5-1 mg/Kg IV) after pre-oxygenation as standard practice for both groups. In the PONV-intervention group, total intravenous anesthesia (TIVA) will be maintained with IV infusions of propofol, and dexmetomidate infusion or intermittent bolus dosing of fentanyl after induction. In the control group, inhalation anaesthetics (sevoflurane or desflurane) and intermittent opioid boluses will be used for maintenance of anesthesia, as standard practice in our institution and across the country. Muscle relaxation will be maintained with boluses of rocuronium (10-20 mg) or vecuronium (1-2 mg) to provide optimal surgical conditions for both groups. Sugammadex (2-4 mg/Kg IV) will be used for reversal of neuromuscular blockade in both groups. Anti-emetic regimen: In the PONV-intervention group, a single dose of dexamethasone 8 mg IV will be administered after induction, and a single dose of ondansetron 4 mg IV will be administered approximately 20 minutes prior to the end of operation. PONV prevention measures in the control group will be limited to dexamethasone 8 mg and ondansetron 4 mg. This contrasts with the PONV-intervention group, which will undergo multimodal therapy [8, 12]. At any point during the study, clinical mandates by either surgeon or anesthesiologist can allow for subject cross-over, or subject withdrawal from the study.

Figure 1: Study protocol for PONV prevention

C) *Post-operatively:* PONV control will include scheduled ondansetron and metoclopramide every 6 hours, using Compazine as a rescue medication (Figure 1). This step will be common for both groups.

Surgery will be performed in a standardized way: antral division will commence at 4 cm from the pylorus, and the gastric sleeve will be calibrated over a 38 Fr bougie (or double channel endoscope, equivalent to 37.6 Fr). All patients will be in the current standardized LSG pathway that includes: avoidance of routine nasogastric decompression or surgical drainage, avoidance of routine urinary catheter placement, early ambulation the same day, early initiation of oral intake as soon as patient is awake, and no routine contrast radiologic studies. Per pathway design, all patients who undergo non-revisional LSG are planned for hospital discharge on POD 1. Pain control consists of scheduled acetaminophen and as needed IV opioids for the day of surgery, followed by as needed oral opiods starting on early morning POD 1.

Specific Aim 1: Evaluate the impact of a PONV-specific intervention on PONV-related prolonged length of hospital stay following SG surgery.

Hypothesis: We hypothesize that the PONV-intervention group will experience a more than 50% relative risk reduction of PONV-related prolonged hospital stay. We hypothesize that a PONV-specific intervention will lead to decrease in incidence and severity of PONV.

Rationale: All patients undergoing LSG are high-risk for PONV [13]. By implementing a series of interventions that individually have been proven efficacious in decreasing nausea or emesis, we anticipate a significant reduction in the incidence of PONV in the experimental group. The impact of nausea and emesis individually on the ability of LSG patients to tolerate oral intake and maintain hydration is unclear. Inability to tolerate oral intake and subsequent dehydration pronounce the effects of PONV, so we anticipate that an early intervention to prevent the incidence and severity of PONV will allow for early hospital discharge without an increased risk for hospital readmission. All items on the PONV-intervention program have been suggested to decrease PONV in bariatric or other high-risk populations [2, 3, 9, 10, 14].

Preliminary data: We have previously completed a prospective cohort study of 65 patients undergoing isolated non-revisional laparoscopic bariatric surgery (subjects undergoing concurrent procedures were excluded), and serially assessed for PONV using a 10-point Likert scale (presented at 2017 SAGES Annual Conference). Using a standardized postoperative PONV management algorithm, we identified that 59 of 65 (90.8%) of patients experienced PONV at some point during their hospitalization following LSG. The study was conducted in a clinical setting with routine radiographic imaging on POD 1 and pathway-targeted hospital discharge on POD 2. We identified that 20.7% of LSG patients experienced a prolonged hospital length of stay (past POD 2) and 6.9% were re-admitted within 30-days for PONV. In a more contemporary clinical practice without routine imaging and early oral intake initiation, the effect of PONV is more pronounced. In our current pathway with these elements of care, patients undergoing LSG are expected to meet criteria for hospital discharge on postoperative day 1. In the 2015-2016 academic year, we identified that 49% of SG patients were unable to be discharged to home on POD 1.

Experimental design: This is a prospective randomized trial of subjects undergoing LSG for morbid obesity. Subjects will be randomized to two groups (control vs PONV-intervention) as described above. ***Assessments***: Subjects will be assessed for the presence and severity of PONV at 1, 4, 12, 24 hours, and 3 weeks following the end of the surgical procedure (table 1). Nausea will be defined as an unsettled feeling in the stomach and urge to vomit. Vomiting will be defined as oral expulsion of gastric contents, and retching as expulsive attempts without any oral content. We will use a 10-point verbal rating scale (VRS) for the assessment of nausea as used previously [3, 9]. Vomiting and retching will be assessed in a binary way. The Rhodes Index of nausea and emesis, an 8-question survey (composite score range 0-32), will be used as an additional assessment instrument at the later time points (12 h and later) since it evaluates PONV over 12-hour intervals [15]. This index has been previously used for the assessment of PONV following LSG [16]. At each time point, total opioids (converted to morphine equivalents) and rescue anti-emetics used will be noted. Visits to the emergency room and hospital re-admissions will be captured; these will be considered PONV-related if the patient presents with inability to tolerate oral intake secondary to PONV, and/or signs and symptoms of dehydration, who are not found to have other pathology during evaluation (i.e. readmission for a patient with nausea due to a systemic infection will not be considered PONV-related). ***Outcome measures***: Primary outcome for this aim will be PONV-related delay in hospital discharge, defined as inability to be discharged from the hospital on POD 1 due to PONV. Secondary outcomes will be hospital length of stay (measured as hours from the end of the surgical procedure), incidence of PONV (incidence of nausea and emesis will also be assessed separately), severity of PONV (based on the VRS and Rhodes Index), PONV-related resource utilization (individually measured presentation to the emergency room and hospital readmission for PONV).

Interpretation, Potential Pitfalls and Alternative Strategies: We anticipate a significant reduction in PONV incidence and PONV-related delayed hospital discharge in the PONV-intervention group. Although unlikely, it is possible that we will be unable to identify a difference in POD1 discharge, as the time of performance of LSG may be a confounder and bias the results (i.e. patients undergoing SG earlier in the day may be more likely

Time points	*Specific Aim 1: PONV*	*Specific Aim 2: PRO*
Baseline	VRS, Rhodes Index	GIQLI, EQ-5D
1 hr	VRS	
4 hr	VRS	
12 hr	VRS, Rhodes Index	
24 hr	VRS, Rhodes Index	QoR-15, GIQLI
3 wk	VRS, Rhodes Index	QoR-15, GIQLI, EQ-5D

Table 1: Patient study assessments for each time point.

to be discharged to home on POD1). In our current practice, LSG procedures are performed earlier in the operating room day, to facilitate earlier hospital discharge the following day. Despite this, we have identified a 49% failure rate for POD1 discharge. In addition, our secondary measures, including incidence/severity of PONV and length of stay (measured in hours from the end of surgery) are not affected by operating room timing, and will allow for efficacy assessment of our PONV-intervention, independent of time of day of LSG completion. It is also possible that we identify no difference between the groups in terms of longer term PONV incidence. Our study will still provide valuable insight on the epidemiology of PONV after hospital discharge following LSG, which is currently poorly characterized. By allowing us to assess the overall incidence of PONV at different timepoints, this study will afford us the opportunity to identify a time period of high incidence and further adjust our prevention efforts accordingly in future studies.

Specific Aim 2: Assess the effect of a PONV-specific intervention on patient reported outcomes (PRO).

Hypothesis: We hypothesize that a PONV-specific intervention will significantly improve patient-reported quality of recovery from surgery and quality of life.

Rationale: PONV significantly affects the late phase of recovery (from hospital discharge to return to baseline), because it impairs the ability to perform activities of daily living, which patients value as an important goal of recovery [7]. In a postoperative survey of 469 patients evaluated two weeks after abdominal surgery, visceral function (including PONV) correlated with physical and functional impairment during recovery. Additionally, one third of patients following ambulatory laparoscopic surgery reported that nausea had a negative effect on their quality of life, during self-assessment on POD 5 [5]. Since PONV is reported commonly in LSG patients, we anticipate that improvement in PONV will significantly improve quality of life and overall experience during the intermediate (from post-anesthesia care unit until hospital discharge) and late phases of recovery. Additionally, the ability to resume physical activity is an important outcome of patient recovery [17]. This is particularly important after bariatric surgery, as an adjunct for weight loss, and recommended as part of clinical practice guidelines [18]. It is plausible that improvements in PONV for SG patients would have a significant benefit in terms of progressive physical activity and resumption of activities of daily living. If the PONV intervention is associated with improved patient experience and PROs, it could improve clinical decision making for patients considering LSG.

Experimental design: Subjects randomized to control versus PONV-intervention from Specific Aim 1, will be assessed in terms of quality of recovery and quality of life at the intermediate and late phases. ***Assessments***: PROs will be obtained at 24 hours, and 3 weeks following LSG surgery (table 1). The Gastrointestinal Quality of Life Index (GIQLI) is a validated instrument for the assessment of quality of life following gastrointestinal surgery, previously used in bariatric surgery research [19-23]. The QoR-15 is a validated reliable instrument to assess the quality of a patient's postoperative recovery [24]. This survey has been also used for quality of recovery assessment in the late phase, up to 30 days following gastrointestinal surgery [25, 26]. The Part A of QoR-15 assesses overall patient experience, as well as physical and functional status without direct assessment of symptoms (e.g. nausea) which are evaluated in Part B. Broad coherent assessment of quality of life will be performed using the EQ-5D index. This is a validated standardized brief instrument that provides a simple descriptive profile in five domains (mobility, self-care, usual activities, pain and anxiety) and a single index value for health status, designed for self-completion. The EQ-5D Crosswalk index calculator will be used to convert the descriptive profiling into a single index. EQ-5D has been extensively used for quality of life assessment in bariatric surgery [27-29].

Outcome measures: Primary outcome from this aim will be difference in the GIQLI index at 2 weeks postoperatively. Secondary outcomes will be difference in GIQLI at 24 hours and 3 weeks, difference in QoR-15 at each time point, difference in QoR-15 Part A at each time point, difference in EQ-5D self-assessed visual score, difference in EQ-5D profiling (score in each category), and difference in EQ-5D index at 3 weeks.

Interpretation, Potential Pitfalls and Alternative Strategies: We anticipate a significantly higher GIQLI in the PONV-intervention group. It is likely that an improvement in PONV will a priori lead to improvements in the quality of life indices selected, since these surveys include assessment of PONV. Although this could be considered bias, we believe that

improvement in these validated indices would remain a significant finding. However, to further assess for global improvements in quality of life, we will be separately analyzing Part A of the QoR-15 survey, which doesn't capture severity and presence of PONV. Additionally, the EQ-5D instrument includes no direct measurement of PONV, and would allow us to control for bias. It is also possible that the PONV-intervention group experiences no significant improvement in quality of life. If we identify an improvement in PONV incidence and severity (specific aim 1) without a concomitant improvement in quality of life after recovery, this finding would suggest the limited impact of PONV on quality of life early after LSG. Such finding would allow us to focus our subsequent PONV intervention methods in the intermediate phase of recovery. The EQ-5D instrument was used over the more widely used Short Form-36 due to the ease of use for patients (five vs 36 questions) and the non-inferiority for postoperative patients.

Statistical analysis: For continuous variables, data distribution will be assessed using the Shapiro-Wilk test. Two-sided t-test (means, standard deviation) and Wilcoxon rank sum test (median, 25^{th}-75^{th} percentiles) will be used accordingly. Categorical variables will be compared using chi-square testing. VRS assessments for all time points combined will be compared using repeated measures ANOVA.

Sample Size Considerations: The primary outcome of the study will be incidence of PONV-related delay of hospital discharge following LSG. Change in proportion will be assessed with chi-square testing. We expect a decrease in delay of POD1 discharge from 49% to 20% [3, 8]. Based on the data above, with two-tailed a=0.05 and b=0.2, we would require 41 subjects per group (total N=82) to detect a significant difference with the PONV-prevention. The Stony Brook Bariatric and Metabolic Weight Loss Center performs 100-150 LSG procedures annually, so we anticipate that the proposed study will be completed within 2 years.

VI. TIMELINE

Milestones	Months							
	1-3	4-6	7-9	9-12	13-15	16-18	19-21	22-24
IRB approval	X							
Study staff training	X							
Subject recruitment		X	X	X	X	X	X	
Data analysis							X	X
Manuscript preparation							X	X

VII. INSTITUTIONAL APPROVALS

Institutional approval will be obtained from the Stony Brook University Institutional Review Board. The review board meets regularly on a bi-monthly basis.

VIII. REFERENCES

1. Spaniolas K, Kasten KR, Brinkley J, Sippey ME, Mozer A, Chapman WH, Pories WJ. The Changing Bariatric Surgery Landscape in the USA. Obes Surg. 2015 Aug;25(8):1544-6.

2. Ziemann-Gimmel P, Goldfarb AA, Koppman J, Marema RT. Opioid-free total intravenous anaesthesia reduces postoperative nausea and vomiting in bariatric surgery beyond triple prophylaxis. Br J Anaesth. 2014 May;112(5):906-11.

3. Benevides ML, Oliveira SS, de Aguilar-Nascimento JE. The combination of haloperidol, dexamethasone, and ondansetron for prevention of postoperative nausea and vomiting in laparoscopic sleeve gastrectomy: a randomized double-blind trial. Obes Surg. 2013 Sep;23(9):1389-96.

4. Sippey M, Kasten KR, Chapman WH, Pories WJ, Spaniolas K. 30-day readmissions after sleeve gastrectomy versus Roux-en-Y gastric bypass. Surg Obes Relat Dis. 2016 Jun;12(5):991-6.

5. Pan PH, Lee SC, Harris LC. Antiemetic prophylaxis for postdischarge nausea and vomiting and impact on functional quality of living during recovery in patients with high emetic risks: a prospective, randomized, double-blind comparison of two prophylactic antiemetic regimens. Anesth Analg. 2008 Aug;107(2):429-38.

6. Carroll NV, Miederhoff P, Cox FM, Hirsch JD. Postoperative nausea and vomiting after discharge from outpatient surgery centers. Anesth Analg. 1995 May;80(5):903-9.

7. Urbach DR, Harnish JL, McIlroy JH, Streiner DL. A measure of quality of life after abdominal surgery. Qual Life Res. 2006 Aug;15(6):1053-61.

8. Apfel CC, Korttila K, Abdalla M, Kerger H, Turan A, Vedder I, Zernak C, Danner K, Jokela R, Pocock SJ, Trenkler S, Kredel M, Biedler A, Sessler DI, Roewer N; IMPACT Investigators. A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. N Engl J Med. 2004 Jun 10;350(24):2441-51.

9. Sinha AC, Singh PM, Williams NW, Ochroch EA, Goudra BG. Aprepitant's prophylactic efficacy in decreasing postoperative nausea and vomiting in morbidly obese patients undergoing bariatric surgery. Obes Surg. 2014 Feb;24(2):225-31.

10. Castro DS Jr, Leão P, Borges S, Gomes L, Pacheco M, Figueiredo P. Sugammadex reduces postoperative pain after laparoscopic bariatric surgery: a randomized trial. Surg Laparosc Endosc Percutan Tech. 2014 Oct;24(5):420-3.

11. Thorell A, MacCormick AD, Awad S, Reynolds N, Roulin D, Demartines N, Vignaud M, Alvarez A, Singh PM, Lobo DN. Guidelines for Perioperative Care in Bariatric Surgery: Enhanced Recovery After Surgery (ERAS) Society Recommendations. World J Surg. 2016 Sep;40(9):2065-83.

12. Gan TJ, Diemunsch P, Habib AS, Kovac A, Kranke P, Meyer TA, Watcha M, Chung F, Angus S, Apfel CC, Bergese SD, Candiotti KA, Chan MT, Davis PJ, Hooper VD, Lagoo-Deenadayalan S, Myles P, Nezat G, Philip BK, Tramèr MR; Society for Ambulatory Anesthesia.. Consensus guidelines for the management of postoperative nausea and vomiting. Anesth Analg. 2014 Jan;118(1):85-113.

13. Apfel CC, Philip BK, Cakmakkaya OS, Shilling A, Shi YY, Leslie JB, Allard M, Turan A, Windle P, Odom-Forren J, Hooper VD, Radke OC, Ruiz J, Kovac A. Who is at risk for postdischarge nausea and vomiting after ambulatory surgery? Anesthesiology. 2012 Sep;117(3):475-86.

14. Apfel CC, Zhang K, George E, Shi S, Jalota L, Hornuss C, Fero KE, Heidrich F, Pergolizzi JV, Cakmakkaya OS, Kranke P. Transdermal scopolamine for the prevention of postoperative nausea and vomiting: a systematic review and meta-analysis. Clin Ther. 2010 Nov;32(12):1987-2002.

15. Rhodes VA, McDaniel RW. The Index of Nausea, Vomiting, and Retching: a new format of the lndex of Nausea and Vomiting. Oncol Nurs Forum. 1999 Jun;26(5):889-94.

16. Afaneh C, Costa R, Pomp A, Dakin G. A prospective randomized controlled trial assessing the efficacy of omentopexy during laparoscopic sleeve gastrectomy in reducing postoperative gastrointestinal symptoms. Surg Endosc. 2015 Jan;29(1):41-7.

17. Feldman LS, Lee L, Fiore J Jr. What outcomes are important in the assessment of Enhanced Recovery After Surgery (ERAS) pathways? Can J Anaesth. 2015. Feb;62(2):120-30.

18. Mechanick JI, Youdim A, Jones DB, Timothy Garvey W, Hurley DL, Molly McMahon M, Heinberg LJ, Kushner R, Adams TD, Shikora S, Dixon JB, Brethauer S. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient--2013 update: cosponsored by American Association of Clinical Endocrinologists, the Obesity Society, and American Society for Metabolic & Bariatric Surgery. Surg Obes Relat Dis. 2013 Mar-Apr;9(2):159-91.

19. Eypasch E, Williams JI, Wood-Dauphinee S, Ure BM, Schmülling C, Neugebauer E, Troidl H. Gastrointestinal Quality of Life Index: development, validation and application of a new instrument. Br J Surg. 1995 Feb;82(2):216-22.

20. Lee WJ, Huang MT, Yu PJ, Wang W, Chen TC. Laparoscopic vertical banded gastroplasty and laparoscopic gastric bypass: a comparison. Obes Surg. 2004 May;14(5):626-34.

21. Freys SM, Tigges H, Heimbucher J, Fuchs KH, Fein M, Thiede A. Quality of life following laparoscopic gastric banding in patients with morbid obesity. J Gastrointest Surg. 2001 Jul-Aug;5(4):401-7.

22. Ignat M, Vix M, Imad I, D'Urso A, Perretta S, Marescaux J, Mutter D. Randomized trial of Roux-en-Y gastric bypass versus sleeve gastrectomy in achieving excess weight loss. Br J Surg. 2016 Nov 30.

23. Nickel F, Schmidt L, Bruckner T, Billeter AT, Kenngott HG, Müller-Stich BP, Fischer L. Gastrointestinal Quality of Life Improves Significantly After Sleeve Gastrectomy and Roux-en-Y Gastric Bypass-a Prospective Cross-Sectional Study Within a 2-Year Follow-up. Obes Surg. 2016 Nov 22.

24. Stark PA, Myles PS, Burke JA. Development and psychometric evaluation of a postoperative quality of recovery score: the QoR-15. Anesthesiology. 2013 Jun;118(6):1332-40.

25. Shida D, Wakamatsu K, Tanaka Y, Yoshimura A, Kawaguchi M, Miyamoto S, Tagawa K. The postoperative patient-reported quality of recovery in colorectal cancer patients under enhanced recovery after surgery using QoR-40. BMC Cancer. 2015 Oct 26;15:799.

26. Kleif J, Vilandt J, Gögenur I. Recovery and convalescence after laparoscopic surgery for appendicitis: A longitudinal cohort study. J Surg Res. 2016 Oct;205(2):407-18.

27. Tarride JE, Breau R, Sharma AM, Hong D, Gmora S, Guertin JR, O'Reilly D, Xie F, Mehran A. The Effect of Bariatric Surgery on Mobility, Health-Related Quality of Life, Healthcare Resource Utilization, and Employment Status. Obes Surg. 2017 Feb;27(2):349-356.

28. Sauerland S, Weiner S, Dolezalova K, Angrisani L, Noguera CM, García-Caballero M, Rupprecht F, Immenroth M. Mapping utility scores from a disease-specific quality-of-life measure in bariatric surgery patients. Value Health. 2009 Mar-Apr;12(2):364-70.

29. Date RS, Walton SJ, Ryan N, Rahman SN, Henley NC. Is selection bias toward super obese patients in the rationing of metabolic surgery justified?--A pilot study from the United Kingdom. Surg Obes Relat Dis. 2013 Nov-Dec;9(6):981-6.