Retrospective Chart Review: Sugammadex vs. Neostigmine/Glycopyrrolate

Pharmacoeconomic Analysis

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Abstract

**Purpose of Project:**
To ascertain the cost-effectiveness of sugammadex versus neostigmine by comparing operating room (OR) and post-anesthesia care unit (PACU) discharge times, that is, who leaves the OR and PACU faster. The overarching goal was to bring awareness to anesthesia providers, that emphasis on acquisition costs with little concern for indirect savings is misguided.

**Methodology:**
1. Pre-intervention data collection of sugammadex, a newer paralytic, and neostigmine, a traditional paralytic, usage and trends over a seven-month period (May – December 2018).
2. Pre-intervention anesthesia provider survey about current usage of sugammadex vs neostigmine, and presentation of pre-intervention data, research, and best practices about sugammadex and neostigmine to anesthesia providers at their monthly meeting at [Corporate Office].
3. Post-intervention data collection of sugammadex as compared to neostigmine usage over a two-month period (August – October 2019).
4. Statistical comparison of data to determine if the initial PowerPoint presentation had an impact on the usage of sugammadex and neostigmine and a subsequent PowerPoint presentation with a post-survey. The independent variables were (1) drugs administered (neostigmine and sugammadex) and ASA status (I-IV). The dependent variables were (1) OR total times in minutes and (2) PACU total time in minutes.

**Results:**
For the first data-set point, a total of 524 cases were analyzed (307 neostigmine/glycopyrrolate and 217 sugammadex). The mean duration time in minutes was shorter for the sugammadex group in both the OR and PACU (16.55-minute difference in the OR and 23.01-minute difference in the PACU). In patients that were considered seriously ill (ASA III and IV), the minute difference in the OR and PACU was even greater in the OR but about the same for PACU respectively (20.51-minute difference in the OR and 22.35-minute difference in the PACU for the seriously ill group). The anesthesia duration time in the OR in both the neostigmine and sugammadex group, independent of ASA, were statistically significant.

For the second data-set point, a total of 568 cases were analyzed (289 neostigmine/glycopyrrolate and 279 sugammadex). Results of the independent t-test suggests that the mean duration time in minutes was longer for the sugammadex group in both the anesthesia and PACU times. The mean difference between the neostigmine and sugammadex groups for anesthesia minutes was (-20.895) and was statistically significant (t=3.3 (539); p = .001). The mean difference between the neostigmine and sugammadex group for PACU minutes was (-11.386) with a strong tendency towards statistical significance (t= 1.9 (566); p=.051).

**Implications for Practice:**
Respiratory complications, such as post-extubation respiratory failure, is the second most common type of postoperative complication. Sugammadex as compared to neostigmine has been found to decrease incidences of post-operative respiratory complications in vulnerable populations like the morbidly obese and those patients with obstructive sleep apnea. Thus, this study has important implications on healthcare quality/safety as it challenges the idea that neostigmine is ideal in every clinical situation.

**Key Words:** sugammadex, neostigmine, discharge times, pharmacoeconomic analysis, PRNB
Retrospective Chart Review: Sugammadex vs. Neostigmine/Glycopyrrolate: A Pharmacoeconomic Analysis

Neuromuscular blocking agents (NMBAs) like rocuronium bromide, vecuronium bromide, and cisatracurium besylate are a mainstay in anesthesia practice. The use of NMBAs provides muscle relaxation which optimizes conditions for tracheal intubation, prevent patient movement during surgical procedures, and enhances surgery which can decrease the risk of surgery-related complications. At the conclusion of a case, patients may either spontaneously recover or be administered a reversal agent for a faster and more complete recovery.

Neostigmine, a cholinesterase inhibitor, has been the traditional agent of choice used to reverse nondepolarizing muscle blockade. It indirectly increases the amount of acetylcholine at the postsynaptic nicotinic receptor by reversibly and competitively inhibiting acetylcholinesterase in the synaptic cleft. Moreover, the effects of neostigmine can usually be seen in five minutes, but peaks at ten (Insinga, Joyal, Goyette, & Galarneau, 2016).

Train-of-four (TOF) testing, a widely used neuromuscular function assessment, helps approximate the degree or percent of neuromuscular blockade. It delivers four separate stimuli every 0.5 seconds at a frequency of two hertz for two seconds. When 100% neuromuscular blockade is attained, no responses can be produced (Nagelhout & Plaus, 2014). Neostigmine can be used for the reversal of a moderate (i.e., when at least two twitches of a TOF stimulation is present) or superficial (i.e., when greater than two twitches are present) neuromuscular blockade. However, “neostigmine is ineffective at reversing deep levels of blockade, because a ceiling effect is reached in which the increase in acetylcholine concentration is insufficient to displace enough NMBA to reverse the neuromuscular block” (Insinga et al., 2016, para. 2). Additionally, due to muscarinic-related side effects like nausea, vomiting, and bradycardia neostigmine is
administered with an antimuscarinic agent, usually glycopyrrolate. More telling is that reversal with neostigmine is neither rapid or predictable. Extubating too early can lead to respiratory failure, aspiration due to depressed reflexes, increased hospital length of stay, and higher hospital costs secondary to postoperative residual neuromuscular blockade (PRNB) (Gaszynski, Szewczyk, & Gaszynski, 2011; Insinga et al., 2016).

Conversely, sugammadex, a modified gamma-cyclodextrin, forms a 1:1 ratio complex with rocuronium (and vecuronium to a lesser extent), which rapidly terminates even profound neuromuscular blocks in a predictable manner. Its effects peak at about three minutes. Sugammadex has been shown to have less side effects, and more notably is that several randomized controlled trials have shown that sugammadex is associated with less incidences of PRNB compared to neostigmine (Carron, Zarantonello, Tellaroli, & Ori, 2016). Although the superiority of sugammadex in comparison to neostigmine has been demonstrated, particularly in the setting of rocuronium-induced neuromuscular blockade, cost concerns remain a major barrier to the widespread use of sugammadex. Indeed, O'Reilly-Shah, Wolf, Jabaley, and Lynde (2017) found that even in the absence of policies restricting sugammadex, 40% of the respondents (anesthesia providers) implemented self-imposed limitation on their use of sugammadex secondary to cost. This finding was telling, because it suggests that anesthesia providers may be making clinical decisions based on a limited understanding of the pharmacoeconomics of sugammadex.

Pharmacoeconomics uses “cost-benefit, cost-effectiveness, cost-minimizatiom, cost-of-illness, and cost-utility analyses to compare pharmaceutical products and treatment strategies” (Arenas-Guzman, Tosti, Hay, & Haneke, 2017, Abstract). Various pharmacoeconomic evaluations suggests that sugammadex may be more cost-effective than neostigmine (Carron,
Zarantonello, Lazzarotto, Tellaroni, & Ori, 2017; Putz et al., 2016). The financial and clinical implications prompted the need for this investigation. Therefore, we conducted a pharmacoeconomic analysis to ascertain the cost-effectiveness of sugammadex compared to neostigmine by assessing operating room (OR) and post-anesthesia care unit (PACU) discharge times, following a retrospective review of medical records covering a span of three months, in adult surgical patients at a large medical center located in southern New Jersey.

**Background and Significance**

Economic constraints impact the way in which healthcare facilities conceptualize cost and potential savings when purchasing drugs, often focusing on up-front costs to the detriment of indirect savings. This view is myopic in nature, as the pharmacoeconomics of certain drugs are multifaceted. For example, although the acquisition costs of sugammadex at the referenced institution above is approximately $173.50 (500 mg per 5 mL vial), compared to neostigmine’s cost of $19 per syringe (stocked as 4 mg per 4 mL prefilled syringes), and glycopyrrolate’s acquisition cost of $4.63 per vial (stocked as 0.4 mg/ 2 mL vial), the slightly higher cost of sugammadex should be weighed against potential advantages like, decreased complications related to PRNB, speedy and predictable reversal, irrespective of the degree of blockade, and faster OR and PACU discharge times (D. Faith, personal communication, March 21, 2019). The magnitude of this effect is worth exploring given the potential clinical and financial implications (Cammu, 2018; O'Reilly-Shah et al., 2017).

Only a paucity of data exists on the cost-benefit analysis of sugammadex. Paton et al. (2010) established two criteria to demonstrate the cost-effectiveness of sugammadex. First, sugammadex must yield faster recovery times when compared to neostigmine. Secondly, any time saved is converted to productive activities. Rapid NMBA reversal can translate into vast
savings in the form of reduced surgery cancellations due to OR time over-run, avoided staff
over-time, and more cases. Additionally, by reducing PRNB related complications, sugammadex
might also reduce the costs related to extra time spent in the PACU (Insinga et al., 2016).

An economic analysis was undertaken to analyze (a) the value of each minute of OR time
saved and (b) the value of each minute of PACU time saved. In the United States, the OR cost
per-minute has been estimated to be about $30. PACU charge times of the implementation
facility will be used and is estimated to be about $21 per-minute. The price of sugammadex was
calculated on the assumption that a patient has a weight of 75 kg. The cheapest combination of
vials was used, and any unused drug was considered wasted.

Needs Assessment

For over 30 years the traditional practice of NMBA reversal has been a cholinesterase
inhibitor such as neostigmine with the concomitant administration of an antimuscarinic agent,
typically glycopyrrolate. Although this practice has been the primary method of NMBA reversal,
largely due to a lack of alternative methods, and given the required coadministration of
glycopyrrolate in order to combat the side effects of neostigmine, suggests that this drug
combination is not optimal (Yang & Keam, 2009). There are several clinical considerations for
neostigmine and glycopyrrolate use that the anesthesia provider must acknowledge, such as
limitations, side effects, and current best practice methods.

According to Brull and Kopman (2017), the primary limitation of using a cholinesterase
inhibitor for NMBA reversal lies mainly in its mechanism of action of competitive inhibition at
the site of the neuromuscular junction, slowing the breakdown of acetylcholine, restoring the
balance of acetylcholine, and resulting in normal function and reversal of the block. Since the
degree of neuromuscular blockade (NMB) reversal is dependent upon the amount of
acetylcholinesterase present in the neuromuscular junction, there is a ‘ceiling effect’ when administering an anticholinesterase. Additionally, neostigmine is ineffective during profound or deep blockade, and during light block only small doses are needed with a full dose resulting in transient neuromuscular weakness.

Due to the nature of the reversal mechanism of cholinesterase inhibitors, limitations further include ineffective dosing potentially resulting in PRNB. The TOF ratio is the ratio of the height of the fourth twitch response compared to the height of the first response, and residual blockade is defined as a TOF ratio less than 0.9 which occurs in up to 20-40% of patients arriving in PACU. (Brull & Kopman, 2017). It is recommended that NMB reversal dosing should be guided by depth of NMB via objective assessment of the quantitative ratio of TOF twitch responses, as well as subjective clinical signs of neuromuscular recovery; however, in clinical practice TOF ratio assessment with quantitative neuromuscular monitoring is rarely used as evidence by high incidences of PRNB (Insinga et al., 2016).

Additional limitations of cholinesterase inhibitors include ineffective timing of administration which can potentially lead to PRNB. According to Jahr et al. (2015) neuromuscular dysfunction due to a recurarization effect can result if the duration of the NMBA outlasts the duration of the cholinesterase inhibitor leading to subsequent life-threatening complications after extubation with increased risks including but not limited to: impaired pharyngeal function, aspiration, weakness of airway muscles, impaired ventilation, partial or complete airway obstruction, anxiety, hypoxemia, need for tracheal reintubation and mechanical ventilation, and a prolonged recovery room stay and/or hospital course. Considering the limitations and the side effects, safer and more effective available alternatives to NMBA reversal should be implemented into standard practice.
As an alternative approach to traditional cholinesterase inhibitor reversal of NMBA, sugammadex was approved by the FDA on December 15, 2015 for use in rocuronium or vecuronium induced NMB (Jahr et al., 2015). The mechanism of action of sugammadex results in rapid encapsulation and removal of NMBA molecules with no action on acetylcholinesterase, therefore, lacking the muscarinic side effects and the need for antimuscarinic agents, along with the potential side effects (Jahr, et al., 2015). Sugammadex use, in comparison to neostigmine, has been associated with a significantly lower risk of respiratory adverse events, cardiovascular adverse events, and postoperative weakness (Carron et al., 2016). The introduction of sugammadex and its highly reliable and reproduceable reversal in comparison to neostigmine suggests that there is a potential for improvement in clinical practice.

Sugammadex has proven to be a superior NMB reversal to neostigmine, and its adoption in practice has been steadily increasing over the past decade; however, the major obstacle to the widespread clinical use continues to be costs (Carron et al., 2016, p. 11). These findings warrant a further investigation of the clinical implications for sugammadex use such as patient characteristics, type of surgery, discharge times, and how those differ from that of neostigmine use.

Additional considerations include the lack of any clinical guidelines or protocols at this university medical center to guide decision making processes when deciding to utilize a cholinesterase inhibitor versus sugammadex, and therefore is largely at the discretion of the provider. Furthermore, at this university medical center, sugammadex is currently only supplied in 500 mg vials at a cost of $173.50 per vial, while outside references indicate that 200 mg vials costs approximately $100 per vial, which may indicate a potential cost-savings advantage if the
smaller dose vials were to be supplied based on the quantity of $\leq 200$ mg doses administered in 2018.

Through the use of a SWOT analysis there were several strengths, weaknesses, opportunities, and threats evident to the project. Internal attributes that help support and strengthen the project includes stakeholder buy-in (i.e., sugammadex, Merck), and facility support, specifically, the chairman of anesthesia, the anesthesiologist liaison between the pharmacy department, as well as the OR statistical analysist. Internal opportunities to help support the project includes the improvement of practice and patient outcomes, the decrease of costs associated with shorter PACU discharge times, and the lack of a current protocol or suggested guidelines for sugammadex use. Threats or weakness to the project includes lack of support from pharmacy personnel, increased costs associated with increased sugammadex use, staff resistance to change, and change of an electronic health record platform projected to go live in September 2019.

**Problem/Purpose Statement**

The problem that needed to be assessed was to ascertain if the use of sugammadex and subsequent reduction in OR and/or PACU discharge times equate to the difference in cost between the use of neostigmine and glycopyrrolate versus sugammadex by a retrospective chart review utilizing a random sample of patients who received sugammadex versus patients who received neostigmine/glycopyrrolate. Comparison and statistical analysis was made between times out of OR after reversal was given, PACU discharge times, with a cost analysis of time differences utilizing the costs per minute in OR and PACU time, and the differences in the cost per vial of sugammadex versus costs of neostigmine and glycopyrrolate.
Clinical Question

The clinical question was, in adult surgical patients who receive neuromuscular blockers during general anesthesia, how cost effective is sugammadex use in comparison to neostigmine in reducing cost by means of reduced postoperative discharge time from the OR to PACU and PACU to discharge, during the perioperative period following a retrospective chart review over three months?

Aims & Objectives

The overall goal of this project was to determine if the use of sugammadex could garner economic advantages in comparison to the combined administration of neostigmine and glycopyrrolate by assessing OR to PACU and PACU discharge times. First, preliminary data pertaining to the administration of sugammadex and the coadministration of neostigmine/glycopyrrolate was analyzed to assess and identify trends. Second, the investigators presented the findings of the preliminary data to anesthesia providers at their monthly meeting. Third, two months of data assessing sugammadex use and associated discharge times from the OR to the PACU as well as discharge times from the PACU in comparison to neostigmine and glycopyrrolate, in the time period following the initial presentation was collected and analyzed. Finally, the two investigators presented the second set of statistical data and pharmacoeconomic analysis to infer whether any changes have occurred in regard to usage, discharge times, and cost.

The differences in times was then evaluated and compared for obvious time lapses between the two courses of treatment. Additional time spent in OR and PACU associated with use of neostigmine was calculated based off minute operation costs, and then added to the costs.
of the medication, to determine if this cost is equivalent, more expensive, or remains less expensive than a one-time dose of sugammadex.

**Review of Literature**

A literature review was conducted to identify and summarize the current research findings relating to the use of sugammadex versus neostigmine from an economical and financial standpoint. An overwhelming amount of studies indicated the rapidity and reliability of rocuronium induced NMB reversal with sugammadex versus that of neostigmine, a well-supported topic. However, the investigators strived to identify what specific barriers led to the limited use of sugammadex use in clinical practice, whether it be institutional restrictions, self-imposed restrictions due to cost concerns, or a lack of acceptance of a superior alternative to NMBA reversal. Reviewing the current literature and research involving sugammadex use in comparison to neostigmine with respect to costs, it became clear that practitioners may be making biased decisions based on experience and opinions, without knowledge of current research.

Upon a narrower search to identify potential factors affecting the pharmacoeconomic components surrounding the use or lack of use, the literature review also found trends in studies identifying PRNB as a commonly occurring incident with traditional cholinesterase inhibitors. PRNB appears to be a primary factor for prolonged discharge times, post-operative complications, and adverse events, potentially contributing to the cost-effectiveness of sugammadex use over neostigmine. Additionally, while reviewing the literature, research also suggested sugammadex use may be most effective when used in patients who are particularly vulnerable to the consequences of PRNB, such as morbidly obese, those with obstructive sleep
apnea, and those with pre-existing respiratory disorders. Furthermore, a complete table of evidence displaying the literature in support of the clinical question can be found in Appendix A.

**Search Strategy/PRISMA**

Literature searches were performed by searching the electronic databases CINAHL, PubMed, and Medline to identify peer reviewed randomized controlled trials, meta-analysis, retrospective case studies, systematic reviews, literature reviews, and any other relevant experimental research between 2009 and 2019 involving. These databases were searched using a variety of topic-related phrases and key words in combinations to narrow the focus. Key words included ‘sugammadex’, ‘neostigmine’, ‘cost analysis’, ‘postoperative outcomes’, ‘discharge times’, and ‘PACU discharge time’. The investigators of this study independently screened the titles and abstract and excluded all nonrelevant articles, and then full texts were assessed to determine if they met predetermined selection criteria. Appropriate studies included adult surgical patients only, in the English language, and were excluded if they included pediatric patients, were unavailable online, or missing an abstract. Using the John Hopkins nursing evidence-based practice individual evidence summary tool, the data was then extracted independently by the two investigators of this study from the included studies. The PRISMA diagram is available for viewing in Appendix B.

**Cost Concern is a Major Barrier to Widespread Sugammadex Use**

Although sugammadex produces a faster and more reliable recovery from rocuronium or vecuronium induced blockade, irrespective of the degree of block (superficial, moderate or deep), without any cholinergic effects and with fewer postoperative adverse effects, cost concerns remain a major barrier to widespread access (Cammu, 2018; Carron et al., 2017; O'Reilly-Shah et al., 2017).
Indeed O'Reilly-Shah et al. (2017) found that most of the respondents (56%) had some form of explicit restriction on sugammadex access secondary to cost. More telling, the study revealed that even in the absence of explicit restrictions, 40% of the respondents self-limited their use of sugammadex citing cost concerns as a primary factor. In this quasi experimental study, the investigators created a mobile application to assess global patterns of clinical practice and experience with sugammadex. There was a total of 11,863 anesthesia provider respondents from 183 countries. Although the study contained limitations like the fact that not all questions were completed by all respondents, the study lacked randomization which can lead to limited generalizability of the results secondary to non-equivalent test groups, and also contained significant variations in terms of national or regional healthcare delivery which can impact the way costs are conceptualized by the respondents. The study findings were still interesting because they suggest that cost concerns are the biggest barrier to widespread use of sugammadex and anesthesia providers are making clinical decisions based on poor economic information concerning sugammadex. The pharmacoeconomics of sugammadex are multifaceted since higher drug costs are likely offset by decreased OR recovery times, faster PACU discharge, and fewer complications related to residual neuromuscular block.

**Potential Economic Advantages of Sugammadex**

Carron et al. 2017 found that compared with neostigmine, sugammadex was associated with a shorter discharge-readiness for patients moving from the OR to the PACU and significantly faster discharge from the OR to the PACU (mean difference = 22.14 mins). This difference was magnified with deep neuromuscular blockades (mean difference 30.05 mins). Moreover, compared with neostigmine, sugammadex was associated with a significantly faster discharge from the PACU to the surgical ward. However, a major limitation to this study was
that it only contained a limited amount of studies (six) and the heterogeneity across the studies were considerable, particularly for the PACU discharge results.

Similarly, Insinga et al. (2016) found that in the presence of sugammadex, 2.4 procedural cancellations due to OR time over-run and 33.5 hours of paid staff overtime were avoided, while saving an average of 62 mins per OR day. In patients who were maintained at a deep level of block to the end of the procedure, it was assumed that 30 minutes of OR time were saved per procedure, and the number of paid hours of staff over-time dropped from 84.1 to 32. A major limitation of this study is that since it is a discrete event simulation model, the results are from secondary data as human subjects were not enrolled. Likewise, Zaouter et al. (2017) confirmed the cost-effectiveness of sugammadex by performing an economic evaluation using real clinical scenarios. Sugammadex as compared to neostigmine both increases the number of cases that can be performed per day and lowers the daily OR cost for surgeries requiring both moderate and deep NMB.

**Postoperative Residual Neuromuscular Blockade (PRNB)**

The associated complications of PRNB can further impact the length of stay in PACU, prolonging hospital discharge, warrant an admission to the ICU, and potentially require reintubation. Insinga et al. (2016) conducted a discrete event simulation model to compare ORs using either neostigmine or sugammadex for NMB reversal over one month to explore the impact on OR efficiency and incidence of PRNB. Insinga et al. (2016) identified the average risk of residual block at extubation with neostigmine use estimated to be 60% when patients are not required to have verification of full neuromuscular recovery (TOF ratio < 0.9) prior to extubation in the OR and sugammadex usage reduced the risk of residual blockade by 93%. These results are telling, and are particularly helpful to the project, considering quantitative TOF ratios with
acceleromyography are not common practice at the university medical center where the study will be conducted, and substitution of sugammadex for neostigmine may likely lead to a reduction in the risk of PRNB and OR procedure times.

Of the many benefits of sugammadex, a major application is that it can be utilized for light, moderate, deep, as well as profound NMB. The meta-analysis conducted by Carron et al. (2016) identified that sugammadex in comparison to neostigmine was faster in reversing moderate and deep rocuronium induced NMB, more likely to be associated with higher train-of-four ratio values at extubation, and showed a lower risk of postoperative residual curarization. Furthermore, Carron et al. (2016) identified that sugammadex use was associated with lower risk of respiratory adverse events (AEs), cardiovascular AEs, and postoperative weakness. The implications of this study may be beneficial to support the theory that patients with pre-existing respiratory, cardiovascular, or neuromuscular disease may benefit from the use of sugammadex.

The prospective cross-sectional pilot investigation conducted by Ledowski et al. (2013) aimed to investigate the impact of sugammadex versus neostigmine or no reversal on patient outcomes by measuring outcome parameters as complications in the recovery room and radiologic diagnosed atelectasis or pneumonia within 30 days. Ledowski et al. (2013) found a high proportion of residual paralysis, and the use of sugammadex resulted in the lowest rate of TOF ratios <0.7 and <0.9, corresponding to a lower rate of oxygen desaturation (defined as SpO2 < 96%) in the recovery room. However, there was no statistical significance noted for patients showing pathological x-ray results after the use of neostigmine or sugammadex when compared to no reversal. Additionally, during the study sugammadex was introduced as an unrestricted alternative to neostigmine and demonstrated a subsequent high acceptance rate as an alternative reversal method. Ledowski et al. (2013) identified cost as a major setback, although
the confirmed lower rate of TOF ratios with sugammadex use and the evidence regarding the impact of PRNB on outcomes should prompt the question of ‘what is the acceptable price for patient safety?’

**PRNB in vulnerable patient populations.**

Carron et al. (2017) states that sugammadex can improve postoperative pulmonary outcomes in populations at risk due to less residual paralysis. The meta-analysis conducted by Carron et al. (2017) sought to analyze whether sugammadex accelerates discharge to the surgical ward compared to neostigmine. Results indicated that compared with neostigmine, sugammadex was associated with a significantly faster discharge from the OR to the PACU, as well as a significantly faster discharge from PACU to the surgical ward. Carron et al. (2017) analyzed a subgroup of morbidly obese patients which showed sugammadex was associated with a significantly faster discharge from PACU. Specifically, the study identified that sugammadex appeared superior for respiratory function and diaphragm recovery compared with neostigmine as evidence by higher tidal volumes and arterial oxygenation as well as a reduced risk of minor respiratory events.

Ünal et al. (2015) identified PRNB can be especially detrimental to those with OSA, and complications are increased with higher diagnosis of post-operative aspiration pneumonia and acute respiratory failure requiring intubation and mechanical ventilation. Ünal et al. (2015) conducted a randomized control trial comparing the efficacy of sugammadex to neostigmine in reversing rocuronium induced NMB in and the incidence of postoperative respiratory complications and costs in patients undergoing treatment for obstructive sleep apnea. Primary outcome measures of the study were time to obtain a TOF ratio 0.9 after reversal and secondary outcome measures were the OR room time, PACU time, frequency of respiratory and circulatory
complications, and associated costs. Ünal et al. (2015) found that TOF ratio 0.9 was achieved faster in the sugammadex group, OR room time and PACU times were also shorter in the sugammadex group and was attributed to the rapid reversal of NMB with sugammadex. Ünal et al. (2015) suggests that the complete and rapid reversal of NMB will result in a decrease of both the frequency of complications and costs in patients with high risk for post-operative respiratory system complications.

The complete and rapid return of neuromuscular function is imperative for prevention of postoperative complications in all patients who receive intraoperative NMBA particularly in morbidly obese patients. De Robertis et al. (2016) claims that perioperative management of morbidly obese patients is undoubtedly challenging, with TOF ratio < 0.9 being associated with increased risk of pulmonary complications and respiratory impairment. De Robertis, et al. (2016) conducted a retrospective study that analyzed data from records of morbidly obese patients (BMI > 40 kg/m2) undergoing elective laparoscopic bariatric surgery in which sugammadex or neostigmine and atropine were used to reverse either rocuronium or cistatracurium induced NMB. The primary endpoint was comparing the latency to achieve a TOF > 0.9 after reversal agent administration, the mean time to achieve an Aldrete score of 10, and costs associated with these drugs. Secondary end points of the study were to evaluate duration of OR time, incidence of postoperative desaturation in PACU, and length of stay in hospital. De Robertis et al. (2016) found that although reversal from NMB was significantly faster with sugammadex there were no desaturation in PACU and differences in length of stay in both groups, but highly encouraged the clinical application of TOF-driven protocol to reverse NMB in morbidly obese patients.

Gaszynski et al. (2012) claims a patent airway and protective upper airway reflexes are crucial in the morbidly obese population because of their borderline vital functions. Gaszynski
et al. (2012) conducted a prospective randomized control trial to compare the effectiveness of neostigmine versus sugammadex and prevent postoperative residual curarization (PORC) in morbidly obese patients undergoing elective bariatric surgery. Sugammadex or neostigmine with atropine were administered and the time to achieve 90% TOF was measured, with TOF reassessed in PACU for PORC (TOF < 90%). In this study the mean time to achieve 90% TOF was 3.5 times shorter in the sugammadex group with no significant associated complications and a greater than 90% TOF in PACU in every case. TOF ratios were less than 90% in the neostigmine group, and observed complications were dangerous profound bradycardia in 10% of patients requiring additional doses of atropine. Overall, Gaszynski et al. (2012) determined that sugammadex was significantly faster reversing rocuronium-induced NMB than neostigmine in morbidly obese patients, and effectively prevents PORC, whereas neostigmine does not.

**Overall Findings from the Literature**

Although sugammadex seems to confer economic advantages, uncertainties remain concerning its cost-effectiveness. To demonstrate the cost-effectiveness of sugammadex, two things need to be established. First, some reduction in patient recovery time can be obtained by using sugammadex as compared to neostigmine. And the time saved can be put to productive use. However, the proportion of time saved that can be put to use is ultimately unknown since there are multiple variables at play. For example, many things may impact OR and PACU discharge times outside of recovery from neuromuscular blocking agents. Indeed, medical personnel accounted for greater than 50% of the delays from PACU to inpatient units, and system problems accounted for 25%. Nevertheless, sugammadex’s potential to accelerate postoperative and PACU discharge times and improve patient outcomes (particularly those with
obstructive sleep apnea and those who are morbidly obese), may offset the slightly higher cost (Carron et al., 2017; Paton et al., 2010).

**Theoretical Framework**

The willingness of clinicians to adopt a new clinical behavior, in this instance, the willingness to use a new drug is influenced by a multitude of factors. Everett Roger’s theory of diffusion of innovations explains these factors most appropriately. Diffusion is the process by which an innovation is communicated over time among the participants in a social system. Innovation is anything (i.e., an idea, practice, or object) that is perceived as new by an individual or other unit of adoption, irrespective of the lapse of time since the product’s first use or discovery. The theory states that four main elements influence the spread of a new idea: (a) the innovation itself; (b) communication style; (c) the decision process; and the (d) social context (see Appendix C for theoretical framework diagram) (Sanson-Fisher, 2004; White & Dudley-Brown, 2012).

**The First Element: The Innovation**

According to the theory, there are five elements of a new idea or innovation that will determine its adoption rate or success: (a) relative advantage; (b) compatibility; (c) complexity, (d) trialability; and (e) observability.

**Relative advantage.**

Relative advantage is defined as the “degree to which an innovation is perceived as better than the idea it supersedes” (Sanson-Fisher, 2004, Relative Advantage). Interestingly enough, adopting a behavior is not only driven by the interest of the patient, but also that of the clinician, and the social system. For example, research may indicate that an innovation is beneficial to patients. However, if the adoption of such practice changes a balance of power
between groups, or is perceived to be antagonistic to the clinician’s interest, the innovation may meet resistance and fail to adopt. Conversely, if the innovation is perceived to be in alignment with the interest of the clinician or that of the social system, the innovation may readily be adopted (Sanson-Fisher, 2004).

Compatibility.

Compatibility is “a measure of the degree to which an innovation is perceived as being compatible with existing values, past experiences, and the needs of potential adopters” (Sanson-Fisher, 2004, Compatibility). Thus, the innovation should solve a perceived problem. Medical exams and screenings that test for cancer, e.g., colonoscopies and mammograms, are readily adopted because they are compatible with the medical beliefs that cancer is a problem and early detection leads to better patient outcomes (Sanson-Fisher, 2004).

Complexity, trialability, and observability.

An innovation is more likely to be adopted if it is perceived as being simple and well defined, and not as complex or difficult to understand or use. Trialability refers to the extent in which the innovation can be trialed and modified. Trialability promotes faith in the innovation and that its purported claims are correct, and that its adoption and implementation is logistically feasible. On the other hand, observability refers to the degree the innovation is seen by others. Observability promotes active participation since it allows the clinician to witness the effects and potential benefits of the innovation firsthand while fostering peer discussion. Increased visibility directly correlates with adoption rates (Sanson-Fisher, 2004).

The Second Element: Communication Style

There are several ways to disseminate information to a group of interest. Examples include, social media, video or audiotapes, lectures, workshops, and/or a face-to-face exchange.
The literature suggests that a face-to-face exchange is an effective communication strategy since it allows real-time tailoring of information to an individual or a group. Moreover, the exchange is more effective when there is more homogeneity among the introducer and the recipient (Sanson-Fisher, 2004).

**The Third Element: The Decision Process**

The third element of Roger’s theory of diffusion of innovations describes a five-step innovation-decision process. The first step is termed *knowledge*, and is the process by which the recipient becomes aware of an innovation and has some idea of how it functions. Secondly, the person forms a favorable or unfavorable attitude or *persuasion* toward the innovation. Thirdly, the recipient *decides* whether to accept or reject the innovation through a series of risk-benefit analysis. Next, the person *implements* the innovation into practice. And lastly, the person evaluates or *confirm* their decision to implement the innovation. People move through the decision process at different rates, and how fast this is done depends on whether the person is an ‘innovator’ (tolerant of risks and likes new ideas), ‘early adopter’ (tend to be opinion leaders of an organization and like to associate with the innovators), ‘early majority’ (risk averse), ‘late majority’ (only adopt after the innovation is status quo), or laggard (likes the tried and true, detest change) (White & Dudley-Brown, 2012, pp. 31-32).

**The Fourth Element: The Social Context**

Systems most permeable to change are those that have a culture of creativity, a mostly flat hierarchical system, and strong leadership that is committed to facilitating change. Altering aspects of the system to better monitor the innovation and streamline feedback may be necessary for desired outcomes. Sadly, most systems are bureaucratic with cultural norms that impede change (Sanson-Fisher, 2004).
Diffusion Theory and Sugammadex

Neostigmine is the traditional agent of choice in terms of reversal agents, whereas sugammadex is a newer reversal agent, approved for use in the United States in December 2015 (Food & Drug Administration [FDA], 2016). As mentioned above, the diffusion of innovation theory states that four main elements influence the spread of a new idea: (a) the innovation itself; (b) communication style; (c) the decision process; and the (d) social context (Sanson-Fisher, 2004).

Characteristics of sugammadex.

Sugammadex offers many advantages over neostigmine. The main advantage is that it is faster in reversing neuromuscular blockade, irrespective of the degree of block and is associated with lower incidences of PRNB compared to neostigmine. Neostigmine is only capable of reversing shallow to moderate neuromuscular blockade. On the other hand, sugammadex, using a recommended dose range of 2 to 16 mg/kg, is capable of reversing any depth of block within three minutes. Another advantage of sugammadex over neostigmine is that it does not have cholinergic-related side effects like neostigmine, thus the coadministration of an anticholinergic agent like glycopyrrolate is not necessary. This potentially reduces the complexity of reversing a patient at the end of case and can serve to increase the use or adoption rate of sugammadex per Roger’s diffusion of innovations theory. Moreover, although the observability or visibility of sugammadex has not been widespread secondary to its acquisition cost, with the recent price hikes of neostigmine as a result of the way the FDA handles grandfathered drugs and the fact that sugammadex’s patent expire in 2021 in the United States, widespread use of sugammadex may soon be the rule and not the exception (Naguib, 2017).

Communication style and the decision process.
As the use of sugammadex increases, anesthesia providers will become aware or gain knowledge of its advantages as documented above. Providers will seek information about sugammadex and will be persuaded one way or the other concerning its use as compared to neostigmine. The person will then decide whether to implement the innovation (sugammadex) into practice or reject its adoption. The last step in the innovation-decision process is confirmation. The person makes the conscious decision on whether to continue to use the innovation or not (White & Dudley-Brown, 2012).

**Social context.**

Systems most permeable to change are those that have a culture of creativity, a mostly flat hierarchical system, and strong leadership that is committed to facilitating change (Sanson-Fisher, 2004). Unfortunately, the implementation hospital in southern New Jersey has a hierarchical system that is mostly bureaucratic. Currently, sugammadex is only stocked in limited Omnicells as compared to neostigmine that is stocked in every area where anesthesia services are provided. The process on how to facilitate greater access to sugammadex is unclear.

**Methodology**

The method of this proposed research project was a retrospective chart review at a large medical center in southern New Jersey in order perform a pharmacoeconomic analysis of neostigmine and glycopyrrolate usage versus that of sugammadex. The goals of the project were to identify if in fact there are faster OR and PACU discharge times associated with sugammadex use versus that of neostigmine and glycopyrrolate, while the pharmacoeconomic analysis goal was to identify if the cost of sugammadex could be offset via the faster OR and PACU discharge times.
After receiving Institutional Review Board (IRB) approval, the 2018 data was collected, statistical interpretation was completed, and findings of this preliminary data was presented to the anesthesia staff during a monthly meeting on August 15, 2019 along with the current literature regarding sugammadex use in a formal PowerPoint presentation created and conducted by the researchers. A second retrospective chart review then took place dating two months after the initial presentation to ascertain if there were any further reductions in OR and PACU discharge times with sugammadex use, or a reduction in patients requiring both reversal agents.

Upon completion of the second retrospective chart review for the period of two months after the initial presentation, data was then analyzed and interpreted with results presented to the anesthesia staff during an anesthesia meeting on January 23, 2020. An anonymous presurvey at the initial presentation was presented at the first presentation and an anonymous postsurvey was provided after the second presentation to all anesthesia providers indicating their perception to the barriers of sugammadex use at the implementation facility as well as if the information presented could influence a change of practice regarding NMB reversal methods. See attached surveys in Appendices D-E.
Setting

This project took place at a large medical center in southern New Jersey. Perioperative records were reviewed from the main OR, EPS/cardiac catheterization lab, ASC, and the endoscopy center on patients who meet the inclusion criteria detailing the dosages of medications given and the time spent in the OR as well as time spent in the respective PACU. These records were analyzed and retrieved from Surgical Information Systems (SIS) analytics, the medical center’s perioperative electronic documentation platform via the center’s surgical services data analyst personnel, whose office is located on the fourth floor directly outside of the OR.

Information in the data retrieval included the case number, age, gender, ASA status, dose of neostigmine, dose of glycopyrrolate, dose of sugammadex, anesthesia starting times, OR discharge times, anesthesia stop times, PACU discharge times, and overall PACU times. The case number is a randomly created number assigned specifically to patients at this medical center and in no way is correlated to a medical record number or any other patient identifier. However, this case number was deleted immediately upon extrapolation of the data, and patient information for each group was reassigned numerically accordingly.

Study Population

The inclusion criteria for the study population was adult surgical patients who received neostigmine/glycopyrrolate, sugammadex, or both agents for the reversal of induced NMB. Patients included will be of American Society of Anesthesiology (ASA) physical status classification I-IV. Per the ASA (2014), an ASA-I is defined as a healthy normal patient, ASA-II is defined as a patient with mild systemic disease, an ASA III is defined as a patient with severe systemic disease.
Exclusion criteria was patients under the age of 18, obstetrical procedures and/or pregnant patients requiring any surgery, patients who underwent open heart surgery, patients who are directly admitted to the ICU, and patients who are to remain intubated post-operatively. Patients are to be grouped based on those who received the traditional cholinesterase inhibitor neostigmine co-administered with the antimuscarinic glycopyrrolate (NG group), and those who received sugammadex (S group), and those who received both neostigmine/glycopyrrolate as well as sugammadex (NGS group) between May 2018 to December 2018. The time frame of May 2018 to December 2018 is implicated due to the fact that sugammadex was not available at the medical center prior to May 2018.

The researchers utilized a research randomizer to randomize the data and then select the corresponding number in the Microsoft Excel spread sheet to identify the specific patient, dose of neostigmine/glycopyrrolate (NG), OR discharge times, PACU discharge times, overall PACU times, as well as ASA status. The same process was repeated for the sugammadex group (S), as well as for the group of patients receiving all three reversal agents (NGS).

Subject Recruitment

Subject recruitment for this study included anesthesia providers who willingly gave an audience to the investigators of this study during the initial and will so during the follow up presentation that will take place at the medical center during a regularly scheduled anesthesia staff meeting. Participation in the presentation indicates an implied consent, which was announced and clearly displayed throughout the power point presentation. Additionally, there was a hard copy of the implied consent available for viewing. Participation in the anonymous surveys that were provided pre and post presentation, also indicates an implied consent. The surveys can be found under Appendices D-E.
The information acquired through the retrospective chart review was presented to anesthesia providers at the medical center as well current literature regarding use of sugammadex via a formal power point presentation created and carried out by the researchers. The first presentation took place Thursday August 15, 2019 during the regularly planned morning anesthesia staff meeting with the second and the second presentation took place on January 23, 2020.

A flyer created by the investigators to inform anesthesia providers of the date, time, and location of the presentation as well as the title of the study and the major research bullet points discussed was created and displayed in the anesthesia staff lounge and e-mailed to all anesthesia providers. The investigators’ names, credentials, and institution were displayed, as well as who the flyer is being promoted towards, the benefits of attending the meeting, and a footer with version number and date is clearly displayed. Please see the Appendix F for the attached flyer.

Consent Procedures

Participation in the presentation indicated an implied consent, which was announced and clearly displayed on the PowerPoint presentation. Additionally, there was a hard copy of the consent available for viewing. Participation in the anonymous surveys that were provided pre and to be provided post presentation, will also indicate an implied consent. The surveys were anonymous, and relevant only to anesthesia practice, thus there was no handling of subject’s personal health information and the study posed no risks or harm to the subjects. Additionally, the only information linking the subject to the research would be the consented document, which therefore would eliminate the anonymous nature of the study. Furthermore, the research involved no procedures that would normally require a written consent outside of the research context. A formal request for a waiver of documentation of consent was requested and approved by the IRB.
Risks/Harms

There are no potential risks to subjects during this study.

Subject Costs and Compensation

Subjects did not incur any costs related to the study and as employees of the medical center, their attendance to the monthly staff meeting, if scheduled to work, is required.

Study Interventions

The interventions conducted are the power point presentation of statistical findings to the anesthesia providers at this medical center.

Outcome Measures

The surveys used include questions with multiple choice responses that was collected and interpreted for specific responses. The statistical software SPSS will be used by the investigators for the interpretation of survey results to identify changes (if any) in the perception of sugammadex costs, efficiency of usage, or a change in practice may occur. Again, the presurvey was administered prior to the first presentation of the preliminary statistical data, and the postsurvey was provided at the end of the second presentation. See attached surveys in Appendices D-E.

Project Timeline

See the attached Gannt chart in Appendix G.

Resources Needed

The overall costs the investigators acquired were minimal with time being the most consuming part of the project. The statistical software used, SPSS, costs $100, and was split between the investigators. Other resources include paper, ink, and pens as well as stationary for the flyers and posters and cost approximately $100 total. Breakfast was provided for the initial
anesthesia meeting and is to be included for the second meeting, costing a total of approximately $150. Overall the total cost to the investigators will be $350, which was split evenly.

**Evaluation Plan**

**Data maintenance/security**

Following IRB approval, the data collection process began. Data collection was overseen by Dr. Entrup, the anesthesiology department chairman. The data-set for ‘phase I’ was e-mailed in a password protected Microsoft Excel spreadsheet to the co-investigators, where it was de-identified. Personal identifiers like patient names, account numbers, and birth dates were replaced with a random numbering system instead. Data from the spreadsheet was analyzed using SPSS Statistics software. The data will be destroyed at the end of the project period, expectedly, May 2020.

**Data analysis**

First the data was screened to assure that it was “clean” or free from error, and that there were no missing values and the data fit between their distribution. Descriptive statistics was then used to describe the sample. Frequencies and percentages were obtained for neostigmine, sugammadex, and ASA physical status classification. The data was determined to be normally distributed, and the parametric test comparing two groups called the t-test was used. The independent t-test evaluated the neostigmine group, the sugammadex group, and the patient’s ASA (the independent variables) against the following dependent variables: (a) OR total time in minutes; and (b) PACU total time in minutes. Following the independent t-test, the Levene’s test was used to assess whether the mean difference between the two groups were statistically significant. Thereafter, a correlations test (Pearson) and regression analysis (repeated measures
ANOVA) were performed to identify any relationships between the independent and dependent variables.

Our first data-set point was between May – December 2018. May was selected because based on the analysis that we received, that is when sugammadex was introduced to the facility. During the aforementioned timeframe, neostigmine was administered 3066 times while sugammadex was only administered 217 times. We ultimately chose 10% of the 3066 in terms of neostigmine usage because we wanted a number that was not only more comparable to sugammadex’s administered amount but also a number that demonstrated that it was administered more than sugammadex Using a random number generator, 307 neostigmine cases were randomly selected. Thus, a total of 524 cases were analyzed (217 sugammadex cases plus 307 neostigmine cases). Again, the main independent variables that were analyzed for this data set were the: (a) cases where patients were administered neostigmine; (b) sugammadex cases; (c) and patients’ ASA classification.

For the 524 total cases that were analyzed in the analysis, an anesthesia duration value was recorded. A value for PACU duration was not recorded for 27 of the neostigmine cases. So, the mean for PACU duration for neostigmine was based on 280 cases. Similarly, the mean for PACU duration for sugammadex was based on 194 cases. The mean duration time in minutes was shorter for the sugammadex group in both the operating room and PACU (16.55-minute difference in the OR and 23.01-minute difference in the PACU). In patients that were considered seriously ill (ASA III and IV), the minute difference in the OR and PACU was even greater in the OR but about the same for PACU (20.51-minute difference in the OR and 22.35-minute difference in the PACU for the seriously ill group). The anesthesia duration time in the OR in both the neostigmine and sugammadex group, independent of ASA, were statistically significant.
Moreover, the Levene’s test showed that the significance value was greater than 0.05, so the null hypothesis that the variances were not equal was rejected (that is, this meets the homogeneity of variances assumption).

The economic analysis was based on a multifactorial evaluation of the OR and PACU costs (i.e., physician, nurse, assistants, and technical staff). At the implementation facility the cost of one opened OR was estimated to be approximately $30 per minute. Whereas per the implementation facility’s internal documentation, PACU charge times were approximated to be about $21 per minute. Thus, using the figures from above, 16.55-minute difference in the OR and 23.01-minute difference in the PACU, we can conclude that on average for cases where sugammadex was administered $806.21 was saved, and for cases where the patient was administered neostigmine and glycopyrrolate on average it cost $1003.71 more than the sugammadex group (see appendices H-J).

Our second data-set point was between August – October 2019 encompassing two months of data collection. During this period of time, neostigmine/glycopyrrolate was administered 519 times while sugammadex was administered a total of 327. In order to obtain a comparable sample size, 327 cases of neostigmine were randomly selected to be compared against the 327 cases of sugammadex. After accounting for extreme outliers, the resultant groups of 289 neostigmine cases and 279 sugammadex cases remained, creating a total of 568 cases.

The independent variables remained the same for the second data set which included: (a) cases where patients were administered neostigmine; (b) sugammadex cases; (c) and patients ASA classification with dependent variables including (a) total anesthesia minutes and (b) total PACU minutes. There were no missing values for either dependent variables recorded, therefore
the mean values were determined for 289 neostigmine cases and 279 sugammadex cases. The first step in the data analysis of mean OR and PACU minutes included an independent t-test.

Results of the independent t-test suggest that the mean duration time in minutes was longer for the sugammadex group in both the anesthesia and PACU times. The Levene’s Test for Equality of Variance p-value was not statistically significant, and we could therefore assume that our variances are equal. Results showed that anesthesia minutes for neostigmine had lower mean times \( \bar{x} = 151.17, \text{SD} = 66.276 \) than the sugammadex group \( \bar{x} = 172.06, \text{SD} = 79.954 \). Furthermore, the mean PACU minutes for neostigmine also had lower mean times \( \bar{x} = 121.66, \text{SD} = 68.924 \) than the sugammadex group \( \bar{x} = 133.04, \text{SD} = 69.667 \). The mean difference between the neostigmine and sugammadex groups for anesthesia minutes was \(-20.895\) and was statistically significant \( t = 3.3 \) (539); \( p = .001 \). The mean difference between the neostigmine and sugammadex group for PACU minutes was \(-11.386\) with a strong tendency towards statistical significance \( t = 1.9 \) (566); \( p = .051 \).

The anesthesia mean time for sugammadex was approximately 21 minutes longer than that of the neostigmine group, and the PACU mean time for sugammadex 11 minutes longer for the sugammadex group than that of the neostigmine group. Unfortunately, this does not equate to a cost savings based upon this information alone. Through the use of a two-way ANOVA study we were able to determine a potential cost savings for sugammadex use when accounting for the interaction effect of the ASA status of the patient.

Upon completing the two-way ANOVA for anesthesia minutes differences between independent variables drugs and ASA status, the Levene’s test determined the significance value was less than 0.05 therefore we rejected the null hypothesis and are violating the assumption of homogeneity for this analysis thus the error variance of the dependent variable was not equal
across the groups and is considered to be a limitation of this analysis. Tests of between subject effects, tests of main effects of Drug and ASA status, and the interaction effect between drug and ASA status were significant for anesthesia minutes while drug scores alone did not prove to have significant effects on anesthesia minutes \( (p=.859) \), however there was a significant ASA effect on anesthesia minutes, \( F(3,560)=3.03, \ p=.029, \ \text{partial } \eta^2=.016. \). Finally, the interaction effect between drug given and ASA status had a significant effect on anesthesia minutes as well \( F(3,560)=2.75, \ p=.042, \ \text{partial } \eta^2=.015. \) The mean differences were relevant findings to the study indicating that the greatest difference between mean anesthesia minutes occurred between ASA 4 patients who received neostigmine \( (M=178.20) \) versus ASA 4 patients who received sugammadex \( (M=140.33) \).

Upon completion of the two-way ANOVA test for PACU minutes and differences between independent variables drugs and ASA status, the Levene’s test determined the significance value was greater than .05 \( (p=.063) \), therefore we failed to reject the null hypothesis and the error variance of the dependent variable was equal across groups. However, there was no significant interaction between drug alone, ASA status alone, or an interaction effect for drug and ASA status and the results are therefore not to be interpreted. Considering the reduction in means for anesthesia minutes a simple pharmacoeconomic analysis could suggest a cost-effective method of giving sugammadex to ASA 4 status patients, however in the term of reducing costs by increasing revenue via quick turnovers, reduction of staff over time, and completion of more cases, these results do not translate into clinical significance due to the small quantity of ASA 4 patients in the sample size. All statistical tables are represented in appendix K.
Anticipated Findings

Implications of study.

Although a statistically significance p-value (0.49) was only obtained for the anesthesia duration time in the OR in both the neostigmine and sugammadex group, independent of ASA, the data, specifically the reduction in OR and PACU time in the sugammadex group, suggests that providers/stakeholders may be overlooking economic advantages that may not be readily apparent. For example, time saved as a result of the use of sugammadex may translate into extra surgical time which confers major economic benefits.

Respiratory complications, such as post-extubation respiratory failure, is the second most common type of postoperative complication (Brueckmann et al., 2015). Sugammadex can be an effective alternative to neostigmine to combat PRNB which can lead to post-extubation respiratory failure. Indeed, sugammadex as compared to neostigmine has been found to decrease incidences of post-operative respiratory complications in vulnerable populations like the morbidly obese and those patients with obstructive sleep apnea (Gaszynski et al., 2011; Ünal et al., 2015). Thus, this study has important implications on healthcare quality/safety as it challenges the idea that neostigmine is ideal in every clinical situation.

Although sugammadex is an effective reversal at every depth of blockade, practitioners may be tempted to forego the use of neuromuscular monitoring altogether. This is ill advised because more profound blocks require larger doses. Sugammadex is an exciting alternative to neostigmine because it has the potential to eradicate or greatly diminish instances of PRNB. However, if formal evaluation of neuromuscular function is sidestepped, PRNB will be here to stay (Naguib, 2017). As of late, official guidelines/policy in the United States concerning the use
of NMB intraoperatively are almost nonexistent. The ASA Task Force on Postanesthetic Care issued a report that states “assessment of neuromuscular function primarily includes physical examination and, on occasion, may include neuromuscular blockade monitoring” (ASA, 2013, expression I). Healthcare organizations are in a prime position to adopt evidence-based research to implement policies that effectively tackles PRNB. This project uses data analysis to influence healthcare policy.

**Plans for sustainability and translation.**

To demonstrate the true pharmacoeconomic impact of sugammadex at the implementation facility, a randomized controlled trial should be conducted, so a pure sample can be evaluated. Moreover, performing an analysis over a greater length of time will increase the sample size which will more likely lead to a greater amount of statistically significant results. Additionally, sugammadex was only stocked in limited Omnicells at this facility at the commencement of the project, as compared to neostigmine which is stocked in multiple locations. This study should be revisited in the setting of comparable sugammadex access.

**Plans for dissemination and professional reporting.**

A presentation of the results of this project may be disseminated at the New Jersey Association of Nurse Anesthetists spring 2020 meeting, Rutgers school of nursing, peer-reviewed science journals, and at the monthly anesthesia meeting of the implementation facility.

**Summary**

The previous section outlined the methodology was used to evaluate the clinical question: in adult surgical patients who receive neuromuscular blockers during general anesthesia, how cost effective is sugammadex use in comparison to neostigmine in reducing cost by means of reduced postoperative discharge time from the OR to PACU and PACU to discharge. A
retrospective chart review adopting a comparative design and utilization of descriptive and inferential statistics was used to answer the question. The independent variables are (a) patients who received sugammadex, (b) patients who received neostigmine, and (c) the ASA physical status classification. The dependent variables are (a) OR total time in minutes and (b) PACU total times in minutes.
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http://dx.doi.org/10.4172/2155-6148.1000740
### Appendix A

#### Table of Evidence

<table>
<thead>
<tr>
<th>Article #</th>
<th>Author &amp; Date</th>
<th>Evidence Type</th>
<th>Sample, Sample Size, Setting</th>
<th>Findings that help answer the EBP Question</th>
<th>Observable measures</th>
<th>Limitations</th>
<th>Evidence level, quality</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Carron, M., Zarantonello, F., Lazzarotto, N., Tellaroni, P., &amp; Ori, C. (2017). Role of sugammadex in accelerating postoperative discharge: A meta-analysis. <em>Journal of Clinical Anesthesia, 39</em>, 38-44. <a href="http://dx.doi.org/10.1016/j.jclinane.2017.03.004">http://dx.doi.org/10.1016/j.jclinane.2017.03.004</a></td>
<td>Meta-analysis</td>
<td>6 studies involving 518 patients</td>
<td>Compared with neostigmine, sugammadex was associated with a significantly faster discharge from the OR to the PACU ( \text{mean difference } [MD] = 22.14 \text{ min, } P &lt; 0.00001 ), particularly when patients with deep NMB were included in the analysis ( [MD] = 30.05 \text{ min, } P &lt; 0.002 )</td>
<td>Discharge-readiness for patients moving from the PACU to the surgical ward ( [MD] = 16.95 \text{ min, } P = 0.0469 )</td>
<td>The number of included studies is limited</td>
<td>Level I</td>
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- Compared with neostigmine, sugammadex was associated with a significantly faster discharge from the OR to the PACU \( [MD] = 22.14 \text{ min, } P < 0.00001 \), particularly when patients with deep NMB were included in the analysis \( [MD] = 30.05 \text{ min, } P < 0.002 \)
- Discharge-readiness for patients moving from the OR to the PACU was shorter for sugammadex than for neostigmine.

- Meta-analyses were performed using arithmetic.
- The number of included studies is limited.
- Heterogeneity across studies was considerable for the PACU discharge results.
Compared with neostigmine, sugammadex was associated with a significantly faster discharge from the PACU to the surgical ward ([MD] = 16.95 min, P = 0.0469).

Subgroup analysis of morbidly obese patients also showed that sugammadex was associated with a significantly faster discharge from the PACU to the surgical ward ([MD] = 8.75 min, p < 0.0001).

Discharge-readiness for patients moving from the PACU to the surgical ward was not significantly different between sugammadex and neostigmine ([MD] = -1.10 min, p = 0.6394).

Instead of geometric means because the latter were not available.
<table>
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<tr>
<td><strong>RCT</strong></td>
<td>100 (50/50 in the neostigmine and sugammadex group respectively) women, undergoing gynecologic laparoscopic surgery, aged 18-80, with ASA grade I or II were enrolled in the study between February 2011 and May 2012. <strong>Setting:</strong> Monocentricic study performed in Belgium</td>
</tr>
<tr>
<td></td>
<td>Shorter and more predictable OR discharges occur after the administration of sugammadex to patients at moderate or deep levels of NMB than after the administration of neostigmine to patients at moderate or even much shallower levels of blockade (P = .064) The financial consequences of deep NMB management based on sugammadex reversal depend on multiple factors: the intraoperative advantages in terms of the surgical conditions, the value of the time spared, and who is charged for the drugs (healthcare system vs hospital vs patient). Sugammadex would be cost-effective only if the reduction in recovery time occurs mainly in the OR (high-value staff time) rather than in the PACU (relatively lower-value staff time)</td>
</tr>
<tr>
<td></td>
<td>Shorter and more predictable OR discharges occur after the administration of sugammadex to patients at moderate or deep levels of NMB than after the administration of neostigmine to patients at moderate or even much shallower levels of blockade (P = .064) No significant results were found in terms of demonstrable benefit of sugammadex reversal in terms of quality or speed of recovery after general anesthesia based on evaluations of recovery using a modified Aldrete score upon arrival in the PACU. Study revealed similar PACU stay durations in both groups The financial consequences of deep</td>
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<td></td>
<td>Based on evaluations of recovery using a modified Aldrete score upon arrival in the PACU, a different result could have been observed if the recovery assessment had been performed closer to tracheal extubation, but this would have raised the question of the clinical relevance of such a potential transient effect</td>
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</table>
NMB management based on sugammadex reversal depend on multiple factors that include the intraoperative advantages in terms of the surgical conditions, the value of the time spared, and who is charged for the drugs (healthcare system vs hospital vs patient).

The economic value of the time saved by improved OR efficiency remains unclear and depends on the ability of the staff to perform other productive activities and the ability of the OR manager to proactively fine-tune the staffing to match the surgical demand.
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<td>Discrete event simulation model</td>
<td>A discrete event simulation (DES) was developed to compare ORs using either neostigmine or sugammadex for NMB reversal over one month in Canada. Selected inputs included OR procedure and turnover times, hospital.</td>
<td>Moderate neuromuscular block: the principal impact of using sugammadex instead of neostigmine is likely to be a reduction in the risk of residual blockade and associated complications. For patients maintained at a deep level of block to the end of the procedure, sugammadex is likely to both enhance OR efficiency and reduce complications of residual block. Where OR efficiency gains occur, potential benefits of sugammadex may include reduced procedural cancellations due to OR time over-run, avoided staff over-time and opportunity to evaluate if procedural throughput may be increased.</td>
<td>For the majority of patients currently managed with moderate neuromuscular block, the principal impact of using sugammadex instead of neostigmine is likely to be a reduction in the risk of residual blockade and associated complications. For patients maintained at a deep level of block to the end of the procedure, sugammadex is likely to both enhance OR efficiency and reduce complications of residual block. Where OR efficiency gains occur, potential benefits of sugammadex may include reduced procedural...</td>
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<td>Model was based on secondary data sources as human or animal subjects were not enrolled.</td>
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<td>Policies for paid staff overtime and procedural cancellations due to OR time over-run, and reductions in RNMB and associated complications with sugammadex use</td>
<td>Cancellations due to OR time over-run, avoided staff over-time and opportunity to evaluate if procedural throughput may be increased</td>
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<td>4</td>
<td>Paton, F., Paulden, M., Chambers, D., Heirs, M., Duffy, S., Hunter, J. M., ... Woolacott, N. (2010). Sugammadex compared with neostigmine/glycopyrrolate for routine reversal of neuromuscular block: A systematic review and economic evaluation. <em>British Journal of Anaesthesia, 105</em>(5), 558-</td>
<td>Sugammadex produces more rapid recovery from moderate (profound) NMB than neostigmine/glycopyrrolate. If the reductions in recovery time associated with sugammadex in the trials are replicated in routine practice, sugammadex would be cost effective if those reductions are</td>
<td>Sugammadex produces more rapid recovery from moderate (profound) NMB than neostigmine/glycopyrrolate. If the reductions in recovery time associated with sugammadex in the trials are replicated in routine practice, sugammadex would be cost effective if those reductions are</td>
<td>Findings are based on limited evidence, and considerable uncertainty remains concerning its clinical effectiveness in</td>
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in the assessment of sugammadex for the reversal of moderate block and 1 for profound block].

Sugammadex has the potential to be cost-effective compared to neostigmine/glycopyrrolate for the reversal of rocuronium-induced blockade provided that the time savings observed in trials can be put to productive use in clinical practice.

Sugammadex would be cost effective if those reductions are achieved in the operating room theatre but not if they are achieved in the recovery room.

The patients in the sugammadex trials were ASA classes I-II and may not represent those who would receive sugammadex in routine clinical practice.

3. The reductions in recovery time with sugammadex seen in the clinical practice and especially its effectiveness.

http://dx.doi.org/10.1093/bja/aeq269
4. The available trials did not compare sugammadex or vecuronium combination with all the commonly used drugs. The maximum that can be achieved pending wider adoption and evaluation may represent the trials may not have reached the maximum that can be achieved pending wider adoption and evaluation.
|   | O'Reilly-Shah, V. N., Wolf, F. A., Jabaley, C. S., & Lynde, G. C. (2017). Using a worldwide in-app survey to explore sugammadex usage patterns: A prospective observational study. *British Journal of Anaesthesia, 119*(2), 333-344. http://dx.doi.org/10.1093/bja/aex171 | 11,863 anesthesia provider respondents in 183 countries | 72% of respondents reported selective usage of sugammadex | 46% reported sugammadex was available and relevant to their practice | Not all questions were completed by all respondents. Lack of randomization leads to limited generalizability of the results secondary to non-equivalent test groups. Variations in national or regional healthcare delivery systems and administration may | NMBA/ reversal agent combinations | Level II |
---|---|---|---|---|---|---|---|
5 | A quasi experimental study, investigators used a tool to deploy a survey assessing global patterns of clinical practice and experience with sugammadex | 72% of respondents reported selective usage of sugammadex | 56% had some form of extrinsic restriction on sugammadex access, primarily due to cost (69%), institutional policies (26%), or drug availability (7.8%). [Cost concerns are the primary driver of limitations in use] | 72% of respondents reported selective usage of sugammadex | 56% had some form of extrinsic restriction on sugammadex access, primarily due to cost (69%), Institutional policies (26%), or drug availability (7.8%). [Cost concerns are the primary driver of limitations in use] | | |
providers appear to be making care decisions with economic concerns of their hospitals and patients in mind]

[Even in the relative absence of policies restricting sugammadex use, about two-thirds of anesthesia providers reported self-imposed limitations on sugammadex administration. Anaesthesia providers appear to be making care decisions with economic concerns of their hospitals and patients in mind]

influence the way in which costs are conceptualized


| 6 | Carron, M., Zarantonello, F., Tellaroli, P., & Ori, C. (2016). Efficacy and safety of sugammadex compared to neostigmine for reversal of neuromuscular blockade: a meta-analysis of randomized controlled trials. *Journal of Clinical Anesthesia*, 35, 1-12. doi:10.1016/j.jclinane.2016.06.018 | Meta-analysis of data about effectiveness and safety of sugammadex compared to neostigmine for reversal of NMB published between January 1, 2005 to 1384 adult patients form 13 RCT | Compared to Neostigmine, Sugammadex was faster in reversing NMB (P<.0001) and more likely to be associated with higher TOF ratio values at extubation (P<.0001), and lower risk of postoperative residual curarization after extubation (P=.0068). Compared to Neostigmine, Sugammadex was associated with lower likelihood of global adverse events (P<.0001), respiratory AEs (P=0.386), cardiovascular AEs (P=.0036), and | Primary outcomes – efficacy outcomes evaluated as the time to reversal of moderate (presence of almost the first twitch, T1, and the second twitch, T2, muscle response of the train-of-four [TOF] at acceleromyography) and deep (presence of posttetanic count [PTC] of 1-5 at acceleromyography monitoring) NMB and the presence of incomplete reversal | Limitations
Size of 13 RCT, Risk of bias | Level I |
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<td>Sugammadex was associated with a more favorable early postoperative recovery in the nociceptive and physiological domains assessed with the PQRS. Patients treated with sugammadex reported significantly better global perspective on the impact of surgery on working capacity and daily activities, as well as higher satisfaction with anesthetic care.</td>
<td>Median time to full recovery TOF ratio &gt;0.9 was 9 minutes in the neostigmine group and 3 minutes in the sugammadex group (P&lt;0.001). PQRS domains: higher percentage of sugammadex treated patients showed recovery in the physiological domain (96.2% vs 70.2%, P=0.001) and in the nociceptive domain</td>
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<td>Prospective Observational cohort study to assess quality of the postoperative recovery with neostig</td>
<td>Convenience sample of 101 adult patients aged 18 years or older undergoing elective surgery (otolaryngology, gynecological, and</td>
<td>small sample size, no sample size calculation was performed and the non-randomized design, the lesser pain intensity in the sugammadex</td>
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<td>org.proxy.libraries.rutgers.edu/10.1111/aas.12389</td>
<td>abdominal surgery (96.2% vs 81.3%, P=0.02) 40 minutes after surgery. Patients fully awake at 40 minutes was 96.2% and 72.9% in the neostigmine group (P=0.001). 100% of patients in the sugammadex group showed no signs of agitation and were able to follow commands completely, although not statistically significant. Patients global perspective on effect of surgery was significantly more favorable for those treated with sugammadex regarding working capacity on day 1 (P&lt;0.001) and day 3 (P&lt;0.001), and daily activities on day 1 (P=0.037) and day 3 (P=0.032) evaluations. More patients in the sugammadex group were very satisfied with anesthetic experience compared with</td>
<td>x group is probably related to type of procedure (fewer sugammadex-treated patients underwent abdominal operations), trends were noted with improved recovery at 40 minutes after surgery with shorter duration of anesthesia</td>
<td>mine versus sugammadex using the Postoperative Quality Recovery Scale (PQRS)</td>
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<td>Rando mized Contro l Trial</td>
<td>Morbidly obese adult patients (BMI &gt; 40 kg m-2) undergoing elective bariatric surgery, 75 patients total requiring general anesthesia and receiving rocuronium 1.0 mg/kg CBW and given two additional doses of 0.06 mg/kg CBW,</td>
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<td>Sugammadex provides fast recovery of neuromuscular function and prevents PORC in the morbidly obese, however Neostigmine does not. Neostigmine group complications include three cases of profound bradycardia requiring additional administration of atropine</td>
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<td>Time to achieve 90% TOF (safe extubation) was measured; patients examined directly after arrival to PACU by a blinded investigator for presence of PORC</td>
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<td>Mean time to 90% TOF for Sugammadex was 2.7 minutes vs 9.6 minutes for Rocuronium (P&lt; 0.05), TOF at PACU was 109.8% for Sugammadex vs 85.5% for Neostigmine (P &lt; 0.05).</td>
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<td>Small sample size, risk of bias, exclusion criteria to study included severe cardiovascular disease (NYHA&gt;2) which may limit benefits of sugammadex over neostigmine for this patient population, doses of all medications were given using CBW; sugammadex Level 1</td>
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randomly assigned to two groups- 35 Patients received Sugammadex 2 mg/kg of corrected body weight (CBW) and 35 received Neostigmine 0.05 mg/kg of CBW administered when response of TOF score of 2

| 9 | Watts, R. W., London, J. A., Van Wijk, R. M., & Lui, Y. (2012). The Influence of Unrestricted Use of Sugammadex on Clinical Anaesthetic Practice in a Tertiary Teaching Hospital. | Retrospective Observational Case-note Study | 374 adult patients requiring intubation for an anesthetic, restricted period 144 | Anesthetic theatre time fell from 143.5 minutes to 120.0 minutes (shorter by 23 minutes on average, P=0.01) and remained statistically significant when adjusted for confounding variables (P=0.02), hospital stay time | Selected patient outcomes- cases of inadequate reversal, mean anesthetic theater time, time spent in PACU, incidence of PONV or incidence of oxygen desaturation in | Risk of bias (Merck supported trial), reliance upon accurate documentation | Level II |
| Anaesthesia and Intensive Care, 40(2), 333-339. doi:10.1177/0310057x1204000218 | patients identified, unrestricted period 188 patients identified; Setting- Australia | fell (P=0.035) but was not statistically significant after adjusted for potential cofounders (P=0.59), Sugammadex use increased from 7.1% to 65.3%, (P < 0.0001); no adverse events attributed to sugammadex during the unrestricted period versus 4 in the restricted period, fewer numbers of inadequate reversal but not significant | PACU, hospital duration | ion and ability to retrieve this information, quality of data could not be verified and a large number of case-notes not available for both groups, not formally powered to detect pre-defined clinically important difference between time periods, single anesthetic unit where rocuronium usage already high, use may have |
increased due to the ‘novelty’ effect, no inferences about causality due to design of study, unclear if study had sufficient power to exclude effects of all potential confounders, testing of multiple outcomes increases probability of making a type-I statistical error

<p>| 10 | De Robertis, E., Zito Marinosci, G., Romano, G. M., Piazza, O., Iannuzzi, M., Cirillo, F., De Simone, S., … | Retrospective study, non- | Records of morbidly obese patients (BMI &gt; 40) | Sugammadex showed shorter times to achieve TOF 0.9 (P&lt;0.05) and an Aldrete score of 10 (P&lt;0.05), higher costs | Time from “starting anesthesia” to when the patient was transferred to the PACU, primary endpoint was | Nature of the study (retrospective non-randomized) | Level II |
|---|---|---|---|
| randomized | kg/m²) undergoing elective laparoscopic bariatric surgery in which Sugammadex or neostigmine were used to reverse NMB. Include 99 patients, 50 patients in group 1 received rocuronium and sugammadex, 49 patients received rocuronium (35 patients) or cisatracurium (14 patients) and (P&lt;0.05), plus a remarkable less duration of operating theater occupancy (23 minutes, P&lt;0.05). Total time saved in Sugammadex group was 19.4 hours, which could be used to perform 12 extra laparoscopic sleeve gastrectomies. Reversal from NMB faster with sugammadex, duration of operating theater occupancy was reduced with potentially workflow increase or personnel reduced cost. |
| comparing the latency to achieve a TOF ratio &gt; 0.9 after reversal, the mean time to achieve an Aldrete score of 10, and the cost associated with these drugs. Secondary endpoints were to evaluate duration of operating theater occupancy, to identify the incidence of postoperative desaturation in PACU, and evaluate length of stay in hospital |
| , single-center design), exclusion of extremely morbidly obese (BMI &gt; 60 kg/m²) patients, potential presence of analytical bias as cisatracurium and rocuronium were both considered in the analysis, time saved by Sugammadex related to anesthesia period and other variables may influence |</p>
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<th>Study</th>
<th>Population</th>
<th>Design</th>
<th>Intervention</th>
<th>Outcomes</th>
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<td>11</td>
<td>Ünal, D. Y., Baran, İ., Mutlu, M., Ural, G., Akkaya, T., &amp; Özlü, O. (2015). Comparison of Sugammadex versus Neostigmine Costs and Respiratory Complications in Patients with Obstructive Sleep Apnoea. <em>Turkish journal of anaesthesiology and reanimation</em>, 43(6), 387-95.</td>
<td>Randomized Controlled Study</td>
<td>ASA I or II patients undergoing surgery for the treatment of obstructive sleep apnea (OSA) aged 19-65 years, 74 patients in two groups; Group S</td>
<td>Time to TOF 0.9 was shorter for Group S (p&lt;0.001), OR time and PACU stay were also shorter in Group S (p&lt;0.001). More respiratory complications noted in Group N (desaturation 32% vs 8% group S, [p=0.048], three patients reintubated group N, eight unplanned ICU admissions (21.6%) versus 1 in Group S, 1 incidence of negative pressure pulmonary edema). Reversal cost higher with Groups were compared regarding time to TOF ratio 0.9, OR time, PACU stay, post-op respiratory complications, costs r/t NMB reversal, anesthesia care and complication treatment. Frequency of complications r/t circulation higher in Group N: 9 patients with HTN (24.3%), 8 with bradycardia (21.6%), 5 with tachycardia (13.5%), Study population includes only ASA I and II and interpretation cannot be made for higher ASA levels, lack of data on the rate of residual NMB since neuromuscular</td>
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Receiving 2 mg/kg Sugammadex or Group N receiving 0.04 mg/kg Neostigmine + 0.5 mg atropine; Setting-Turkey.

Sugammadex but complication treatment cost and total cost were lower in Group S. and 5 with arrhythmia (13.5%). Group N, six patients were given additional dose of atropine d/t bradycardia, NTG given to one patient d/t HTN. Frequencies of desaturation (p<0.001), cough (p=0.012), and HTN (p=0.004) higher in patients with high AHI (Apnea-Hypoapnea index) score.

Monitoring not performed in PACU, costs incurred may not be exactly the same as those in other hospitals because of differences in billing techniques.

12. Ledowski, T., Hillyard, S., O'Dea, B., Archer, R., Vilas-Boas, F., & Kyle, B. (2013). Introduction of sugammadex as standard reversal agent: Impact on the incidence of residual neuromuscular blockade and postoperative patient outcome. Indian Journal of Anaesthesia, 57(1), 46. Prospective cross-sectional pilot investigation to investigate clinicians. All paralyzed and tracheally intubated patients within main operating theaters during TOF ratios assessed quantitatively by an independent observer, sugammadex use resulted in significantly lower numbers of patients with TOF ratios <0.7 and <0.9 when compared with neostigmine-based or no reversal (P<0.0005). only studied a non-randomized convenience sample (two weeks) limiting conclusions that can be
<p>| doi:10.4103/0019-5049.108562 | 8:00 am to 6:00 pm during two epochs of seven consecutive days, data of 146 patients analyzed. Setting: tertiary teaching hospital | PACU episodes of desaturation, any other airway related incidents, cardiac arrhythmias and nausea/vomiting. Data from postoperative chest x-rays performed within 30 days from operation date reviewed for findings consistent with atelectasis or pneumonia, compared to patients with no abnormal x-ray results (either not performed or reported as ‘normal’). Those with reported pneumonia or atelectasis had a significantly lower median TOF ratio prior to extubation (0.71 [0.44/0.86] vs 0.94 [0.84/0.98]; P&lt;0.001). | drawn firmly from results. The use of kinemyometric (KMG) quantitative neuromuscular monitoring for assessment of TOF ratios may not be ideal for research purposes, definition of “outcome” defined as x-ray findings consistent with atelectasis or pneumonia as undesirable “mid-term” outcome. |</p>
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|   | Jahr, J. S., Miller, J. E., Hiruma, J., Emaus, K., You, M., & Meistelman, C. (2015). Sugammadex: A scientific review including safety and efficacy, update on Literature Review | N/A | Neostigmine and Pyridostigmine have profound negative cholinergic side effects such as bradycardia, bronchoconstriction, nausea, and excessive salivation; No significant differences in postoperative bleeding in patients undergoing laparotomy for oncologic surgery with subsequent drain |
|   |   |   | Nature of research (literature review), further studies suggested |
| 2 |   |   | IV |
and therefore, require concomitant administration of glycopyrrolate or atropine. Duration of NMBA may outlast DOA of anticholinesterase leading to recurarization effect. Incomplete reversal (TOF ratio less than 0.9) of NMB risks prolong recovery room stay and/or hospital course. Sugammadex reduced the time to a 0.9 TOF ratio by 14-17 minutes during shallow block and 47 minutes and 61 minutes for rocuronium and vecuronium-induced deep NMB. Time saved in operating room at a value of $E4.44$ per minute sugammadex was cost effective for routine reversal of shallow and deep NMB, if reductions in recovery times were obtained in the OR and associated for improvement in productivity and more efficient use of staff members. Placement, addressing FDA concerns regarding coagulation concerns.

- No significant differences in QTc interval prolongation occurred in patients with cardiovascular disease undergoing cardiac surgery and in healthy volunteers, addressing FDA concerns of potential for sugammadex to cause QTc prolongation.
- Hypersensitivity and anaphylaxis incidence not statistically significant from that of placebo at 95% confidence limits - however a modest increased risk being associated with the 16 mg/kg dose.
- Reproducibility of the reversal is a main benefit; predictability of response was greater with Sugammadex than neostigmine. 98% of

- Cost-effective economic evaluation revealed that sugammadex could decrease OR costs allowing to perform a higher number of surgical interventions with the same daily operation schedule time.

Cost per case corresponds to: $y$ (costs of case using sugammadex) = $Z$ (sugammadex cost per case) - $K$ (time saved per case) – $x$ (operation staff value per minute):

$y=Z-K-Z$

In patients with superficial blockade (4 twitches)- Sugammadex reduces mean time to reach TOF ratio of 0.9 by 17 minutes. $Y= $100 – 17 min x $30; $y= $410; OR time saved will lower cost related to surgery by $410; Moderate NMB (TOF count 1-3)-

Does not take into consideration the rate of both surgery cancellations and emergency intervention.

Calculation of the OR time cost was based on an investigation conducted in a teaching hospital |

| | | | sugammadex patients versus 11% of neostigmine recovering from TOF ratio of 0.9 within 5 minutes- in comparison it took 101 minutes for 98% of patients receiving neostigmine to recover to a 0.9 TOF ratio | V |
Rapid NMB reversal can lower OR occupancy with the consequential potential to increase the OR workflow especially for short cases.

- By eliminating postoperative residual curarization and related pulmonary complications, sugammadex might reduce costs related to time necessary to discharge patients from PACU resulting in more rapid turnover between surgeries.

Sugammadex reduces mean time to reach a TOF ratio of 0.9 by 18.6 minutes, requiring up to 2 200mg vials ($200): $y=200-18.6 \times 30; y=-358; might save up to $358.

- Deep NMB (PTC 1-2): requires 4 mg/kg sugammadex, corresponds to 300 mg, obtained with 2 vials ($200); sugammadex reduces mean time to obtain a TOF ratio >0.9 by 47.5 minutes; $y=200-47.5 \times 30; y=1225; OR time saved will lower the cost related to the surgery by $1225 and length of the procedure encompassing teaching time could be longer in comparison with a non-teaching hospital. Value of each minute of PACU and length of hospital stay saved may depend on institutional habits due to the large differences in staff practice and logistics from one center to another, and a lack of
prospective large sample size conducted in North America on this topic.
Appendix B

PRISMA Diagram

Records identified through database searching (n = 404)

Records after duplicates removed (n = 314)

Records screened (n = 314)

Records excluded (n = 274)

Full-text articles assessed for eligibility (n = 40)

Full-text articles excluded, excluded for not pertaining to clinical question, included pediatric studies (n = 28)

Studies included in qualitative synthesis (n = 1)

Studies included in quantitative synthesis (meta-analysis) (n = 11)
Appendix C

Concept Map

Roger’s Innovation-decision 5 Step Process

Knowledge

As the use of sugammadex increases, anesthesia providers will gain knowledge on how it functions.

Persuasion

Providers form a favorable or unfavorable attitude towards sugammadex based upon perceived characteristics of the innovation (e.g., relative advantage & complexity).

Decision

Providers decide to adopt or reject the use of sugammadex.

Implementation

Providers put an innovation into use. Until this stage, the process has been a mental exercise.

Confirmation

Occurs when an individual seeks reinforcement of an innovation-decision already made.

INNOVATORS ——— LAGGARDS
Appendix D

Pre-Survey

Participation in this minimal-risk survey is entirely voluntary. The survey is conducted by the co-investigators and research team at Rutgers University who will not be sharing this information with other health authorities. No identifying information will be collected. By participating and answering questions, you are providing consent to participate in this study. If at any time you do not wish to participate in the survey, you may choose to not answer these questions. The information in the statement does not expire. Thank you for your participation.

1. Please check the box you identify with
   CRNA
   Anesthesiologist
   SRNA
   Other: Please specify_______

2. How long have you been in clinical practice?
   a. 1-2 years
   b. 3-10 years
   c. 10-15 years
   d. 15 + years

3. Do you consider any of the following a self-limitation to sugammadex use? Please check all that apply.
   High costs compared to neostigmine
   Lack of accessibility in every OR
   Preference of neostigmine over sugammadex
   Lack of sugammadex familiarity

4. After administration of neostigmine and glycopyrrolate, how often have you been required to also administer sugammadex for suspected post-operative residual neuromuscular blockade?
   a. 0-3 times
   b. 4-6 times
   c. 6-10 times
   d. 10 +

5. Do you feel that post-operative residual neuromuscular blockade is a significant post-operative complication?
   a. Yes
   b. No
   c. Unsure

6. What dose of sugammadex would you give for a train-of-four (TOF) twitch-response of two twitches? Check all that apply
   4 mg/kg
   1 mg/kg
2 mg/kg
None of these doses
I’m not sure

7. When educating females of child bearing age taking hormonal oral contraceptives, for how many days do you recommend a secondary form of birth control?
   a. 3 days
   b. 5 days
   c. 7 days
   d. I’ve never made this recommendation

8. Which of the following patients do you feel may benefit most from sugammadex? Choose all that apply.
   BMI > 40
   Diagnosed obstructive sleep apnea
   History of lung disease
   Surgeries requiring deep NMB
   None
Appendix E

Post-Survey

Participation in this minimal-risk survey is entirely voluntary. The survey is conducted by the co-investigators and research team at Rutgers University who will not be sharing this information with other health authorities. No identifying information will be collected. By participating and answering questions, you are providing consent to participate in this study. If at any time you do not wish to participate in the survey, you may choose to not answer these questions. The information in the statement does not expire. Thank you for your participation.

1. Please check the box you identify with
   - CRNA
   - Anesthesiologist
   - SRNA
   - Other: Please specify_______

2. How long have you been in clinical practice?
   - e. 1-2 years
   - f. 3-10 years
   - g. 10-15 years
   - h. 15 + years

3. Do you consider any of the following a self-limitation to sugammadex use? Please check all that apply.
   - High costs compared to neostigmine
   - Lack of accessibility in every OR
   - Preference of neostigmine over sugammadex
   - Lack of sugammadex familiarity

4. After administration of neostigmine and glycopyrrolate, how often have you been required to also administer sugammadex for suspected post-operative residual neuromuscular blockade?
   - a. 0-3 times
   - b. 4-6 times
   - c. 6-10 times
   - d. 10 +

5. Do you feel that post-operative residual neuromuscular blockade is a significant post-operative complication?
   - a. Yes
   - b. No
   - c. Unsure

6. What dose of sugammadex would you give for a train-of-four (TOF) twitch-response of two twitches? Check all that apply
   - 4 mg/kg
   - 1 mg/kg
74 SUGAMMADEX VS. NEOSTIGMINE

2 mg/kg
None of these doses
I’m not sure

7. When educating females of child-bearing age taking hormonal oral contraceptives, for how many days do you recommend a secondary form of birth control?
   a. 3 days
   b. 5 days
   c. 7 days
   d. I’ve never made this recommendation

8. Which of the following patients do you feel may benefit most from sugammadex? Choose all that apply.
   BMI > 40
   Diagnosed obstructive sleep apnea
   History of lung disease
   Surgeries requiring deep NMB
   None

9. Do you feel the information provided may lead to a change in your practice?
   a. Maybe
   b. Yes
   c. No
Appendix F

Recruitment Flyer

Invitation to Participate in a Research Study

Join Rutgers Student Nurse Anesthetists Shari Herron BSN, CCRN and Natalie Joseph, BSN, CCRN for a power point presentation of research findings on

A Retrospective Chart Review: Sugammadex vs Neostigmine/Glycopyrrolate a Pharmacoeconomic Analysis

Purpose of Study: A retrospective chart review focusing on the investigational use of sugammadex vs neostigmine/glycopyrrolate with an emphasis on determining faster OR and PACU discharge times, economic implications and associated costs with both treatments, current use of sugammadex, and assessing barriers to sugammadex use

Included in chart review: ASA I-IV, including emergency cases adult surgical patients who received neostigmine/glycopyrrolate, sugammadex, or both agents for the reversal of induced neuromuscular blockade

All research conducted at:

Principal Investigator: Dr. Michael McLaughlin

For more information contact:
Shari Herron SRNA
Natalie Joseph SRNA

8/7/2019 Version# 3
Appendix G

Gantt Chart

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Project: Shari DNP
Date: Mon 4/15/19
Appendix G

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Project: Shari DNP
Date: Mon 4/15/19

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- Milestone
- Summary
- Project Summary
- Inactive Task
- Inactive Milestone
- Manual Task
- Duration-only
- Manual Summary Rollup
- Manual Summary
- Start-only
- Finish-only
- External Tasks
- External Milestone
- Deadline
- Progress
- Manual Progress

Page 2
Appendix G

Gantt Chart Continued
Appendix G

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Page 4
Appendix H

Anesthesia vs. PACU Duration in Minutes

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Anesthesia Duration-Minutes

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PACU Duration-Minutes

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### Appendix I

#### Independent Samples Test

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| **PACU Duration Minutes** |                         |                            |
| F                   | 0.611                   | -0.595                     |
| Sig.                | 0.435                   | 0.552                      |
| t                   | -0.561                  | -0.752                     |
| df                  | 471                     | 466.607                    |
| Sig. (2-tailed)     | 0.575                   | 0.552                      |
| Mean Difference     | -7.594                  | -7.594                     |
| Std. Error Difference | 13.531                 | 12.771                     |
| Lower               | -34.183                 | -32.690                    |
| Upper               | 18.994                  | 17.502                     |

#### Standardized Coefficients

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*a. Dependent Variable: Anes Duration-Minutes*
Appendix J

Cost comparison of Neostigmine vs Sugammadex May -December 2018

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<td>PACU cost/minute: $21</td>
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# Appendix K

## Group Statistics

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## Levene's Test

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### Levene's Test of Equality of Error Variances

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## Tests of Between-Subjects Effects

Dependent Variable: Anesthesia minutes

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