IMPLEMENTATION OF A SUGAMMADEX CLINICAL PRACTICE GUIDELINE

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Abstract

Background: Residual paralysis is the presence of muscle weakness postoperatively and leads to increased rates of respiratory complications. In a study of more than 200,000 cases where paralytics were administered, 64% of cardiac arrests were related to airway complications secondary to residual paralysis in the post anesthesia care unit. Of these cases, there was a mortality rate of 29%. A medium-sized hospital in Maryland reported postoperative complications associated with residual paralysis. It was identified that sugammadex was used 103 times over an 8-month period due to failed neostigmine reversal resulting in low tidal volumes and muscle weakness. Currently there is no guideline for the use of sugammadex at this institution. Sugammadex offers a definitive solution to the safety profile found lacking with neostigmine. If the use of neostigmine was replaced by sugammadex administration, these negative consequences would be abated—especially in high-risk populations. High risk populations include: can't intubate, can't ventilate situations, deep blockade, elderly, morbidly obese, pulmonary disease and neuromuscular disease. The focus of this doctorate project was to develop a Clinical Practice Guideline for the use of sugammadex in the prevention of residual paralysis for high risk patients.

Intervention: A residual paralysis problem was identified. The solution was to develop a guideline for the use of sugammadex. A literature review was conducted for supporting evidence for the guideline. The project proposal was then submitted for a Non-Human Subjects Research determination. The guideline was revised and assessed using the gold standard guideline evaluation tool. The final guideline was presented to the anesthesia department. Practitioner Feedback Questionnaires were distributed to those in attendance. All data collected from the evaluation phase was then synthesized, analyzed, and evaluated. The final manuscript was submitted for review.

Results: The results of the Appraisal of Guidelines for Research and Evaluation II Tool were 100% across the six domains and for overall assessment. Each appraiser had a total score of 161/161 and an overall of 322/322. The project leaders received 100% return rate of the Practitioner Feedback Questionnaires (n=22). In reviewing the data, majority of anesthesia providers felt the guideline should be approved for practice (95.5%), they would use it in their own practice (100%) and they would apply the recommendations to their patients (100%). This analysis demonstrated buy-in and acceptance of the guideline by the department.

Conclusion: Study results indicate sugammadex compared to neostigmine is safe and effective in the reversal of muscle relaxants and reduces adverse events—especially in high-risk populations. The ability of sugammadex to rapidly reverse blockade can play a critical role in high-risk patients. A guideline of sugammadex use will help decrease postoperative complications at the local hospital. The guideline, the sugammadex algorithm and patient education handout will be incorporated into provider daily practice and placed in all operating rooms as a result.

Overview

One of the commonly observed challenges of anesthesia is generalized muscle weakness or residual neuromuscular blockade (RNMB) after administration of neuromuscular blocking agents (NMBAs) (Murphy et al., 2011). Neuromuscular blocking agents are most often used in general anesthesia to produce neuromuscular blockade (NMB) or muscle paralysis intra-operatively. Muscle paralysis facilitates intubation and decreases patient movement which optimizes operating conditions. The degree of paralysis can be monitored with the use of an electronic peripheral nerve stimulator that activates muscle contraction. Nerve stimulators are used to produce a train-of-four (TOF) ratio or post tetanic counts (PTC) that allow the provider to assess the depth of NMB. The train-of-four ratio will produce four equal muscle contractions, or "twitches," if there is no neuromuscular blockade; but if NMB is present there will be loss of twitch height, or muscle contraction secondary to the blocking agent, and/or the number of twitches. The fourth twitch is compared to the first twitch to get the TOF ratio and indicates the degree of blockade. For example, a TOF ratio of 0.9 is equivalent to 90% (Srivastava & Hunter, 2009).

Residual neuromuscular blockade is "incomplete neuromuscular recovery in the early postoperative period defined as a TOF ratio of less than 0.9" or less than 90% (Murphy et al., 2011, p.946). Risks of RNMB are multi-factorial including patient factors (i.e. age, co-morbidities, weight), pharmacological causes (i.e. drug interactions), duration and type of anesthesia (i.e. opioid use, benzodiazepine use), and metabolic causes (i.e. acidosis,) (Srivastava & Hunter, 2009). Residual neuromuscular blockade impairs airway patency increasing the risk of post-operative complications such as reduced upper airway volumes, airway obstruction and hypoxemia events. In fact, 38 – 64% of patients who receive intermediate- acting NMBAs

experience RNMB. Awake volunteers, with a TOF ratio of 0.7-0.75, described RNMB as "unpleasant symptoms" such as generalized fatigue, decreased grip strength, visual disturbances, facial weakness, difficulty speaking, difficulty keeping their eyes open and difficulty swallowing (Murphy et al., 2011, p. 947).

In 2006, a publication of a study about the first use of sugammadex in humans was published. Over the past decade, the number of studies regarding sugammadex and clinical practice using sugammadex has greatly increased proving that sugammadex eliminates post-operative complications, such as RNMB, and improves surgical conditions (Carron, Zarantonello, & Tellaroli, 2016). Sugammadex is a modified γ-cyclodextrin, created to bind to free plasma molecules of aminosteroid NMBAs, most specifically the NMB drug, rocuronium. The use of sugammadex allows for full reversal with deep NMB within 5 minutes; however, full reversal after sugammadex use most often occurs even faster, within 2-3 minutes (Martini, Boon, Bevers, Aarts, & Dahan, 2013).

Sugammadex is proven to be superior, reliable and faster compared to its competition neostigmine. Neostigmine can result in incomplete reversal or RNMB and has potent parasympathetic activity that causes adverse effects, such as bradycardia, nausea and vomiting. The difference between these drugs is a result of their mechanism of action (Carron et al., 2016). Unlike the ceiling effect and adverse effects seen with neostigmine, sugammadex encapsulates the rocuronium and rarely causes RNMB or any adverse events. The sugammadex-rocuronium complex has a high association and low dissociation rate. It is estimated that for every 25 million complexes one complex will dissociate (Nag et al., 2013). By encapsulating the rocuronium it is removed from the neuromuscular junction and allows return of muscle function. Neostigmine increases the concentration of acetylcholine at the neuromuscular junction to

compete and displace the rocuronium from the site; however, the rocuronium is not completely removed and can paradoxically compete for the receptor site causing RNMB (Carron et al., 2016).

Evidence supports that sugammadex use is effective, safe, allows rapid reversal of NMB and reduces the incidences of RNMB (Brueckmann et al., 2015). The purpose of this project was to create a policy, at a community hospital, regarding the use of sugammadex. At this institution sugammadex had been used 103 times over an eight-month period. The primary indication for sugammadex use was failed neostigmine reversal resulting in muscle weakness and low tidal volumes.

The goal of this project was to develop and implement an evidence-based clinical practice guideline (CPG) that clearly identifies when sugammadex can and cannot be used at this Maryland hospital. The anticipated outcome was adoption and implementation of the CPG at the institution. Short-term goals were 1) recruitment of expert panel, 2) draft the CPG, 3) initial, secondary and third revisions of CPG, 4) proposal of CPG to anesthesia department, 5) analysis, synthesis and evaluation of CPG based on feedback, 6) final revisions and draft of CPG. Long-term goals were 1) adoption and implementation of the CPG, 2) greater than 75% of clinicians will correctly use sugammadex for reversal of NMB when indicated and 3) to reduce incidences of RNMB and its associated complications (see Figure 1).

Theoretical Framework

The Ottawa Model of Research Use (OMRU) by Graham and Logan (2004) was chosen as its key elements can be used to design and implement a CPG. This model is used to identify issues and create the steps to resolve the identified issues. The model consists of six components that are inter-related creating a web of connection that work with the three stages of the model.

These stages are a) Assessment, b) Monitoring and c) Evaluation (Graham & Logan, 2004). The *Assessment stage* involves identifying barriers and support within the practice environment, potential adapters, and the evidence-based innovations—three components of the model. It is during the *Assessment stage* that data of available resources and influences about the intervention are collected. The data collected in the *Assessment stage* is used to create the best possible intervention with the least amount of resistance. *Monitoring* is the second stage which includes intervention and adoption—two more components of the model. In the *Monitoring stage*, the Evidence-based intervention will be implemented and the progression will be tracked. The last stage, the *Evaluation stage*, monitors outcomes and examines the impact of the intervention—the last component of the model (Graham & Logan, 2004).

The OMRU was chosen due to its inter-related model focusing on adapting to changes throughout each stage. It was created to aid healthcare providers in translating research into practice, and therefore can be used to guide development of a CPG to decrease the incidence of residual neuromuscular blockade from failed neostigmine reversal (Graham and Logan, 2004). The medical institution of interest will use the structure and organization of the OMRU model to implement the use of sugammadex. Using the elements of OMRU, the sugammadex concepts and intervention will be linked. The first component, Evidence-based innovation, is the use of sugammadex to rapidly reverse NMB no matter the depth of the NMB. The second component, Potential adopters, is the anesthesia providers at the institution which includes the certified registered nurse anesthetist and the anesthesiologist. The third component, Practice environment, is the institution where sugammadex will be implemented. The fourth component, Interventions, and the fifth component, Adoption, will be the introduction of sugammadex use during the emergence phase of anesthesia. The final component, Outcomes, will use internal

data collected from implementation to be analyzed. Furthermore, the Assessment stage of the OMRU model will be used as a guide to the literature review and identifying potential barriers at the identified institution for the CPG to increase the use of sugammadex (see table 1). The data collected during the Assessment stage will be used to develop the CPG and implementation process specific to the institution of interest. The Monitoring stage will implement the CPG while ensuring the CPG is being used accurately and for its intended purpose with the least resistance. Lastly, after implementation the Evaluation stage will be carried out to analyze the outcomes and impact of the CPG.

Literature Review

The use of sugammadex compared to neostigmine for reversal of NMBAs is the focus for this literature review. All evidence was reviewed for level of evidence rating based on the Melnyk and Fineout-Overholt (2014) rating system for the hierarchy of evidence and critiqued using the *Quality Rating Scheme* (Table 1-3) (Newhouse, 2006). The review begins with a broad overview of routine reversal comparing the efficacy of the two reversal agents—sugammadex and neostigmine—and continues to compare the drugs specifically based on post-operative RNMB and safety. Finally, the review concludes discussing the benefits and risks of using sugammadex. The overall objective of this literature review is to analyze and synthesize the evidence supporting the use of sugammadex to reduce the incidence of RNMB.

Investigators of two phase III clinical trials established the efficacy of sugammadex for reversal of rocuronium or vecuronium during moderate and deep NMB. The clinical trials were four separate randomized control trials (RCTs) that shared the same objectives and methodology—to determine the efficacy of sugammadex at reversing moderate and deep NMB compared to neostigmine with glycopyrrolate. NMB was measured using TOF

acceleromyograph to measure the response at the adductor pollicis muscle in each trial. Recovery of TOF to a value of 0.9 or greater was the primary outcome measured (Blobner et al., 2010; Khuenl-Brady et al., 2010; Jones, Caldwell, Brull & Soto, 2008; Lemmens, El-Orbany, Berry, Morte & Martin, 2010). In the trial by Blobner et al., (2010) a total of 96 were randomized to receive either sugammadex, 2 mg/kg, (n=48) or neostigmine, 10 mcg/kg, (n=48) with rocuronium for intubation, 0.6 mg/kg, and for maintenance, 0.1-.0.2 mg/kg, as needed (N=96). Reversal was given when the second twitch of the TOF was present. The authors results showed that the sugammadex group was faster than neostigmine at reversing rocuronium (1.5 min. vs. 18.6 min.; $p<0.0001$) (Blobner et al., 2010). In the trial by Khuenl-Brady et al. (2010) a total of 93 patients were randomized to receive either sugammadex, 2 mg/kg, (n=48) or neostigmine, 10 mcg/kg, (n=45) with vecuronium, 0.1 mg/kg, for intubation and for maintenance, 0.02-0.03 mg/kg, as needed (N=93). Reversal was given when the second twitch of the TOF was present. The authors of the trial showed that the sugammadex group was faster than neostigmine at reversing vecuronium (2.7 min. vs. 17.9 min.; $p <0.0001$) (Khuenl-Brady et al., 2010).

In the trial by Jones et al. (2008) comparing sugammadex and neostigmine, a total of 74 patients received 0.6 mg/kg of rocuronium for intubation and 0.15 mg/kg as needed for maintenance (N=74). All patients were randomized to receive sugammadex 4 mg/kg (n=37) or neostigmine 70 mcg/kg with glycopyrrolate 14 mcg/kg (n=37) which was administered at the appearance of 1-2 PTCs for reversal of NMB. The authors of the trial demonstrated that the sugammadex was faster than neostigmine at reversing rocuronium (2.9 min. vs. 50.4 min) (Jones et al., 2008). In the trial by Lemmens et al. (2010) a total of 83 patients received vecuronium 0.1 mg/kg for intubation and 0.015 mg/kg as needed for maintenance (N=83). All patients were

randomized to receive sugammadex 4 mg/kg (n=46) or neostigmine 70 mcg/kg with glycopyrrolate 14 mcg/kg (n=36) which was administered at the appearance of 1-2 PTCs for reversal of NMB. Similar to the earlier trials described in this review, the authors of the trial showed sugammadex was faster than neostigmine at reversing vecuronium (4.5 min. vs. 66.2 min.; $p < 0.0001$) (Lemmens et al., 2010).

Additionally, the previously mentioned studies showed a stronger safety profile with sugammadex compared to neostigmine. The adverse events examined by the authors were dry mouth, nausea, vomiting, hemodynamic changes and albumin in the urine (Blobner et al., 2010; Khuenl-Brady et al., 2010; Jones et al., 2008; Lemmens et al., 2010). Blobner et al. (2010) showed after moderate rocuronium-induced NMB the sugammadex group had 14.3% (n=7) vs. neostigmine 20.4% (n=10) incidences of adverse events. Khuenl-Brady et al. (2010) demonstrated after moderate vecuronium-induced NMB the sugammadex group had 14.6% (n=7) vs. neostigmine 22.2% (n=10) of adverse events. Jones et al. (2008) showed after deep rocuronium-induced NMB the sugammadex group had 27% (n=10) vs. neostigmine 31.6% (n=12) of adverse events. Lastly, Lemmens et al. (2010) proved after deep vecuronium-induced NMB the sugammadex group had 19.6% (n=9) vs. neostigmine 27.8% (n=10) incidences of adverse events. Overall, the synthesis of the evidence shows that sugammadex has a higher safety profile when compared to neostigmine.

Additionally, in a meta-analysis performed by Carron et al. (2016) 13 RCTs were analyzed (N=1384) comparing neostigmine to sugammadex in reversing moderate and deep NMB induced by vecuronium and rocuronium. The authors of the meta-analysis showed sugammadex was significantly faster than neostigmine in reversing moderate NMB in both groups (Carron et al., 2016). Furthermore, several investigators have conducted trials to

determine if sugammadex may reduce RNMB. In a trial by Brueckmann et al. (2015) a total of 150 patients undergoing abdominal surgery and receiving rocuronium were randomized into two groups (N=150). One group was randomized to receive sugammadex 2-4 mg/kg (n=74) whereas the other group received a neostigmine/glycopyrrolate combination using standard dosing (n=76). The primary outcome of this trial was sugammadex had a significantly lower rate of RNMB in the post anesthesia care unit (PACU) as compared to neostigmine (0% vs. 43% with a TOF ratio <0.9; p<0.0001). The authors of the trial also showed that the median times from drug administration to OR discharge and PACU discharge was significantly different between the groups (14.7 min vs. 18.6 min., respectively; p=0.021) (Brueckmann et al., 2015).

In a large systematic review by Abad-Gurumeta et al. (2015) 14 RCTs (N= 1553) were analyzed comparing sugammadex to neostigmine for reversal of rocuronium and vecuronium-induced NMB. The primary outcome was to assess rate of post-operative RNMB. The authors found that sugammadex significantly reduced the rate of RNMB and the patients exhibited no signs of RNMB as compared to neostigmine (3.9/100 patients vs. 8.4/100 patients, respectively). The authors also reported that 1 in 22 patients avoided RNMB when given sugammadex as compared to neostigmine and that minor weakness after NMB was also decreased in the sugammadex group (4.7/100 patients vs. 9.4/100 patients, respectively) (Abad-Gurumeta et al., 2015). Overall, synthesis of the evidence proves that sugammadex use results in fewer incidences of RNMB.

Moreover, many researchers have examined the safety of sugammadex compared to neostigmine. One systematic review by Hristovska, Duch & Afshari (2017) analyzed 30 RCTs (N=2259) that compared sugammadex recovery time and adverse effects to neostigmine after nondepolarizing NMBAs were administered at any dose. The primary outcome of recovery time

comparison showed the same results as the studies mentioned earlier. The adverse effects observed were bradycardia, post-operative nausea vomiting (PONV), desaturation and need for supplemental oxygen. The authors of the review showed that sugammadex had 40% less incidence of adverse events compared to neostigmine (159/1000 patients vs. 283/1000 patients, respectively) (Hristovska, Duch & Afshari, 2017).

Evidence supports the use of sugammadex as a safe and efficient drug to reverse NMBAs. The benefits include shorter recovery time, less adverse events, decreased residual neuromuscular blockade and overall increased muscle strength after NMB. The biggest challenge is the cost of sugammadex compared to neostigmine. The risks of sugammadex are similar to standard reversal with neostigmine such as hemodynamic changes, nausea and vomiting.

Implementation Plan

A quality improvement project was designed for a medium-sized community hospital to create a CPG for the use of sugammadex for patients undergoing general anesthesia requiring NMB. The targeted patient population for this CPG is adults (> or equal to 18 years of age) who are undergoing general anesthesia requiring the use of the NMBAs rocuronium or vecuronium that meet the inclusion/exclusion criteria mentioned below. The target audience of this CPG was Certified Registered Nurse Anesthetists (CRNAs) and Anesthesiologists. The guideline was used to inform standard of care with the use of sugammadex. Three phases of the project were implemented over several months. A step by step procedures and timeline plan for the completion of the quality improvement project can be found in Appendix A. This chart was created in collaboration with all group members of the project. Phase one of the project consisted of identifying the clinical problem, expert panel and current evidence. Literature was

reviewed and a CPG draft was created. An Appraisal of Guidelines for Research and Evaluation (AGREE II tool) was used to revise the CPG. Phase two of the project, involved including recommendations from the chief anesthesiologist and again revising the CPG which was then presented at Anesthesia Grand Rounds. Phase three was used to evaluate feedback from the presentation and create a definitive CPG incorporating all feedback.

Phase one began in February 2018, the first two weeks consisted of recruiting an expert panel to develop the CPG. The expert panel included a CRNA with a terminal degree and one anesthesiologist or Medical Director of Anesthesia at the institution of interest. An email was sent to this panel with the tentative timeline of meetings, the purpose of the project and everyone's role in the project. A draft of the CPG will be emailed to the panel (Appendix C) with instructions to review using the AGREE II tool (Appendix D). Following review of the CPG, a meeting was held with the expert panel to discuss the results and go over any recommendation for change. The CPG was then revised to include recommendations from the panel. The expert panel received the revised CPG for review. Succeeding the panel's review, the project progressed to phase two. During this stage of the quality improvement project, the chief anesthesiologist received a copy of the CPG for review. The recommendations from the chief anesthesiologist were incorporated into the CPG. The revised CPG with the chief's changes were emailed to the expert panel during phase two.

After the expert panel reviewed the final CPG, the CPG was approved. A date was selected to present the CPG to the Department of Anesthesia Grand Rounds at the institution of interest. Phase three took place during the last month which included provider feedback of the CPG. The providers were asked to complete a practitioner feedback questionnaire (PFQ) after the presentation (Appendix E). The panel collected the data and performed an analysis (see

analysis and results section). Once the data was analyzed, a meeting with the expert panel and chief anesthesiologist took place. The data was discussed and the final edits were made to the CPQ. The final CPG was then disseminated through a poster presentation at the Maryland Association of Nurse Anesthetists (MANA) Spring Meeting.

Data Collection and Analysis

A data collection and analysis plan was used to evaluate this quality improvement project. The CPG was evaluated, in phase one of the project, using the AGREE II tool as it is considered the gold standard for guideline evaluation and has construct validity (Brouwers et. al., 2010). The AGREE II tool was created by the AGREE Next Steps Consortium to evaluate the quality of CPG's. The tool consists of 23 items within six distinct domains and one section for an overall assessment of the CPG being evaluated (Appendix D). A seven point Likert scale ranging from "strongly agree" to "strongly disagree" is used to grade each item of the AGREE II tool. Each item is scored and the results are summarized within each domain to compare the CPG quality in that domain (AGREE Next Steps Consortium, 2009). Each member of the expert panel received an electronic copy of the AGREE II tool to evaluate the CPG. Using the AGREE II tool, each domain is separately examined with corresponding scores denoting the quality of data in that domain. The scores from each domain and from each expert panel member were totaled then the maximum score and the minimum score were subtracted. A percentage was given by dividing the difference of the maximum and minimum scores by the totaled number from each domain. The percentage was used to quantify the quality of the CPG as good or poor (AGREE Next Steps Consortium, 2009). Any domain that receives a poor-quality score was discussed with the expert panel and revised for the final CPG.

Additionally, in phase three of the project, a PFQ (Appendix E) was used to evaluate the anesthesia provider's attitudes towards the CPG. The PFQ was used because of its content validity and reliability that was established by Cronbach's alpha coefficient (Brouwers, Graham, Hanna, Cameron, & Browman, 2004). The PFQ is a twenty-three-item questionnaire using a three point Likert scale ranging from "strongly agree" to "strongly disagree" except for four items (#10, 13, 14, & 15) which are negative items reverse scored. A PFQ is designed specifically for adopters of a CPG. The purpose of the PFQ is to identify potential barriers to implementation by assessing the CPG for quality, applicability and acceptability (Brouwers, Graham, Hanna, Cameron, & Browman, 2004). The PFQ was given to each attendee at the presentation of the CPG in a paper/pen format. The data obtained from the PFQ was grouped by the number of years' experience of the provider. There are six groups of experience categories ranging from 0-5 years of experience to greater than 25 years of experience (see Figure 3). A univariate frequency table was used to show the frequency of each score for each item. The frequency of each item was then divided by the total number of questions and made a percent. These statistical tests are used to investigate the response to each question and compare among the three groups.

Human Rights Protection

The University of Maryland Baltimore Institutional Review Board determined that the project was quality improvement and gave a determination of Non-Human Subjects Research. The participants acknowledged verbal disclosure of voluntary involvement in this project. To protect the privacy of the participants, no identifiers were collected. Furthermore, to protect the data, the PFQs were submitted via a secure system using a secure box that was stored in a locked office. Any electronic data was stored in a password-protected computer for analysis.

Results

Using the data analysis plan outlined above the collected data was analyzed by the stakeholders using descriptive statistics. Each member of the expert panel received an electronic copy of the AGREE II tool to evaluate the CPG. Any domain that received a poor-quality score was discussed with the expert panel and revised for the final CPG. The results of the final AGREE II Tool were 100% across the 6 domains and for the overall assessment. Each appraiser had a total score of 161/161 points and an overall of 322/322 points. This indicates that the providers feel the CPG has specifically explained the objective, health questions and population target (domain 1), the target population preferences/views were sought (domain 2), the external review of evidence was adequate and consistent with the recommendations made in the guideline (domain 3), has clarity (domain 4), overcomes potential barriers and is applicable (domain 5), and has no competing interest or influence from a funded source (domain 6). The percentage of each domain is used to quantify the quality of the CPG as good or poor (AGREE Next Steps Consortium, 2009).

Additionally, the PFQ was used to assess potential barriers to implementation by assessing the adopters of the CPG. The PFQ provided demographic data about the adopters of the CPG. This included provider type (see Figure 2) and provider years of experience (see Figure 3). There was a total of twenty-two providers (N=22) at the presentation and a 100% return rate of the attendees was received. The providers were Certified Registered Nurse Anesthetists (CRNAs) (n= 10; 46%), Anesthesiologist (n=8; 36%) and Student Registered Nurse Anesthetist (SRNAs) (n=4; 18%). The years of experiences ranged from less than 5 years to more than 25 years with a majority being less than 5 years (32%) and 5-10 years (32%).

A univariate frequency table was used to show the frequency of each score for each item (see Figure 4). In reviewing the data, the PFQ's received "strongly agree" and "strongly disagree" where appropriate for acceptance of the CPG. Item 1 was excluded from the table as it required a yes or no response which differed from the Likert scale responses. For an example of the PFQ questions see Appendix E. For items 2-8, 11-12, 16, 20, 22-23 all providers strongly agreed. These items assessed the CPG for rationale for development, need for guideline, relevant and complete literature search, agreement with methodology used to summarize evidence, evidence in guideline is consistent with external review, recommendations are clear, agreement with recommendations, produces more benefit than harm, presents options acceptable to patients, likely to be supported by a majority of colleagues, comfortability with recommendations, if approved would use in practice and would apply to patients. Item 9 assessed suitability for target population, 95% of providers strongly agreed and 5% neither agreed or disagreed. Item 10 assessed if the CPG was too rigid to apply to each patient, 18% neither agreed or disagreed and 82% strongly disagreed. Item 13 assessed if reorganization of care in the practice setting was needed, 32% neither agreed or disagreed and 68% strongly disagreed. Item 14 and 15 assessed if recommendations were technically challenging and too expensive to apply, 18% neither agreed or disagreed and 82% strongly disagreed. These four items (10, 13, 14, & 15) are negative items with reverse scores. Item 17 assessed if used the expected effects on outcomes will be obvious, 91% strongly agree and 9% neither agree or disagree. Item 18 assessed if recommendations reflect a more effective approach for improving outcomes than current practice, 96% strongly agree and 4% neither agree or disagree. Item 19 assessed if use will result in better use of resources, 91% strongly agree, 5% neither agree or disagree, and 4% strongly disagree. Item 21 assessed approval of guideline, 96% strongly agree

and 4% strongly disagree. This analysis demonstrated buy-in and acceptance of the CPG by the majority of the department.

Sustainability and Generalization

The use of sugammadex to decrease RNMB outlined by this CPG will be sustained through continuous efforts by the hospital's anesthesia and perioperative staff previously mentioned. Audits of electronic databases will be used to assess if patients are receiving sugammadex. Additionally, incidence of RNMB and length of stay will be managed using electronic data bases to continuously assess the effectiveness of the outcomes identified in this CPG. One feature of this organization that will contribute to the sustainability of this CPG is the engagement of senior leaders in administration, such as the chief anesthesiologist, early in the planning stages of the project. Another contributor to sustainability will be the inclusion of mentors and champions, such as the CRNA and MDA, from the organization to facilitate the change and encourage continual usage. Furthermore, using the PFQ allows the expert panel to take into consideration the attitudes, culture and potential barriers present at the medical institution of interest. This allows the expert panel to use this feedback from the PFQ to make changes to the final CPG, incorporating this data to create a sustainable and realistic CPG. Lastly, the ability to audit electronic medical records (EMR) will contribute to ongoing sustainability, as EMR's can provide data collection of outcomes and quality improvement activity data. This CPG was designed to solely be used at the community hospital identified. It will be used in this medical institution's perioperative area and is not intended to be generalized outside of this setting.

Discussion

Evidence reviewed in this manuscript demonstrates that sugammadex use is effective, safe, allows rapid reversal of NMB and reduces the incidences of RNMB thus supporting the short and long-term goals of this project (Brueckmann et al., 2015). The occurrence of residual paralysis after reversal with neostigmine was identified at the community hospital of interest. This is consistent with the current literature available stating neostigmine can result in incomplete reversal or RNMB and has potent parasympathetic activity that causes adverse effects, such as bradycardia, nausea and vomiting (Carron et al., 2016). Abad-Gurumeta et al. (2015) found that sugammadex significantly reduced the rate of RNMB and the patients exhibited no signs of RNMB as compared to neostigmine. The authors also reported that 1 in 22 patients avoided RNMB when given sugammadex as compared to neostigmine and that minor weakness after NMB was also decreased in the sugammadex group (Abad-Gurumeta et al., 2015). Sugammadex is proven to be superior, reliable and faster compared to its competition neostigmine thus creating a policy would benefit the identified institution (Carron et al., 2016). The project leaders and members of the anesthesia department identified the need to create a policy on the use of sugammadex since it is available at the hospital of interest. A CPG was developed to be approved to decrease the incidence of residual paralysis and demonstrate when sugammadex can and cannot be used at the facility. A cost analysis (Table 4) was performed due to restrictions from pharmacy on wide spread use. The cost analysis identified a higher price in the use of sugammadex compared to neostigmine which was an unexpected outcome of the project. When reviewing the literature this is a common concern of pharmacies in hospitals (Carron et al., 2016). The Project leaders did not see it being an issue since it was available at the institution; however, there was push back on everyday use. As a result, the final CPG was

modified for the use of sugammadex in the high-risk patient population because the benefit of sugammadex outweighed the costs of the associated complications in this patient population.

Overall, the intervention was achieved, which was acceptance of the CPG, due to the large amount of supporting literature. The outcome of the final CPG was evaluated using the AGREE II tool and found to have high scores demonstrating a high quality CPG. Each domain of the CPG received a score of 100%. According to Brouwers et al., 2010, a CPG is considered high quality for any calculated domain score greater than 70 percent. Since each domain received 100% this demonstrates a high quality CPG; therefore, no more recommendations or changes need to be made for the CPG at this time. A PFQ was used to evaluate the final CPG. This evaluation received high scores as well and identified buy-in from the anesthesia department to accept and adapt their practice using the CPG. Providers felt the benefits of sugammadex in high risk patients out-weighted the cost compared to neostigmine (Table 5).

One strength of the project was that the department felt the presentation by the project leaders and the creation of the algorithm was quite beneficial to their practice. The algorithm as a result was placed in every operating room to provide reference to providers. The providers at this institution strongly believe in the use of sugammadex and incorporating evidence-based research into their practice. This has been vital to the implementation and acceptance of the CPG for sugammadex use. Majority of the staff are familiar with sugammadex and are eager to see its use at the institution. Each member of the expert panel has been eager, knowledgeable and a suitable resource for the creation of the CPG. Following the presentation to the anesthesia department, the project leaders received a lot of positive feedback about the CPG in person and via e-mail. This was also evident in the results of the PFQ analysis. The staff was open to the implementation of the CPG (Appendix C), algorithm for sugammadex use (Appendix G), and

education hand-out for patients of child bearing age who are on birth control (Appendix H) which aided in practice change.

Additionally, the providers appreciated the evidence that was presented to the pharmacy to allow the CPG to be approved. Another strength of the project was the early buy-in from stakeholders and providers in the department. Many providers were eager to have a policy created for sugammadex use. Lastly, the evidence supporting the use of sugammadex is high quality. Using meta-analysis and randomized control trials to create this CPG is beneficial to its sustainability and acceptance. Over the next decade, the use of sugammadex will be more prominent with a reduction in the cost as the current patent expires. This is a benefit to the institution for adopting a CPG into practice before it is widely approved in the industry.

One limitation of the project is the use of sugammadex for all patients receiving general anesthesia at the institution due to the cost as previously mentioned. Pharmacy was very hesitant to spend the money on a drug whose effects can be achieved with a cheaper drug with a different mechanism of action. This was overcome by narrowing the CPG down to the high-risk patients where the benefits outweigh the cost. Secondly, the price of sugammadex will vary at all institutions which makes the use of this CPG not generalizable outside of the medium-sized community hospital it was designed for. To overcome for this limitation the CPG was designed to only be used at this facility. Additionally, the CPG was designed to meet the needs of the hospital of interest. Therefore, it is not generalizable for that reason as well. It is made specific for their needs and evaluated for acceptance and quality based on the providers at this institution. The providers were eager to create a policy and to use sugammadex which is a limitation to the study due to internal bias. This limitation was minimized by presenting a non-bias review of the literature on sugammadex and neostigmine. The last limitation was found in the PFQ analysis.

Some attendees did not completely read and complete the PFQ's. As a result, any PFQ that was not filled out was not included in the final PFQ analysis. This adjusted for the limitation.

Conclusion

The sugammadex clinical practice guideline was created in hopes to increase patient outcomes in high risk patients who receive general anesthesia with neuromuscular blockade. Additionally, the guideline was created to standardize and guide providers on the approved use of sugammadex at the hospital of interest. The algorithm and patient education handout within the CPG will be useful tools for anesthesia providers to guide their practice. All together this should decrease residual paralysis in high risk patients after general anesthesia. By decreasing residual paralysis its associated complications of increased length of stay, cost and respiratory complications will also be decreased.

Overall, practice has been affected because of this CPG. Providers are more aware of sugammadex overall especially for use in the high-risk population. Providers, at the institution of interest, can now ensure high-risk patients are managed appropriately and safely with the approval of the sugammadex CPG in this patient population. Clinically providers are assessing patients at risk and using the CPG algorithm and determining if sugammadex is the reversal of choice. The CPG algorithm was laminated and placed in every operating room on the anesthesia machine for reference and use because of the CPG.

Although sugammadex cannot be used freely, it can now be used in high risk patients which is common among the literature reviewed. Use in high risk patients will help to limit the increased cost associated with adverse events such as residual paralysis. The project can be sustained to collect data on the use of sugammadex in high risk patients and show the benefits it is having. A second cost analysis can then be performed to show the effectiveness of the CPG.

This data can then be presented to the pharmacy and anesthesia department in hopes to further expand the use of sugammadex to other patient populations. This can be done on a quarterly basis reviewing electronic health records and by creating a committee to be in charge of monitoring use and effectiveness.

Potentially this CPG can be spread to other facilities. The CPG would need to be modified slightly to incorporate policies and procedures specific to that institution. Additionally, a cost analysis would need to be performed to compare price of neostigmine and sugammadex as this varies at every hospital. An area for quality improvement using this project is continued education of residual paralysis and the use of sugammadex with patients on birth control. Educating the PACU staff and any potential unit that would receive patients post-operatively such as surgical units or intensive care units. It is important they understand the significance of the drug interactions as well as signs and symptoms to identify if a patient is experience residual paralysis. Overall, the sugammadex guideline was accepted to be adopted into clinical providers practice at the institution of interest. The guideline should decrease post-operative complications associated with neuromuscular blockade in high-risk patients.

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Table 1

Evidence Review

Author/Year	Study objective	Design	Sample (N)	Outcomes studied (how measured)	Results	Level of evidence
Abad-Gurumeta, A., Ripolles-Melchor, J., Casans-Frances, R., Espinosa, A., Martinez-Hurtado, E., Fernandez-Perez, C., . . . Calvo-Vecino, J. (2015)	The study evaluated the rate of post-operative RNM after administration of sugammadex or neostigmine.	Systematic review of RCTs	N=1553 14 RCTs	The study used TOF to measure outcomes of the study that were measured.	The results showed that sugammadex reduced overall signs of RNMB (HR 0.46 95% CI 0.29 -0.71; p=0.0004). Secondary results were that critical respiratory events were not reduced; however, this was underpowered as only 9 total events were identified and therefore not significant. Lastly, PONV was similar among the two groups.	1A
Blobner, M., Eriksson, L., Scholz, J., Motsch, J., Rocca, G., Prins, M. (2010)	The study evaluated mean time to TOF ratio 0.9 or greater using sugammadex compared to neostigmine after moderate NMB with rocuronium. It also evaluated adverse events and the safety profile of sugammadex compared to neostigmine.	Phase III clinical RCT	N=96 Group 1= Sugammadex (n=48) Group 2= Neostigmine + glycopyrrolate (n=49)	NMB was measured using TOF acceleromyograph at the adductor pollicis muscle. The outcomes measured were efficacy and adverse events of sugammadex compared to neostigmine in rocuronium-induced moderate NMB.	Time to TOF ratio of 0.9 or greater in the sugammadex group was 1.5 minutes and in the neostigmine/glycopyrrolate group 18.6 minutes ($p<0.0001$). Adverse events possibly or probably related to the study drug were 14.3% (n=6) in the sugammadex group and 20.4% (n=10) in the neostigmine group.	2A

Brueckmann, B., Saski, N., Grobara, P., Li, M.K., Woo. T., de Bie, J., Maktabi, M., Lee, J., Pino, R., Sabouri, A., McGovern, F., Saehr-Rye, A., & Eikermann, M. (2015)	The study evaluated if there was a decreased incidence of residual blockade and increased operating room discharge promptness with the use of sugammadex to reverse rocuronium-induced neuromuscular blockade (NMB).	Randomized Control Trial (RCT)	N=150 Group 1 (n=74) Sugammadex recipients Group 2 (n=76) Standard of care	The outcome studied was the incidence of residual blockade with the use of sugammadex compared to standard of care with neostigmine and glycopyrrolate. A Train-of-four measurement was taken upon arrival to the Post Anesthesia Care Unit (PACU). Pain scores were also recorded in the PACU.	The study proved that recovery from neuromuscular blockade with sugammadex showed no residual blockade (n=0) compared to the standard of care with neostigmine and glycopyrrolate (n=33; $p <$ 0.0001). Additionally, the readiness to discharge was shorter in the sugammadex than the standard of care group (14.7 v. 18.6 respectively; $p = 0.02$).	2A
Carron, M., Zarantonello, F., & Tellaroli, P. (2016)	The analysis reviewed RCTs to prove Sugammadex is effective and safe in reversing neuromuscular blockade compared to standard of care (Neostigmine).	Meta-Analysis of RCTs	N=1384 Sugammadex v. Neostigmine for reversal of NMB	The outcome studied was the effectiveness and safety of Sugammadex use. A PRISMA methodology was used to perform a data analysis of randomized control trials. Primary outcomes were efficacy of Sugammadex measured by time to reversal with moderate neuromuscular block (MNMB) and deep neuromuscular block (DNMB) using the Train of Four (TOF) Ratio. Incomplete reversal measured by TOF Ratio was also measured. The secondary outcome was safety evaluation by a blinded safety assessor.	The study proved Sugammadex had a faster recovery time compared to Neostigmine ($p<0.0001$). Higher TOF ratios post extubation were noted in the Sugammadex group ($p < 0.0001$) and lower recurarization risk after extubation ($p = 0.0068$). Overall, Sugammadex had reduced cardiovascular ($p =$ 0.0036) and respiratory ($p =$ 0.0386) adverse events.	1A

Hristovska, Duch, Allingstrup, & Afshari, (2017)	The review compared reversal of NMB in adults using Sugammadex to Neostigmine looking at efficacy and safety of both drugs.	Systematic Review of RCTs	N=4206 based on 41 RCTs	The outcome studied was the efficacy and safety of Sugammadex and Neostigmine. The outcome was measured using the Cochrane risk of bias tool. It evaluates the risk of random error through trial sequential analysis. An overall assessment of the quality of evidence was examined using the GRADE approach. The primary outcome was recovery time which was measured using TOF. The secondary outcome was adverse events and was measured by calculating risk ratios.	The study proved that NMB was more rapidly reversed using Sugammadex. The depth of the NMB did not affect the speed of Sugammadex. Patients who received Sugammadex had a 40% less incidence of harmful events compared to the standard of care using Neostigmine.	1A
Jones, R., Caldwell, J., Brull, S., & Soto, R. (2008)	The study evaluated mean time to TOF ratio 0.9 or greater using sugammadex compared to neostigmine after deep NMB with rocuronium. It also evaluated adverse events and the safety profile of sugammadex compared to neostigmine.	Phase III clinical RCT	N=74 Group 1= Sugammadex (n=37) Group 2= Neostigmine + glycopyrrolate (n=37)	NMB was measured using TOF acceleromyograph at the adductor pollicis muscle. The outcomes measured were efficacy and adverse events of sugammadex compared to neostigmine in rocuronium-induced deep NMB.	Time to TOF ratio of 0.9 or greater in the sugammadex group was 2.9 minutes and in the neostigmine/glycopyrrolate group 50.4 minutes ($p<0.0001$). Adverse events possibly or probably related to the study drug were 27% (n=10) in the sugammadex group and 31.6% (n=12) in the neostigmine group.	2A

Khuenl-Brady, K. Wattwil, M., Vanacker, B., Lora-Tamayo, J., Rietbergen, H., Alvarez-Gomez, J. (2010)	The study evaluated mean time to TOF ratio 0.9 or greater using sugammadex compared to neostigmine after moderate NMB with vecuronium. It also evaluated adverse events and the safety profile of sugammadex compared to neostigmine.	Phase III clinical RCT	N=93 Group 1= Sugammadex (n=48) Group 2= Neostigmine + glycopyrrolate (n=45)	NMB was measured using TOF acceleromyograph at the adductor pollicis muscle. The outcomes measured were efficacy and adverse events of sugammadex compared to neostigmine in vecuronium-induced moderate NMB.	Time to TOF ratio of 0.9 or greater in the sugammadex group was 2.7 minutes and in the neostigmine/glycopyrrolate group 12.9 minutes ($p<0.0001$). Adverse events possibly or probably related to the study drug were 14.6% (n=7) in the sugammadex group and 22.2% (n=10) in the neostigmine group.	2A
Lemmens, H., El-Orbany, M., Berry, J., Morte, J., & Martin, G. (2010)	The study evaluated mean time to TOF ratio 0.9 or greater using sugammadex compared to neostigmine after deep NMB with vecuronium. It also evaluated adverse events and the safety profile of sugammadex compared to neostigmine.	Phase III clinical RCT	N=83 Group 1= Sugammadex (n=46) Group 2= Neostigmine + glycopyrrolate (n=36)	NMB was measured using TOF acceleromyograph at the adductor pollicis muscle. The outcomes measured were efficacy and adverse events of sugammadex compared to neostigmine in vecuronium-induced deep NMB.	Time to TOF ratio of 0.9 or greater in the sugammadex group was 4.5 minutes and in the neostigmine/glycopyrrolate group 66.2 minutes ($p<0.0001$). Adverse events possibly or probably related to the study drug were 19.6 % (n=9) in the sugammadex group and 27.8% (n=10) in the neostigmine group.	2A

(Melnyk & Fineout-Overholt, 2014; Newhouse, 2006)

Table 2

Rating System for Hierarchy of Evidence

Level of the Evidence	Type of the Evidence
I	Evidence from systematic review, meta-analysis of randomized controlled trails (RCTs), or practice-guidelines based on systematic review of RCTs.
II	Evidence obtained from well-designed RCT
III	Evidence obtained from well-designed controlled trials without randomization
IV	Evidence from well-designed case-control and cohort studies
V	Evidence from systematic reviews of descriptive and qualitative studies
VI	Evidence from a single descriptive or qualitative study
VII	Evidence from the opinion of authorities and/or reports of expert committees

(Melnyk & Fineout-Overholt, 2014)

Table 3

Rating Scale for Quality of Evidence

Quality Rating Level	Quality Rating Description
A	High – consistent results with sufficient sample, adequate control, and definitive conclusions; consistent recommendations based on extensive literature review that includes thoughtful reference to scientific literature.
B	Good – reasonably consistent results; sufficient sample, some control, with fairly definitive conclusions; reasonably consistent recommendations based on fairly comprehensive literature review that includes some reference to scientific evidence.
C	Low/major flaw – Little evidence with inconsistent results; insufficient sample size; conclusions cannot be drawn

(Newhouse, 2006)

Table 4

Cost Analysis

Sugammadex (200mg/2ml)	$95 per vial/ approx. $95/dose
Sugammadex (500mg/5ml)	*lower cost; pharmacy here does not stock
Neostigmine (10mg/10ml)	$57.70 per vial $28.85/dose
Glycopyrrolate (0.4mg/2ml)	$13.87 per vial $27.74/dose ($56.59 total with N&G)

Table 5

Sugammadex Compared to Neostigmine

Neostigmine	**vs. Sugammadex**
Co-administered with glycopyrrolate	Single drug
Widely available	Limited availability
Inexpensive	Expensive (see Table 1)
Reverses all non-depolarizing agents	Only reverses steroidal NDMB
Cannot reverse deep blockade	Can reverse deep blockade
Longer peak time (7-10 mins)	Shorter peak time (3 mins)
Causes weakness if given s/p full recovery	No problems if given s/p full recovery
May increase PONV	Does not increase PONV
Non-allergenic	Allergenic

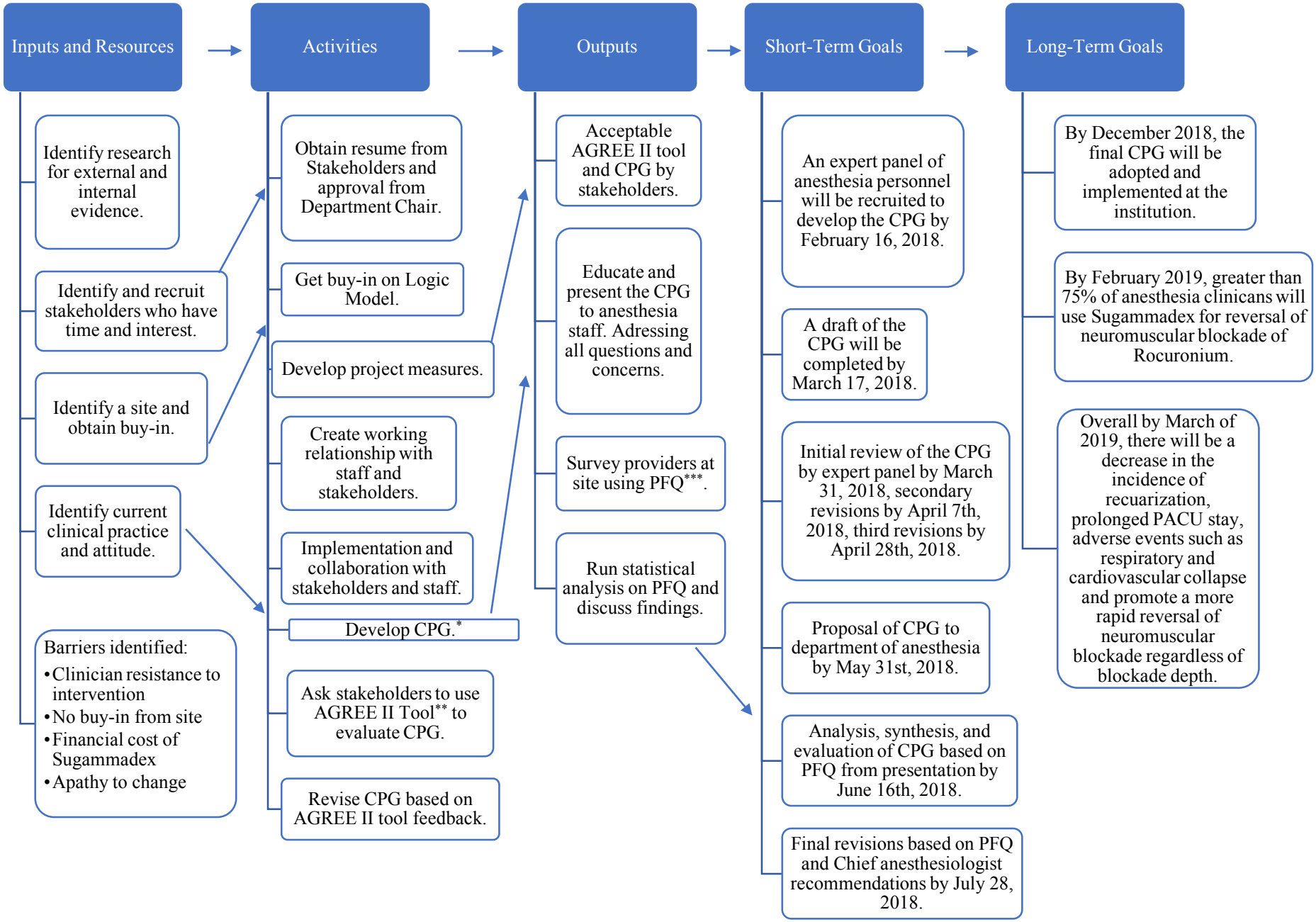


Figure 1. Logic Model. *Clinical Practice Guideline; **Appraisal of Guidelines for Research and Evaluation (AGREE) II tool; ***Practitioner Feedback Questionnaire.

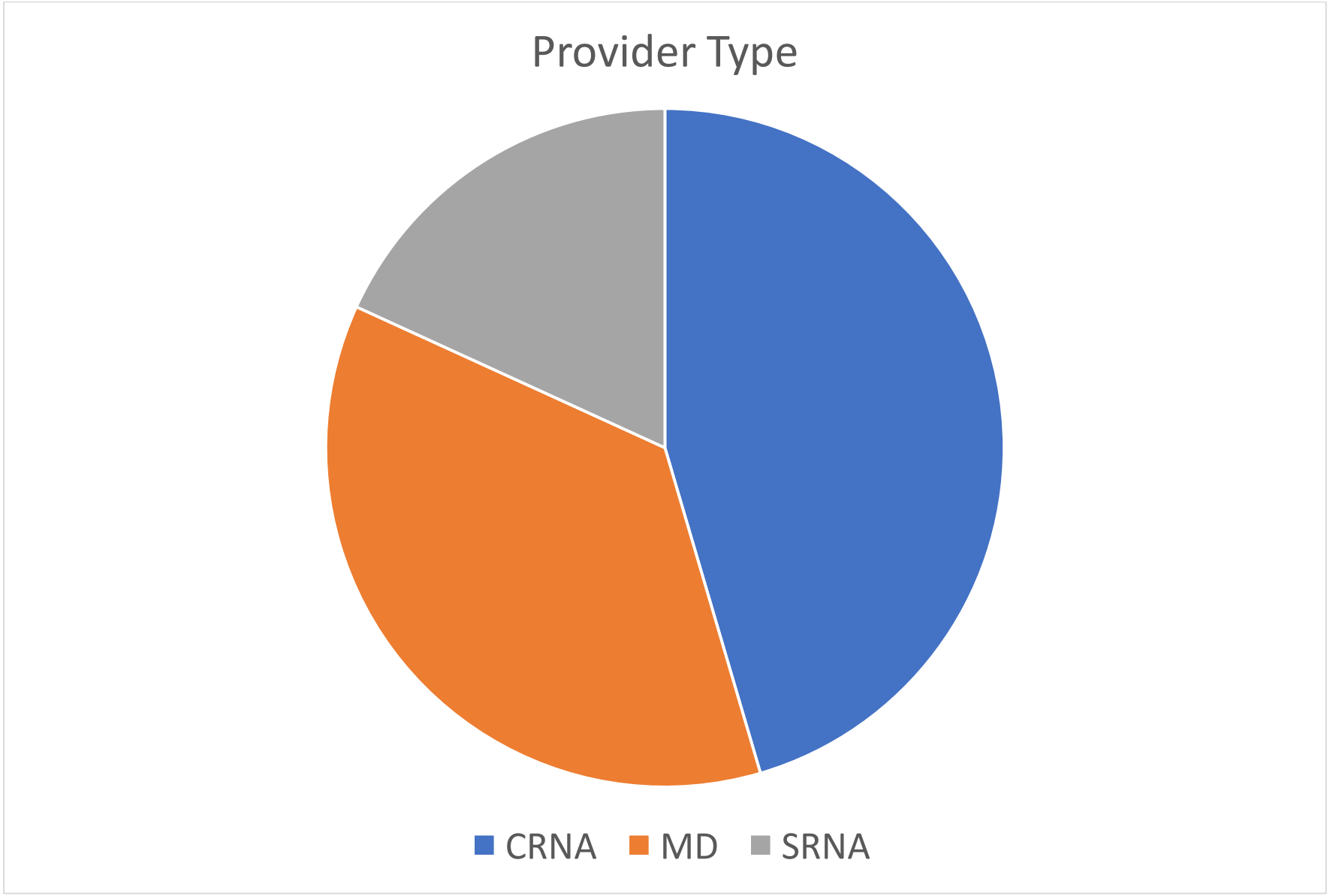


Figure 2. Provider type. CRNA: Certified Registered Nurse Anesthetist, MD: Anesthesiologist, SRNA: Student Registered Nurse Anesthetist.

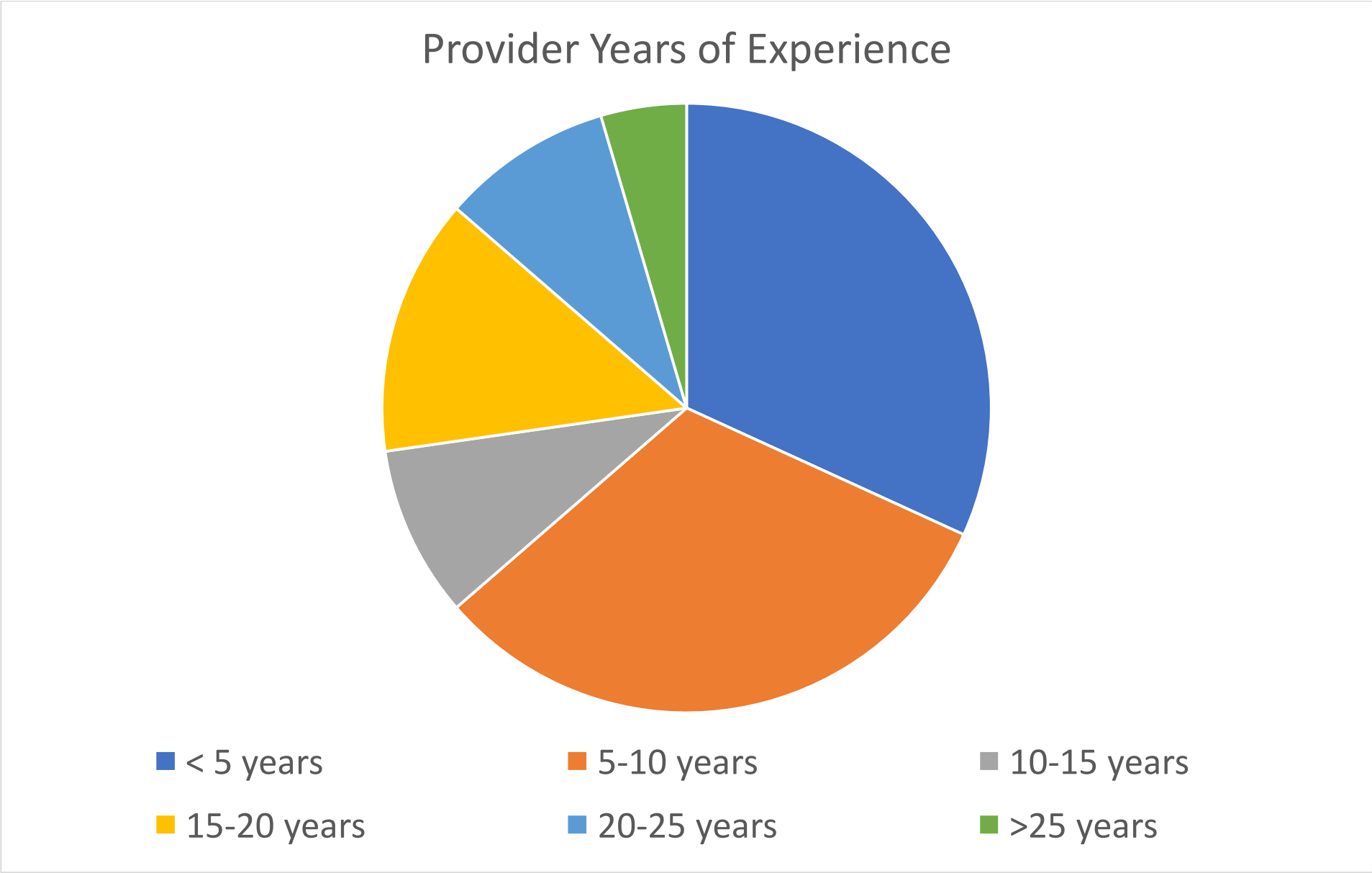


Figure 3. Provider years of experience.

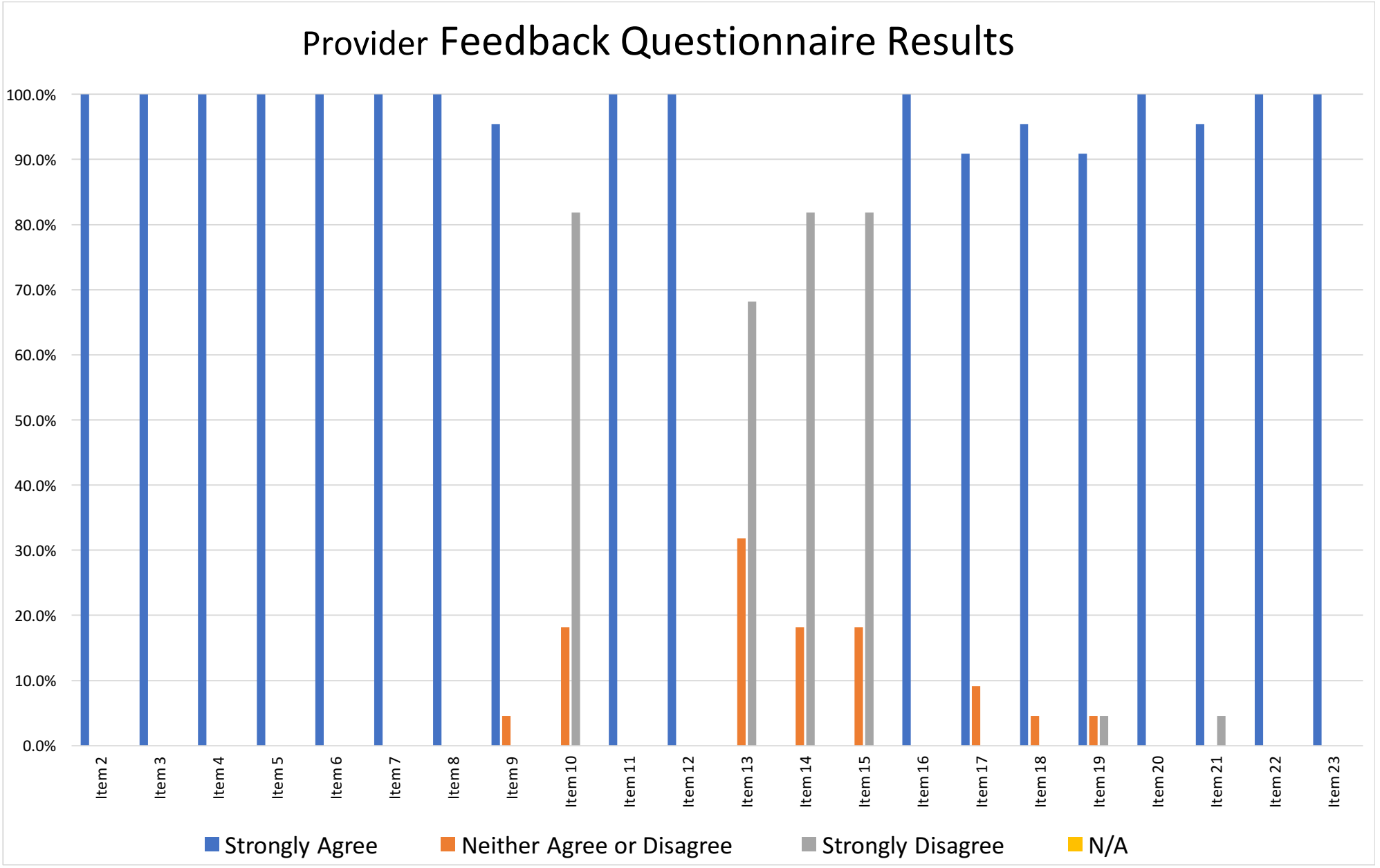


Figure 4. Provider Feedback Questionnaire Results.

Appendix A

Timeline of Anticipated Completion Dates for Quality Improvement Project

Anticipated Date for Completion	Description
June 2018	Submission of proposal to committee members/stakeholders for initial review.
June 2018	Secondary review of CPG with committee members/stakeholders.
July 2018	Submission of project proposal to UMSON IRB and hospital IRB.
December 2018	Proposal presentation to committee members/stakeholders containing recommended (final) revisions.
December 2018	Implementation of DNP project via presentation of CPG during grand rounds/Thursday morning meeting. Feedback via PFQ's obtained.
January 2019	Analysis, synthesis and evaluation of data from PFQ's.
February 2019	Final manuscript submission to committee/stakeholders for review.

Appendix B

MAP-IT

DNP Project Name: Implementation of a CPG for the use of sugammadex

DNP Project Purpose Statement: The aim of this project is implementation of a Clinical Practice Guideline for the use of sugammadex at a community hospital in Maryland by January 2019. The CPG will decrease the incidence of residual neuromuscular blockade, prolonged Post Anesthesia Care Unit (PACU) stay, adverse events such as respiratory and cardiovascular collapse and promote a more rapid reversal of neuromuscular blockade regardless of blockade depth.

Short-Term SMART Objectives:

1. By February 16, 2018, an expert panel of anesthesia personnel will be recruited to develop the CPG.
2. By March 17, 2018, a draft of the CPG will be completed.
3. By March 31, 2018, initial review of the CPG by expert panel, secondary revisions by April 7th, 2018, third revisions by April 28th, 2018.
4. By May 31st, 2018 there will be proposal of CPG to department of anesthesia.
5. By June 16th, 2018, analysis, synthesis, and evaluation of CPG based on PFQ from presentation.
6. By July 28, 2018, final revisions based on PFQ and Chief anesthesiologist recommendations.

Long-Term SMART Objectives:

1. By December 2018, the final CPG will be adopted and implemented at the institution.
2. By February 2019, greater than 75% of anesthesia clinicians will use sugammadex for reversal of neuromuscular blockade of rocuronium.
3. By March of 2019, there will be a decrease in the incidence of residual neuromuscular blockade, prolonged PACU stay, adverse events such as respiratory and cardiovascular collapse and promote a more rapid reversal of neuromuscular blockade regardless of blockade depth.

Population/Context: Anesthesia providers at a community hospital

in Maryland will be the audience for this guideline. The patient population targeted by this CPG will be any patient > or equal 18 years of age who is undergoing general anesthesia requiring the use of the NMBA's rocuronium or vecuronium. Patients excluded include pediatric patients (< or equal to 17 years of age), neuromuscular disease, pregnancy patients, women breast-feeding and patients with severe renal impairment requiring dialysis.

Mobilize: *WHO will help facilitate the changes in structures and processes (practices)?*

List of Core Team Members:

1. Dr. Htut – Anesthesiologist (MD)
2. Debra Curtits – Certified Registered Nurse Anesthetists (CRNA)
3. Danielle Goeren – Student Registered Nurse Anesthetists (SRNA)
4. Karissa Hansen – Student Registered Nurse Anesthetists (SRNA)
5. Jennifer Lewin – Student Registered Nurse Anesthetists (SRNA)

Others I will mobilize after the draft plans have been developed:

1. Dr. Joseph Pellegrini – Certified Registered Nurse Anesthetists (CRNA)/ Director of Nurse Anesthesia Program at the University of Maryland, Baltimore
2. Dr. Markas – Chief Anesthesiologist (MD)
3. Kathy Crowley – Chief Certified Registered Nurse Anesthetists (CRNA)

Assess: *WHAT structures and processes (practices) need to change and WHY? What structure, process, and outcome measures will be used to measure progress?*

- At this community hospital, it was recognized that the current sugammadex policy needed to be modified to explicitly state when sugammadex can and cannot be used secondary to the number of RNMB occurring (approximately 20x per year).

- An internal audit within this community hospital in Maryland was conducted to identify the amount of times sugammadex has been used over an eight-month period (n=103), the reasoning for the use of sugammadex and the number of patients who had RNMB in the past year (n=20). Providers examined if sugammadex was being used appropriately according to the current policy and found that it was not being used according to policy. The main reason being failed neostigmine reversal resulting in muscle weakness and low tidal volumes. Additionally, an external review of the literature was conducted to identify appropriate times to use sugammadex and compare it to the standard of care neostigmine and glycopyrrolate. Furthermore, the external review of the literature looked at best practice use of sugammadex, the history of the drug, treatment modalities and cost analysis.
- Without a practice guideline providers are inappropriately using sugammadex. By creating a CPG, providers will have a standard of care to direct the use of sugammadex at this community hospital in Maryland. The use of sugammadex will replace the current standard of care using neostigmine and glycopyrrolate for reversal of NMB.
- The CPG will be evaluated using the Appraisal of Guidelines for Research and Evaluation (AGREE) II tool which is considered the gold standard for guideline evaluation due to its construct validity (Brouwers et. al., 2010). The AGREE II tool was created by the AGREE Next Steps Consortium to evaluate the quality of CPG's. The tool consists of 23 items within six distinct domains and one section for an overall assessment of the CPG being evaluated (Appendix D). A seven point Likert scale ranging from "strongly agree" to "strongly disagree" is used to grade each item of the AGREE II tool. Each item is scored and the results are summarized within each domain to compare the CPG quality in that domain (AGREE Next Steps Consortium, 2009). Each member of the expert panel will receive an electronic copy of the AGREE II tool to evaluate the CPG. Using the AGREE II tool, each domain is separately examined with corresponding scores denoting the quality of data in that domain. The scores from each domain and from each expert panel member will be totaled then the maximum score and the minimum score will be subtracted. A percentage will be given by dividing the difference of the maximum and minimum scores by the totaled number from each domain. The percentage is then used to quantify the quality of the CPG as good or poor (AGREE Next Steps Consortium, 2009). Any domain that receives a poor-quality score will be discussed with the expert panel and revised for the final CPG.
- The practitioner feedback questionnaire (PFQ) will be used to evaluate the provider's attitudes towards the CPG. The PFQ was used because of its content validity and reliability that was established by Cronbach's alpha coefficient (Brouwers, Graham, Hanna, Cameron, & Browman, 2004). The PFQ is a twenty-three-item questionnaire using a three point Likert scale ranging from "strongly agree" to "strongly disagree" except for four items (#10, 13, 14, & 15) which are negative items reverse scored. A PFQ is designed specifically for adopters of a CPG. The purpose of the PFQ is to identify potential barriers to implementation by assessing the CPG for quality, applicability and acceptability (Brouwers, Graham, Hanna, Cameron, & Browman, 2004). The PFQ was given to each attendee at the presentation of the CPG in a paper/pen format. The data obtained from the PFQ was grouped by the number of years' experience of the provider. There were three groups: 0-5 years of experience, 5-10 years of experience, and greater than 10 years of experience. A univariate frequency table is used to show the frequency of each score for each item. The frequency of each item is then divided by the total number of questions and made a percent. These statistical tests are used to investigate the response to each question and compare among the three groups.

Plan: *HOW will these changes be made (strategies and tactics)? WHEN will these changes be made?*

Phase One:

1. February 2018
    a. Review of current literature and recruit expert panel to develop clinical practice guideline
2. March 2018
    a. Initial meeting with expert panel
    b. Create tentative schedule with meetings, everyone's role in project and purpose of project
3. May 2018
    a. Complete first draft of CPG
    b. Email the first draft of CPG to all stakeholders for review with instructions to use the AGREE II tool to evaluate
4. June 2018
    a. Initial review of CPG completed by expert panel
    b. Meeting to go over CPG recommendations from initial review and make necessary changes to send back to expert panel
    c. Submission of project proposal second draft to UMSON IRB and hospital IRB
5. June 2018
    a. Secondary review of CPG by expert panel completed
    b. Meeting to go over CPG recommendations from second review and make necessary changes to send back to expert panel
    c. Submit third draft to expert panel and Dr. Pellegrini for final review before chief anesthesiologist
6. July 2018

a. Third revisions of CPG from expert panel and Dr. Pellegrini recommendations completed
b. Meeting to go over CPG recommendations from third review and make necessary changes

Phase Two:

1. July 2018
   a. Proposal of CPG to Department of Anesthesia including Dr. Markas, MD (Chief Anesthesiologist) and Kathy Crowley, CRNA (Chief CRNA) for approval
2. August 2018
   a. Completed review by Dr. Markas and Kathy Crowley
   b. Meeting to go over CPG recommendations from fourth review and make necessary changes from feedback received
   c. Final CPG sent to back to Dr. Markas for approval

Phase Three:

1. December 2018
   a. Presentation to the anesthesia providers during department meeting
   b. At end of presentation give providers PFQ questionnaire with instructions to complete
   c. Collect at minimum of 75% of the PFQ questionnaires
2. January 2019
   a. Analysis, synthesis and evaluation of CPG based on PFQ questionnaire
2. January 2019
   a. Final revisions based on PFQ and Chief Anesthesiologist recommendations
   b. Meet with Dr. Markas, MD and Kathy Crowley, CRNA for final review and edits
3. February 2019
   a. Final CPG will be implemented at the institution
4. August 2019
   a. Greater than 75% of the anesthesia clinicians will use sugammadex appropriately and according to the new guidelines
5. August 2019
   a. There will be a decrease in the incidence of RNMB, prolonged PACU stay, adverse events such as respiratory and cardiovascular collapse and promote a more rapid reversal of NMB regardless of blockade depth

Implement: *WHAT strategies and tactics were used? WHEN were the desired changes made?*

Step 1: Perform small tests of change

- By December 2018, all anesthesia staff will be educated on the new CPG and policy changes regarding the use of sugammadex. This will occur at the presentation by the students at the Thursday morning meeting to the department. The students will educate and inform the staff to increase the level of comfort with sugammadex use.

Step 2: Full-scale implementation

- By February 2019, all anesthesia staff will be re-educated and reminded that the CPG has been adopted and implemented at the institution. All questions and concerns will be addressed at Thursday morning meetings throughout the month. Students will be educating and taking any feedback from providers.

Track: *WHAT structures and processes (practices) were changed based on the metrics we used to measure progress (including frequency of assessment)? HOW did these changes affect outcomes? WHAT do we need to do differently to make greater progress toward improving outcomes?*

1. March 2019, PFQs will be given out to anesthesia providers every 6 months to review how implementation of CPG is going.
2. March 2019, internal data will be reviewed every year to access use of sugammadex, reason for use and RNMB cases.
3. March 2019, a decrease in the incidence of RNMB, prolonged PACU stay, adverse events such as respiratory and cardiovascular collapse and promote a more rapid reversal of NMB regardless of blockade depth will be noted at the community hospital in Maryland
4. Based on PFQs and internal review all recommendations will be used to revise CPG if applicable.

Date: April 30th, 2018 **Re-Assessment Date 1:** June 2018 **Re-Assessment Date 2:** July 2018

Plan Developed by (List all contributors): Danielle Goeren, Karissa Hansen, Jennifer Lewin, Debra Curtis, Dr. Htut, and Joseph Pellegrini

Reference: Guidry, M., Vischi, T., Han, R., & Passons, O. MAP-IT: a guide to using healthy people 2020 in your community. U.S. Department of Health and Human Services. The Office of Disease Prevention and Health Promotion, Washington, D.C. https://www.healthypeople.gov/2020/tools-and-resources/Program-Planning

Appendix C

CLINICAL PRACTICE GUIDELINE: SUGAMMADEX TREATMENT MODALITIES TO REDUCE RESIDUAL NEUROMUSCULAR BLOCKADE

Background and Significance

One of the commonly observed challenges of anesthesia is generalized muscle weakness or residual neuromuscular blockade (RNMB) after administration of neuromuscular blocking agents (NMBAs) (Murphy et al., 2011). Neuromuscular blocking agents are most often used in general anesthesia to produce neuromuscular blockade (NMB) or muscle paralysis intraoperatively. Muscle paralysis facilitates intubation and decreases patient movement which increases operating conditions. The degree of paralysis can be monitored with the use of a nerve stimulator that activates muscle contraction. Nerve stimulators are used to produce a train-of-four (TOF) or post tetanic counts (PTC) that allow the provider to assess the depth of neuromuscular blockade (Srivastava & Hunter, 2009).

Residual neuromuscular blockade is "incomplete neuromuscular recovery in the early postoperative period defined as a TOF ratio of less than 0.9" (Murphy et al., 2011, p.946). Risks of RNMB are multifactorial including patient factors (i.e. age, comorbidities, etc.), pharmacological causes (i.e. drug interactions), duration and type of anesthesia (i.e. opioid use, benzodiazepine use, etc.), and metabolic causes (i.e. acidosis, etc.) (Srivastava & Hunter, 2009). Residual neuromuscular blockade impairs airway patency increasing the risk of post-operative complications such as reduced upper airway volumes, airway obstruction and hypoxemia events. In fact, 38 – 64% of patients who receive intermediate- acting NMBAs experience RNMB. In a study of more than 200,000 cases where paralytics were administered, 64% of cardiac arrests were related to airway complications in the PACU (Ellis et al., 2014). 23% of these cases occurred within the first 24 hours of the perioperative period, with a mortality rate of 29% (Ellis et al., 2014). The absence of residual paralysis not only can decrease poor outcomes, but more importantly the capability to save a patient's life. Awake volunteers, with a TOF ratio of 0.7-0.75, described RNMB as "unpleasant symptoms" such as generalized fatigue, decreased grip strength, visual disturbances, facial weakness, difficulty speaking, keeping their eyes open and swallowing (Murphy et al., 2011, p. 947).

Delayed discharge from the PACU has been shown to be a concerning direct result of residual paralysis. In a study of 248 patients, 22% experienced residual paralysis. This resulted in a 114-minute increase in PACU length of stay (Butterly et al., 2010). Regarding the surgical patient population as a whole, the absence of residual paralysis would allow anesthesia providers and PACU nurses the ability to recover, extubate, and progress patients to the next level of care without fear of consequences associated with its presence. This translates into increased efficiency in overall PACU flow and scheduling of surgical cases. According to Miller et al. (2010), a shorter length of stay can lead to decreased institutional costs by lessening the need for overtime personnel such recovery room nurses and nursing aids. In turn, this has the potential for enhanced staff satisfaction. Decreased wait times, faster discharges, and better outcomes naturally lead to a rise in patient and family satisfaction.

In 2006, a publication of a study about the first use of sugammadex in humans was published. Over the past decade, the number of studies regarding sugammadex and clinical practice using sugammadex has greatly increased proving that sugammadex eliminates post-operative complications, such as RNMB, and improves surgical conditions (Carron, Zarantonello, & Tellaroli, 2016). Sugammadex is a modified y-cyclodextrin, created to bind to free plasma molecules of aminosteroid NMBAs, specifically rocuronium, which it has high affinity for. The use of sugammadex allows for full reversal with deep NMB within 5 minutes; however, full reversal after sugammadex use most often occurs even faster within 2-3 minutes (Martini, Boon, Bevers, Aarts, & Dahan, 2013).

Sugammadex is proven to be superior, reliable and faster compared to its competition neostigmine. Neostigmine can result in incomplete reversal or RNMB and has potent parasympathetic activity that causes adverse effects, such as bradycardia, nausea and vomiting. The difference between these drugs is a result of their mechanism of action (Carron et al., 2016). Unlike the ceiling effect and adverse effects seen with neostigmine, sugammadex encapsulates the rocuronium and rarely causes RNMB or any adverse events. The sugammadex-rocuronium complex has a high association and low dissociation rate. It is estimated that for every 25 million complexes one complex will dissociate (Nag et al., 2013). By encapsulating the rocuronium it is removed from the neuromuscular junction and allows return of muscle function. Neostigmine increases the concentration of acetylcholine at the neuromuscular junction to compete and displace the rocuronium from the site; however, the rocuronium is not completely removed and can paradoxically compete for the receptor site causing RNMB (Carron et al., 2016).

Evidence supports that sugammadex use is effective, safe, allows rapid reversal of NMB and reduces the incidences of RNMB (Brueckmann et al., 2015). The purpose of this Doctorate in Nursing Practice (DNP) project is to modify the current policy, at a community hospital, regarding the use of sugammadex. Currently, at this institution sugammadex has been used 103 times over an eight-month period. The main reason being failed neostigmine reversal resulting in muscle weakness and low tidal volumes. An evidence-based clinical practice guideline (CPG) will be implemented that clearly identifies when sugammadex can and cannot be used at this Maryland hospital. The anticipated outcome is adoption and implementation of the CPG at the institution. Short-term goals are 1) recruitment of expert panel, 2) draft the CPG, 3) initial, secondary and third revisions of CPG, 4) proposal of CPG to anesthesia department, 5) analysis, synthesis and evaluation of CPG based on feedback, 6) final revisions and draft of CPG. Long-term goals are 1) adoption and implementation of the CPG, 2) greater than 75% of clinicians will use sugammadex for reversal of NMB and 3) to reduce incidences of RNMB and its associated complications.

Scope and Purpose

The purpose of this Doctor of Nursing Practice project is to develop a clinical practice guideline (CPG) for the administration of sugammadex as a reversal agent for paralytics used by anesthesia personnel. This CPG will address the question: Does the use of sugammadex as a reversal agent for rocuronium and vecuronium induced neuromuscular blockade reduce the incidence of residual neuromuscular blockade in adult patients undergoing general anesthesia requiring neuromuscular blockade agents. Presentation of this CPG will facilitate education of Anesthesia Department staff of a medium-sized community hospital on the superiority of sugammadex over Neostigmine in its ability to effectively reverse NMB and thus decrease the incidence of residual paralysis, with additional benefits as a rescue drug in the emergent "cannot ventilate, cannot intubate" scenario. The anticipated outcome is that sugammadex will be more effective in the reversal of neuromuscular blockade with fewer side effects, and no residual paralysis. The audience targeted by this CPG presentation are the anesthesia providers and Post Anesthesia Care Unit (PACU) registered nurses. The targeted patient population for this CPG will be adults (> or equal to 18 years of age) who are undergoing general anesthesia requiring the use of the neuromuscular blocking agents rocuronium or vecuronium that meet the inclusion/exclusion criteria mentioned below.

Inclusion/Exclusion Criteria

For this guideline, the following inclusion criteria will be used: male/females, $\geq$ 18 years old, patients undergoing general anesthesia requiring the use of the neuromuscular blocking agents rocuronium or vecuronium. Exclusion criteria includes pediatric patients (< or equal to 17 years of age), neuromuscular disease, pregnancy patients, women breast-feeding and patients with severe renal impairment requiring dialysis.

Stakeholders Involvement

Residual neuromuscular blockade has been identified as an area of improvement for this community hospital. Anesthesia providers responsible for patient care in the perioperative period at this location have identified RNMB as a potential contributor to prolonged PACU stays. Interest in the use of sugammadex as a reversal agent for RNMB has been recognized. An extensive literature reviewed (see below) describes how the information for the CPG was gathered and how practice recommendations were decided upon. Collaboration among an expert panel will facilitate the creation, presentation, and implementation of this sugammadex CPG. A Certified Registered Nurse Anesthetist (CRNA) with a terminal DNP degree, an Anesthesiologist, and three Student Registered Nurse Anesthetists (SRNAs) practicing at this community hospital are members of the expert panel. Additionally, a faculty member at the University of Maryland School of Nursing with a PhD or DNP degree will be a part of the expert panel. Each member will be invested in using their expertise to collaborate on the development and implementation of sugammadex use at this institution. The CRNA, Anesthesiologist and school faculty member will use the AGREE II Tool to aid the students in revising and making changes to the CPG. The final CPG will be finalized by the Chief Anesthesiologist and CRNA at the community hospital. The target audience of this CPG will be perioperative providers such as CRNAs, Anesthesiologists, and Registered Nurses in this area. The guideline will be used to inform standard of care with the use of sugammadex.

Literature Review, Analysis and Synthesis

PubMed, CINAHL, and Cochrane Library electronic databases were searched for literature. The search was limited to articles published between January 2008 to March 2018. Medical Subject Heading (MeSH) terms were used to search for articles and included words such as "sugammadex," "neostigmine," "neuromuscular blockade," "residual neuromuscular blockade," "residual paralysis," "anesthesia," and "neuromuscular blocking agents." This resulted in 128 articles, which were further narrowed to only include RCTs, meta analyses, and systematic reviews. A total of 6 articles were identified as being most relevant to the development of this CPG and included in the literature review.

The literature review highlights the significance of four articles, two systematic reviews of randomized control trials (RCTs), one meta-analysis of RCTs, and one RCT. The review will discuss the safety and efficacy of sugammadex, and the decrease of residual neuromuscular blockade when sugammadex is used. Carron, Zarantonello & Tellaroli (2016), completed a meta-analysis of randomized control trials (RCTs) to compare the safety and effectiveness of sugammadex administration versus Neostigmine in the reversal of neuromuscular blockade. The study concluded that when compared to neostigmine, sugammadex was notably faster in reversing neuromuscular blockade ($P < 0.0001$), and was associated with a higher train-of-four ratio at extubation ($P < 0.0001$). Sugammadex was also concluded to have lower adverse respiratory events ($P = 0.0386$), lower cardiac adverse events ($P = 0.0036$), and significantly lower global adverse events ($P = < 0.0001$) (Carron, Zarantonello, & Tellaroli, 2016). Hristovska, Duch, Allingstrup & Afshari (2017), similarly compared the efficacy and safety of sugammadex to neostigmine. the review found sugammadex to be 6.6 times faster than neostigmine in reversal of moderate NMB and 16.8 times faster in reversal of deep NMB (Hristovska, Duch, & Afshari, 2017). With the use of sugammadex adverse events such as bradycardia and postoperative nausea and vomiting are reduced up to 40 percent (Hristovska et al., 2017).

Ledowski (2015) completed a systematic review of RCTs to examine the optimal use of sugammadex and determine its place in clinical practice. The review concluded that sugammadex is more rapid and more reliable in the reversal of NMBAs. The use of sugammadex results in a more rapid return of muscle strength which assists with easier

management of difficult airway situations. Lastly, Brueckmann et al. (2015), completed a RCT to determine if the use of sugammadex in the reversal of rocuronium induced neuromuscular blockade was effective in preventing residual paralysis. The study revealed that no residual blockade was found in patients in group 1, those who received sugammadex, but 43.4 percent of those in group 2 who received neostigmine had residual blockade (n = 33). Sugammadex was shown to be 3 to 18 times faster in the reversal of rocuronium-induced NMBA when compared to neostigmine. Operating room discharged time was faster following sugammadex (14.7 minutes, $p = 0.02$) when compared to neostigmine (18.6 minutes).

The results of these recent studies indicate that sugammadex is safe and effective for the reversal of NMBAs, and results in reduced adverse events. This is in comparison to the current reversal agent, neostigmine, which has a numerous amount of undesirable side effects. Sugammadex's ability to reverse NMBAs has major implications for routine anesthesia practice. The ability of sugammadex to rapidly reverse NMBAs could play a critical role in the dangerous 'cannot intubate, cannot ventilate" situations. All the studies discussed conclude that sugammadex is superior in reversal of NMBAs in terms of speed, efficacy and side effects

Methods

The CPG was created by the collaboration of five people who were vested in the success of the CPG to establish a clear standard of care for the use of sugammadex at this community hospital. The expert panel that developed the CPG included three doctoral candidate SRNAs, a CRNA with a terminal degree and an Anesthesiologist at the medical institution of interest. The process used to create, assess and evaluate the CPG is listed below:

1. Identification of the problem, expert panel and current evidence to be used to address the identified problem at the medical institution of interest.
2. Review of literature addressing the use of preoperative carbohydrate loading to decrease postoperative nausea and vomiting.
3. Expert panel completed a review of the preliminary guideline using the AGREE II tool.
4. Several meetings were conducted with the expert panel to address recommendations and comments from the AGREE II tool results. Revisions of the preliminary guidelines were made based on feedback provided.
5. Target users were given a questionnaire to evaluate the attitudes and feasibility of implementing the guideline.
6. The expert panel developed a final guideline incorporating all the feedback of both the AGREE II tool and questionnaire.

Benefits and Risk

Benefits:

- Decreased incidence of residual paralysis
- Increased safety profile with less adverse events such as cardiovascular and respiratory side effects
- Increased muscle strength after NMB
- Decreased PACU length of stay/shorter recovery time
- Useful in "cannot ventilate, cannot intubate" scenarios after NMB

Risks:

- Cost compared to neostigmine
- Rare reports of bradycardia, nausea, vomiting and allergic reaction
- Interacts with contraceptives, decreasing their effectiveness.

Practice Recommendations

Surgical patients older than 18 years of age undergoing surgical procedures necessitating the use of paralytics should receive sugammadex as the agent of choice in the reversal of NMB. Consequently, the negative effects associated with the use of Neostigmine such as residual paralysis would be negated. Incorporating sugammadex will reduce postoperative residual neuromuscular blockade and increased patient's outcomes. This CPG is recommended to be used by perioperative providers such as CRNAs, MDAs, Surgeons and Registered Nurses in perioperative areas. The outcomes of the CPG should be continually monitored by the anesthesia staff and evaluated after implementation. Every two to three years a literature review of the current evidence should be conducted to update the CPG. The targeted patient population for this CPG will be adult (> or equal to 18 years old) surgical patients. This guideline should not to be used for patients with any of the following:

- pediatric patients (< or equal to 17 years of age)
- neuromuscular disease
- pregnancy
- women breast-feeding

- patients with severe renal impairment requiring dialysis

Facilitators and Barriers

The implementation of this CPG may create potential barriers. These potential barriers include the cost of the sugammadex, education and training of the perioperative and anesthesia staff and resistance to change by the providers. Facilitators of the sustainability of the CPG include education of staff, staff involvement and feedback, accessibility of the affordable sugammadex and user-friendly guideline that is clear and concise.

Appendix D

AGREE II Tool

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA
DOMAIN 1: SCOPE AND PURPOSE	
1. OBJECTIVES *Report the overall objective(s) of the guideline. The expected health benefits from the guideline are to be specific to the clinical problem or health topic.*	Health intent(s) (i.e., prevention, screening, diagnosis, treatment, etc.) Expected benefit(s) or outcome(s) Target(s) (e.g., patient population, society)
2. QUESTIONS *Report the health question(s) covered by the guideline, particularly for the key recommendations.*	Target population Intervention(s) or exposure(s) Comparisons (if appropriate) Outcome(s) Health care setting or context
3. POPULATION *Describe the population (i.e., patients, public, etc.) to whom the guideline is meant to apply.*	Target population, sex and age Clinical condition (if relevant) Severity/stage of disease (if relevant) Comorbidities (if relevant) Excluded populations (if relevant)
DOMAIN 2: STAKEHOLDER INVOLVEMENT	
4. GROUP MEMBERSHIP *Report all individuals who were involved in the development process. This may include members of the steering group, the research team involved in selecting and reviewing/rating the evidence and individuals involved in formulating the final recommendations.*	Name of participant Discipline/content expertise (e.g., neurosurgeon, methodologist) Institution (e.g., St. Peter's hospital) Geographical location (e.g., Seattle, WA) A description of the member's role in the guideline development group

5. TARGET POPULATION PREFERENCES AND VIEWS *Report how the views and preferences of the target population were sought/considered and what the resulting outcomes were.*	Statement of type of strategy used to capture patients'/publics' views and preferences (e.g., participation in the guideline development group, literature review of values and preferences) Methods by which preferences and views were sought (e.g., evidence from literature, surveys, focus groups) Outcomes/information gathered on patient/public information How the information gathered was used to inform the guideline development process and/or formation of the recommendations
6. TARGET USERS *Report the target (or intended) users of the guideline.*	The intended guideline audience (e.g. specialists, family physicians, patients, clinical or institutional leaders/administrators) How the guideline may be used by its target audience (e.g., to inform clinical decisions, to inform policy, to inform standards of care)
DOMAIN 3: RIGOUR OF DEVELOPMENT	
7. SEARCH METHODS *Report details of the strategy used to search for evidence.*	Named electronic database(s) or evidence source(s) where the search was performed (e.g., MEDLINE, EMBASE, PsychINFO, CINAHL) Time periods searched (e.g., January 1, 2004 to March 31, 2008) Search terms used (e.g., text words, indexing terms, subheadings) Full search strategy included (e.g., possibly located in appendix)
8. EVIDENCE SELECTION CRITERIA *Report the criteria used to select (i.e., include and exclude) the evidence. Provide rationale, where appropriate.*	Target population (patient, public, etc.) characteristics Study design Comparisons (if relevant) Outcomes Language (if relevant) Context (if relevant)
9. STRENGTHS & LIMITATIONS OF THE EVIDENCE *Describe the strengths and limitations of the evidence. Consider from the perspective of the individual studies and the body of evidence aggregated across all the studies. Tools exist that can facilitate the reporting of this concept.*	Study design(s) included in body of evidence Study methodology limitations (sampling, blinding, allocation concealment, analytical methods) Appropriateness/relevance of primary and secondary outcomes considered Consistency of results across studies Direction of results across studies Magnitude of benefit versus magnitude of harm Applicability to practice context

10. FORMULATION OF RECOMMENDATIONS *Describe the methods used to formulate the recommendations and how final decisions were reached. Specify any areas of disagreement and the methods used to resolve them.*	Recommendation development process (e.g., steps used in modified Delphi technique, voting procedures that were considered) Outcomes of the recommendation development process (e.g., extent to which consensus was reached using modified Delphi technique, outcome of voting procedures) How the process influenced the recommendations (e.g., results of Delphi technique influence final recommendation, alignment with recommendations and the final vote)
11. CONSIDERATION OF BENEFITS AND HARMS *Report the health benefits, side effects, and risks that were considered when formulating the recommendations.*	Supporting data and report of benefits Supporting data and report of harms/side effects/risks Reporting of the balance/trade-off between benefits and harms/side effects/risks Recommendations reflect considerations of both benefits and harms/side effects/risks
12. LINK BETWEEN RECOMMENDATIONS AND EVIDENCE *Describe the explicit link between the recommendations and the evidence on which they are based.*	How the guideline development group linked and used the evidence to inform recommendations Link between each recommendation and key evidence (text description and/or reference list) Link between recommendations and evidence summaries and/or evidence tables in the results section of the guideline
13. EXTERNAL REVIEW *Report the methodology used to conduct the external review.*	Purpose and intent of the external review (e.g., to improve quality, gather feedback on draft recommendations, assess applicability and feasibility, disseminate evidence) Methods taken to undertake the external review (e.g., rating scale, open-ended questions) Description of the external reviewers (e.g., number, type of reviewers, affiliations) Outcomes/information gathered from the external review (e.g., summary of key findings) How the information gathered was used to inform the guideline development process and/or formation of the recommendations (e.g., guideline panel considered results of review in forming final recommendations)
14. UPDATING PROCEDURE *Describe the procedure for updating the guideline.*	A statement that the guideline will be updated Explicit time interval or explicit criteria to guide decisions about when an update will occur Methodology for the updating procedure
DOMAIN 4: CLARITY OF PRESENTATION	
15. SPECIFIC AND UNAMBIGUOUS RECOMMENDATIONS *Describe which options are appropriate in which situations and in which population groups, as informed by the body of evidence.*	A statement of the recommended action Intent or purpose of the recommended action (e.g., to improve quality of life, to decrease side effects) Relevant population (e.g., patients, public) Caveats or qualifying statements, if relevant (e.g., patients or conditions for whom the recommendations would not apply) If there is uncertainty about the best care option(s), the uncertainty should be stated in the guideline
16. MANAGEMENT OPTIONS *Describe the different options for managing the condition or health issue.*	Description of management options Population or clinical situation most appropriate to each option

17. IDENTIFIABLE KEY RECOMMENDATIONS *Present the key recommendations so that they are easy to identify.*	Recommendations in a summarized box, typed in bold, underlined, or presented as flow charts or algorithms Specific recommendations grouped together in one section
DOMAIN 5: APPLICABILITY	
18. FACILITATORS AND BARRIERS TO APPLICATION *Describe the facilitators and barriers to the guideline's application.*	Types of facilitators and barriers that were considered Methods by which information regarding the facilitators and barriers to implementing recommendations were sought (e.g., feedback from key stakeholders, pilot testing of guidelines before widespread implementation) Information/description of the types of facilitators and barriers that emerged from the inquiry (e.g., practitioners have the skills to deliver the recommended care, sufficient equipment is not available to ensure all eligible members of the population receive mammography) How the information influenced the guideline development process and/or formation of the recommendations
19. IMPLEMENTATION ADVICE/TOOLS *Provide advice and/or tools on how the recommendations can be applied in practice.*	Additional materials to support the implementation of the guideline in practice. For example: Guideline summary documents Links to check lists, algorithms Links to how-to manuals Solutions linked to barrier analysis (see Item 18) Tools to capitalize on guideline facilitators (see Item 18) Outcome of pilot test and lessons learned
20. RESOURCE IMPLICATIONS *Describe any potential resource implications of applying the recommendations.*	Types of cost information that were considered (e.g., economic evaluations, drug acquisition costs) Methods by which the cost information was sought (e.g., a health economist was part of the guideline development panel, use of health technology assessments for specific drugs, etc.) Information/description of the cost information that emerged from the inquiry (e.g., specific drug acquisition costs per treatment course) How the information gathered was used to inform the guideline development process and/or formation of the recommendations
21. MONITORING/ AUDITING CRITERIA *Provide monitoring and/or auditing criteria to measure the application of guideline recommendations.*	Criteria to assess guideline implementation or adherence to recommendations Criteria for assessing impact of implementing the recommendations Advice on the frequency and interval of measurement Operational definitions of how the criteria should be measured

DOMAIN 6: EDITORIAL INDEPENDENCE	
22. FUNDING BODY *Report the funding body's influence on the content of the guideline.*	The name of the funding body or source of funding (or explicit statement of no funding) A statement that the funding body did not influence the content of the guideline
23. COMPETING INTERESTS *Provide an explicit statement that all group members have declared whether they have any competing interests.*	Types of competing interests considered Methods by which potential competing interests were sought A description of the competing interests How the competing interests influenced the guideline process and development of recommendations

(AGREE Next Steps Consortium, 2009)

Appendix E

Practitioner Feedback Questionnaire

Please select the appropriate demographic category that most accurately describes you.

Type of anesthesia provider:	Years practiced in current role:
CRNA ☐ Anesthesiologist ☐ SRNA ☐	<5 ☐ 5-10 ☐ 10-15 ☐ 15-20 ☐ 20-25 ☐ >25 ☐

For each item, please check off the box that most adequately reflects your opinion.

1. Are you responsible for the care of patients for whom this draft guideline report is relevant? This may include the referral, diagnosis, treatment, or follow-up of patients.	Yes ☐	No ☐	Unsure ☐
If you answered "*No*" or "*Unsure*", there is no need to answer or return this questionnaire. If you answered "*Yes*", please answer the questions below and return to **[enter expected destination of surveys]**.			
	Strongly agree	Neither agree or disagree	Strongly disagree
2. The rationale for developing a guideline is clear.	☐	☐	☐
3. There is a need for a guideline on this topic.	☐	☐	☐
4. The literature search is relevant and complete (e.g., no key evidence was missed nor any included that should not have been) in this draft guideline.	☐	☐	☐
5. I agree with the methodology used to summarize the evidence included in this draft guideline.	☐	☐	☐
6. The results of the evidence described in this draft guideline are interpreted according to my understanding of the evidence.	☐	☐	☐
7. The draft recommendations in this report are clear.	☐	☐	☐
8. I agree with the draft recommendations as stated.	☐	☐	☐
9. The draft recommendations are suitable for the patients for whom they are intended.	☐	☐	☐
10. The draft recommendations are too rigid to apply to individual patients.	☐	☐	☐
11. When applied, the draft recommendations will produce more benefits for patients than harms.	☐	☐	☐
12. The draft guideline presents options that will be acceptable to patients.	☐	☐	☐
13. To apply the draft recommendations will require reorganization of services/care in my practice setting.	☐	☐	☐
14. To apply the draft guideline recommendations will be technically challenging.	☐	☐	☐
15. The draft guideline recommendations are too expensive to apply.	☐	☐	☐
16. The draft guideline recommendations are likely to be supported by a majority of my colleagues.	☐	☐	☐
17. If I follow the draft guideline recommendations, the expected effects on patient outcomes will be obvious.	☐	☐	☐
18. The draft guideline recommendations reflect a more effective approach for improving patient outcomes than is current usual practice. (If they are the same as current practice, please tick NA). *NA* ☐	☐	☐	☐
19. When applied, the draft guideline recommendations will result in better use of resources than current usual practice. (If they are the same as current practice, please tick NA). *NA* ☐	☐	☐	☐
20. I would feel comfortable if my patients received the care recommended in the draft guideline.	☐	☐	☐
21. This draft guideline should be approved as a practice guideline.	☐	☐	☐
22. If this draft guideline were to be approved as a practice guideline, I would use it in my own practice.	☐	☐	☐
23. If this draft guideline were to be approved as a practice guideline, I would apply the recommendations to my patients.	☐	☐	☐

Adapted from: Brouwers, M.C., Graham, I.D., Hanna, S.E., Cameron, D.A., & Browman, G.P. (2004). Clinicians' assessments of practice guidelines in oncology: The CAPGO survey**.** *International Journal of Technology Assessment in Health Care, 20*(4), 421-6.

Appendix F

Project Proposal Summary

Background: Residual neuromuscular blockade (RNMB) is "incomplete neuromuscular recovery in the early postoperative period defined as a TOF ratio of less than 0.9" (Murphy et al., 2011, p.946). RNMB impairs airway patency increasing the risk of post-operative complications such as reduced upper airway volumes, airway obstruction and hypoxemia events. In fact, 38 – 64% of patients who receive intermediate- acting NMBAs experience RNMB (Murphy et al., 2011). Over the past decade, the number of studies regarding sugammadex and clinical practice using sugammadex has greatly increased proving that sugammadex eliminates post-operative complications, such as RNMB, and improves surgical conditions (Carron, Zarantonello, & Tellaroli, 2016). Sugammadex is proven to be superior, reliable and faster compared to its competition neostigmine.

Purpose Statement: The aim of this project is to modify the current policy, at a community hospital, regarding the use of sugammadex. Currently, at this institution sugammadex has been used 103 times over an eight-month period. The main reason being failed neostigmine reversal resulting in muscle weakness and low tidal volumes. An evidence-based clinical practice guideline (CPG) will be implemented that clearly identifies when sugammadex can and cannot be used at this Maryland hospital.

Evidence to Support Practice Change: Evidence supports that sugammadex use is effective, safe, allows rapid reversal of NMB and reduces the incidences of RNMB (Brueckmann et al., 2015). The use of sugammadex will replace the current standard of care using neostigmine and glycopyrrolate for reversal of NMB. Neostigmine can result in incomplete reversal or RNMB and has potent parasympathetic activity that causes adverse effects, such as bradycardia, nausea and vomiting. Unlike neostigmine, sugammadex encapsulates the rocuronium and rarely causes RNMB or any adverse events. The sugammadex-rocuronium complex has a high association and low dissociation rate. It is estimated that for every 25 million complexes one complex will dissociate (Nag et al., 2013). By encapsulating the rocuronium it is removed from the neuromuscular junction and allows return of muscle function (Carron et al., 2016).

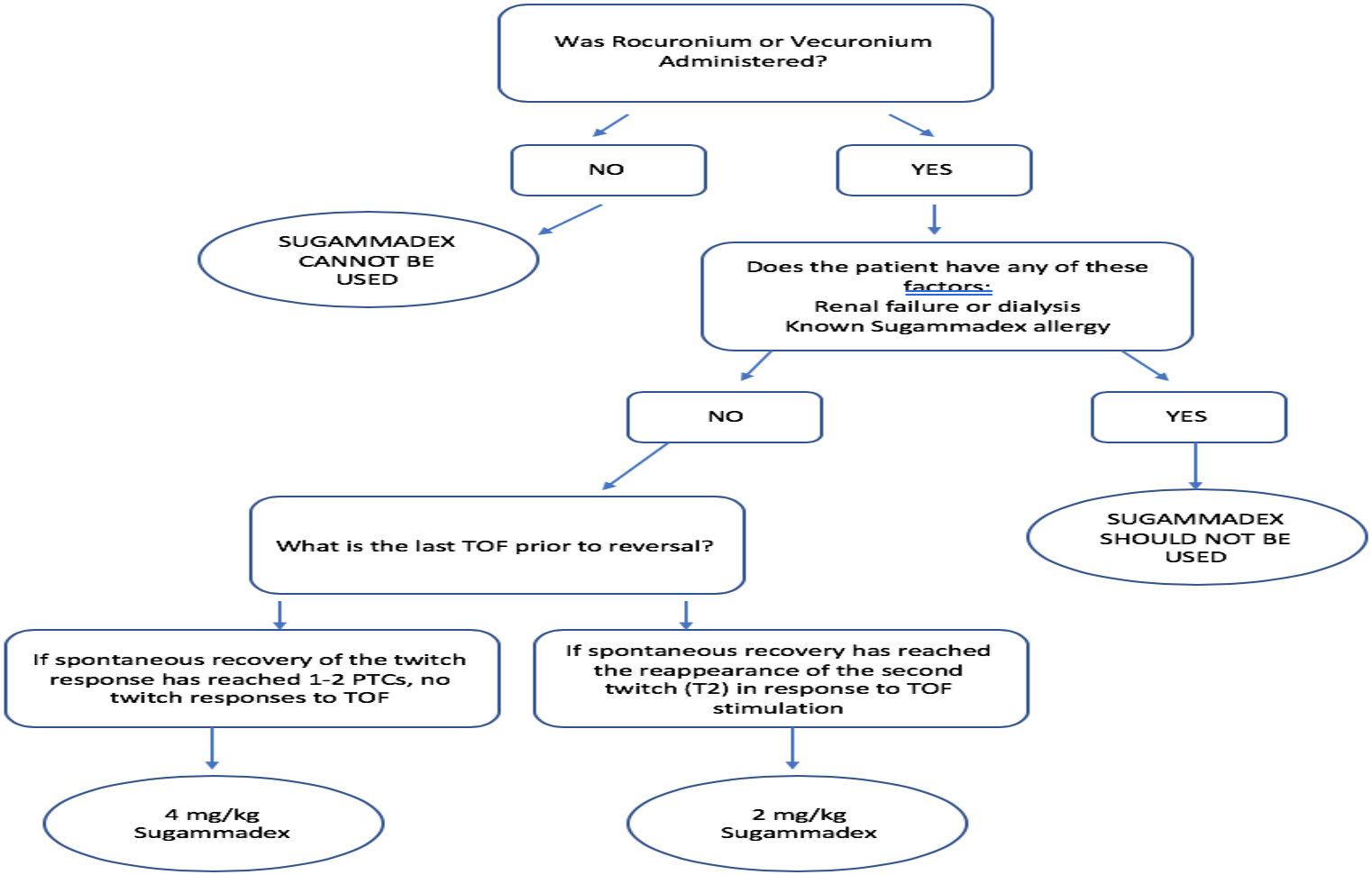
Implementation Plan: Three phases of the project will be implemented from February 2018-August 2019. Phase one of the project will consist of identifying the clinical problem, expert panel and current evidence. A CPG draft is created and an Appraisal of Guidelines for Research and Evaluation (AGREE II tool) will be used to revise the CPG. The expert panel includes a CRNA with a terminal degree and one MDA at the institution of interest. Phase two of the project, involves including recommendations from the chief anesthesiologist and revising the CPG which will then be presented at Anesthesia Grand Rounds. Phase three is used to evaluate feedback from the presentation and create a final CPG with all feedback.

Data Collection and Analysis Plan: The CPG will be evaluated using the AGREE II tool as it is considered the gold standard for guideline evaluation and has construct validity (Brouwers et. al., 2010). The tool consists of 23 items within six distinct domains and one section for an overall assessment of the CPG being evaluated. A seven point Likert scale ranging from "strongly agree" to "strongly disagree" is used to grade each item of the AGREE II tool. Each item is scored and the results are summarized within each domain to compare the CPG quality in that domain (AGREE Next Steps Consortium, 2009). Each member of the expert panel will receive an electronic copy of the AGREE II tool to evaluate the CPG. Any domain that receives a poor-quality score will be discussed with the expert panel and revised for the final CPG. The practitioner feedback questionnaire (PFQ) will be used because of its content validity and reliability established by Cronbach's alpha coefficient. The PFQ is a twenty-three-item questionnaire using a three point Likert scale ranging from "strongly agree" to "strongly disagree" except for four items (#10, 13, 14, & 15) which are negative items reverse scored. The purpose of the PFQ is to identify potential barriers to implementation by assessing the CPG for quality, applicability and acceptability (Brouwers, Graham, Hanna, Cameron, & Browman, 2004).

Measures to Protect Human Rights: The University of Maryland Baltimore Institutional Review Board for a Non-Human Subjects Research will receive a submission of proposal of this project for determination. The participants acknowledge verbal disclosure of voluntary involvement in this project. To protect the privacy of the participants, no identifiers will be collected. Furthermore, to protect the data, the PFQs will all be submitted via a secure system using a secure box that is stored in a locked office. Any electronic data will be stored in a password-protected computer for analysis.

Appendix G

Sugammadex Algorithm



NOTE: 16 mg/kg Sugammadex is recommended if there is a clinical need to reverse NMB soon (approximately 3 minutes) after administration of a single dose of 1.2 mg.kg of Rocuronium or for cannot intubate cannot ventilate situations.

Appendix H

Sugammadex Patient Education Handout

Sugammadex (Bridion) Drug Interactions Counseling for Female Patients

You have been given a medication called sugammadex (Bridion) during your procedure or surgery on _____ (insert day).

Sugammadex (Bridion) interacts with hormonal contraceptives (including but not limited to oral birth control pills ("the pill"), injectable Depo Provera, Nuvaring, and patch) and may make this method of contraception (birth control) **less effective for the next 7 days**.

If you are not sure if you are taking a hormonal contraceptive, check with your doctor or pharmacist.

If you use hormonal contraceptives as your method of birth control, **you must use an additional, NON-HORMONAL method of contraception** (birth control) **for the next 7 days following sugammadex (Bridion)** administration.

You may continue taking your hormonal contraception (birth control) as prescribed by your doctor but use an additional NON-HORMONAL method of contraception for the next 7 days after the date of your surgery (listed above).

NON-HORMONAL methods of contraception (birth control) include:

- Male condom and spermicide
- Female condom and spermicide
- Female diaphragm
- Female cervical sponge
- Your male partner is sterilized (vasectomy)

An alternative to NON-HORMONAL contraception (birth control) is not having sexual intercourse or engaging in any sexual activity that may result in pregnancy for the 7 days after your procedure date.

Please contact your doctor or pharmacist with any questions. A doctor, pharmacist, or nurse can also assist you with questions while you are in the hospital or surgical center.

References:
Bridion (sugammadex) prescribing information. December 2015. Association of Reproductive Health Professionals. Non-hormonal contraceptive methods. July 2013.

Appendix I

AGREE II Tool Domain Scores

AGREE II Tool Domain Scores

Summary of Domain Scores	
Domain 1	100%
Domain 2	100%
Domain 3	100%
Domain 4	100%
Domain 5	100%
Domain 6	100%
Overall assessment	100%

		Appraiser 1	Appraiser 2	Total
Domain 1	Item 1	7	7	14
	Item 2	7	7	14
	Item 3	7	7	14
Obtained Scores				42
Calculated Domain Scores				100%
Domain 2	Item 4	7	7	14
	Item 5	7	7	14
	Item 6	7	7	14
Obtained Scores				42
Calculated Domain Scores				100%
Domain 3	Item 7	7	7	14
	Item 8	7	7	14
	Item 9	7	7	14
	Item 10	7	7	14
	Item 11	7	7	14
	Item 12	7	7	14
	Item 13	7	7	14

	Item 14	7	7	14
Obtained Scores				112
Calculated Domain Scores				100%
Domain 4	Item 15	7	7	14
	Item 16	7	7	14
	Item 17	7	7	14
Obtained Scores				42
Calculated Domain Scores				100%
Domain 5	Item 18	7	7	14
	Item 19	7	7	14
	Item 20	7	7	14
	Item 21	7	7	14
Obtained Score				56
Calculated Domain Scores				100%
Domain 6	Item 22	7	7	14
	Item 23	7	7	14
Obtained Scores				28
Calculated Domain Scores				100%
Overall Guideline Assessment		7	7	14
Calculated Domain Scores				100%
Total Obtained Scores		161	161	322

Appendix J

Practitioner's Feedback Questionnaire (PFQ) Scores

Please select the appropriate demographic category that most accurately describes you. Title: **Anesthesiologist:** 8 (36.4%) **CRNA:** 10 (45.5%) **SRNA:** 4 (18.2%) Years of Experience: **0-5 years:** 7 (31.8%) **5-10 years:** 7 (31.8%) **10-15 years:** 2 (9.1%) **15-20 years:** 3 (13.6%) **20-25 years:** 2 (9.1%) **>25 years:** 1 (4.5%)

1. Are you responsible for the care of patients for whom this guideline report is relevant? This may include the referral, diagnosis, treatment, or follow-up of patients.	Yes 22 (100%)	No 0 (0%)	Unsure 0 (0%)
If you answered "*No*" or "*Unsure*", there is no need to answer or return this questionnaire. If you answered "*Yes*", please answer the questions below and return to the anesthesia department secretary/or designated personnel.			
	Strongly agree	Neither agree or disagree	Strongly disagree
2. The rationale for developing a guideline is clear.	22 (100%)	0 (0%)	0 (0%)
3. There is a need for a guideline on this topic.	22 (100%)	0 (0%)	0 (0%)
4. The literature search is relevant and complete (e.g., no key evidence was missed nor any included that should not have been) in this guideline.	22 (100%)	0 (0%)	0 (0%)
5. I agree with the methodology used to summarize the evidence included in this guideline.	22 (100%)	0 (0%)	0 (0%)
6. The results of the evidence described in this guideline are interpreted according to my understanding of the evidence.	22 (100%)	0 (0%)	0 (0%)
7. The CPG's recommendations in this report are clear.	22 (100%)	0 (0%)	0 (0%)
8. I agree with the recommendations as stated.	22 (100%)	0 (0%)	0 (0%)
9. The recommendations are suitable for the patients for whom they are intended.	21 (95.5%)	1 (4.5%)	0 (0%)
10. The recommendations are too rigid to apply to individual patients.	0 (0%)	4 (18.2%)	18 (81.8%)
11. When applied, the recommendations will produce more benefits for patients than harm.	22 (100%)	0 (0%)	0 (0%)
12. The guideline presents options that will be acceptable to patients.	22 (100%)	0 (0%)	0 (0%)
13. Application of recommendations will require reorganization of services/care in my practice setting.	0 (0%)	7 (31.8%)	15 (68.2%)
14. To apply the guideline, recommendations will be technically challenging.	0 (0%)	4 (18.2%)	18 (81.8%)

15. The guideline recommendations are too expensive to apply.	0 (0%)	4 (18.2%)	18 (81.8%)
16. The guideline recommendations are likely to be supported by a majority of my colleagues.	22 (100%)	0 (0%)	0 (0%)
17. If I follow the guideline recommendations, the expected effects on patient outcomes will be obvious.	20 (90.9%)	2 (9.1%)	0 (0%)
18. The guideline recommendations reflect a more effective approach for improving patient outcomes than is current usual practice. (If they are the same as current practice, please tick ☐ NA).	21 (95.5%)	1 (4.5%)	0 (0%)
19. When applied, the draft guideline recommendations will result in better use of resources than current usual practice. (If they are the same as current practice, please tick *NA* ☐)	20 (90.9%)	1 (4.5%)	1 (4.5%)
20. I would feel comfortable if my patients received the care recommended in the guideline.	22 (100%)	0 (0%)	0 (0%)
21. This proposed guideline should be approved as a practice guideline.	21 (95.5%)	0 (0%)	1 (4.5%)
22. If this proposed guideline were to be approved as a practice guideline, I would use it in my own practice/apply the recommendations to my patients.	22 (100%)	0 (0%)	0 (0%)