

# New Frontiers for Neuromuscular Blockade Use and Reversal

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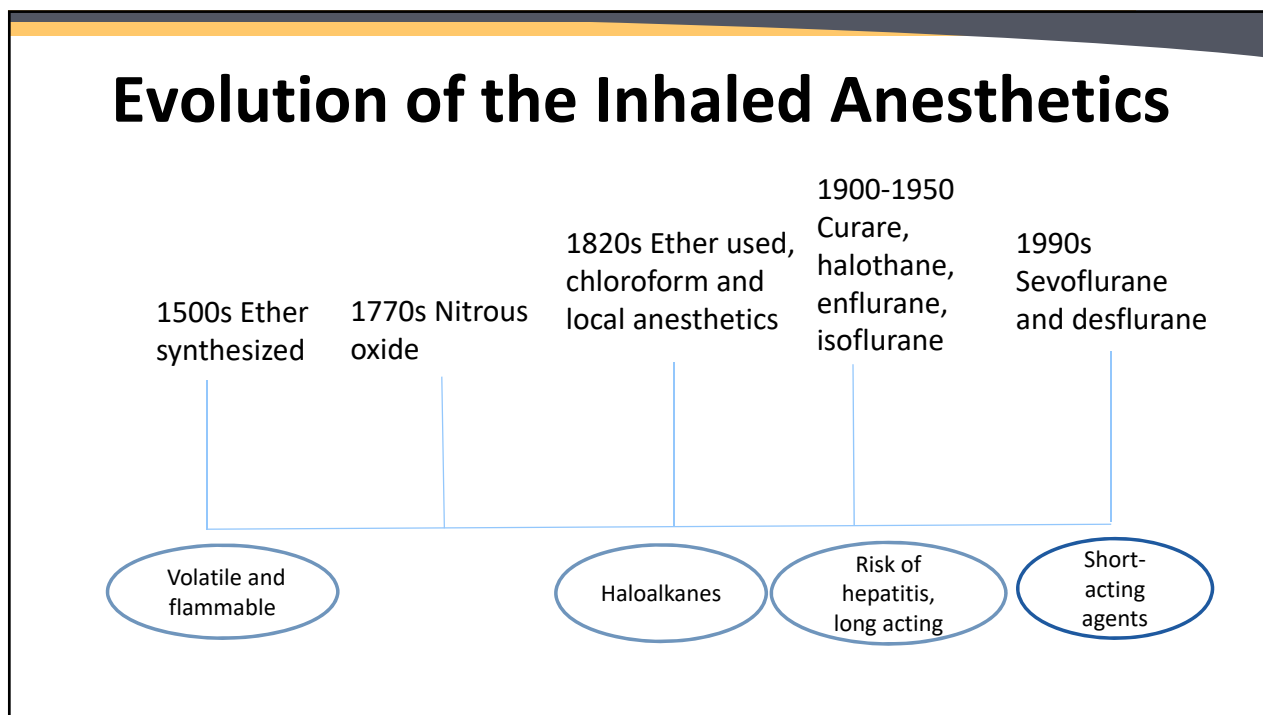
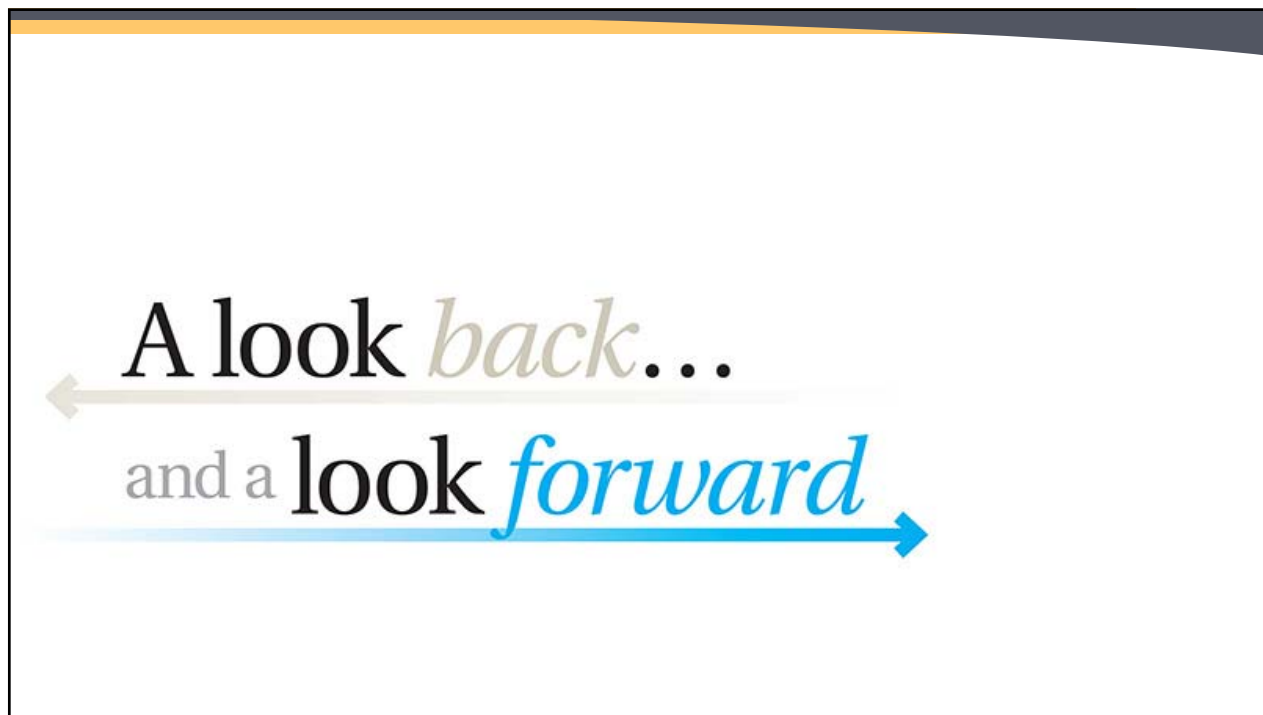
### **Learning Objectives**

At the conclusion of this application-based educational activity, participants should be able to

- Explain the science of neuromuscular blockade (NMB) and reversal
- Consider patient and procedural risk factors when managing reversal of neuromuscular blockade
- Improve communication between the anesthesia clinician and recovery team about the NMB reversal strategy
- Begin the process of conducting a drug-use evaluation or developing guidelines related to the use of neuromuscular reversal agents in your institution

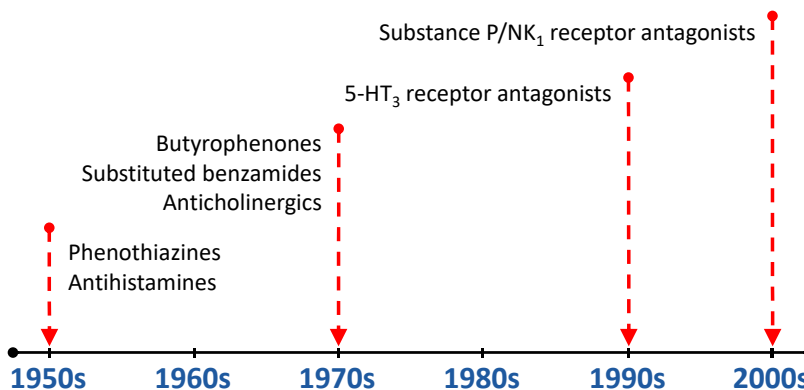
### **Factors Influencing the Use of Neuromuscular Blocking Agents and Reversal**

# New Frontiers for Neuromuscular Blockade Use and Reversal



# New Frontiers for Neuromuscular Blockade Use and Reversal

## Evolution of Antiemetics for PONV

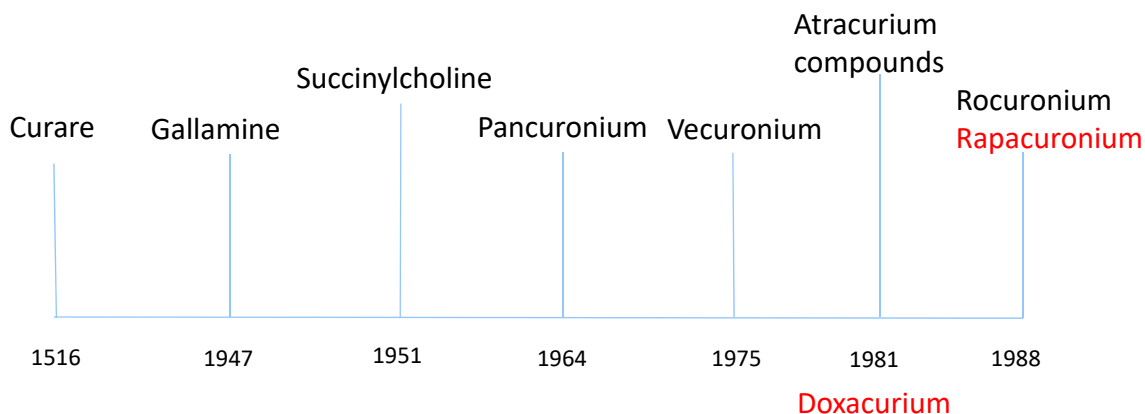


PONV = postoperative nausea and vomiting

5-HT<sub>3</sub> = serotonin receptor type 3

P/NK<sub>1</sub> = substance P, neurokinin 1 receptors

## Evolution of Neuromuscular Blockers and Reversal Agents



### Why Use a Neuromuscular Blocker?

- Decrease incidence of adverse postoperative upper airway symptoms
- Results in better intubating conditions
- Reduce rate of adverse hemodynamic effects



Combes X et al. *Br J Anaesth.* 2007; 99:276-81.

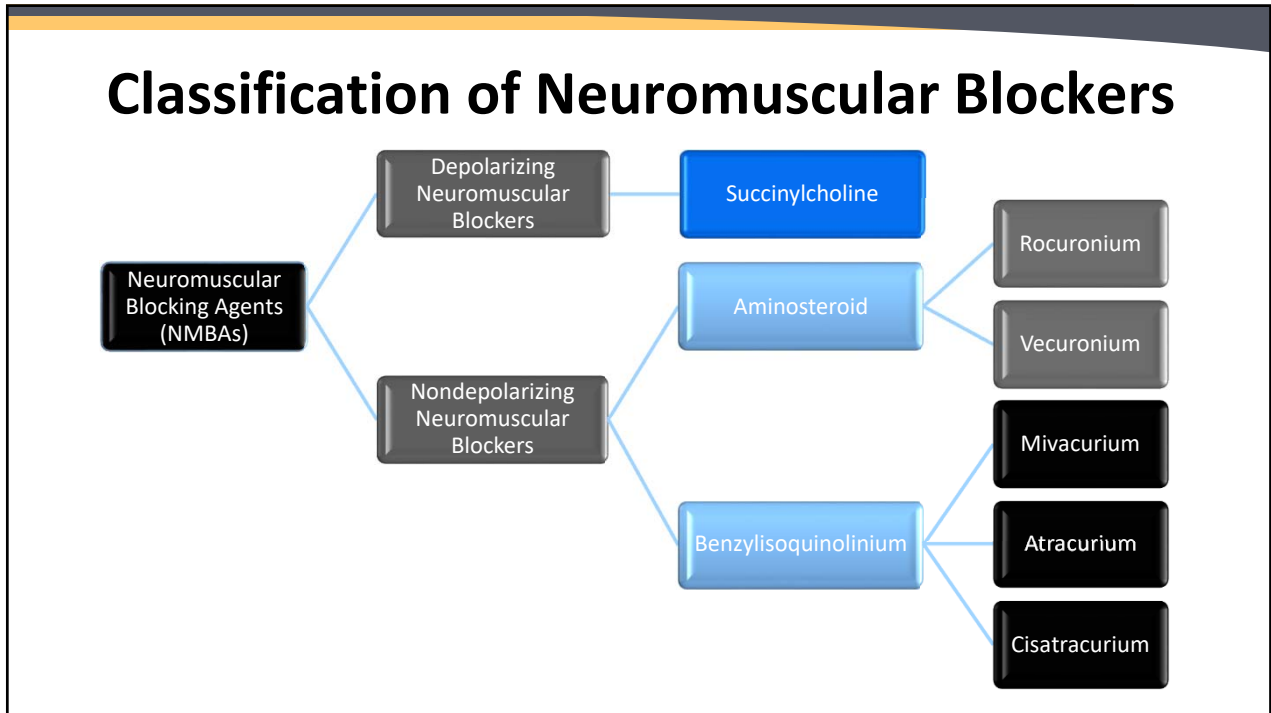
### Choice of Neuromuscular Blocker and Reversal Agent

- Duration of procedure
- General anesthetic to be used
- Adverse effect profile
- Patient characteristics
  - Age
  - Renal and hepatic function
- Cost



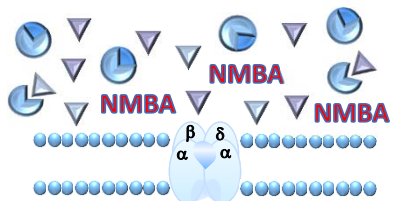
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# New Frontiers for Neuromuscular Blockade Use and Reversal

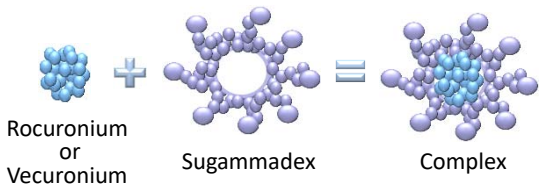


## Options for NMB Reversal

- Neostigmine ▽ (plus glycopyrrolate)
  - Acetylcholinesterase (AChE) inhibitor
    - Prevents breakdown of acetylcholine (ACh) ▽
    - Increased competition at the nicotinic receptor



- Sugammadex
  - Selective relaxant binding agent
  - Forms a complex with selected aminosteroid NMBAs
    - Sugammadex affinity
      - Rocuronium > vecuronium
      - No affinity for other NMBAs



## New Frontiers for Neuromuscular Blockade Use and Reversal

### Case Scenario Presentation



- 69-year-old male, ASA class II, height 70 in, BMI >35 kg/m<sup>2</sup>, allergies to diphenhydramine and tramadol, history of sleep apnea
- General anesthesia planned for exploratory laparotomy with hernia repair and possible resection at an ambulatory surgery center (ASC)
- Induction with succinylcholine 100 mg, midazolam 1 mg, and fentanyl 200 mcg at 9:15 am
- Inhaled anesthetic, induction with isoflurane, maintenance with desflurane, discontinued at 11:45 am
- Intraoperatively received morphine 12 mg, ondansetron 4 mg, phenylephrine for blood pressure control, and rocuronium for maintenance

ASA = American Society of Anesthesiologists, BMI = body mass index

### Association of Anaesthetists of Great Britain and Ireland 2015 Recommendations



“A peripheral nerve stimulator must be used whenever neuromuscular blocking drugs are given. A quantitative peripheral nerve stimulator is recommended.”

Checketts MR et al. *Anaesthesia*. 2016; 71:85-93.



## New Frontiers for Neuromuscular Blockade Use and Reversal

### Humans vs. the Machine

- TOF watch vs. TOF count by providers
- 75 patients/687 observations
- Agreement 56%
  - 87% at TOF = 0 or 4
  - 36% at TOF = 1, 2, or 3
- No influence by the type of healthcare provider



TOF = train-of-four

Bhananker SM et al. *Can J Anaesth.* 2015; 62:1089-96.

### Practice Considerations from the American Association of Nurse Anesthetists

- When considering the combination of rocuronium and sugammadex for a difficult or emergent airway, have the drug dose and supplies necessary to prepare the drug available in the anesthetizing location
- If rocuronium is used in place of succinylcholine, sugammadex should be available as a rapid reversal agent

[https://www.aana.com/docs/default-source/practice-aana-com-web-documents-\(all\)/airway-management-use-of-succinylcholine-or-rocuronium.pdf?sfvrsn=fc0049b1\\_4](https://www.aana.com/docs/default-source/practice-aana-com-web-documents-(all)/airway-management-use-of-succinylcholine-or-rocuronium.pdf?sfvrsn=fc0049b1_4) (accessed 2019 Oct 28).

### Survey of Sugammadex Availability

- 11,863 anesthesia providers
- 183 countries
- 46% had ready availability
- 56% had some sort of restrictions on use



O'Reilly-Shah VN et al. *Br J Anaesth.* 2017; 119:333-5.

### What about Pulmonary Complications

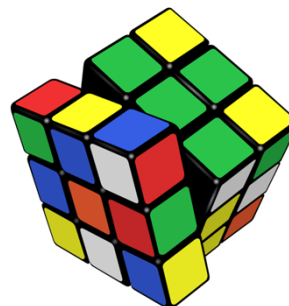
- Observational study from the Multicenter Perioperative Outcomes Group (MPOG)
- Adults with inpatient surgery 2014-2018
- Outcomes for postoperative pulmonary complications based on ICD9/10 diagnoses
- 18,086 matched sugammadex or neostigmine patients
- Sugammadex resulted in a 29% reduction in risk



Kheterpal S et al. *Eur J Anaesthesiol.* 2019; 36(e-Suppl 57). Abstract 01AP12-4.

### Surgical Complexity Impact on an Ambulatory Surgery Center

- Patient selection often driven by potential adverse effects
  - Postoperative pain
  - Perioperative bleeding
  - Duration of surgical procedure
  - Patient comorbidities



### Saving \$\$\$

- Healthcare costs in U.S. are expanding faster than the rate of inflation
- Surgery costs make up a significant portion of total healthcare expenditures
- Costs of ASC procedures are approximately 60% of hospital costs
- Estimated that Medicare would save over \$2.4 billion/yr if just 50% of procedures were shifted to ASCs
- Bipartisan Budget Act of 2015 levels the reimbursement landscape
- Increased patient satisfaction
- 340B pricing

Mundy R. <https://ankura.com/insights/healthcare-outlook-2017-ambulatory-surgery-centers>. Published May 30, 2017 (accessed 2019 October 2019).



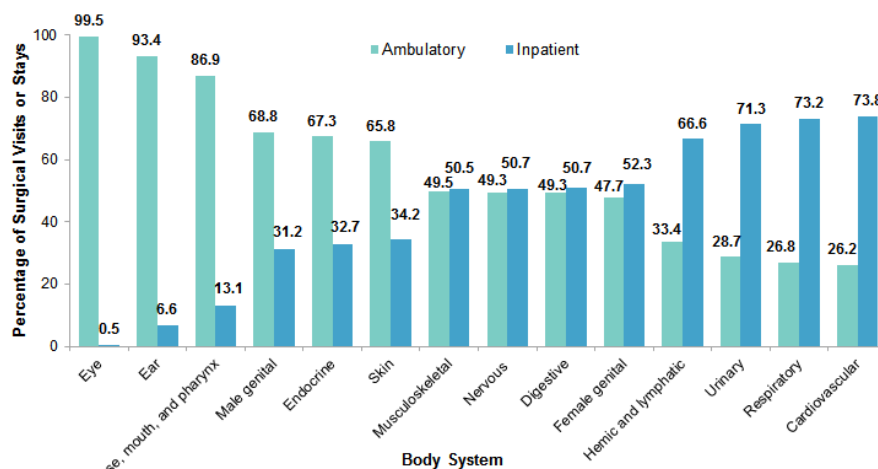
# New Frontiers for Neuromuscular Blockade Use and Reversal

## Key Trends for ASCs in the Next Decade

- Outpatient volumes will grow 15% across the U.S.
- Orthopedic and spine surgeries to grow 35%
- Shift in cardiovascular care
- Health systems expand their ambulatory footprint
- Hospital-based ASCs estimated to reach \$70 billion and multispecialty ASCs \$77 billion by 2027

<https://globenewswire.com/news-release/2017/09/27/1133626/0/en/Ambulatory-Surgical-Centres-Market-to-Garner-US-113-046-7-Mn-By-End-of-2027-Future-Market-Insights.html>. Published Sept 27, 2017 (accessed 2019 Oct 28).

## Ambulatory vs. Inpatient Surgery Types (2014)



Steiner CA. <https://hcup-us.ahrq.gov/reports/statbriefs/sb223-Ambulatory-Inpatient-Surgeries-2014.pdf> (accessed 2019 Oct 28).

## New Frontiers for Neuromuscular Blockade Use and Reversal

### Patient Selection for Ambulatory Procedures

- A growing outpatient population has led to a higher complexity of care
- A safe anesthetic is necessary for high risk patients
  - Prevents the need for mechanical ventilation
  - Reduces risk for conversion to an inpatient status
  - Facilitates discharge to home following surgeries
- Risk factors for increased mortality in an ASC
  - Overweight and/or obese
  - Respiratory issues
  - History of transient ischemic attack and/or stroke
  - Hypertension and/or cardiovascular disease
  - Prolonged surgery time



Lee JH. *Korean J Anesthesiol.* 2017; 70:398-406.

### Why Safety is Critical in an ASC

- 1 of every 31 patients receiving care in an outpatient surgery center was admitted to hospital or visited emergency department within 7 days of discharge



Rice S. <https://www.modernhealthcare.com/article/20140428/NEWS/304289965/better-communication-could-curb-er-visits-after-outpatient-surgery-study>. Published Apr 28, 2014. (accessed 2019 Oct 28).

## New Frontiers for Neuromuscular Blockade Use and Reversal

### The Aging Population

- In the next 4 decades, people aged  $\geq 60$  years will account for 22% of the world population
- Approximately 50% will require anesthesia for surgical intervention
- Patients will be sicker and at greater risk for postoperative complications
- Age-related decrease in reserve capacity of organs can affect drug clearance
  - Delayed recovery from neuromuscular blocking agents
  - Prolonged duration of action of neostigmine

Bloom DE et al. *Lancet*. 2015; 385:649-57; Sear JW. *Curr Opin Anaesthesiol*. 2003; 16:373-8; McDonagh DL et al. *Anesthesiology*. 2011; 114:318-29.



### The Aging Population and the ASC

- Multiple health conditions that affect the ability to recover from surgical procedures
- More rapid clinical deterioration
- Less physiologic reserve



## New Frontiers for Neuromuscular Blockade Use and Reversal

### Age Demographics of ASC Patients

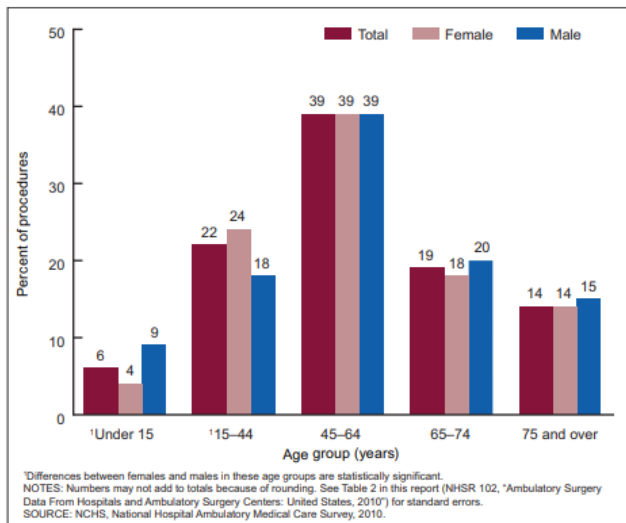


Figure 2. Percent distribution of ambulatory surgery procedures in hospitals and ambulatory surgery centers, by age and sex: United States, 2010

Hall MJ et al. National Health Statistics Reports. No. 102; February 28, 2017. <https://www.cdc.gov/nchs/data/nhsr/nhsr102.pdf> (accessed 2019 Oct 28).

### Use of Reversal Agents and Time in the ASC

- Turnover time = time patient is transported to PACU and time to induction of the next patient
  - Patients cannot be extubated until NMB is reversed
  - Encapsulating agents (sugammadex) work faster than anticholinesterase agents
  - Faster turnover improves the financial viability of the ASC

PACU = post anesthesia care unit

# New Frontiers for Neuromuscular Blockade Use and Reversal

## What about differences in recovery time?

- Outpatient surgery with rocuronium + sugammadex compared with succinylcholine and spontaneous recovery
  - 150 patients with a primary end point of TOF = 0.9
  - Time from sugammadex to TOF = 0.9: 1.8 min
  - Time from succinylcholine to TOF = 0.9: 10.8 min



Soto R et al. *Am J Therap.* 2016; 23:e1654-e1662.

## Back to Our Patient - Recap



- 69-year-old male, ASA class II, height 70 in, BMI >35 kg/m<sup>2</sup>, allergies to diphenhydramine and tramadol, history of sleep apnea
- General anesthesia planned for exploratory laparotomy with hernia repair and possible resection at an ambulatory surgery center (ASC)
- Induction with succinylcholine 100 mg, midazolam 1 mg, and fentanyl 200 mcg at 9:15 am
- Inhaled anesthetic, induction with isoflurane, maintenance with desflurane, discontinued at 11:45 am
- Intraoperatively received morphine 12 mg, ondansetron 4 mg, phenylephrine for blood pressure control, and rocuronium for maintenance



## New Frontiers for Neuromuscular Blockade Use and Reversal

### Back to Our Patient – Recovery Progress

- Twitch monitoring documented
  - 11:00 am 1/4
  - 11:15 am 1/4
  - 11:30 am 1/4
  - 11:45 am 2/4
  - 12:00 pm 2/4
- Reversal agents administered
  - 12:14 pm neostigmine 5 mg and glycopyrrolate 0.8 mg
- Reversal complete at 12:51 pm (4/4 twitches) but significant respiratory support required with possible pulmonary edema, supplemental oxygen needed
- Discharge from PACU 16:15 pm

Time for

TURNOVER



### Why is the PACU Handover Timeout Important?

- Information loss can occur during all phases of care
- During a handover, information is at risk of degradation and miscommunication
- Transfer of care from the operating room to the PACU is an especially vulnerable time

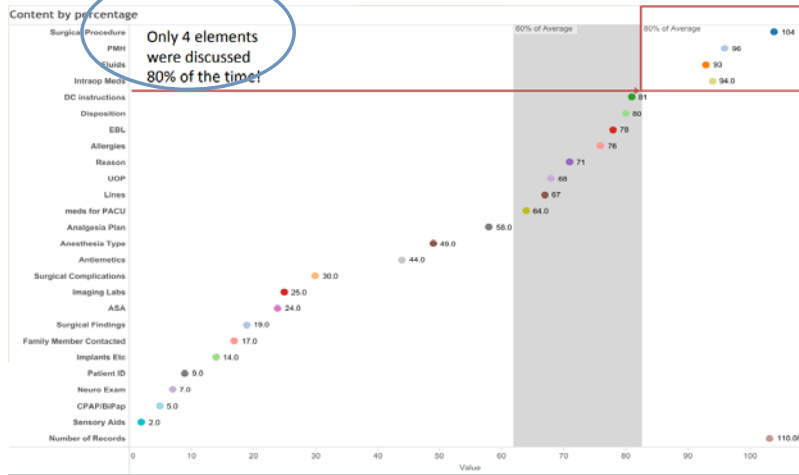
### Michigan Medicine Pre-implementation Observations

- 110 observed handovers in the Adult Main PACU
- Elements observed
  - Duration of handover process
  - Which healthcare personnel were present at the bedside
  - When the patient arrived and departed
  - Type of information discussed during the handover process
  - Quality of teamwork and communication



# New Frontiers for Neuromuscular Blockade Use and Reversal

## Results of Observations



### M PACU Handover Timeout

"All Stay for the All Stop"

\*\*If an item does not apply to your patient, verbalize that it is "n/a" \*\*

1. Prior to Patient Arrival	3. Anesthesia Provider to PACU RN & Surgical/Proceduralist Designee	5. PACU RN Wrap-up
<p><b>PACU RN:</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Review "MICHART PACU Summary" including allergies</li> <li><input type="checkbox"/> Complete Chart Review (H&amp;P)</li> </ul>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Allergies &amp; Contact Precautions</li> <li><input type="checkbox"/> PMH, PSH</li> <li><input type="checkbox"/> Anesthetic Type</li> <li><input type="checkbox"/> Airway type</li> <li><input type="checkbox"/> Airway status</li> <li><input type="checkbox"/> Relevant Intraop &amp; Preop Meds (PONV Plan, vasopressive, relaxants, reversal)</li> <li><input type="checkbox"/> Anesthetic Complications</li> <li><input type="checkbox"/> Assessment Parameters (Vital signs, Labs, etc.)</li> <li><input type="checkbox"/> Vascular Access</li> <li><input type="checkbox"/> Pain Management Plan</li> <li><input type="checkbox"/> Intraop fluids (crystalloid, colloid, Blood products, Cell Saver, Cryo)</li> <li><input type="checkbox"/> Urine &amp; EBL</li> <li><input type="checkbox"/> Type and location of sensory aids</li> </ul>	<p><b>Nurse reviews with Team:</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Nurse states their concerns</li> <li><input type="checkbox"/> Nurse asks team, "What other questions/concerns do you have?"</li> <li><input type="checkbox"/> If no other questions/concerns, PACU RN announces, "Handover complete".</li> </ul>
<p><b>2. Patient Arrival</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Anesthesia announces patient name, age and procedure</li> <li><input type="checkbox"/> Team connects monitors</li> <li><input type="checkbox"/> PACU RN completes brief assessment &amp; checks ID band</li> <li><input type="checkbox"/> PACU RN announces, "Timeout", introduces self and asks for introductions*</li> <li><input type="checkbox"/> PACU RN leads the handover process</li> </ul> <p><b>Introductions</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Surgery Reps name &amp; pager #</li> <li><input type="checkbox"/> Primary surgical contact for f/u questions</li> <li><input type="checkbox"/> What are the primary surgical concerns?</li> <li><input type="checkbox"/> Anesthesia providers name &amp; pager #</li> <li><input type="checkbox"/> What are the primary anesthesia concerns?</li> </ul> <p style="font-size: x-small; text-align: center;">*following patient stabilization</p>	<p><b>4. Surgical/Proceduralist Designee to PACU RN &amp; Anesthesia Provider</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Surgical Findings</li> <li><input type="checkbox"/> Postop Diagnosis</li> <li><input type="checkbox"/> Surgical Complications</li> <li><input type="checkbox"/> Intraop Position</li> <li><input type="checkbox"/> Drains/Devices</li> <li><input type="checkbox"/> Procedure Specific: Pulses, Grafts, Transplants, Implants, Dressings</li> <li><input type="checkbox"/> Neuro Exam</li> <li><input type="checkbox"/> Responsible family member contacted</li> <li><input type="checkbox"/> Disposition</li> </ul>	<div style="text-align: center;"> </div> <p style="font-size: x-small;">Sidenotes: Medical Students may not act as a handover designee All designees are to remain at the patient's bedside until handover is complete</p>

# New Frontiers for Neuromuscular Blockade Use and Reversal

Anesthesiology Performance Improvement and Reporting Exchange (ASPIRE), a statewide BCBSM CQI, has a transfer of care metric related to the PACU handover process.



ASPIRE

**Measure Abbreviation:** TOC 02 (MIPS 426)\*

*\*TOC 02 is built to the specification outlined by the Merit Based Incentive Program (MIPS) 426: Post-Anesthetic Transfer of Care Measure: Procedure Room to a Post Anesthesia Care Unit (PACU) measure. MIPS measure specifications are available for download at <https://app.cms.gov/resources/education>*

**Description:** Percentage of patients, regardless of age, who are under the care of an anesthesia practitioner and are admitted to a PACU in which a post-anesthetic formal transfer of care protocol or checklist which includes the key transfer of care elements is utilized.

**NQS Domain:** Communication and Care Coordination

**Measure Type:** Process

**Scope:** Measured on a per case basis

**Measure Summary:**

This measure is a two-part measure:

- 1) Documentation of PACU or ICU handoff complete in the electronic anesthesia record as a yes/no question. The percentage of handoffs will be calculated as number of handoffs documented as "yes" in the electronic anesthesia record where the denominator equals the number of transfer to PACU events.
- 2) Development of a standardized audit process to determine quality of handoff. Each site will be expected to submit a minimum of 10 audit results per month to ASPIRE using a paper-based tool (see table below) and then submitted using a web-based password protected spreadsheet.

## Questions to be Answered

- Is one reversal drug superior to two?
- What is the cost of predictable NMB reversal?
- Should high risk patients be stratified?
- How does the cost effectiveness compare between choices for reversal?
- What is best practice for NMB monitoring and reversal?



### Complications of Residual Neuromuscular Blockade

### Case Scenario Presentation

- A 72-year-old, 80-kg male presents for exploratory laparotomy and bowel resection for perforated diverticulum.
- He presents with acute renal insufficiency, likely from hypovolemia. He has a history of chronic obstructive pulmonary disease (COPD), stable on chronic inhaled beta agonists.
- He is induced with propofol and rocuronium 1.2 mg/kg for rapid sequence induction. Neuromuscular blockade is maintained with interval dosing of rocuronium to facilitate exposure through closing.

## New Frontiers for Neuromuscular Blockade Use and Reversal

### Case Scenario, Continued

- Blockade is monitored at the facial nerve with a qualitative train-of-four count.
- After laparotomy closure, 2/4 twitches are appreciated at the facial nerve, and the blockade is reversed with neostigmine 5 mg and glycopyrrolate 1 mg.
- After reversal 4 twitches are appreciated by qualitative analysis.
- The patient recovers spontaneous ventilation with a tidal volume of 6 mL/kg.
- He wakes up, is extubated, and taken to PACU for recovery.

### Case Scenario, Continued

- In the PACU, his oxygen saturation is 90% despite O<sub>2</sub> by facemask. BiPap non-invasive ventilation is initiated, but the saturations do not recover well.
- A chest x-ray in the PACU is suspicious for aspiration demonstrating consolidation in the right lower lobe. The decision is made to re-intubate the patient and transfer to the ICU.
- He recovers from a diagnosed pneumonia and is discharged from the ICU on postop day 4, and from the facility on postop day 7 without further complications.

BiPap = bilevel positive airway pressure

## New Frontiers for Neuromuscular Blockade Use and Reversal

### Discussion Points

- Risk factors for postoperative respiratory complications
- Metabolism of rocuronium
- Monitoring strategies (qualitative vs. quantitative, site of measurement)
- Assessment of recovery of neuromuscular function based on diaphragmatic function
- Outcomes associated with residual neuromuscular blockade
- Optimal reversal strategies
- Costs associated with postoperative pulmonary complications

### Risk Factors for Postoperative Pulmonary Complications

- Advanced age
- High BMI
- Cancer
- Impaired cognition
- Upper abdominal surgery
- Smoking
- COPD
- Abnormal pulmonary function test
- Prolonged duration of anesthesia

Brooks-Brunn JA. *Chest*. 1997; 111:564-71.

### Monitoring at the Face vs. Hand

- Eye muscles are more sensitive to nerve stimulation than hand muscles
- This results in false negative tests for residual blockade
- The hand may not always be accessible

Thilen SR et al. *Anesthesiology*. 2012; 117:964-72.

### PACU Events and Residual Blockade

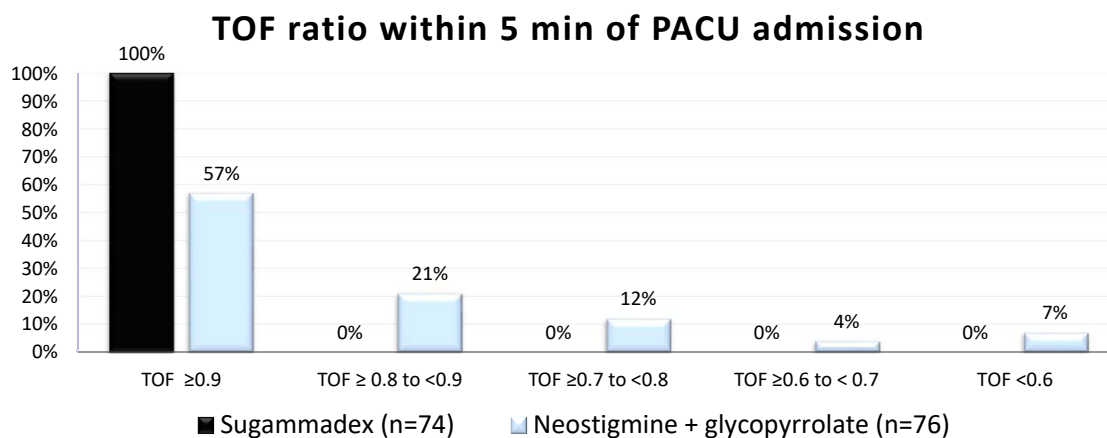
- Patients who suffered pulmonary events early in their PACU stay had quantitative measurements of neuromuscular function
- These cases were matched against a control group
- Residual blockade was prevalent in the cohort of patients who suffered events while absent in the matched control group
- Data confirm that residual blockade is associated with these events, and a causal inference is worth exploring

Murphy GS et al. *Anesth Analg*. 2008; 107:130-7.



## New Frontiers for Neuromuscular Blockade Use and Reversal

### Incidence of Postoperative Residual NMB



Brueckmann B et al. *Br J Anaesth.* 2015; 115:743-51.

### Cost of Care Associated with Residual Blockade

- Total costs of hospital care are not affected
- Increased rate of ICU admission
- Increased hospital length of stay (LOS)

Grabitz SD et al. *Anesth Analg.* 2019; 128:1129-36.

### **Cost of Care Associated with Postoperative Pulmonary Complications**

- Year 2000 data
- \$5,771 added cost per case
- \$24,000 if respiratory failure ensues

Shander A et al. *Crit Care Med.* 2011; 39:2163-72.

### **Association of Postoperative Outcomes with NMB Reversal Practice**

- Observational study of reversal practices
- Significantly higher rate of postoperative nausea or vomiting with neostigmine reversal than sugammadex reversal
- No significant differences in PACU or hospital LOS
- Pulmonary outcomes deteriorated significantly with advanced age
  - Not observed in the sugammadex group

Ledowski T et al. *Eur J Anaesthesiol.* 2014; 31:423-9.

### **Risk of Postoperative Pulmonary Complications**

- Large multicenter observational study
- Use of neuromuscular blockade was associated with pulmonary complications
- However, choice of reversal agent and method of assessment of block carried no association

Kirmeier E et al. *Lancet Respir Med.* 2019; 7:129-40.

### **Costs of Care Related to Reversal Choice**

- Observational study of abdominal surgery cases over 7-year period
- Propensity score matching was used to pair a neostigmine cohort with a sugammadex cohort
- Sugammadex was associated with lower 30-day unplanned readmission rate, shorter hospital stay, and lower related hospital charges than neostigmine

Oh TK et al. *Br J Anaesth.* 2019; 122:370-8.

## Identifying Opportunities for Improvement

### Case Scenario

- Barnes-Jewish Hospital added sugammadex to the hospital formulary 3 years ago after collaborative discussions between the departments of pharmacy and anesthesia.
- Criteria for sugammadex included moderate to deep block, failed airway, PACU respiratory event with suspected residual NMB, and any situation in which there were concerns about the use of neostigmine due to potential adverse effects or disease-related issues (e.g., myasthenia gravis, bradycardia).
- All non-urgent use required anesthesia Attending physician approval.
- Inventory of sugammadex was maintained in the OR pharmacy satellites.
- Due to high comparative cost, it was recommended a drug-use evaluation (DUE) be conducted to determine adherence to the established criteria.

# New Frontiers for Neuromuscular Blockade Use and Reversal

## Pharmacoeconomics

Dose of Sugammadex	Agent	Level of NMB According to TOF Monitoring	Example Dose for 85-kg Patient	Sugammadex Cost (WAC)	Comparative \$ * Neostigmine + Glycopyrrolate (WAC)
2 mg/kg	Rocuronium or VECuronium	If spontaneous recovery has reached TOF $\geq 2$ twitches	170 mg	\$100	\$ 22-90 Price fluctuation: (2016: \$70-140)
4 mg/kg	Rocuronium or VECuronium	If spontaneous recovery has reached $\geq 1$ PTC and TOF of 0 - 1 twitch	340 mg	\$183 (500 mg vial) \$200 (200 mg vial)	N/A
16 mg/kg	Rocuronium only	If reversal is required for failed airway immediately after an induction dose of rocuronium.  Not for non-urgent reversal or for reversal of a PTC of 0	1360 mg	\$510-540 (500 mg vial) \$665-700 (200 mg vial)	N/A

\*Variable due to depth of NMB and the stocked formulation (Typical neostigmine dose 30-70 mcg/kg)

Neostigmine 1 mg/mL 3 mL Simplist Syringe: \$14  
Neostigmine 1 mg/mL 3 mL 503b syringe: \$15-25  
Neostigmine 1 mg/mL 10 mL vial: \$10

Glycopyrrolate 0.2 mg/mL 2 mL Simplist Syringe: \$13  
Glycopyrrolate 0.2 mg/mL 3 mL 503b syringe: \$20  
Glycopyrrolate 0.2 mg/mL 5 mL : \$12

WAC = wholesale acquisition cost, PTC = post-tetanic count

## Key Components of a DUE

- Interprofessional collaboration
- Pharmacy's understanding of the perioperative space and clinician workflow
- Consideration of clinical outcomes, workflow outcomes, patient safety, and cost
  - Cost-effectiveness of sugammadex is difficult to determine due to various confounders

## New Frontiers for Neuromuscular Blockade Use and Reversal

### Common Confounding Factors in the Perioperative Space

- Retrospective documentation
- Omission of key documentation
- Inaccurate or incomplete documentation
- Neuromuscular monitoring
  - Compliance and methods: qualitative vs. quantitative
- Neuromuscular monitoring documentation
- Art of anesthesia: timing of sedation and NMB reversal
- Team dependent workflows and goals
- Inpatient bed capacity and patient placement

### Barnes-Jewish Hospital and Washington University Physicians

9,236 Employees	1,698 Attending physicians	883 Residents and fellows
1,638 Licensed beds / 1,266 staffed	53,428 Inpatient admissions	78 OR suites
350 Anesthesia clinicians	18,515 Inpatient surgeries	23,989 Outpatient surgeries



2018 Annual hospital report.

# New Frontiers for Neuromuscular Blockade Use and Reversal

## Drug-Use Evaluation



### Date

- June 2018-September 2019
- Live data extract



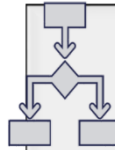
### Neuromuscular blockade

- Rocuronium (n=23,993)
- Vecuronium (n=994)



### NMB Reversal

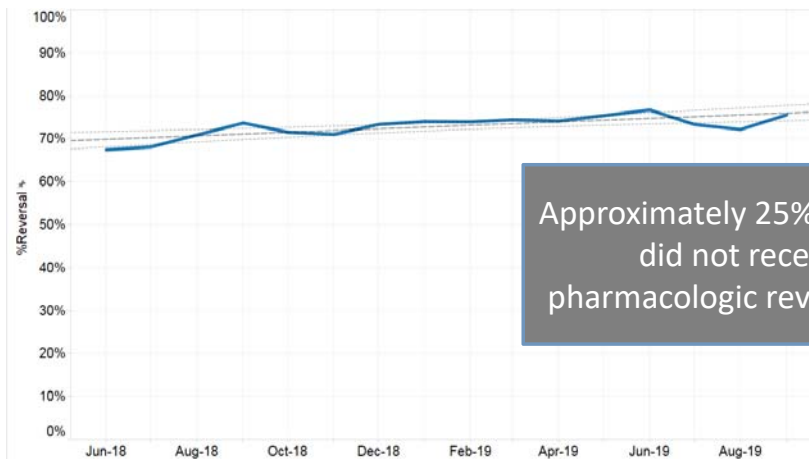
- Sugammadex (n=3,975)
- Neostigmine (n=14,893)



### Endpoints

- Rate of NMB reversal, dose assessment
- Clinician use, NMB monitoring, recovery times
- Demographics (age, ASA class)

## Rate of NMB Reversal



Approximately 25% of patients did not receive a pharmacologic reversal agent

Title  
Percent of Surgical Cases Utilizing Non-Depolarizing Neuromuscular Blockers with Pharmacologic Reversal of Blockade

BARNES JEWISH  
Hospital  
HealthCare

Washington  
University in St. Louis  
Physicians

NATIONAL LEADERS IN MEDICINE

# New Frontiers for Neuromuscular Blockade Use and Reversal

## Respiratory Complications Without Reversal

- Retrospective observational study of 11,355 adult patients undergoing general anesthesia for noncardiac surgery at 5 Veterans Health Administration (VA) hospitals

Unadjusted Outcomes	Reversal Agent (n=7047)	No Reversal Agent (n=1937)
Respiratory complications	3.6%	13.5%
Non-respiratory complications	10.4%	19.5%
30-day mortality	1.1%	5.0%
Long-term mortality	29.1%	39.9%

Bronsert MR. *Anesth Analg.* 2017; 124:1476-83.

## Respiratory Complications without Reversal

Analysis	OR/HR (95% CI)	p value
Respiratory complication		
Unadjusted	4.20 (3.51-5.03)	<0.0001
Multivariable adjusted	1.71 (1.24-2.37)	<0.0001
Propensity matched	1.75 (1.23-2.50)	<0.001
30-day mortality		
Unadjusted	4.71 (3.48-6.37)	<0.001
Multivariable adjusted	1.78 (1.02-3.13)	0.04
Propensity matched	1.83 (0.99-3.37)	0.06

- NO reversal was associated with the following:
  - 70-75% increase in odds of respiratory complications
  - Marginal association with increased 30-day all-cause mortality
  - No association with **non-respiratory** complications or long-term all-cause mortality

Bronsert MR et al. *Anesth Analg.* 2017; 124:1476-83.



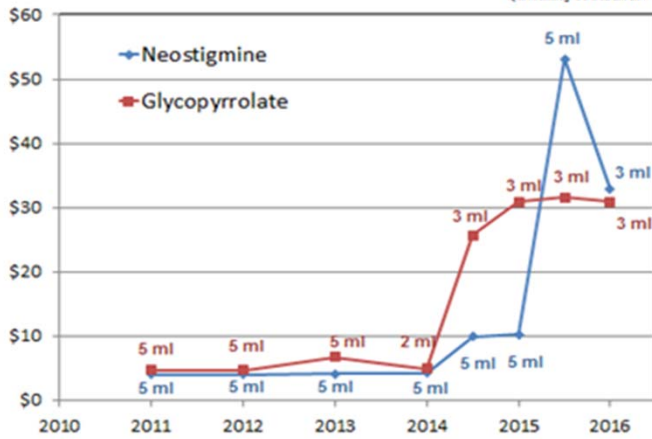
# New Frontiers for Neuromuscular Blockade Use and Reversal

## Cost-Conscious Clinicians

### The high cost of reversal

BJH Pharmacy (May 2016)

(Thank you Rachel Wolfe)

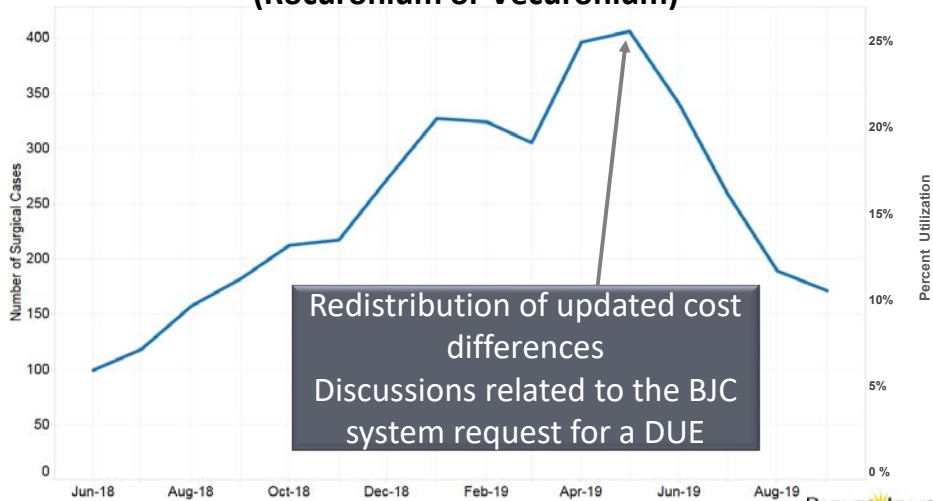


### Increase cost transparency

- 2016
  - 1 vial of sugammadex 200 mg cheaper than 2 syringes of neostigmine + 2 syringes of glycopyrrolate
- 2019
  - Sugammadex price steady
  - Neostigmine and glycopyrrolate cost have decreased

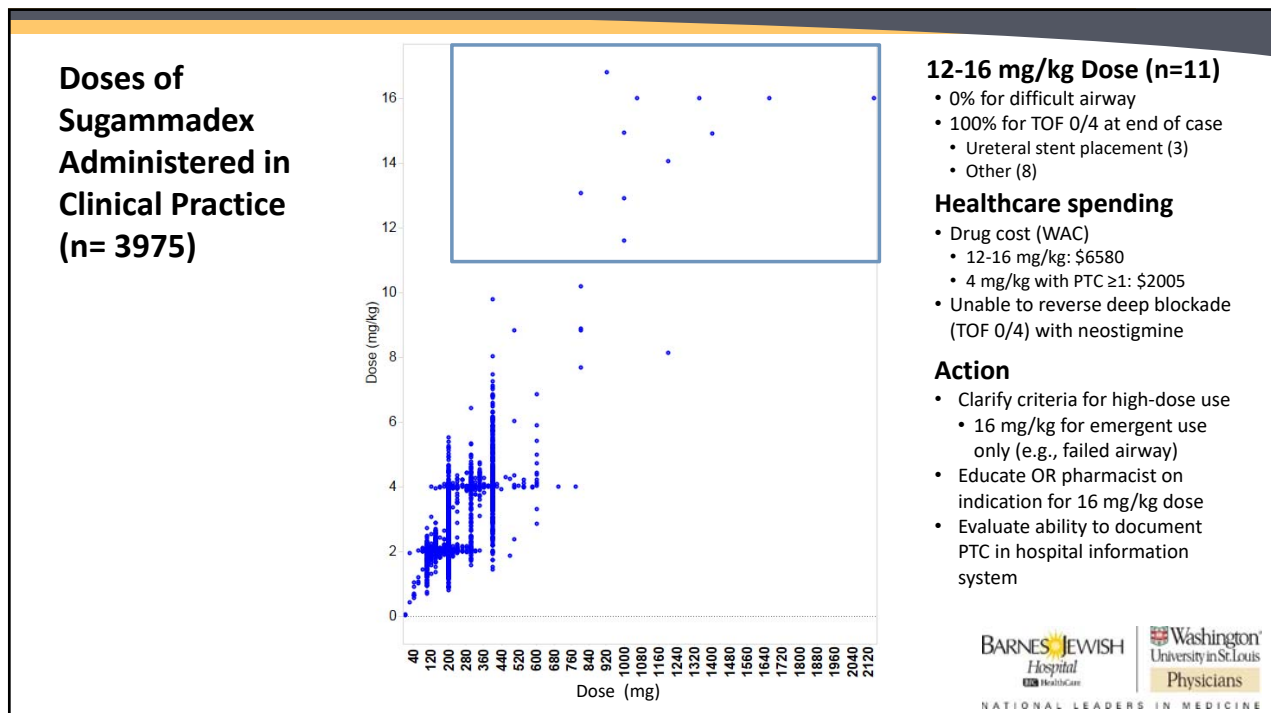
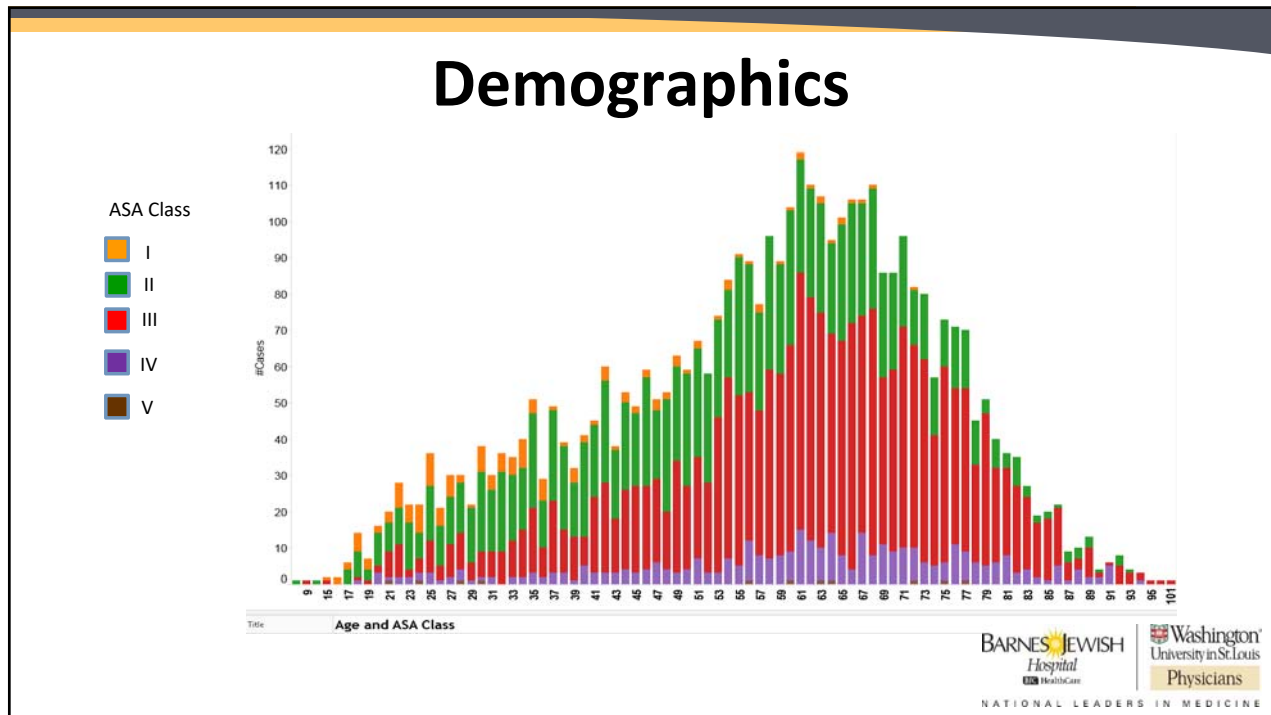
## Rate of Sugammadex Reversal

(Rocuronium or Vecuronium)

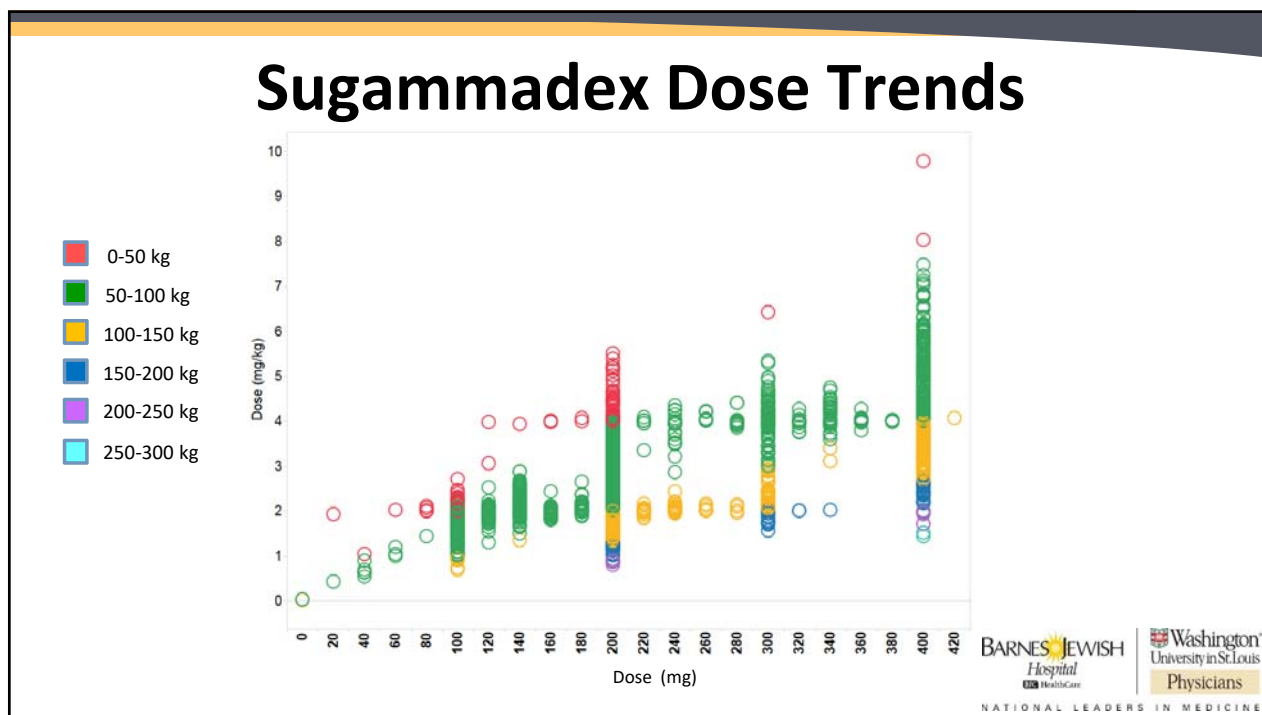


Redistribution of updated cost differences  
Discussions related to the BJC system request for a DUE

# New Frontiers for Neuromuscular Blockade Use and Reversal



## New Frontiers for Neuromuscular Blockade Use and Reversal

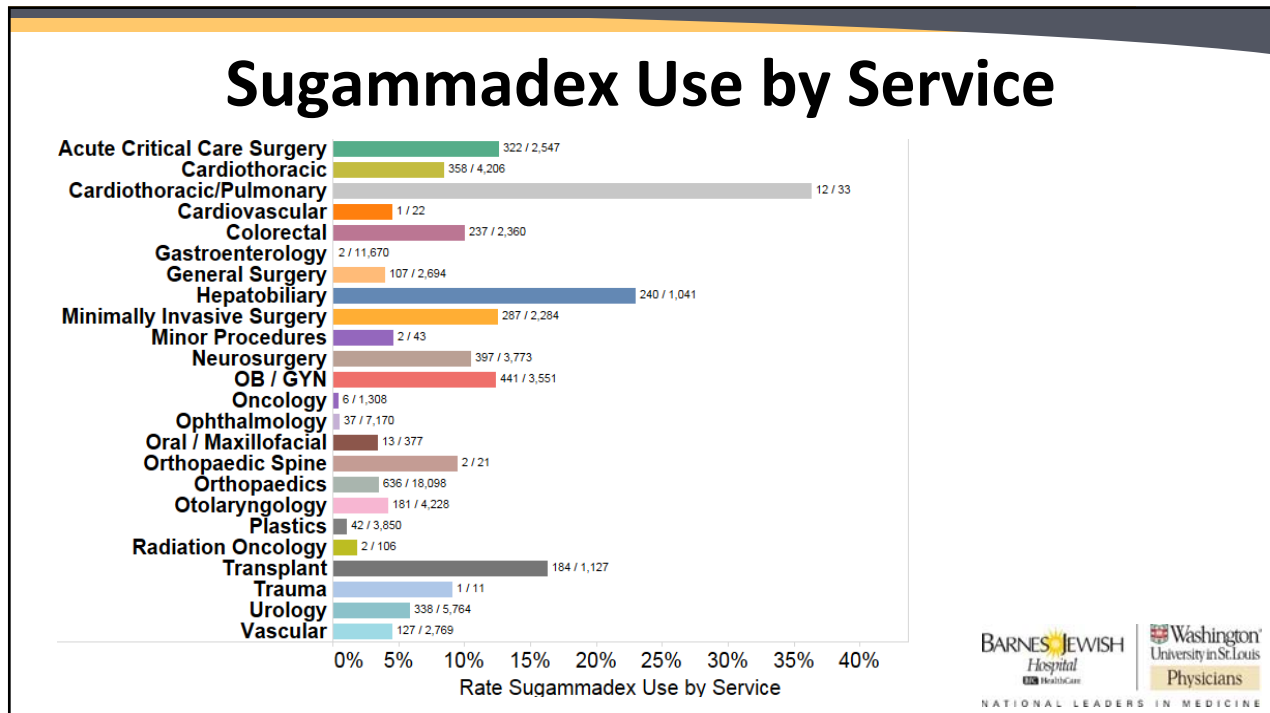


## Lower-Dose Sugammadex

- Several studies have evaluated lower-than-recommended doses of sugammadex
  - Underdosing is often part of cost-reduction strategies
    - Increased risk of recurrence of neuromuscular blockade after initial successful (but transient) reversal
    - Increased risk of residual neuromuscular blockade
    - Increased risk of postoperative complications

de Boer HD et al. *BMC Anesthesiol.* 2018; 18:159.

# New Frontiers for Neuromuscular Blockade Use and Reversal



## Short Procedures and Deep Blockade

- Example surgical procedure: Laryngeal micro-surgery
  - Intubation conditions may be improved with deep blockade
    - Many patients with history of or anticipated difficult airway
  - Surgical conditions may be improved with deep blockade
    - Larynx is in close proximity to centrally located muscles that are relatively resistant to neuromuscular blockade
      - e.g., jaw and diaphragmatic muscles
  - Short procedure
    - Average surgery duration ~ 30 minutes

## Laryngeal Micro-surgery

- Evaluate surgical conditions and recovery profile

Moderate Blockade (n=19)

Deep Blockade (n=21)

Choi ES et al. *Anesthesia*. 2017; 72:1185-90.

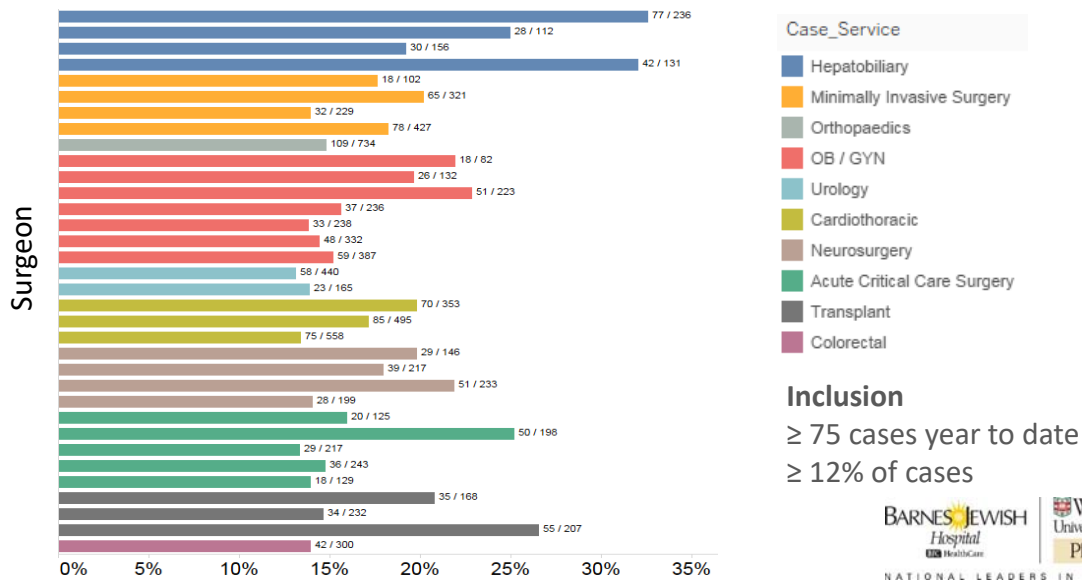
## Laryngeal Micro-surgery

Outcomes	Moderate Blockade	Deep Blockade	p value
Intubation conditions			< 0.001
Poor	2	0	
Good	15	0	
Excellent	4	19	
Intraoperative laryngoscopy conditions			< 0.001
Poor	1	0	
Good	11	0	
Excellent	9	19	
Surgical rating scale (1-7 extremely dissatisfied to extremely satisfied)			< 0.001
3	1	0	
4	0	0	
5	5	0	
6	14	3	
7	1	16	

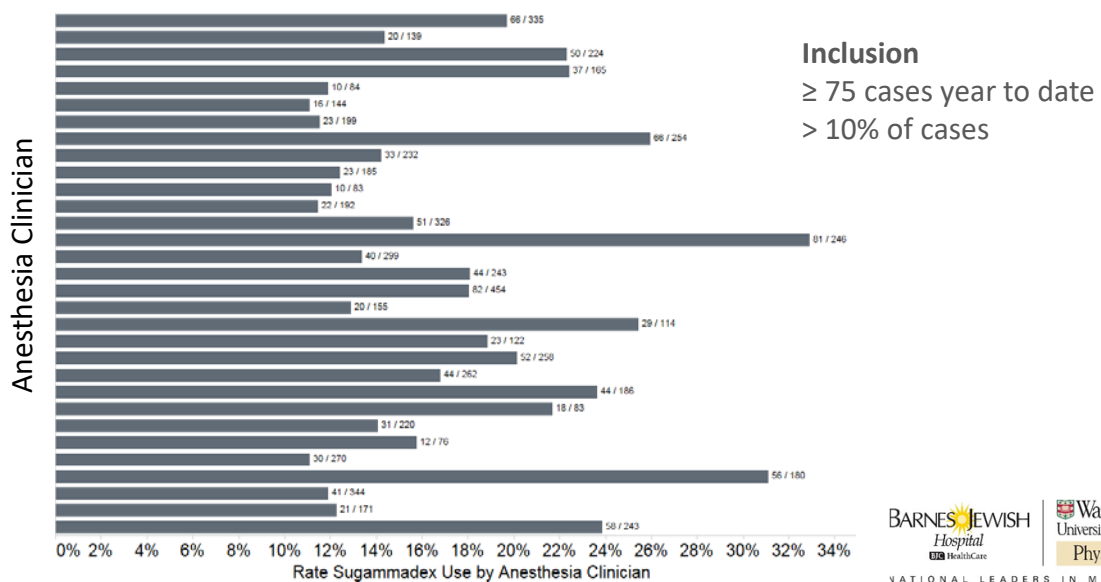
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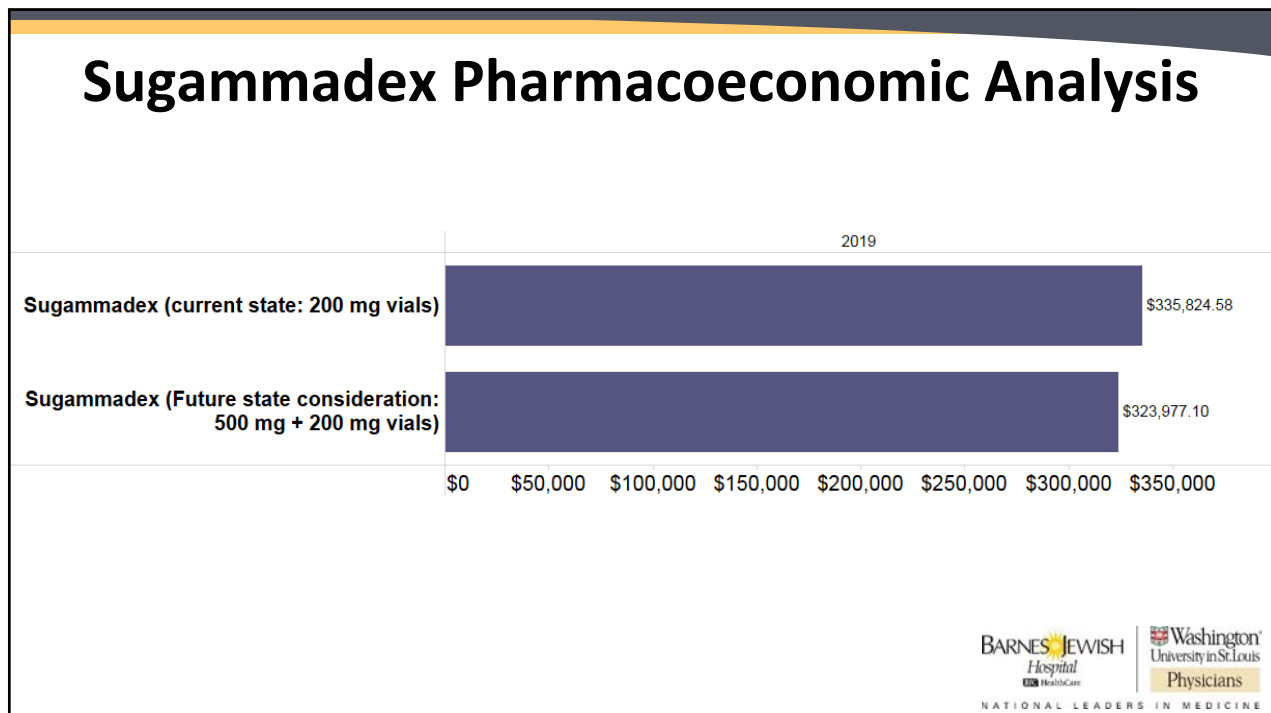
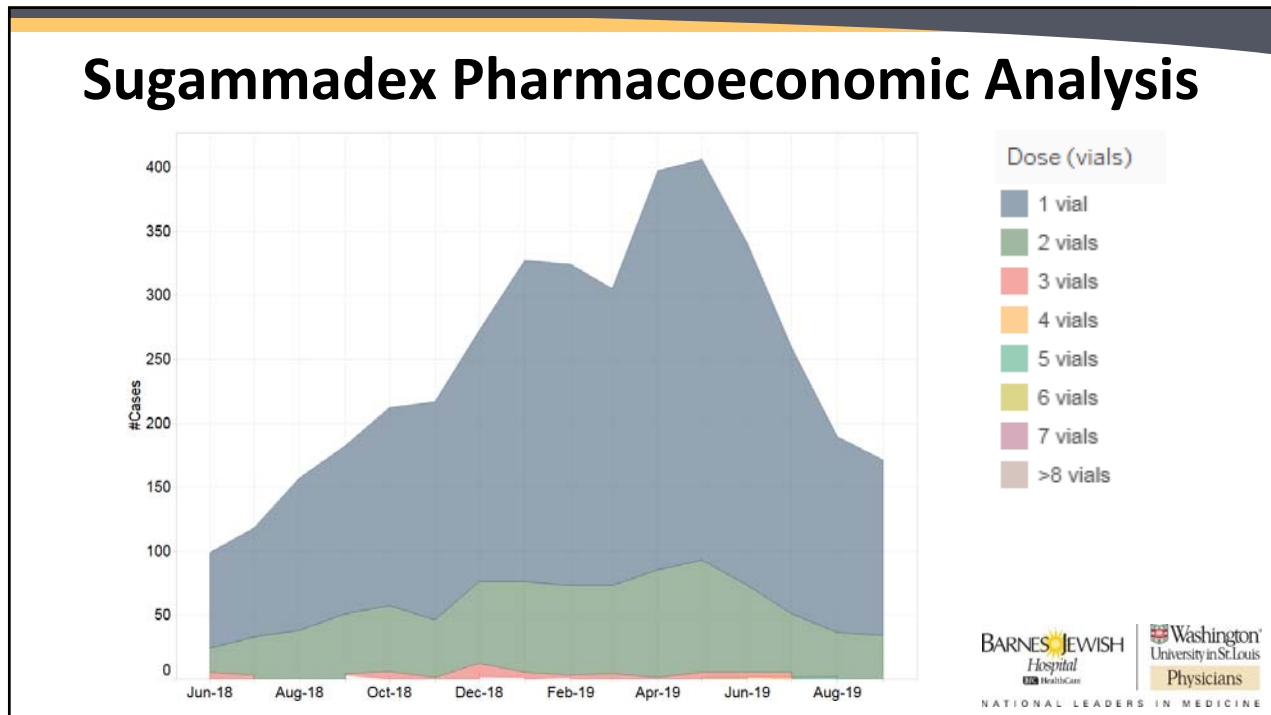
## Rate of Sugammadex Use by Surgeon



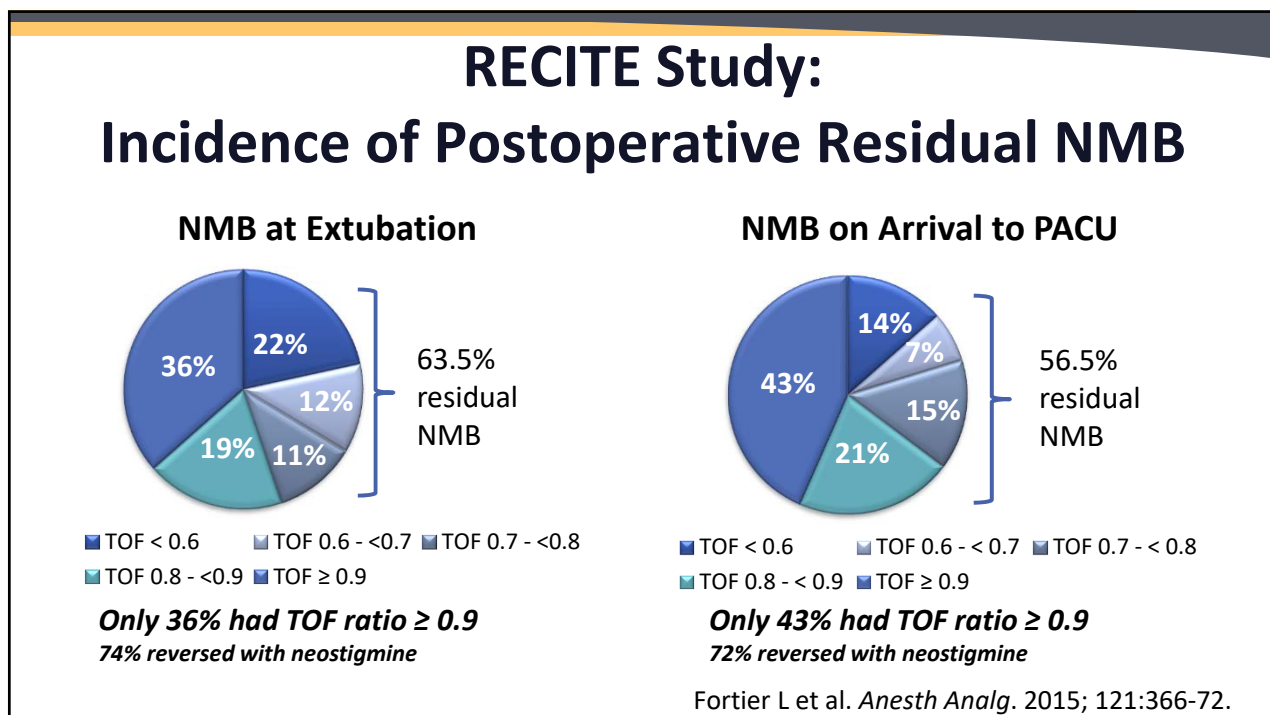
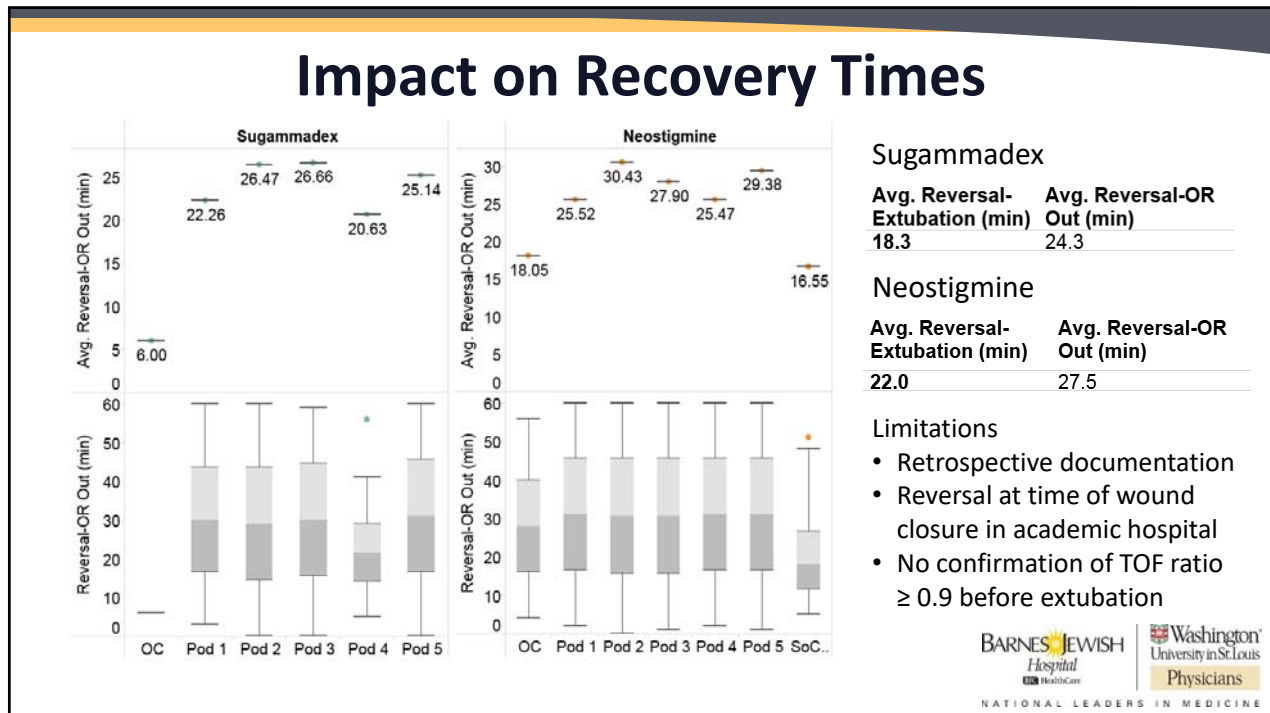
## Rate of Sugammadex Use by Anesthesia Clinicians



# New Frontiers for Neuromuscular Blockade Use and Reversal



# New Frontiers for Neuromuscular Blockade Use and Reversal





### Residual NMB and PACU Respiratory Events

- Incidence of critical respiratory events (CRE) within 15 min of PACU admission was 0.8% (61/7459)
  - Reintubation rate of 0.1% (8/7459)
    - Similar to previous estimates of 0.1-0.2%
- 42 of the 61 patients were matched with controls
  - Criteria: age, sex, type of procedure
  - Significant residual NMB in cases with CRE vs. controls
    - TOF ratio  $0.62 \pm 0.2$  vs. TOF ratio  $0.98 \pm 0.07$ ,  $p < 0.0001$
  - Severe residual NMB (TOF ratio  $< 0.7$ ) was present in 73.8% of cases with CRE vs. 0% in the control group

Murphy GS et al. *Anesth Analg.* 2008; 107:130-7.

### Pertinent Findings from DUE Provide Opportunities for Improvement

- Inappropriate use of 16 mg/kg dose
- High incidence of spontaneous recovery
- Low use of quantitative monitoring where available (i.e., TOF ratio)
- Lack of neuromuscular monitoring documentation
- Recovery times in clinical practice differ from those in structured, controlled trial settings
  - Influenced by multiple confounding factors

## Who Will Benefit Most?

- Change in approach
  - Risk-based algorithms
  - Goal: Reduce postoperative complications



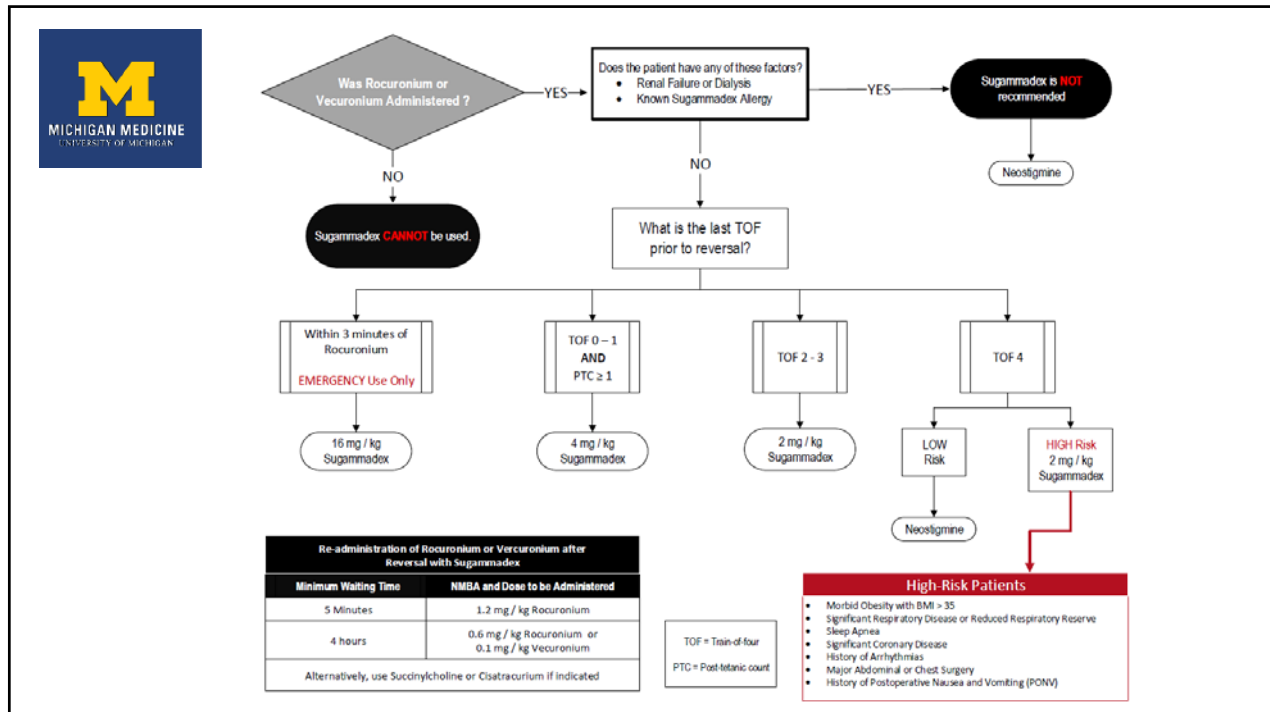
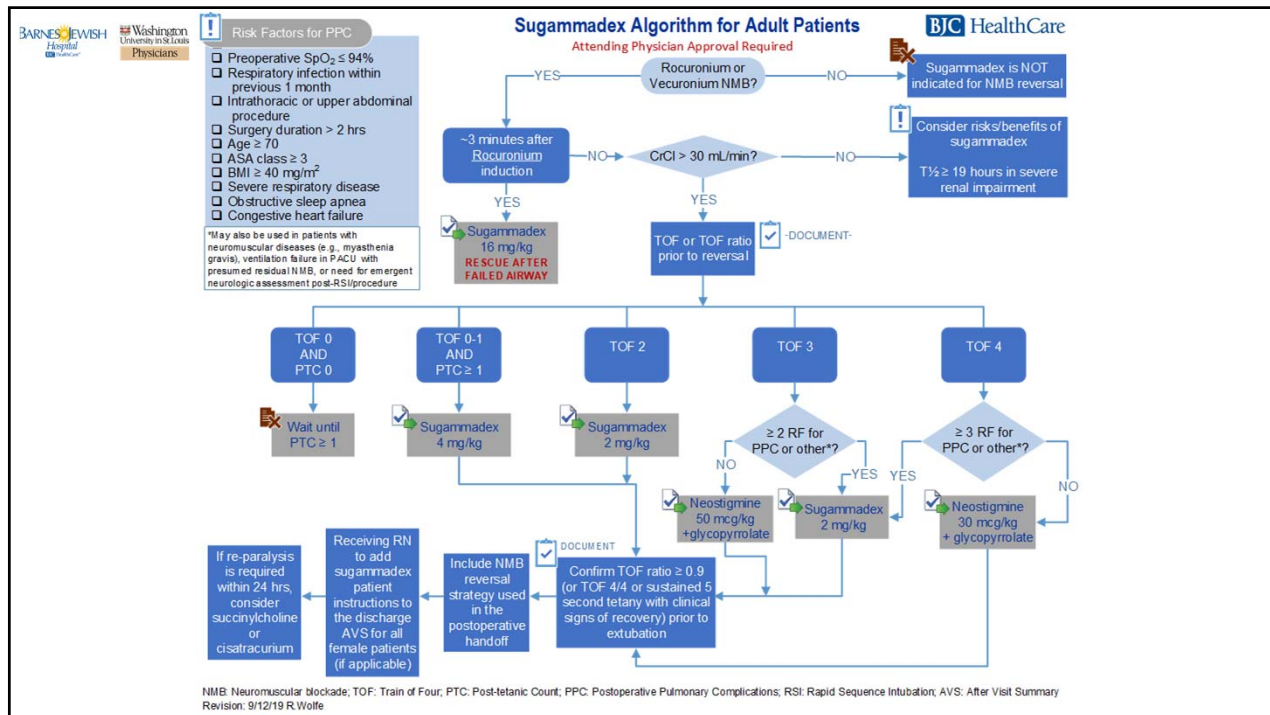
Miskovic A et al. *Br J Anaesth.* 2017; 118:317-34.

## Risk-Based Algorithms

- Use current data
- Provide direction
  - Provide education
- Anticipated result
- Provide value



# New Frontiers for Neuromuscular Blockade Use and Reversal



### Key Takeaways

- Failure to reverse is associated with postoperative residual neuromuscular blockade
- Sugammadex may reduce postoperative pulmonary complications
- The ambulatory care surgery center population is at risk for postoperative residual NMB
- Challenges still exist for measurement of NMB

### Time to Reflect

**After today's program, which of these practice changes will you consider making?**

- a. Work with interprofessional team to develop standard handover process in PACU
- b. Assess postop reintubations and other pulmonary events
- c. Review access to reversal agents for moderate/deep block and rapid sequence intubation
- d. Ensure appropriate use of sugammadex 16 mg/kg dose
- e. Initiate a drug-use review as step in developing guidelines for use of NMB reversal agents



# PACU Handover Timeout

"All Stay for the All Stop"

\*\*If an item does not apply to your patient, verbalize that it is "n/a" \*\*

## 1. Prior to Patient Arrival

### PACU RN:

- Review "MiChart PACU Summary" including allergies
- Complete Chart Review (H&P)

## 2. Patient Arrival

- Anesthesia announces patient name, age and procedure
- Team connects monitors
- PACU RN completes brief assessment & checks ID band
- PACU RN announces, "Timeout", introduces self and asks for introductions\*
- PACU RN leads the handover process

### Introductions

- Surgery Reps name & pager #
- Primary surgical contact for f/u questions
- What are the primary surgical concerns?
- Anesthesia providers name & pager #
- What are the primary anesthesia concerns?

\*following patient stabilization

## 3. Anesthesia Provider to PACU RN & Surgical/Proceduralist Designee

- Allergies & Contact Precautions
- PMH, PSH
- Anesthetic Type
- Airway type
- Airway status
- Relevant Intraop & Preop Meds (PONV Plan, vasoactive, relaxants, reversal)
- Anesthetic Complications
- Assessment Parameters (Vital signs, Labs, etc.)
- Vascular Access
- Pain Management Plan
- Intraop fluids (crystalloid, colloid, Blood products, Cell Saver, Cryo)
- Urine & EBL
- Type and location of sensory aids

## 4. Surgical/Proceduralist Designee to PACU RN & Anesthesia Provider

- Surgical Findings
- Postop Diagnosis
- Surgical Complications
- Intraop Position
- Drains/Devices
- Procedure Specific: Pulses, Grafts, Transplants, Implants, Dressings
- Neuro Exam
- Responsible family member contacted
- Disposition

## 5. PACU RN Wrap-up

### Nurse reviews with Team:

- Nurse states their concerns
- Nurse asks team, "What other questions/concerns do you have?"
- If no other questions/concerns, PACU RN announces, "Handover complete".



**MICHIGAN MEDICINE**  
UNIVERSITY OF MICHIGAN

### Sidenotes:

Medical Students may **not** act as a handover designee

All designees are to remain at the patient's bedside until handover is complete

# Michigan Medicine PACU Handover Tool

Background	Yes	No	NA
Introduction (Provider names and roles: PACU RN and anesthesia team members)			
Identification of patient*			
Pertinent PMH/PSH			
Discussion of surgical/procedure course			
Allergies			
Contact Precautions			
Anesthetic Management			
Airway management (ETT/ LMA)			
Type of anesthetic			
Anesthetic Complications			
Medications			
Preoperative Meds			
Sedations medications & amount administered. Reversal administered?			
Muscle relaxants: Time/Amount administered. Reversal administered?			
Pain Management Plan			
PONV Risk & Meds Administered			

Fluids			
Vascular access			
Total Intraoperative Fluids/Blood Products Administered			
Intraoperative labs			
Expectations/Plans			
Identify primary anesthesia concerns for this patient.			
Allow opportunity for questions/acknowledgement of understanding of report from receiving PACU team			

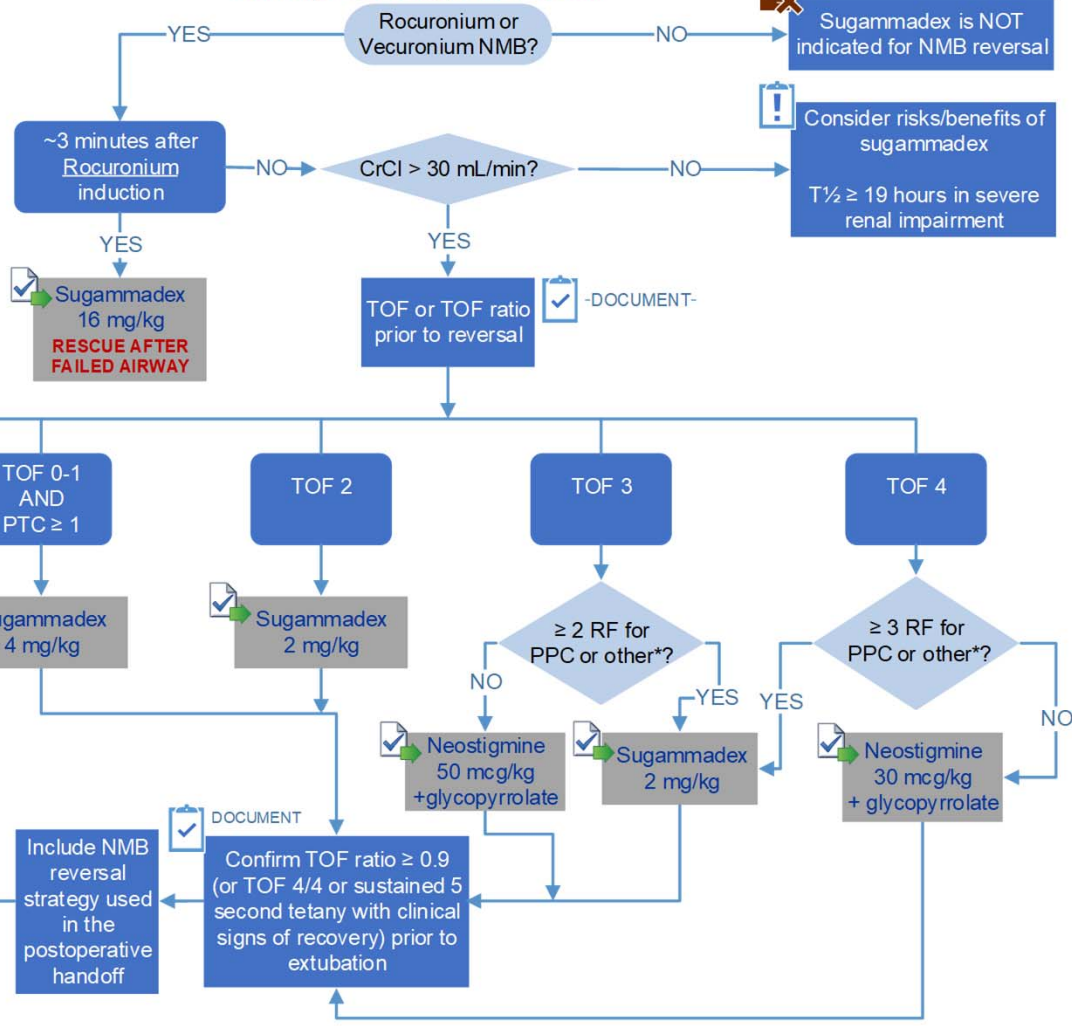
### Sugammadex Algorithm for Adult Patients

Attending Physician Approval Required

**Risk Factors for PPC**

- Preoperative SpO<sub>2</sub> ≤ 94%
- Respiratory infection within previous 1 month
- Intrathoracic or upper abdominal procedure
- Surgery duration > 2 hrs
- Age ≥ 70
- ASA class ≥ 3
- BMI ≥ 40 mg/m<sup>2</sup>
- Severe respiratory disease
- Obstructive sleep apnea
- Congestive heart failure

\*May also be used in patients with neuromuscular diseases (e.g., myasthenia gravis), ventilation failure in PACU with presumed residual NMB, or need for emergent neurologic assessment post-RSI/procedure



NMB: Neuromuscular blockade; TOF: Train of Four; PTC: Post-tetanic Count; PPC: Postoperative Pulmonary Complications; RSI: Rapid Sequence Intubation; AVS: After Visit Summary  
 Revision: 9/12/19 R.Wolfe

