

Evaluation of Procedural Neuromuscular Blockade Reversal Time with Sugammadex versus Neostigmine plus Glycopyrrolate

Alex Metzger PharmD

PGY1 Pharmacy Practice Resident - SSM Health DePaul Hospital

Residency Program Director: Anthony Lucido PharmD, BCPS

Project Mentors: Heather Malcom PharmD, BCPS &

Kim Doerhoff PharmD, BCPS

Disclosure

- No conflicts (financial or otherwise) to disclose

Learning Objective

- Identify differences in efficacy, safety, and cost between sugammadex and neostigmine plus glycopyrrolate for neuromuscular blockade reversal.

Research Question

- Do adult patients undergoing elective surgeries who received sugammadex for reversal of rocuronium or vecuronium induced neuromuscular blockade have a shorter neuromuscular blockade reversal time compared to patients who received neostigmine plus glycopyrrolate?

Background

- Rocuronium and vecuronium induced neuromuscular blockade reversal historically has been performed with neostigmine plus glycopyrrolate
- Sugammadex approved in 2015
- Price Differences:
 - Sugammadex 200mg/2ml: \$119.68
 - Neostigmine 10mg/10ml: \$22.00
 - Glycopyrrolate 0.4mg/2ml: \$6.72

Hristovska A, *Cochrane Database Syst Rev.* 2017.
Carron M, *J Clin Anesth.* 2016;35:1-12. 3.
Jones K, *Survey Anesthesiol.* 2008;52(3):139-140.
Paton F, *Br J Anaesth.* 2010;105(5):558-567.

Background cont.

	Hristovska et al ¹	Carron et al ²	Paton et al ⁴
Study Type	Meta-analysis	Meta-analysis	Systematic Review
Aim	To evaluate the efficacy and safety of sugammadex versus neostigmine in both moderate and profound neuromuscular blockade reversal	To evaluate the efficacy and safety of sugammadex versus neostigmine in neuromuscular blockade reversal	Economical evaluation of the difference in time saved with sugammadex versus neostigmine in neuromuscular blockade reversal
Results	Moderate: 10.22 min reduction Profound: 45.78 min reduction	Statistically significant quicker reversal Statistically significant lower adverse effects	Economically cost-effective when used in the operating room
Year	2017	2016	2010

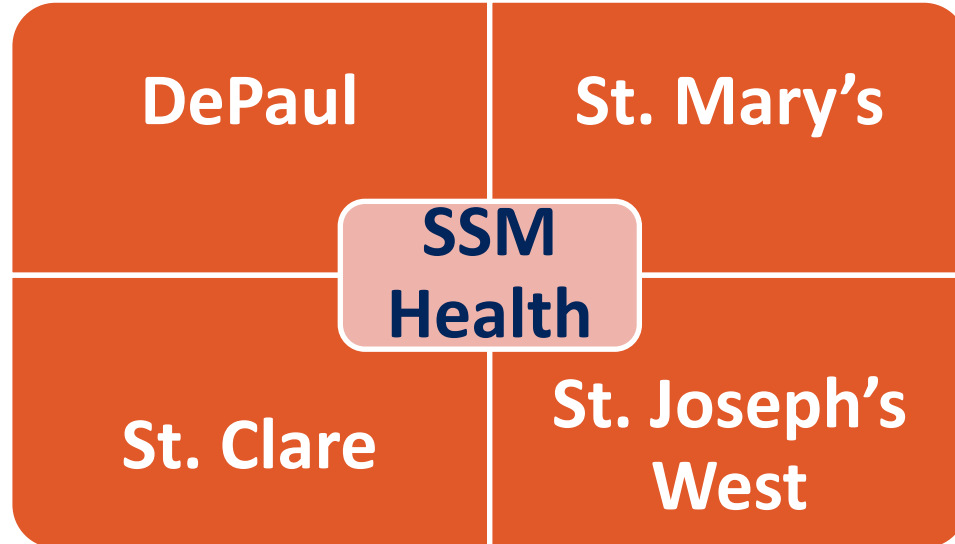
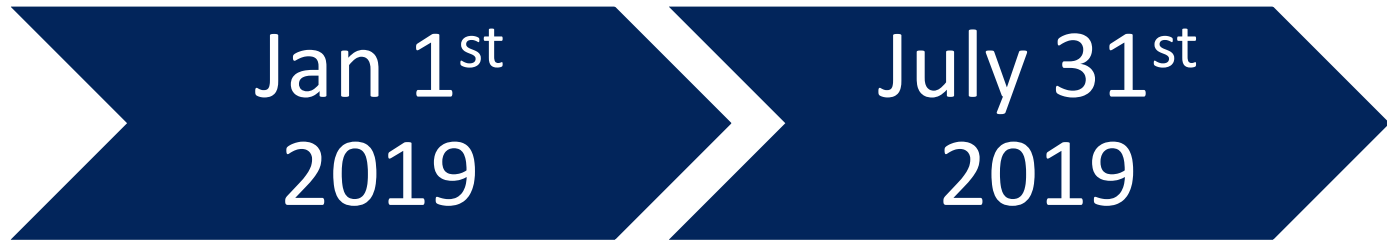
Hristovska A, *Cochrane Database Syst Rev.* 2017.

Carron M, *J Clin Anesth.* 2016;35:1-12. 3.

Paton F, *Br J Anaesth.* 2010;105(5):558-567.

Study Design

- Multi-center, non-blinded, retrospective study



Treatment Arms

Retrospective cohort arms

Neostigmine plus glycopyrrolate for neuromuscular blockade reversal

Sugammadex for neuromuscular blockade reversal

Inclusion & Exclusion

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none">- ≥ 18 years old- Vecuronium or rocuronium neuromuscular blockade- Elective surgery- Located at SSM Health: DePaul, St. Mary's, St. Clare, or St. Joseph's West	<ul style="list-style-type: none">- Creatinine clearance ≤ 50 ml/min- Pregnant- Breastfeeding

Study Endpoints

Primary Endpoint

- Neuromuscular blockade reversal time

Secondary Endpoints

- Hypotension up to 6 hours following the procedure
- Bradycardia up to 6 hours following the procedure

Statistical Analysis

Mann-Whitney U

- Neuromuscular blockade reversal time

Chi-Square

- Hypotension up to 6 hours following procedure
- Bradycardia up to 6 hours following procedure

Descriptive statistics

- Baseline characteristics

* All statistical tests performed with Minitab v19 software

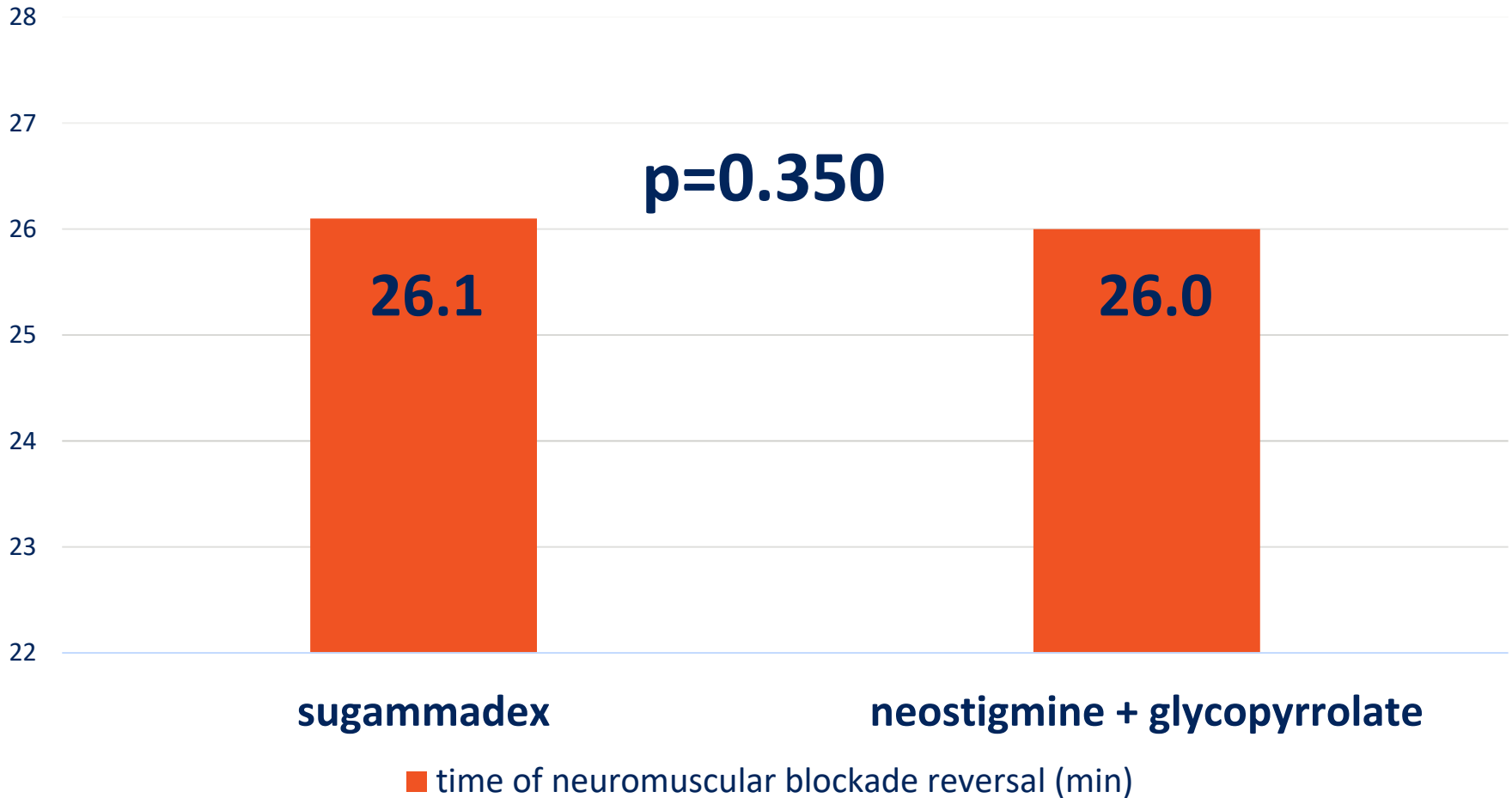
Gaddis, *Annals of Emergency Medicine*, 19(1), pp.86-89.
DiCenzo, ACCP; 2011.

Baseline Characteristics

	Sugammadex (n=60)	Neostigmine/glycopyrrolate (n=60)	P-value
Age	51.4	43.2	0.003
Gender	42 females 18 males	45 females 15 males	0.540
Hospital Breakdown			0.007
- DPHC	25	10	
- SMHC	13	14	
- SCHC	13	28	
- SJHW	9	8	
Weight (kg)	102	91.9	0.025
BMI (kg/m²)	35.2	32.4	0.129
Height (in)	67	66.2	0.557
S.Cr	0.8	0.82	0.727
CrCl	84.1	87.1	0.170
ASA Score	2.5	2.1	0.001

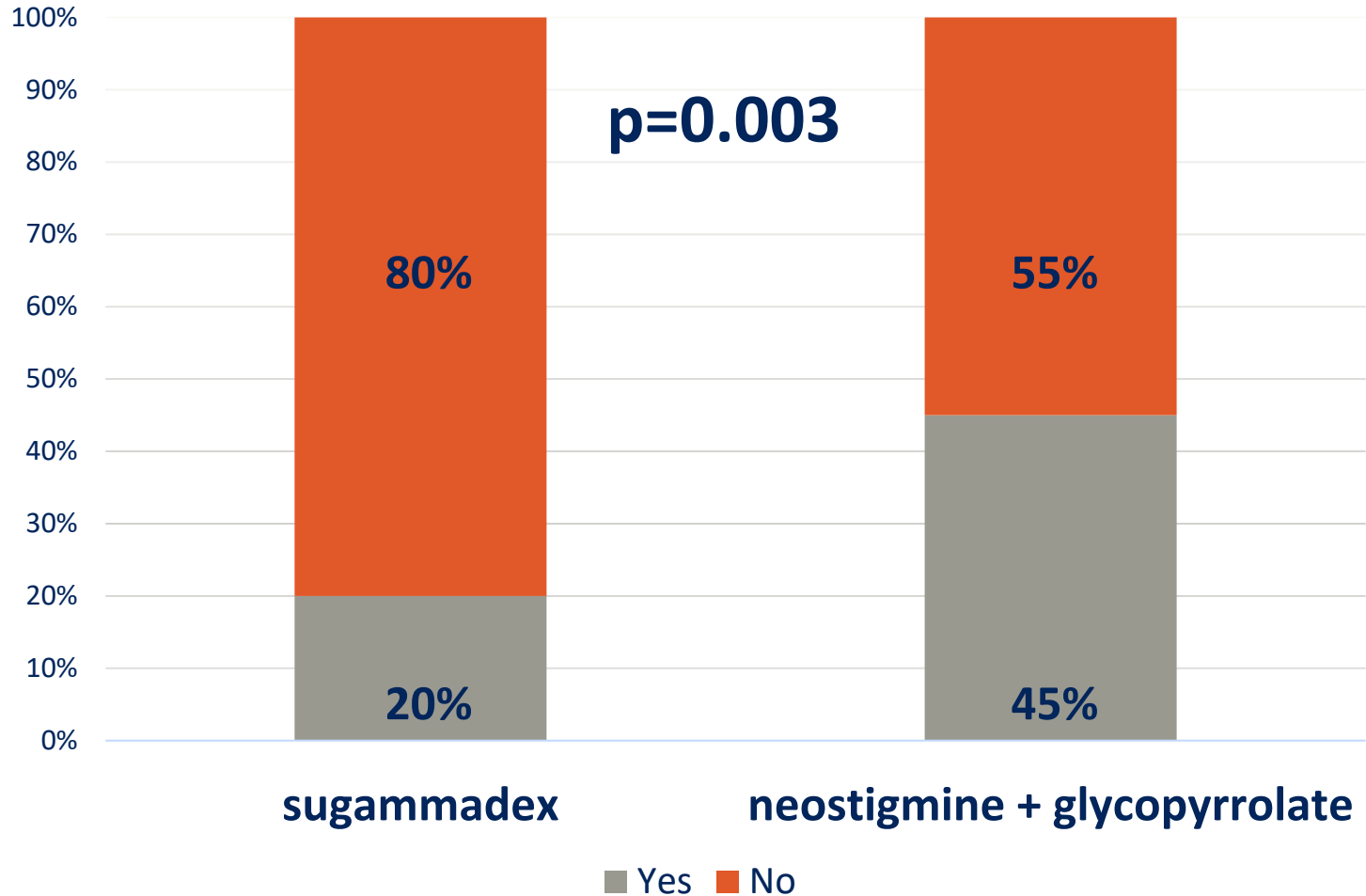
Primary outcome

Neuromuscular Blockade Reversal Time



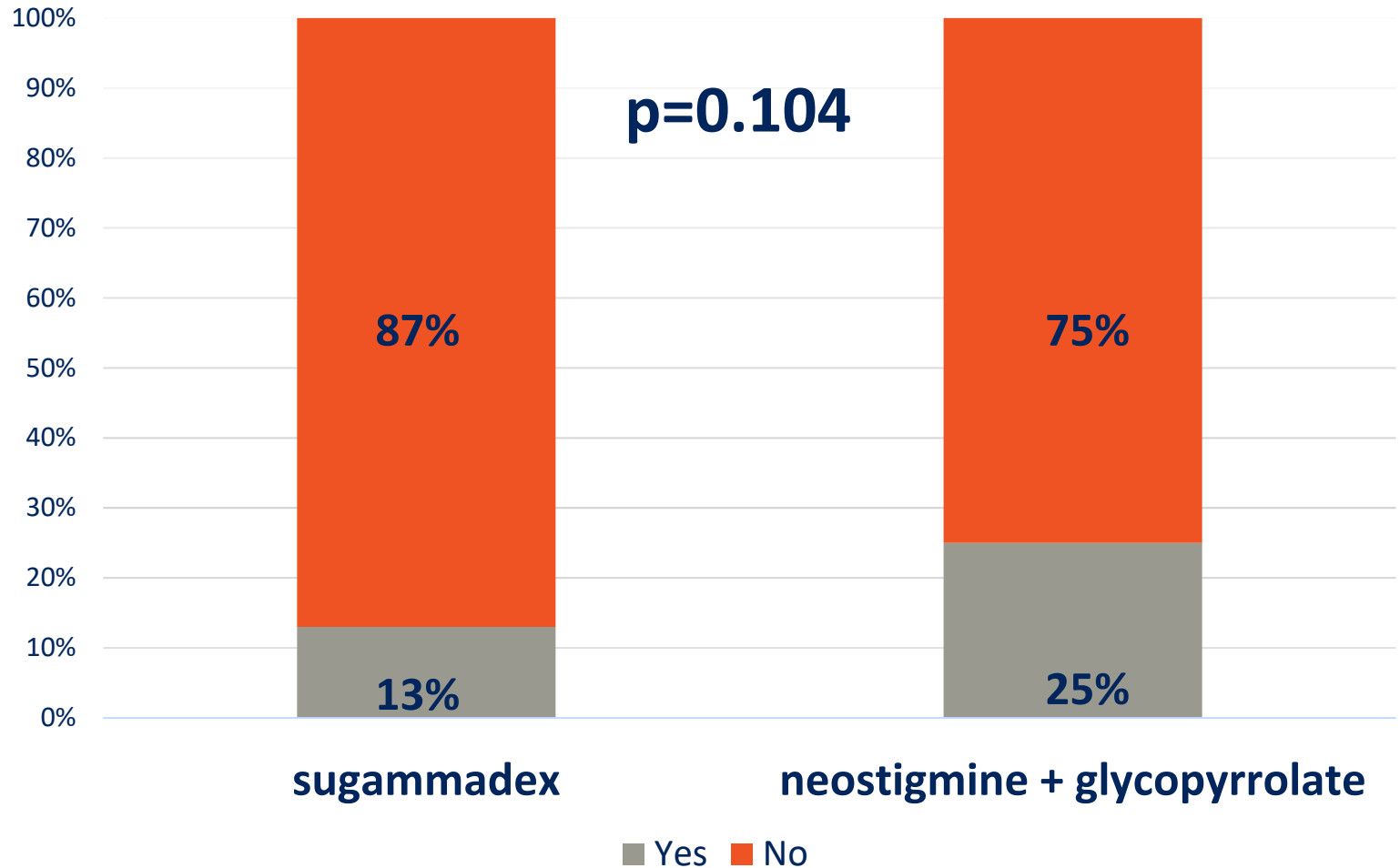
Secondary Outcomes

Hypotension up to 6 hrs post-procedure



Secondary Outcomes Cont.

Bradycardia up to 6 hrs post-procedure



Cost and Dosing Data

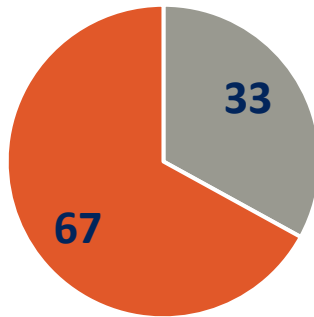
- average cost per minute in operating room: **\$31.31**
 - neostigmine + glycopyrrolate would result in **\$3.13** in savings based on operating room time
- neostigmine + glycopyrrolate would result in **\$113.97** in savings based on the average amount of each medication utilized
- time + medications = total savings of **\$117.10**

Strengths & Limitations

Strengths	Limitations
<ul style="list-style-type: none">- Multi-center- Cost data- Strict inclusion and exclusion criteria	<ul style="list-style-type: none">- Small patient population- Differences in surgical type- Baseline characteristic differences- Limited safety data- Low percent of accurate dosing

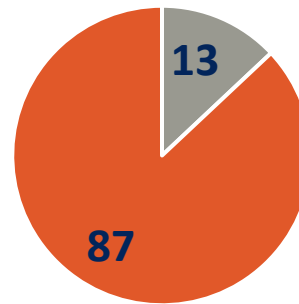
Correct Dosing Percentages

neostigmine



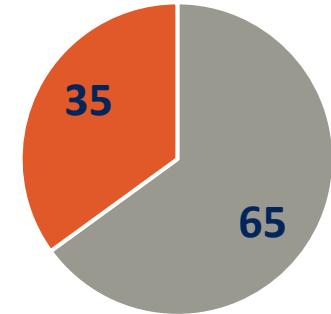
■ correct ■ incorrect

glycopyrrolate



■ correct ■ incorrect

sugammadex



■ correct ■ incorrect

Summary

- Efficacy:
 - There was no difference in neuromuscular blockade reversal time between the two arms
- Safety:
 - Sugammadex showed statistical significance in reducing rates of hypotension
 - No statistical difference seen in rates of bradycardia
- Cost:
 - Neostigmine + glycopyrrolate resulted in a \$117.10 average cost savings per procedure

Future Plans

- Dosing issues:
 - Educate anesthesia staff about proper dosing per package inserts
 - Stress the risks and benefits of over or under dosing
 - Re-evaluate data to see if there is a difference when correct dosing is utilized

Future Plans Cont.

- Operating room staff:
 - Present the efficacy, safety, and cost data
 - Discuss any limitations they identify
 - Evaluate the switching back to neostigmine + glycopyrrolate
 - Standardize train of four

References

- 1. Hristovska A, Duch P, Allingstrup M, Afshari A. Efficacy and safety of sugammadex versus neostigmine in reversing neuromuscular blockade in adults. *Cochrane Database Syst Rev.* 2017.
- 2. Carron M, Zarantonello F, Tellaroli P, Ori C. Efficacy and safety of sugammadex compared to neostigmine for reversal of neuromuscular blockade: a meta-analysis of randomized controlled trials. *J Clin Anesth.* 2016;35:1-12.
- 3. Jones K, Caldwell J, Brull S, Soto R. Early Reversal of Profound Rocuronium-Induced Neuromuscular Blockade by Sugammadex in a Randomized Multicenter Study. *Survey Anesthesiol.* 2008;52(3):139-140.
- 4. Paton F, Paulden M, Chambers D et al. Sugammadex compared with neostigmine/glycopyrrolate for routine reversal of neuromuscular block: a systematic review and economic evaluation. *Br J Anaesth.* 2010;105(5):558-567.
- 5. Gaddis, M., Gaddis, G. (1990). Introduction to biostatistics: Part 1, basic concepts. *Annals of Emergency Medicine*, 19(1), pp.86-89.
- 6. DiCenzo, R. Clinical Pharmacist's Guide to Biostatistics and Literature Evaluation. ACCP; 2011.
- 7. Krause M, McWilliams S, Bullard K et al. Neostigmine Versus Sugammadex for Reversal of Neuromuscular Blockade and Effects on Reintubation for Respiratory Failure or Newly Initiated Noninvasive Ventilation. *Anesthesia & Analgesia.* 2019:1.
- 8. Brideon [package insert]. Whitehouse Station, NJ. Merck & Co Inc; 2015.
- 9. Bloxiverz [package insert]. Chesterfield, MO. Avadel Legacy Pharmaceuticals; 2017.
- 10. Robinul [package insert]. Deerfield, IL. Baxter Healthcare Corporation; 2018.

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