Neuromuscular Blockade and Reversal: Patient Safety Considerations for the Interprofessional Team

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Learning Objectives

At the conclusion of this activity, participants should be able to

- Discuss the rationale for relevant depth of neuromuscular blockade needed to achieve ideal surgical operating conditions
- Explain approaches for reviewing medications for reversal of neuromuscular blockade that take into account patient safety, clinical outcomes, and pharmacoeconomics
- Address challenges faced by the interprofessional team in influencing changes that improve perioperative medication safety and outcomes related to residual paralysis

Achieving the Appropriate Depth of Neuromuscular Blockade

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Muscle Relaxation Often Needed During Surgery

- Serves as a major component of providing anesthesia in many surgical cases
  - *Analgesia, Amnesia,* ***Muscle Relaxation***
- Does not produce unconsciousness, analgesia or amnesia
  - Should never be given without sedation medication
- Prevents patient from moving while surgeon operates
- Relaxes muscle, making operating conditions ideal for surgeon to operate

Muscle Relaxation

- May occur from regional nerve block or neuromuscular blocking agents (muscle relaxants)
- May be potentiated by inhalational agents in a dose-related manner or by certain medications, such as magnesium or aminoglycosides (e.g., gentamicin)
- Can be antagonized by calcium and by anticholinesterases (reversal agents)

McCall EJ. Antibiotics. In: Ouellette RG et al., eds. Pharmacology for nurse anesthesiology; 2011:212-3.

Muscle Relaxation

- Neuromuscular blocking agents have varying effects on different muscles
  - Diaphragm is less susceptible to the effects compared with both peripheral muscles and pharyngeal upper airway dilator muscles
  - Diaphragmatic function returns more rapidly than peripheral muscles

Lien CA et al. Neuromuscular blockers and reversal drugs. In: Hemmings HC et al., eds. Pharmacology and physiology for anesthesia: foundations and clinical application; 2013:326.

Muscle Relaxants

- Risk of residual neuromuscular blockade (NMB) is one of the most feared complications of anesthesia
- Intermediate-acting neuromuscular blockers (e.g., rocuronium, vecuronium, atracurium) have an incidence of residual NMB of over 20%, even after short surgical procedures
- Residual NMB may also occur after a single intubating dose of intermediate-acting neuromuscular blockers
- Quantitative monitoring is presently considered the only recommended method to diagnose residual NMB

Bettelli G. *Curr Opin Anaesthesiol*. 2006; 19:600-5.

To Paralyze or Not Paralyze

- Some anesthesia providers think muscle relaxants should always be administered as part of the anesthetic regimen to ensure patient safety (unless contraindicated due to EMG or motor monitoring)
- Other anesthesia providers advocate for not administering a muscle relaxant as part of the anesthetic regimen

EMG = electromyography

Muscle Relaxation with Anesthetic Induction

- Reverses muscle rigidity that may occur from opioids given with induction
- Eases ventilation after induction of anesthesia
- Allows the vocal cords to relax and open for placement of the endotracheal tube into the trachea without injury to the vocal cords
- Prevents laryngospasm during intubation
- Prevents patient from clenching teeth or moving during intubation

Cammu G. *Acta Anaesth Belg*. 2007; 58:7-14.

Muscle Relaxation During Surgery

- Allows muscles of abdomen to be relaxed for surgeon
- Deep NMB provides better operating conditions for a variety of surgeries compared with moderate, shallow, or no NMB
- Prevents coughing and movement during certain surgeries
- Allows relaxation of hip joint for laparoscopic hip surgery

Ledowski T. *Surg Laparosc Endosc Percutan Tech*. 2015; 25:281-5.
Bettelli G. *Curr Opin Anaesthesiol*. 2006; 19:600-5.

Muscle Relaxation for Abdominal Surgery

- Provides adequate surgical operating conditions
- Eliminates abdominal muscle tone
  - Allows surgical exposure and closure with ease
- Prevents spontaneous breathing and diaphragmatic movement during surgery
- May decrease incisional herniation
- May decrease bleeding
- May decrease morbidity and mortality

Ledowski T. *Surg Laparosc Endosc Percutan Tech*. 2015; 25:281-5.
Bettelli G. Curr Opin *Anaesthesiol*. 2006; 19:600-5.

Muscle Relaxation for Laparoscopic Surgery

- Increasing evidence suggests that "only deep NMB may achieve best operating conditions during laparoscopic surgery"
- Deep muscle relaxation superior vs. surgeon increasing intraabdominal pressure
- Allows intraabdominal pressure to be lower (8-10 mm Hg vs. 10-15 mm Hg), which can lead to
  - Significantly reduced postoperative pain
  - Improved patient outcomes and improved quality of life ratings
  - Earlier hospital discharge
  - Less impaired organ perfusion and organ dysfunction (renal, hepatic, cardiac) from macrovascular or microvascular changes that may occur with higher pressures

Ledowski T. *Surg Laparosc Endosc Percutan Tech*. 2015; 25:281-5.

Muscle Relaxation for Cardiac Surgery

- Facilitates tracheal intubation
- Decreases oxygen consumption during cardiopulmonary bypass by up to 30%
- Prevents movement during cannulation
- Attenuates shivering
- Decreases skeletal muscle contraction with defibrillation

Contrera MA et al. Anesthesia for cardiac surgery.
In: Nagelhaut JJ et al., eds. Nurse anesthesia, 6th ed. St. Louis: Elsevier; 2018:494.
Cammu G. *Acta Anaesthesiol Belg*. 2007; 58:7-14. Irish CL et al. *J Cardiothorac Vasc Anesth*. 1991; 5:132-4.

Paralyzing the Patient for Surgery

Advantages

- Better operating conditions for surgeon due to muscle relaxation
- Patient will not move or cough despite surgical stimulation
- Lighter anesthetic can be given without risk of patient movement
- Emergence from anesthesia will be quicker

Disadvantages

- Muscle relaxants have no anesthetic or hypnotic effects (risk of awareness)
- Increased complications: histamine release, anaphylaxis, myalgia with succinylcholine, residual NMB with nondepolarizing agents
- Increased HR and BP may occur with sympathetic stimulation and lighter anesthesia
- Reversal agents needed if any depth of NMB is present at end of surgery

HR = heart rate
BP = blood pressure

Bettelli G. *Curr Opin Anaesthesiol*. 2006; 19:600-5.
Ledowski T. *Surg Laparosc Endosc Percutan Tech*. 2015; 25:281-5.

Adverse Effects of Anticholinesterase Inhibitors: Neostigmine

- Confusion
- Bronchoconstriction
- Abdominal cramping, nausea, vomiting
- Parasympathetic stimulation: bradycardia, asystole
- Muscle weakness
- Increased intestinal tone
- Loss of bowel or bladder control
- Excessive salivation

Lien CA et al. Neuromuscular blockers and reversal drugs. In: Hemmings HC et al., eds. Pharmacology and physiology for anesthesia: foundations and clinical application; 2013:326.

Not Paralyzing the Patient for Surgery

Advantages

- Decreases anesthetic awareness
  - If patient moves, anesthesia provider will deepen anesthetic, preventing recall
- No need for reversal agents
- Prevents residual NMB

Disadvantages

- Deeper anesthetic needed to prevent movement
- If patient coughs, may lead to injury
  - Head in pins → lacerations at pin site; injury to neck
  - Trocar inserted for laparoscopic surgery → accidental injury to major vessel
- Prolongs emergence - deeper anesthetic
- Patient may need vasopressor support

Bettelli G. *Curr Opin Anaesthesiol*. 2006; 19:600-5. Avidan MS et al. *Anaesthesia*. 2013; 68:333-42. Ledowski T. *Surg Laparosc Endosc Percutan Tech*. 2015; 25:281-5.

If patient is paralyzed, what depth of NMB is needed?

Depth of Block	Quantitative Measurement	Qualitative Measurement	Comments
Complete block	PTC = 0	PTC = 0	Head in pins; laparoscopic abdominal or hip surgery
Deep block	PTC ≥ 1; TOF = 0	PTC ≥ 1; TOF = 0	No breathing or diaphragmatic movement
Moderate block	TOF = 1-3	TOF = 1-3	Many surgeries where deep block not needed
Shallow block	TOF ratio < 0.4	TOF = 4; fade present	Muscle relaxant not necessarily needed
Minimal block	TOF ratio = 0.4-0.9	TOF = 4; fade not detected	Not yet ready for extubation
Acceptable recovery	TOF ratio ≥ 0.9	Cannot be determined	Ready for extubation

PTC = post-tetanic count, TOF = train-of-four

Modified from Naguib M et al. *Anesth Analg.* 2018; 127:71-80.

Depth of Neuromuscular Blockade

- Anesthesia providers and surgeons must work together to agree on an acceptable depth of NMB to ensure patient safety
- If muscle relaxation is needed, paralysis should be reversed to decrease the risk of residual NMB

Key Takeaways

- Muscle relaxation may provide ideal operating conditions for the surgeon
- However, this may not always be the safest method in providing anesthesia to the patient
- Surgeons and anesthesia providers must work together to ensure that the anesthetic given is what is best for the patient

Approaches for Reviewing Medications for Reversal of Neuromuscular Blockade

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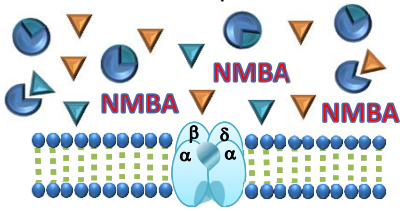
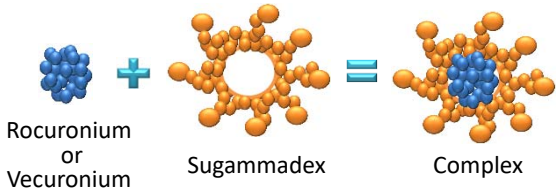
Neuromuscular Blocking Agent (NMBA) Reversal

- Neostigmine
  - 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



Key Attributes of the Reversal Agents

Neostigmine

- Competitive mechanism of action that has the ability to reverse all NMBAs
- Ineffective for reversing profound or deep neuromuscular block
- May reverse moderate block, but takes a significant amount of time
- Effectively reverses minimal to light block within 10-15 minutes in most patients
- Anticholinergic (e.g., glycopyrrolate) coadministration required to prevent bradycardia
- Adverse effects, such as PONV and bradycardia, are more prevalent than with sugammadex
- Residual NMB (defined as a TOF ratio < 0.9) is more prevalent than with sugammadex

Sugammadex

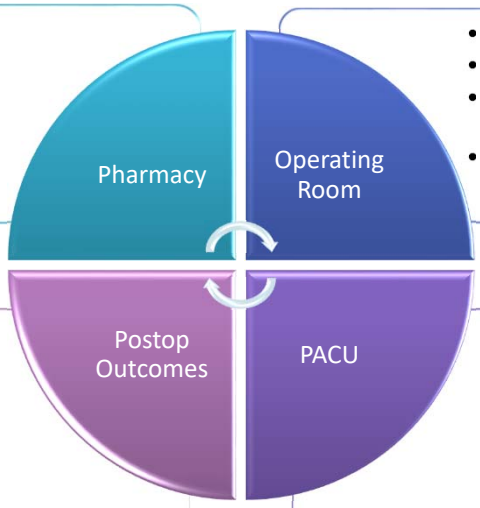
- Predictable, highly effective reversal agent for rocuronium and vecuronium only
- Effectively reverses shallow to deep, and even profound block
- Emergent reversal (~3 min from induction) is only approved for rocuronium-induced blockade
- Associated with hypersensitivity reactions (mechanism unknown, unlikely IgG- or IgE-mediated)
- Drug cost is higher than the combination of neostigmine + glycopyrrolate

PONV = postoperative nausea and vomiting

Brull SJ et al. *Anesthesiology*. 2017; 126:173-90.
Hristovska AM et al. *Cochrane Database Syst Rev*. 2017; 8:CD012763.

Pharmacoeconomic Considerations

- Medication efficacy
- Medication safety
- Medication cost
- Medication use
- Adjunctive medications



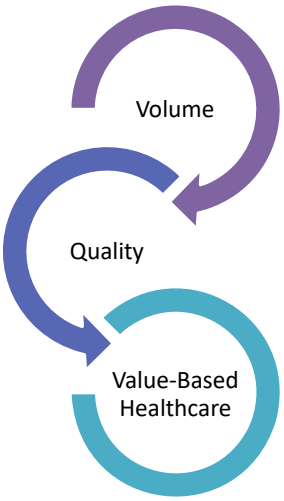
- OR time and OR cost
- OR efficiency
- NMB monitoring: equipment availability, use practices, and cost
- Patient safety: ADE, emergent reversal option

- Postoperative complications: pneumonia, aspiration pneumonitis, atelectasis
- Readmissions
- Patient satisfaction

- Residual NMB: reintubation, ICU admission, PACU respiratory event
- PONV incidence
- Readiness for discharge
- PACU time and PACU cost
- Patient education

PACU = post anesthesia care unit; ADE = adverse drug event

Shift in the Healthcare Mindset



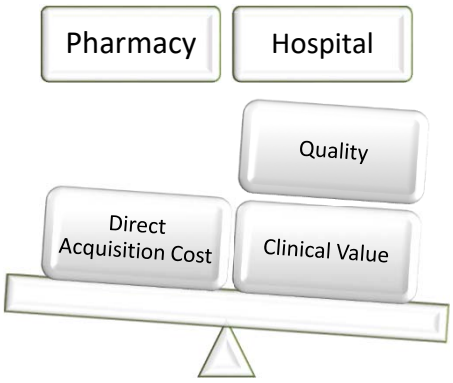
- Agency for Healthcare Research and Quality (AHRQ)
  - U.S. Department of Health and Human Services
  - Value-based care is a core healthcare priority
  - Goal: 20% reduction in hospital-acquired conditions (HACs) between 2014-2019
  - Category: All other HACs
    - Postoperative respiratory failure
    - Postoperative pneumonia
- Potential strategies to reduce postoperative HACs
  - Optimize use of NMM and NMB reversal agents

NMM = neuromuscular monitoring

https://www.ahrq.gov (accessed 2018 Oct 30).

Quality and Value-Based Healthcare

- Budgetary silos
  - Have the potential to constrain medication use
  - No direct return on investment
- All are tasked to improve health outcomes, reduce unnecessary use, and control healthcare expenditures



Interprofessional Approach

- Clinical tactics to NMM and NMB reversal are strategically evaluated to optimize return on investment (ROI)

$$\text{ROI} = \frac{\text{Net return from reduced postoperative HACs}}{\text{Investment in optimal management of NMB}}$$

Center for Health Care Strategies, Inc. http://www.chcsroi.org. 2007 (accessed 2018 Oct 30).

Pharmacy Department Investment

Investment

- Drug cost*
  - NMB Reversal - Shallow
    - Neostigmine plus glycopyrrolate $30-65
    - Sugammadex $90
  - NMB Reversal - Moderate
    - Neostigmine plus glycopyrrolate $30-130
    - Sugammadex $90-165
  - NMB Reversal - Deep†
    - Sugammadex $165
  - NMB Reversal - Emergent†
    - Sugammadex $495

*Based on average health-system purchase price of a single-dose or single-use vial or prefilled syringe & weight of 85 kg.
†Neostigmine is ineffective for reversing profound or deep neuromuscular block.

Perioperative and Anesthesiology Investment

Investment

- Neuromuscular monitoring equipment (quantitative preferred)
  - Availability and accessibility of user-friendly devices
  - Device acquisition costs ($800-2400 per device)
- Equipment training and competency maintenance
  - Difference in clinical, subjective, and objective monitoring
  - Appropriate electrode placement sites
  - Pre-planning with quantitative monitors (e.g., placement and calibration before NMBA)
  - NMM required for sugammadex as well as neostigmine
- Institutional practice guideline on clinical management and monitoring of NMB

Brull S et al. *Anesthesiology*. 2017; 126:173-90.

Workflow Efficiency

Return on Investment

- Meta-analysis: sugammadex vs. neostigmine
  - Operating room recovery time
    - Sugammadex faster discharge
      - MD 22.14 min, 95% CI (14.62-29.67), p<0.00001
      - Inclusion of patients with deep block: MD 30.05 min, 95% CI (11.11-48.99), p<0.002
  - PACU length of stay
    - Sugammadex faster discharge
      - MD 16.95 min, 95% CI (0.23-33.67), p=0.0469

- Impact on intraoperative & PACU efficiency
  - Reduction in staffing costs
  - Reduction in overtime pay
  - Enhanced employee satisfaction
  - Enhanced patient satisfaction
- Key considerations
  - Discharge vs. discharge-readiness
  - Clinical significance of time saved
    - Enough time saved for an additional case
    - Avoidance of placing OR on hold and case cancellation

MD = mean difference

Carron M et al. *J Clin Anesth*. 2017; 39:38-44.
Carron M et al. *Clinicoecon Outcomes Res*. 2016; 8:43-52.

Clinical Outcomes

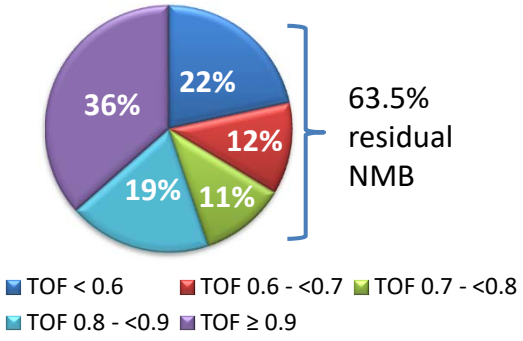
Potential Return on Investment

- Reduced mechanical ventilation in PACU
- Reduced respiratory events in PACU
- Reduced postoperative pulmonary complications
- Decreased unplanned ICU admissions
- Faster recovery of bowel function
- Decreased readmissions

Carron M et al. *Clinicoecon Outcomes Res*. 2016; 8:43-52.
O'Reilly-Shah VN et al. *Korean J Anesthesiol*. 2018; 71:374-85.

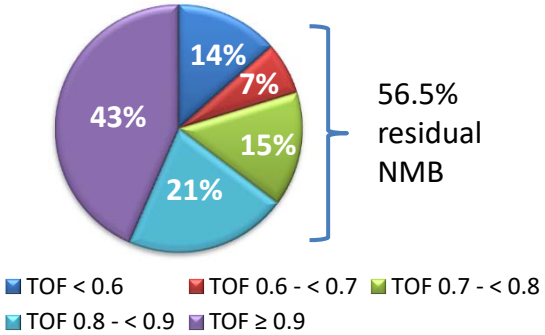
RECITE Study:
Incidence of Postoperative Residual NMB

NMB at Extubation



Only 36% had TOF ratio ≥ 0.9
73.9% reversed with Neostigmine

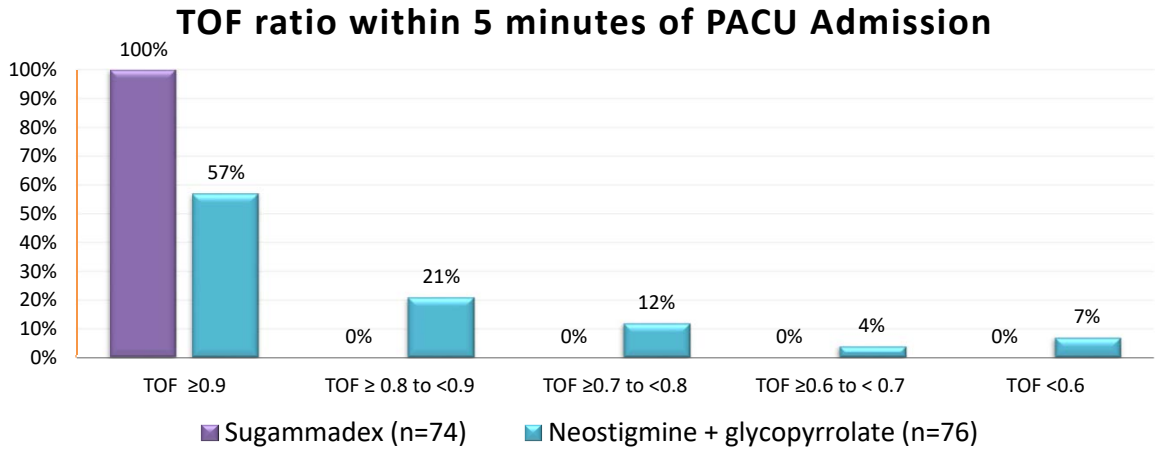
NMB on Arrival to PACU



Only 43% had TOF ratio ≥ 0.9
72 % reversed with Neostigmine

Fortier L et al. *Anesth Analg*. 2015; 121:366-72.

Incidence Postoperative Residual NMB



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

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%
- 42/61 patients were matched with controls
  - Criteria: age, sex, procedure
  - Significant residual NMB in cases with CRE vs. controls
    - TOF ratio 0.62 ± 0.2 vs. TOF ratio 0.98 ± 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.

Postoperative Pulmonary Complications

Author & Journal	Study Design	Intervention	Primary Outcome	Results
Grosse-Sundrup M. BMJ. 2012; 345:e6329	Prospective PMC N=18,579 (matched)	Receipt of intermediate-acting NMBA	Desaturation after extubation (O_2 Sat < 90% and with decrease in O_2 Sat after extubation) and reintubation within 7 days	NMBA increased risk of postop desaturation • (OR 1.36, 95% CI 1.23-1.51) NMBA increased risk of reintubation • (OR 1.4, 95% CI 1.09-1.80)
Bulka CM. Anesthesiology 2016; 125:647-55	Retrospective PMC N=1,455 NMBA vs. No NMBA N=1,320 Neostigmine vs. No reversal	Receipt of intermediate-acting NMBA	Incidence of pneumonia within 30 days after surgery	NMBA increased incidence of postoperative pneumonia • 9 vs. 5.22 per 10,000 person-days at risk (1.79; 95% CI, 1.08-3.07) No reversal increased incidence of postoperative pneumonia • (2.26, 95% CI, 1.65-3.03)

PMC = Propensity matched cohort, OR = odds ratio, CI = confidence interval

Postoperative Pulmonary Complications

Design	Intervention	Primary Outcome	Results

Multicenter, prospective, observational European cohort study 211 hospitals	Observational study of patients receiving general anesthesia for non-cardiac surgery	Incidence of postoperative pulmonary complications (PPC) at 28 days	• PPC incidence: 7.6% (1,658/21,694)
			  • PPC incidence with NMBA: 8.4% (1,441/17,150)
			  • Increased risk with NMBA (ARR_{adj} -4.4, 95% CI -5.5 to -3.2)
			Major risk factors for PPC
			• Intrathoracic or open upper abdominal surgery
			• Surgery duration > 2 hr
			• Preoperative SpO_2 of ≤ 94%
			• Emergent surgery
			• ASA class ≥ 3
			• Age > 60 yr
			Subgroup analysis (selective NMM and reversal agent use)
			• NMBA increased incidence of PPC (OR_{adj} 1.86, 95% CI 1.53-2.26)
			• NMM did not decrease risk of PPC (OR_{adj} 1.31, 95% CI 1.15-1.49)
			• Reversal agents did not decrease risk of PPC (OR_{adj} 1.23, 95% CI 1.07-1.41)

n=21,694 NMBA=17,150 NMB reversal=8,795 NMM= 6,868 • (TOF ratio in 60.9% [4,182/6,868])			

ARR_{adj} = adjusted absolute risk reduction; ASA = American Society of Anesthesiologists; OR_{adj} = adjusted odds ratio

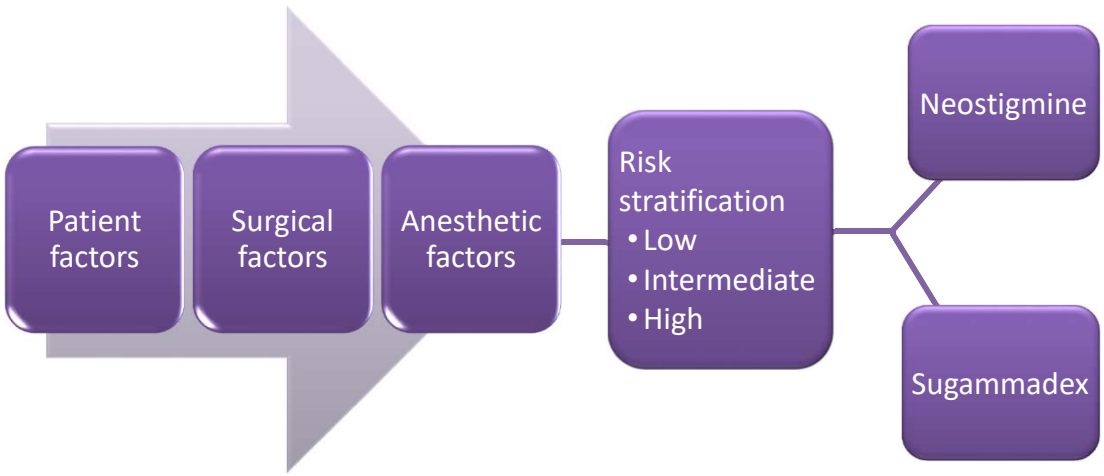
Kirmeier E et al. *Lancet Respir Med*. 2018 Sept 14. Epub ahead of print.

Optimizing ROI

- Postoperative pulmonary complications
  - Increase patient morbidity and mortality
  - Increase healthcare expenditures
  - Relatively common
- Preventative measures could be a significant source of cost savings
  - Optimal clinical management of NMB
- Identify patients at high risk for pulmonary complications
  - Enhance return on investment

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

Risk Prediction Models



Risk Stratification

Patients at High Risk for Postoperative Pulmonary Complications	
Preoperative $SpO_2 \leq 94\%$	Severe respiratory disease
ASA class ≥ 3	Obstructive sleep apnea
Age ≥ 60 yr	BMI > 40 kg/m^2
Duration of procedure > 2 hr	Chronic renal insufficiency
Intrathoracic or upper abdominal surgery	Significant cardiovascular disease
Long-acting NMBA	History of recent respiratory infection

Miskovic A et al. *Br J Anaesth*. 2017; 118:317-34.
Kirmeier E et al. *Lancet Respir Med*. 2018 Sept 14. Epub ahead of print.
Hristovska AM et al. *Cochrane Database Syst Rev*. 2017; 8:CD012763.

Reviewing Reversal Agents

- Interprofessional collaboration
- Multidepartment investment
- Value-based healthcare focus
- Strategy to optimize ROI
- Leadership support
- Continued focus on clinical outcomes
- Understanding of clinical practice

Understanding Clinical Practice

- Utilization
  - % of patients with general anesthesia
  - % of patients receiving NMBAs
  - % using neostigmine
  - % using sugammadex
- Dosage and vial size
  - Appropriate for patient's weight
  - Appropriate for depth of blockade
  - Appropriate for renal function
- NMM
  - Qualitative vs. quantitative
  - TOF or TOF ratio prior to extubation
  - Competency
- Accessibility impact
  - Stored in ADC, Rx satellite
- Neostigmine with sugammadex rescue
  - Failed reversal with neostigmine ($$$)
  - Neostigmine-related neuromuscular weakness
- Sugammadex 16 mg/kg use for emergent reversal
- Postoperative clinical outcomes
  - PACU respiratory events
  - Reintubation rates
  - Unplanned ICU admissions
  - Postoperative pulmonary complications
  - Complications from use of anticholinergic agents
  - Hypersensitivity reactions

Key Takeaways

- Pharmacy review of NMB reversal agents must consider impact beyond the pharmacy budget
- Interprofessional effort is required to obtain the best return on investment
- Clinical outcome data on sugammadex are limited
- Optimal clinical management of NMB is undefined

Influencing Change to Improve Perioperative Medication Safety and Outcomes

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Elements of Implementation Success

- Intervention characteristics
- Outer setting
- Inner setting
- Characteristics of individuals
- Implementation process

Damschroder LJ et al. *Implement Sci*. 2009, 4:50.

Intervention Characteristics

Intervention Source	Perception of key stakeholders about whether the intervention is externally or internally developed
Evidence Strength & Quality	Stakeholders' perceptions of the quality and validity of evidence supporting the belief that the intervention will have desired outcomes
Relative Advantage	Stakeholders' perception of the advantage of implementing the intervention versus an alternative solution
Adaptability	Degree to which an intervention can be adapted, tailored, refined, or reinvented to meet local needs

Damschroder LJ et al. *Implement Sci*. 2009, 4:50.

Trialability	Ability to test the intervention on a small scale in the organization and ability to reverse course (undo implementation) if warranted
Complexity	Perceived difficulty of implementation, reflected by duration, scope, radicalness, disruptiveness, centrality, and intricacy and number of steps required to implement
Design Quality and Packaging	Perceived excellence in how the intervention is bundled, presented, and assembled
Cost	Costs of the intervention and costs associated with implementing that intervention, including investment, supply, and opportunity costs

Damschroder LJ et al. *Implement Sci*. 2009, 4:50.

Outer Setting

Patient Needs & Resources	Extent to which patient needs, as well as barriers and facilitators to meet those needs, are accurately known and prioritized by the organization
Cosmopolitanism	Degree to which an organization is networked with other external organizations
Peer Pressure	Mimetic or competitive pressure to implement an intervention; typically because most or other key peer or competing organizations have already implemented or are in a bid for a competitive edge

Damschroder LJ et al. *Implement Sci*. 2009, 4:50.

External Policy & Incentives	Broad construct that includes external strategies to spread interventions, including policy and regulations (governmental or other central entity), external mandates, recommendations and guidelines, pay-for-performance, collaborations, and public or benchmark reporting

Damschroder LJ et al. *Implement Sci*. 2009, 4:50.

Inner Setting

Structural Characteristics	Social architecture, age, maturity, and size of an organization
Networks & Communications	The nature and quality of webs of social networks and the nature and quality of formal and informal communications within an organization
Culture	Norms, values, and basic assumptions of a given organization
Implementation Climate	Absorptive capacity for change, shared receptivity of involved individuals to an intervention and the extent to which use of that intervention will be rewarded, supported, and expected within the organization
Readiness for Implementation	Tangible and immediate indicators of organizational commitment to the decision to implement an intervention

Damschroder LJ et al. *Implement Sci*. 2009, 4:50.

Characteristics of Individuals

Characteristics of Individuals

- Knowledge and beliefs about the intervention
- Self-efficacy
- Individual stage of change
- Individual identification with organization
- Other personal attributes

Damschroder LJ et al. *Implement Sci*. 2009, 4:50.

The Joint Commission Journal on Quality and Patient Safety

Infection Prevention and Control

How Active Resisters and Organizational Constipators Affect Health Care–Acquired Infection Prevention Efforts

Sanjay Saint, M.D., M.P.H.; Christine P. Kowalski, M.P.H.; Jane Banaszak-Holl, Ph.D.; Jane Forman, Sc.D., M.H.S.; Laura Damschroder, M.S., M.P.H.; Sarah L. Krein, Ph.D., R.N.

Saint S et al. *Jt Comm J Qual Patient Saf*. 2009; 35:239-46.

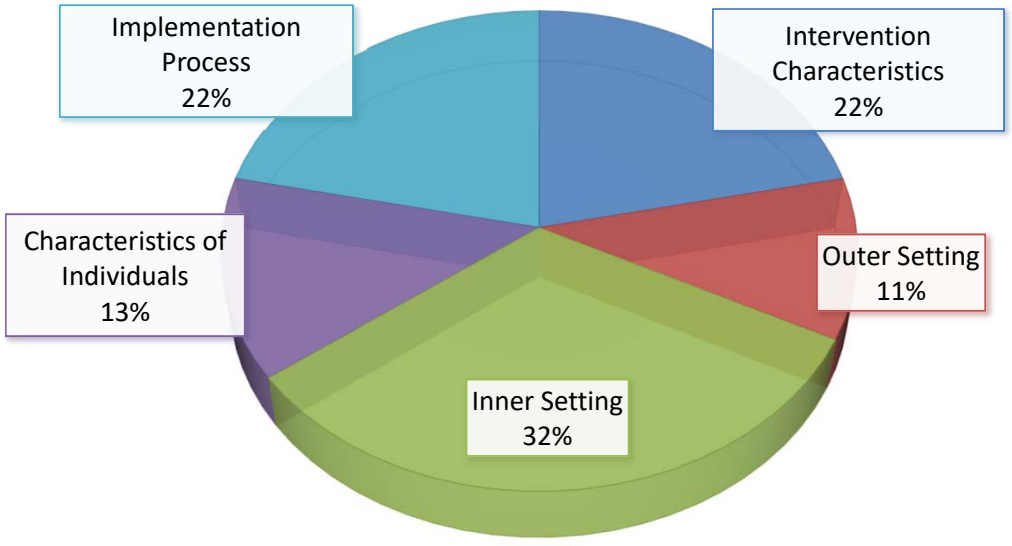
Implementation Process

Implementation Process

- Planning
- Engaging
  - Opinion leaders
  - Formally appointed internal implementation leaders
  - Champions
  - External change agents
- Executing
- Reflecting and evaluating

Damschroder LJ et al. *Implement Sci*. 2009, 4:50.

Relative Numbers of Constructs



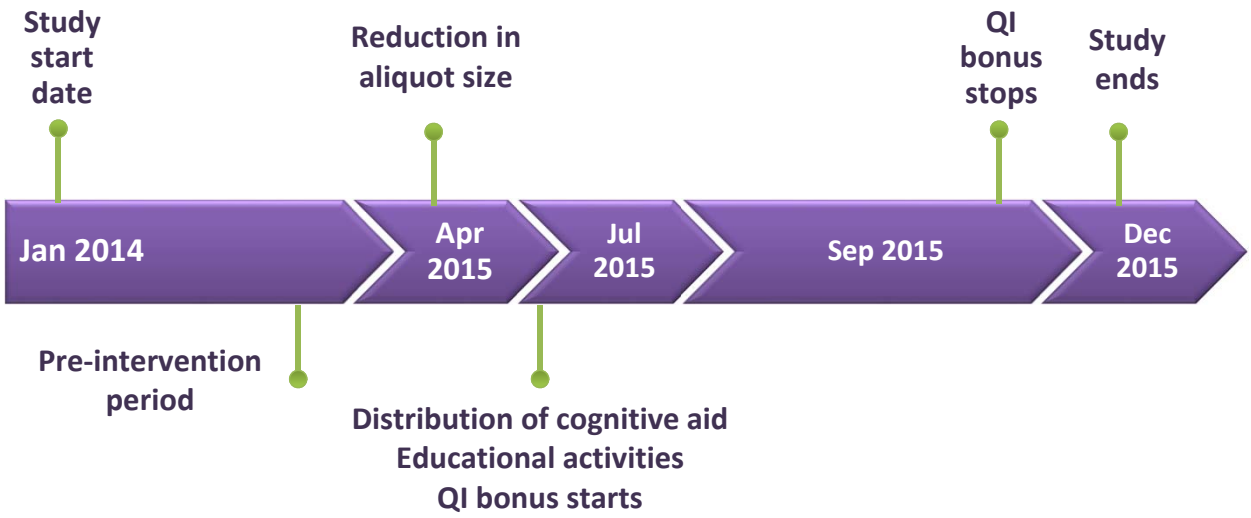
Damschroder LJ et al. *Implement Sci*. 2009, 4:50.

So What Actually Works?

Strong Differentiators	Low Implementation Success		High Implementation Success	
INTERVENTION CHARACTERISTICS				
Relative advantage	-2	+1	+2	+2
OUTER SETTING				
Patient needs and resources	-2	0 (mixed)	+2	+2
INNER SETTING				
Networks and communications	-2	-2	+2	+2
Implementation climate				
Tension for change	0	0	+1	+1
Relative priority	-1	-2	+1	+2
Goals and feedback	-2	-1	+1	+2
Learning climate	Missing	-1	+1	+2
Readiness for implementation				
Leadership engagement	-2	-1	+2	+2
IMPLEMENTATION PROCESS				
Planning	-1	Missing	+1	+1
Reflecting and evaluating	-1	-2	+1	+2

Damschroder et al. *Implementation Science.* 2013, 8:51.

Study Design



QI = quality improvement

Rudolph MI et al. *Anaesthesia.* 2018; 73:1067-78.

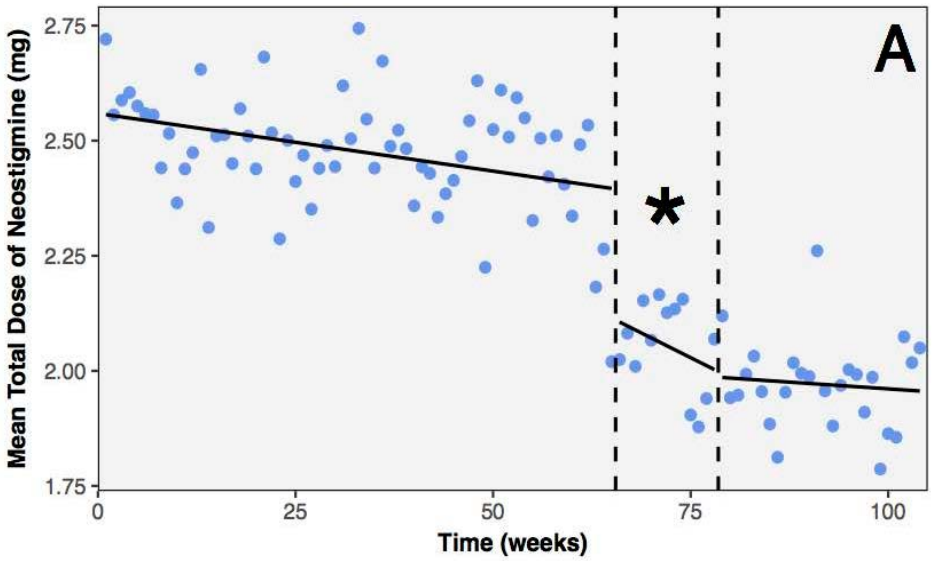
Neostigmine Reversal Guide

Type of Monitoring		Neostigmine Dose	
Qualitative	Quantitative	Weight-Based	70-kg patient
No twitch	No twitch	WAIT	WAIT
1 twitch	1 twitch	WAIT	WAIT
2-3 twitches	2-3 twitches	~50 mcg/kg	3-4 mg
4 twitches with fade	TOF ratio <0.4	~40 mcg/kg	2-3 mg
4 twitches without fade	TOF ratio 0.4-0.9	15-30 mcg/kg	1-2 mg
	TOF ratio >0.9	NONE	NONE

Risk factors for Residual Weakness
High total dose of NMBA >1.5 mcg/kg rocuronium or >0.4 mg/kg cisatracurium
High dose neostigmine reversal >60 mcg/kg
ALWAYS DOSE NMBA AND REVERSAL ACCORDING TO MONITORING AND CLINICAL CONDITION

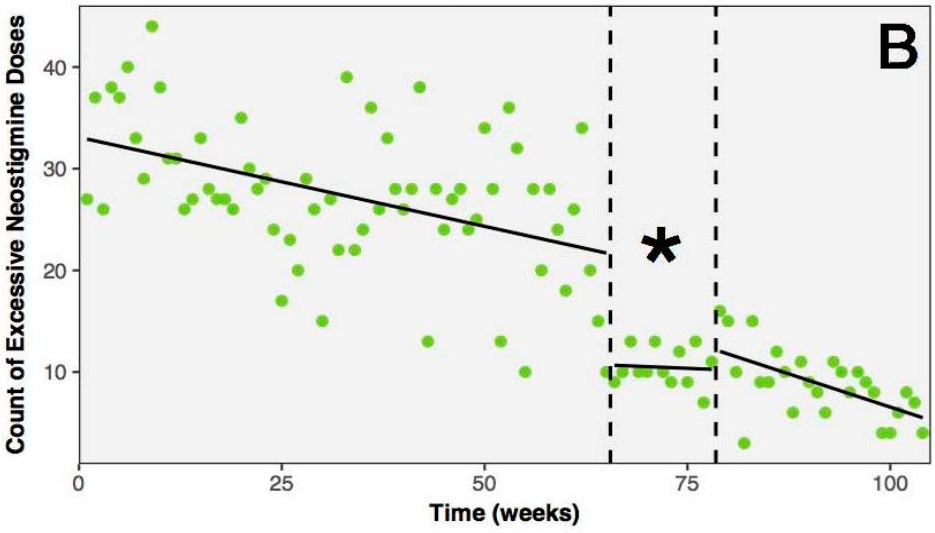
Rudolph MI et al. *Anaesthesia.* 2018; 73:1067-78.

Mean Neostigmine Dose



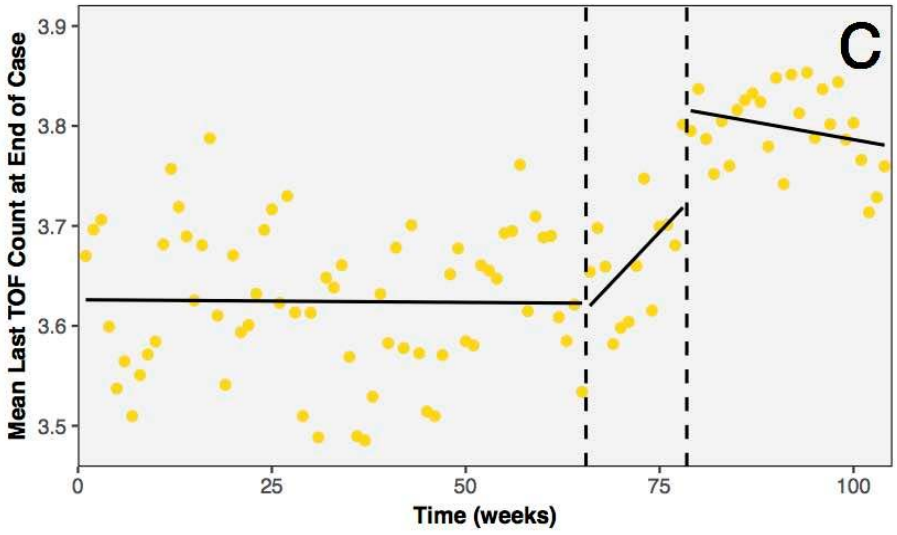
Rudolph MI et al. *Anaesthesia.* 2018; 73:1067-78.

Excessive Neostigmine Dose (>60 mcg/kg)



Rudolph MI et al. *Anaesthesia.* 2018; 73:1067-78.

TOF Count at the End of the Case



Rudolph MI et al. *Anaesthesia.* 2018; 73:1067-78.

Clinical Outcomes

Outcome	Pre-QI Intervention n= 2,937	Post-QI Intervention n=9,088	Adjusted OR (95% CI) IRR (95% CI)	p-value
PRC[a]	220 (7.5%)	568 (6.3%)	0.73 (0.61-0.88)	0.001
Hospital LOS [b] Mean ± SD	5.3 ± 7.5	5.0 ± 7.2	0.91 (0.87-0.94)	<0.001
Costs ($)[b] Median [IQR]	14943 [9121, 24836]	14493 [8804, 24017]	0.95 (0.93-0.97)	<0.001

[a]Odds ratio, derived from logistic regression.
[b]Incidence rate ratio, derived from zero-truncated negative binomial regression.

IRR = incidence rate ratio, IQR = interquartile range,
PRC = postoperative respiratory complications, LOS = length of stay

Rudolph MI et al. *Anaesthesia*. 2018; 73:1067-78.

I. INTERVENTION CHARACTERISTICS	
Evidence Strength and Quality	x
Intervention Source	
I. INNER SETTING	
Networks and Communications	
Implementation Climate	
Tension for change	x
Relative priority	x
Goals and Feedback	x
Learning climate	
Readiness for Implementation	
Leadership Engagement	x
V. PROCESS	
Planning	x
Reflecting and Evaluating	x

Why was this intervention successful?

Evidence for Dosing and Monitoring

- Use of NMBA independently associated with PRC
- Higher doses of intermediate-acting NMBA associated with dose-dependent increases in incidence of PRC
- Appropriate reversal may limit risk of PRC associated with high dose NMBA
- Use of quantitative monitoring may be associated with lower risk of PRC

Kirmeier E et al. *Lancet Respir Med*. 2018 Sept 14. Epub ahead of print.
McLean DJ et al. *Anesthesiology.* 2015; 122:1201-13.

Appropriate Reversal Can Be a QI Target

	Appropriate Reversal		Inappropriate Reversal	
NMBA Dose Quintiles (x ED95 dose)	PRC rate	Effect Size	PRC rate	Effect Size
I (Lowest)	0.39%	n/a	0.43%	n/a
II	0.45%	1.04 (0.7-1.6)	0.56%	1.03 (0.8-1.3)
III	0.60%	1.16 (0.8-1.7)	0.65%	1.06 (0.8-1.3)
IV	0.63%	0.95 (0.6-1.4)	0.89%	1.20 (1-1.5)
V (Highest)	0.91%	0.98 (0.6-1.5)	1.49%	1.41 (1.1-1.8)

Appropriate reversal (neostigmine ≤0.06 mg/kg at TOF count of at least 2)

Inappropriate reversal (no neostigmine administration, neostigmine administration not guided by TOF count or doses >0.06 mg/kg)

ED95 = effective dose to produce 95% depression in twitch height

McLean DJ et al. *Anesthesiology*. 2015; 122:1201-13.

Key Takeaways

- Process modification through change management in the OR is complex
  - Art of anesthesia
- Implementation science constructs are valid
  - Reflect on how past interventions succeeded or failed in your environment
- Residual NMB is largely preventable through effective change management

Selected Resources

- Brull SJ et al. Current status of neuromuscular reversal and monitoring: challenges and opportunities. *Anesthesiology*. 2017; 126:173-90.
- Damschroder LJ et al. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. *Implement Sci*. 2009, 4:50.
- Hemmings HC, Egan TD, eds. Pharmacology and physiology in anesthesia. Philadelphia: Elsevier-Saunders; 2013.
- Rudolph MI et al. Implementation of a new strategy to improve the peri-operative management of neuromuscular blockade and its effects on postoperative pulmonary complications. *Anaesthesia.* 2018; 73:1067-78.

Strategies for the Interprofessional Team: Faculty Discussion and Questions

- Providing ventilation support for patients in the PACU who have deep block
- Using quantitative monitoring
- Incorporating cost-effectiveness studies into P&T evaluations
- Providing patient education about interaction of sugammadex and hormonal contraceptives
- Enhancing patient safety after neuromuscular blockade
- Paying attention to definitions (e.g., postoperative respiratory complications) when assessing outcomes

About the Faculty

Rachel C. Wolfe, Pharm.D., BCCCP,
Activity Chair

Clinical Pharmacy Specialist
Perioperative Services and Surgical Critical Care
Barnes-Jewish Hospital
St. Louis, Missouri

Rachel C. Wolfe, Pharm.D., BCCCP, is Clinical Pharmacy Specialist of Perioperative Services and Surgical Critical Care at Barnes-Jewish Hospital and Washington University Medical Center in St. Louis, Missouri. She is also Adjunct Clinical Instructor for the Barnes-Jewish Hospital Goldfarb School of Nursing and St. Louis College of Pharmacy.

Dr. Wolfe earned her Doctor of Pharmacy degree from St. Louis College of Pharmacy. She completed her residency training at University of Kentucky HealthCare, and she is board certified in critical care.

At Barnes-Jewish Hospital, Dr. Wolfe is responsible for the provision of clinical pharmacy services in the perioperative and periprocedural environment and for the coordination of clinical services provided by four operating room pharmacy satellites. She also serves as a preceptor for Doctor of Pharmacy students and pharmacy residents and is co-chair of the analgesia subcommittee of the Pharmacy & Therapeutics committee. Dr. Wolfe collaborates closely with the Department of Anesthesiology to develop and implement evidenced-based protocols and plays an integral role in the enhanced surgical recovery initiatives that span across several surgical services. She has led several medication safety and standardization initiatives in addition to initiatives that focus on quality of perioperative care and postoperative patient outcomes.

Dr. Wolfe is a member of the Society of Critical Care Medicine and American College of Clinical Pharmacy. In 2011 she received Barnes-Jewish Hospital's David A. Gee Meritorious Service Award and Team Award for Quality Improvement for Anesthesia Medication Management.

Bernadette Henrichs, Ph.D., CRNA, CCRN

Director, Nurse Anesthesia Program
Barnes-Jewish College Goldfarb School of Nursing

Director, CRNA Education and Research
Washington University Department of Anesthesiology
St. Louis, Missouri

Bernadette Henrichs, Ph.D., CRNA, CCRN, is Professor and Director of the Nurse Anesthesia Program at the Goldfarb School of Nursing at Barnes-Jewish College in St. Louis, Missouri. She is also Director of CRNA Education and Research in the Department of Anesthesiology at Washington University School of Medicine in St. Louis. In addition, Dr. Henrichs administers anesthesia several days a week.

Dr. Henrichs received her anesthesia training from Washington University School of Medicine, later earning her M.S.N. and Ph.D. degrees from St. Louis University in St. Louis, Missouri.

Dr. Henrichs is an active member of the Missouri Association of Nurse Anesthetists (MoANA), American Association of Nurse Anesthetists (AANA), American Association of Critical-Care Nurses (AACN), Sigma Theta Tau International Honor Society of Nursing, and Society for Simulation in Healthcare. She served on the AANA Board of Directors as Region 4 Director and on the AANA Foundation Board of Trustees.

In addition to authoring several articles and book chapters on anesthesia-related topics, Dr. Henrichs co-edited *A Resource for Nurse Anesthesia Educators,* 2nd ed. She served on the editorial board and is a reviewer for *AANA Journal*. In 2017, Dr. Henrichs received the AANA Program Director of the Year Award. She also received the Beverly Krause Outstanding CRNA Clinical Instructor Award in 2014, an honor bestowed by graduates.

S. Krishna Ramachandran, M.D.

Associate Professor of Anaesthesia
Harvard Medical School

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Boston, Massachusetts

S. Krishna Ramachandran, M.D., is Associate Professor of Anaesthesia at Harvard Medical School and Vice Chair of Quality, Safety, and Innovation in the Department of Anesthesiology at Beth Israel Deaconess Medical Center in Boston.

Dr. Ramachandran is a nationally recognized leader in patient safety and perioperative quality. As the Vice-Chair of Anesthesiology, he has developed several programs, including a unique quality tool that connects clinician medication management behaviors with patient and efficiency outcomes. He also led anesthesia clinical change management and surveillance of safety in response to the shortage of intravenous opioids.

Dr. Ramachandran began his career in anesthesia in Pondicherry, India, and developed it further as a specialist registrar in the Oxford Deanery in England. After a successful decade leading quality and safety initiatives at the University of Michigan, he moved to Harvard and Beth Israel Deaconess Medical Center in 2016. He is a faculty member on the Master of HealthCare Quality and Safety program at Harvard Medical School. In addition, he is a busy clinician, educator, and researcher.

Dr. Ramachandran serves on the editorial board of prestigious journals and has published over 60 peer-reviewed studies in top anesthesiology journals, primarily around perioperative cardiorespiratory outcomes. Most recently he co-authored a study looking at the relationship between reducing neostigmine syringe size to 3 mL from the standard 5-mL vial and perioperative respiratory failure rates.

Additional Learning Activities in this Initiative

- Neuromuscular Blockade and Reversal: An Overview of Key Concepts (1.0 hr CE)—available NOW on-demand
- Two e-newsletters (total 0.5 hr CE)—available Spring 2019

www.ashpadvantagemedia.com/nmbsafety

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