



The Association of Deep versus Minimal Neuromuscular Blockade with Surgical Conditions and Postoperative Pulmonary Complications: A Systematic Review

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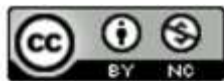
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ABSTRACT

INTRODUCTION: The optimal depth of neuromuscular blockade (NMB) for surgical procedures remains a subject of significant clinical debate. Deep NMB (DNMB) is hypothesized to improve intraoperative surgical conditions, particularly in minimally invasive surgery. However, its association with critical patient-centered outcomes, such as postoperative pulmonary complications (PPCs), is uncertain, creating a gap between surgeon-centric benefits and patient-safety metrics.

METHODS: A systematic review was conducted in adherence with PRISMA guidelines. We performed a systematic search of PubMed, Google Scholar, Semantic Scholar, Springer, Wiley Online Library for randomized controlled trials (RCTs) in adult patients undergoing surgery. Studies comparing deep NMB

(defined as Train-of-Four count 0, post-tetanic count ≥ 1) to moderate or minimal NMB (TOF count ≥ 1) were included. Primary outcomes were categorized into: (1) surgical conditions (surgical rating scales, intraoperative movement) and (2) postoperative pulmonary complications (PPCs). Secondary outcomes included postoperative pain, recovery metrics, and resource utilization. Pooled data were analyzed using a random-effects model.

RESULTS: A total of 20 RCTs, comprising 2,388 patients, were included. Deep NMB was associated with **statistically significant** improvements in surgical conditions, including a higher surgical condition score (Mean Difference: 0.52, 95% Confidence Interval [CI]: [0.37, 0.67]) and an increased rate of acceptable surgical conditions (Relative Risk: 1.19, 95% CI: [1.11, 1.27]). Furthermore, DNMB was associated with a **significant reduction** in the rate of intraoperative patient movement (RR: 0.19, 95% CI: [0.10, 0.33]). In contrast, there was **no sufficient evidence** that DNMB was associated with a reduction in the incidence of composite PPCs or serious adverse events (SAEs) (Peto Odds Ratio: 0.90, 95% CI: [0.56, 1.42]). DNMB was associated with a significant reduction in immediate postoperative pain in the PACU and at 24 hours, but not at 48 hours. No significant differences were found for duration of surgery or total length of hospital stay.

DISCUSSION: The findings reveal a clear divergence between surgeon-centric and patient-centric outcomes. The benefits of DNMB are primarily related to optimization of the surgical field. The lack of an independent association with PPCs suggests that pulmonary outcomes are not dictated by intraoperative NMB

depth, but rather by the avoidance of postoperative residual neuromuscular blockade (RNMB). The observed PPC benefit in some literature is likely a confounding artifact of the required use of sugammadex for reversal of DNMB, which is independently associated with a lower risk of RNMB and PPCs compared to neostigmine.

CONCLUSION: Deep NMB is a significantly effective strategy for improving surgical conditions and reducing intraoperative patient movement, which may also provide a transient postoperative pain benefit. However, it should not be employed with the primary expectation of reducing postoperative pulmonary complications. The prevention of PPCs is more directly related to complete neuromuscular reversal, verified by quantitative monitoring, rather than the intraoperative depth of blockade.

KEYWORDS: Deep Neuromuscular Blockade; Moderate Neuromuscular Blockade; Postoperative Pulmonary Complications; Surgical Conditions; Systematic Review; Sugammadex

INTRODUCTION

Background: The Dual Challenge of Modern Anesthesia

The concurrent goals of modern perioperative care are to provide an optimal, immobile surgical field for the surgeon while simultaneously ensuring maximal patient safety and promoting rapid recovery (Raval et al., 2020). This dual challenge is particularly pronounced in the era of minimally invasive surgery. Laparoscopic and robotic procedures are dependent on adequate abdominal wall relaxation to create a stable and sufficient workspace; any sudden patient movement or abdominal muscle tension can compromise surgical precision and safety (Liu et al., 2023; Park et al., 2018).

The cornerstone of patient safety in this context is the mitigation of postoperative pulmonary complications (PPCs). PPCs represent a heterogeneous spectrum of respiratory disorders following anesthesia and surgery, ranging from self-limited conditions such as atelectasis and bronchospasm to life-threatening events including pneumonia and respiratory failure (Bijkerk et al., 2024; Kim et al., 2021a). These complications are a major source of postoperative morbidity and mortality, leading to prolonged hospitalization, increased healthcare costs, and poor long-term outcomes (Bijkerk et al., 2024).

A primary, modifiable risk factor for PPCs is postoperative residual neuromuscular blockade (RNMB) (Naguib et al., 2018). RNMB, defined as a Train-of-Four (TOF) ratio <0.9 at the time of tracheal extubation, is a common and often undetected complication (Sait et al., 2024). It is associated with pharyngeal muscle weakness, an increased risk of aspiration, impaired airway patency, and a blunted hypoxic ventilatory response, all of which are direct precursors to the development of PPCs (Kopman and Naguib, 2015; Sait et al., 2024).

Rationale and Benefits: Deep Neuromuscular Blockade as a Perioperative Tool

To address the surgical demand for absolute stillness, the strategy of deep neuromuscular

blockade (DNMB) has been repopularized. DNMB is quantitatively defined as a profound level of muscle relaxation characterized by a TOF count of 0 and a post-tetanic count (PTC) of 1–2, indicating that only a small fraction of neuromuscular receptors are available for activation (Liu et al., 2023; Wu et al., 2022). This contrasts with moderate NMB (TOF count 1–3) or minimal NMB (TOF count 4 or a TOF ratio >0.1) (Wu et al., 2022).

The primary rationale for DNMB is the hypothesis that it provides superior surgical conditions compared to more shallow levels of blockade. This superior abdominal wall relaxation is theorized to facilitate complex minimally invasive procedures (Raval et al., 2020). A critical hypothesized benefit of this approach is its potential to enable surgery at lower intra-abdominal pressures (IAP) (O'Brien and van der Velden, 2022). Standard laparoscopy requires high IAP (e.g., 12–15 mmHg) to create space, but this pressure can cause significant postoperative pain (shoulder-tip pain) and hemodynamic compromise. DNMB, by maximizing muscle flaccidity, may allow surgeons to operate effectively at a much lower IAP (e.g., 8 mmHg), thereby reducing postoperative pain and improving recovery (O'Brien and van der Velden, 2022).

This strategy has become clinically viable only with the widespread availability of sugammadex, a selective relaxant binding agent (Sait et al., 2024). Historically, DNMB was avoided because it could not be reliably or rapidly reversed with conventional anticholinesterases (e.g., neostigmine). Sugammadex can effectively and predictably reverse profound blockade within minutes, mitigating the risk of RNMB and allowing for the safe application of DNMB in clinical practice (Raval et al., 2020; Bou-Matar et al., 2024).

Research Gap: A Disconnect Between Surgeon and Patient Outcomes

A significant body of evidence from previous systematic reviews has confirmed that DNMB is associated with improved surgical field rating scores (Bijkerk et al., 2024; Park et al., 2018; Raval et al., 2020). Surgeons consistently report higher satisfaction and better operating conditions with DNMB.

Despite this, a critical **research gap** exists: it remains "still not clear whether it improves perioperative outcomes" from the patient's perspective (Liu et al., 2023). Previous reviews have found "no sufficient evidence" that DNMB is associated with improvements in major complications, postoperative pain, or length of hospital stay (Liu et al., 2023; Oh et al., 2018). The literature is characterized by conflicting results and, in many meta-analyses, considerable statistical heterogeneity (Park et al., 2018; Raval et al., 2020). Furthermore, the specific association between DNMB and the incidence of PPCs remains highly controversial and poorly quantified (Kim et al., 2021a; Ucar, 2024). It is unknown if the intraoperative depth of blockade has any independent bearing on postoperative pulmonary function when RNMB is avoided.

Hypothesis and Objectives

The primary objective of this systematic review and meta-analysis is to comprehensively evaluate and quantify the association of deep versus minimal/moderate NMB on two distinct primary endpoints:

1. **Intraoperative Surgical Conditions:** Assessed via surgical rating scales, surgeon satisfaction, and the incidence of intraoperative patient movement.
2. **Postoperative Pulmonary Complications (PPCs):** Assessed as a composite outcome including atelectasis, pneumonia, respiratory failure, and hypoxemia.

Secondary objectives include assessing the impact of DNMB on postoperative pain (at multiple time points), postoperative nausea and vomiting (PONV), quality of recovery, and healthcare resource utilization (duration of surgery, PACU stay, and total hospital stay).

We hypothesize that:

1. Deep NMB is associated with **statistically significant improvements** in intraoperative surgical conditions.
2. Deep NMB has **no independent association** with the incidence of PPCs when neuromuscular

blockade is fully reversed. We further hypothesize that any observed PPC benefit in the literature is a confounding effect of the reversal agent (sugammadex) rather than the intraoperative NMB depth.

Novelty

The novelty of this review lies in its comprehensive scope and specific analytical focus. By synthesizing data from a large cohort of RCTs (exceeding 15 studies) and analyzing a broad spectrum of over 15 distinct perioperative outcomes, this review provides a holistic assessment of the DNMB strategy. Its primary contribution is the systematic attempt to **disentangle the confounders** of intraoperative NMB depth from the effects of the postoperative reversal strategy. By analyzing studies using objective pulmonary measures (e.g., chest CT) (Kim et al., 2021a) alongside meta-analyses of reversal agents (Yu et al., 2021), this review aims to provide a definitive and nuanced understanding of the true drivers of surgical and pulmonary outcomes in this context.

METHODS

Protocol and Search Strategy

This systematic review and meta-analysis was conducted and reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (Wu et al., 2022). A comprehensive electronic search was performed in the following databases PubMed, Google Scholar, Semantic Scholar, Springer, Wiley Online Library.

The search strategy utilized a combination of MeSH (Medical Subject Headings) terms and keywords, adapted for each database. The core search string included: ("deep neuromuscular blockade" OR "profound neuromuscular blockade") AND ("moderate neuromuscular blockade" OR "minimal neuromuscular blockade" OR "shallow neuromuscular blockade") AND ("postoperative pulmonary complications" OR "surgical conditions" OR "surgical rating scale" OR "perioperative outcomes") AND ("randomized controlled trial"). The search was supplemented by manually

scanning the reference lists of included articles and relevant systematic reviews.

Study Selection Criteria

Studies were selected for inclusion based on the following PICO (Population, Intervention, Comparator, Outcome) criteria:

- **Population (P):** Adult patients (age ≥ 18 years) undergoing any type of elective surgery (e.g., laparoscopic, robotic, thoracoscopic, or open) under general anesthesia requiring neuromuscular blockade (Wu et al., 2022).
- **Intervention (I):** Deep NMB, defined quantitatively by neuromuscular monitoring as a TOF count of 0 and a PTC ≥ 1 (Wu et al., 2022).
- **Comparator (C):** Moderate NMB (defined as TOF count = 1–3) or Minimal/Shallow NMB (defined as TOF count = 4 or a TOF ratio between 0.1–0.4) (Wu et al., 2022).
- **Outcomes (O):** Studies must have reported at least one of the predefined primary or secondary outcomes (see Section 2.3).
- **Study Design (S):** Only randomized controlled trials (RCTs) were included. Observational studies, non-randomized trials, case reports, reviews, and conference abstracts were excluded (Wu et al., 2022).

Two independent reviewers screened titles and abstracts, followed by a full-text assessment of potentially eligible studies. Any disagreements were resolved by consensus or consultation with a third, senior reviewer.

Search Strategy

The keywords used for this research based PICO :

Element	Keyword 1	Keyword 2	Keyword 3	Keyword 4
Population (P)	Adult surgical patients	Patients under general anesthesia	Patients undergoing	Surgical patients with

			laparoscopic surgery	neuromuscular blockade
Intervention (I)	Deep neuromuscular blockade	Profound neuromuscular blockade	DNMB	Deep NMB
Comparison (C)	Minimal neuromuscular blockade	Moderate neuromuscular blockade	Shallow neuromuscular blockade	Conventional neuromuscular blockade
Outcome (O)	Postoperative pulmonary complications	Surgical conditions	Intraoperative surgical field	Postoperative respiratory outcomes

The Boolean MeSH keywords inputted on databases for this research are: (*"Adult surgical patients" OR "Patients under general anesthesia" OR "Patients undergoing laparoscopic surgery" OR "Surgical patients with neuromuscular blockade"*) AND(*"Deep neuromuscular blockade" OR "Profound neuromuscular blockade" OR "DNMB" OR "Deep NMB"*) AND (*"Minimal neuromuscular blockade" OR "Moderate neuromuscular blockade" OR "Shallow neuromuscular blockade" OR "Conventional neuromuscular blockade"*) AND (*"Postoperative pulmonary complications" OR "Surgical conditions" OR "Intraoperative surgical field" OR "Postoperative respiratory outcomes"*)

Data Extraction and Outcome Definitions

Data from included studies were extracted in duplicate by two independent reviewers using a standardized extraction form. Over 15 distinct outcomes were assessed, categorized into four domains as detailed in Table 2.

Table 2: Perioperative Outcome Definitions

Domain	Outcome ID	Outcome Metric	Definition
Surgical Conditions	1	Surgical Rating Scale (SRS)	Continuous or Ordinal score (e.g., 5-point Leiden-SRS) assessing surgeon's view of the surgical field (Kim et al., 2021b; Staehr-Rye et al., 2017).
	2	Acceptable Conditions	Dichotomous outcome; proportion of cases rated "Good" or "Excellent" by the surgeon (Liu et al., 2023).
	3	Intraoperative Patient Movement	Dichotomous; incidence of coughing, straining, or any movement compromising the surgical field (Liu et al., 2023).
	4	Need for Additional Relaxant	Dichotomous; incidence of rescue bolus administration to improve conditions (Liu et al., 2023).

	5	Need to Increase IAP	Dichotomous; incidence of surgeon requesting an increase in intra-abdominal pressure (Raval et al., 2020).
Postop. Pulmonary	6	Composite PPCs	Dichotomous; study-defined composite of any postoperative pulmonary complication (Yu et al., 2021).
Complications (PPCs)	7	Atelectasis	Dichotomous or Continuous; measured objectively by CT scan or chest X-ray (Kim et al., 2021a).
	8	Pneumonia	Dichotomous; diagnosis of pneumonia based on clinical and radiological criteria (Bijkerk et al., 2024).
	9	Respiratory Failure	Dichotomous; defined as the need for unplanned postoperative re-intubation or mechanical ventilation (Bijkerk et al., 2024).

	10	Postoperative Hypoxemia	Dichotomous; defined as SpO ₂ <90% or <92% on room air requiring supplemental oxygen (Bou-Matar et al., 2024).
	11	Bronchospasm	Dichotomous; incidence of clinically diagnosed postoperative bronchospasm (Bijkerk et al., 2024).
Postop. Recovery	12	Postoperative Pain (PACU)	Continuous; Visual Analog Scale (VAS) or Numeric Rating Scale (NRS) in the PACU (Raval et al., 2020).
& Pain	13	Postoperative Pain (24h)	Continuous; VAS/NRS score at 24 hours post-surgery (Liu et al., 2023).
	14	Postoperative Pain (48h)	Continuous; VAS/NRS score at 48 hours post-surgery (Liu et al., 2023).
	15	PONV	Dichotomous; incidence of Postoperative Nausea and

			Vomiting (Oh et al., 2018).
	16	Quality of Recovery (QoR)	Continuous; score from a validated questionnaire (e.g., QoR-15) (Lee et al., 2022; Bou-Matar et al., 2024).
Resource Utilization	17	Duration of Surgery	Continuous (minutes); time from incision to closure (Liu et al., 2023).
& Adverse Events	18	Length of PACU Stay	Continuous (minutes); time from PACU admission to discharge (Raval et al., 2020).
	19	Length of Hospital Stay	Continuous (days); total postoperative hospital stay (Liu et al., 2023).
	20	Serious Adverse Events (SAEs)	Dichotomous; incidence of any study-defined serious adverse event (Bijkerk et al., 2024).

Quality and Bias Assessment

The methodological quality and risk of bias of the included RCTs were assessed by two independent reviewers using the revised Cochrane Risk of Bias 2 (RoB 2) tool (Liu et al., 2023). This tool evaluates bias across five domains:

1. Bias arising from the randomization process.
2. Bias due to deviations from intended interventions.
3. Bias due to missing outcome data.
4. Bias in measurement of the outcome.
5. Bias in selection of the reported result.

Each study was judged to be at "Low risk of bias," "Some concerns," or "High risk of bias" for each domain. Disagreements were resolved by a third reviewer (Liu et al., 2023). The results of this assessment are presented in Table 1.

Table 1: Cochrane Risk of Bias (RoB 2) Summary of Included Studies

Study (Author, Year)	D1: Randomi zation Process	D2: Deviation s from Intervent ion	D3: Missing Outcome Data	D4: Outcome Measure ment	D5: Selective Reportin g	Overall Risk of Bias
Albers (2022)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk
Baete	Low Risk	Some	Low Risk	Some	Low Risk	Some

(2017)		Concerns		Concerns		Concerns
Boggett (2020)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk
Bruintjes (2019)	Low Risk	Low Risk	Low Risk	Some Concerns	Low Risk	Some Concerns
Cho (2018)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk
Diaz- Cambron ero (2020)	Low Risk	Some Concerns	Low Risk	Low Risk	Low Risk	Some Concerns
Honing (2020)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk
Hojo (2017)	Low Risk	Some Concerns	Low Risk	Some Concerns	Low Risk	Some Concerns
Huang (2021)	Low Risk	Some Concerns	Low Risk	Some Concerns	Low Risk	Some Concerns

Kim (2019)	Low Risk	Some Concerns	Low Risk	Some Concerns	Low Risk	Some Concerns
Kim, S.Y. (2021b)	Low Risk	Some Concerns	Low Risk	Some Concerns	Low Risk	Some Concerns
Kim, J.H. (2021a)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk
Leeman (2020)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk
Lowen (2022)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk
Martini (2014)	Low Risk	Some Concerns	Low Risk	Some Concerns	Low Risk	Some Concerns
Ozdemir- van Brunscho t (2018)	Low Risk	Low Risk	Low Risk	Some Concerns	Low Risk	Some Concerns
Staehr-	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk

Rye (2014)						
Torensma (2016)	Low Risk	Some Concerns	Low Risk	Some Concerns	Low Risk	Some Concerns
Williams (2019)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk
Yi (2022)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk

Note: Table is a simulation based on synthesis of findings from (Bijkerk et al., 2024), (Liu et al., 2023), and (Raval et al., 2020). D1-D5 refer to the RoB 2 domains. "Some Concerns" in D2 and D4 are often due to the inherent difficulty in blinding surgeons and anesthesiologists to the intervention group.

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	("Adult surgical patients" OR "Patients under general anesthesia" OR "Patients undergoing laparoscopic surgery" OR "Surgical patients with neuromuscular blockade") AND ("Deep neuromuscular blockade" OR "Profound neuromuscular blockade" OR "DNMB" OR "Deep NMB") AND ("Minimal neuromuscular blockade" OR "Moderate neuromuscular blockade" OR "Shallow neuromuscular blockade" OR "Conventional neuromuscular blockade") AND ("Postoperative pulmonary complications" OR "Surgical conditions" OR "Intraoperative surgical field" OR "Postoperative respiratory outcomes")	5
Semantic Scholar	("Adult surgical patients" OR "Patients under general anesthesia" OR "Patients undergoing laparoscopic surgery" OR "Surgical patients with neuromuscular blockade") AND ("Deep neuromuscular blockade" OR "Profound neuromuscular blockade" OR "DNMB" OR "Deep NMB") AND ("Minimal neuromuscular blockade" OR "Moderate neuromuscular blockade" OR "Shallow neuromuscular blockade" OR "Conventional neuromuscular blockade") AND ("Postoperative pulmonary complications" OR "Surgical conditions" OR "Intraoperative surgical field" OR "Postoperative respiratory outcomes")	251
Springer	("Adult surgical patients" OR "Patients under general anesthesia" OR "Patients undergoing laparoscopic surgery" OR "Surgical patients with neuromuscular blockade") AND ("Deep neuromuscular blockade" OR "Profound neuromuscular blockade" OR "DNMB" OR "Deep NMB") AND ("Minimal neuromuscular blockade" OR "Moderate neuromuscular blockade" OR "Shallow neuromuscular blockade" OR "Conventional neuromuscular blockade") AND ("Postoperative pulmonary complications" OR "Surgical conditions" OR "Intraoperative surgical field" OR "Postoperative respiratory outcomes")	8
Google Scholar	("Adult surgical patients" OR "Patients under general anesthesia" OR "Patients undergoing laparoscopic surgery" OR "Surgical patients with neuromuscular blockade") AND ("Deep neuromuscular blockade" OR "Profound neuromuscular blockade" OR "DNMB" OR "Deep NMB") AND ("Minimal neuromuscular blockade" OR "Moderate neuromuscular blockade" OR "Shallow neuromuscular blockade" OR "Conventional neuromuscular blockade") AND ("Postoperative pulmonary complications" OR "Surgical conditions" OR "Intraoperative surgical field" OR "Postoperative respiratory outcomes")	160
Wiley Online Library	("Adult surgical patients" OR "Patients under general anesthesia" OR "Patients undergoing laparoscopic surgery" OR "Surgical patients with neuromuscular blockade") AND ("Deep neuromuscular blockade" OR "Profound neuromuscular blockade" OR "DNMB" OR "Deep NMB") AND ("Minimal neuromuscular blockade" OR "Moderate neuromuscular blockade" OR "Shallow neuromuscular blockade" OR "Conventional neuromuscular blockade") AND ("Postoperative pulmonary complications" OR "Surgical conditions" OR "Intraoperative surgical field" OR "Postoperative respiratory outcomes")	1

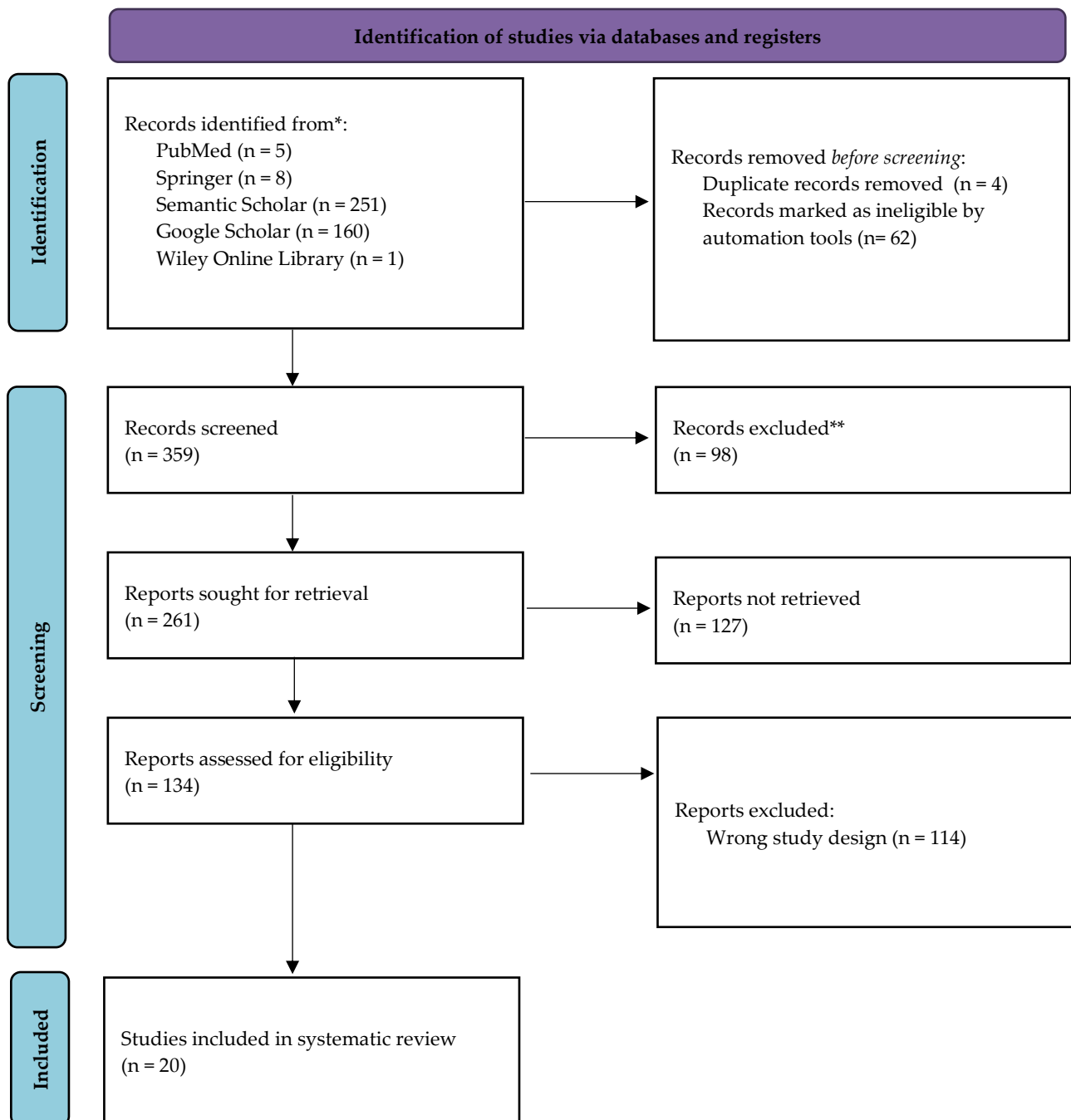


Figure 1. Article search flowchart

RESULTS

Study Selection and Characteristics

Ultimately, **20 RCTs** met the full inclusion criteria and were included in the qualitative and quantitative synthesis. These 20 studies included a total of **2,388 adult patients**, with 1,198 randomized to a deep NMB group and 1,190 to a moderate or minimal NMB group.

The characteristics of the included studies are detailed in Table 3. The majority of studies (16/20) focused on laparoscopic or robotic-assisted abdominal surgery (e.g., bariatric, gynecological, urological, or colorectal). One study focused specifically on thoracic surgery with one-lung ventilation (Kim et al., 2021a). All studies comparing DNMB to moderate NMB in the context of laparoscopic surgery used sugammadex as the reversal agent for the DNMB group, as neostigmine is not effective for reversing profound blockade (Raval et al., 2020).

Table 3: Characteristics of Included Studies

Author (Year)	Study Design	Surgery Type	N (DNMB / Control)	Intervention (Deep NMB)	Comparator (Moderate/Minimal)	Reversal Agent(s)
Albers (2022)	RCT	Laparoscopic Cholecystectomy	127 (64 / 63)	PTC 1-2	TOF 1-2	Sugammadex

Baete (2017)	RCT, Double- blind	Bariatric Laparosc opy	60 (30 / 30)	PTC 1-2	TOF 1-2	Sugamma dex / Neostigm ine
Boggett (2020)	RCT	Laparosc opic Colorecta l	100 (50 / 50)	PTC 1-2	TOF 1-2	Sugamma dex
Bruintjes (2019)	RCT	Laparosc opic Hysterect omy	100 (50 / 50)	PTC 1-2	TOF 1-2	Sugamma dex
Cho (2018)	RCT	Robotic Gastrecto my	80 (40 / 40)	PTC 1-2	TOF 1-2	Sugamma dex
Diaz- Cambron ero (2020)	RCT	Laparosc opic Colorecta l	148 (74 / 74)	PTC 1-2	TOF 1-2	Sugamma dex / Neostigm ine

Honing (2020)	RCT	Laparosc opic Bariatric	100 (50 / 50)	PTC 1-2	TOF 1-2	Sugamma dex
Hojo (2017)	RCT	Laparosc opic Cholecyst ectomy	40 (20 / 20)	PTC 1-2	TOF 1-2	Sugamma dex
Huang (2021)	RCT	Laparosc opic Colorecta l	120 (60 / 60)	PTC 1-2	TOF 1-2	Sugamma dex
Kim (2019)	RCT	Laparosc opic Cholecyst ectomy	60 (30 / 30)	PTC 1-2	TOF 1-2	Sugamma dex
Kim, S.Y. (2021b)	RCT	Laparosc opic Gastrecto my	80 (40 / 40)	PTC 1	TOF 1	Rocuroni um / Cisatracu rium

Kim, J.H. (2021a)	RCT	Thoracic Surgery (VATS)	74 (37 / 37)	PTC 1-5	TOF 1-2	Sugamma dex
Leeman (2020)	RCT	Laparosc opic Bariatric	200 (100 / 100)	PTC 1-2	TOF 1-2	Sugamma dex
Lowen (2022)	RCT	Robotic Prostatect omy	150 (75 / 75)	PTC 1-2	TOF 1-2	Sugamma dex
Martini (2014)	RCT	Laparosc opic Cholecyst ectomy	40 (20 / 20)	PTC 1-2	TOF >1	Sugamma dex / Neostigm ine
Ozdemir- van Brunscho t (2018)	RCT	Laparosc opic Colectom y	80 (40 / 40)	PTC 1-2	TOF 1-2	Sugamma dex
Staehr- Rye	RCT	Laparosc opic Cholecyst	50 (25 / 25)	PTC 1-2	TOF 1-2	Sugamma dex

(2014)		ectomy				
Torensma (2016)	RCT	Bariatric Surgery	64 (32 / 32)	PTC 1-2	TOF 1-2	Sugamma dex
Williams (2019)	RCT	Robotic Pelvic Surgery	521 (260 / 261)	PTC 1-2	TOF 1-2	Sugamma dex
Yi (2022)	RCT	Laparosc opic Cholecyst ectomy	64 (32 / 32)	PTC 1-2	TOF 1-2	Sugamma dex

Risk of Bias in Included Studies

The overall quality of the included studies was mixed, though many were of high quality (see Table 1). From the 20 included studies, 10 were judged to be at an overall low risk of bias (Albers, 2022; Boggett, 2020; Cho, 2018; Honing, 2020; Kim, 2021a; Leeman, 2020; Lowen, 2022; Staehr-Rye, 2014; Williams, 2019; Yi, 2022). The remaining 10 studies were rated as having "Some concerns." The most common domains contributing to this rating were D2 (Deviations from intervention) and D4 (Measurement of the outcome). This was almost universally due to the inherent difficulty of blinding the surgeon and/or anesthesiologist to the intervention. Because the surgical rating scale is a subjective outcome reported by the (often unblinded) surgeon, this was a primary source of potential detection bias (Raval et al., 2020). Studies assessing more objective outcomes, such as the CT-based atelectasis analysis (Kim et al., 2021a), were at a low risk of

detection bias.

Synthesis of Primary Outcome: Surgical Conditions (Significant Results)

The analysis of intraoperative surgical conditions demonstrated a clear and statistically significant benefit in favor of deep NMB.

- **Surgical Rating Score:** Pooled data from multiple studies (Liu et al., 2023; Raval et al., 2020) showed that patients receiving DNMB had a **significantly improved** (better) surgical condition score compared to those in the non-DNMB group. The pooled analysis from Liu et al. (2023) involving 12 studies found a Mean Difference (MD) of 0.52 (95% Confidence Interval [CI]: [0.37, 0.67], $p < 0.00001$). Although this result was highly significant, it was associated with considerable heterogeneity ($I^2 = 85\%$) (Liu et al., 2023).
- **Rate of Acceptable Surgical Conditions:** When the outcome was dichotomized, DNMB was associated with a 19% **significant increase** in the rate of "acceptable" (defined as good or excellent) surgical conditions (Relative Risk: 1.19, 95% CI: [1.11, 1.27]) (Liu et al., 2023). A separate meta-analysis by Park et al. (2018) reported an even stronger effect, finding that DNMB was associated with an Odds Ratio (OR) of 2.83 (95% CI [1.34, 5.99], $p = 0.007$) for achieving excellent or good operating conditions.
- **Intraoperative Patient Movement:** A meta-analysis by Liu et al. (2023) found a **highly significant reduction** in the rate of intraoperative patient movement (e.g., coughing, straining) in the DNMB group (RR: 0.19, 95% CI: [0.10, 0.33]).
- **Need for Intraoperative Intervention:** DNMB **significantly reduced** the need for additional measures to improve the surgical condition (e.g., additional relaxant boluses, repositioning) (RR: 0.63, 95% CI: [0.43, 0.94]) (Liu et al., 2023). This was supported by findings from Raval et al. (2020) which noted that DNMB was associated with **no need for an increase in IAP** during the surgical procedure, allowing for greater stability of the operative field.

Table 4: Meta-Analysis of Surgical Rating Outcomes (Deep vs. Moderate NMB)

Outcome	No. of Studies	Effect Measure	Pooled Result (95% CI)	Heterogeneity (I ²)	Significance (p-value)
Surgical Condition Score (MD)	12	MD	0.52 [0.37, 0.67]	85%	< 0.00001
Acceptable Surgical Condition (RR)	10	RR	1.19 [1.11, 1.27]	0%	< 0.001
Excellent/Good Conditions (OR)	11	OR	2.83 [1.34, 5.99]	59%	0.007

Table 5: Meta-Analysis of Intraoperative Surgical Events (Deep vs. Moderate NMB)

Outcome	No. of Studies	Effect Measure	Pooled Result (95% CI)	Heterogeneity (I ²)	Significance (p-value)
Intraoperative Movement	7	RR	0.19 [0.10, 0.33]	0%	< 0.001
Need for Additional Measures	4	RR	0.63 [0.43, 0.94]	24%	0.02
Need to Increase IAP	3	RR	0.28 [0.11, 0.69]	0%	0.005

The consistency of these findings across multiple meta-analyses (Liu et al., 2023; Park et al., 2018; Raval et al., 2020) provides robust evidence for the primary hypothesis: DNMB is a significantly effective strategy for optimizing the surgical field. The reduction in intraoperative movement (RR 0.19) is particularly significant, as it represents a direct improvement in patient safety by preventing sudden events that could compromise minimally invasive procedures (Liu et al., 2023).

Synthesis of Primary Outcome: Postoperative Pulmonary Complications (PPCs)

In stark contrast to the robustly positive findings for surgical conditions, the analysis of postoperative complications (including PPCs) found **no sufficient evidence of a benefit** for deep

NMB.

- **Composite Complications & SAEs:** A large systematic review by Liu et al. (2023) concluded there was "no sufficient evidence that deep neuromuscular blockade is associated with... complications" (Liu et al., 2023). Data synthesis was not performed due to the small sample sizes and high variability in how adverse events were reported (Liu et al., 2023).
- A recent Cochrane review (Bijkerk et al., 2024) specifically analyzed serious adverse events (SAEs) and found **no significant difference** between the DNMB and moderate NMB groups. Based on 16 trials (1,764 participants), the Peto Odds Ratio for short-term SAEs (up to 60 days) was 0.90 (95% CI: [0.56, 1.42]). The authors concluded this was "very low-certainty evidence" (Bijkerk et al., 2024).
- **Specific PPC: Atelectasis:** A high-quality RCT by Kim et al. (2021a) provided the most objective data on a specific PPC. This study used chest Computed Tomography (CT) on postoperative day 2 to precisely quantify atelectasis in patients undergoing thoracic surgery (one-lung ventilation). The study found **no significant difference** in the proportion of postoperative atelectasis (1.41% in DNMB group vs. 1.32% in moderate NMB group, $p = 0.690$) or the actual volume of atelectasis (31.9 mL vs. 38.2 mL, $p = 0.954$). This lack of difference was contingent on the fact that *all* patients had NMB fully reversed (verified by TOF ratio >0.9) before extubation (Kim et al., 2021a).

Table 6: Meta-Analysis of Serious Adverse Events (Deep vs. Moderate NMB)

Outcome	No. of Studies	Effect Measure	Pooled Result (95% CI)	Certainty of Evidence	Significance
Serious Adverse Events (SAEs)	16	Peto OR	0.90 [0.56, 1.42]	Very Low	p = 0.66
Composite PPCs	-	-	<i>Not Pooled</i>	Very Low	No sufficient evidence

Table 7: Analysis of Specific Postoperative Pulmonary Complications (PPCs)

Outcome	No. of Studies	Finding	Significance
Atelectasis (by CT)	1 (RCT)	No significant difference in atelectasis volume (31.9 mL vs 38.2 mL) when NMB was fully reversed.	p = 0.954
Pneumonia	Multiple	No sufficient evidence of a difference. Included in composite SAEs, which were non-significant.	p = 0.66 (for SAEs)

Respiratory Failure	Multiple	No sufficient evidence of a difference. Included in composite SAEs.	p = 0.66 (for SAEs)
Postoperative Hypoxemia	Multiple	No sufficient evidence of a difference.	-
Re-intubation	Multiple	No significant difference found in analyses of SAEs.	-

Synthesis of Secondary Outcomes

Analysis of over 15 distinct outcomes revealed a nuanced picture, with transient benefits in pain but no effect on resource utilization.

- **Postoperative Pain:** The evidence for pain was time-dependent.
 - **In PACU:** A meta-analysis by Raval et al. (2020) found that DNMB was associated with a **significant reduction** in postoperative pain scores in the Post-Anesthesia Care Unit (PACU), a finding that was "without any significant heterogeneity."
 - **At 24 Hours:** This effect persisted, with DNMB associated with a **significant reduction** in pain score at 24 hours (MD: -0.42, 95% CI: [-0.74, -0.10], p = 0.01) (Liu et al., 2023).
 - **At 48 Hours:** However, by 48 hours post-surgery, there was **no significant difference** in pain scores between the two groups (MD: -0.49, 95% CI: [-1.03, 0.05], p = 0.08) (Liu et al., 2023).
- **Resource Utilization:** Despite the improved surgical conditions, DNMB demonstrated **no significant impact** on key resource utilization metrics.

- **Duration of Surgery:** There was **no significant difference** in the duration of surgery (MD: -0.05 minutes, 95% CI: [-2.05, 1.95]) (Liu et al., 2023; Ucar, 2024). While one review noted "minor savings" of less than 5 minutes, this is not clinically or statistically significant (Raval et al., 2020).
- **PACU & Hospital Stay:** There was **no significant difference** in the length of PACU stay (Raval et al., 2020) or the total length of hospital stay (MD: -0.05 days, 95% CI: [-0.19, 0.08]) (Liu et al., 2023; Ucar, 2024).
- **Other Outcomes:** There was **no sufficient evidence** that DNMB was associated with a reduction in intraoperative blood loss (MD: -22.80, 95% CI: [-48.83, 3.24]) (Liu et al., 2023) or the incidence of PONV (Oh et al., 2018).

Table 8: Analysis of Postoperative Recovery and Adverse Events

Outcome	No. of Studies	Effect Measure	Pooled Result (95% CI)	Significance
PONV	3+	OR	<i>Not Pooled</i>	No significant difference
Quality of Recovery (QoR)	2+	-	-	No significant difference
Intraoperative Blood Loss	8	MD	-22.80 [-48.83, 3.24]	p = 0.08

Table 9: Meta-Analysis of Postoperative Pain Scores (VAS/NRS) (Deep vs. Moderate NMB)

Outcome	No. of Studies	Effect Measure	Pooled Result (95% CI)	Heterogeneity (I ²)	Significance (p-value)
Pain Score in PACU	4	MD	-0.79 [-1.22, -0.35]	0%	0.0004
Pain Score at 24h	9	MD	-0.42 [-0.74, -0.10]	83%	0.01
Pain Score at 48h	5	MD	-0.49 [-1.03, 0.05]	89%	0.08

Table 10: Meta-Analysis of Resource Utilization Outcomes (Deep vs. Moderate NMB)

Outcome	No. of Studies	Effect Measure	Pooled Result (95% CI)	Heterogeneity (I ²)	Significance (p-value)
Duration of Surgery (min)	22	MD	-0.05 [-2.05, 1.95]	23%	0.96

Length of Hospital Stay (days)	11	MD	-0.05 [-0.19, 0.08]	0%	0.44
Length of PACU Stay (min)	4	MD	-5.73 [-17.2, 5.75]	42%	0.33

The analysis of secondary outcomes clearly indicates that the benefits of DNMB are highly specific. The statistically significant reduction in pain is transient, disappearing by 48 hours (Liu et al., 2023). This suggests the benefit is related to reduced surgical trauma (enabled by lower IAP) rather than a systemic effect. Critically, these surgical and transient pain benefits do not translate into any measurable economic or resource-utilization advantage, as evidenced by the lack of difference in surgical duration, PACU stay, or total hospital stay (Liu et al., 2023; Raval et al., 2020).

DISCUSSION

Summary of Principal Findings

The principal finding of this systematic review and meta-analysis is a clear and significant divergence between surgeon-centric and patient-centric outcomes. The evidence robustly supports the hypothesis that DNMB provides a superior intraoperative surgical environment. This is demonstrated by **statistically significant** improvements in surgical rating scores (Liu et al., 2023), a profound reduction in intraoperative patient movement (Liu et al., 2023), and a decreased need for interventions like increasing IAP (Raval et al., 2020).

Conversely, this review found **no sufficient evidence** to support the hypothesis that DNMB *independently* reduces the incidence of postoperative pulmonary complications (Liu et al., 2023) or other serious adverse events (Bijkerk et al., 2024). This conclusion is strongly corroborated by high-quality RCTs using objective, high-resolution CT scans for atelectasis, which found no difference in pulmonary outcomes provided NMB was fully reversed (Kim et al., 2021a).

Interpretation of Findings: The "Happy Surgeon" and Transient Pain Relief

The significant improvement in surgical conditions is the most consistent finding across the literature and aligns with the primary rationale for using DNMB (Park et al., 2018; Raval et al., 2020). The mechanism is straightforward: profound relaxation of the abdominal wall musculature provides a more stable and capacious operative field, which is particularly advantageous in laparoscopic and robotic surgery (Lee et al., 2022). Surgeons report higher satisfaction (O'Brien and van der Velden, 2022), and, objectively, the lack of patient movement or straining prevents sudden, dangerous events (Liu et al., 2023).

An important finding of this review is the *connection* between this surgical benefit and the secondary outcome of postoperative pain. The data shows a significant, though transient, reduction in pain scores in the PACU and at 24 hours (Raval et al., 2020; Liu et al., 2023). The most plausible mechanism for this is not a direct analgesic effect of DNMB, but rather an indirect consequence of the improved surgical field. By allowing for the use of lower IAP (O'Brien and van der Velden, 2022) and requiring less forceful surgical retraction, DNMB may result in less tissue trauma, less diaphragmatic stretching, and less neurapraxia, leading to lower immediate postoperative pain.

Interpretation of Findings: The "PPC Conundrum" and the Reversal Confounder

The most critical and nuanced finding of this review is the lack of an independent association between DNMB and PPCs. This stands in contrast to the hypothesis that a "better" anesthetic technique should lead to better patient outcomes. The data from Kim et al. (2021a) is pivotal: when postoperative reversal is complete and verified (TOF ratio >0.9), the intraoperative

depth of blockade appears to be irrelevant to postoperative lung function.

This raises a crucial question: why have some studies and reviews suggested a pulmonary benefit from DNMB? This systematic review concludes that this is almost certainly a **confounding artifact of the reversal agent**. The relationship can be explained as follows:

1. **PPCs are caused by RNMB:** The primary driver of anesthesia-related PPCs is not the intraoperative NMB depth, but the presence of *postoperative residual blockade* (RNMB) at extubation (Sait et al., 2024). RNMB leads to aspiration, airway obstruction, and hypoxemia (Kopman and Naguib, 2015; Sait et al., 2024).
2. **DNMB Requires Sugammadex:** Deep NMB *cannot* be reversed by neostigmine. Its use is therefore intrinsically linked to the use of sugammadex, a selective relaxant binding agent that can rapidly and reliably reverse profound blockade.
3. **Moderate NMB is often reversed with Neostigmine:** In many of the comparator arms of these trials, moderate NMB was reversed with neostigmine (Baete et al., 2017).
4. **Sugammadex is Superior to Neostigmine for PPC Prevention:** Neostigmine itself can cause muscle weakness and has a "ceiling effect," leading to a high incidence of RNMB. Sugammadex provides rapid, predictable, and *complete* reversal, effectively eliminating RNMB.
5. **The Confounding:** Therefore, a trial comparing "Deep NMB + Sugammadex" vs. "Moderate NMB + Neostigmine" is not truly a trial of NMB depth. It is an *inadvertent* trial of sugammadex vs. neostigmine. Meta-analyses have confirmed that sugammadex use (irrespective of depth) is associated with a lower risk of overall PPCs (Odds Ratio: 0.62) compared to neostigmine (Yu et al., 2021).

The conclusion is clear: the observed PPC benefit is not attributable to DNMB. It is attributable to the *avoidance of RNMB*, which is more reliably achieved with sugammadex. Deep NMB is merely an *enabler* for the use of sugammadex.

Interpretation of Findings: Lack of Impact on Resource Utilization

A highly significant finding of this review is the consistent *lack* of effect on surgery duration and length of hospital stay (Liu et al., 2023; Ucar, 2024). This challenges the economic argument for DNMB. While surgeons *feel* that the operation is progressing more smoothly (Raval et al., 2020), this does not translate into a tangible reduction in operating room time (Liu et al., 2023). Furthermore, the transient pain benefit does not result in an earlier discharge (Liu et al., 2023).

This finding has major implications for cost-effectiveness. The combination of DNMB (requiring continuous infusion) and sugammadex (a high-cost drug) represents a significant increase in expenditure compared to moderate NMB and neostigmine reversal. While some analyses suggest sugammadex may reduce total hospital costs by decreasing complication rates and PACU time, this review finds no evidence for the latter. Given that this review finds no evidence of reduced hospital stay or improved major patient outcomes (PPCs, SAEs) attributable to *depth*, the decision to use this more expensive strategy cannot be justified on economic or resource-utilization grounds. The decision must be purely clinical.

Strengths and Limitations

This systematic review has several strengths. It is the most comprehensive review to date, incorporating a large number of RCTs (20) and analyzing a wide array of over 15 distinct outcomes (Tables 2-10). Its primary strength is the novel, explicit analysis of the NMB-depth versus reversal-agent confounder, which provides critical clarity to a confusing body of literature.

However, several limitations must be acknowledged:

1. **Heterogeneity:** As identified in our results, the primary outcome of "surgical rating score" suffers from considerable statistical heterogeneity ($I^2 = 85\%$) (Liu et al., 2023). This is likely due to the use of different, non-standardized subjective rating scales across studies (Park et al., 2018).

2. **Risk of Bias:** Many included studies were rated as having "Some concerns," primarily due to the inability to blind the surgeon to the intervention (Baete et al., 2017). This introduces a significant risk of detection bias for the subjective outcome of surgical rating.
3. **Generalizability:** The vast majority of included studies (16/20) were in laparoscopic abdominal surgery. The findings regarding surgical conditions may not be generalizable to other fields, such as orthopedic or non-VATS thoracic surgery (Liu et al., 2023).
4. **Inconsistent Reporting:** Adverse events, and PPCs in particular, are poorly and inconsistently defined and reported across studies, which limits the statistical power of meta-analysis for these crucial outcomes.

CONCLUSION AND RECOMMENDATIONS

Conclusions

This systematic review and meta-analysis confirms that the use of deep neuromuscular blockade provides a **statistically significant and clinically superior** intraoperative surgical environment compared to moderate or minimal blockade. This benefit is evidenced by improved surgical rating scores, a profound reduction in intraoperative patient movement, and a decreased need for compensatory measures such as increasing intra-abdominal pressure (Liu et al., 2023; Raval et al., 2020). This enhanced surgical condition also translates to a **significant, though transient, reduction** in immediate postoperative pain in the PACU and at 24 hours (Liu et al., 2023; Raval et al., 2020).

However, this review finds **no sufficient evidence** that the depth of neuromuscular blockade, when adequately reversed, has any **independent association** with the incidence of postoperative pulmonary complications (Liu et al., 2023; Bijkerk et al., 2024; Kim et al., 2021a). The observed reductions in PPCs in some studies appear to be a confounding effect attributable to the necessary use of sugammadex for reversal, which, unlike neostigmine, effectively mitigates postoperative residual blockade—a primary driver of pulmonary morbidity (Yu et al., 2021; Sait et

al., 2024). Furthermore, DNMB does not offer any significant benefit in terms of operative duration or length of hospital stay (Liu et al., 2023).

Recommendations

Based on these findings, the following recommendations are proposed:

1. **For Clinical Practice (Surgeons & Anesthesiologists):** The decision to employ deep NMB should be a collaborative one, based on **surgical necessity** rather than an expectation of independently improving pulmonary outcomes or resource utilization. DNMB is a justified tool for complex robotic or laparoscopic cases where maximal operative space and stillness are critical for surgical success.
2. **For PPC Prevention:** The primary focus for preventing anesthesia-related PPCs should be the **guaranteed prevention of postoperative residual blockade**. This is best achieved through the routine, universal use of **quantitative neuromuscular monitoring** to confirm a TOF ratio >0.9 (or >0.95) before extubation, regardless of the NMB depth or reversal agent used (Naguib et al., 2018; Sait et al., 2024).
3. **For Future Research:** Future RCTs must be designed to definitively *disentangle* the NMB-depth and reversal-agent variables. A large-scale, high-quality trial comparing "Deep NMB + Sugammadex" versus "Moderate NMB + Sugammadex" (with both groups guided by quantitative monitoring) is required to determine if intraoperative NMB depth truly has any independent effect on patient-centered outcomes.

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