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Review: Opioid-Sparing Pharmacological Strategies for Pain Management After Lumbar Spine Surgery: A Narrative Review

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ABSTRACT

Postoperative pain after lumbar spine surgery is generated by skin and muscle injury, periosteal and osseous nociception, neural manipulation, and pre-existing neuropathic sensitization. Opioids remain effective rescue analgesics, but dose-related nausea, ileus, sedation, respiratory depression, delirium, and the risk of persistent postoperative use have accelerated adoption of multimodal, opioid-sparing pathways. This narrative review synthesizes contemporary evidence for pharmacological strategies after lumbar discectomy, decompression/laminectomy, and lumbar fusion, emphasizing procedure intensity, patient risk, and the strength of spine-specific data. PubMed/MEDLINE and reference lists of major systematic reviews, meta-analyses, randomized trials, and consensus guidance were searched through September 14, 2026. The most consistent foundation is scheduled acetaminophen plus a nonsteroidal anti-inflammatory drug (NSAID) or cyclooxygenase-2 inhibitor when not contraindicated, with local anesthetic techniques and rescue opioids. Intravenous acetaminophen can reduce early opioid use versus placebo after lumbar disc surgery, but a recent ambulatory-spine randomized trial did not establish a clinically important advantage over oral acetaminophen. Short-course NSAIDs reduce pain and opioid consumption; newer fusion data suggest that risk to arthrodesis is exposure-dependent rather than a class-wide absolute contraindication, with prolonged or high-dose ketorolac warranting particular caution. Ketamine has the clearest role in painful fusion procedures and opioid-tolerant patients. Gabapentinoids show opioid-sparing signals in spine-specific trials but should not be routine because clinically modest benefits must be balanced against dizziness, sedation, and respiratory risk when combined with opioids. Evidence for dexmedetomidine and intravenous lidocaine is inconsistent; magnesium is promising but less standardized. A risk-stratified strategy that prioritizes non-opioid foundations, adds adjuvants selectively, and treats opioids as rescue therapy offers the most defensible approach while preserving analgesic efficacy and functional recovery.

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1. Introduction

Lumbar spine operations span a wide spectrum, from single-level microdiscectomy to multilevel decompression and instrumented fusion. Their common postoperative problem is clinically important pain arising from incisional injury, paraspinal muscle retraction, facet and periosteal manipulation, bone work, and neural tissue irritation. The intensity and phenotype of pain therefore vary substantially between procedures and among patients, particularly when chronic radicular pain, central sensitization, anxiety, sleep disturbance, or preoperative opioid exposure is present. Procedure-specific consensus statements increasingly favor multimodal analgesia over opioid-centered regimens because no single agent reliably controls all components of postoperative pain (1-6).

Opioids remain indispensable for severe breakthrough pain, but their adverse-effect profile is highly relevant after spine surgery. Sedation and ventilatory impairment may interfere with early mobilization and are especially concerning in patients with obstructive sleep apnea, obesity, frailty, or concomitant sedatives. Nausea, vomiting, constipation, ileus, urinary retention, pruritus, and delirium can also delay recovery. Beyond the immediate perioperative period, lumbar fusion is associated with clinically meaningful rates of prolonged opioid use, and persistent use can also arise in previously opioid-naive patients after spine surgery (7-9). Consequently, the contemporary goal is opioid minimization rather than opioid elimination: analgesic foundations should reduce baseline nociceptive burden, while opioids are reserved and titrated for rescue when pain remains function-limiting.

The purpose of this narrative review is to synthesize the efficacy, safety, and practical positioning of opioid-sparing pharmacological strategies after adult lumbar spine surgery. Particular attention is paid to acetaminophen, NSAIDs and cyclooxygenase-2 (COX-2) inhibitors, gabapentinoids, ketamine, alpha-2 agonists, intravenous lidocaine, glucocorticoids, magnesium, and local-anesthetic techniques. The review also addresses two recurring clinical controversies: whether NSAIDs should be avoided after lumbar fusion and whether sedating adjuvants should be deployed routinely or selectively.

2. Methods

This narrative review was informed by a focused PubMed/MEDLINE search through September 14, 2026, supplemented by the reference lists of relevant reviews and procedure-specific guidance. Search concepts covered adult lumbar discectomy, decompression/laminectomy, fusion, postoperative pain, multimodal and opioid-sparing analgesia, and the principal agents and techniques discussed in this article. Priority was given to recent systematic reviews and meta-analyses, randomized trials, consensus recommendations, and large observational studies with direct clinical relevance to lumbar spine surgery. Sources were selected for relevance to the narrative rather than by a prespecified systematic-review protocol, and findings were integrated qualitatively; no formal risk-of-bias assessment, GRADE process, or de novo meta-analysis was performed.

3. Why an Opioid-Sparing Strategy Is Clinically Relevant

The strongest argument for opioid sparing is not that opioids are intrinsically inappropriate, but that opioid dose is a modifiable contributor to postoperative adverse events and downstream exposure. In a meta-analysis of lumbar fusion cohorts, prolonged opioid use was common and was strongly associated with preoperative opioid exposure and other patient-level risk factors (7). Large claims analyses further show that new persistent opioid use occurs after spine surgery even in patients who were opioid-naive before the procedure (8,9). These data support three linked objectives: reduce unnecessary inpatient opioid requirements, avoid discharge prescriptions that greatly exceed expected need, and identify patients

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likely to require a tailored taper rather than an abrupt transition from high inpatient doses.

A pharmacologically coherent multimodal regimen targets different steps in nociception. Acetaminophen provides centrally mediated analgesia without platelet inhibition; NSAIDs and COX-2 inhibitors attenuate prostaglandin-mediated peripheral inflammation; local anesthetics reduce afferent transmission; ketamine and magnesium modulate N-methyl-D-aspartate (NMDA)-dependent sensitization; alpha-2 agonists reduce sympathetic tone and nociceptive transmission; and gabapentinoids reduce excitatory neurotransmitter release through the alpha-2-delta calcium-channel subunit. Combining mechanistically distinct drugs can produce additive opioid sparing, but additive toxicity is also possible. Thus, multimodal analgesia should not become 'maximal polypharmacy.' The appropriate endpoint is the smallest effective combination matched to procedure and patient risk.

4. Acetaminophen (Paracetamol): A Low-Risk Analgesic Foundation

Acetaminophen is a logical baseline component because it is non-sedating, has no clinically important platelet effect at usual doses, and can be continued across the perioperative period in most patients. Procedure-specific lumbar and complex-spine recommendations support routine paracetamol as part of a multimodal regimen (1-3). In a 2022 meta-analysis of five RCTs including 271 patients undergoing lumbar disc surgery, intravenous paracetamol reduced cumulative 24-hour opioid consumption by a mean of 10.61 mg compared with placebo and also improved several early pain scores, although statistical heterogeneity was substantial and overall certainty was low to moderate (10). An earlier randomized lumbar-discectomy trial similarly reported improved postoperative analgesia with intravenous paracetamol (11).

The clinically important question, however, is usually route rather than whether acetaminophen should be used. In a randomized ambulatory-spine trial published in 2025, intravenous acetaminophen did not establish a clinically important superiority over preoperative oral acetaminophen for opioid use or patient-centered recovery outcomes (12). This finding supports an oral-first strategy when enteral administration is feasible, reserving the intravenous formulation for patients who cannot take oral medication or when institutional pathways identify a specific perioperative advantage. Usual adult ceiling doses must be reduced in hepatic disease, low body weight, malnutrition, or substantial alcohol exposure, and duplicate acetaminophen in combination opioid products should be counted toward the daily total.

5. NSAIDs and COX-2 Inhibitors: Effective Opioid Sparing with Fusion-Specific Nuance

NSAIDs have among the most reproducible opioid-sparing effects in lumbar surgery. A meta-analysis of 17 randomized trials involving 789 lumbar-surgery patients found that adding an NSAID to opioid analgesia improved pain control and reduced opioid requirements without a clear signal of major short-term harm (13). Procedure-specific recommendations for laminectomy, complex spine surgery, and lumbar fusion therefore include an NSAID or COX-2 inhibitor unless contraindicated (1-3). COX-2 selective agents are attractive when platelet effects are a concern, although renal, cardiovascular, and gastrointestinal risk still requires assessment.

The major controversy is bone healing after fusion. The older literature created a broad perception that all NSAID exposure should be avoided, but subsequent syntheses indicate a dose- and duration-dependent relationship. A cross-disciplinary review concluded that short courses at lower doses appear less concerning than prolonged or high-dose exposure (14). A 2011 meta-analysis specifically associated high-dose ketorolac with impaired fusion while normal-dose short-term NSAID exposure did not show the same signal (15). More recent posterior-spine systematic review data

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similarly distinguish short-term analgesic use from prolonged postoperative exposure (16).

The 2026 systematic review and meta-analysis of perioperative ketorolac and spinal union provides especially useful contemporary context. Across 41,365 patients, ketorolac was not associated with a significant overall increase in nonunion; however, exposure longer than 48 hours or total doses above 240 mg was associated with higher nonunion risk (17). These findings do not prove that any NSAID regimen is risk-free, particularly in multilevel fusion, smokers, patients with osteoporosis, or those with other impaired-healing risk factors. They do, however, argue against treating NSAIDs as an absolute class contraindication after fusion. A reasonable evidence-informed position is to use the shortest effective, dose-limited course when the surgeon and perioperative team agree, while avoiding prolonged high-dose therapy and respecting renal, gastrointestinal, bleeding, and cardiovascular contraindications.

6. Gabapentinoids: Selective Rather Than Routine Use

Gabapentin and pregabalin have an intuitive role in spine surgery because many patients present with radicular or neuropathic symptoms. Older spine-specific meta-analyses found reductions in early pain and morphine consumption when gabapentinoids were given preoperatively (18). A 2023 network meta-analysis of 27 RCTs and 1,861 spine-surgery patients also found analgesic and opioid-sparing differences among gabapentin and pregabalin dosing strategies, with gabapentin 900 mg/day ranking favorably for pain outcomes (19). A 2025 lumbar-spine meta-analysis comparing the two agents suggested lower 24-hour morphine consumption with gabapentin, while between-drug pain-score differences were limited (20). The 2026 lumbar-discectomy review also identified opioid-sparing signals for both gabapentin and pregabalin, but rated the evidence as low to very low certainty (5).

These spine-specific signals must be balanced against larger perioperative evidence. A major 2020 systematic review and meta-analysis of 281 trials and 24,682 participants across surgical specialties found that gabapentinoids produced statistically detectable but generally clinically unimportant pain reductions and increased adverse effects such as dizziness and visual disturbance (21). Sedation is especially relevant when gabapentinoids are combined with opioids in older adults, patients with obstructive sleep apnea, renal impairment, or other respiratory risk factors. Therefore, routine administration to every lumbar-surgery patient is difficult to justify. A more defensible approach is selective use in younger or otherwise low-risk patients with a prominent neuropathic pain phenotype or established preoperative therapy, using renal-adjusted doses and avoiding escalation solely to achieve marginal opioid sparing. Abrupt discontinuation of chronic high-dose therapy should also be avoided.

7. Ketamine: The Strongest Systemic Adjunct for High-Pain and Opioid-Tolerant Patients

Low-dose ketamine reduces NMDA-mediated central sensitization and is particularly relevant when tolerance or opioid-induced hyperalgesia may blunt conventional analgesia. A meta-analysis of 14 randomized spine-surgery trials involving 649 patients found reduced opioid consumption and pain during the first 24 postoperative hours without a clear increase in serious adverse events (22). A later systematic review of low-dose ketamine in spine surgery similarly supported reductions in postoperative opioid use and pain scores, though protocols varied substantially (23). Procedure-specific recommendations for complex spine surgery include intraoperative ketamine as part of multimodal analgesia (3). The signal is especially compelling in opioid-tolerant populations. In a randomized trial of opioid-dependent patients with chronic back pain undergoing major back surgery, intraoperative ketamine reduced perioperative opioid consumption (24). Another randomized trial in opioid-tolerant

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patients undergoing spinal fusion showed better pain control with subanesthetic ketamine added to the postoperative regimen (25). These studies support prioritizing ketamine for instrumented or multilevel fusion, patients taking long-term opioids, or individuals with high expected nociceptive burden rather than giving it indiscriminately after minor decompression. Commonly studied regimens use a small induction bolus followed by a low-dose infusion, but exact dosing should follow local anesthesia protocols. Psychotomimetic symptoms, hypertension, tachyarrhythmia, and selected psychiatric or cardiovascular conditions require consideration.

8. Alpha-2 Agonists: Dexmedetomidine and Clonidine

Dexmedetomidine provides sympatholysis, sedation, and analgesic-sparing effects without the same degree of ventilatory depression as opioids. A 2018 systematic review and meta-analysis of randomized spine-surgery trials reported reductions in intraoperative and postoperative opioid requirements, but heterogeneity was substantial (26). In contrast, a well-conducted randomized trial in major spine surgery found that intraoperative dexmedetomidine did not reduce postoperative opioid consumption or pain and increased bradycardia and vasopressor requirements (27). A 2025 systematic review focused on spinal fusion again suggested potential opioid-sparing benefit, while underscoring variation in age, dosing, and comparators (28).

These mixed findings make dexmedetomidine an anesthetic-context adjuvant rather than a universal postoperative analgesic. It may be useful when an anesthesiologist also seeks a propofol- or opioid-sparing intraoperative technique, smoother emergence, or reduced sympathetic activation. It is less attractive in patients with significant baseline bradycardia, conduction disease, or limited hemodynamic reserve. Evidence for clonidine is less extensive in modern lumbar pathways, and its oral or neuraxial use should likewise be protocol-driven.

9. Intravenous Lidocaine: Biologically Plausible but Clinically Inconsistent

Systemic lidocaine has anti-hyperalgesic and anti-inflammatory properties, and several early spine trials were favorable. A 2020 meta-analysis of four RCTs involving 275 spine-surgery patients reported reduced pain and an approximately 15 mg reduction in morphine-equivalent consumption (29). A separate meta-analysis comparing intravenous lidocaine with wound or epidural bupivacaine also concluded that both local-anesthetic approaches reduced postoperative opioid use, with a larger pooled effect for lidocaine (30). The foundational complex-spine RCT by Farag and colleagues reported benefits in pain-related outcomes with perioperative lidocaine (31), and another lumbar-surgery RCT found lower postoperative pain with systemic lidocaine (32).

However, a 2021 meta-analysis restricted to randomized spine-surgery trials found no significant reduction in 48-hour opioid use or pain (33). Differences in lidocaine dose, infusion duration, surgical complexity, baseline multimodal therapy, and sample size probably contribute to the discordance. Given the narrow therapeutic window and risk of local-anesthetic systemic toxicity, intravenous lidocaine should not be treated as a default component of lumbar enhanced-recovery pathways. Its use is best confined to institutions with established dosing, monitoring, and toxicity-management protocols, particularly when stronger evidence-based options are contraindicated.

10. Glucocorticoids: Modest Analgesic Benefit with Useful Antiemetic Effects

Dexamethasone is routinely used for postoperative nausea and vomiting prophylaxis and may provide a modest analgesic bonus. In an 80-patient randomized,

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triple-blind trial of lumbar decompressive laminectomy, 0.2 mg/kg intravenous dexamethasone reduced 48-hour morphine consumption from 42.5 mg to 34.5 mg, but did not significantly improve pain scores at rest or with movement (34). This magnitude of effect is smaller than that expected from a complete multimodal foundation, but it can still be clinically useful when dexamethasone is already indicated for antiemetic prophylaxis.

Local steroid strategies have also been studied. In a randomized lumbar-discectomy study, adding methylprednisolone to wound bupivacaine was evaluated for postoperative pain control (35). Although such approaches can reduce local inflammation, heterogeneous formulations and theoretical concerns about wound healing or infection limit routine extrapolation. Systemic dexamethasone should be used cautiously in patients with poorly controlled diabetes because perioperative hyperglycemia can offset its recovery benefits.

11. Magnesium Sulfate: An NMDA-Modulating Adjunct with Emerging Evidence

Magnesium reduces NMDA-receptor activity and calcium influx and has been studied as a low-cost perioperative adjunct. A randomized placebo-controlled trial in lumbar laminectomy found that intraoperative magnesium as part of multimodal analgesia reduced 24-hour morphine-equivalent consumption by approximately 9 mg and improved aspects of postoperative pain control (36). A 2024 meta-analysis of eight spinal-surgery studies involving 541 patients found significantly lower opioid consumption and a small reduction in 24-hour pain with magnesium, although protocols and comparators varied (37).

Magnesium may therefore be a useful second-line adjunct for patients expected to have moderate-to-severe pain when ketamine is undesirable or when an institution already has a validated magnesium protocol. It is not yet as standardized as acetaminophen, NSAIDs, or ketamine. Renal dysfunction, neuromuscular weakness, hypotension, and interactions with neuromuscular blocking agents deserve attention, and prolonged infusion requires appropriate monitoring.

12. Local Anesthetic Techniques and Erector Spinae Plane Block

Although regional techniques are procedural, their opioid-sparing effect is pharmacologically mediated by local anesthetics and is directly relevant to a medication-focused strategy. Procedure-specific recommendations support local anesthetic wound infiltration for lumbar decompression and recognize local/epidural techniques for more complex spine surgery (1-3). These approaches can reduce afferent nociceptive input without adding systemic sedation. Their main limitations are operator dependence, duration of action, and the need to account for total local-anesthetic dose when multiple techniques are combined.

The erector spinae plane block (ESPB) has accumulated a substantial randomized literature. A 2024 meta-analysis of lumbar-spine RCTs found lower postoperative pain and opioid consumption with ESPB (38). A 2026 fusion-specific systematic review likewise reported lower 24-hour opioid requirements and improved pain outcomes, although heterogeneity remained (39). An even larger updated 2026 meta-analysis of 60 RCTs (4,167 patients) across vertebral surgery reported an approximately 8.9 mg reduction in 24-hour morphine-milligram equivalents, fewer rescue-analgesic requirements, and less postoperative nausea and vomiting; certainty was limited by substantial heterogeneity (40). In practical terms, ESPB or local infiltration is a reasonable add-on when expertise is available, particularly for fusion, but it should complement rather than replace scheduled non-opioid systemic analgesia. A concise comparison of the evidence, opioid-sparing signal, major cautions, and suggested role of these strategies is provided in Table 1.

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Table 1. Evidence summary for major opioid-sparing pharmacological strategies after lumbar spine surgery.

Strategy	Key evidence	Opioid-sparing signal	Main cautions	Suggested role
Acetaminophen	Lumbar-disc meta-analysis: 5 RCTs, n=271; lower 24-h opioid use. A 2025 RCT found no clear IV advantage over oral administration (10-12).	Moderate and consistent as a baseline agent	Hepatic disease, low body weight, alcohol exposure; count combination products	Routine foundation; oral preferred when feasible
NSAID / COX-2 inhibitor	A 17-RCT lumbar meta-analysis showed better pain control and lower opioid use. Modern fusion evidence suggests dose- and duration-dependent rather than absolute nonunion risk (13-17).	Strong for early opioid sparing	Renal, GI, CV, and bleeding risk; fusion exposure should be short and dose-limited	Routine if no contraindication; surgeon alignment for fusion
Gabapentin / pregabalin	Spine-specific meta-analyses show early opioid reduction, but broad perioperative evidence indicates small clinical benefit with more dizziness and visual adverse effects (18-21).	Variable; patient-selection dependent	Sedation, dizziness, respiratory risk with opioids; renal dose adjustment	Selective use for neuropathic phenotype or established therapy
Ketamine	Multiple spine RCT meta-analyses show lower opioid use and early pain; RCTs support benefit in opioid-tolerant fusion patients (22-25).	Strongest systemic add-on for high-risk cases	Psychotomimetic effects, sympathetic stimulation; protocolized monitoring	High-pain fusion, chronic opioid exposure, or opioid tolerance
Dexmedetomidine	Meta-analytic signal for opioid reduction, but a major-spine RCT showed no postoperative benefit and more bradycardia/vasopressor use (26-28).	Inconsistent	Bradycardia, hypotension, and limited hemodynamic reserve	Selective intraoperative adjunct
IV lidocaine	Some reviews suggest less pain and opioid use; an RCT-only meta-analysis found no significant 48-h benefit (29-33).	Inconsistent / low certainty	Local-anesthetic systemic toxicity; narrow therapeutic window	Protocolized use only; not routine
Glucocorticoids	A lumbar-laminectomy RCT showed a modest reduction in 48-h morphine without pain-score improvement; local steroid strategies are heterogeneous (34,35).	Modest	Hyperglycemia; infection or wound-healing concerns in selected patients	Useful primarily when antiemetic prophylaxis is also desired
Magnesium sulfate	A lumbar RCT and 2024 meta-analysis (8 studies, n=541) found lower opioid use and a small pain reduction (36,37).	Promising, less standardized	Renal impairment, hypotension, and neuromuscular effects	Conditional second-line adjunct
Local anesthetic / ESPB	Lumbar and fusion meta-analyses show lower opioid use and pain; an updated 2026 vertebral-surgery meta-analysis included 60 RCTs (38-40).	Consistent signal; heterogeneous protocols	Dose summation, local-anesthetic toxicity, and operator dependence	Strong add-on when expertise is available

Abbreviations: COX-2, cyclooxygenase-2; CV, cardiovascular; ESPB, erector spinae plane block; GI, gastrointestinal; IV, intravenous; NSAID, nonsteroidal anti-inflammatory drug; RCT, randomized controlled trial. Effect estimates are summarized from cited source reviews and should not be interpreted as a new pooled analysis.

13. Building a Risk-Stratified Multimodal Regimen

The most defensible opioid-sparing pathway is layered rather than drug-maximal (Figure 1). The first layer is a universal foundation: scheduled oral acetaminophen and an NSAID/COX-2 inhibitor unless contraindicated, plus antiemetic prophylaxis and local anesthetic infiltration when feasible. For limited discectomy or decompression in opioid-naive patients, this foundation may be sufficient with small amounts of rescue opioid. For multilevel decompression, instrumented fusion, marked preoperative pain, or chronic opioid exposure, the regimen can be intensified with ketamine and a local/regional anesthetic technique. Magnesium or dexmedetomidine can be considered where institutional experience is strong. Gabapentinoids and intravenous lidocaine should be selective rather than routine because their benefit-to-harm ratio is more context dependent (1-6,18-33).

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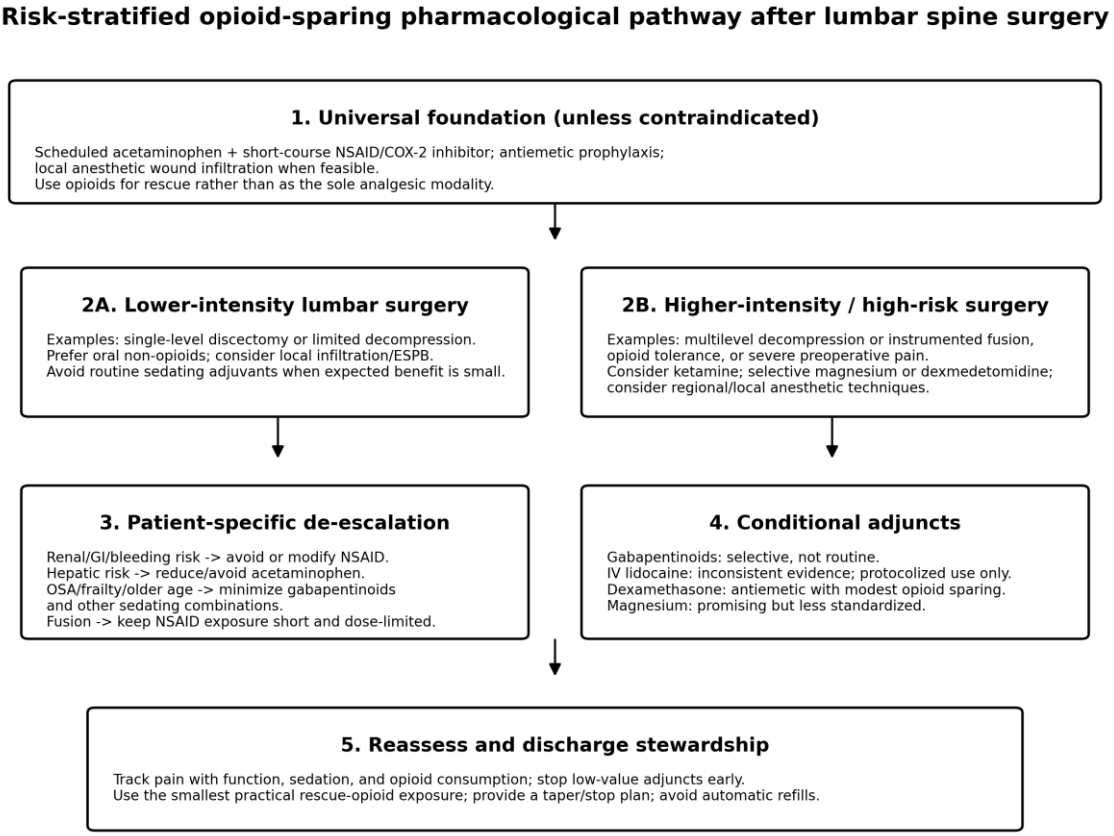


Figure 1. Risk-stratified opioid-sparing pharmacological pathway for adult lumbar spine surgery.
The pathway emphasizes a low-risk non-opioid foundation, selective escalation for higher-intensity surgery or opioid tolerance, explicit de-escalation for organ-specific and sedation risk, conditional use of less consistently supported adjuncts, and rescue rather than routine opioid use. COX-2, cyclooxygenase-2; CV, cardiovascular; ESPB, erector spinae plane block; GI, gastrointestinal; IV, intravenous; NSAID, nonsteroidal anti-inflammatory drug; OSA, obstructive sleep apnea.

Risk stratification should also remove drugs, not just add them. Patients with chronic kidney disease, active gastrointestinal ulceration, major bleeding risk, or certain cardiovascular conditions may not be candidates for NSAIDs. Acetaminophen dose should be reduced in significant hepatic risk. Older, frail, or obstructive-sleep-apnea patients are particularly vulnerable to sedation from gabapentinoid-opioid combinations. Patients undergoing fusion may receive a short NSAID course in many modern pathways, but prolonged high-dose exposure should be avoided and the final decision should be aligned with the operating surgeon (14-17).

Opioid rescue should be functional and reassessed rather than automatically scheduled. Pain scores alone are poor guides to recovery; ambulation, sleep, respiratory status, nausea, and ability to participate in physiotherapy are equally important. If oral opioids are needed at discharge, the prescription should reflect the last 12-24 hours of inpatient use and the expected recovery trajectory, with explicit stop or taper instructions. Patients on chronic opioids require a different plan: baseline opioid dependence should be prevented from becoming withdrawal, while escalation for surgical pain should be time-limited and coordinated with the preoperative prescriber whenever possible. The phase-based perioperative application of these principles is summarized in Table 2.

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Table 2. Practical perioperative framework for opioid-sparing analgesia.

Phase	Primary task	Preferred opioid-sparing actions	Stewardship / safety check
Preoperative	Assess opioid exposure, OSA/frailty, renal/hepatic/GI/CV risk, neuropathic phenotype, and fusion/nonfusion status.	Oral acetaminophen; NSAID/COX-2 inhibitor if appropriate. Avoid routine high-dose gabapentinoid loading in patients at high sedation risk.	Agree on chronic-opioid continuation and the postoperative taper/rescue plan.
Intraoperative	Match adjunct intensity to surgical magnitude and patient risk.	Local anesthetic infiltration or ESPB; ketamine for painful fusion or opioid tolerance. Consider dexmedetomidine or magnesium selectively.	Avoid stacking sedating adjuncts without a defined benefit; use protocolized infusion stop times.
PACU / first 24 h	Prioritize function, ventilation, nausea control, and mobilization in addition to NRS/VAS.	Continue scheduled acetaminophen plus short-course NSAID/COX-2 inhibitor if eligible; use the oral route when feasible.	Use opioids only for uncontrolled function-limiting pain; reassess after each escalation.
24-72 h / discharge	De-escalate adjuncts and convert to a simple oral regimen.	Stop infusions; continue only high-value non-opioids for a defined duration.	Base discharge opioid quantity on recent use; provide stop/taper instructions and avoid automatic refills.

Abbreviations: COX-2, cyclooxygenase-2; CV, cardiovascular; ESPB, erector spinae plane block; GI, gastrointestinal; NRS, Numeric Rating Scale; NSAID, nonsteroidal anti-inflammatory drug; OSA, obstructive sleep apnea; PACU, post-anesthesia care unit; VAS, Visual Analog Scale.

14. Procedure-Specific Considerations

Lumbar discectomy and limited decompression generally produce a shorter, less intense nociceptive course than multilevel fusion. In these lower-intensity procedures, scheduled oral acetaminophen plus an NSAID/COX-2 inhibitor and local anesthetic infiltration can often provide the majority of analgesic coverage. The 2026 lumbar-discectomy systematic review found opioid-sparing effects across several classes, but the certainty for individual interventions was low to very low, reinforcing the value of choosing low-risk foundational agents rather than stacking every positive trial intervention (5).

Instrumented lumbar fusion has a different risk-benefit profile. More extensive muscle dissection and bony work increase early pain, while concerns about arthrodesis influence NSAID prescribing. Ketamine and regional/local anesthetic strategies have a stronger rationale in this setting, especially for opioid-tolerant patients (3,22-25,39). NSAID use should be short, protocolized, and dose-limited if chosen, rather than prolonged by default (14-17). Because fusion patients may have longer hospital stays, daily de-prescribing is important: an adjunct started in the operating room should not automatically continue for several postoperative days if its benefit is uncertain.

15. Safety, Monitoring, and Drug-Selection Pitfalls

Multimodal analgesia can reduce opioid toxicity while creating new adverse-event combinations if applied indiscriminately. The most important preventable error is additive sedation: opioids, gabapentinoids, benzodiazepines, antihistamines, and other sedatives can produce disproportionate respiratory impairment when combined. The second is unrecognized organ-specific toxicity, such as NSAID-associated acute kidney injury or gastrointestinal bleeding and excessive acetaminophen exposure from multiple products. The third is protocol drift, in which infusions such as lidocaine, ketamine, dexmedetomidine, or magnesium are continued without a defined indication, stop time, or monitoring standard.

A successful pathway therefore specifies both inclusion and exclusion criteria. Baseline renal and hepatic function, bleeding risk, cardiovascular disease, frailty, sleep apnea, chronic opioid dose, neuropathic symptoms, and fusion status should be reviewed before selecting adjuncts. Sedation and respiratory status should be monitored at least as deliberately as numeric pain scores. The net goal is not the lowest possible opioid count at any cost, but lower opioid exposure with preserved alertness, mobilization, gastrointestinal function, and patient-reported recovery.

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16. Limitations of the Evidence Base

The evidence is limited by heterogeneity at almost every level. Studies combine microdiscectomy, laminectomy, minimally invasive procedures, deformity surgery, and multilevel fusion; background analgesia differs; opioid outcomes are reported in different equivalents and time windows; and some trials predate contemporary enhanced-recovery pathways. Small positive trials can overestimate benefit, while meta-analyses may pool clinically dissimilar protocols. This is particularly relevant for intravenous lidocaine, dexmedetomidine, and gabapentinoids, where conclusions change depending on trial selection and baseline care (18-33).

The fusion-NSAID literature also contains a substantial observational component and is vulnerable to confounding by indication, dose, duration, smoking, surgical complexity, and bone-health status. The large 2026 ketorolac analysis strengthens the case for exposure-dependent risk but does not establish a universally safe dose for every construct (17). Recommendations should therefore be implemented as pathway principles and adapted to institutional protocols rather than interpreted as prescriptive dosing standards.

17. Conclusion

After lumbar spine surgery, the most evidence-supported opioid-sparing strategy is a multimodal, risk-stratified regimen rather than reliance on a single 'best' adjuvant. Scheduled acetaminophen and a short-course NSAID/COX-2 inhibitor, when not contraindicated, form the pharmacological backbone. Local anesthetic techniques can further reduce nociceptive input without systemic sedation. Ketamine is the most consistently supported systemic add-on for painful fusion procedures and opioid-tolerant patients. Gabapentinoids should be selective, especially in patients at risk for sedation or respiratory compromise. Dexmedetomidine and intravenous lidocaine have inconsistent evidence and are best reserved for protocolized use; dexamethasone offers useful antiemetic effects with modest opioid sparing, and magnesium is a promising but less standardized adjunct. For fusion, current evidence favors short, dose-limited NSAID exposure rather than a blanket prohibition, with prolonged or high-dose ketorolac avoided. Opioids remain appropriate rescue therapy, but minimizing unnecessary exposure during hospitalization and at discharge is a core component of postoperative safety and recovery.

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Conflicts of interest

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References

1. Debono B, Wainwright TW, Wang MY, et al. Consensus statement for perioperative care in lumbar spinal fusion: Enhanced Recovery After Surgery (ERAS) Society recommendations. Spine J. 2021;21(5):729-752.

2. Peene L, Le Cacheux P, Sauter AR, Joshi GP, Beloeil H. Pain management after laminectomy: a systematic review and procedure-specific post-operative pain management (PROSPECT) recommendations. Eur Spine J. 2021;30(10):2925-2935.

3. Waelkens P, Alsabbagh E, Sauter A, Joshi GP, Beloeil H. Pain management after complex spine surgery: a systematic review and procedure-specific postoperative pain management recommendations. Eur J Anaesthesiol. 2021;38(9):985-994.

4. Geisler A, Zachodnik J, Koppen K, Chakari R, Bech-Azeddine R. Postoperative pain treatment after spinal fusion surgery: a systematic review with meta-analyses and trial sequential analyses. Pain Rep. 2022;7(3):e1005.

5. Zachodnik J, Bech-Azeddine R, Sandberg M, et al. Postoperative pain management after lumbar discectomy: a systematic review with meta-analyses and trial sequential analyses. Eur J Pain. 2026;30(4):e70261.

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6. Devin CJ, McGirt MJ. Best evidence in multimodal pain management in spine surgery and means of assessing postoperative pain and functional outcomes. J Clin Neurosci. 2015;22(6):930-938.

7. Kuo CC, Soliman MAR, Iskander J, et al. Prolonged opioid use after lumbar fusion surgery: a meta-analysis of prevalence and risk factors. World Neurosurg. 2022;168:e132-e149.

8. Schultz E, Zhuang T, Shapiro LM, et al. Is outpatient spine surgery associated with new, persistent opioid use in opioid-naive patients? A retrospective national claims database analysis. Spine J. 2023;23(10):1451-1460.

9. Bologheanu R, Bilir A, Kapral L, Gruber F, Kimberger O. New persistent opioid use after surgery. JAMA Netw Open. 2025;8(2):e2460794.

10. Yin F, Wang XH, Liu F. Effect of intravenous paracetamol on opioid consumption in multimodal analgesia after lumbar disc surgery: a meta-analysis of randomized controlled trials. Front Pharmacol. 2022;13:860106.

11. Shimia M, Parish M, Abedini N. The effect of intravenous paracetamol on postoperative pain after lumbar discectomy. Asian Spine J. 2014;8(4):400-404.

12. Schwenk ES, Ferd P, Torjman MC, et al. Intravenous versus oral acetaminophen for pain and quality of recovery after ambulatory spine surgery: a randomized controlled trial. Reg Anesth Pain Med. 2025;50(6):483-488.

13. Jirarattanaphochai K, Jung S. Nonsteroidal antiinflammatory drugs for postoperative pain management after lumbar spine surgery: a meta-analysis of randomized controlled trials. J Neurosurg Spine. 2008;9(1):22-31.

14. Sivaganesan A, Chotai S, White-Dzuro G, McGirt MJ, Devin CJ. The effect of NSAIDs on spinal fusion: a cross-disciplinary review of biochemical, animal, and human studies. Eur Spine J. 2017;26(11):2719-2728.

15. Li Q, Zhang Z, Cai Z. High-dose ketorolac affects adult spinal fusion: a meta-analysis of the effect of perioperative nonsteroidal anti-inflammatory drugs on spinal fusion. Spine (Phila Pa 1976). 2011;36(7):E461-E468.

16. Singh R, Kopilak E, Rajan R, Bauer J, Razi AE, Ng M. The impact of non-steroidal anti-inflammatory drugs on postoperative outcomes in posterior spinal surgery: a systematic review. Global Spine J. 2026;16(4):2012-2027.

17. Ononogbu-Uche FC, Ahmed R, Giarola I, et al. Does perioperative ketorolac use impact union rate in spine surgery: a systematic review and meta-analysis. Spine J. 2026;26(5):893-901.

18. Liu B, Liu R, Wang L. A meta-analysis of the preoperative use of gabapentinoids for the treatment of acute postoperative pain following spinal surgery. Medicine (Baltimore). 2017;96(37):e8031.

19. Tsai SHL, Hu CW, El Sammak S, et al. Different gabapentin and pregabalin dosages for perioperative pain control in patients undergoing spine surgery: a systematic review and network meta-analysis. JAMA Netw Open. 2023;6(8):e2328121.

20. Ebada A, Bever N, Carron CJ, Odiase P, Wolfe C, Al Tamimi M, Aoun SG. Comparing gabapentin and pregabalin for perioperative pain management in lumbar spine surgery: a systematic review and meta-analysis. World Neurosurg. 2025;201:124284.

21. Verret M, Lauzier F, Zarychanski R, et al. Perioperative use of gabapentinoids for the management of postoperative acute pain: a systematic review and meta-analysis. Anesthesiology. 2020;133(2):265-279.

22. Pendi A, Field R, Farhan SD, Eichler M, Bederman SS. Perioperative ketamine for analgesia in spine surgery: a meta-analysis of randomized controlled trials. Spine (Phila Pa 1976). 2018;43(5):E299-E307.

23. Zhou L, Yang H, Hai Y, Cheng Y. Perioperative low-dose ketamine for postoperative pain management in spine surgery: a systematic review and meta-analysis of randomized controlled trials. Pain Res Manag. 2022;2022:1507097.

24. Loftus RW, Yeager MP, Clark JA, Brown JR, Abdu WA, Sengupta DK, Beach ML. Intraoperative ketamine reduces perioperative opiate consumption in opiate-dependent patients with chronic back pain undergoing back surgery. Anesthesiology. 2010;113(3):639-646.

25. Urban MK, Ya Deau JT, Wukovits B, Lipnitsky JY. Ketamine as an adjunct to postoperative pain management in opioid tolerant patients after spinal fusions: a prospective randomized trial. HSS J. 2008;4(1):62-65.

26. Tsaousi GG, Pourzitaki C, Aloisio S, Bilotta F. Dexmedetomidine as a sedative and analgesic adjuvant in spine surgery: a systematic review and meta-analysis of randomized controlled trials. Eur J Clin Pharmacol. 2018;74(11):1377-1389.

27. Naik BI, Nemergut EC, Kazemi A, et al. The effect of dexmedetomidine on postoperative opioid consumption and pain after major spine surgery. Anesth Analg. 2016;122(5):1646-1653.

28. Rodriguez MJ, Vazquez A, Rodriguez-Dominguez V, Mata PR, Mariscal G. Safety and efficacy of dexmedetomidine in spinal fusion: a systematic review and meta-analysis. J Pain Palliat Care Pharmacother. 2025;39(4):500-517.

29. Bi Y, Ye Y, Ma J, Tian Z, Zhang X, Liu B. Effect of perioperative intravenous lidocaine for patients undergoing spine surgery: a meta-analysis and

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systematic review. Medicine (Baltimore). 2020;99(48):e23332.

30. Tsai SHL, Yolcu YU, Hung SW, et al. The analgesic effect of intravenous lidocaine versus intrawound or epidural bupivacaine for postoperative opioid reduction in spine surgery: a systematic review and meta-analysis. Clin Neurol Neurosurg. 2021;201:106438.

31. Farag E, Ghobrial M, Sessler DI, et al. Effect of perioperative intravenous lidocaine administration on pain, opioid consumption, and quality of life after complex spine surgery. Anesthesiology. 2013;119(4):932-940.

32. Kim KT, Cho DC, Sung JK, et al. Intraoperative systemic infusion of lidocaine reduces postoperative pain after lumbar surgery: a double-blinded, randomized, placebo-controlled clinical trial. Spine J. 2014;14(8):1559-1566.

33. Haratian A, Musa A, Field R, et al. Intravenous lidocaine in spine surgery: a meta-analysis of randomized controlled trials. N Am Spine Soc J. 2021;7:100079.

34. Wittayapairoj A, Wittayapairoj K, Kulawong A, Huntula Y. Effect of intermediate dose dexamethasone on post-operative pain in lumbar spine surgery: a randomized, triple-blind, placebo-controlled trial. Asian J Anesthesiol. 2017;55(3):73-77.

35. Ersayli DT, Gurbet A, Bekar A, Uckunkaya N, Bilgin H. Effects of perioperatively administered bupivacaine and bupivacaine-methylprednisolone on pain after lumbar discectomy. Spine (Phila Pa 1976). 2006;31(19):2221-2226.

36. Tsaousi G, Nikopoulou A, Pezikoglou I, Birba V, Grosomanidis V. Implementation of magnesium sulphate as an adjunct to multimodal analgesic approach for perioperative pain control in lumbar laminectomy surgery: a randomized placebo-controlled clinical trial. Clin Neurol Neurosurg. 2020;197:106091.

37. Campos J, Bas JL, Campos C, Mariscal G, Bas T, Bas P. Efficacy and safety of intravenous magnesium sulfate in spinal surgery: a systematic review and meta-analysis. J Clin Med. 2024;13(11):3122.

38. Wilson AA, Schmid AM, Pestana P Jr, Tubog TD. Erector spinae plane block on postoperative pain and opioid consumption after lumbar spine surgery: a systematic review and meta-analysis of randomized controlled trials. J Perianesth Nurs. 2024;39(1):122-131.

39. Mobinikhaledi A, Amiri AK. TMSCl-catalysed condensation of α-diketone compounds with urea/thiourea derivatives under solvent-free conditions. J Chem Sci. 2013;125(5):1055-1062.

40. Ye J, Wu J, Zhou Y, Mao C. Efficacy of erector spinae plane block in lumbar fusion surgery: a systematic review and meta-analysis on opioid-sparing and postoperative pain outcomes. J Pain Res. 2026;19:573516.

Dost B, Turunc E, Karapinar YE, Beldagli M, Turan EI, Dokmeci H, De Cassai A. Erector spinae plane block for postoperative analgesia in vertebral surgery: an updated meta-analysis of randomized controlled trials with trial sequential analysis and meta-regression. J Clin Anesth. 2026;111:112184.

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