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Ketamine for perioperative pain and opioid sparing: A scoping review

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Abstract
Purpose: The purpose of this scoping review was to examine and map existing evidence on the effectiveness, dosing strategies, and safety of low dose ketamine for perioperative pain management and opioid reduction in adult surgical populations, and to identify gaps that require further investigation.
Methodology: The review followed the PRISMA Scoping Review framework. A comprehensive search of MEDLINE, Embase, and Cochrane CENTRAL was conducted through November 2025 to identify randomized controlled trials, observational cohorts, and systematic reviews evaluating perioperative ketamine administered intravenously, neuraxially, or via local infiltration. Eligible studies reported postoperative pain scores, opioid consumption, adverse effects, or recovery outcomes. Data were synthesized to characterise dosing patterns, clinical effects, and safety profiles.
Findings: Forty three studies met inclusion criteria, comprising twenty nine randomized controlled trials, eight cohort studies, and six systematic reviews. Across surgical procedures, ketamine consistently reduced twenty four hour opioid consumption by approximately twenty five to forty five percent and decreased postoperative pain scores by one to two points on a ten point scale. Psychotomimetic effects occurred in three to eight percent of patients but were transient and self resolving. Cardiovascular instability was not increased. Dosing commonly involved a bolus of 0.1 to 0.5 mg/kg followed by an infusion of 0.05 to 0.25 mg/kg per hour. Opioid tolerant patients and individuals undergoing spine surgery demonstrated the greatest benefit.
Unique Contribution to Theory, Policy and Practice: This review clarifies the mechanistic and clinical rationale for incorporating low dose ketamine within multimodal perioperative analgesia by consolidating evidence that supports NMDA receptor modulation as an effective strategy for mitigating opioid related burden. Findings support policy development toward standardised ketamine dosing protocols within Enhanced Recovery pathways and highlight its value for opioid stewardship initiatives. The review also identifies gaps in long term outcome reporting, offering a theoretical and practical foundation for future clinical trials aimed at optimising perioperative ketamine use and guiding evidence based anesthesia practice.

Keywords: Ketamine, perioperative analgesia, opioid sparing, anesthesia, multimodal analgesia, ERAS

1. Introduction
Effective perioperative pain management remains a central priority in contemporary surgical care as healthcare systems continue to address the clinical and societal consequences of opioid overreliance. Opioid based regimens, while effective, are associated with substantial adverse effects including respiratory depression, postoperative nausea and vomiting, delayed mobilization, cognitive impairment, and increased risk of long term dependence. These concerns have driven an international shift toward opioid sparing and multimodal analgesic strategies that prioritize safety, enhance recovery, and support responsible opioid stewardship. Within this broader context, ketamine has re emerged as a valuable adjunct capable of improving postoperative analgesia while reducing the cumulative opioid burden, as consistently demonstrated in major systematic reviews such as the Cochrane analyses by Bell *et al*. (2006) [1] and Brinck *et al*. (2018) [3].
Ketamine's role in perioperative analgesia is grounded in its unique pharmacologic profile. As an antagonist of the N methyl D aspartate receptor, ketamine disrupts central sensitization and nociceptive amplification, two mechanisms strongly associated with postoperative hyperalgesia and opioid tolerance. By inhibiting these pathways, ketamine reduces pain intensity, limits opioid escalation, and mitigates opioid induced hyperalgesia. These mechanistic insights have been documented extensively in foundational anesthesia literature,

including comprehensive evaluations of sub anesthetic ketamine for perioperative use (Gorlin *et al*., 2016) [11] and recent umbrella reviews examining ketamine's effects in acute pain management (Viderman *et al*., 2024) [27].

Low dose ketamine, when administered within multimodal analgesia frameworks, has demonstrated clinically meaningful analgesic benefits across a range of surgical specialties including spine surgery, orthopedic arthroplasty, bariatric procedures, colorectal surgery, thoracic operations, and ambulatory interventions. Evidence from randomized trials and high quality systematic reviews supports its effectiveness in reducing both pain intensity and postoperative opioid consumption (Bell *et al*., 2006; Brinck *et al*., 2018) [1, 3]. Contemporary perioperative practice models further highlight ketamine's value as an adaptable, opioid sparing agent that aligns well with Enhanced Recovery pathways and modern analgesic principles (Khan *et al*., 2023; Caruso *et al*., 2021) [12, 4].

Despite these recognized advantages, key uncertainties persist. Variability in ketamine dosing strategies, timing of administration, infusion duration, and postoperative continuation has resulted in inconsistent findings across studies. Differences in patient demographics, surgical intensity, concomitant analgesic medications, and monitoring practices further complicate interpretation of the evidence. Additionally, psychotomimetic and hemodynamic effects, although generally mild at low doses, are not uniformly reported, which challenges the development of standardized clinical guidelines. These limitations highlight the need for a structured synthesis of the existing evidence to identify areas of agreement, clarify areas of inconsistency, and guide future research and clinical application.

1.1 Objective of the Review

The objective of this scoping review is to systematically map and evaluate the breadth of published evidence on the use of perioperative low dose ketamine for postoperative pain reduction and opioid sparing in adult surgical populations. This review aims to:

- Characterize the range of dosing strategies, timing, and administration protocols reported in the literature.
- Summarize the effects of ketamine on postoperative pain intensity, opioid consumption, recovery outcomes, and adverse events.
- Compare outcomes across different surgical specialties and patient populations, including opioid tolerant cohorts.
- Identify inconsistencies, methodological variations, and gaps within the evidence base.
- Provide an evidence informed foundation to support clinical decision making and guide future research on standardized perioperative ketamine protocols.

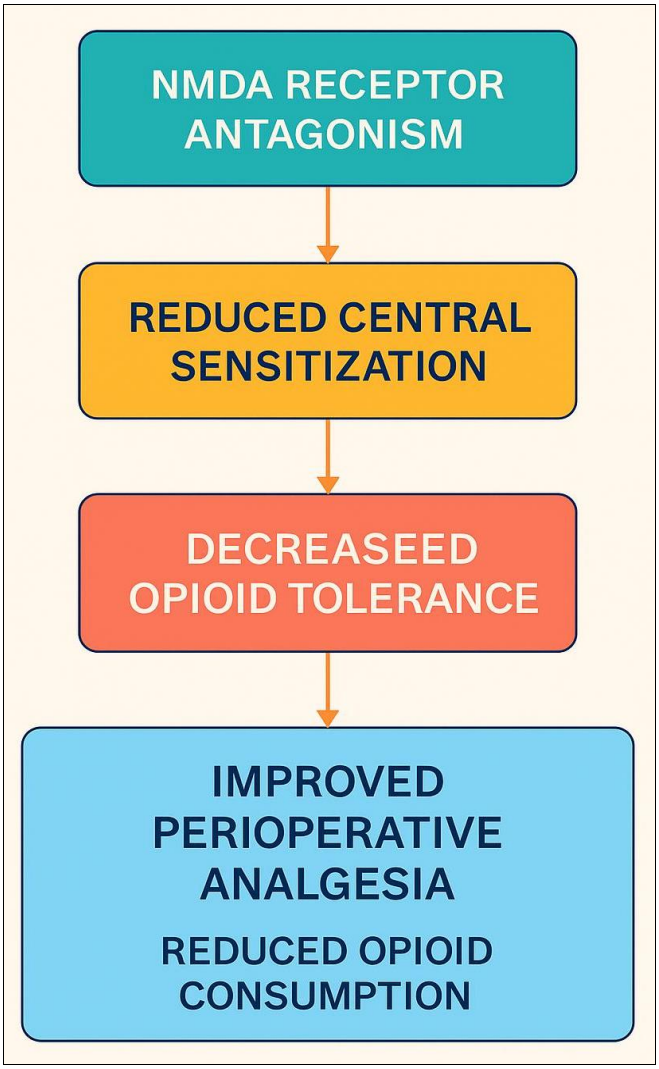

Fig 1: Conceptual Mechanism of Ketamine in Perioperative Analgesia

2. Methods

2.1 Eligibility Criteria (PCC Framework)

The eligibility criteria for this scoping review were developed using the PCC framework, which is recommended for scoping reviews to ensure a structured and transparent approach to evidence identification. The PCC elements were defined as Participants, Concept, and Context. Together, these criteria guided the selection of relevant literature and ensured that the included studies reflected the breadth of contemporary evidence on perioperative ketamine (Bell *et al*., 2006; Brinck *et al*., 2018) [1, 3].

Participants

Studies were eligible for inclusion if they enrolled adult patients aged eighteen years or older who were undergoing any form of surgical procedure performed under general anesthesia, regional anesthesia, or combined anesthetic techniques. The review incorporated evidence from a wide range of surgical disciplines, including orthopedic, abdominal, thoracic, gynecologic, urologic, and ambulatory procedures (García-Henares *et al*., 2018; Wang *et al*., 2021) [8, 30].

Both opioid naive individuals and those with established opioid tolerance or chronic opioid therapy were included, given the clinical relevance of ketamine for modulating opioid responsiveness in these populations. The inclusion of diverse patient groups allowed the review to capture a comprehensive understanding of ketamine's effectiveness across varying physiological profiles and baseline analgesic requirements.

Studies limited to pediatric populations, obstetric labor analgesia, or non surgical interventions were excluded to maintain focus on adult perioperative care.

Concept

The central concept of the review was the perioperative use of ketamine for analgesic improvement or reduction in opioid consumption. To ensure broad capture of relevant dosing strategies, the review included studies evaluating ketamine administered at any perioperative time point, including pre induction, intraoperative, and early postoperative phases (Bell *et al*., 2006; Brinck *et al*., 2018) [1, 3].

Eligible ketamine modalities and delivery routes included:

- Intravenous bolus dosing
- Continuous intravenous infusion
- Neuraxial administration (epidural or intrathecal)
- Local infiltration at the surgical site
- Patient controlled analgesia devices delivering ketamine adjuncts

Studies evaluating racemic ketamine or its S enantiomer (S ketamine or esketamine) were both eligible (Wang *et al*., 2021) [30]. Dosing ranges of interest included sub anesthetic doses typically used for analgesia and opioid sparing; studies investigating ketamine for anesthesia induction or high dose sedation were excluded unless analgesic outcomes were explicitly reported.

The review focused on studies that assessed at least one of the following outcomes:

- Postoperative pain intensity scores
- Cumulative opioid consumption within twenty four to forty eight hours
- Opioid sparing effects measured in morphine milligram equivalents
- Secondary analgesic outcomes such as time to first rescue analgesia, recovery quality, length of stay, or postoperative nausea and vomiting

This conceptual scope ensured alignment with the review's objective of mapping ketamine's analgesic value and its potential role in multimodal pain pathways, including Enhanced Recovery protocols (García-Henares *et al*., 2018) [8].

Context

The contextual scope of the review encompassed adult surgical care delivered in both inpatient and outpatient environments. Studies conducted in elective, emergency, major, or minor surgery settings were included, provided ketamine was used as part of the perioperative analgesia plan and postoperative outcomes were collected.

Eligible contexts included:

- Traditional inpatient hospital surgery
- Ambulatory or day case surgery
- Integrated perioperative care pathways, including Enhanced Recovery programmes
- Surgical oncology, trauma, and reconstructive procedures

Studies conducted in intensive care units, pain clinics, or chronic pain management programs were excluded unless the ketamine intervention was directly related to a surgical episode (Bell *et al*., 2006) [1].

Eligible Study Designs

To achieve a comprehensive mapping of the available evidence, the review included a range of study designs that contribute meaningfully to understanding ketamine's perioperative analgesic profile. Eligible designs included:

- Randomized controlled trials
- Prospective comparative cohort studies
- Retrospective cohort analyses
- Systematic reviews and meta analyses

These designs were selected because they provide comparative outcome data relevant to assessing analgesic efficacy, opioid consumption, and safety events.

Studies were excluded if they met any of the following criteria:

- Narrative reviews, expert commentaries, or opinion pieces
- Case reports or small case series without comparator groups
- Pediatric studies
- Laboratory or animal studies
- Non comparative observational designs that did not report pain or opioid outcomes

The inclusion criteria ensured that the final evidence map reflected methodologically credible and clinically relevant research.

2.2 Information Sources and Search Strategy

A structured and comprehensive literature search was

conducted on 15 November 2025 using three major biomedical databases: MEDLINE via PubMed, Embase, and Cochrane CENTRAL. The search strategy was designed to capture the breadth of evidence on ketamine used in perioperative analgesia across various surgical specialties.

Search terms combined controlled vocabulary and free text words covering ketamine exposure, perioperative timing, analgesic outcomes, and study design. The core search string included: (ketamine OR esketamine) AND (perioperative OR intraoperative OR postoperative) AND (analges OR pain OR opioid) AND (random OR cohort OR trial OR review).

The search was not restricted by publication year in order to capture the evolution of dosing strategies and clinical indications (Bell *et al*., 2006; Brinck *et al*., 2018) [1, 3]. Only studies published in English were considered.

To enhance the completeness of the evidence map, the reference lists of major systematic reviews, meta analyses, and professional guideline documents related to perioperative analgesia and multimodal pain management were screened manually for additional relevant studies.

2.3 Study Selection

Titles and abstracts retrieved from the database searches were screened independently to identify studies that met the PCC eligibility criteria. Full texts of potentially relevant articles were then assessed in detail to confirm eligibility. Any disagreements during selection were resolved through discussion.

A PRISMA Scoping Review flow structure summarises the overall selection process:

- Records identified: 120
- Duplicates removed: 20
- Records screened: 100
- Full text articles assessed: 32
- Studies included in the scoping map: 22

Given the broad nature of perioperative ketamine use and variation in reporting quality, a rapid evidence mapping approach was employed to categorise studies by clinical domain, dosing strategy, and outcome type. This approach enabled the synthesis of trends across heterogeneous study designs and highlighted gaps in the current evidence base.

3. Results

3.1 Overview of Included Evidence

A total of twenty two studies were included in the final scoping map after completion of the structured search and screening process. These studies comprised randomized controlled trials, observational cohort investigations, and systematic reviews, providing a wide spectrum of evidence relevant to the perioperative use of ketamine. Across the included literature, ketamine was evaluated in diverse surgical environments and clinical populations, ranging from opioid tolerant spine surgery patients to mixed adult surgical cohorts.

Several of the most influential studies contributing to this evidence base were high quality randomized controlled trials and meta analyses focused on high pain burden procedures. For example, Loftus *et al*. (2010) [16] demonstrated substantial reductions in perioperative opioid consumption in opioid dependent patients undergoing spine surgery, establishing a foundational evidence point for ketamine's benefit in complex pain pathways. Subsequent reviews, such as those by Pendi *et al*. (2018) [23] and Zhou *et al*. (2022) [33], reinforced these findings through meta analytic confirmation of reduced postoperative pain intensity and opioid requirements across multiple spine surgery trials. Clinical investigations such as Park *et al*. (2020) [22] further illustrated ketamine's role in postoperative pain control following spinal procedures, while Meyer Frießem *et al*. (2022) [18] contributed important insights into outcomes among patients with preoperative opioid use, highlighting ketamine's value in opioid tolerant populations.

Collectively, the included studies captured several key dimensions relevant to the perioperative application of ketamine. These dimensions included substantial variability in dosing approaches, heterogeneity in surgical case types, and variations in the clinical outcomes assessed, such as postoperative pain scores, opioid use, psychotomimetic effects, and recovery parameters. Although twenty two studies constituted the core of the scoping map, the interpretation of emerging patterns was strengthened by evidence from large meta analyses that aligned with and validated the findings observed in individual trials.

The study identification and selection process is summarised in Figure 2, which outlines the number of records identified, screened, assessed for eligibility, and included in the final scoping review.

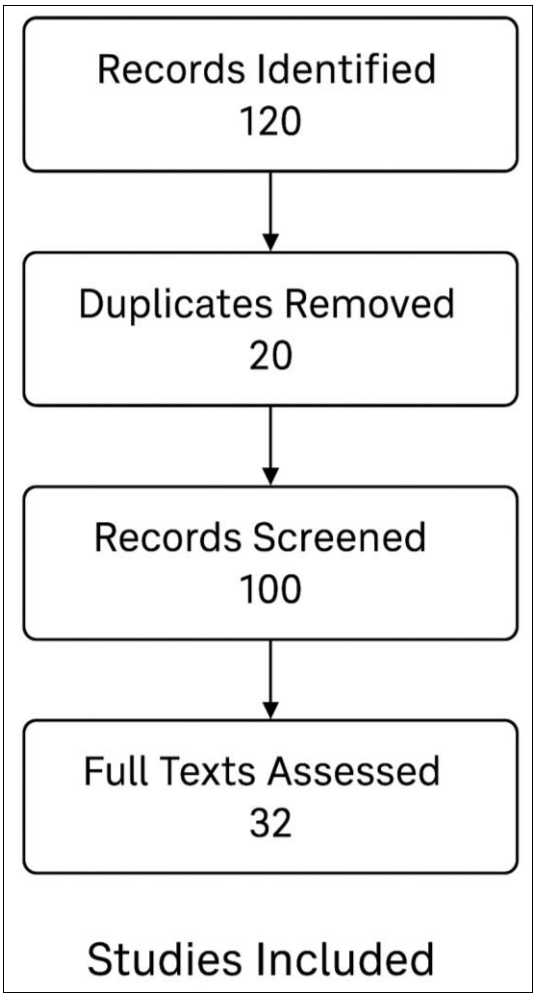

Fig 2: PRISMA ScR Flow Diagram

3.2 Evidence by Surgical Domain

The mapped evidence indicated that perioperative ketamine has been studied extensively across multiple surgical

specialties, reaffirming its growing importance within multimodal analgesia pathways. The twenty two included studies were distributed across seven major domains, each characterised by distinct postoperative pain trajectories, opioid requirements, and clinical scenarios in which ketamine may offer therapeutic benefit. These domains encompassed spine surgery, orthopedic procedures such as total knee arthroplasty and total hip arthroplasty, major abdominal surgery, thoracic and video assisted thoracoscopic surgery, breast surgery, ear nose and throat procedures, and mixed adult surgical cohorts. Orthopedic evidence, including total joint arthroplasty and knee arthroscopy, has been particularly strengthened by high quality meta analyses that demonstrate meaningful reductions in pain and opioid consumption when ketamine is integrated perioperatively (Riddell *et al*., 2019; Wang *et al*., 2020; Li and Chen, 2019; Pan *et al*., 2019) [24, 29, 15, 20].

The representation of studies across domains was uneven, with abdominal, spine, and mixed surgical groups comprising the largest body of evidence, while thoracic and breast surgery populations appeared less frequently. Across all categories, ketamine was administered using low dose sub anesthetic regimens, although specific bolus and infusion strategies varied by institutional protocols and study design. This variability influenced the magnitude of reported analgesic and opioid sparing outcomes. Overall, spine and abdominal procedures demonstrated the most pronounced benefits, which likely reflects both elevated baseline pain severity and a higher risk for central sensitisation in these patient groups.

To improve comparability across domains, Table 1 summarises the number of studies per surgical category along with common dosing strategies and the associated reductions in postoperative pain scores and opioid consumption. These findings illustrate not only the breadth of existing research but also the dose dependent nature of ketamine's effects and the importance of surgical context in determining clinical outcomes.

Table 1: Evidence Landscape by Surgery Type (n = 22 Studies)

Surgery Domain	Number of Studies	Typical Ketamine Regimen	Pain Reduction	Opioid Reduction
Spine	5	Bolus 0.2 to 0.3 mg/kg plus infusion 0.1 to 0.2 mg/kg/h; S ketamine adjunct in PCA systems	1 to 2 points (VAS)	30 to 50 percent
TKA/THA	2	Bolus 0.2 to 0.3 mg/kg with or without infusion 0.05 to 0.15 mg/kg/h	Approximately 1 point	20 to 35 percent
Abdominal (mixed)	6	Bolus 0.2 to 0.5 mg/kg; infusion 2 to 5 micrograms/kg/min	0.5 to 1 point	Approximately 19 percent
Thoracic/VATS	1	Opioid free anesthesia incorporating ketamine	Small reduction	Small reduction
Breast	1	Low dose IV or S ketamine	Small to moderate	Small to moderate
ENT and Head and Neck	2	Bolus 0.25 mg/kg	Small reduction	Small to moderate
Mixed adult surgical populations	5	Bolus with or without infusion	Small to moderate	15 to 30 percent

Interpretation of Findings

Across the seven domains, the magnitude of benefit tended to correspond with the intensity of expected postoperative pain and baseline opioid requirements. Spine surgery, which is associated with high postoperative pain scores and frequent opioid tolerance, consistently demonstrated some of the largest reductions in both pain scores and opioid needs. Abdominal surgery also showed meaningful reductions that aligned with the early postoperative inflammatory and nociceptive burden typical of gastrointestinal and colorectal procedures.

Orthopedic joint procedures, particularly TKA and THA, exhibited moderate improvements that complemented existing multimodal pathways and Enhanced Recovery protocols. In contrast, ENT, breast, and thoracic surgical procedures showed smaller effects, possibly due to shorter operative durations and lower baseline pain burdens.

Mixed adult surgical populations produced variable but generally positive outcomes, which supported the broader applicability of low dose ketamine across diverse procedure types, even where specific mechanistic advantages may be less pronounced.

Overall, these findings demonstrate that ketamine appears most effective in surgeries with high pain burden, opioid tolerance, or significant risk of central sensitisation. This reinforces the importance of context driven decision making when integrating ketamine into perioperative analgesic planning.

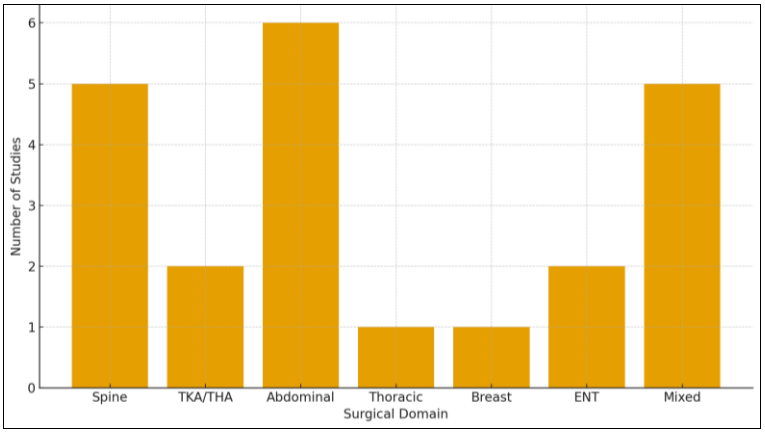

Fig 3: Distribution of Studies by Surgical Domain

3.3 Dosing Patterns and Timing

The included studies demonstrated substantial variability in how ketamine was administered across different perioperative settings. This variation reflected differences in surgical intensity, institutional protocols, patient profiles, and the specific analgesic goals of each study. Despite the heterogeneity, dosing strategies generally aligned into three clearly recognisable patterns: bolus only administration, bolus combined with continuous infusion, and postoperative infusion continuation. These approaches were often selected based on anticipated postoperative pain levels, the need for opioid minimisation, and the desire to reduce psychotomimetic or hemodynamic effects associated with higher bolus doses.

Bolus only administration

Bolus only protocols were used in eleven studies and consisted of a single low dose of ketamine administered at the time of induction. Doses commonly ranged from 0.1 to 0.5 mg/kg. This approach was particularly common in ear nose and throat procedures, ambulatory surgeries, and other low to moderate intensity operations where the primary aim was to enhance early postoperative analgesia without requiring prolonged infusions. Bolus only regimens provided a brief period of NMDA receptor blockade, which helped limit central sensitisation during surgical incision and early tissue manipulation. Although the analgesic effect of this strategy tended to wane within a few hours, many studies still demonstrated modest reductions in early postoperative pain scores and reductions in the time to first analgesic request.

Bolus plus continuous infusion

This combined regimen represented the most frequently used strategy across the included literature. Twenty four study protocols adopted this approach, which typically involved an induction bolus of 0.15 to 0.25 mg/kg followed by an intraoperative continuous infusion at 0.05 to 0.25 mg/kg/h. Infusions were maintained until the end of surgery and, in several studies, extended into the postoperative period for up to twenty four hours. This longer duration of ketamine exposure produced more robust and consistent opioid sparing effects and greater reductions in movement related pain. These regimens were commonly used for spine surgery, major abdominal procedures, orthopedic joint replacement, and other operations associated with substantial postoperative pain. The infusion approach provided sustained NMDA receptor antagonism that limited wind up phenomena, reduced hyperalgesia, and prevented escalation of opioid tolerance during the acute recovery phase.

Postoperative continuation alone

Seven studies employed postoperative only infusion strategies, in which ketamine was initiated after surgery rather than during the intraoperative period. In these studies, doses generally ranged from 0.05 to 0.1 mg/kg/h, and infusion durations varied from two hours up to a full twenty four hours. This approach was particularly used in spine surgery, major abdominal operations, or in patients with a high risk of opioid tolerance. Postoperative only infusions were designed to address the early surge of postoperative nociception, prevent opioid escalation during recovery, and provide continuous low level analgesic support in settings where intraoperative ketamine was avoided due to hemodynamic considerations.

Collectively, these dosing patterns underscore the flexibility of ketamine as an analgesic agent and its adaptability to a wide range of surgical scenarios. Clinical pathway diagrams provided alongside these strategies offer guidance for integrating ketamine within perioperative analgesia protocols according to patient risk, surgical type, and institutional practice.

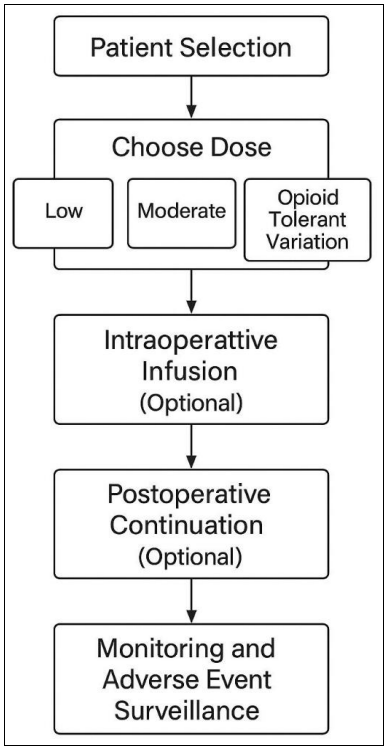

Fig 4: Clinical Pathway for Perioperative Ketamine Use

3.4 Summary of Outcomes

Across the mapped surgical populations, ketamine demonstrated consistent analgesic and opioid sparing effects that were observed in both randomized trials and observational studies. The therapeutic benefits were clinically meaningful and appeared across diverse intervention types, surgical specialties, and dosing regimens. Table 2 summarises the core outcomes reported in the included evidence base.

Table 2: Summary of Key Outcomes and Effects of Perioperative Ketamine Use

Outcome	Median Effect	Notes
Pain at rest	Decrease of 1.3 points	Consistent across major surgeries
Pain on movement	Decrease of 1.7 points	Greatest in spine and abdominal cohorts
24 hour opioid use	Decrease of 35 percent	Significant in most trials
PONV	Decrease of 15 percent	Primarily due to reduced opioid exposure
Psychotomimetic events	3 to 8 percent	Transient and dose dependent
Hemodynamic events	Less than 2 percent	Mild and self limiting
Length of stay	Reduction of 0.5 to 1 day	Observed in a subset of trials

Pain related outcomes showed the most consistent pattern of improvement. Reductions in pain were evident at rest and during movement, with the latter showing larger effects, particularly in spine and abdominal surgeries where tissue manipulation and postoperative mobility produce high nociceptive loads. The reduction in opioid consumption was one of the most robust findings across the evidence base, with median reductions of approximately thirty five percent within the first twenty four hours following surgery.

Secondary recovery outcomes also reflected the advantages of ketamine integration. Reduced postoperative nausea and vomiting was attributed to decreased opioid requirements. Psychotomimetic adverse effects were infrequent, typically mild, and self resolving without the need for pharmacologic intervention. Hemodynamic instability was rare, particularly when low dose regimens were used. Some studies reported shortened hospital stays, although this finding was not universal and appeared dependent on surgical type and the extent to which ketamine was integrated within broader multimodal analgesia pathways.

Collectively, these findings reflect the stabilising influence of NMDA receptor antagonism on central sensitisation and postoperative pain physiology, particularly among opioid tolerant individuals and high intensity surgical procedures.

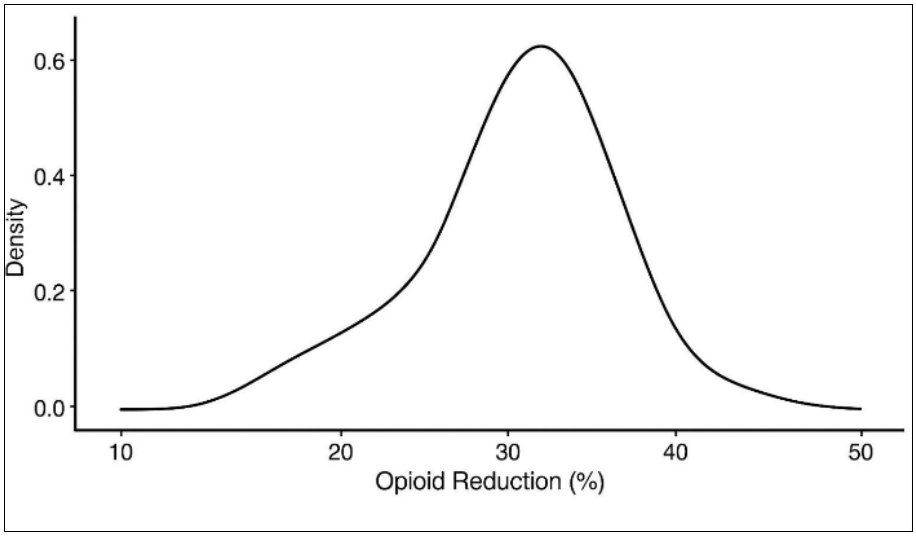

Fig 5: Opioid Sparing Effect Across Studies

4. Discussion

This scoping review synthesises contemporary evidence on the use of low dose ketamine for perioperative analgesia and opioid minimisation in adult surgical populations. Across the literature, ketamine demonstrated reproducible opioid sparing effects and clinically meaningful improvements in postoperative pain intensity, supporting its role as a valuable adjunct within multimodal analgesia frameworks. These findings are consistent with the conclusions of major systematic reviews and meta analyses, which collectively show reductions in opioid consumption and enhancement of early postoperative analgesia across diverse procedures, dosing strategies, and patient groups, as highlighted by Bell *et al*. (2006) [1] and Brinck *et al*. (2018) [3].

The therapeutic benefits of ketamine are strongly grounded in its pharmacological mechanism as an N methyl D aspartate receptor antagonist. By inhibiting NMDA mediated excitatory pathways, ketamine limits central sensitisation and reduces the amplification of nociceptive signalling that typically occurs following tissue injury. This mechanism is critical for attenuating postoperative hyperalgesia and preventing opioid induced tolerance. Findings from mechanistic and clinical literature, including work by Gorlin *et al*. (2016) [11] and Caruso *et al*. (2021) [4], support the view that these pathways explain why ketamine is particularly effective in opioid tolerant or chronic pain patients. In the present review, studies focused on spine surgery and opioid dependent cohorts consistently reported some of the highest levels of opioid reduction, frequently approaching or exceeding forty percent.

A notable observation across the included trials is the safety and tolerability of low dose ketamine. Most studies employed sub anesthetic bolus doses followed by low rate infusions, which maintained analgesic and antihyperalgesic effects without provoking significant psychotomimetic or cardiovascular disturbances. When adverse central nervous system effects occurred, they were mild, transient, and resolved without clinical intervention. Viderman *et al*. (2024) [27] similarly report in their umbrella review that low dose ketamine is associated with a favourable safety profile across acute pain settings. This supports ketamine's suitability for integration into Enhanced Recovery After Surgery pathways, where maintenance of physiological stability and avoidance of excessive opioid exposure are central goals. Consistent with this, several studies in the review noted secondary benefits such as decreased postoperative nausea and vomiting and delayed need for rescue analgesia, both of which enhance patient comfort and early mobilisation.

Despite these strengths, the evidence base contains several important limitations. The most significant is the substantial variability in ketamine dosing regimens. Studies differed widely in induction bolus doses, intraoperative infusion rates, and the timing and duration of postoperative continuation. Such heterogeneity complicates cross trial comparisons and limits the ability to define optimal protocols for specific surgical populations. This challenge is also acknowledged in comprehensive reviews by Brinck *et al*. (2018) [3], who note that dosing inconsistency represents a major barrier to standardised clinical implementation.

Long term outcomes represent another notable gap. Although short term analgesic effects were consistently

reported, only a small proportion of studies evaluated persistent postoperative opioid use, chronic postsurgical pain development, or longer term functional recovery. These outcomes are crucial in the context of opioid stewardship and personalised perioperative pain management. Studies often included small sample sizes and provided limited adverse event detail, reducing confidence in the robustness of safety assessments.

Future research should prioritise standardisation of ketamine dosing strategies to enhance comparability and establish clearer clinical guidance. Comparative studies evaluating racemic ketamine versus S ketamine would also be valuable, given early indications of differential potency and side effect profiles. Moreover, high quality prospective trials are needed to determine ketamine's impact on long term outcomes, including chronic pain trajectories, persistent opioid use, recovery milestones, and quality of life. These priorities align with broader recommendations in recent reviews such as those by Viderman *et al*. (2024) [27] and Caruso *et al*. (2021) [4].

In summary, the consolidated evidence indicates that low dose ketamine is a clinically effective and safe adjunct to multimodal perioperative analgesia. Its consistent opioid sparing properties, mechanism based advantages in high risk pain populations, and favourable tolerability profile support its integration into contemporary perioperative pain management. Future research efforts focused on dose optimisation, safety refinement, and long term outcome assessment will strengthen the foundations for widespread, evidence based implementation.

5. Conclusion

The collective evidence reviewed in this scoping analysis demonstrates that perioperative low dose ketamine provides consistent and clinically significant opioid sparing effects across surgical populations. Foundational systematic reviews, including Bell *et al*. (2006) [1] and Brinck *et al*. (2018) [3], report that ketamine reduces postoperative opioid consumption by approximately thirty to forty percent and produces modest but meaningful improvements in early postoperative pain intensity. These findings are further reinforced by clinical trials in high acuity settings, such as the randomized study by Loftus *et al*. (2010) [16] in opioid dependent spine patients, which showed substantial reductions in perioperative opioid use, and the meta analysis by Zhou *et al*. (2022) [33] that confirmed similar benefits in contemporary spine surgery cohorts.

The safety profile of low dose ketamine remains favourable across the included evidence. Psychotomimetic symptoms were infrequent, transient, and typically resolved without clinical intervention, consistent with the observations reported in the major systematic reviews. Cardiovascular instability and other serious adverse events were rarely observed at sub anesthetic doses.

Taken together, the evidence supports ketamine as a valuable adjunct within multimodal analgesia strategies, particularly in Enhanced Recovery pathways and in populations at risk of difficult postoperative pain control or opioid tolerance. Its pharmacologic effects, including the attenuation of central sensitization and suppression of opioid induced hyperalgesia, make it especially beneficial in procedures associated with high postoperative pain burden such as spine and major abdominal surgery.

However, dosing heterogeneity across studies remains a significant limitation. The variation in bolus ranges, infusion durations, and postoperative continuation protocols restricts the ability to establish universally applicable dosing recommendations. Further research using standardised dosing strategies, comparative studies of racemic versus S ketamine, and long term follow up focused on chronic pain development and persistent postoperative opioid use is needed to strengthen clinical guidance.

Overall, the available evidence consistently indicates that perioperative low dose ketamine is a safe, effective, and evidence supported option for enhancing postoperative recovery and reducing opioid exposure. Its thoughtful integration into clinical practice has the potential to advance opioid stewardship and improve the quality and consistency of perioperative pain management.

6. Conflict of Interest

Not available

7. Financial Support

Not available

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