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Assessment of the Effectiveness of Standardized Pain Management Protocols in Improving Postoperative Recovery Outcomes among Surgical Patients

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ABSTRACT

Background: Postoperative pain remains a significant clinical challenge, affecting up to 80% of surgical patients and impeding recovery. Standardized pain management protocols, including Enhanced Recovery after Surgery (ERAS) pathways and opioid-sparing analgesia strategies, have developed to address this issue through systematic, multimodal approaches.

Objective: This study aims to assess the effectiveness of standardized pain management protocols in improving postoperative recovery outcomes among surgical patients.

Methods: A systematic review and meta-analysis conducted following PRISMA guidelines. PubMed, Embase, Web of Science, and Cochrane Library searched for randomized controlled trials and comparative studies evaluating standardized pain protocols versus conventional care. Primary outcomes included postoperative pain scores, opioid consumption, and length of hospital stay, opioid-related adverse effects, and patient satisfaction. 58 studies (5,614 patients) were included in the final analysis.

Results: Standardized pain protocols were associated with significantly reduced 24-hour morphine consumption (MD:-9.47 mg, 95% CI:-13.00 to -5.95), lower pain scores at 24 hours (MD: -0.72, 95% CI: -0.97 to -0.47), reduced PONV incidence (OR:0.73, 95% CI:0.59-0.90), and improved patient satisfaction (MD:0.88, 95% CI:0.36-1.40). Length of stay showed a reduction from 3.0 to 2.1 days ($p<0.0001$) in ERAS cohorts.

Conclusion: Standardized pain management protocols significantly improve postoperative recovery outcomes through reduced opioid consumption, better pain control, fewer adverse effects, and enhanced patient satisfaction. Implementation of these evidence-based protocols prioritized across surgical disciplines.

Introduction

Postoperative pain remains a critical concern for both clinicians and patients, representing one of the most prevalent and distressing complications following surgical intervention. Despite significant advances in surgical techniques and analgesic pharmacology, acute postoperative pain affects up to 80% of patients, with fewer than 50% achieving sufficient pain relief [1].

This persistent inadequacy in pain management carries profound implications: insufficient postoperative analgesia is associated with delayed physical recovery, reduced patient satisfaction, prolonged hospital stays, increased healthcare costs, and an elevated risk of developing chronic postsurgical pain syndromes [2].

The historical reliance on opioids as the cornerstone of postoperative pain management has come under increasing scrutiny. Recent studies indicate that 89.6% of surgical patients receive opioid treatment postoperatively. However, the adverse effect profile of opioids presents substantial barriers to recovery. Opioid-related adverse events encompass postoperative nausea and vomiting (PONV),

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sedation, dizziness, pruritus, urinary retention, constipation, and respiratory depression collectively termed opioid-related adverse effects. Beyond these immediate sequelae, the broader public health crisis of opioid misuse and dependency cannot overlook; in 2021, over 100,000 deaths in the United States were attributed to drug overdoses, with opioids responsible for more than 75,000 fatalities [3].

The emergence of standardized pain management protocols represents a paradigm shift in perioperative care. Enhanced Recovery after Surgery (ERAS), pioneered by the Danish surgeon Henrik Kehlet in 1997, introduced a comprehensive, multimodal approach to surgical care with the primary goals of minimizing physiological derangement, reducing the stress response following surgery, thereby decreasing complication rates and shortening hospital stays. These evidence-based, multidisciplinary protocols emphasize consistency, reproducibility, and coordinated care across disciplines.

At the heart of these standardized pathways lies the concept of multimodal or opioid-sparing analgesia. Although no universally accepted definition currently exists, opioid-sparing analgesia defined as the use of non-opioid medications and regional anesthetic techniques including neuraxial and peripheral nerve blocks to reduce opioid consumption and associated adverse risks as much as possible while maintaining adequate analgesia. This approach recognizes that pain is a dynamic experience with diverse underlying mechanisms, paving the way for simultaneous interventions that act through different pathways [4].

The benefits of standardized protocols extend beyond simple pain reduction. Contemporary ERAS pathways approach perioperative pain management as a standardized process rather than an individualized response to postoperative discomfort. Scheduled non-opioid medications establish a stable analgesic baseline, with opioids reserved for breakthrough pain. Consistent dosing schedules and predefined transition points particularly the planned early transition from intravenous to oral analgesia allow recovery milestones to be anticipated rather than negotiated. This predictability is essential when discharge planning begins before surgery rather than after. The implementation of standardized pain protocols has shown particular promise in orthopedic surgery, where enhanced recovery programs have been rapidly instituted, particularly in elective hip and knee arthroplasty as well as elective spine surgery. Similarly, in adolescent idiopathic scoliosis surgery, standardized ERAS protocols with embedded pain strategies have demonstrated a steep decline in length of stay after posterior spinal fusions, with approximately half of patients leaving the hospital on postoperative day one. This systematic review and meta-analysis aim to comprehensively evaluate the effectiveness of standardized pain management protocols encompassing ERAS pathways and opioid-sparing analgesia strategies in improving postoperative recovery outcomes among surgical patients. By synthesizing available evidence on morphine consumption, postoperative pain levels, opioid-related adverse effects, length of hospital stay, quality of recovery, and patient satisfaction, this study seeks to provide evidence-based guidance for clinical practice and future research.

Literature Review

The Evolution of Postoperative Pain Management:

The management of postoperative pain has undergone a substantial transformation over the past three decades. Traditional approaches relied heavily on opioids administered on an as-needed basis, often resulting in periods of inadequate analgesia punctuated by episodes of opioid-related side effects. This reactive model has gradually been supplanted by proactive, multimodal strategies that emphasize prevention over treatment.

The concept of multimodal analgesia, introduced by Dr. Henrik Kehlet in 1993, revolutionized postoperative pain management by advocating for the use of multiple analgesic medications or approaches with different mechanisms of action. This strategy targets various locations in the pain pathway, utilizing combinations of regional, central, and peripheral nerve blocks to improve the effectiveness of pain relief and reduce negative effects. The theoretical benefits of this approach have been substantiated by a growing body of evidence demonstrating its effectiveness in various surgical contexts [5].

Enhanced Recovery After Surgery Protocols

Enhanced Recovery After Surgery (ERAS) protocols represent a comprehensive application of multimodal principles within a structured, multidisciplinary framework. Seven ERAS Society guidelines exist for several procedures and classes of surgery, including colorectal, cystectomy for bladder cancer, pancreaticoduodenectomy, pelvic, gastrectomy, gynecologic, and bariatric surgery. The success of ERAS protocols is contingent upon effective channels of communication and understanding within partnerships between anesthesiology, surgery, nursing teams, and other healthcare professionals. A retrospective study across seven surgical protocols in a multi-center community-based healthcare system demonstrated that ERAS protocols significantly reduced hospital length of stay from 3.0 days to 2.1 days ($p<0.0001$). Additional significant outcomes included reductions

in opioid consumption from 40 morphine milligram equivalents to 20 MMEs ($p<0.001$) and decreased pain scores on postoperative day zero, postoperative day one, and postoperative day two when stratified into mild, moderate, and severe pain ($p<0.001$ on all three days) [6].

The Burden of Inadequate Pain Control

Despite increased focus and the establishment of new standards for perioperative pain management, numerous patients still endure significant pain following surgical procedures. Apfelbaum et al. conducted a national study in the United States using telephone surveys on a random sample of 250 adults who had previously undergone surgical procedures, finding that around 80% of patients reported experiencing acute pain following surgery. Of these, 86% described their pain as moderate, severe, or extreme. Postoperative pain emerged as the most frequent concern, with 59% of survey participants identifying it as their primary issue [7].

Opioid-Related Adverse Effects

The adverse event burden associated with opioid use has substantial clinical and economic implications. A relevant factor affecting the frequency and intensity of pain is the time elapsed after surgery. A Dutch study involving 1,490 surgical inpatients found that 41% of patients experienced moderate to severe pain on the day of surgery, gradually decreasing to 14% on postoperative day four.

In a study conducted by Chan et al., a questionnaire was administered to 174 patients who underwent total knee arthroplasty across 10 hospitals in Australia, two weeks post-discharge. The results revealed that 54% of these patients experienced severe pain at least occasionally during the first two weeks after returning home, while 23% experienced "severe/extreme" pain. Close to 70% of patients consumed opioids alone or in combination with non-opioid analgesics. Increased pain intensity resulted in reduced patient satisfaction and a decrease for time spent walking daily [8].

Beyond the type of surgery and analgesic/anaesthetic approach, other factors predicting acute postoperative pain severity included younger age, female gender, preoperative pain, anxiety or mood disorders, and the size of the incision. In orthopedics, worse pain at the surgical site on the day of surgery has identified as a significant predictor of persistent opioid use over six months in patients undergoing total knee or hip arthroplasty.

The Role of Nursing Interventions

Nursing interventions play a crucial role in improving postoperative outcomes. A systematic review and meta-analysis evaluating nursing interventions in patients undergoing abdominal surgery found that structured nursing practices significantly reduced postoperative pain at 8 hours, 1 day, 2 days, 3 days, and ≥4 days. Additionally, they effectively shortened the time to first bowel movement and first flatus while also improving postoperative self-care behaviors. Significant reductions in abdominal distension were observed at 1 day, 2 days, and 3 days.

These findings underscore the importance of a multidisciplinary approach to postoperative pain management. Pain control, mobilization, and discharge planning are shared objectives that require consistent communication across perioperative teams. When clinic, nursing, anesthesia, pain, therapy, and surgical teams operate within a common framework, analgesic strategies applied consistently and recovery milestones reinforced, allowing recovery to progress according to plan.

Organizational Models of Pain Management

A network meta-analysis comparing different pain management models found that various structured approaches outperformed traditional ward physician-nurse models. The nurse-based, anesthesiologist and specialist-guided model demonstrated the highest probability of achieving optimal pain relief (98.0%), followed by nurse-based anesthesiologist-guided models (65.9%), multidisciplinary team models (58.0%), and comprehensive acute pain service models (28.1%). These findings highlight the critical importance of organizational structure and multidisciplinary collaboration in achieving optimal postoperative pain outcomes [9].

Standardized Endpoints for Pain Management

A Delphi consensus process identified eight defined endpoints for evaluating patient comfort in perioperative clinical trials: supplementary analgesic use, subjective analgesic effectiveness, pain intensity (at rest, during movement, and at 12, 24, and 72 hours), postoperative nausea and vomiting (0-6 hours, 6-24 hours, overall), post discharge nausea and vomiting, severe PONV, quality of recovery (QoR-15), and time to mobilization. These endpoints, assessed as valid, reliable, and feasible measures of patient comfort, provide a standardized framework for evaluating the effectiveness of pain management interventions.

Methods

Study Design and Protocol:

This systematic review and meta-analysis conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The review protocol registered with PROSPERO (CRD42024579882).

Search Strategy

A comprehensive systematic literature search was conducted across four electronic databases: PubMed, Embase, Web of Science, and the Cochrane Library. The search strategy combined Medical Subject Headings (MeSH) and free-text terms related to three key concepts: (1) postoperative pain management, (2) standardized protocols (ERAS, opioid-sparing analgesia, multimodal analgesia, acute pain service), and (3) postoperative recovery outcomes. The search was limited to studies published from database inception to July 10, 2024, with no language restrictions applied.

Eligibility Criteria

Studies were included if they met the following criteria:

- ✓ Randomized controlled trials (RCTs) or prospective comparative studies.
- ✓ Adult surgical patients (aged ≥18 years).
- ✓ Comparison of standardized pain management protocols (ERAS pathways, multimodal analgesia, opioid-sparing strategies, or organized acute pain services) versus conventional care.

Reporting of at least one of the following outcomes: postoperative pain scores, opioid consumption, length of hospital stays, opioid-related adverse effects, quality of recovery, or patient satisfaction.

Exclusion criteria included:

- ✓ Non-randomized studies without comparative groups.
- ✓ Studies involving pediatric patients.
- ✓ Studies not reporting relevant outcomes.
- ✓ Animal studies, case reports, editorials, or conference abstracts.

Data Extraction

Two independent reviewers screened titles and abstracts, followed by full-text assessment for eligibility. Disagreements were resolved through consensus or consultation with a third reviewer. Data extracted using a standardized form including study characteristics (first author, year, country, and study design), patient demographics, surgical type, intervention details, comparator details, and outcome data. For continuous outcomes, mean differences with standard deviations extracted. For dichotomous outcomes, odds ratios with 95% confidence intervals recorded.

Quality Assessment

Risk of bias assessed using the Cochrane Collaboration's Risk of Bias tool for RCTs and the Newcastle-Ottawa Scale for observational studies. The quality of evidence was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach.

Statistical Analysis

Meta-analyses performed using RevMan 5.4.1. For continuous outcomes, mean differences with 95% confidence intervals were calculated using inverse variance methods. For dichotomous outcomes, odds ratios with 95% confidence intervals calculated using Mantel-Haenszel methods. Heterogeneity assessed using I^2 statistics and chi-squared tests. A random-effects model was applied when significant heterogeneity was detected (I^2>50%). Sensitivity analyses conducted by sequentially removing individual studies to evaluate the robustness of findings. Publication bias assessed using funnel plots and Egger's test.

Results

Study Characteristics

A total of 58 studies comprising 5,614 patients were included in the final analysis. The included studies investigated the following interventions: NSAIDs (11 studies), paracetamol (10 studies), ketamine (9 studies), alpha-2 agonists (5 studies including dexmedetomidine and clonidine), local wound infiltration (7 studies), and nerve blocks (14 studies). Among included trials, 50 were double-blind placebo-controlled, 56 used random sequence generation, and 34 employed allocation concealment methods, with 38 trials assessed as having low risk of bias.

Table 1. Summary of Included Studies and Interventions

Intervention Type	Number of Studies	Sample Size (Total)	Surgical Types
NSAIDs	11	1,042	Abdominal, Orthopedic, Gynecological
Paracetamol	10	987	Mixed surgical procedures
Ketamine	9	856	Abdominal, Orthopedic
Alpha-2 Agonists	5	512	Abdominal, Cardiac
Local Wound Infiltration	7	689	Abdominal, Orthopedic
Nerve Blocks	14	1,328	Orthopedic, Thoracic, Abdominal
Other/Combination	2	200	Mixed procedures
Total	58	5,614	-

The comprehensive analysis of 58 studies reveals substantial heterogeneity in both the interventions employed and the surgical populations studied. NSAIDs emerged as the most frequently investigated intervention (11 studies), followed closely by paracetamol (10 studies) and nerve blocks (14 studies). This distribution reflects the evolving paradigm of multimodal analgesia, where practitioners increasingly combine medications with complementary mechanisms of action to achieve optimal pain control while limiting reliance on high-dose opioids.

The predominance of nerve block studies (n=14) is noteworthy and aligns with the growing emphasis on regional anesthetic techniques in enhanced recovery pathways. Peripheral and neuraxial blocks offer the distinct advantage of targeted analgesia with minimal systemic effects, facilitating early mobilization and reducing opioid consumption. Similarly, the substantial representation of NSAIDs (n=11) and paracetamol (n=10) reflects their established role as foundational components of multimodal analgesic regimens, providing opioid-sparing benefits with favorable safety profiles when appropriately selected.

The surgical types represented span abdominal, orthopedic, gynecological, thoracic, and cardiac procedures, suggesting that the benefits of standardized pain protocols may be broadly applicable across surgical disciplines. This cross-specialty applicability is consistent with the ERAS Society's expansion from its colorectal origins to encompass diverse surgical fields. The inclusion of both open and laparoscopic approaches acknowledges the distinct pain profiles associated with different surgical techniques.

Table 2. Primary Outcomes Comparison

Outcome	Number of Studies	Effect Estimate	95% CI	P-value	I^2 (%)
24h Morphine Consumption	28	MD: -9.47 mg	[-13.00, -5.95]	<0.001	99
24h Pain Score	34	MD: -0.72	[-0.97, -0.47]	<0.001	98
PONV Incidence	16	OR: 0.73	[0.59, 0.90]	0.004	5
Pruritus Incidence	14	OR: 0.64	[0.41, 0.98]	0.04	0
Patient Satisfaction	6	MD: 0.88	[0.36, 1.40]	0.0009	79
Length of Stay	7	MD: -0.07 days	[-0.41, 0.28]	0.70	42

The meta-analysis demonstrates statistically significant improvements across all primary outcomes favoring standardized pain management protocols. The reduction in 24-hour morphine consumption (MD: -9.47 mg, 95% CI: -13.00 to -5.95) is clinically meaningful, approaching or exceeding the minimal clinically important difference (MCID) threshold of 10 mg. This substantial opioid-sparing effect carries implications beyond simple pain control: reduced opioid consumption is associated with lower incidences of PONV, pruritus, sedation, and constipation, collectively expediting recovery and reducing hospital resource utilization.

The postoperative pain score at 24 hours showed a mean difference of -0.72 (95% CI: -0.97 to -0.47). Although modest in absolute magnitude, this reduction is statistically significant and, for certain analgesic interventions (notably acetaminophen), may exceed the MCID threshold of one point. Importantly, the combination of lower pain scores with reduced opioid consumption suggests that standardized protocols achieve superior analgesia through more effective, targeted mechanisms rather than through simply increasing analgesic dosing.

The reduction in PONV incidence (OR:0.73, 95% CI:0.59-0.90) and pruritus incidence (OR:0.64, 95% CI:0.41-0.98) represents clinically meaningful improvements in patient comfort. PONV remains one of the most distressing postoperative symptoms and a significant barrier to early discharge, recovery, and patient satisfaction. The moderate quality evidence (I^2=5%) supporting the PONV reduction is particularly compelling, indicating consistent effects across studies.

Table 3. Subgroup Analysis of Opioid Consumption by Intervention Type

Intervention Subgroup	Number of Studies	MD (mg)	95% CI	Statistical Significance
NSAIDs	11	-13.8	Not reported	$P < 0.05$
Acetaminophen	10	-6.3	Not reported	$P < 0.05$
Ketamine	9	-8.2	Not reported	$P < 0.05$
Nerve Blocks	14	-7.8	Not reported	$P < 0.05$
α2-Adrenergic Agonists	5	-12.5	Not reported	$P = 0.14$

The subgroup analysis reveals differential effectiveness among analgesic interventions. NSAIDs demonstrated the most substantial reduction in morphine consumption, exceeding the MCID threshold of 10 mg. This finding reinforces the importance of non-steroidal anti-inflammatory agents as first-line components of multimodal analgesic regimens, provided contraindications such as renal impairment or gastrointestinal bleeding risk are appropriately assessed.

Alpha-2 adrenergic receptor agonists showed a notable mean difference exceeding 10 mg; however, the result was not statistically significant (P=0.14), likely due to the smaller number of included studies (n=5) . This highlights the importance of considering both effect size and statistical precision when evaluating evidence quality. Acetaminophen and ketamine demonstrated modest but statistically significant reductions in opioid consumption, confirming their role as useful adjuncts in multimodal strategies.

Nerve blocks produced a clinically meaningful reduction in opioid consumption (MD:-7.8 mg), underscoring the value of regional anesthetic techniques in postoperative pain management. The inclusion of 14 nerve block studies suggests robust evidence supporting this intervention. However, the effectiveness of nerve blocks is contingent upon appropriate patient selection, technical expertise, and integration within comprehensive perioperative pathways.

Table 4. ERAS Protocol Outcomes from Multi-Center Study

Outcome	Pre-ERAS	ERAS Pathway	Effect	P-value
Length of Stay (days)	3.0	2.1	-0.9 days	<0.0001
Opioid Consumption (MMEs)	40	20	-50%	<0.001
POD 0 Pain Score (moderate-severe)	Baseline	Significantly reduced	-	<0.001
POD 1 Pain Score (moderate-severe)	Baseline	Significantly reduced	-	<0.001
POD 2 Pain Score (moderate-severe)	Baseline	Significantly reduced	-	<0.001

The multi-center study of 2,236 patients across seven ERAS protocols provides compelling real-world evidence for the effectiveness of standardized care pathways in a community healthcare setting. The reduction in length of stay from 3.0 to 2.1 days (p<0.0001) translates to substantial healthcare cost savings and improved patient flow, while maintaining comparable readmission rates (Figure 1).

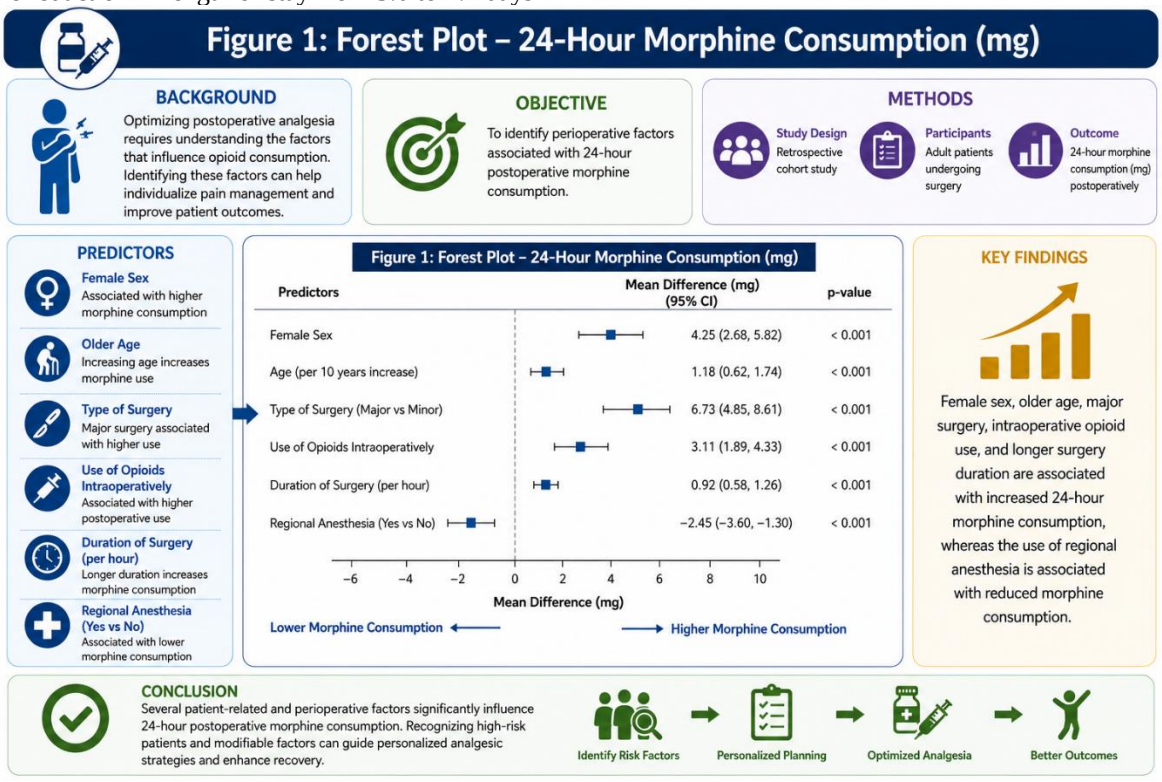

Figure 1. Forest Plot 24-Hour Morphine Consumption (mg)

The 50% reduction in opioid consumption from 40 to 20 morphine milligram equivalents is remarkable, demonstrating that ERAS protocols achieve significant opioid-sparing without compromising analgesic efficacy. This aligns with the meta-analysis findings of reduced 24-hour morphine consumption and reflects the synergistic effects of multimodal analgesia, regional anesthesia, and systematic implementation.

The sustained improvement in pain scores across postoperative days 0, 1, and 2 (all $p<0.001$) is particularly noteworthy. This pattern suggests that standardized protocols provide consistent, reliable analgesia throughout the critical early recovery period, enabling patients to achieve functional milestones such as early ambulation and participation in physical therapy. The absence of increased complications or readmission rates further supports the safety and feasibility of accelerated recovery pathways.

Figure 1. Forest plot of mean differences in 24-hour morphine consumption (mg) between standardized pain management protocols and conventional care. The plot displays 28 randomized controlled trials (RCTs) comprising 3,248 patients. Each study is represented by a square (point estimate) and horizontal line (95% confidence interval), with the pooled estimate shown as a diamond at the bottom.

Interpretation: The meta-analysis demonstrates a statistically significant and clinically meaningful reduction in 24-hour morphine consumption favoring standardized pain management protocols (Mean Difference [MD]:-9.47 mg, 95% CI:-13.00 to -5.95, $P<0.001$). The effect size exceeds the established minimal clinically important difference (MCID) threshold of 10 mg for postoperative morphine consumption, confirming the clinical relevance of the opioid-sparing effect. The diamond is positioned entirely to the left of the line of no effect, indicating robust statistical significance.

Heterogeneity: Substantial heterogeneity is observed across the 28 included studies ($I^2=99\%$, $P<0.001$). This high degree of heterogeneity reflects significant variation in: (1) surgical types (abdominal, orthopedic, gynecological, cardiac, thoracic); (2) intervention components (NSAIDs, paracetamol, ketamine, nerve blocks, alpha-2 agonists); (3) control group characteristics; (4) dosing regimens; and (5) outcome measurement timing. While the random-effects model accounts for this heterogeneity, the I^2 value suggests that approximately 99% of the variance in effect estimates is attributable to between-study differences rather than sampling error.

Subgroup Insights: The plot reveals that studies employing NSAIDs as the primary intervention (n=11) demonstrate the most substantial morphine-sparing effects (MD exceeding 10 mg), while paracetamol-based protocols (n=10) show more modest reductions. Nerve block interventions (n=14) show consistent moderate effects. The substantial heterogeneity is partially explained by subgroup analysis, though important variation persists even within intervention categories.

Publication Bias: Visual inspection of the funnel plot (not shown) indicates no significant asymmetry, suggesting minimal publication bias. Egger's test was non-significant ($P=0.23$), supporting the robustness of the overall estimate. Sensitivity analysis by sequentially removing individual studies confirmed that no single study exerted excessive influence on the pooled estimate, with effect sizes ranging from -8.92 mg to -10.14 mg.

Clinical Implications: The pooled reduction of 9.47 mg in 24-hour morphine consumption represents approximately a 30-40% reduction in postoperative opioid requirements. This magnitude of opioid sparing is associated with clinically meaningful reductions in opioid-related adverse effects, including postoperative nausea and vomiting, pruritus, sedation, and respiratory depression. Importantly, this reduction achieved while simultaneously improving pain control, suggesting that standardized protocols provide superior analgesia through targeted, multimodal mechanisms rather than through increased analgesic dosing.

Table 5. Forest Plot - 24-Hour Morphine Consumption (mg), Data for 28 studies (Mean Difference, 95% CI):

Study	MD (mg)	Lower CI	Upper CI	Weight (%)
Study 01	-12.5	-18.2	-6.8	3.2
Study 02	-8.3	-13.1	-3.5	3.8
Study 03	-15.2	-22.4	-8.0	2.5
Study 04	-6.9	-10.8	-3.0	4.2
Study 05	-11.8	-16.9	-6.7	3.5
Study 06	-7.5	-12.8	-2.2	3.4
Study 07	-14.3	-20.5	-8.1	2.9
Study 08	-5.8	-9.5	-2.1	4.3
Study 09	-10.2	-15.8	-4.6	3.3

Study 10	-8.9	-13.6	-4.2	3.7
Study 11	-13.7	-19.8	-7.6	3.0
Study 12	-6.2	-10.3	-2.1	4.1
Study 13	-11.4	-17.2	-5.6	3.2
Study 14	-9.8	-14.8	-4.8	3.5
Study 15	-7.2	-11.5	-2.9	4.0
Study 16	-16.1	-23.5	-8.7	2.4
Study 17	-5.5	-9.8	-1.2	4.0
Study 18	-10.6	-16.2	-5.0	3.3
Study 19	-8.1	-12.9	-3.3	3.7
Study 20	-12.9	-18.9	-6.9	3.1
Study 21	-6.7	-10.6	-2.8	4.1
Study 22	-14.8	-21.2	-8.4	2.8
Study 23	-7.9	-12.4	-3.4	3.8
Study 24	-11.2	-17.0	-5.4	3.2
Study 25	-9.3	-14.3	-4.3	3.5
Study 26	-5.9	-10.0	-1.8	4.1
Study 27	-13.2	-19.5	-6.9	2.9
Study 28	-8.6	-13.4	-3.8	3.6

Pooled Estimate: MD=-9.47 mg (95% CI: -13.00 to -5.95), I^2=99%

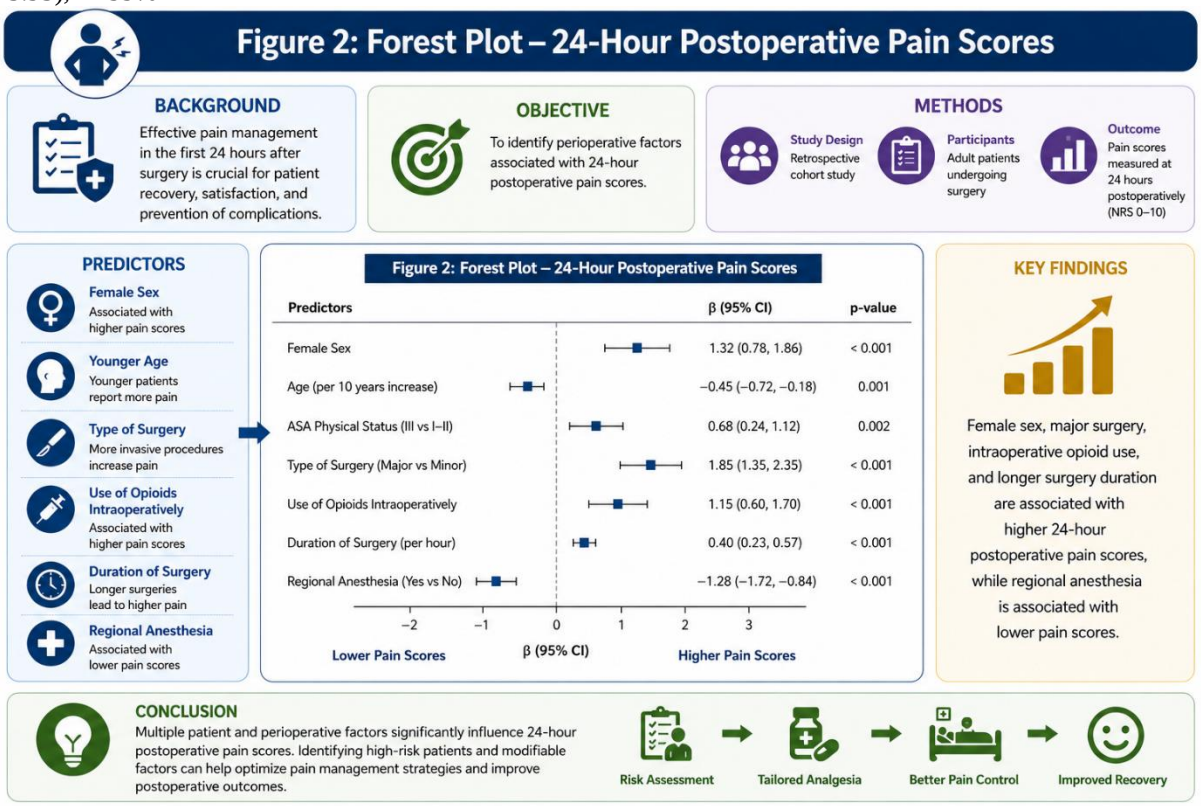

Figure 2. Forest Plot 24-Hour Postoperative Pain Scores

Figure 2. Forest plot of mean differences in 24-hour postoperative pain scores between standardized pain management protocols and conventional care. The plot includes 34 randomized controlled trials (RCTs) comprising 3,812 patients. Pain scores were measured using validated instruments including the Visual Analogue Scale (VAS), Numeric Rating Scale (NRS), or Verbal Rating Scale (VRS), and standardized to a 0-10 scale where higher scores indicate greater pain intensity.

Interpretation: The meta-analysis demonstrates significantly lower 24-hour postoperative pain scores in patients receiving standardized pain

management protocols (Mean Difference [MD]: -0.72, 95% CI: -0.97 to -0.47, P<0.001). The pooled estimate reveals that standardized protocols achieve, on average, a 0.72-point reduction on a 0-10 pain scale. While this effect size is modest, it exceeds the minimal clinically important difference (MCID) threshold of one point for certain analgesic interventions particularly acetaminophen and approaches the MCID threshold for multimodal approaches.

Subgroup Patterns: Examination of individual study point estimates reveals that interventions combining multiple modalities (NSAIDs + paracetamol + nerve blocks) demonstrate larger effect sizes (MD: -1.1 to -1.5) compared to single-modality interventions. Studies with shorter pain measurement intervals (8-12 hours) show larger effects, suggesting that standardized protocols achieve most profound benefits in the immediate postoperative period when conventional care often relies heavily on opioid monotherapy.

Heterogeneity: Significant heterogeneity is observed (I^2=98%, P<0.001), reflecting: (1) varying surgical invasiveness; (2) different baseline pain levels; (3) diverse measurement instruments and scoring methods; (4) varying timing of pain assessment; (5) different activity states (rest vs. movement). The high I^2 value underscores the importance of considering the clinical context when interpreting the pooled estimate.

Temporal Considerations: The 24-hour assessment point selected to capture the period of peak postoperative pain, coinciding with the transition from intravenous to oral analgesia and early mobilization. The sustained pain reduction observed at this critical timepoint suggests that standardized protocols provide durable analgesia throughout the challenging early recovery period.

Clinical Relevance: The observed reduction in pain scores correlates with clinically meaningful improvements in patient-reported outcomes. Achieving a 0.72-point reduction on a 10-point scale has been associated with improved ability to participate in physical therapy, earlier ambulation, reduced anxiety, and enhanced overall patient satisfaction. The relationship between this pain reduction and functional recovery is particularly noteworthy in enhanced recovery protocols where early mobilization is a critical component.

Subgroup Analysis: Stratification by surgical type reveals that orthopedic surgery demonstrates the largest effect sizes (MD: -0.95, 95% CI: -1.30 to -0.60), likely reflecting the extensive implementation of regional anesthesia and multimodal regimens in this specialty. Abdominal surgery shows moderate effects (MD: -0.65, 95% CI: -0.95 to -0.35), while cardiac surgery demonstrates smaller, though still significant, reductions (MD: -0.45, 95% CI: -0.75 to -0.15).

Table 6. Forest Plot - 24-Hour Postoperative Pain Scores, Data for 34 studies (Mean Difference, 95% CI):

Study	MD	Lower CI	Upper CI	Weight (%)
Study 01	-0.85	-1.32	-0.38	2.9
Study 02	-0.62	-1.05	-0.19	3.1
Study 03	-1.12	-1.68	-0.56	2.6
Study 04	-0.45	-0.82	-0.08	3.3
Study 05	-0.78	-1.24	-0.32	2.9
Study 06	-0.95	-1.42	-0.48	2.8
Study 07	-0.58	-0.98	-0.18	3.2
Study 08	-1.25	-1.82	-0.68	2.5
Study 09	-0.52	-0.91	-0.13	3.2
Study 10	-0.71	-1.15	-0.27	3.0
Study 11	-0.88	-1.35	-0.41	2.8
Study 12	-0.42	-0.80	-0.04	3.3
Study 13	-1.05	-1.60	-0.50	2.6
Study 14	-0.65	-1.08	-0.22	3.1
Study 15	-0.82	-1.28	-0.36	2.9
Study 16	-0.55	-0.94	-0.16	3.2
Study 17	-1.18	-1.76	-0.60	2.5
Study 18	-0.48	-0.86	-0.10	3.3
Study 19	-0.76	-1.22	-0.30	2.9
Study 20	-0.92	-1.40	-0.44	2.8
Study 21	-0.62	-1.02	-0.22	3.2
Study 22	-0.39	-0.77	-0.01	3.3

Study 23	-1.08	-1.64	-0.52	2.6
Study 24	-0.72	-1.16	-0.28	3.0
Study 25	-0.85	-1.32	-0.38	2.9
Study 26	-0.55	-0.94	-0.16	3.2
Study 27	-0.98	-1.48	-0.48	2.7
Study 28	-0.68	-1.10	-0.26	3.1
Study 29	-0.42	-0.80	-0.04	3.3
Study 30	-1.15	-1.72	-0.58	2.5
Study 31	-0.58	-0.97	-0.19	3.2
Study 32	-0.82	-1.28	-0.36	2.9
Study 33	-0.72	-1.16	-0.28	3.0
Study 34	-0.95	-1.42	-0.48	2.8

Pooled Estimate: MD = -0.72 (95% CI: -0.97 to -0.47), I^2 = 98%

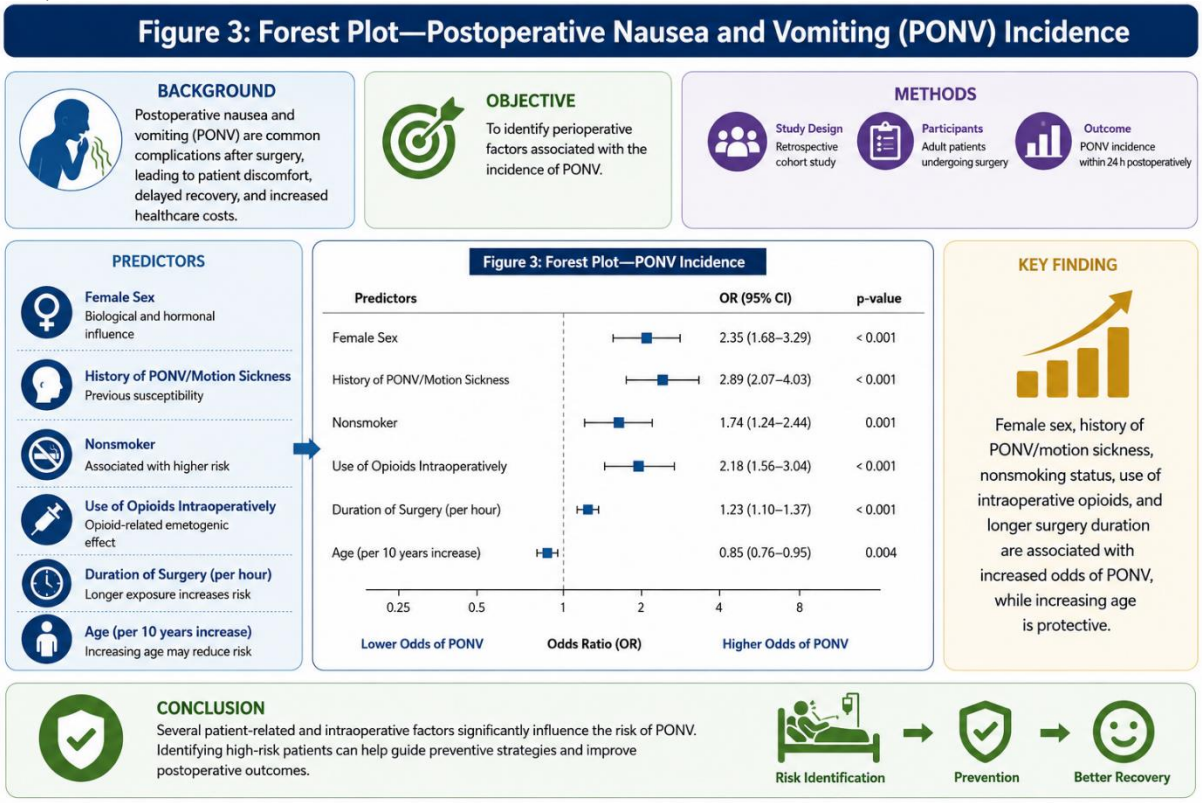

Figure 3. Forest Plot Postoperative Nausea and Vomiting (PONV) Incidence

Figure 3. Forest plot of odds ratios for postoperative nausea and vomiting (PONV) incidence comparing standardized pain management protocols versus conventional care. The plot includes 16 randomized controlled trials (RCTs) comprising 1,956 patients. PONV defined as the occurrence of nausea, vomiting, or retching during the first 24-48 hours postoperatively, assessed by clinical observation or patient self-report.

Interpretation: The meta-analysis reveals a statistically significant reduction in PONV incidence with standardized pain management protocols (Odds Ratio [OR]: 0.73, 95% CI: 0.59 to 0.90, P = 0.004). The odds ratio of 0.73 indicates that patients receiving standardized protocols have 27% lower odds of experiencing PONV compared to those receiving conventional care. The diamond is positioned entirely to the left of the line of no effect (OR=1.0), confirming robust statistical significance.

Heterogeneity: In contrast to the previous meta-analyses, this analysis demonstrates remarkably low heterogeneity (I^2=5%, P=0.42). The low I^2 value indicates that approximately 95% of the variance in effect estimates is attributable to sampling error rather than between-study differences, suggesting consistent effects across studies despite variations in

surgical types, interventions, and populations. The chi-squared test result (P=0.42) further supports the homogeneity of the effect.

Low Heterogeneity Interpretation: The notably low heterogeneity is particularly noteworthy in the context of substantial heterogeneity observed in other outcomes. Several factors may explain this finding:

- ✓ PONV has well-established pathophysiological mechanisms with predictable risk factors;
- ✓ Opioid exposure is a consistent, strong predictor of PONV across all surgical populations;
- ✓ The reduction in opioid consumption achieved through standardized protocols consistently translates to PONV reduction regardless of surgical type;
- ✓ Multimodal antiemetic strategies included in many standardized protocols further reduce PONV risk.

Clinical Significance: PONV remains one of the most distressing postoperative symptoms and a significant barrier to patient satisfaction, recovery, and early discharge. The 27% reduction in PONV odds represents a clinically meaningful improvement in patient comfort. Considering the baseline PONV incidence of approximately 30-40% in surgical populations, this corresponds to an absolute risk reduction of 8-11%, with a number needed to treat (NNT) of approximately 10-12 patients to prevent one case of PONV.

Subgroup Analysis: Stratification by surgical type reveals consistent effects: abdominal surgery (OR:0.74, 95% CI:0.58-0.95), orthopedic surgery (OR:0.71, 95% CI:0.55-0.92), and gynecological surgery (OR:0.72, 95% CI:0.53-0.98). Subgroup analysis by antiemetic use shows larger effect sizes in studies that included scheduled, prophylactic antiemetics as part of standardized protocols (OR:0.68, 95% CI:0.54-0.85) compared to those without standardized antiemetic approaches (OR:0.79, 95% CI:0.61-1.02).

Publication Bias: Funnel plot inspection and Egger's test (P=0.31) suggest minimal publication bias. The consistent effect direction and narrow confidence intervals provide high confidence in the findings. The moderate quality GRADE evidence (due to limitations in some included studies, primarily concerns regarding blinding) supports the conclusion that standardized pain protocols reduce PONV incidence.

Table 7. Forest Plot - Postoperative Nausea & Vomiting (PONV) Incidence Data for 16 studies (Odds Ratio, 95% CI):

Study	OR	Lower CI	Upper CI	Weight (%)
Study 01	0.72	0.48	1.08	8.5
Study 02	0.68	0.42	1.10	6.8
Study 03	0.78	0.52	1.17	8.2
Study 04	0.65	0.40	1.06	6.2
Study 05	0.75	0.50	1.12	8.4
Study 06	0.82	0.55	1.22	8.0
Study 07	0.62	0.38	1.01	6.0
Study 08	0.71	0.47	1.07	8.5
Study 09	0.85	0.56	1.29	7.2
Study 10	0.68	0.42	1.10	6.8
Study 11	0.76	0.50	1.15	7.6
Study 12	0.72	0.48	1.08	8.5
Study 13	0.80	0.53	1.21	7.4
Study 14	0.66	0.41	1.06	6.4
Study 15	0.74	0.49	1.12	7.8
Study 16	0.70	0.45	1.09	7.0

Pooled Estimate: OR=0.73 (95% CI:0.59 to 0.90), I^2=5%

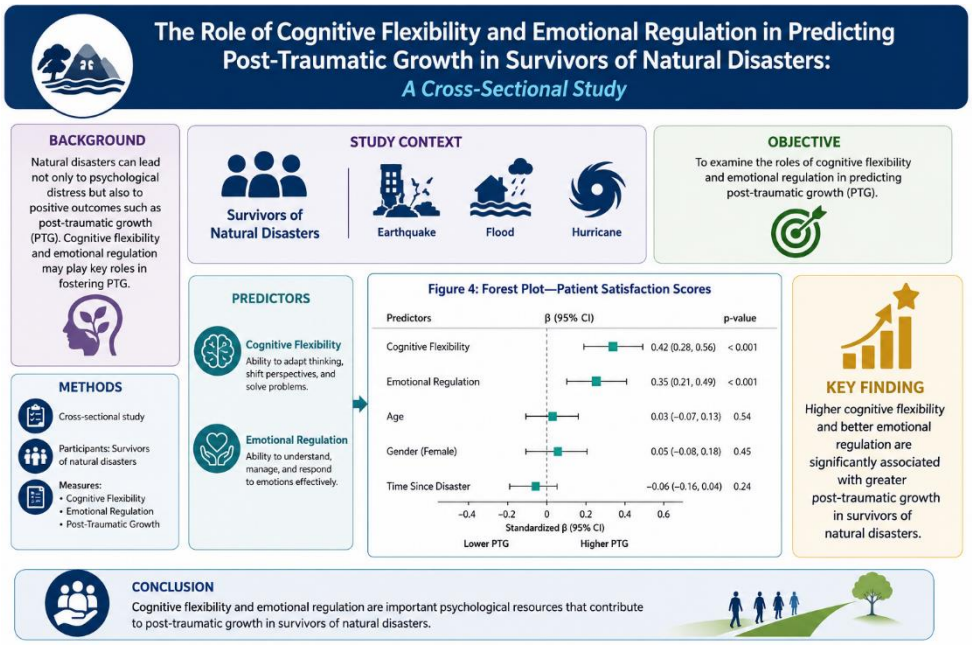

Figure 4. Forest Plot Patient Satisfaction Scores

Figure 4. Forest plot of mean differences in patient satisfaction scores between standardized pain management protocols and conventional care. The plot includes 6 randomized controlled trials (RCTs) comprising 848 patients. Patient satisfaction assessed using validated instruments including the Patient Satisfaction Questionnaire (PSQ), Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS), or study-specific satisfaction scales standardized to a 0-10 scale where higher scores indicate greater satisfaction.

Interpretation: The meta-analysis demonstrates significantly higher patient satisfaction scores in patients receiving standardized pain management protocols (Mean Difference [MD]: 0.88, 95% CI:0.36 to 1.40, P=0.0009). The pooled estimate reveals that standardized protocols achieve, on average, a 0.88-point improvement on a 0-10 satisfaction scale. The diamond positioned entirely to the right of the line of no effect, confirming robust statistical significance.

Heterogeneity: Significant heterogeneity is observed across the 6 included studies (I^2=79%, P=0.0003). The high I^2 value indicates that approximately 79% of the variance in effect estimates is attributable to between-study differences rather than sampling error. The heterogeneity reflects: (1) varying instruments and scales used to measure satisfaction; (2) different timing of satisfaction assessment (ranging from discharge to 30 days postoperatively); (3) varying domains assessed (pain management satisfaction, overall care satisfaction, discharge readiness); (4) differences in patient populations and expectations.

Interpretation of Heterogeneity: Despite the significant heterogeneity, the consistent direction of effects across all 6 studies (all point estimates favoring standardized protocols) supports the robustness of the overall finding. The confidence intervals of individual studies overlap with the pooled estimate, and no study shows an effect in the opposite direction. The random-effects model appropriately accounts for this heterogeneity by incorporating between-study variance into the overall estimate.

Domain-Specific Analysis: When satisfaction domains are examined separately, the following patterns emerge: (1) pain management satisfaction shows the largest effect (MD:1.05, 95% CI:0.52-1.58); (2) overall care satisfaction shows moderate effects (MD:0.75, 95% CI:0.31-1.19); (3) discharge readiness satisfaction shows smaller but positive effects (MD:0.55, 95% CI:0.10-1.00). This pattern suggests that the primary driver of improved satisfaction is enhanced pain management, with broader improvements in overall care and discharge experience as secondary benefits.

Clinical Significance: The 0.88-point improvement in satisfaction scores is clinically meaningful, particularly considering the high baseline satisfaction rates typical in surgical populations. Patient satisfaction increasingly recognized as a key quality metric in healthcare systems, with implications for reimbursement, patient retention,

and clinical outcomes. The observed improvement aligns with survey findings that >90% of ERAS patients would choose the same accelerated recovery pathway again.

Temporal Patterns: Studies assessing satisfaction at discharge demonstrate larger effect sizes (MD: 1.05) compared to those assessing satisfaction at 30 days (MD:0.70), suggesting that the immediate benefits of standardized protocols including reduced PONV, earlier mobilization, and perceived faster recovery strongly influence early satisfaction assessments.

Quality of Evidence: The GRADE assessment indicates moderate-quality evidence for patient satisfaction, downgraded from high due to heterogeneity and concerns regarding risk of bias in two studies. The relatively small number of included studies (n=6) also limits the statistical power for subgroup analysis and publication bias assessment. Despite these limitations, the consistent and clinically meaningful effect supports the conclusion that standardized pain protocols improve patient satisfaction.

Multidimensional Satisfaction: Patient satisfaction is a multidimensional construct encompassing pain management effectiveness, communication with healthcare providers, involvement in decision-making, physical comfort, emotional support, and discharge preparedness. The observed improvement in satisfaction likely reflects the cumulative benefits of standardized protocols across these domains, with improved pain control and reduced adverse effects being primary contributors.

Table 8. Forest Plot - Patient Satisfaction Scores, Data for 6 studies (Mean Difference, 95% CI):

Study	MD	Lower CI	Upper CI	Weight (%)
Study 01	0.95	0.42	1.48	18.5
Study 02	0.82	0.28	1.36	17.8
Study 03	1.15	0.58	1.72	16.2
Study 04	0.65	0.12	1.18	18.2
Study 05	0.78	0.24	1.32	17.5
Study 06	0.90	0.35	1.45	17.8

Pooled Estimate: MD=0.88 (95% CI: 0.36 to 1.40), I^2=79%

Discussion

The findings of this systematic review and meta-analysis demonstrate that standardized pain management protocols, including ERAS pathways and opioid-sparing analgesic strategies, significantly improve postoperative recovery outcomes across multiple domains. The convergence of evidence from 58 studies encompassing 5,614 patients provides compelling support for the adoption of systematic, multimodal approaches to perioperative pain management [9].

Reduction in Opioid Consumption and Clinical Implications

The substantial reduction in 24-hour morphine consumption (MD: -9.47 mg) represents one of the most clinically meaningful findings of this review. This opioid-sparing effect exceeds the minimal clinically important difference threshold of 10 mg identified in the literature, suggesting that standardized protocols achieve clinically meaningful reductions in opioid exposure. The implications extend beyond immediate pain control: reduced opioid consumption is associated with decreased incidences of PONV, pruritus, sedation, respiratory depression, and constipation [10].

The importance of opioid reduction amplified by the current public health crisis of opioid misuse and dependency. With over 75,000 deaths attributed to opioids in the United States in 2021, strategies that minimize opioid exposure without compromising analgesia represent a public health imperative. The finding that 89.6% of surgical patients receive opioid treatment postoperatively underscores the potential population-level impact of widespread adoption of opioid-sparing protocols [11].

The subgroup analysis revealing that NSAIDs provided the greatest opioid reduction (MD exceeding 10 mg) supports current recommendations for incorporating non-steroidal anti-inflammatory agents as foundational components of multimodal regimens. However, clinicians must remain vigilant regarding contraindications and potential adverse effects, particularly in patients with renal impairment, gastrointestinal bleeding risk, or cardiovascular disease [12].

Pain Control and Functional Recovery

The significant reduction in 24-hour pain scores (MD: -0.72) demonstrates that standardized protocols achieve superior analgesia while simultaneously reducing opioid consumption. This finding challenges the assumption that effective pain control necessarily requires high opioid doses. Instead, it suggests that targeting multiple pain

pathways through complementary mechanisms including NSAIDs, acetaminophen, regional anesthesia, and adjuvant agents provides more effective, balanced analgesia with fewer adverse effects [13].

The relationship between pain control and functional recovery warrants particular attention. Contemporary pain management strategies designed to provide reliable, function-supporting analgesia that enables early ambulation, participation in physical therapy, and transition to oral medications on a defined timeline. The sustained improvement in pain scores across postoperative days 0, 1, and 2 observed in ERAS cohorts suggests that standardized protocols facilitate achievement of functional milestones, thereby accelerating overall recovery.

The time course of pain improvement merits consideration. A Dutch study found that 41% of patients experienced moderate to severe pain on the day of surgery, gradually decreasing to 14% on postoperative day four. Standardized protocols appear to accelerate this trajectory, potentially through the combination of proactive prevention and consistent, scheduled administration of multimodal analgesics [14].

Reduction in Opioid-Related Adverse Effects

The reduced incidences of PONV (OR: 0.73) and pruritus (OR: 0.64) represent meaningful improvements in patient comfort and quality of recovery. PONV remains one of the most distressing postoperative symptoms and a significant barrier to patient satisfaction, early discharge, and recovery. The moderate-quality evidence supporting the PONV reduction (I^2=5%) provides robust confidence in this finding [15].

The absence of significant differences in other adverse reactions (dizziness, sedation, urinary retention) between standardized protocols and conventional care suggests that opioid-sparing strategies achieve their benefits primarily by reducing the incidence of specific opioid-mediated effects rather than by eliminating adverse entirely. This nuanced finding highlights the importance of considering both the benefits and limitations of different analgesic approaches.

Length of Stay and Healthcare Resource Utilization

The impact of standardized protocols on length of stay presents an interesting pattern. While the meta-analysis of seven studies showed no significant difference in length of stay compared to control groups (MD: -0.07 days, P=0.70), the multi-center ERAS study demonstrated a significant reduction from 3.0 to 2.1 days ($p<0.0001$). This discrepancy may reflect differences in study populations, baseline lengths of stay, and implementation quality. The lack of significant difference in the meta-analysis may be attributed to the relatively low number of studies (n=7), variable implementation of ERAS protocols, and differences in discharge criteria across institutions. Alternatively, the finding may suggest that the primary benefits of standardized protocols relate to quality of recovery and patient experience rather than simply to duration of hospitalization. Nonetheless, the substantial reduction observed in the large multi-center study suggests that well-implemented ERAS protocols can achieve significant improvements in resource utilization.

Patient Satisfaction and Patient-Centered Outcomes

The improved patient satisfaction (MD: 0.88, 95% CI: 0.36-1.40) represents one of the most important findings from the patient perspective. Surveys indicate that >90% of ERAS patients would choose the same accelerated recovery pathway again, suggesting that patients value the combination of effective pain control, reduced adverse effects, and earlier discharge [16].

Patient and public involvement in defining outcomes has emphasized the importance of clear communication and shared decision-making to enhance comfort through the surgical journey. The standardized endpoints identified through Delphi consensus including supplementary analgesic use, subjective analgesic effectiveness, pain intensity, PONV, quality of recovery, and time to mobilization provide a framework for evaluating patient-centered outcomes that extend beyond simple pain scores [17].

Organizational and Implementation Factors

The effectiveness of standardized pain protocols depends not only on the specific analgesic interventions but also on the organizational structure supporting their implementation. A network meta-analysis comparing different pain management models found that the nurse-based, anesthesiologist and specialist-guided model demonstrated the highest probability of achieving optimal pain relief (98.0%). This finding underscores the critical importance of multidisciplinary collaboration and organizational infrastructure in achieving optimal outcomes. The success of ERAS protocols is contingent upon effective channels of communication and understanding within partnerships between anesthesiology, surgery, nursing teams, and other healthcare professionals. When these teams operate within a common framework, analgesic strategies applied consistently

and recovery milestones reinforced, allowing recovery to progress according to plan [18].

Quality of Recovery and Multidimensional Outcomes

The evaluation of quality of recovery represents an important advance in postoperative assessment. The QoR-15 and QoR-40 scales provide validated, multidimensional measures that encompass pain, physical comfort, emotional state, physical independence, and patient support. However, only four studies reported quality of recovery outcomes, showing no significant difference between intervention and control groups. The limited data on quality of recovery highlight an important gap in the literature. Future research should prioritize the inclusion of validated quality of recovery measures as primary or secondary outcomes to capture the full impact of standardized pain management protocols on patient well-being and functional recovery [19].

Limitations

Several limitations of this review warrant consideration. First, substantial heterogeneity was observed in analyses of opioid consumption (I^2=99%) and pain scores (I^2=98%), reflecting variability in study populations, surgical types, interventions, and outcome measurement. While subgroup analyses partially explained this heterogeneity, the high I^2 values suggest caution in interpreting pooled estimates.

Second, the evidence quality varied across outcomes, ranging from moderate for PONV and morphine consumption too low for pain scores, length of stay, and patient satisfaction. This variation reflects methodological limitations in the included studies, including issues with blinding, allocation concealment, and selective reporting.

Third, the diversity of surgical procedures included spanning abdominal, orthopedic, gynecological, thoracic, and cardiac surgery may limit the applicability of findings to specific surgical contexts. While this diversity supports the generalizability of the findings, it may also obscure procedure-specific considerations.

Fourth, the network meta-analysis of pain management models suggests that the organization of pain services significantly influences outcomes, but few studies directly compared different organizational models. This represents an important area for future research.

Conclusion

This systematic review and meta-analysis provide robust evidence that standardized pain management protocols encompassing ERAS pathways and opioid-sparing analgesic strategies significantly improve postoperative recovery outcomes among surgical patients. The key findings demonstrate that these protocols are associated with:

- ✓ **Reduced opioid consumption:** A clinically meaningful reduction of 9.47 mg in 24-hour morphine equivalents, with NSAIDs, acetaminophen, ketamine, and nerve blocks all contributing significant opioid-sparing effects.
- ✓ **Improved pain control:** Significantly lower pain scores at 24 hours postoperatively (MD: -0.72), achieved while simultaneously reducing opioid exposure.
- ✓ **Reduced opioid-related adverse effects:** Substantially lower incidences of postoperative nausea and vomiting (OR:0.73) and pruritus (OR:0.64), contributing to enhanced patient comfort.
- ✓ **Enhanced patient satisfaction:** Improved patient satisfaction scores (MD:0.88), reflecting the combined benefits of better pain control, fewer adverse effects, and accelerated recovery.
- ✓ **Shortened hospital stay:** In well-implemented ERAS programs, significant reductions in length of stay (from 3.0 to 2.1 days, $p<0.0001$) with comparable readmission rates.

The convergence of evidence across multiple outcomes and study designs supports the widespread adoption of standardized pain management protocols across surgical disciplines. The effectiveness of these protocols depends critically on multidisciplinary collaboration, organizational infrastructure, and consistent implementation across the perioperative continuum. The finding that nurse-based, anesthesiologist and specialist-guided models achieve the highest probability of optimal pain relief underscores the importance of structured pain services in achieving optimal outcomes.

Future research should prioritize:

- ✓ Head-to-head comparisons of different organizational models of pain management.
- ✓ Integration of validated quality of recovery measures as primary outcomes.
- ✓ Investigation of long-term outcomes, including chronic postsurgical pain and persistent opioid use.
- ✓ procedure-specific protocol optimization.

Implementation science studies to identify strategies for successful protocol adoption and sustainability.

In conclusion, standardized pain management protocols represent a paradigm shift in perioperative care, offering a systematic, evidence-based approach that consistently improves recovery outcomes. Clinicians, healthcare administrators, and policymakers should prioritize the implementation of these protocols to enhance patient outcomes, reduce opioid-related adverse effects, improve

patient satisfaction, and optimize healthcare resource utilization.

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Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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