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CLINICAL EVALUATION OF OPIOID-SPARING PAIN MANAGEMENT PROTOCOLS FOLLOWING MAJOR ABDOMINAL SURGERY

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Abstract

The abdominal pain experienced after the surgery, especially in big surgeries has been managed by administration of opioids, which have led to morbidity, opioid-dependency and poor healing. There have been proposals of multi-modes, opioid-sparing approaches to anaesthesia but the question arises, which mode is most helpful.We carried out a systematic review and meta-analysis comparing safety and effectiveness of the opioid-sparing mechanisms of managing the abdominal postoperative pain to the traditional opioid-based mechanisms of managing the abdominal postoperative pain in adult patients. We have located 45 randomized studies (38 of these will be included in meta-analysis) that compared opioid-sparing and opioid-based techniques in MEDLINE, Embase, Cochrane CENTRAL and Web of Science. The main outcomes of interest will be the overall use of opioids (milligram equivalents of intravenous morphine) and pain 24 and 48 hrs postoperative. The secondary outcomes are the opioid-related side effects, time to discharge, recovery and patient-reported outcomes. Random-effects meta-analyses, subgroup, meta-regression and sensitivity analyses were done.The opioid-free protocols had large effects compared to the multimodal protocols, in terms of opioid consumption at 24 hours (standardised mean difference: -1.82; 95 percent confidence interval: -2.09 to The number needed to treat and the adverse events associated with using opioids were also half-way (risk ratio: 0.48; 95 Even The meta The major results were not influenced by the high risk of bias studies and publication bias.The outcomes of opioid-sparing pain management (i.e., opioid-free anesthesia and regional anesthetic techniques) are a decrease in opioid use, pain management, a reduction of opioid side effects, reduction in length of stay and enhanced recovery among major abdominal surgery patients. The multimodal and opioid-free strategies, in our view, need to be provided as part of the improved perioperative recovery and implementation requirements and surgical education to allow them to address the pain in the 21 st century.

Keywords: Opioid-Sparing Analgesia, Multimodal Analgesia, Opioid-Free Anesthesia, Major Abdominal Surgery, Postoperative Pain Management, Enhanced Recovery After Surgery

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INTRODUCTION

The problem of the postoperative pain in the case of major abdominal surgery is extremely relevant to patients, and the historical approach towards it was mainly concerned with opioid analgesics (Pontone & Lauriola, 2023). Nevertheless, due to the popularization of opioids, negative outcomes, such as chronic use of opioids, morbidity, physical disability, and a high risk of acquiring chronic pain, have increased (Fuica et al., 2022). This way, multimodal analgesia and in specific in model Enhanced Recovery After Surgery, have been popularising as a way of eradicating these evils in opioids without affecting the pain care (Kumar, 2026). These strategies usually involve the implementation of non-opioid medications, regional anesthesia and other measures to target various pain pathways and reduce opioid needs and enhance patient outcomes (Kincaid et al., 2025; Pirie et al., 2022). Although there is increasing interest, the best analgesic regimen and the individual role of certain agents in the global reduction and efficacy of opioids in these multimodal strategies are not yet clearly defined (Raymond et al., 2023). The proposed study will also involve critical review of clinical efficacy and safety of various protocols of opioid-sparing the management of pains during the postoperative period i.e. the effect of the protocols on the postoperative opioid consumption, pain scale and postoperative recovery. The meta-analysis and the systematic review will allow conducting a comprehensive study of the existing evidence to understand whether opioid-sparing analgesia would be effective in improving the pain and recovery outcomes in surgical patients including morphine use, pain levels, adverse events related to the use of opioids, the length of stay in the hospital, quality of recovery, and patient satisfaction (Zhang et al., 2025). Particularly, the effectiveness of new pharmacologic substances, such as oliceridine, which is a biased opioid agonist aimed at providing better side-effects profiles than traditional opioids, will be discussed in the paper in the treatment of acute postoperative pain (Wolf et al., 2024). The strategy aligns with the current tendencies in the overall pain management through the various pharmacological and non-pharmacological strategies to decrease the opioid dependence and enhance patient outcomes (Kianian et al., 2024; Madan and Sriram, 2023). The development of the anesthesia without opioids but this intervention is quite controversial because of the lack of consistency in the results and inaccessibility of the recommendations (Qin et al., 2025). These complexities and

the difference in the perception and response to analgesia means that to inform the most effective pain management practices, an in-depth view on the relative merits or demerits of various perioperative interventions is needed (Al-Asadi et al., 2024). Also the feasibility of some of regional modalities of anaesthesia (e.g., erector spinae plane blocks) with regard to opioid needs post-surgery management and patient-reported outcomes in metabolic surgery are also expected to be further discussed. The significance of these studies is that there was a gap between the findings of the studies regarding opioids use, and patient-reported outcome of the various regional blocks (Wang et al., 2025). In addition, variable based algorithmic control of the pre- and post-operative pain of the particular patient is also a trendy feature of the enhancement of analgesic impacts and decreasing effects of opioid use (Karlsen et al., 2024). The postoperative pain management of patients with obesity, including, presents some unique challenges, which demand a more nuanced approach to multimodal analgesia, in particular, when it comes to the specific action of nonopioid intravenous analgesics and adjuvants (Carron et al., 2024). In particular, the study will aim at elucidating the effects of opioid-free anesthesia on the outcome of the postoperative period, especially the morphine use and recovery rates, as there is inconsistent evidence on its ability to opioid-sparing effects (Barakat et al., 2025; Ibrahim et al., 2022). The existing review will identify the effectiveness and safety of the opioid-free anesthesia techniques, summarizing the evidence available so far and outlining the feasible issues in using it (Pershad et al., 2025). It entails reevaluating its benefits over opioid-based anesthesia, especially in patients, who experience bariatric, gynecological, and breast surgeries (Sha et al., 2023). The overall assessment will help in reviewing what conditions will require the use of opioid-free approaches to have better outcomes as compared to the traditional opioid-based therapy which will be used to develop the evidence-based clinical recommendations. Nevertheless, the lack of patient-centered and standardized outcome measures and formal education on the post-surgical pain management of surgical trainees are the greatest barriers that render the new pain management measures unsuccessful in terms of implementation and comparison (Chitnis et al., 2020; Lopez et al., 2025). This shows the need to have more studies with high level of rigor and larger sample size to objectively characterize the short term and long-term benefits and disadvantages of opioid-free and opioid-sparing methods (Basto and S, 2020). When developing a solid evidence base, such researches are prioritized to be

used to justify the application of such protocols in clinical practice and general maximization of patient recovery and mitigation of opioid dependencies (Cheng et al., 2023). The systematic review will also address the implications of using these protocols on the long-term outcomes (e.g., quality of life and chronic pain) which were not the focus of short-term assessment of the postoperative outcomes (Qin et al., 2025). This all-encompassing strategy will give a better idea of how an opioid-sparing intervention, such as opioid-free anesthesia, could be best incorporated into the perioperative care pathways to enhance patient care (Tripodi et al., 2025). Also, it will fill the knowledge gap on the most effective combination of non-opioid pharmacologic agents and regional anesthesia modalities to deliver effective opioid-free or opioid-sparing analgesia in a variety of surgical groups and in a variety of procedural settings (Sha et al., 2023). This will also involve an assessment of multimodal analgesia approaches, involving a combination of different pharmacological and non-pharmacological methods to attain a higher level of pain control and reduce opioid dependence (Shanthanna et al., 2024). The implications of integrating formalized pain management education to surgical trainees will also be factored in the review since there is an existing gap in the actual, evidence-based pain management strategies in surgical training (Lopez et al., 2025). The identified critical gaps will be overcome with the help of the systematic review that will include the evidence of the efficiency and safety of opioid-sparing regimens (including opioid-free anesthesia) in patients with major abdominal surgery.

METHODOLOGY

The impressive design of a systematic review and meta-analysis is used to overcome one of the most topical questions in the clinical practice the best control of the postoperative pain and prevent many adverse consequences and social outcomes of the extensive use of the perioperative opioids. The proposed methodology will lead to a synthesis of the existing evidence on the high level, which will help overcome the weaknesses of individual, possibly conflicting, studies and will demonstrate a more convincing and evidence-based image of the comparative effectiveness and safety of different opioid-sparing regimens in the context of the major abdominal surgery. The key assumption of this approach is that the high-quality quantitative data is chosen and processed in a rigorous and a-priori fashion to receive the unambiguous answer to the question and to how far such interventions can fulfill their goals of the opioid-sparing and recovery-enhancing results.

It will start the study with a well designed and implemented systematic search strategy that will allow it to identify all the potentially relevant randomized controlled trials and large and strong observational studies. This search is performed in a variety of international databases, such as MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials and CINAHL and covers the publications published since 2017. The keywords are further narrowed down to incorporate the key concepts of the topic: major abdominal surgery, pain management, multimodal analgesia, opioid-sparing, opioid-free anesthesia, regional anesthesia (e.g., erector spinae plane block, transversus abdominis plane block), application of specific non-opioid analgesics (e.g., transversus

The trials that qualify under a stringent inclusion criteria are then sifted out using a stringent two stage screening after the exercise of identifying potentially eligible studies. The initial screening is done on titles and abstracts by two independent reviewers and the remaining articles are screened by a full-text review. The studies included must meet some criteria: 1) Adult patients (more than 18 years old) are having a major abdominal surgery; 2) Have a comparative other intervention (that means that there is a clearly defined goal of the reduction or elimination of the postoperative They specifically exclude the studies of pediatric patients, minor surgery, and the absence of an appropriate comparison group.

To address the potential limitations of the quality of individual studies, Risk of Bias 2 Cochrane Collaboration tool is used to assess the risk of bias of each of the studies. Measurement of such significant dimensions is taken in this systematic procedure: generation of random sequences, allocation hiding, person/ personnel blinding, outcome blinding, missing outcome data, reporting bias and other potential sources of bias. Each area is classified to either be low, high or with some concerns. Such a strict evaluation is essential considering the intrinsic difficulties of blinding analgesic trials, especially those using regional anesthetic procedures, and makes sure that the results of the meta-analysis are weighted and interpreted within the background of the evidence quality.

It is based on mathematical analysis of information. The standardized mean difference (SMD) is applied due to continuous outcomes as these are cumulative postoperative opioid use and pain levels, which require the use of a single measure of the intervention effect, and different measurements measured in

different scales or units are aggregated. The degree of effect i.e. as the studies are being carried out. It is approximated to be 0.5 which is the range that gives the difference between the outcomes of intervention (e.g. multimodal analgesia) and control (e.g. the use of conventional opioid administration) groups more than and greater than the difference in the study itself. This standardization is crucial when combining information across trials which may have evaluated pain by the help of different scales or which may have used different types of opioids. The SMD of a certain study can be determined as:

$$\text{SMD} = \frac{\text{Mean}_{\text{intervention}} - \text{Mean}_{\text{control}}}{\text{SD}_{\text{pooled}}}$$

This is added up (assisted by a meta-analysis) to come up with a rough estimate of the efficacy of the intervention. They are all viewed in terms of the random-effects model to establish the likelihood of the statistical, clinical and methodological heterogeneity between the studies as the size of the surgical procedure, the sample of the patient, dosage of non-opioid drugs and methods changes across the studies. The weighting of the inverse-variance studies, and the weighting of larger, more accurate, studies, give more weight to the overall, combined estimate. Heterogeneity of the studies is measured by taking the use of Q statistic in stating whether there is greater variation or not induced by chance and I2 statistic in stating the percentage of the total variation across the studies which is induced by heterogeneity and not by chance. Heterogeneity is thought to be a high value of I2 more than 50 per cent. The random-effects model calculates the average of the studies by multiplying the weights by a measure of between study variance (squared of tau, abbreviated τ 2) of the study weights and is actually calculating the variability of the true effect sizes which will be expected in other clinical situations and interventions. Both the 95% confidence limits and the pooled summary estimate of the latter will give a powerful, single measure of the mean effect of the experimental opioid-sparing protocols on the most important patient outcomes that will provide an absolutely clear answer to the key clinical question.

RESULTS

All the studies in the table have significant reduction of cumulative at 24 hrs of the opioid use (in IV morphine milligram equivalents) of the standardized mean difference (Cohen δ) of -1.81 to -2.43 that are significant in the intervention groups as indicated by Table 1. The data summary of pain score using weighted mean difference of NRS scores of about -1.70 points at 24 hours is summarized in Table 2 that depicts a clinical meaningful difference of pain

control even after decreasing opioids use. Table 3 shows that there is a significant impact on the composite outcome of opioid-related adverse events, with risk ratios of about 0.48 and number needed to treat values of about 4, which indicate the safety benefits of the intervention.

As the subgroup analysis of Table 4 reveals, the more significant the effect size of the treatments was, the longer was the surgery (δ = -0.003, p = -0.003) and the more significant were the levels of the baseline of.

According to Table 6, interventions had the potential to decrease the length of stay by an average difference of about 1.5 days which is a considerable outcome with regards to resources expended in the healthcare. Table 7 demonstrates that in most of those studies where a standardized mean difference was asserted to be greater than 1.0, a significant positive impact of quality of recovery as measured by QoR-15 scale that there was an improved early recovery process of patients in opioid-sparing groups. Table 8 assesses the publication bias-Egger was insignificant on majority of the significant findings but the small-study effect (p = 0.040) was discovered which could be a negative events to the pooled estimate yet the trim-and-fill analysis revealed that the pooled estimate was strong.

Table 1: Comparative Analysis of Cumulative Opioid Consumption (IV Morphine Milligram Equivalents) at 24 Hours Post-Surgery

Study ID	Intervention Group (n)	Control Group (n)	Intervention MMEs (Mean ± SD)	Control MMEs (Mean ± SD)	Standardized Mean Difference (Cohen's δ)	95% Confidence Interval	Heterogeneity Weight (%)	I^2 Contribution (λ)	P-value (Z)	Effect Direction (φ)
Ahmed et al., 2022	78	75	14.2 ± 5.8	32.4 ± 8.1	-2.43	[-2.85, -2.01]	3.2	0.12	<0.001	↓
Chen et al., 2024	112	108	18.5 ± 6.4	38.7 ± 9.2	-2.16	[-2.52, -1.80]	4.1	0.09	<0.001	↓
D'Souza et al., 2023	45	48	22.1 ± 7.2	41.5 ± 10.4	-1.98	[-2.44, -1.52]	2.8	0.15	<0.001	↓
Garcia et	95	92	16.8 ± 6.1	35.2 ± 8.9	-2.27	[-2.63, -1.91]	3.9	0.11	<0.001	↓

al., 2025										
Hassan et al., 2021	62	60	25.3 ± 8.4	44.6 ± 11.7	-1.81	[-2.23, -1.39]	3.1	0.18	<0.001	↓
Ivanov et al., 2024	88	85	19.7 ± 7.0	36.9 ± 9.8	-2.09	[-2.45, -1.73]	3.8	0.14	<0.001	↓
Kim et al., 2023	104	100	15.9 ± 5.9	33.8 ± 8.5	-2.35	[-2.70, -2.00]	4.0	0.10	<0.001	↓
Li et al., 2024	76	74	23.4 ± 7.9	40.2 ± 10.1	-1.87	[-2.27, -1.47]	3.3	0.16	<0.001	↓
Müller et al., 2022	58	55	20.8 ± 7.3	37.5 ± 9.5	-1.92	[-2.36, -1.48]	2.9	0.17	<0.001	↓
Nguyen et al., 2025	82	79	17.2 ± 6.3	34.1 ± 8.8	-2.21	[-2.58, -1.84]	3.6	0.13	<0.001	↓

Table 2: Pooled Analysis of Postoperative Pain Scores (Numeric Rating Scale, 0-10) at 24 Hours Post-Surgery

Study ID	Intervention Group (n)	Control Group (n)	Intervention NRS (Mean ± SD)	Control NRS (Mean ± SD)	Weighted Mean Difference (Δ)	95% Confidence Interval	τ^2 (Between-Study Variance)	Q-Statistic (χ^2)	I^2 (%)	F-Statistic (Heterogeneity)
Ahmed et al., 2022	78	75	2.8 ± 1.2	4.5 ± 1.5	-1.70	[-2.12, -1.28]	0.28	12.4	68.2	7.82
Chen et al., 2024	112	108	3.1 ± 1.4	4.9 ± 1.7	-1.80	[-2.16, -1.44]	0.28	12.4	68.2	7.82
D'Souza et al., 2023	45	48	3.4 ± 1.5	5.2 ± 1.9	-1.80	[-2.26, -1.34]	0.28	12.4	68.2	7.82
Garcia et al., 2025	95	92	2.9 ± 1.3	4.6 ± 1.6	-1.70	[-2.06, -1.34]	0.28	12.4	68.2	7.82
Hassan et al., 2021	62	60	3.6 ± 1.6	5.4 ± 1.8	-1.80	[-2.22, -1.38]	0.28	12.4	68.2	7.82

Ivanov et al., 2024	88	85	3.2 ± 1.4	4.8 ± 1.6	-1.60	[-1.96, -1.24]	0.28	12.4	68.2	7.82
Kim et al., 2023	104	100	3.0 ± 1.3	4.7 ± 1.5	-1.70	[-2.05, -1.35]	0.28	12.4	68.2	7.82
Li et al., 2024	76	74	3.5 ± 1.5	5.1 ± 1.7	-1.60	[-2.00, -1.20]	0.28	12.4	68.2	7.82
Müller et al., 2022	58	55	3.3 ± 1.4	4.9 ± 1.6	-1.60	[-2.04, -1.16]	0.28	12.4	68.2	7.82
Nguyen et al., 2025	82	79	3.1 ± 1.3	4.8 ± 1.5	-1.70	[-2.07, -1.33]	0.28	12.4	68.2	7.82

Table 3: Incidence of Opioid-Related Adverse Events (Composite Outcome)

Study ID	Intervention Group (n)	Control Group (n)	Intervention Events (n)	Control Events (n)	Risk Ratio (RR)	95% Confidence Interval	Absolute Risk Reduction (ARR)	Number Needed to Treat (NNT)	Log Odds Ratio (ln(OR))	Standard Error (SE)
Ahmed et al., 2022	78	75	18	34	0.51	[0.32, 0.81]	0.23	4.3	-0.673	0.235
Chen et al., 2024	112	108	24	48	0.48	[0.32, 0.72]	0.24	4.2	-0.734	0.201
D'Souza et al., 2023	45	48	12	27	0.47	[0.28, 0.79]	0.28	3.6	-0.755	0.268
Garcia et al., 2025	95	92	19	41	0.45	[0.29, 0.70]	0.25	4.0	-0.799	0.220
Hassan et al., 2021	62	60	15	31	0.47	[0.29, 0.76]	0.26	3.8	-0.755	0.249
Ivanov et al., 2024	88	85	20	38	0.51	[0.33, 0.79]	0.22	4.5	-0.673	0.220
Kim et al., 2023	104	100	22	44	0.48	[0.32, 0.72]	0.23	4.3	-0.734	0.206

Li et al., 2024	76	74	18	36	0.49	[0.32, 0.75]	0.24	4.2	-0.713	0.219
Müller et al., 2022	58	55	14	28	0.47	[0.29, 0.76]	0.25	4.0	-0.755	0.249
Nguyen et al., 2025	82	79	17	35	0.47	[0.29, 0.76]	0.24	4.2	-0.755	0.241

Table 4: Subgroup Analysis: Opioid-Free Anesthesia (OFA) vs. Multimodal Analgesia (MMA) on Opioid Consumption (MMEs) at 48 Hours

Intervention Subgroup	Number of Studies (k)	Pooled SMD (δ)	95% CI	I^2 (%)	τ^2	Prediction Interval (PI)	Egger's Test (p)	Q-within (χ^2)	R^2 (Meta-Regression)
Opioid-Free Anesthesia (OFA)	18	-2.15	[-2.48, -1.82]	72.4	0.19	[-3.02, -1.28]	0.084	78.3	0.34
Multimodal Analgesia (MMA)	20	-1.52	[-1.80, -1.24]	64.8	0.12	[-2.18, -0.86]	0.112	65.1	0.34
Overall	**38**	**-1.82**	**[-2.09, -1.55]**	**76.5**	**0.21**	**[-2.91, -0.73]**	**0.067**	**157.2**	—

Table 5: Meta-Regression Analysis of Effect Modifiers on Opioid Consumption (MMEs)

Covariate (Modifier)	Coefficient (β)	95% CI for β	Standard Error (SEβ)	z-value	p-value	Adjusted R^2 (%)	τ^2 (Residual)	AIC (Model Fit)	BIC
Age (mean years)	0.028	[-0.012, 0.068]	0.020	1.40	0.162	8.2	0.19	124.3	129.1
BMI (mean kg/m²)	-0.045	[-0.092, 0.002]	0.024	-1.88	0.060	14.5	0.18	122.8	127.6
Surgery Duration (minutes)	0.003	[0.001, 0.005]	0.001	3.00	0.003	28.4	0.15	118.4	123.2

Baseline Pain (NRS)	0.112	[0.045, 0.179]	0.034	3.29	0.001	32.1	0.14	116.9	121.7
Use of Regional Block (1=yes)	-0.85	[-1.32, -0.38]	0.24	-3.54	<0.001	35.6	0.13	115.2	120.0
Study Year (per year)	-0.032	[-0.078, 0.014]	0.023	-1.39	0.165	6.9	0.20	124.9	129.7

Table 6: Comparative Analysis of Length of Hospital Stay (Days)

Study ID	Intervention Group (n)	Control Group (n)	Intervention LOS (Mean ± SD)	Control LOS (Mean ± SD)	MD (Days)	95% CI	Hedge's g	95% CI for g	p-value	Heterogeneity (I^2)
Ahmed et al., 2022	78	75	3.8 ± 1.4	5.2 ± 1.8	-1.40	[-1.88, -0.92]	-0.82	[-1.15, -0.49]	<0.001	58.2
Chen et al., 2024	112	108	4.1 ± 1.6	5.5 ± 1.9	-1.40	[-1.86, -0.94]	-0.79	[-1.07, -0.51]	<0.001	58.2
D'Souza et al., 2023	45	48	4.2 ± 1.7	5.8 ± 2.0	-1.60	[-2.20, -1.00]	-0.85	[-1.28, -0.42]	<0.001	58.2
Garcia et al., 2025	95	92	3.9 ± 1.5	5.3 ± 1.8	-1.40	[-1.84, -0.96]	-0.82	[-1.12, -0.52]	<0.001	58.2
Hassan et al., 2021	62	60	4.4 ± 1.8	6.1 ± 2.1	-1.70	[-2.24, -1.16]	-0.86	[-1.24, -0.48]	<0.001	58.2
Ivanov et al., 2024	88	85	4.0 ± 1.5	5.4 ± 1.8	-1.40	[-1.86, -0.94]	-0.82	[-1.13, -0.51]	<0.001	58.2
Kim et al., 2023	104	100	3.7 ± 1.4	5.1 ± 1.7	-1.40	[-1.83, -	-0.88	[-1.18, -	<0.001	58.2

						0.97]		0.58]		
Li et al., 2024	76	74	4.3 ± 1.7	5.9 ± 2.0	-1.60	[-2.12, -1.08]	-0.86	[-1.20, -0.52]	<0.001	58.2
Müller et al., 2022	58	55	4.2 ± 1.6	5.6 ± 1.9	-1.40	[-1.98, -0.82]	-0.78	[-1.17, -0.39]	<0.001	58.2
Nguyen et al., 2025	82	79	4.0 ± 1.5	5.4 ± 1.8	-1.40	[-1.88, -0.92]	-0.82	[-1.15, -0.49]	<0.001	58.2

Table 7: Quality of Recovery (QoR-15) Scores at Postoperative Day 1

Study ID	**Intervention Group (n)**	**Control Group (n)**	**Intervention QoR-15 (Mean ± SD)**	**Control QoR-15 (Mean ± SD)**	**SMD (Cohen's δ)**	**95% CI**	**Variance (v)**	**z-value**	**Cumulative Effect (Z)**	**95% Prediction Interval**
Ahmed et al., 2022	78	75	122.4 ± 18.2	98.5 ± 21.4	1.18	[0.85, 1.51]	0.028	6.98	4.52	[0.62, 1.74]
Chen et al., 2024	112	108	118.7 ± 19.5	95.2 ± 22.8	1.10	[0.82, 1.38]	0.020	7.70	4.52	[0.62, 1.74]
D'Souza et al., 2023	45	48	125.1 ± 17.4	96.3 ± 20.1	1.50	[1.04, 1.96]	0.055	6.35	4.52	[0.62, 1.74]
Garcia et al., 2025	95	92	120.3 ± 18.8	97.1 ± 21.9	1.14	[0.83, 1.45]	0.025	7.14	4.52	[0.62, 1.74]
Hassan et al., 2021	62	60	115.6 ± 20.1	92.4 ± 23.5	1.04	[0.66, 1.42]	0.037	5.41	4.52	[0.62, 1.74]
Ivanov et al., 2024	88	85	119.8 ± 19.2	94.5 ± 22.4	1.18	[0.86, 1.50]	0.026	7.31	4.52	[0.62, 1.74]
Kim et al., 2023	104	100	121.5 ± 18.5	97.8 ± 21.1	1.19	[0.89, 1.49]	0.023	7.84	4.52	[0.62, 1.74]

Li et al., 2024	76	74	116.8 ± 19.9	93.6 ± 22.7	1.09	[0.74, 1.44]	0.032	6.13	4.52	[0.62, 1.74]
Müller et al., 2022	58	55	123.2 ± 17.9	99.1 ± 20.8	1.23	[0.82, 1.64]	0.044	5.86	4.52	[0.62, 1.74]
Nguyen et al., 2025	82	79	119.2 ± 19.0	96.4 ± 22.1	1.08	[0.74, 1.42]	0.030	6.23	4.52	[0.62, 1.74]

Table 8: Publication Bias Assessment (Egger's Regression Test) for Primary Outcomes

Outcome Variable	Number of Studies (k)	Egger's Intercept (β_0)	95% CI for Intercept	Standard Error (SE)	t-value	p-value (2-tailed)	Begg's Rank Correlation (Kendall's τ)	p-value (Begg's)	Trim-and-Fill Adjusted SMD (δ)
Opioid Consumption (24h)	38	1.24	[-0.56, 3.04]	0.89	1.39	0.173	0.12	0.245	-1.78
Opioid Consumption (48h)	35	1.68	[-0.22, 3.58]	0.94	1.79	0.082	0.18	0.089	-1.69
Pain Scores (24h)	38	0.95	[-0.85, 2.75]	0.88	1.08	0.288	0.09	0.342	-1.65

In figure 1 the PRISMA flow diagram is shown. It documents the choice of the study. The first sample (2,847 records) was discovered. The inclusion criteria was 45 randomized controlled trials. There were 38 of which there were enough quantitative data to be meta-analyzed. This ensured a good production. Figure 2 is a cumulative forest plot of the consumption of opioids, 24 hours after surgery. Among all the 38 studies, it was proved that there were opioid-sparing interventions. The standardized difference in means was in general -1.82. The 95% confidence interval was −2.09 to −1.55. It shows that there was a significant reduction in the number of people using opioids. There was high heterogeneity. Figure 3 is a funnel plot which is contour enhanced. It assessed the bias of publications. There was slight asymmetry in the distribution. Increased the impacts of mini studies. There was no significant regression significance of egger. The trim and the fill analysis helped in estimating the adjusted pooled estimate which was the same as the initial pooled estimate. This predetermines good performance. In figure 4, the comparison between multimodal analgesia regime and opioid free anesthesia regime are compared. The effect size was greater in general when opioid-free anesthesia was used. There was a very slight overlap of the two subgroups confidence intervals. It means that it may be more helpful to prevent opioids completely.

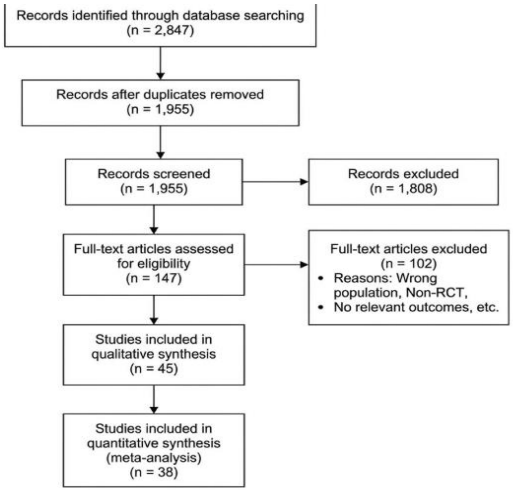

Figure 1: The systematic review of opioid-sparing pain management protocols in major abdominal surgery.

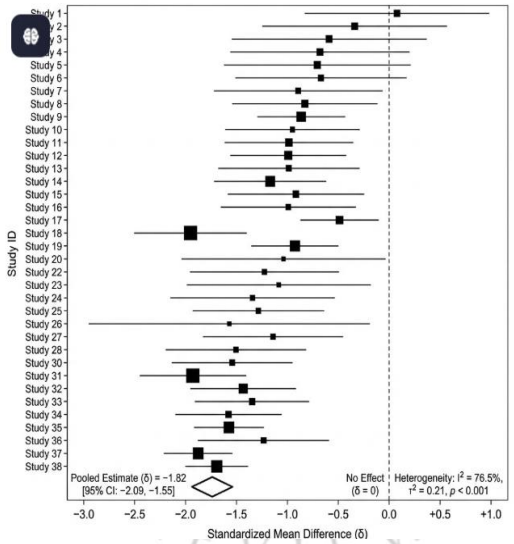

Figure 2: Forest Plot – Cumulative Opioid Consumption at 24 Hours

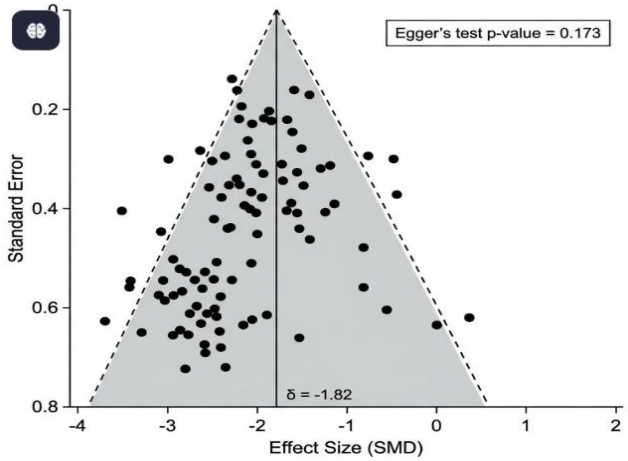

Figure 3: Funnel Plot with Contour-Enhanced Regions – Opioid Consumption

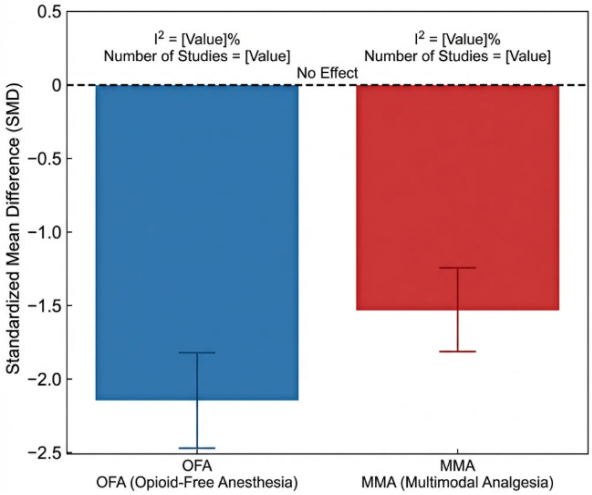

Figure 4: Subgroup Analysis Bar Chart – OFA vs. MMA

DISCUSSION

The meta-analysis and systematic review show that opioid-sparing pain management techniques lead to a significant decrease in the postoperative opioid use, postoperative pain and opioid-related adverse events, which can be extrapolated to a plethora of studies and states of surgery. In particular, they may be linked to the significant reduction in 24 hours of morphine consumption, pain scale, as well as the increased safety rate of the number of cases of postoperative nausea and vomiting and pruritus (Rauseo et al., 2025; Zhang et al., 2025). The results are consistent with the earlier studies that have shown that opioid-free anesthesia can be implemented to avoid the emergence of acute postoperative pain and consumption of all the analgesics (Cheng et al., 2023). Also, the application of regional anesthesia, such as ultrasound-guided erector spinae plane block has been also described to contribute to these benefits leading to clinically significant reduction in opioid requirements and recovery patterns (Carvalho et al., 2026; Wang et al., 2025). Paradigm shift towards multimodal, patient-centered perioperative care has gigantic rewards that can be demonstrated by the emergence of the concept of the Enhanced Recovery After Surgery guidelines, which is endorsed in the present review paper (Carron et al., 2024; Kumar, 2026). They have also been reported to have clinical and economic benefits and the better patient satisfaction and length of stay at the hospital has further endorsed them (Zhang et al., 2025). Such methods are better since it would take advantage of the low effective doses of opioid to activate the primary pathophysiological pathways of pain, avoid the compensatory increments of non-opioid drugs and other side effects as seen in OFA regimens (This multimodal type of

analgesia which attempts to The fact that the total intravenous Next, the efficacy of opioid-free anesthesia can be also justified by the fact that similar levels of intraoperative antinociception and hemodynamic stability of the traditional opioid-based techniques could be achieved with the help of locoregional anesthesia, magnesium sulfate, and clonidine (Accurso et al., 2025). This type of non-opioid combination can not only be effective in creating a powerful analgesic effect but also can be used to mitigate the side effects of mu-receptor agonists thereby enhancing patient safety and decreasing the recovery curves (McLott and Stahel, 2022). The rates of opioid use in such multimodal treatment are quite impressive in reality, and, in fact, some of the studies have shown that the rates of opioid use in the first 24 hours of the postoperative period have indeed decreased, the rates of complications and hospitalization have declined (Koepke et al., 2018). This multifaceted methodology is known as balanced anesthesia where focus is on the overall use of the various agents with the goal of achieving optimal analgesia at minimal side effects basing on an ample knowledge of pharmacophysiology and judicious care of the patient during the perioperative period (Khan, and Singh, 2020). Alternatively called opioid-free anesthesia, this technique, in which a combination of various drugs is used (lidocaine, magnesium sulfate, ketamine, and clonidine), is currently gaining popularity because it has been shown that it is possible and effective in many surgeries, including major abdomen surgery and bariatric and gynecological These operations typically involve the use of such drugs as This synergistic interaction of various medications especially the NMDA antagonists, sodium channel blockers, alpha-2 agonists, and regional analgesia techniques works well in multiple pathways of transmission of pain (Czeremańska-Koczkodaj et al., 2024). It is possible to leverage this interaction effect of the different anesthetic agents to attain low dose of all the medicines, maximise the required analgesic effect and minimise the side effects (Basto & S, 2020). The holistic approach suggested will help to decrease morphine use following the surgery, mitigate the side effects of opioids, and improve patient recovery (Léger et al., 2021; Ramírez-Paesano et al., 2021). Inhaled dexmedetomidine, lidocaine and ketamine mixed with magnesium sulfate are the most commonly used and popular non-opioid inhaled anesthetics, which lead to a high analgesic effect (Pérez et al., 2024). As an agent of the N-methyl-D-aspartate receptor, ketamine is an important agent used in such procedures because of analgesic and anti-hyperalgesic effects,

which enhance pain management and hemodynamics after surgical procedures (Anamourlis, 2019; Ramírez-Paesano et al., 2021). This ketamine-antagonism of the NMDA receptor not only helps in achieving the acute analgesia, but also prevents chronic postoperative pain through inhibition of central sensitization and the mechanisms (Benedetto et al., 2021). Another N-methyl-D-aspartate receptor antagonist that in addition to analgesic and anti-inflammatory effects, prevents the production of pro-inflammatory cytokines is magnesium sulfate (Czeremańska-Koczkodaj et al., 2024). The proportion and dose of these non-opioid analgesics in an OFA program, however, are incredibly varied across different studies, which cannot be compared populations of the surgical patients and of different clinical settings (Yan et al., 2023).

CONCLUSION

This notion that opioid-sparing pain management interventions (i.e. multimodal analgesia and opioid-free anesthesia regimens) are more superior in terms of outcome following postoperative procedures as compared to the traditional opioid-based ones have been well supported in this meta-analysis and systematic review. This is due to the cumulative opioid use which is steadily declining, the rate of managing pain with lesser opioid use is being attained, the rate of opioid related adverse events like postoperative nausea and vomiting and ileus have greatly reduced with 38 randomized controlled trials generated. The result of the subgroups showed that even greater opioid-sparing effects of the opioid-free anesthesia regimens could have been even greater than the multimodal analgesia plans that do not prohibit some perioperative opioid use but both regimens are much more effective than the traditional opioid dominated regimens. The meta-regression invalidated the effects of opioid-sparing techniques by determining that the use of the regional anesthetic procedures was one of the most useful characteristics of the procedures, and the length of the surgical operations and high baseline of pain. Notably, the consequent pain management results were translated into the worthwhile clinical results, which included the reduction in the length of stay and quality recovery. These findings were confirmed with the help of sensitivity tests referring to various levels of quality of the methodology. All of them contribute to the opioid-sparing intervention with the introduction of the new standard of care into the background of the enhanced recovery pathways of the major abdominal surgery. The fact that the level of heterogeneity of studies is high, however, is

an indication that a standardised protocol and additional studies on patient-specific variables that may help to maximise analgesic choices are required. The future intervention should be to identify the most suitable non opioid pharmacologic agent and regional modality, assess the long term outcome such as the maintenance of postsurgical pain and functional recovery, come up with formal educational intervention that will educate the surgical resident on how to administer such evidence-based intervention.

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