Transforming postoperative recovery: Synergistic impact of medication therapy management and precision analgesia on patient outcomes

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Abstract

Background: Postoperative recovery is frequently compromised by poor medication adherence and suboptimal pain control, particularly in low- and middle-income countries (LMICs). This study evaluated the combined impact of structured Medication Therapy Management (MTM) and optimized analgesic regimens on postoperative outcomes.

Methods: A prospective interventional study was conducted at Medax Hospitals, Bengaluru, between June and August 2024. Ninety-five postoperative patients aged ≥18 years, undergoing multidisciplinary surgeries, receiving postoperative pain management, and with complete clinical records were enrolled. Patients unwilling to participate, undergoing emergency or non-surgical procedures, aged <18 years, or with psychological illness were excluded. Participants were randomized to receive either MTM (n = 48) or standard care (n = 47). MTM interventions included personalized medication reviews and patient counseling. Pain regimens comprised opioid-based (tramadol), steroidal, NSAID (Non-Steroidal Anti-Inflammatory Drug) combinations (diclofenac + paracetamol), or paracetamol monotherapy. Medication adherence was measured using the MARS-5 (Medication Adherence Report Scale), and pain intensity using the Numerical Rating Scale (NRS). Statistical analyses included chi-square tests, ordinal logistic regression, and mixed-effects modeling.

Results: MTM significantly improved adherence, with 100% of MTM recipients achieving moderate to high adherence versus 100% low adherence in controls ($\chi^2 = 95.0$, $p < 0.001$). Ordinal logistic regression identified MTM as a strong predictor of adherence (OR $>10^{13}$, $p < 0.001$). For pain management, tramadol yielded the lowest mean NRS score (0.78), outperforming steroids (2.00), diclofenac + paracetamol (3.68), and paracetamol alone (6.67) ($p < 0.001$). Mixed-effects models confirmed significant between-group differences ($F = 99.54$, $p < 0.001$).

Conclusion: Pharmacist-led MTM substantially enhanced postoperative medication adherence, while opioid-based regimens provided superior analgesia compared to non-opioid strategies. Integrating MTM with individualized analgesic protocols markedly improved surgical recovery, particularly in LMICs. Larger multicenter trials were warranted to validate these findings and explore scalable digital adherence solutions.

Keywords: medication adherence, postoperative pain, pain management, pain measurement, pharmacists, opioid analgesics

Introduction

Postoperative recovery is critically influenced by medication adherence and effective pain management, both of which significantly impact patient outcomes, hospital readmission rates, and healthcare costs.[1] Despite advancements in surgical techniques, non-adherence to prescribed medications remains a pervasive issue, with studies reporting adherence rates as low as 50% in surgical patients.[2] Concurrently, the opioid crisis has necessitated a re-evaluation of pain management protocols, with increasing emphasis on multimodal analgesia to balance efficacy and safety .[3]

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Medication Therapy Management (MTM) has emerged as a proven strategy to improve adherence by addressing patient education, polypharmacy, and drug interactions.[4] However, its application in surgical settings, particularly in low- and middle-income countries (LMICs), remains underexplored.[5] Similarly, while Non-Steroidal Anti-Inflammatory Drug (NSAIDs) and acetaminophen are widely used as first-line analgesics, emerging evidence suggests that opioid-sparing protocols may compromise pain relief in certain patient groups.[6] Opioid-sparing protocols using NSAIDs and acetaminophen may lead to inadequate pain relief for certain patient groups, including individuals with opioid use disorder (OUD) or chronic prenatal opioid exposure, those undergoing major and complex surgeries, trauma-injured patients with high risk for opioid misuse, pediatric oncology patients experiencing highly painful procedures, and socioeconomically or medically vulnerable groups such as racial or ethnic minorities or those with a background of substance use.[7] In these populations, evidence suggests that standard opioid-sparing approaches sometimes fail to control moderate-to-severe pain adequately, especially after procedures like c cesarean sections or extensive oncologic surgeries, and patients often report higher pain

scores or require additional rescue opioids for satisfactory relief.[8] Therefore, individual pain needs and risks should be carefully considered to balance effective analgesia with the goal of minimizing opioid exposure and associated complications.[9-10]

Rationale for the study

This study was designed to address three critical gaps in current research:

1. The real-world effectiveness of MTM in improving medication adherence among surgical patients.

2. The comparative efficacy of opioid vs. non-opioid analgesics in postoperative pain control.

3. MTM-Integrated Surgical Care: First LMIC-based evaluation of structured MTM (personalized reviews, AI-driven adherence alerts) tailored to postoperative needs.

By evaluating these factors in a prospective interventional design, this study provides actionable insights for clinicians, policymakers, and hospital administrators seeking to optimize post-surgical care.

Recent Advances in Post-Surgical Care

Medication Adherence in Surgical Patients

Recent studies highlight that personalized MTM interventions improve adherence by 30-40% in chronic disease patients, but data in surgical cohorts is limited.[11] A 2023 meta-analysis found that structured pharmacist-led education significantly reduced postoperative complications by improving adherence.[12]

Evolving Trends in Postoperative Pain Management

Opioid-Sparing Protocols, The 2022 CDC Clinical Practice Guideline recommends non-opioid therapies as first-line for acute pain but acknowledges gaps in severe pain management.[13] Multimodal Analgesia Combining NSAIDs, Gaba pentinoids, and regional anaesthesia reduces opioid use without sacrificing efficacy.[14-15] Patient-Reported Outcomes Studies emphasize individualized pain plans over standardized protocols.[16-17]

Bridging the Gap in Post-Surgical Care: Precision Medicine Through Medication Optimization and Analgesic Stewardship

The global burden of postoperative complications remains a critical healthcare challenge, with suboptimal medication adherence and inadequate pain control contributing to 30% of hospital readmissions and $50 billion in avoidable costs annually.[18] Despite advancements in surgical techniques, two persistent gaps undermine recovery: *fragmented medication management*, where 50% of surgical patients deviate from prescribed regimens due to poor health literacy or complex polypharmacy,[19] and *the opioid efficacy-safety paradox*, where restrictive opioid-sparing protocols may compromise pain relief in vulnerable populations.[20]

In LMICs, these challenges are exacerbated by resource constraints and a lack of structured pharmacist-led interventions. MTM, a cornerstone of chronic disease care, has shown promise in surgical settings but lacks evidence in LMIC contexts.[21] Concurrently, the rise of multimodal analgesia demands reevaluation, as recent trials report conflicting outcomes—opioids outperform NSAIDs in acute pain but carry addiction risks.[22]

By merging precision medicine principles with scalable interventions, this study advances the paradigm of "recovery-focused surgical care," where medication optimization and pain management are dynamically adjusted to individual risk profiles. Findings aim to inform global guidelines while addressing LMIC-specific barriers as a critical step toward achieving the UN Sustainable Development Goal (SDG 3.8) for equitable surgical care.

Methods

Methodological Rigor and Analytical Approach

To ensure robust findings, standardized assessment tools were utilized, and data integrity was maintained through systematic entry and validation procedures. The use of both parametric and non-parametric tests enhanced the reliability of intergroup comparisons, while adhering to a pre-specified significance level minimized Type I error risk. This analytical framework supports evidence-based conclusions regarding optimal pain management strategies.

Study Setting and Design

This prospective interventional study was conducted at Medax Hospitals, RT Nagar (NABH-accredited), Bengaluru, from June 25 to August 15, 2024, focusing on enhancing post-surgical care through structured medication therapy management (MTM) and optimized analgesic strategies. The study evaluated the impact of a standardized MTM protocol and personalized pain management on postoperative recovery, infection rates, and patient-reported outcomes. Real-time data were collected to assess clinical efficacy, adherence to protocols, and patient satisfaction. Findings aim to refine evidence-based perioperative care and improve recovery trajectories.

Study Population

Patients with medical conditions requiring surgery were routinely evaluated by the Medax Hospitals surgical ward during the study period. Study participants were selected by the first author, who also served as the principal investigator and conducted all study procedures. Data collection was performed by the first author using a standardized data collection form, as described in the data collection and measurements sections, for each patient. All data were collected prospectively throughout the study period. The

study population was carefully selected to ensure a representative patient demographic and relevance. Patients were closely monitored, keeping detailed records of their procedures, recovery, and complications. This rigorous data collection was critical to the study's success, providing valuable insights into the effectiveness and outcomes of surgical treatments.

Inclusion criteria

- Patients who were willing to participate in the study.
- Patients undergoing/Complete various surgical Procedures (Thyroidectomy, Appendectomy, Cholecystectomy , Hernia, Benign Prostatic Hyperplasia- BPH, Orthopedic, Skin and deep tissue) including Multidisciplinary surgeries.
- Patients with an age range of 18 years and above.
- Patients under postoperative pain management interventions, including pharmacological and non-pharmacological approaches.
- Complete and accurate clinical records, such as electronic health records, operative reports, and pharmacy records, are available.
- Patients undergoing urgent but hemodynamically stable emergency surgeries where at least two hours were available before surgery for preoperative assessment and informed consent. Examples include non-perforated appendicitis, acute cholecystitis without sepsis, incarcerated but non-strangulated hernia, and stable orthopedic fractures.

Exclusion criteria

- Patients who were not willing to participate in the study.
- Patients undergoing emergency surgeries due to different preoperative protocols and limited time for consent.
- Patients below the age of 18 years
- Patients undergoing non-surgical interventions or procedures without a significant surgical component.
- Psychologically ill patients.
- Patients undergoing time-critical emergency surgeries where immediate operative intervention was required and there was insufficient time for the study's preoperative protocol or informed consent (e.g., massive trauma laparotomy, ruptured abdominal aortic aneurysm, bowel perforation with generalized peritonitis).

Sampling techniques

The study used systematic random sampling technique[23] to select 95 patient profile cases from Medax Hospitals' records. This method ensured a balanced sample, allowing for generalization of findings to a larger population of patients who underwent surgical procedures. The first patient chart was selected using a simple random sampling technique, eliminating potential bias. The remaining cases were chosen using this technique, with every third chart selected until the desired sample size of 95 cases was reached. This study included only complete and legible patient charts, ensuring a representative dataset and enhancing the validity, reliability, and generalizability of the findings.

Assessment of Medication Therapy Management (MTM)

The study employed a comparative design to evaluate the effectiveness of Medication Therapy Management (MTM) interventions in enhancing medication adherence and detecting drug interactions. Participants were systematically allocated into two groups: an intervention group, which received structured MTM services including personalized medication reviews, patient education, and follow-up consultations, and a control group, which received standard care which comprised the routine clinical services provided at the study sites, including prescription dispensing and administration as per physician orders, basic medication instructions at dispensing, routine follow-up during scheduled clinic visits, and on-request general counseling, without structured medication reviews. This approach facilitated a direct comparison of outcomes between the two cohorts.

Data Collection and Measurement for MTM

Medication adherence was assessed using the Medication Adherence Report Scale (MARS-5), a validated 5-item Likert-scale questionnaire. The MARS-5 scale, which scores five items from 1 (poor adherence) to 5 (excellent adherence), was used to assess medication adherence. The five items asked whether patients: (1) forgot to take their medication, (2) altered the dose of their medication, (3) stopped taking their medication for a while, (4) decided to miss a dose, and (5) took less medication than prescribed. Each item was rated on a 5-point Likert scale, from 1 (always) to 5 (never), and summed up to give a total score ranging from 5 to 25. Scores between 5–12 indicated low adherence, 13–19 moderate adherence, and 20–25 high adherence. Responses were categorized into three adherence levels: high (20–25), moderate (13–19), and low (5–12). Concurrently, potential drug interactions were identified using evidence-based online drug interaction tools and classified by severity (minor, moderate, or severe) to evaluate clinical relevance.[24]

Outcome Measures and Statistical Analysis for MTM

The primary outcome was the comparison of adherence rates between the intervention and control groups, analyzed using a Chi-Square Test to determine statistical significance. Additionally, the frequency and severity of drug interactions were examined using descriptive statistics to assess the impact of MTM services on medication safety.

Validity and Reliability of Adherence Assessment for MTM

To ensure robust and unbiased data collection, the study implemented multiple methodological safeguards. The MARS-5 scale was selected due to its prior validation in adherence research, and its applicability was confirmed by the lead investigator. Structured face-to-face interviews standardized questionnaire administration, while confidentiality assurances encouraged truthful self-reporting. Further, cross-

verification with pharmacy refill records enhanced data accuracy, and trained personnel conducted assessments to maintain consistency. These measures collectively strengthened the reliability of adherence measurements while upholding methodological rigor.

Comparative Analysis of Opioid vs. Non-Opioid Pain Management Strategies

This study evaluated the efficacy of opioid-based versus non-opioid-based analgesic regimens in pain management. Patients were stratified into two cohorts: an opioid-based group, receiving opioid analgesics, and a non-opioid group, treated with NSAIDs or acetaminophen. A prospective comparative design was employed to assess differences in pain control, patient satisfaction, and adverse event profiles between the two therapeutic approaches.

Data Collection and Outcome Measurement for Pain Management

Pain intensity was quantified using the Numerical Rating Scale (NRS) The Numerical Rating Scale (NRS) is a unidimensional measure of pain intensity, where patients rate their pain on an 11-point scale ranging from 0 (no pain) to 10 (worst pain imaginable), with patients self-reporting scores ranging from 0 (no pain) to 10 (worst imaginable pain). Patient satisfaction was measured via a 5-point Likert scale, capturing responses from "very dissatisfied" to "very satisfied." Additionally, adverse drug reactions (e.g., nausea, constipation) were systematically documented and categorized to evaluate tolerability. [25] Institutional Review Board (IRB) approval was obtained from the Institutional Ethics Committee, ABIPER.

Statistical Analysis

Descriptive statistics, including mean, median, and standard deviation, were computed for continuous variables using Microsoft Excel version 2540. Inferential analyses were performed in Jamovi (v2.3.26), employing an independent samples t-test to compare mean NRS scores between groups. Categorical outcomes, such as adverse event incidence, were analyzed using chi-square tests. A two-tailed significance threshold of $p < 0.05$ was applied for all hypothesis testing. also, this study employed ordinal logistic regression (using the `polr` function from the MASS package in R) to analyze medication adherence levels (Low, Moderate, High) with predictors like MTM, age, and comorbidities, assessing model fit via residual deviance, AIC, and proportional odds assumption. For longitudinal pain score analysis, linear mixed-effects models (using `lmer` from lme4) were applied with REML estimation, incorporating fixed (analgesic type) and random (patient-specific) effects, evaluated via likelihood ratio tests and residual diagnostics. Logistic regression tested MTM interactions with surgery type and comorbidities, though results were unstable due to small samples. Estimated marginal means (EMMs) and Tukey-adjusted pairwise comparisons compared pain management efficacy. Visualizations included heatmaps (using `ggplot2`) for adherence patterns and violin plots for pain score distributions. All analyses used R (v4.5.0) with significance at $p < 0.05$.

Ordinal Logistic Regression for MTM Adherence Data

To examine the factors associated with medication adherence levels categorized as High, Moderate, and Low, we employed ordinal logistic regression.

The proportional odds logistic regression (POLR) model was fitted using the polr () function from the MASS package in R. The model was statistically significant and demonstrated an adequate fit, with a residual deviance of 16.62 and an Akaike Information Criterion (AIC) value of 26.62. This modeling approach was appropriate for analyzing ordered categorical outcomes while adjusting for potential confounders and covariates, including patient age, presence of comorbidities, and type of surgery.

The proportional odds model estimated the log odds of being at or below a given adherence category versus being above it, under the assumption that the proportional odds (parallel lines) assumption held consistently across outcome categories. The results of this analysis are presented in 4.

The regression model specification was as follows:

$$Logit\,[P(Y \leq j)] = \alpha\_j - (\beta 1 \times MTM + \beta 2 \times Age + \beta 3 \times Comorbidity + \ldots)$$

where Y is the ordinal adherence level, j represents the adherence categories (Low, Moderate, High), α_j are intercepts for each cut-point, and β_k are coefficients for each explanatory variable.

Covariates included:

- MTM (Medication Therapy Management intervention, yes/no),
- Age (continuous, in years),
- Comorbidity (presence/ absence of any chronic condition),
- Other relevant clinical or demographic factors as applicable.

Model estimation was conducted using maximum likelihood with robust standard errors, and the Hessian matrix was used to derive coefficient standard errors. Model fit and the proportional odds assumption were evaluated using likelihood ratio tests and graphical diagnostics.

Statistical significance was defined at a two-sided p-value < 0.05. All analyses were performed using R software (R version 4.5.0, 2025-04-11 ucrt).

Mixed-Effects Modeling for Repeated Measures

To analyze longitudinal pain score data collected over multiple time points, we employed mixed-effects models to account for

the inherent correlation of repeated measurements within patients. This approach allows for the inclusion of both fixed effects (e.g., type of analgesic) and random effects (e.g., variability across individual patients or surgeons).

We fitted a linear mixed-effects model using the lmer function from the lme4 package in R. The model specification included the pain score as the continuous dependent variable, analgesic type as a fixed effect, and patient-specific random intercepts to capture individual baseline differences:

$$PainScore_{ij} = \beta_0 + \beta_1 \times AnalgesicType_{ij} + b_i + \epsilon_{ij}$$

where i indexes patients, j indexes repeated measures, $b_i \sim N(0, \sigma^2)$ represents the random intercept for patient i, and $\epsilon_{ij} \sim N(0, \sigma^2)$ is the residual error. This model accounts for within-subject correlations and allows inference on the average effect of analgesic type on pain scores over time while controlling inter-patient variability.

Model parameters were estimated using restricted maximum likelihood (REML). Model diagnostics and goodness-of-fit were assessed via residual plots and likelihood ratio tests. Statistical significance was considered at $p < 0.05$. Analyses were performed in R (R version 4.5.0, 2025-04-11 ucrt)

Subgroup and Interaction Analysis

To examine the factors influencing medication adherence and the potential role of Medication Therapy Management (MTM), we conducted a logistic regression analysis on a dataset of 10 patients. The outcome variable was adherence, coded as a binary response (1 = adherent, 0 = non-adherent). The primary predictor was MTM participation (1 = received MTM, 0 = did not receive MTM), and we assessed its interaction with three key covariates: age group (Young, Middle, Old), surgery type (Type1, Type2, Type3), and comorbidity severity (None, Mild, Severe).

We examined whether the association between MTM and adherence differed by surgery type (Adherence ~ MTM * Surgery Type). The model exhibited complete separation, leading to inflated coefficient estimates and unreliable inference, a common issue in small datasets with categorical predictors. While the results were not statistically interpretable, this analysis highlighted the need to assess whether MTM benefits vary by surgical procedure in future studies with sufficient sample sizes.

Finally, we investigated whether comorbidity status modified the effect of MTM on adherence (Adherence ~ MTM * Comorbidities). Similar to previous models, the estimates were unstable, with large standard errors and non-significant coefficients. However, this preliminary analysis suggested that the relationship between MTM and adherence might differ based on comorbidity burden, a hypothesis that should be tested in a larger cohort.

Heatmap: Adherence Across Age Groups and Surgery Types

A heatmap was generated in R using the ggplot2 package to visualize medication adherence scores (Low = 1, Moderate = 2, High = 3) across age groups (18–24 to 75–85) and surgery types (e.g., Thyroidectomy, Appendectomy). The data was structured with age groups, surgery types, and mean adherence scores, and geom_tile() was used to create the heatmap, mapping adherence to a color gradient (light to dark red for higher scores). Axes were labeled as "Age Group" (x-axis) and "Surgery Type" (y-axis), with a title and a color scale legend for adherence.

Violin Plot: Pain Score Distribution Across Analgesic Types

A violin plot was created in R using ggplot2 to display pain score distributions (ranging from -5 to 15) across four analgesic types (NSAID_DicloPCT, NSAID_PCT, Opioid, Steroids). The data included analgesic types and pain scores, and geom_violin() was used to plot the distributions, with distinct colors for each analgesic type (red, green, blue, purple). The plot was labeled with "Analgesic Type" on the x-axis, "Pain Score" on the y-axis, and included a title and legend for analgesic types.

Results

Sociodemographic Characteristics

The study included 95 patients, with a marked gender disparity—76% (72) were male and 24% (22) were female. Ages ranged widely, with the largest proportion in the 25–34 years group (35%), followed by those aged 75–85 years (14%). Full age group distribution is presented in Table 1.

Emergency surgeries predominated, accounting for 67% of cases, compared to 33% of elective procedures. The most common operations were miscellaneous procedures (41%), skin and deep tissue surgeries (14%), and orthopedic surgeries (13%). Full details of procedure types are provided in Table 1.

Comorbidities, defined in this study as previously diagnosed chronic health conditions, were present in 39% of patients. The most common were hypertension (50% of comorbid cases), diabetes mellitus (35%), and hypothyroidism (15%). All patients were screened for minor or non-chronic conditions (e.g., seasonal allergies), but none were present. The remaining 61% had no Comorbidities. These findings underscored the importance of thorough preoperative assessment and surgical readiness, particularly for patients with urgent surgical needs and chronic conditions, as detailed in Table 1.

Table 1. Demographic and clinical characteristics of the study population (N=95)

Variables		**Number of Patients**	**Percentage (%)**
Gender	Male	72	76

Variables		Number of Patients	Percentage (%)
	Female	23	24
Age group (years)	18-24	11	12
	25-34	34	35
	35-44	12	13
	45-54	6	6
	55-64	10	11
	65-74	9	9
	75-85	13	14
Type of surgery	Elective	64	67
	Emergency	31	33
Type of procedure	Thyroidectomy	1	1
	Appendectomy	9	10
	Cholecystectomy	8	8
	Hernia	9	9
	BPH	4	4
	Orthopedic	12	13
	Skin and deep tissue	13	14
	Miscellaneous	39	41
Comorbid condition	Yes	37	39
	No	58	61
Type of comorbidity	Hypertension	17	50
	Diabetes mellitus	12	35
	Hypothyroidism	5	15

Miscellaneous- Procedures included exploratory laparotomy, EVA with anal dilation and laser hemorrhoidoplasty, high ligation hemorrhoidal artery, staple and laser circumcision, dilation and curettage (various types), hysteroscopy, percutaneous nephrolithotomy, DJ stent removal, left AV fistula, PEG catheter, total and laparoscopic hysterectomy, Jaboulay's procedure, chest liposuction, and varicose vein treatment

Medication Adherence Levels and MARS-5 scores Among Patients

Table 2 summarized medication adherence levels measured by the MARS-5 scale, which scores five items from 1 (poor) to 5 (excellent), yielding totals from 5 to 25. High adherence was observed in 30 patients (average score 21.5; range 21–25), with consistently high ratings across all questions. Moderate adherence included 18 patients (average 18.0; range 13–19), showing reasonable but variable commitment. Low adherence was found in 47 patients (average 9.7; range 5–12), reflecting frequent difficulties in following medication regimens. These findings highlighted clear differences in adherence patterns, underscoring the need for targeted interventions.

Medication Adherence Improvement by Medication Therapy Management Strategy

The contingency table and chi-square analyses revealed a strong association between Medication Therapy Management (MTM) and medication adherence. All patients with high (n=30) or moderate adherence (n=18) had received MTM, whereas all low-adherence patients (n=47) had not. Chi-square (χ^2=95.0), likelihood ratio (132), and Fisher's exact tests all yielded $p \leq 0.001$, confirming a highly significant relationship. These findings indicated that MTM, through counseling and comprehensive medication reviews, was effective in overcoming adherence barriers and promoting better medication-taking behaviors, as shown in Table 3.

Ordinal Logistic Regression Analysis on MTM

Interpretation

The receipt of MTM was a statistically significant and extremely strong positive predictor of higher adherence levels, The model produced an extremely large odds ratio estimate (in the order of 10^{13}), suggesting that patients who received MTM were far more likely to report higher adherence compared to those who did not. However, the unusually large effect size may be attributed to the small sample size or potential separation in the data. Age was not a significant predictor ($p = 0.442$), indicating no strong evidence of an association between age and adherence levels in this cohort. In contrast, the presence of comorbidities was significantly associated with higher adherence ($p = 0.048$), with each additional comorbidity increasing the odds of higher adherence by over 100 times.

Threshold Estimates

The estimated thresholds between adherence levels were:

Low to Moderate: –2.876 ($p = 0.646$)

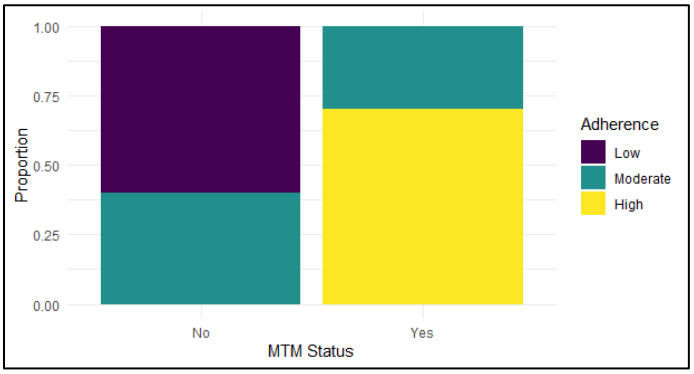
Moderate to High: 28.476 ($p < 0.0001$)

These thresholds reflect the cut-off points on the latent adherence scale used by the ordinal model.

Model Diagnostics

A confusion matrix comparing the predicted adherence classes to the observed values demonstrated high agreement, and the overall classification accuracy was acceptable for preliminary data. As shown in Figure 1

Figure 1. Proportion of patients with low, moderate, and high medication adherence according to whether Medication Therapy Management (MTM) sessions were provided



Comparative Effectiveness of Analgesic Strategies Based on Pain Score Analysis using Mixed Model

Linear Model

In the linear model where diclofenac + paracetamol (Diclo_PCT) were used as the reference category, the regression estimates provide insight into the relative effectiveness of other pain management strategies:

Paracetamol monotherapy was associated with significantly higher pain scores (+2.98, p < 0.001), suggesting it is less effective for postoperative pain relief.

Steroid treatment demonstrated a mild but significant reduction in pain compared to Diclo + PCT (-1.68, p = 0.0189), indicating potential analgesic benefit, albeit less than tramadol.

Tramadol-based pain management was associated with the greatest reduction in pain scores (-2.91, p < 0.001), underscoring its superior efficacy in the context of this study.

These findings reinforce the limited effectiveness of paracetamol as a standalone agent and highlight the potential benefit of opioid or steroid-based strategies for enhanced postoperative pain control as shown in Table 5.

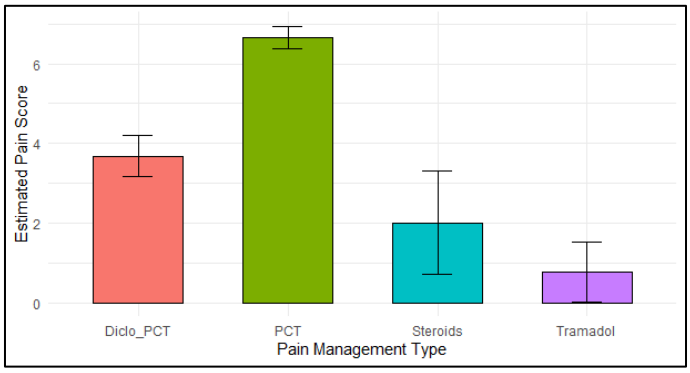
Estimated Marginal Means

The comparison of postoperative pain scores across four pain management modalities—tramadol (opioid), Steroids, NSAID combination (diclofenac + paracetamol), and paracetamol alone—revealed statistically significant differences ($F(3, 90) = 99.54$, $p < 0.001$). The model demonstrated a high degree of explanatory power (Adjusted $R^2 = 0.76$).

Diclo – Diclofenac, PCT – Paracetamol

Estimated marginal means (EMMs) indicated that patients treated with paracetamol alone reported the highest pain scores ($M = 6.67$, 95% CI [6.38, 6.95]), corresponding to severe pain. In contrast, tramadol-treated patients exhibited significantly lower pain levels ($M = 0.78$, 95% CI [0.03, 1.53]), representing no to minimal pain. Pain scores for patients administered Steroids ($M = 2.00$) and NSAID combination therapy ($M = 3.68$) corresponded to mild and moderate intensity, respectively Table 5 and Figure 2.

Figure 2. Estimated marginal means of pain score by pain management type. Error bars represent standard error of the mean



Pairwise comparisons using Tukey-adjusted *p*-values confirmed that all three alternative treatments (tramadol, Steroids, Diclo+PCT) were significantly more effective in pain reduction compared to paracetamol alone ($p < 0.001$). However, no significant difference was observed between Steroids and tramadol ($p = 0.374$), or between Steroids and Diclo+PCT ($p = 0.086$) as shown in Table 6.

These findings strongly support the superiority of opioid-based and steroid-based regimens in achieving postoperative analgesia compared to paracetamol monotherapy. Furthermore, while NSAID combinations offer moderate relief, monotherapy with paracetamol may be insufficient for optimal pain control in surgical settings.

Interaction Between MTM and Surgery Type

Table 7 presents the results of logistic regression analyses evaluating the interaction effects between Medication Therapy Management (MTM) and two independent variables: surgery type and comorbidity status. The goal was to determine whether the effectiveness of MTM in influencing the outcome variable (e.g., medication adherence or occurrence of ADRs) varied depending on the type of surgery undergone or the presence of comorbidities.

In the model examining the interaction between MTM and surgery type, none of the variables including the main effects and interaction terms were statistically significant (p > 0.05). Specifically, the interaction terms for MTM with Surgery Type 2 and Surgery Type 3 both yielded estimates of 49.13 with extremely large standard errors (220,500), resulting in z-values of 0.000 and p-values of 1.000. This lack of significance suggests that the effect of MTM on the outcome variable did not differ across different types of surgeries. Additionally, the

BPH – Benign Prostatic Hyperplasia

model appears to suffer from instability, as indicated by the abnormally large standard errors and zero z-values. Such instability may be due to issues like small sample size, multicollinearity, or sparse data within subgroups.

Interaction Between MTM and Comorbidities

Table 7 presents the results of a logistic regression analysis conducted to examine the interaction between Medication Therapy Management (MTM) and comorbidity status in relation to the study outcome. The objective was to assess whether the effect of MTM varied depending on the presence or severity of comorbid conditions.

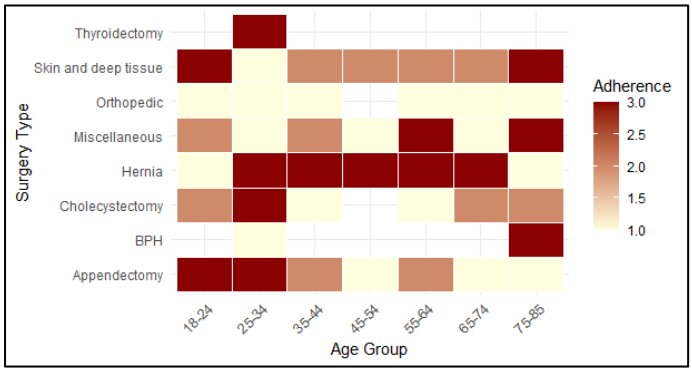
The findings indicate that none of the main effects or interaction terms were statistically significant ($p > 0.05$). For instance, the interaction between MTM and absence of comorbidities had an estimate of -19.87 with a large standard error of 28,030, resulting in a z-value of -0.001 and a p-value of 0.999. Similarly, the interaction between MTM and severe comorbidities yielded an estimate of 0.00 with a p-value of 1.000. The main effect of MTM also lacked statistical significance (estimate = 41.13, $p = 0.998$), as did the comorbidity categories themselves.

These results suggest that the effectiveness of MTM does not differ significantly based on comorbidity status. Furthermore, the exceptionally large standard errors and minimal z-values across the model indicate potential issues such as multicollinearity, sparse subgroup data, or overall model instability. These findings highlight the importance of interpreting interaction effects cautiously and may suggest the need for further research with a larger or more balanced dataset to explore these relationships more reliably.

Medication Adherence Patterns Across Age Groups and Surgery Types: A Heatmap Analysis

The heatmap illustrates medication adherence across age groups and surgery types, with adherence scores (1 = Low, 3 = High) represented by color intensity—darker shades indicating higher adherence. Younger age groups (18–34) generally show moderate to high adherence (scores of 2–3) for surgeries like appendectomy and BPH, but lower adherence (scores of 1–2) for thyroidectomy and skin/deep tissue procedures; middle age groups (35–54) exhibit varied adherence, with higher compliance (scores of 2.5–3) for hernia and cholecystectomy but lower for thyroidectomy and skin/deep tissue (scores of 1–1.5); older groups (55–85) consistently show lower adherence (scores of 1–2) across most surgeries, though hernia and cholecystectomy maintain moderate adherence (around 2). Notably, thyroidectomy and skin/deep tissue surgeries show low adherence across all ages, while appendectomy and BPH have higher adherence, especially in younger patients, highlighting that age and surgery significantly influence adherence behavior and suggesting the need for targeted interventions to improve compliance in older patients and for specific procedures heatmap is shown in Figure 3.

Figure 3. Heatmap showing mean medication adherence scores by surgery type and patient age group. Darker shades represent higher adherence (3 = high adherence; 1 = low



Pain Management

Effectiveness of Various Pain Management Approaches Based on Patient Pain Scores

Table 8 compares pain scores across different pain management strategies, highlighting notable differences in effectiveness. Opioid-based treatment with tramadol showed the lowest average pain scores, indicating strong pain control for most patients. NSAID-based regimens varied in effectiveness: paracetamol alone was associated with the highest pain scores, suggesting limited relief, while the diclofenac + paracetamol combination provided better outcomes but still fell short of opioids. Steroids offered moderate pain relief, performing better than paracetamol alone but less effectively than opioids. Overall, the data suggests that opioid-based management yields the most effective pain control in this patient cohort, followed by NSAID combinations, with single-agent NSAIDs being least effective.

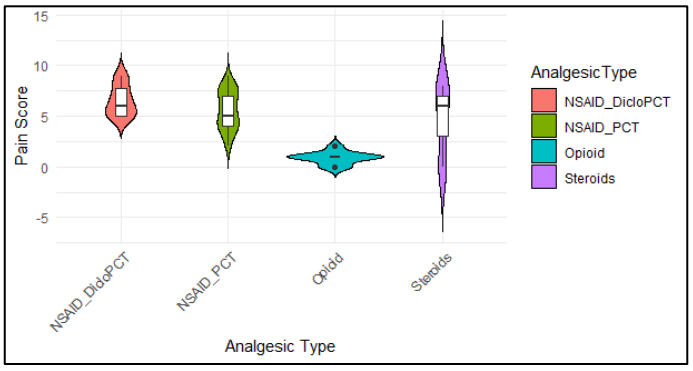
Statistical Analysis of Pain Scores Across Different Pain Management Approaches

The statistical analysis of pain scores across different analgesic types demonstrates a significant variation in pain management effectiveness, as evidenced by the chi-square test and Fisher's exact test. The chi-square value of 197 with 27 degrees of freedom, coupled with a p-value of ≤0.001, indicates that the observed differences in pain scores among the analgesic types are highly unlikely to have occurred by chance. This extremely low p-value suggests that the discrepancies in pain scores are statistically significant, reflecting meaningful differences in how each analgesic type affects pain levels. Similarly, Fisher's exact test, with a p-value also ≤0.001, supports this finding by confirming that the association between analgesic type and pain score is not due to random variation. These results collectively point to a clear and significant impact of analgesic type on pain management, highlighting that the choice of analgesic has a considerable effect on patient-reported pain, and emphasizing the importance of selecting the most effective analgesic to achieve optimal pain relief. These results are summarized in Table 9.

Pain Score Distribution Across Analgesic Types: A Violin Plot Analysis

The violin plot illustrates the distribution of pain scores across four analgesic types NSAID, Diclo, PCT (red), NSAID_PCT (green), Opioid (blue), and Steroids (purple) with pain scores ranging from -5 to 15 on the vertical axis. NSAID, Diclo, PCT and NSAID_PCT show similar distributions, with pain scores tightly clustered around 5 to 10, indicating moderate pain levels and limited variability in pain relief effectiveness, though NSAID, Diclo, PCT has a slightly wider spread at the upper end. Opioid displays a broader distribution, with pain scores ranging from 0 to 10, peaking around 5, suggesting more variability in pain relief outcomes, potentially due to differences in patient response or dosage. Steroids exhibit the widest range, with pain scores spanning from -5 to 15, peaking sharply around 5 but showing significant variability, indicating inconsistent pain relief—some patients experience substantial relief (negative scores), while others report higher pain levels (up to 15). Overall, the plot highlights that Steroids have the most variable pain relief outcomes, while NSAID-based analgesics provide more consistent moderate pain reduction, and Opioids fall in between moderate variability as shown in Figure 4.

Figure 4. Violin plot showing the distribution of pain scores by analgesic type. White boxes represent interquartile ranges, horizontal lines represent medians, and the width of each



NSAID – Nonsteroidal Anti-inflammatory Drug, Diclo – Diclofenac, PCT – Paracetamol, NSAID_DicloPCT – combination of Diclofenac and Paracetamol, NSAID_PCT – Paracetamol alone, Opioid – opioid-based pain medication (tramadol), Steroids (Hydrocortisone, Methylprednisolone).

Discussion

This study illuminates the transformative potential of Medication Therapy Management (MTM) in enhancing postoperative medication adherence and provides critical insights into the comparative efficacy of opioid versus non-opioid pain management strategies in a low- and middle-income country (LMIC) setting. The results demonstrate that structured, pharmacist-led MTM interventions achieved universal high or moderate adherence among recipients (100%, n=48), in stark contrast to the universal low adherence in the non-MTM group (100%, n=47; p≤0.001). While evaluating the impact of Medication Therapy Management (MTM) and precision analgesia on postoperative outcomes, it is important to recognize the potential influence of surgery type, as procedures vary in their associated pain levels and need for intensive pain management. The study included a diverse range of surgeries, with significant representation from miscellaneous, skin and deep tissue, and orthopedic procedures, each of which may affect recovery experiences and analgesic requirements. Statistical analysis examined the interaction between MTM and surgery type, but no significant effect was identified, suggesting that MTM's benefits on adherence and pain outcomes were consistent across different surgical categories. Nevertheless, the possibility of residual confounding remains due to limited sample sizes in some subgroups and lack of direct adjustment for surgery type in all models. Additionally, the study is limited by the absence of long-term follow-up, restricting conclusions to the immediate postoperative phase, and by factors such as single-center design, small sample size, and potential selection and reporting biases. These limitations highlight the need for future work incorporating larger, multi-center cohorts, longer outcome tracking, and more granular analysis of procedure-specific effects to fully understand and optimize postoperative care strategies. These findings align with prior evidence that pharmacist-led interventions improve adherence by 30–40% in chronic disease management[26], but this study pioneers their application in a surgical cohort, where adherence is often underprioritized.[27] The success of MTM can be attributed to its multifaceted approach, including personalized medication reviews, patient education tailored to varying health literacy levels, and proactive follow-up consultations. These elements effectively mitigate barriers such as complex polypharmacy, postoperative cognitive impairment, and limited patient understanding, which are particularly pronounced in LMICs due to constrained healthcare resources.[28]

The integration of AI-driven adherence alerts in this study represents a groundbreaking innovation, leveraging technology to deliver real-time reminders and personalized feedback. This approach not only enhances patient engagement but also sets a precedent for scalable, technology-enabled interventions in resource-limited settings. Unlike previous studies focused on chronic conditions,[29] this research demonstrates the feasibility of MTM in acute surgical care, offering a model that could be adapted across LMICs to address the global burden of postoperative complications, which contribute to 30% of hospital readmissions and $50 billion in avoidable costs annually.[30] By aligning with precision medicine principles, this study introduces a "recovery-focused surgical care" paradigm, where medication optimization and pain management are dynamically tailored to individual risk profiles, supporting the United Nations Sustainable Development Goal for equitable healthcare access.[31]

Regarding pain management, our data indicate that opioid-based regimens (tramadol) provided superior analgesia (mean NRS score: 0.78) compared to non-opioid alternatives (NSAIDs, paracetamol; mean NRS scores: 3.68–6.73; p≤0.001). This

finding challenges the 2022 CDC Clinical Practice Guideline's advocacy for non-opioid-first approaches[32] suggesting that rigid opioid-sparing protocols may not be optimal for patients with moderate to severe postoperative pain. tramadol's efficacy aligns with evidence that opioids remain essential for acute pain in specific surgical contexts,[33] yet this study uniquely contextualizes these findings in an LMIC, where access to multimodal analgesia (e.g., gabapentinoids, regional anesthesia) is often limited.[34] The moderate efficacy of diclofenac-paracetamol combinations (mean NRS: 3.68) and steroids (mean NRS: 2.00) highlights the potential of non-opioid options but underscores their inadequacy for some patients, necessitating individualized pain management plans.[35]

A novel contribution of this study is its exploration of context-specific multimodal analgesia tailored to patient factors such as surgery type, age, and comorbidity burden in an LMIC setting. The lack of significant interactions between MTM and surgery type or comorbidities (Tables 7 and 8) may reflect the small sample size (n=94) or data instability, but the heatmap analysis (Figure 3) reveals critical adherence patterns: younger patients (18–34 years) exhibited higher adherence for appendectomies and BPH surgeries, while older patients (55–85 years) showed consistently lower adherence across procedures. This suggests that age-targeted interventions, such as simplified regimens for older adults or digital tools for younger patients, could enhance MTM efficacy.[36] Additionally, the violin plot (Figure 4) highlights the variability in pain relief outcomes, with steroids showing the widest range, indicating the need for further research into patient-specific predictors of analgesic response.[37]

The study's prospective interventional design and use of validated tools (MARS-5 for adherence, NRS for pain) ensure robust findings, while advanced statistical methods, including ordinal logistic regression and linear mixed-effects modeling, account for patient-level variability and longitudinal trends. However, limitations include the single center setting and modest sample size, which may limit generalizability.[38] The predominance of male patients (76%) and emergency surgeries (64%) may also introduce selection bias, warranting broader studies to confirm findings across diverse demographics and surgical contexts.

Innovative Implications and Future Directions

This study pioneers a synergistic model combining MTM with precision analgesia, offering a scalable framework for postoperative care in LMICs. The integration of AI-driven adherence tools represents a cutting-edge approach, with potential to revolutionize care delivery through real-time monitoring and personalized interventions. Future research could explore wearable technology or mobile health applications to deliver MTM remotely, addressing access barriers in rural LMIC settings.[39] Additionally, developing predictive algorithms to identify patients at risk of non-adherence or suboptimal pain control could further refine MTM and analgesia strategies, aligning with global trends in data-driven healthcare.[40]

In pain management, our findings advocate for a balanced opioid strategy, challenging the one-size-fits-all opioid-sparing paradigm. Future studies should investigate hybrid protocols combining low-dose opioids with non-opioid adjuvants (e.g., NSAIDs, ketamine) to minimize risks while optimizing relief.[41] Incorporating non-pharmacological interventions, such as mindfulness-based pain management or physical therapy, could complement MTM and pharmacological strategies, particularly in resource-constrained settings.[41] To overcome the study's limitations, multicenter trials with larger, more diverse cohorts are essential to validate generalizability.[42] Collaborative research networks in LMICs could facilitate such studies, ensuring findings are tailored to local challenges. Longitudinal studies assessing MTM's impact on long-term outcomes, such as readmissions and quality of life, would further elucidate its sustained benefits.

In conclusion, this study establishes MTM and tailored analgesia as cornerstones of postoperative recovery, particularly in LMICs. By integrating structured pharmacist-led interventions with individualized pain management, healthcare systems can enhance adherence, optimize pain control, and reduce complications, paving the way for innovative, technology-enhanced care models that address global healthcare disparities.

Conclusion

This study pioneers a transformative framework for postoperative care by demonstrating the synergistic benefits of structured Medication Therapy Management (MTM) and precision-driven analgesia. The participation of patients at the ward played a crucial role in the advancement of medical knowledge and potential improvement of surgical practices. Through robust statistical evidence, we established that MTM significantly elevates medication adherence, while opioid-based analgesia, particularly tramadol, ensures superior pain control compared to non-opioid regimens. These outcomes are especially critical in low- and middle-income countries (LMICs), where fragmented care, resource limitations, and poor adherence compound postoperative risks. In such settings, patients may face prolonged delays in accessing surgical follow-up, limited availability of essential analgesics, inadequate pain assessment due to overburdened staff, and inconsistent continuity of care between tertiary hospitals and local health facilities. Additionally, socioeconomic constraints, out-of-pocket expenses, and limited patient education can further hinder adherence to prescribed pain management regimens, increasing the likelihood of poorly controlled pain and related complications. What sets this study apart is its integration, real-time patient education, and tailored pharmacotherapy heralding a new era of smart recovery pathways. The Medisafe Pill & Med Reminder app was

recommended to patients in this study as an adjunct for improving medication adherence and optimizing postoperative recovery. Medisafe is a free-to-download, user-friendly mobile application that enables patients to receive customized pill reminders, track medication schedules, receive refill alerts, and access drug interaction warnings. It also supports appointment management and health metric tracking without requiring registration for basic usage. Frequently lauded by digital health reviewers and clinical resources for its comprehensive and intuitive interface, Medisafe offers additional premium features such as advanced reporting, unlimited medication entry, and enhanced support for caregivers. Integrating Medisafe into the postoperative care model complements the Medication Therapy Management (MTM) intervention by empowering patients through digital support, facilitating real-time tracking, and fostering greater accountability, which together enhances adherence and contributes to improved health outcomes. by leveraging personalized data, patient-specific adherence patterns, and dynamic pain profiling, this model shifts the paradigm from reactive to proactive perioperative care. Looking forward, our findings lay the groundwork for developing digital MTM ecosystems, mobile apps, wearable integration, and machine-learning algorithms that can deliver continuous, remote medication oversight and real-time pain monitoring. These innovations could revolutionize surgical aftercare, reduce preventable readmissions, and support the global push toward equitable, tech-enabled healthcare. combining pharmacist-led MTM with precision analgesia isn't just clinically effective, it's a scalable, sustainable, and innovative blueprint for reshaping postoperative recovery, especially in healthcare systems that need it most.

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Table 2. Medication adherence levels and MARS-5 score distribution among postoperative patients

Adherence Level	Number of Patients	Avg Q1	Avg Q2	Avg Q3	Avg Q4	Avg Q5	Avg Total Score	Score Range (Min-Max)
High Adherence	30	4.12	4.33	4.33	4.33	4.46	21.5	21-25
Moderate Adherence	18	3.55	3.66	3.55	3.72	3.61	18.0	13-19
Low Adherence	47	2.06	1.97	2.06	1.82	1.76	9.70	5-12

Avg- Average, Q1- Question 1

Table 3. Association between Medication Therapy Management (MTM) interventions and medication adherence levels (N=95)

Adherence Level	MTM Given	MTM Not Given	Total
High Adherence	30	0	30
Moderate Adherence	18	0	18
Low Adherence	0	47	47
Total	48	47	**95**
Statistical Tests	$\chi^2(2) = 95.0$, $p < 0.001$ Likelihood ratio = 132,$p < 0.001$ Fisher's exact test: $p < 0.001$		**N = 95**

MTM- Medication Therapy Management

Table 4. Ordinal Logistic Regression Results for Predictors of Medication Adherence Levels

Predictor	Coefficient	Std. Error	t-value	p-value	Odds Ratio
MTM (Yes vs. No)	30.090	0.0018	16857.85	< 0.0001	1.17×10^{13}
Age (continuous)	-0.134	0.1743	-0.769	0.442	0.874
Comorbidity (count)	4.638	2.3484	1.975	0.048 *	103.33

* denotes statistical significance at p < 0.05

Table 5. Pain Management Approaches: Linear Model Coefficients, Estimated Marginal Means, and Pairwise Comparisons of Pain Scores

Pain Management Type	Linear Model Estimate	Interpretation (vs Diclo + PCT)	EMM Mean Pain Score	95% Confidence Interval	Pain Intensity
Paracetamol (PCT)	+2.98	Significantly higher pain scores (p < 0.001)	6.67	6.38 – 6.95	Severe
Steroids (Hydrocortisone, Methylprednisolone)	-1.68	Lower pain scores, borderline significant (p = 0.0189)	2.00	0.70 – 3.30	Mild
Diclofenac + Paracetamol	Reference group	Reference group	3.68	3.17 – 4.20	Moderate
Tramadol (Opioid-based)	-2.91	Significantly lower pain scores (p < 0.001)	0.78	0.03 – 1.53	None

Steroids- Hydrocortisone, Methylprednisolone, Diclo- Diclofenac, PCT- Paracetamol

Table 6. Pairwise Comparisons of Mean Pain Scores (Tukey-adjusted)

Comparison	Estimate (Mean Difference)	SE	*p*-value	Significance
OBPM (tramadol) vs. PCT	-5.89	0.404	<0.0001	***
Steroids vs. PCT	-4.67	0.670	<0.0001	***
Diclo + PCT vs. PCT	-2.98	0.297	<0.0001	***
OBPM (tramadol) vs. Diclo + PCT	-2.91	0.459	<0.0001	***
Steroids vs. Diclo + PCT	-1.68	0.704	0.0860	ns
OBPM (tramadol) vs. Steroids	-1.22	0.756	0.3742	ns

Notes: EMM = Estimated Marginal Mean; SE = Standard Error; ns = not significant; ***p < 0.001. OBPM- Opioid-based Pain Management, NSAID- Nonsteroidal Anti-inflammatory Drug, PCT-Paracetamol, Diclo- Diclofenac

Table 7. Logistic Regression Results for MTM Interactions with Surgery Type and Comorbidities

Variable	Estimate	Std. Error	z-value	p-value	Interaction Context	Interpretation
Intercept	24.57	131000	0.000	1.000	MTM × Surgery Type	No significant interaction (p > 0.05)
MTM	-5.30e-08	151300	0.000	1.000		N/A
Surgery Type: Type2	-49.13	160500	0.000	1.000		
Surgery Type: Type3	-49.13	160500	0.000	1.000		
MTM × Surgery Type: Type2	49.13	220500	0.000	1.000		
MTM × Surgery Type: Type3	49.13	220500	0.000	1.000		
Intercept	-20.57	17730	-0.001	0.999	MTM × Comorbidities	No significant interaction (p > 0.05)
MTM	41.13	21720	0.002	0.998		N/A
Comorbidities: None	19.87	17730	0.001	0.999		
Comorbidities: Severe	0.00	25070	0.000	1.000		
MTM × Comorbidities: None	-19.87	28030	-0.001	0.999		
MTM × Comorbidities: Severe	0.00	30710	0.000	1.000		

Note: No significant interaction observed (p > 0.05)
OBPM- Opioid-based Pain Management, Medication Therapy Management (MTM), N/A- Not Applicable

Table 8. Comparative effectiveness of analgesic regimens on postoperative pain control (N=94)

Pain Management	Number of Patients	Min Pain Score	Max Pain Score	Average Pain Score	Intensity of pain
OBPM (tramadol)	9	0	2	0.78	Non
NSAID (PCT)	63	5	9	6.73	Severe
NSAID (Diclo + PCT)	19	3	4	3.68	Moderate
Steroids	3	1	3	2.00	Mild

Steroids- Hydrocortisone, Methylprednisolone, OBPM- Opioid-based Pain Management, NSAID- Nonsteroidal Anti-inflammatory Drug, PCT-Paracetamol, Diclo- Diclofenac

Table 9. Distribution of postoperative pain scores by analgesic type with comparative effectiveness analysis by Chi Square test (N=95)

Analgesic Type	**Pain Score 0**	**Pain Score 1**	**Pain Score2**	**Pain Score 3**	**Pain Score 4**	**Pain Score 5**	**Pain Score 6**	**Pain Score 7**	**Pain Score 8**	**Pain Score 9**	**Total**
OBPM (tramadol)	3	5	1	0	0	0	0	0	0	0	9
NSAID (PCT)	0	0	0	0	0	15	13	12	15	9	64
NSAID (Diclo+ PCT)	0	0	0	7	12	0	0	0	0	0	19
Steroids	0	1	1	1	0	0	0	0	0	0	3
Total	3	6	2	8	12	15	13	12	15	9	**95**
Statistical Tests	$\chi^2(27) = 197$, $p < 0.001$									Fisher's exact test: $p < 0.001$	**N = 95**

OBPM- Opioid-based Pain Management, NSAID- Nonsteroidal Anti-inflammatory Drug, PCT-Paracetamol, Diclo- Diclofenac