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Anesthetic Requirements in Chronic Cannabis Users: A Systematic Review and Meta-Analysis

Perez Sui-Ling[1], Hernandez Suarez Enmanuel[1], Ubeda Arias Karla[1], D'Angelo Samuel[2], Narayanan Adhav[2], Berkun Rose[2] and Nader Nader D[2]*

[1]Herbert Wertheim College of Medicine, Florida International University, Miami, Florida, USA.

[2]Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, New York, USA.

***Correspondence:**
Berkun Rose, Jacobs School of Medicine and Biomedical Sciences, UB Downtown Gateway, 77 Goodell St., Ste 550, Buffalo, New York, USA, Tel: 716-829-6108, Fax: 716-842-4170.

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ABSTRACT

Introduction: *Chronic cannabis use is increasingly prevalent among surgical patients, yet its effects on anesthetic drug requirements remain unclear. This systematic review and meta-analysis evaluated whether chronic cannabis users require higher doses of propofol or intraoperative opioids compared with non-users undergoing procedural sedation or general anesthesia.*

Methods: *A systematic search of PubMed was performed from January 1, 2000 to January 1, 2025. Eligible studies included adult chronic cannabis users undergoing procedural sedation or general anesthesia and reported total intraoperative propofol dose or opioid administration convertible to morphine milligram equivalents (MME). Two reviewers independently extracted data and assessed risk of bias using the Cochrane Risk of Bias tool. Mean differences with 95% confidence intervals were pooled using a fixed-effects model. A prespecified subgroup analysis stratified studies by propofol outcome definition (induction dose vs. total intraoperative dose).*

Results: *Four studies (617 patients) reported propofol dosing and three studies (557 patients) reported intraoperative opioid administration. Cannabis users required significantly more propofol than non-users (mean difference 35.30 mg, 95% CI 17.25–53.35; $I^2 = 0\%$). In subgroup analysis, the three studies reporting total intraoperative propofol dose demonstrated a mean difference of 32.53 mg (95% CI 12.94–52.13; $p = 0.001$; $I^2 = 0\%$), and the test for subgroup differences was non-significant ($\chi^2 = 0.51$, $p = 0.48$). Cannabis users also required higher intraoperative opioid doses (mean difference 1.48 mg MME, 95% CI 0.69–2.27; $I^2 = 0\%$).*

Conclusions: *Chronic cannabis use is associated with increased propofol requirements and modestly increased intraoperative opioid administration. These findings were robust across subgroup analyses stratifying by propofol outcome definition, supporting the importance of preoperative cannabis use assessment and individualized anesthetic management.*

Keywords

Cannabis, Anesthesia, Propofol, Opioids, Procedural sedation, Meta-analysis.

Introduction

Cannabis is among the most widely used psychoactive substances in the United States, with expanding legalization contributing to rising prevalence among adults presenting for surgery [1,2]. Anesthesiologists increasingly encounter patients who use

cannabis regularly, yet the perioperative implications of chronic exposure remain insufficiently defined. Case reports, retrospective studies, and clinical observations suggest that chronic cannabis users may require higher doses of sedative–hypnotic or analgesic agents during procedural sedation and general anesthesia [3-6].

Repeated exposure to Δ9-tetrahydrocannabinol (THC) is associated with CB1 receptor downregulation, desensitization, and reduced receptor availability, particularly in cortical and subcortical regions involved in arousal, nociception, and anesthetic processing [7,8]. Because propofol produces hypnosis primarily through potentiation of gamma-aminobutyric acid type A (GABAA) receptor–mediated inhibition—a pathway modulated by cannabinoid signaling—chronic THC exposure may shift the propofol dose–response relationship [9,10]. Experimental work also demonstrates bidirectional cross-talk between cannabinoid and μ-opioid systems, providing a potential mechanism for altered opioid responsiveness after chronic cannabis use [11]. Additionally, prior reviews have hypothesized that propofol may interact directly with the endocannabinoid system, although this mechanism remains speculative [12].

Clinical data are consistent with these mechanistic hypotheses but remain inconsistent across studies. Several analyses reported significantly higher propofol doses in cannabis users during endoscopy, oral and maxillofacial surgery, and general anesthesia [3-6], while other studies relying on toxicology-based THC detection rather than chronic use history found no differences after adjusting for confounders [13]. Prospective pharmacology work in healthy volunteers showed minimal interaction between inhaled THC and opioid respiratory effects, though such studies involved acute administration rather than chronic exposure [14].

Given the heterogeneity of findings and lack of standardized outcome reporting, a quantitative synthesis is needed. We conducted a systematic review and meta-analysis to evaluate whether chronic cannabis users require higher doses of propofol and intraoperative opioids compared with non-users.

Methods

Study design and reporting

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline. The study protocol, including eligibility criteria, outcomes of interest, and analytic approach, was defined a priori. This review was not prospectively registered in PROSPERO; this is acknowledged as a limitation.

Search strategy

A comprehensive literature search of PubMed was performed covering January 1, 2000 to January 1, 2025. The search combined Medical Subject Headings (MeSH) and free-text terms related to cannabis (including marijuana and Δ9-tetrahydrocannabinol), anesthesia, sedation, perioperative care, and surgical procedures. Reference lists of relevant studies and reviews were manually screened to identify additional eligible articles.

Eligibility criteria

Studies were eligible if they included adult patients (≥18 years) undergoing procedural sedation or general anesthesia and compared anesthetic drug requirements between chronic cannabis users and non-users. Chronic cannabis use was variably defined across studies, typically including self-reported daily, weekly, or regular use documented during preoperative assessment. Eligible designs included randomized trials and observational cohort studies reporting extractable continuous data on intraoperative propofol or opioid dosing. Studies involving pediatric populations, acute or occasional cannabis use, cannabidiol-only products, volunteers not undergoing anesthesia, or lacking extractable dose data were excluded.

Data extraction and risk of bias

Two reviewers independently screened studies, extracted data, and assessed risk of bias, with disagreements resolved by consensus. Extracted variables included study design, patient demographics, definition of cannabis exposure, procedure type, anesthetic technique, propofol outcome definition, and total intraoperative doses of propofol and opioids. Risk of bias was assessed using the Cochrane Risk of Bias tool, with particular attention to selection bias, exposure misclassification, and confounding.

Statistical analysis

The primary outcome was total intraoperative propofol dose. The secondary outcome was total intraoperative opioid dose, standardized to intravenous morphine milligram equivalents (MME) using established equianalgesic conversion ratios. Unadjusted group means were pooled even when adjusted estimates were available, to ensure methodological consistency across studies. When standard deviations (SD) were not reported, they were reconstructed from available summary statistics using Cochrane-recommended methods. Mean differences (MD) with 95% confidence intervals (CI) were pooled using a fixed-effects model due to low observed heterogeneity. Statistical heterogeneity was assessed using the I^2 statistic and Cochran's Q test.

Because the definition of propofol requirement varied across studies (induction dose vs. total intraoperative dose), a prespecified subgroup analysis was performed stratifying studies by propofol outcome definition. A test for subgroup differences was used to evaluate whether pooling across outcome definitions was appropriate. Funnel plots were visually inspected to assess publication bias. All analyses were performed using Review Manager (RevMan) version 5.4 (The Cochrane Collaboration, Copenhagen, Denmark).

Results

Study selection

The electronic database search identified 106 records. An additional 11 studies were identified through manual citation

searching, yielding 117 records. After removal of two duplicates, 115 records underwent title and abstract screening. Thirteen articles were reviewed in full text, of which nine were excluded due to ineligible outcomes, inappropriate study design, unavailable full text, or incorrect patient population. Four studies met inclusion criteria for the propofol dosing meta-analysis, and three studies contributed data to the intraoperative opioid dosing meta-analysis. The study selection process is summarized in the PRISMA flow diagram (Figure 1).

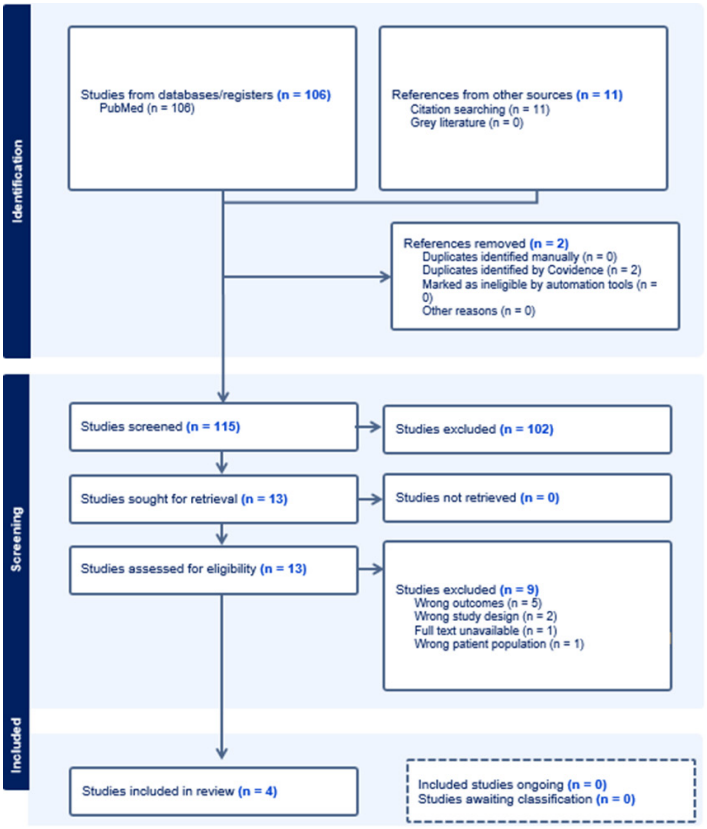

Figure 1: PRISMA flow diagram of study selection.

Characteristics of included studies

The four studies contributing propofol data [3-6] included one prospective, randomized, single-blind clinical trial [4] and three retrospective cohort studies [3,5,6], published between 2009 and 2023. Studies were conducted in the United States or Europe and encompassed gastrointestinal endoscopy under procedural sedation [3], ambulatory oral and maxillofacial surgery [6], orthopedic surgery under general anesthesia [5], and day-case general anesthesia with a laryngeal mask airway [4]. Notably, the propofol outcome definition varied: one study [4] measured induction dose required to achieve a target bispectral index (BIS) and successful laryngeal mask insertion, while the remaining three studies [3,5,6] measured total intraoperative propofol dose administered throughout the procedure. Study characteristics are summarized in (Table 1).

Across all studies, cannabis exposure was defined by self-report obtained during preoperative evaluation or anesthesia intake. Definitions of chronic use varied and included regular use, daily or weekly use, or any reported use within a defined preoperative window. No study incorporated biochemical confirmation of cannabis exposure. Information regarding cannabis potency, route of administration, and timing of last use was inconsistently reported.

Intraoperative opioid administration was reported in three studies [3,5,6] and included fentanyl and hydromorphone. Opioid doses were converted to intravenous MME for pooled analysis. Although some studies reported adjusted analyses, unadjusted group means and SD were used for meta-analysis to maintain consistency.

Risk of bias assessment

Risk of bias assessments are summarized in (Figures 2 and 3). Most included studies were judged to be at high risk of selection bias due to the absence of random sequence generation and allocation concealment in the retrospective cohort studies. One study [4] employed a prospective randomized, single-blind design and was judged to be at lower risk of selection bias. Detection bias was considered low risk across all studies, as anesthetic dosing outcomes were derived from electronic anesthesia records or prospectively recorded anesthesia charts. Performance bias was judged to be unclear, reflecting the retrospective nature of most studies.

Table 1: Characteristics of included studies.

Study	Design	Cannabis n	Total N	Setting	Propofol outcome definition	Opioid data	Cannabis exposure definition
Flisberg 2009 [4]	Prospective RCT, single-blind	30	60	Day-case GA, LMA insertion (Europe)	Induction dose to achieve BIS < 60 and successful LMA insertion	No	Self-report: cannabis use > 1x/week
Twardowski 2019 [3]	Retrospective cohort	25	250	GI endoscopy, procedural sedation (USA)	Total intraoperative propofol dose	Yes	Self-report: regular cannabis use
Holmen 2020 [5]	Retrospective cohort	30	118	Orthopedic surgery, GA (USA)	Total intraoperative propofol dose	Yes	Self-report: preoperative cannabis use
Ripperger 2023 [6]	Retrospective cohort	57	189	Ambulatory OMS, GA (USA)	Total intraoperative propofol dose	Yes	Self-report: daily/weekly cannabis use

BIS: bispectral index, GA: general anesthesia, GI: gastrointestinal, LMA: laryngeal mask airway, OMS: oral and maxillofacial surgery, RCT: randomized controlled trial.

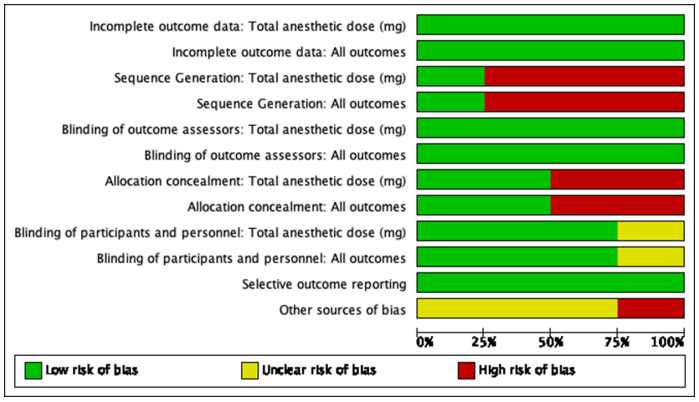

Figure 2: Risk of bias graph summarizing authors' judgments across all included studies.

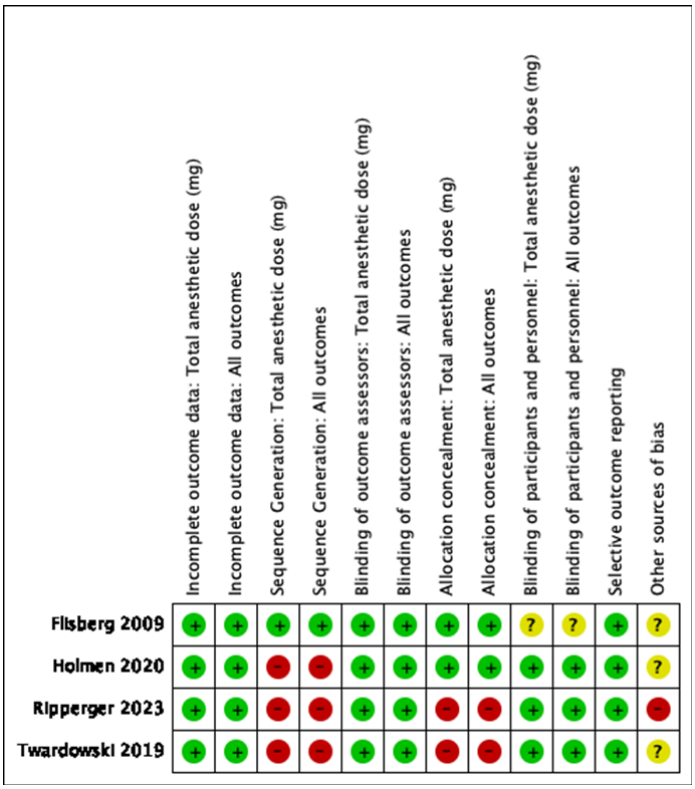

Figure 3: Risk of bias summary for individual included studies.

Incomplete outcome data and selective outcome reporting were assessed as low risk across studies. Other sources of bias, including residual confounding and exposure misclassification, were judged to be unclear to high risk due to reliance on self-reported cannabis use and inconsistent adjustment for procedural duration, concurrent sedative administration, and comorbid conditions. Overall, the evidence base was assessed as having moderate risk of bias, primarily attributable to selection bias and residual confounding.

Primary outcome: Total propofol requirement

All four studies demonstrated higher propofol dosing among cannabis users. Meta-analysis using a fixed-effects model yielded an overall MD of 35.30 mg (95% CI 17.25–53.35; p = 0.0001; I^2 = 0%; χ^2 = 0.59, p = 0.90) (Figure 3).

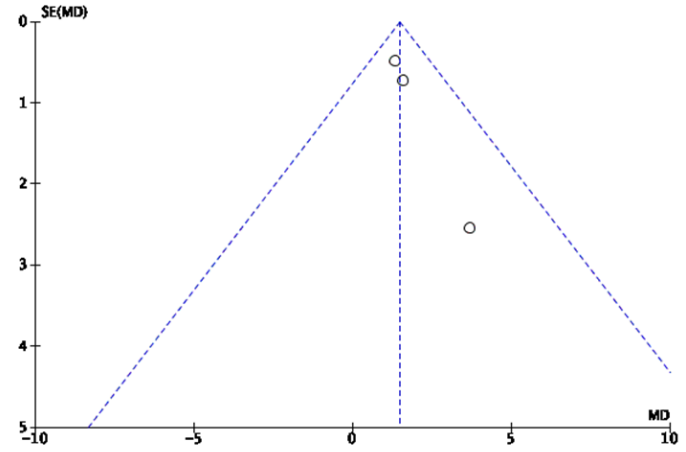

Figure 3: Forest plot of total intraoperative propofol dose comparing chronic cannabis users with non-users (fixed-effects model).

Subgroup analysis by propofol outcome definition

Because one study [4] measured induction dose while the remaining three [3,5,6] measured total intraoperative propofol dose, a prespecified subgroup analysis was performed. Among the three studies reporting total intraoperative propofol dose, the pooled MD was 32.53 mg (95% CI 12.94–52.13; p = 0.001; I^2 = 0%; χ^2 = 0.08, p = 0.96). The single study reporting induction dose [4] demonstrated an MD of 50.80 mg (95% CI 4.45–97.15; p = 0.03). The test for subgroup differences was non-significant (χ^2 = 0.51, df = 1, p = 0.48; I^2 = 0%), indicating no evidence that the effect differed by propofol outcome definition and supporting the validity of the pooled analysis (Figure 4).

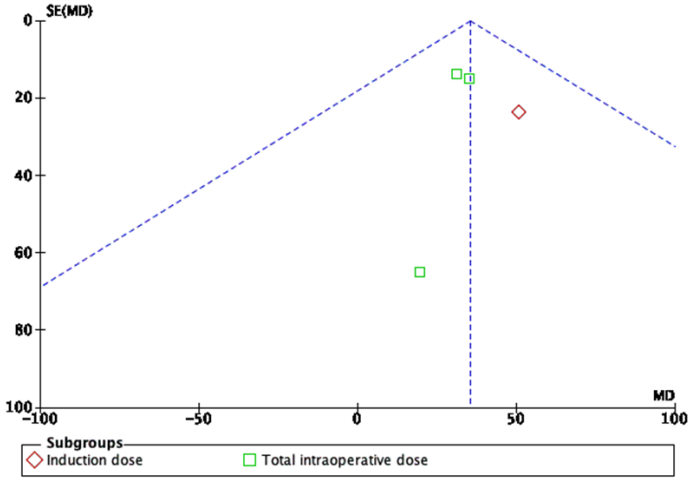

Figure 4: Forest plot of propofol dose with subgroup analysis by outcome definition (induction dose vs. total intraoperative dose).

Secondary outcome: total intraoperative opioid requirement

Three studies reported intraoperative opioid administration. After

standardization to MME, pooled analysis yielded an MD of 1.48 mg MME (95% CI 0.69–2.27; p = 0.0002; I^2 = 0%; χ^2 = 0.87, p = 0.65) (Figure 5).

Publication bias

Visual inspection of funnel plots for propofol and opioid outcomes demonstrated no apparent asymmetry (Figures 6 and 7). Given the small number of included studies, formal statistical testing for publication bias was not performed.

Additional analyses

Several studies reported co-administration of adjunct sedatives, including midazolam; however, these data were not pooled due to inconsistent reporting formats and variability in sedation protocols. One study contributing opioid data required reconstruction of SD from reported summary statistics. Sensitivity analyses using alternative variance estimates did not meaningfully alter pooled effect sizes.

Discussion

In this systematic review and meta-analysis, chronic cannabis use was associated with significantly higher anesthetic drug requirements during procedural sedation and general anesthesia. Across four studies—one randomized trial and three retrospective cohorts—cannabis users required an average of 35.30 mg more propofol than non-users, with no observed statistical heterogeneity. The association remained significant when restricted to the three studies measuring total intraoperative propofol dose (MD 32.53 mg, 95% CI 12.94–52.13; p = 0.001), and the test for subgroup differences confirmed no significant variation across propofol outcome definitions (p = 0.48). Three studies demonstrated a modest but statistically significant increase in intraoperative opioid administration of 1.48 mg MME.

The increase in propofol requirements is biologically plausible. Chronic THC exposure produces CB1 receptor downregulation and desensitization, as demonstrated in positron emission tomography studies of daily cannabis users showing approximately 20% reduction in CB1 receptor availability in cortical and subcortical regions relevant to anesthetic action [7,8]. Because cannabinoid signaling modulates GABAergic neurotransmission—the primary mechanism through which propofol exerts its hypnotic effects—disruption of this pathway may necessitate higher doses to achieve equivalent sedation or hypnosis [9,10]. Preclinical studies further demonstrate that cannabinoids interact with glutamatergic and serotonergic pathways, which may additionally alter anesthetic sensitivity.

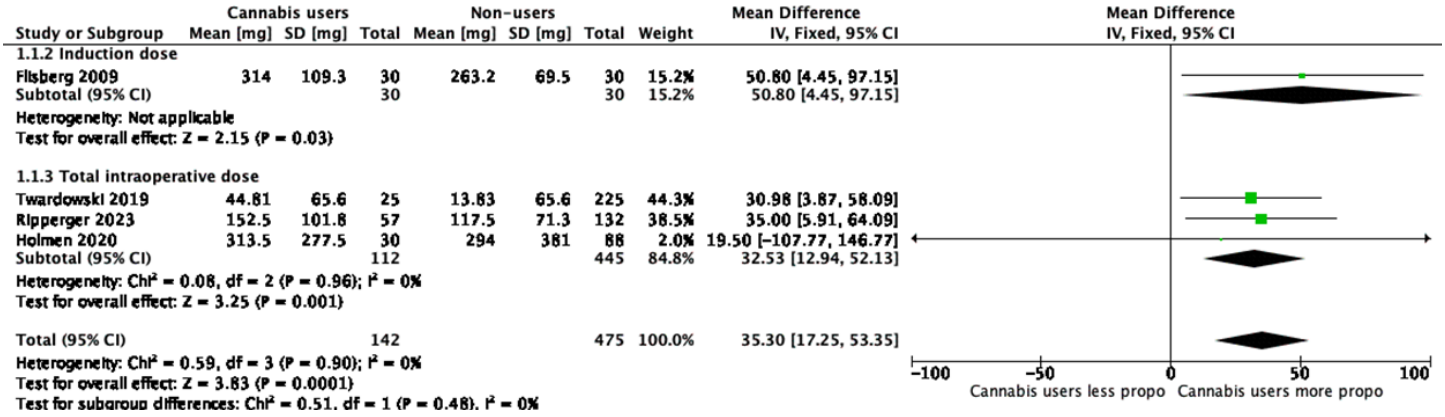

Figure 5: Forest plot of total intraoperative opioid dose (morphine milligram equivalents) comparing chronic cannabis users with non-users (fixed-effects model).

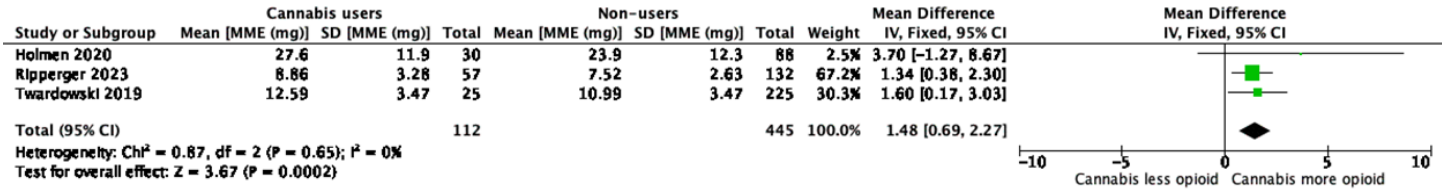

Figure 6: Funnel plot of total intraoperative propofol dose comparing chronic cannabis users with non-users.

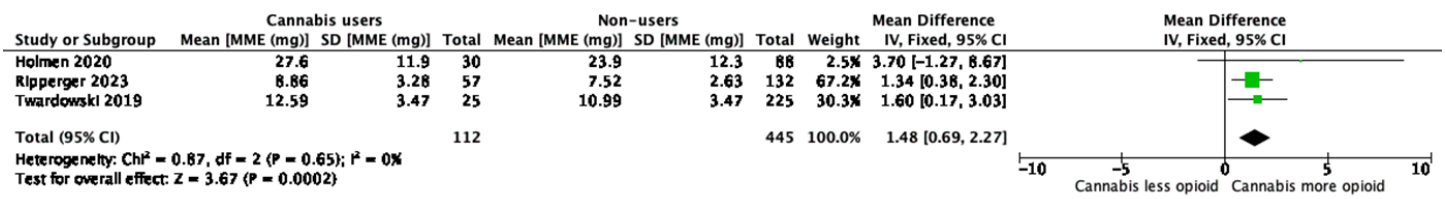

Figure 7: Funnel plot of total intraoperative opioid dose (morphine milligram equivalents) comparing chronic cannabis users with non-users.

The modest increase in opioid requirements is consistent with known interactions between the cannabinoid and opioid systems, including shared intracellular signaling pathways and reciprocal modulation of μ-opioid receptor function following chronic cannabinoid exposure [11]. Although the absolute difference in opioid dosing was smaller than that observed for propofol, this finding suggests partial cross-tolerance affecting intraoperative analgesic requirements.

Our results align with recent observational studies and meta-analyses. Goudra and Green [15] demonstrated that marijuana use independently predicted higher propofol and adjunct sedative dosing during gastrointestinal endoscopy.

Baker et al. [16] reported an average increase of 47 mg in propofol requirements among cannabis users, with subgroup analysis showing increases of 30.57 mg during general anesthesia and 53.02 mg during endoscopic procedures. Ekrami et al. [17] reported increased postoperative opioid consumption among cannabis users. Conversely, other cohorts have reported no significant differences in anesthetic dosing between THC-positive and THC-negative patients [13].

Differences in exposure classification, cannabis potency, timing of last use, and institutional protocols likely contribute to these discrepancies.

Several limitations should be acknowledged. The included studies comprised one randomized trial and three retrospective cohorts, introducing potential selection bias and residual confounding. Cannabis exposure was based on self-report without biochemical verification, which may result in exposure misclassification and bias toward the null.

Definitions of cannabis use varied across studies, with limited information on potency, route of administration, or recency of use. The number of included studies was small, precluding additional subgroup analyses and limiting assessment of publication bias. One study required reconstruction of SD from summary statistics, although sensitivity analyses indicated minimal impact on pooled estimates. The definition of propofol requirement varied across studies; however, subgroup analysis demonstrated no significant difference by outcome definition, and heterogeneity remained at 0% in both the overall and subgroup analyses. Finally, this review was not prospectively registered in PROSPERO, which limits the ability to verify adherence to a prespecified analytic plan, though eligibility criteria, outcomes, and analytic methods were defined a priori.

Despite these limitations, the consistency of effect sizes and absence of heterogeneity strengthen confidence in the observed association. These findings have clinical relevance given the high prevalence of cannabis use, which affects nearly 20% of U.S. adults and is more common among younger populations [18]. Failure to anticipate increased anesthetic requirements may increase the risk of inadequate sedation, patient movement, or hemodynamic instability during induction. Routine preoperative assessment of cannabis use should be incorporated into anesthetic evaluation, and clinicians should be prepared to titrate sedative and analgesic agents accordingly.

Conclusion

Chronic cannabis use is associated with increased propofol requirements and modestly increased intraoperative opioid dosing during procedural sedation and general anesthesia. These findings were robust across subgroup analyses stratifying by propofol outcome definition. As cannabis use becomes increasingly prevalent, anesthesiologists should recognize cannabis exposure as a clinically relevant factor influencing anesthetic management. Prospective studies with standardized exposure definitions and mechanistic endpoints are needed to further refine dosing strategies and optimize perioperative care in this population.

References

1. Azofeifa A, Mattson ME, Schauer G, et al. National estimates of marijuana use and related indicators—National Survey on Drug Use and Health, United States, 2002–2014. MMWR Surveill Summ. 2016; 65: 1-28.
2. Hasin DS, Kerridge BT, Saha TD, et al. Prevalence and correlates of DSM-5 cannabis use disorder, 2012–2013: findings from the National Epidemiologic Survey on Alcohol and Related Conditions–III. Am J Psychiatry. 2016; 173: 588-599.
3. Twardowski MA, Link MM, Twardowski NM. Effects of cannabis use on sedation requirements for endoscopic procedures. J Am Osteopath Assoc. 2019; 119: 307-311.
4. Flisberg P, Paech MJ, Shah T, et al. Induction dose of propofol in patients using cannabis. Eur J Anaesthesiol. 2009; 26: 192-195.
5. Holmen IC, Beach JP, Kaizer AM, et al. The association between preoperative cannabis use and intraoperative inhaled anesthetic consumption: a retrospective study. J Clin Anesth. 2020; 67: 109980.
6. Ripperger D, Atte A, Ritto F. Cannabis users require more anesthetic agents for general anesthesia in ambulatory oral and maxillofacial surgery procedures. J Oral Maxillofac Surg. 2023; 81: 1460-1465.
7. Hirvonen J, Goodwin RS, Li CT, et al. Reversible and regionally selective downregulation of brain cannabinoid CB1 receptors in chronic daily cannabis smokers. Mol Psychiatry. 2012; 17: 642-649.
8. D'Souza DC, Cortes-Briones J, Creatura G, et al. Rapid changes in CB1 receptor availability in cannabis-dependent males after abstinence from cannabis. Biol Psychiatry Cogn Neurosci Neuroimaging. 2016; 1: 60-67.
9. Franks NP. Molecular targets underlying general anaesthesia. Br J Pharmacol. 2006; 147: S72-S81.
10. Bloomfield MAP, Hindocha C, Green SF, et al. The neuropsychopharmacology of cannabis: a review of human imaging studies. Pharmacol Ther. 2019; 195: 132-161.

11. Scavone JL, Sterling RC, Van Bockstaele EJ. Cannabinoid and opioid interactions: implications for opiate dependence and withdrawal. Neuroscience. 2013; 248: 637-654.
12. Sajdeya R, Treggiari MM, Narouze S. Review of cannabis use and propofol anesthesia: recent insights and clinical implications. Curr Opin Anaesthesiol. 2025; 38: 660-668.
13. King DD, Stewart SA, Collins-Yoder A, et al. Anesthesia for patients who self-report cannabis (marijuana) use before esophagogastroduodenoscopy: a retrospective review. AANA J. 2021; 89: 205-212.
14. van Dam CJ, Schrier R, van Velzen M, et al. Inhaled Δ9-tetrahydrocannabinol does not enhance oxycodone-induced respiratory depression: randomized controlled trial in healthy volunteers. Br J Anaesth. 2023; 130: 485-493.
15. Goudra B, Green M. Perioperative repercussions of cannabis use—implications for GI endoscopy sedation. J Clin Med. 2025; 14: 7028.
16. Baker MB, Binda DD, Nozari A, et al. Quantitative analysis of propofol dosage in cannabis users: a systematic review and meta-analysis. J Clin Med. 2025; 14: 858.
17. Ekrami E, Sari S, Kopac O, et al. Association between cannabis use and opioid consumption, pain, and respiratory complications after surgery: a retrospective cohort analysis. Anesth Analg. 2024; 139: 724-733.
18. Substance Abuse and Mental Health Services Administration. Key substance use and mental health indicators in the United States: results from the 2022 National Survey on Drug Use and Health. Rockville (MD): SAMHSA. 2023.
19. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021; 372: n71.