Introduction: Perioperative low-dose intravenous ketamine may be a useful addition in pain management regimens. Randomised Controlled Trials (RCTs) of IV ketamine have produced remarkably variable efficacy results. It would be useful to know the evidence for the correct role of ketamine in postoperative pain control. Previous systematic reviews have included all routes of ketamine administration and assumed a fixed-effects model. Heterogeneity between studies is significant and this was addressed by narrowing inclusion criteria, using a random effects model, and performing subgroup analyses on groups designated prior to data collection. Metaregression was used to analyse the effect of total dose of ketamine.

Methods: High-quality RCTs that were randomized, double-blinded and placebo-controlled using intravenous ketamine as the treatment group were included. PubMed, Embase, and the Cochrane Library were searched, and manufacturers contacted to find RCTs. Primary outcome was total dose of narcotic consumed postoperatively. Studies were excluded if they used regional anesthesia. No limitation was placed on patient age or language of publication. P-values of subgroups were corrected for multiple comparisons. Analysis was by standard differences in means.

Results: Sixty-three studies were analyzed, with 80 comparison arms. A clear reduction in total narcotic consumed was observed across all studies (p<0.0001). Calculations of publication bias were negative. Ketamine was unhelpful for prostate, dental, head & neck, hernia, laminectomy/disectomy, lower abdominal, or coronary artery bypass graft surgery. It was helpful for orthopedic/limb, mid- or upper- abdominal, and thoracic surgery. Efficacy was not different between adult and pediatric studies. The dose of ketamine had little influence on outcome. Timing of administration (pre- or post-incision) had no influence. In particular, there was no pre-emptive effect. There was no difference from placebo for psychic side-effects, postoperative nausea and vomiting measures, or sedation.

Discussion: Implications for clinicians: Perioperative low-dose ketamine is especially useful when the anticipated postoperative pain is severe, and it may be given at any point (preemptively, intraoperatively, postoperatively) and in any method (bolus, infusion, PCA co-administration). Intuitively, an increased postoperative VAS score correlates with painful surgery such as upper abdominal and thoracic incisions. Future research: There is little to be gained from more RCTs of surgery known to produce mild pain. Further study should be directed towards unanswered questions, and should concentrate on studying patients at risk for severe postoperative pain, for respiratory depression, and patients who continue to experience severe postoperative pain despite routine treatment. There may be benefit in those patients for whom narcotic sparing is important, such as patients that are intolerant to narcotic side effects and those with significant histories of postoperative nausea and vomiting.