

# INPLASY PROTOCOL

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**Review Stage at time of this  
submission:** Data analysis.

**Conflicts of interest:** N/A.

## Lidocaine infusion on bowel function recovery after major colorectal surgery: a systematic review with meta-analysis, trial sequential analysis, and meta-regression

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**Review question / Objective:** Do lidocaine infusion shorten the time to flatus / defecation in patients receiving major colorectal surgery?

**Condition being studied:** However, some limitations were observed in these meta-analyses. They did not give any grading on the certainty of evidence (CoE) for their positive results. They also did not discuss the influence of risk of bias (RoB) in enrolled RCTs, which is one of the critical domain in the appraisal tool "A Measurement Tool to Assess systematic Reviews 2 (AMSTAR2)".

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 July 2020 and was last updated on 25 July 2021 (registration number INPLASY202070023).

### INTRODUCTION

**Review question / Objective:** Do lidocaine infusion shorten the time to flatus / defecation in patients receiving major colorectal surgery?

**Rationale:** Intravenous lidocaine infusion (IVF-Lido) during perioperative period is

currently one of the most promising potential candidates to speed up bowel function recovery after major colorectal surgery (mCRS). However, inconsistent conclusions were shown in previous meta-analyses.

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analyses. They did not give any grading on the certainty of evidence (CoE) for their positive results. They also did not discuss the influence of risk of bias (RoB) in enrolled RCTs, which is one of the critical domain in the appraisal tool “A MeaSurement Tool to Assess systematic Reviews 2 (AMSTAR2)”.

## METHODS

**Search strategy:** The two key concepts used in the search, "colorectal surgery" and "lidocaine", included their synonyms (42 free-text terms plus truncation symbols when appropriate) and controlled vocabulary (19 MeSH terms and 22 Emtree terms). Embase was used as the initial database for the development of search strategy, and the search syntax was appropriately translated to individual databases. The highly sensitive search filters were adopted for identifying randomized trials. The authors extended the searching date till 5 April 2021.

**Participant or population:** Patient receiving major colorectal surgery.

**Intervention:** Continuous lidocaine infusion (+).

**Comparator:** Continuous lidocaine infusion (-).

**Study designs to be included:** The inclusion criteria were: 1) randomized controlled trials (RCTs) that involved patients undergoing major colorectal surgery; 2) intervention groups

**Eligibility criteria:** RCTs not only enrolling patients with colorectal surgery, or no available results.

**Information sources:** Embase, MEDLINE\_Ovid, Cochrane CENTRAL, Scopus, CNKI, Index to Taiwan Periodical Literature System, WHO ICTRP, Other sources: clinicaltrials.gov, references in review/ other systemic review articles.

**Main outcome(s):** Time to first flatus and time to first defecation.

**Additional outcome(s):** Meta-regression of time to flatus or time to defecation about surgical type, unit body weigh unit time of lidocaine dosage, changes of lidocaine treatment, and pain control condition in control groups

**Data management:** Data were extracted from the eligible studies included by two authors (Chen PC, Lai PC), and a senior author (Huang YT) finalized the data. The data extracted from the eligible studies included authors, publication year, number of patients, procedure type, lidocaine injection dosage in intervention and control groups, and outcomes of bowel function recovery and visual pain analog scores.

**Quality assessment / Risk of bias analysis:** The risk of bias and internal validity were assessed by two authors (Lai PC and Huang YT) independently using the “Risk-of-bias tool 2.0 (RoB 2.0)” for RCTs developed by the Cochrane collaboration. Divergences were resolved by consensus. The results of RoB 2.0 was drawn through the “Risk-of-Bias Visualization tool”.

**Strategy of data synthesis:** The primary outcome was bowel function recovery, including first flatus passage and first defecation after surgery. Secondary outcome included lidocaine dosage and visual analog score (VAS).

**Subgroup analysis:** Subgroup meta-analysis: some concerned or low overall risk of bias, another one: high overall risk of bias. Meta-regression about surgical type, unit body weigh unit time of lidocaine dosage, changes of lidocaine treatment, and pain control condition in control groups

**Sensibility analysis:** Meta-regression of time to flatus or time to defecation about surgical type, unit body weigh unit time of lidocaine dosage, changes of lidocaine treatment, and pain control condition in control groups

**Language:** no restriction.

**Country(ies) involved:** Taiwan.

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**Other relevant information:** This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA) 2020. A priori power of the meta-analysis was calculated by the R package “dmetar” with random effect model. Regarding publication bias, it was assessed through visual inspection using funnel plots and quantified by the Doi plot with Luis Furuya-Kanamori (LFK) index (MetaXL version 5.3, EpiGear International Pvt., Ltd.). Values of LFK index outside the interval between -1 and +1 were defined as asymmetry, indicating the probability of publication bias. We assessed the certainty of evidence in each outcome by using GRADE methodology.

**Keywords:** lidocaine, colorectal surgery, flatus, defecation, meta-analysis, trial sequential analysis, meta-regression.

**Contributions of each author:**

**Author 1 - Po-Chuan Chen** - database search, data extraction, and drafting of the manuscript.

**Author 2 - Chao-Han Lai** - critical analysis, interpretation of the data, and providing informative suggestions for the preparation of the manuscript.

**Author 3 - Ching-Ju Fang** - database search, PRISMA completion, reference editing of the manuscript.

**Author 4 - Pei-Chun Lai** - double confirmation of the enrolled studies and data, concept of the meta-analysis, statistical analyses, grading of bias risk, and revision of the manuscript.

**Author 5 - Yen-Ta Huang** - double confirmation of the enrolled studies and data, concept of the meta-analysis, statistical analyses, grading of bias risk, and revision of the manuscript.