**Meta-Analysis** 

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# INPLASY PROTOCOL

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### INTRODUCTION

Review question / Objective: (P), Adults with a scheduled surgery or intervention; (I), patients administrated analgesia before surgical insult; C) patients administrated analgesia after surgical insult; (O)postoperative pain or other postoperative outcomes available in the study .How does pre-emptive analgesia prevent the use of analgesia on postoperative pain.

Condition being studied: Adults with a scheduled surgery or intervention, patients administrated analgesia before surgical insult, patients administrated analgesia after surgical insult, and postoperative pain

**Review question / Objective:** (P), Adults with a scheduled surgery or intervention; (I), patients administrated analgesia before surgical insult; C) patients administrated analgesia after surgical insult; (O)postoperative pain or other postoperative outcomes available in the study .How does preemptive analgesia prevent the use of analgesia on postoperative pain.

Pre-emptive versus Preventive Analgesia for Postoperative Pain: A Systematic Review and

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Condition being studied: Adults with a scheduled surgery or intervention, patients administrated analgesia before surgical insult, patients administrated analgesia after surgical insult, and postoperative pain or other postoperative outcomes available in the study.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 June 2023 and was last updated on 01 June 2023 (registration number INPLASY202360005). or other postoperative outcomes available in the study.

# **METHODS**

Search strategy: A literature search was conducted on five databases (PubMed, ProQuest, Scopus, ScienceDirect, ClinicalKey) on March 8, 2022. Handsearching was also done to retrieve more studies. The following query search was utilized in all five major databases: preemptive AND preventive analgesia AND postoperative pain. electronic bibliographic databases include PubMed, ProQuest, Scopus, ScienceDirect, ClinicalKey.

Participant or population: Adult participant.

Intervention: The intervention group that being bevaluate in this review is an adult who is scheduled to get a surgery and administered to get an analgesia before and after the surgical insult.

**Comparator:** All articles were RCT studies comparing pre-emptive analgesia with preventive analgesia.

Study designs to be included: double-blind, randomized, controlled trials study design.

Eligibility criteria: Inclusion: double-blind, randomized, controlled trials study design. Exclusion criteria of articles are: the study design is other than RCT, the study has undesirable intervention or population, and the study is not available in English.

Information sources: Article searching was done on five databases (PubMed, ProQuest, Scopus, ScienceDirect, ClinicalKey). Hand-searching was also done to search for additional articles. We have only included double-blind, randomized, controlled trials (RCT). A total of fifteen articles were included. All articles were RCT studies comparing pre-emptive analgesia with preventive analgesia. The quality of the included studies was evaluated with Cochrane risk-of-bias assessment tools. Quantitative analysis was performed by Review Manager 5.4. Main outcome(s): The outcome measures were defined below (i) visual analogue scale (VAS): a psychometric measuring instrument designed to rate the severity of pain; (ii) verbal rating scale (VRS): adjectives used to describe the severity of pain; (iii) numerical rating scale (NRS): a numeric scale used to rate the severity of pain; (iv) duration of analgesia (DA): time elapsed during analgesia; (v) time to rescue analgesic (TRA): time needed from the postoperative period to the first request for additional analgesic use; (vi) analgesic use (AU): analgesic usage experienced by all patients; and (vii) adverse effects (AEs): Total patients experiencing adverse effects such as nausea and vomiting. Among all the outcomes, VAS/VRS/NRS was considered the primary outcome. We included these three because each of them had a uniform rating of pain, which starts from 0 (no pain at all) to 10 (maximum imaginable pain).

Data management: The process of literature selection is based on the "PRISMA 2009 Flow Diagram" as seen in Figure 1. From database searching and other sources, a total of 661 study articles were found. One study was found from manual searching. After the removal of duplicates. 627 articles were left for initial screening. The selection of articles was conducted with a consensus of 3 investigators (RF, APN, and MAIM), 610 articles were eventually excluded as they did not meet our inclusion criteria based on the title and abstract. The full-text screening was conducted on the 17 articles left, 2 articles were left out because one article was not available in English and the other study has the pediatric population as the subject of the study. Therefore, we have 15 articles eligible to be included in this systematic review and meta-analysis.

Quality assessment / Risk of bias analysis: Cochrane risk-of-bias assessment tools. Evaluations were carried out by ART and RF. independently. Each study will be assessed as "low-risk", "high-risk" or "unclear risk" based on seven evidencebased domains. The domains are: "Random sequence generation (selection bias)". "Allocation concealment (selection bias)", "blinding of participants and personnel (performance bias)", "blinding of outcome assessment (detection bias)", "incomplete outcome data (attrition bias)", "selective reporting (reporting bias)", "other bias".

Strategy of data synthesis: Statistical analysis was performed using Review Manager version 5.4. Weighted mean differences (MDs) were used to evaluate continuous data. These continuous data include VAS, VRS, NRS, DA, TRA, and AU. Meanwhile, risk ratio (RR) was used to evaluate dichotomous data such as AEs. The Mantel-Haenszel  $\chi$ 2 test and the I2 test were used to evaluate the heterogeneity of the study. If the I2 value was more than 50%, this indicated a high level of heterogeneity.

Subgroup analysis: Statistical methods: methods include subgroup-specific metaanalyses

Interpretation of results: The process of literature selection is based on the "PRISMA 2009 Flow Diagram" a total of 661 study articles were found. One study was found from manual searching. After the removal of duplicates, 627 articles were left for initial screening. 34 articles records after duplicates removed. 627 record screened and 610 articles that being excluded. Full text articles aasessed for eligibility and 2 articles being excluded because the text is in korean and include pediatric population. the rest 15 studies included in qualitative synthesis.

Sensitivity analysis: Independently. Each study will be assessed as "low-risk", "highrisk" or "unclear risk" based on seven evidence-based domains. The domains are: "Random sequence generation (selectionbias)".

Language restriction: English.

Country(ies) involved: Indonesia.

**Keywords:** Pre-emptive analgesia, preventive analgesia, postoperative pain, randomized controlled trial.

#### Contributions of each author:

Author 1 - aida rosita tantri - Conception and design of the case series, Interpretation and analysis of data, Final approval of the manuscript.

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Author 3 - Hansen Angkasa - Interpretation and analysis of data, Drafting the manuscript.

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Author 5 - Muhammad A. I. Maulana -Interpretation and analysis of data, Drafting the manuscript.