INPLASY

Predictors of clinically meaningful pain relief after surgery for spinal metastases: a systematic review and meta-analysis protocol

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ADMINISTRATIVE INFORMATION

Support - Nil.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202640011

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 4 April 2026 and was last updated on 4 April 2026.

INTRODUCTION

Review question / Objective Objective: To identify and synthesize evidence on preoperative, intraoperative, and postoperative predictors of clinically meaningful pain relief following surgery for spinal metastases.

Review question: Among adults with spinal metastases undergoing surgical treatment (P), which demographic, tumor, neurological, surgical, and adjuvant treatment factors (E) are associated with clinically meaningful pain relief (O) compared with non-response (C)?

PICO framework:
P (Population): Adults (≥18 years) with spinal metastases undergoing surgical treatment
E (Exposure): Pre-/peri-/postoperative prognostic factors (demographic, tumor, neurological, surgical, adjuvant)
C (Comparator): Within-study comparison: pain responders vs non-responders
O (Outcome): Clinically meaningful pain relief defined by MCID-based thresholds (≥2-point VAS/NRS reduction or ≥30% relative reduction) as primary definition; any author-defined threshold as sensitivity definition.

Rationale Spinal metastases affect up to 40% of patients with systemic malignancy and represent a major source of pain and disability. Surgery, including decompression, stabilization, and separation surgery, is commonly performed to alleviate pain. However, pain relief following surgery is not uniform, and a meaningful proportion of patients continue to experience significant pain postoperatively. The concept of the minimal clinically important difference (MCID) has gained increasing attention in spine surgery outcomes research, yet no prior systematic review has specifically synthesized evidence on predictors of clinically meaningful pain response in the spinal metastasis surgical population. Identifying preoperative factors that predict which patients will achieve meaningful pain relief would enhance surgical decision-making, facilitate informed

consent, and allow for tailored multimodal treatment planning.

A search of PROSPERO, INPLASY, and the Cochrane Library confirmed that no ongoing or completed systematic review addresses this specific question.

Condition being studied Spinal metastases (metastatic tumors affecting the vertebral column) in adult patients. Spinal metastases can cause severe pain, neurological deficits, spinal instability, and reduced quality of life. Surgical management includes posterior decompression, spinal stabilization with instrumentation, corpectomy, separation surgery, and minimally invasive techniques. The condition of interest is pain experienced by these patients and the factors that predict whether surgery will result in clinically meaningful pain improvement.

METHODS

Search strategy Four electronic databases were searched: PubMed/MEDLINE, Embase, Cochrane CENTRAL, and Scopus, from January 2010 through April 2026. The search combined three concept blocks using Boolean operators:

Block A (Spinal metastases): MeSH terms ("Spinal Neoplasms"; "Spine" AND "Neoplasm Metastasis") + free-text (spinal metastas*, vertebral metastas*, MSCC, MESCC, separation surgery)

Block B (Surgery): MeSH terms ("Spinal Fusion"; "Decompression, Surgical"; "Laminectomy") + free-text (surgery, decompression, corpectomy, stabilization, instrumentation, fusion, en bloc, resection)

Block C (Pain): MeSH terms ("Pain"; "Pain Measurement"; "Visual Analog Scale") + free-text (pain, VAS, NRS, numeric rating, pain score, pain relief, analgesia)

Combined: A AND B AND C

Database-specific syntax was adapted for each platform (MeSH for PubMed, Emtree for Embase, MeSH descriptors for Cochrane, TITLE-ABS-KEY for Scopus). The complete search strategies are available in the supplementary file.

Supplementary searches: backward citation screening of included studies, forward citation tracking via Google Scholar, trial registry searches (ClinicalTrials.gov, WHO ICTRP), and conference abstract screening (AANS, CNS, AOSpine, Eurospine).

Participant or population Inclusion: Adults (≥18 years) with histologically or radiologically confirmed spinal metastases undergoing any surgical treatment.

Exclusion: Primary spinal tumors (chordoma, chondrosarcoma, osteosarcoma, intradural tumors); pediatric patients (<18 years); studies where metastatic-specific data cannot be extracted from mixed cohorts.

Intervention Any surgical treatment for spinal metastases, including: posterior decompression (laminectomy), spinal stabilization with instrumentation (pedicle screw fixation), corpectomy, separation surgery, spondylectomy (en bloc resection), and minimally invasive surgical (MIS) approaches. Surgery may be performed alone or in combination with adjuvant radiotherapy and/or systemic therapy.

Excluded interventions: Vertebroplasty or kyphoplasty alone (without open/MIS decompression or stabilization); radiation therapy alone; systemic therapy alone; stereotactic radiosurgery alone (without surgical component).

Comparator Within-study comparison: pain responders vs non-responders. No between-group comparator is required, as this review examines prognostic factors (predictors) rather than comparing interventions. Studies reporting multivariable or univariable predictor analyses of pain outcomes are eligible.

Study designs to be included Randomized controlled trials (RCTs), prospective cohort studies, retrospective cohort studies, and registry-based studies. Case series with ≥10 patients are eligible if they report predictor-outcome associations for pain.Excluded: Case reports, case series <10 patients, editorials, letters, conference abstracts without full text, narrative reviews, and systematic reviews (used for backward citation screening only).

Eligibility criteria Inclusion criteria:
1. Adults ≥18 years with spinal metastases undergoing surgery
2. Pain measured by a validated instrument (VAS, NRS, BPI, or equivalent)
3. At least one pre-/peri-/postoperative factor analyzed for association with pain outcome
4. Published 2010–2026 (inclusive)

5. English language (or non-English with extractable data from tables/figures)
6. Sample size ≥10 patients

Exclusion criteria:
1. Primary spinal tumors
2. Vertebroplasty/kyphoplasty alone
3. Radiation or systemic therapy alone
4. Mixed primary + metastatic cohorts (unless metastatic subgroup extractable)
5. No pain outcome or no predictor analysis
6. Reviews, editorials, case reports.

Information sources Electronic databases: PubMed/MEDLINE, Embase, Cochrane CENTRAL, Scopus
Trial registries: ClinicalTrials.gov, WHO ICTRP
Grey literature: AANS, CNS, AOSpine, Eurospine, CSRS conference abstracts (last 5 years)
Other: Backward citation screening of included studies; forward citation tracking (Google Scholar).

Main outcome(s) Primary outcome: Clinically meaningful pain relief after surgery for spinal metastases.

Primary definition: Pain response defined by MCID-based thresholds (≥2-point reduction on 0–10 NRS/VAS or ≥30% relative reduction from baseline).

Sensitivity definition: Any author-defined threshold of clinically meaningful pain improvement.

Measurement: VAS (0–10 or 0–100 mm), NRS (0–10), BPI (Brief Pain Inventory), or equivalent validated pain instrument.

Additional outcome(s) Secondary outcomes:
1. Absolute mean pain score change (pre- vs postoperative VAS/NRS)
2. Quality of life improvement (EQ-5D, COMI, ODI, SOSGOQ, SF-36)
3. Functional/neurological improvement (Frankel/ASIA grade, ambulatory status, KPS/ECOG)
4. Postoperative complication rate
5. Analgesic use change (morphine equivalent daily dose).

Data management Records were managed using EndNote for deduplication and screening. Deduplication was performed using a three-step algorithm: (1) DOI matching, (2) exact normalized title matching, and (3) fuzzy title matching (Jaccard similarity ≥0.85). Title screening was performed using a validated keyword-based classification system. Full-text screening was performed independently against eligibility criteria.

Data were extracted into a standardized Excel template with four domains: study characteristics, pain outcomes, predictor data (one row per predictor-outcome association), and quality assessment.

All statistical analyses were performed using Python 3.12 (SciPy, NumPy, Matplotlib).

Quality assessment / Risk of bias analysis Study quality was assessed using the Newcastle-Ottawa Scale (NOS) for cohort studies, with a maximum of 9 stars across three categories: Selection (4 stars), Comparability (2 stars), and Outcome (3 stars).

Quality thresholds: Good quality ≥7 stars; Fair quality 5–6 stars; Poor quality <5 stars.

Certainty of evidence was assessed using the GRADE framework (Grading of Recommendations, Assessment, Development, and Evaluations) for each outcome, starting at LOW for observational studies and applying downgrade criteria for risk of bias, inconsistency, indirectness, imprecision, and publication bias.

Strategy of data synthesis Quantitative synthesis:
1. Pain improvement was pooled across studies using a DerSimonian-Laird random-effects model (mean difference on 0–10 scale).
2. Heterogeneity was assessed using I^2, Cochran's Q, and prediction intervals.
3. For predictor-specific data: odds ratios (OR) with 95% CIs were planned for pooling when ≥3 studies reported compatible outcomes. Given insufficient homogeneous data, a direction-of-effect synthesis framework (SWiM guideline) was used.

Sensitivity analyses:
1. Leave-one-out analysis
2. Restriction to studies with reported (non-estimated) SDs
3. Restriction to prospective studies only
4. Restriction to good-quality studies (NOS ≥7)

Publication bias: Funnel plot + Egger's test planned for outcomes with k≥10; not performed when k<10 (stated per Cochrane Handbook §13.3.5).

Narrative synthesis: Direction-of-effect table and harvest plot used to synthesize predictor-level evidence across studies with heterogeneous effect measures.

Subgroup analysis Pre-specified subgroup analyses:
1. Study design: prospective vs retrospective

2. Pain instrument: VAS/NRS vs BPI vs multi-instrument
3. Follow-up timepoint: short-term (≤1 month) vs medium-term (1–6 months) vs long-term (>6 months)
4. Study quality: good (NOS ≥7) vs fair/poor (NOS <7)

Note: Subgroup analyses were planned contingent on sufficient studies (k≥3) per subgroup. If insufficient, results are reported narratively.

Sensitivity analysis 1. Leave-one-out: sequential removal of each study to assess influence on the pooled estimate.
2. Model sensitivity: comparison of DerSimonian-Laird vs REML estimators.
3. SD estimation sensitivity: restriction to studies with reported/calculated SDs (excluding estimated values).
4. Risk of bias sensitivity: restriction to good-quality studies (NOS ≥7).
5. Study design sensitivity: restriction to prospective studies only.
6. Outcome definition sensitivity: separate analysis of MCID-based vs author-defined pain response thresholds.

Language restriction English.

Country(ies) involved Taiwan (review conducted at Chang Gung Memorial Hospital, Taoyuan).

Other relevant information Author contributions:
Ying-Ching Li: Conceptualization, methodology, search strategy, screening, data extraction, statistical analysis, manuscript drafting, project administration.
Cheng-Yu Li: Screening, data extraction, quality assessment.
Sheng-Han Huang: Screening, data verification.
Hong Kai Wang: Data extraction, quality assessment.
Kuan-Hung Chen: Data verification, manuscript review.
Yu-Jen Lu: Supervision, methodology review, manuscript review.

All authors contributed to and approved the final protocol.

Reporting guidelines: This systematic review follows the PRISMA 2020 statement and the SWiM (Synthesis Without Meta-analysis) reporting guideline.

Target journal: The Spine Journal.

Estimated completion date: April 2026.

Keywords spinal metastases; pain; surgery; predictors; systematic review; meta-analysis; minimal clinically important difference; MCID.

Dissemination plans The findings of this systematic review will be submitted for publication in a peer-reviewed spine surgery journal (The Spine Journal). Additionally, results may be presented at international spine surgery conferences (AOSpine, Eurospine, or CSRS). The complete dataset, statistical analysis scripts, and supplementary materials will be made available from the corresponding author upon reasonable request.

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