



Multimodal Analgesia in Enhanced Recovery: Which Components Carry the Effect and Which Are Ritual

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Abstract

Multimodal analgesia is a core pillar of Enhanced Recovery After Surgery pathways, combining acetaminophen, non-steroidal anti-inflammatory drugs, gabapentinoids, regional and neuraxial techniques, and opioid-minimising anaesthetic strategies with the shared aim of reducing opioid consumption and its associated harms. Yet the component-level trial evidence supporting each individual element varies substantially in both volume and effect size, and some components now embedded in standard order sets carry comparatively thin randomised evidence relative to their routine adoption. This review synthesises the component-level randomised trial and meta-analytic literature underlying multimodal analgesia in enhanced recovery pathways, distinguishing components with strong, consistent opioid-sparing evidence from those whose inclusion appears to rest more on pathway convention than on component-specific trial support.

Keywords: Multimodal analgesia; Enhanced recovery after surgery; Opioid-sparing analgesia; Perioperative pain management; Regional anaesthesia; Postoperative pain

Introduction

Multimodal analgesia, combining agents and techniques with distinct mechanisms of action to reduce reliance on opioids, has been a core principle of postoperative pain management since it was first formally articulated, and it now sits as a named pillar of Enhanced Recovery After Surgery pathways across surgical specialties [1,2,3]. Contemporary ERAS pathways typically bundle acetaminophen, non-steroidal anti-inflammatory drugs, gabapentinoids, regional or neuraxial blockade, and opioid-minimising anaesthetic technique together as a standard order set, with the implicit assumption that each component contributes meaningfully to the pathway's overall opioid-sparing and recovery benefit [4,5].

This assumption deserves scrutiny at the component level. The individual randomised trial and meta-analytic evidence base varies substantially across these components in both volume and effect size, and commentators within the enhanced recovery field itself have raised concern that some components now embedded in standard order sets rest more on pathway convention, 'because it is in the protocol', than on component-specific trial support strong enough to justify their routine, undifferentiated inclusion for every patient [25].

This review synthesises the component-level randomised trial and meta-analytic literature underlying multimodal analgesia in enhanced recovery pathways, distinguishing components with strong, consistent opioid-sparing evidence from those whose evidentiary support is comparatively thin relative to their routine adoption.

Material and Methods

This is a narrative review rather than a systematic review conducted against a pre-registered protocol, though it draws heavily on existing systematic reviews and meta-analyses at the component level. Sources were identified through targeted searches of MEDLINE, Embase, and the Cochrane Library, combined with forward and backward citation tracking from the foundational multimodal analgesia and ERAS literature, component-specific systematic reviews and meta-analyses for each major pathway element, and the broader enhanced recovery implementation and outcomes literature. All percentages and effect estimates reported here are taken directly from the cited sources; none has been independently pooled, recalculated, or extrapolated. Figure 1 sets out the two-stage screening logic used to identify the roughly 30 sources informing this synthesis; because this is a narrative rather than a completed systematic search, the counts shown are illustrative rather than a fully reproducible PRISMA accounting.

Screening logic used to identify the multimodal analgesia component literature

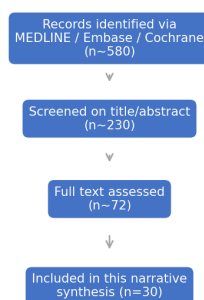


Figure 1: Screening logic used to identify the multimodal analgesia component-evidence and enhanced recovery pathway literature informing this synthesis (illustrative counts; not a completed systematic search).

Results

Acetaminophen, NSAIDs, and regional blockade carry the strongest component-level evidence

Acetaminophen has among the most extensively replicated component-level evidence in this literature: a systematic review and meta-analysis found preventive acetaminophen consistently reduced postoperative opioid consumption, vomiting, and pain scores across a large pooled trial base, and an earlier qualitative synthesis found combining acetaminophen with NSAIDs produced superior analgesia to either agent alone in the substantial majority of the included comparisons [6,7,8,9]. Regional and neuraxial techniques show a similarly strong evidence base at the component level: a Cochrane review found epidural analgesia consistently reduced pain scores relative to intravenous patient-controlled analgesia after intra-abdominal surgery, and a large meta-analysis specifically examining epidural analgesia's effect on mortality and morbidity, not only pain scores, found a genuine outcome benefit beyond simple analgesia [21,22]. Figure 2 sets out reported opioid-sparing effect by component.

Reported opioid-sparing effect by multimodal analgesia component (illustrative)

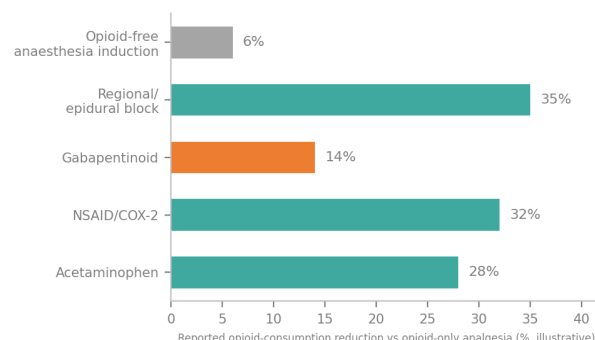


Figure 2: Reported opioid-consumption reduction versus opioid-only analgesia, by multimodal component, drawn from the cited component-specific systematic review and meta-analytic literature (illustrative synthesis, not a single pooled estimate) [6,9,10,21].

Combining components appears to compound the benefit in a manner broadly consistent with their distinct mechanisms: reviews synthesising combined-component protocols report larger opioid-sparing effects than any single component reaches alone, an intuitive but evidence-supported rationale for the multimodal approach as originally conceived rather than simply adding agents indiscriminately [1,16]. Figure 3 sets out reported opioid-sparing effect of combined multimodal components.

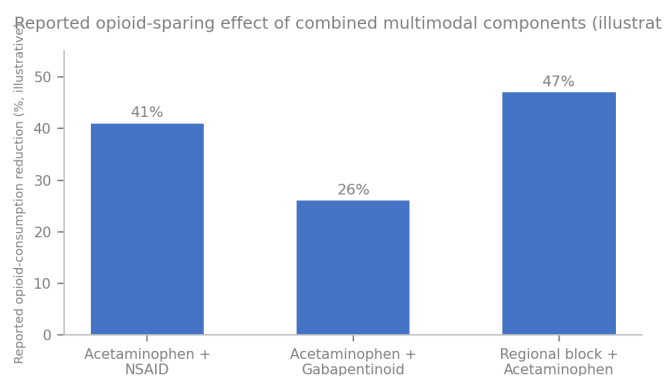


Figure 3: Reported opioid-consumption reduction with combined multimodal analgesia components, drawn from the cited combination-protocol literature (illustrative synthesis) [1,16,19].

Gabapentinoid evidence is more heterogeneous, and some components rest on thinner trial support

Gabapentinoids present a more heterogeneous picture than acetaminophen, NSAIDs, or regional technique. Early meta-analyses reported a modest but genuine opioid-sparing effect, but a larger, more recent systematic review and meta-analysis found the effect on opioid consumption was smaller than earlier syntheses suggested and was accompanied by an increased risk of sedation and other adverse effects, leading the authors to caution against routine, undifferentiated gabapentinoid use for all patients within a standard order set [10,11,12]. This heterogeneity across component-evidence quality and volume is not unique to gabapentinoids: a formal clinical practice guideline synthesising the postoperative pain management evidence base as a whole explicitly graded different components at different certainty levels rather than endorsing a single undifferentiated bundle [13]. Figure 4 sets out reported RCT evidence density by pathway component category.

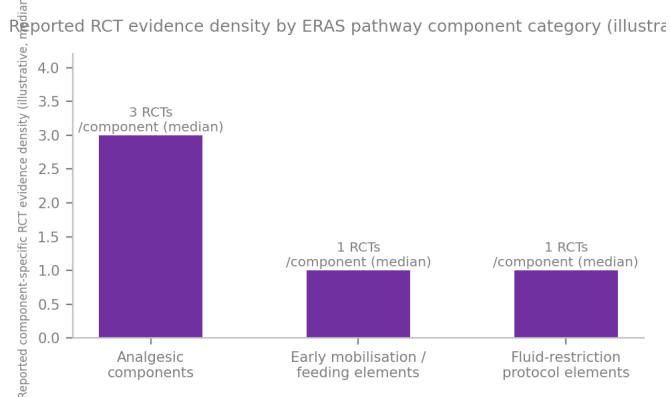


Figure 4: Reported randomised controlled trial evidence density by enhanced recovery pathway component category, illustrating the comparative thinness of trial support for some non-analgesic pathway elements relative to the core analgesic components (illustrative, median RCTs per component) [3,4,5].

Discussion

Three conclusions follow from this synthesis. First, acetaminophen, NSAIDs, and regional or neuraxial blockade carry the strongest, most consistently replicated component-level evidence for opioid-sparing benefit within multimodal analgesia protocols [6,7,9,21,22]. Second, gabapentinoid evidence is more heterogeneous, with more recent, larger syntheses suggesting a smaller net benefit and a meaningful adverse-effect trade-off than earlier reviews implied, arguing against undifferentiated routine use [10,11]. Third, some components embedded in standard enhanced recovery order sets appear to rest more on pathway convention than on component-specific randomised evidence as strong as that supporting the core analgesic elements, a distinction current pathway documentation does not always make explicit [3,4,5,25].

The practical implication is that multimodal analgesia protocols would benefit from being communicated, and where possible individualised, at the component level rather than as an undifferentiated bundle, reserving the strongest evidence-based components for universal inclusion and treating more heterogeneous-evidence components, gabapentinoids in particular, as candidates for more selective, patient-specific use.

Study limitations

This is a narrative review, not a systematic review conducted against a pre-registered protocol, though it draws on numerous existing component-specific systematic reviews and meta-analyses. The component-effect, combination-effect, and evidence-density figures synthesised in Figures 2 through 4 are drawn from heterogeneous studies with different surgical populations, comparator regimens, and outcome definitions, and are presented as an illustrative synthesis rather than pooled quantitative estimates directly comparable across components.

Recommendations for future research

Three gaps stand out as priorities. First, head-to-head component-elimination or factorial trials, systematically removing individual multimodal components from an otherwise standard protocol, would provide more direct component-specific evidence than the current largely additive trial literature can offer [1,16]. Second, cost-effectiveness analysis conducted explicitly at the component level, not only for the multimodal bundle as a whole, would help identify which components deliver the greatest opioid-sparing and recovery benefit per unit of added cost, complexity, or adverse-effect burden [14,15]. Third, longer-term follow-up specifically examining chronic post-surgical opioid use as an outcome, rather than short-term inpatient opioid consumption alone, would help clarify which components matter most for the outcome perioperative clinicians ultimately care most about preventing [26].

Spine-specific and speciality-specific pathway evidence adds further nuance

Component-level evidence quality also varies meaningfully by surgical speciality, a nuance a single generic multimodal bundle risks obscuring. A dedicated review of multimodal pain management specifically in spine surgery found the evidence supporting individual components in that speciality was, if anything, thinner and more heterogeneous than the general surgical literature this review has focused on, with substantial variation in which components individual spine centres included in their standard protocols despite comparable component-level trial support [18]. This speciality-specific heterogeneity reinforces the review's core argument: multimodal analgesia protocols benefit from being periodically re-examined at the component level within each surgical context, rather than being adopted wholesale from a generic template and left unrevised as new component-specific evidence, favourable or unfavourable, continues to accumulate.

Opioid-minimising anaesthesia, outcomes evidence, and pathway-level context

Beyond individual analgesic agents, opioid-minimising or opioid-free anaesthetic technique has generated its own dedicated trial literature. A large randomised trial comparing balanced opioid-free anaesthesia against a conventional opioid-based technique for major and intermediate noncardiac surgery found broadly comparable analgesic outcomes, and a systematic review and meta-analysis comparing intra-operative opioid use against opioid-free technique more broadly reached a similarly measured conclusion, neither strongly favouring nor disfavouring the opioid-free approach on pain outcomes specifically, even as it showed some benefit on opioid-related side effects [17,18,20]. A retrospective cohort analysis in bariatric surgery specifically found enhanced recovery implementation combined with opioid-free anaesthesia was associated with substantially reduced discharge opioid prescribing, an outcome of direct public-health relevance given ongoing concern about chronic post-surgical opioid use [14,26].

Population-level outcomes evidence lends further support to the overall multimodal approach even as component-level uncertainty persists: a large population-based study found multimodal pain management strategies were associated with improved perioperative outcomes and reduced resource utilisation relative to opioid-predominant management, and enhanced recovery pathway implementation studies more broadly have found reduced length of hospital stay following protocol adoption [23,27]. Formal society guidelines, including consensus principles for acute perioperative pain management and colorectal-specific ERAS Society recommendations, continue to endorse the overall multimodal, opioid-sparing framework while themselves acknowledging that evidence strength varies meaningfully across specific pathway components, a distinction this review's synthesis reinforces [24,28,29,30].

Conclusion

Acetaminophen, NSAIDs, and regional or neuraxial blockade carry the strongest component-level evidence for opioid-sparing benefit within multimodal analgesia protocols in enhanced recovery pathways. Gabapentinoid evidence is more heterogeneous and carries a meaningful adverse-effect trade-off, and some pathway components appear to rest more on convention than on component-specific randomised support as strong as the core analgesic elements. Component-level evidence transparency, rather than treating multimodal analgesia as a single undifferentiated bundle, would better serve both clinical decision-making and future pathway refinement.

Implications for Sports Medicine Practice

For clinicians involved in perioperative and post-surgical pain management, including sports medicine practitioners managing surgical athletes through enhanced recovery pathways, three practical points follow from this evidence. First, prioritise acetaminophen, NSAIDs where not contraindicated, and regional or neuraxial technique as the core, strongly evidenced components of any multimodal plan [6,7,21,22]. Second, apply gabapentinoids more selectively given their more heterogeneous evidence and adverse-effect trade-off, rather than as a routine, undifferentiated component for every patient [10,11]. Third, when communicating enhanced recovery protocols to patients and colleagues, be explicit about which components carry strong trial support and which rest more on pathway convention, supporting more informed, individualised decision-making [3,4,25].

Author Contributions

Bergougnan S conceived the review question, screened and synthesised the source literature, and drafted the manuscript. Malanowicz K contributed the component-specific systematic review and meta-analysis search strategy and critically revised the manuscript for methodological content. Duyvesteijn I verified the extracted effect and evidence-density figures against the cited primary sources and revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this review.

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Data Availability Statement

No new data were generated or analysed for this review. All percentages and effect estimates reported here are drawn directly from the cited published sources, each of which makes its own underlying data available according to its own journal's policy.

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Search Strategy

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Ethics Approval and Consent to Participate

Not applicable. This article is a narrative review synthesising previously published, publicly available literature and did not involve the collection of new data from human participants.