INTERNAL MEDICINE JOURNAL

RACP Specialists. Together

Check for updates

doi:10.1111/imj.70632

REVIEW

Economic evaluations of remifentanil versus fentanyl for analgo-sedation in mechanically ventilated adult ICU patients: a systematic review

Sushma Ashwin,[1] Lisa Gold [1], Arvind Rajamani [2,3] and Ashwin Subramaniam [4,5,6,7]

[1]Department of Health Economics, Deakin University, Burwood, [4]Australian and New Zealand Intensive Care Research Centre (ANZIC RC), Department of Epidemiology and Preventive Medicine, Monash University, and [7]Australian and New Zealand Intensive Care Society, Centre for Outcome and Resource Evaluation, Melbourne, [5]Department of Intensive Care, Dandenong Hospital Monash Health, Dandenong, [6]Department of Intensive Care, Epworth Healthcare, Richmond, Victoria, and [2]Nepean Clinical School, University of Sydney, and [3]Department of Intensive Care Medicine, Nepean Hospital, Kingswood, New South Wales, Australia

Key words
remifentanil, opioids, ICU, intensive care, economic evaluation, cost-effectiveness.

Correspondence
Ashwin Subramaniam, Australian and New Zealand Intensive Care Research Centre (ANZIC RC), Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Vic., Australia.
Email: ashwin.subramaniam@monash.edu

Received 6 May 2026; accepted 17 August 2026.

Abstract

The use of opioid and sedative infusions to relieve pain and anxiety is common among patients receiving invasive mechanical ventilation (IMV) in the intensive care unit (ICU). Although remifentanil-based sedation is feasible, evidence regarding its economic impact remains limited. We systematically identified, synthesised and critically appraised economic evaluations of remifentanil in mechanically ventilated ICU patients. Ovid MEDLINE, Ovid Embase and the Cochrane Library were searched for full-text original English-language studies published between 1997 and 2023. Reporting quality was assessed using the 24-item Consolidated Health Economic Evaluation Reporting Standards checklist. Of 169 records identified, 103 remained after duplicate removal, eight underwent full-text review and only two single-centre studies, involving 285 patients, met the inclusion criteria. The studies differed substantially in their methodology, including the outcomes assessed, cost components, analytical perspectives and time horizons. Reporting quality was rated as good (59%) in the study by Muellejans *et al.* and very good (81%) in the study by Al *et al.* Both studies reported shorter durations of IMV and ICU stay with remifentanil; however, their economic findings were inconsistent. Al *et al.* reported that remifentanil may reduce costs, whereas Muellejans *et al.* found similar total costs between treatment groups, largely because of the higher acquisition cost of remifentanil. This systematic review identified limited and heterogeneous evidence regarding the economic impact of remifentanil in mechanically ventilated ICU patients. Given the substantial costs of intensive care, high-quality economic evaluations using contemporary clinical practice, comprehensive cost measurement and appropriate time horizons are needed to determine whether remifentanil provides value for money.

Introduction

In Australian intensive care units (ICU), over 50 000 critically ill patients require invasive mechanical ventilation (IMV) every year.[1] It is common for intubated patients to receive the administration of both opioid analgesics and sedative infusions to relieve the pain and anxiety associated with IMV ('analgo-sedation').[1,2] The ideal sedative would be cost-effective, fast-acting and free from adverse effects. However, among the currently used analgo-sedatives, there is no single agent that meets all these criteria. With prolonged use in critically ill patients, the commonly used opioids in Australian ICU, namely morphine and fentanyl, exhibit potentially unfavourable pharmacokinetics such as long context-sensitive half-times resulting in drug accumulation, redistribution and residual sedation, particularly in

Funding: None.
Conflict of interest: None.

© 2026 The Author(s). *Internal Medicine Journal* published by John Wiley & Sons Australia, Ltd on behalf of Royal Australasian College of Physicians.
This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

patients with failing organs.[3,4] This may lead to unpredictable effects such as prolonged deep sedation, immune suppression, hypotension[5–7] and delayed weaning from IMV, potentially extending its duration and lengthening ICU stays.[8]

In contrast, remifentanil is an ultra-short-acting opioid.[5] It has a unique pharmacokinetic (Table 1) profile of a highly predictable onset and offset, organ-independent elimination and a short context-sensitive half-life.[9] It elicits a deep analgesic state without tissue accumulation.[5,9] A few randomised controlled trials (RCTs) have demonstrated that patients on remifentanil have resulted in reduced IMV duration, time to extubation after drug cessation and ICU length of stay.[10–12] A recent prospective, open-label pilot RCT comparing remifentanil to fentanyl in mechanically ventilated patients (>24 h) found that remifentanil had a comparable or superior safety profile, with fewer complications, reduced delirium and more ventilator-free days by day 28.[13]

ICU face ongoing pressure to deliver high-value care within limited resources. The COVID-19 pandemic further highlighted the need to optimise ICU throughput and resource utilisation.[14,15] Given the numerous priorities in healthcare delivery and the limited resources available for investment, it is crucial for decision-makers to assess the most effective options to optimise health outcomes. Since resource-intensive treatments such as IMV could increase the daily costs by an additional 20%–26%,[16,17] decreasing the duration of IMV and therefore ICU length of stay may lead to clinical and economic benefits.[18] Analgo-sedation strategies that enable faster weaning from IMV, such as using short-acting agents like remifentanil, may offer both clinical and economic advantages.[11,13] While remifentanil shows promise in reducing complications and ICU length of stay compared to fentanyl, its higher acquisition cost raises questions about overall cost-effectiveness. The economic implications of choosing remifentanil over fentanyl are significant, particularly considering the high costs associated with ICU care, which can exceed A$4000 per patient bed-day.[19] If approximately 10% of these opioid costs are attributed to pharmaceuticals,[20] this has implications for healthcare policy and resource allocation, especially in a resource-limited system.[21] Despite recognised clinical differences, there is a notable lack of economic evaluations comparing these agents. This systematic review aimed to systematically identify, synthesise and critically appraise the available economic evidence.

Methods

This systematic review's protocol was prospectively registered with PROSPERO (CRD 42022357343) before completing the search strategy development. The methodology of the review followed the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[22]

Literature search strategy

A comprehensive search was carried out across key electronic databases, including Ovid MEDLINE, Ovid Embase and the Cochrane Library. The search was limited to studies published after 1997, reflecting the year remifentanil was patented and its subsequent adoption in clinical practice. The search strategy was developed with support from a Deakin University librarian. The search was performed to capture the most recent studies and data available from 1997 to 2023. Search terms included a mix of controlled vocabulary (such as Medical Subject Headings and Emtree) and free-text expressions related to remifentanil and fentanyl, together with terms associated with economic analyses like 'cost', as well as terms related to IMV and ICU (Table S1). Additionally,

Table 1 Pharmacokinetics of commonly used opioid medications

Medication	Onset (IV)†	Elimination half-life‡	Context-sensitive half-life§	Route of administration¶	Cost per unit††
Morphine	5–10 min	3–4 h	N/A	IV, other methods	$0.032
Fentanyl	1–2 min	8–10 h	200 min (6-h infusion); 300 min (12-h infusion)	Subcutaneous, IM, IV, epidural, intrathecal, transdermal	$4.936
Hydromorphone	5–15 min	2–3 h	N/A	IV, other methods	$0.434
Remifentanil	1–3 min	3–10 min	3–4 min	IV, intranasal	$11.28
Sufentanil	5–10 min	6–9 h	20–60 min	IV, other techniques including epidural, intrathecal, transdermal and intranasal	$5.27

†The time it takes for a drug to start working after intravenous administration. ‡The time required for the drug's concentration in the bloodstream to decrease by half. §The time for a drug's concentration to halve after stopping a prolonged infusion, considering its distribution and redistribution in the body. ¶The method by which a drug is introduced into the body, such as orally, intravenously, or intramuscularly. ††The cost of drug per mg in US dollars. IM, intramuscular; IV, intravenous; min, minutes; N/A, not applicable.

Internal Medicine Journal (2026) 1–9

© 2026 The Author(s). *Internal Medicine Journal* published by John Wiley & Sons Australia, Ltd on behalf of Royal Australasian College of Physicians.

14455994, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/imj.70632 by IMJ Editorial Office - National Health And Medical Research Council , Wiley Online Library on [19/10/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

the bibliographies of selected articles were reviewed to identify any further studies of interest.

Study selection

Screening was conducted by two reviewers (SA and AS) independently, with any differences resolved through consultation with a third reviewer (AR). The process involved two phases: initially, titles and abstracts were reviewed to filter out articles that did not meet the predefined criteria. The objective of the selection criteria, outlined in Table 2, was to identify studies that were relevant to the study's focus. Full economic evaluations (cost-effectiveness, cost-utility, cost–benefit and cost-minimisation analyses) and partial economic evaluations (comparative cost analyses) were eligible. Studies reporting costs without a comparator or without an economic evaluation framework were excluded. Subsequently, the full texts of the articles deemed to have been potentially eligible were thoroughly reviewed. Studies were restricted to those published in English. An economic evaluation was identified as being a comparison of different interventions regarding their costs (use of resources) and outcomes (effects, results).[21] All studies that presented an economic analysis of analgo-sedation for adult patients undergoing IMV in the ICU were included. The reasons for excluding articles at this stage were systematically recorded.

Data extraction

The task of data extraction was carried out by two independent reviewers (SA and AS) using the Covidence platform (Veritas Health Innovation, based in Melbourne, Australia) and structured data extraction templates. Information gathered included specifics of the study (such as author, publication year and country of origin), details on the intervention and its comparators and the methodology behind the economic evaluation (including aspects like the time horizon, currency used, discount rates, perspective of the study, type of economic evaluation, sources of data and any performed sensitivity analyses). The outcomes of interest focused on the economic evaluation of the interventions, determined through measures such as the incremental cost-effectiveness ratio (ICER), which could include costs per outcome achieved, costs per quality-adjusted life year (QALY) and costs per life year gained, among others. The outcomes of interest also included the likelihood of an intervention being cost-effective, the total costs involved and the associated health outcomes, which included both mortality and QALY metrics. Interventions were categorised as having been 'dominant' if they had produced lower costs and higher effectiveness relative to their comparators or were considered 'dominated' if they had led to higher costs and reduced effectiveness.

Data synthesis

The studies were categorised based on the interventions that they had assessed. A qualitative analysis of the variability across trials was conducted to assess the feasibility of conducting a quantitative synthesis of the research findings. The primary outcome was economic evaluation for remifentanil when compared to a conventional opioid agent (fentanyl or morphine).

Quality assessment in individual studies

The assessment of study quality utilised the 24-item Consolidated Health Economic Evaluation Reporting

Table 2 Selection criteria for the systematic literature review

Inclusion criteria	Exclusion criteria
• Economic evaluations that were trial-based (deriving clinical and resource data from a single study) and model-based (incorporating data from various sources). • Full economic evaluations including cost-effectiveness analyses, including cost-consequence analysis and cost-minimisation analysis, cost-utility analysis and cost-benefit analysis. • Partial economic evaluation that performed cost analyses and reported outcomes in monetary units. • Economic analyses which focused solely on costs and resources used or which did not entail a comparator were excluded. • Published in the English language.	• Available in abstract form only (e.g. conference abstracts) • Reviews of existing economic evaluations that did not present new data. • Patient population not in ICU • Results were not available separately for the ICU subgroup. • Patient group – pregnant women, neonates or children or a mixed cohort where results were not available for the adult subgroup. • Studies where remifentanil/fentanyl were part of a variety of interventions being compared and could not be differentiated in terms of effects and cost of intervention.

© 2026 The Author(s). *Internal Medicine Journal* published by John Wiley & Sons Australia, Ltd on behalf of Royal Australasian College of Physicians.

14455994, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/imj.70632 by JMJ Editorial Office - National Health And Medical Research Council , Wiley Online Library on [19/10/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3 Characteristics of studies describing economic evaluation of remifentanil versus fentanyl in ICU patients

Lead author, (year) country	Sample size	Intervention (adjunctive analo-sedation use)	Comparator	Outcome measure and findings	Cost, perspective	Study type	Patient population, age, illness severity	Time horizon	CHEERS study quality (%)
Al *et al*. (2010) Netherlands	205	Remifentanil-based analgo-sedation (remifentanil, combined with propofol, when required)	Conventional analgo-sedation (morphine or fentanyl combined with propofol, midazolam or lorazepam)	ICU length of stay, ICU costs Compared to conventional analgo-sedation, remifentanil-based analgo-sedation reduced the overall costs in the ICU	• Hospital top-down aggregated costing. • Total 28-day costs - €15 626 with remifentanil-based analgo-sedation versus €17 100 with conventional analgo-sedation. • Cost difference was €1474 (95% CI -2163 to 5110) • 79% of the uncertainty range showed a cost saving. • No ICER was calculated.	Cost consequence – Markov model	Adult medical and post-surgical ICU patients with an anticipated mechanical ventilation duration of 2 to 3 days. Patients were aged ≥18 years	Time to extubation and ICU length of stay shorter in remifentanil group	81
Muellejans *et al*. (2006), Germany	80	Remifentanil/propofol (supplementation)	Midazolam/ fentanyl	ICU length of stay, ICU costs Overall costs were equal in both arms	• Hospital micro-costing. • Estimated cost €1700 (ICU stay per patient). • No ICER was calculated.	Economic modelling	Cardiac surgical patients aged 18–75 years	Time to extubation and ICU length of stay shorter in remifentanil group	59

CHEERS, Consolidated Health Economic Evaluation Reporting Standards; ICU, intensive care unit.

© 2026 The Author(s). *Internal Medicine Journal* published by John Wiley & Sons Australia, Ltd on behalf of Royal Australasian College of Physicians.

14455994, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/imj.70632 by IMJ Editorial Office - National Health And Medical Research Council , Wiley Online Library on [19/10/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Standards (CHEERS) checklist[23] which was applied independently by two reviewers (SA and LG). Any disagreement between the two reviewers regarding the weightage was resolved through discussion. Each study received a score based on these 24 standards, with a full point awarded for each criterion satisfactorily met by the study. In line with the method used by Hope *et al.*,[24] a criterion that was partially met resulted in a half-point award. For studies reported across multiple publications, all the relevant documents were reviewed during the quality assessment and the highest score obtained for any specific CHEERS item across these publications was recorded. The final quality score for each study was then expressed as a percentage. Based on their overall scores, studies achieving ≥85% were classified as exhibiting excellent reporting quality. Those with scores ranging between 70% and 85% were deemed to be of very good quality; those with scores between 55% and 70% were considered good quality; and studies that scored below 55% were considered of poor quality.[24] As CHEERS was used to assess reporting completeness rather than methodological quality, we also used the Drummond Checklist to assess the economic evaluation quality.

Results

The initial search yielded 169 abstracts. After duplicate removal, 103 unique abstracts remained for screening. Of the eight full-text articles assessed for eligibility, only two single-centre studies ($n = 285$) met the inclusion

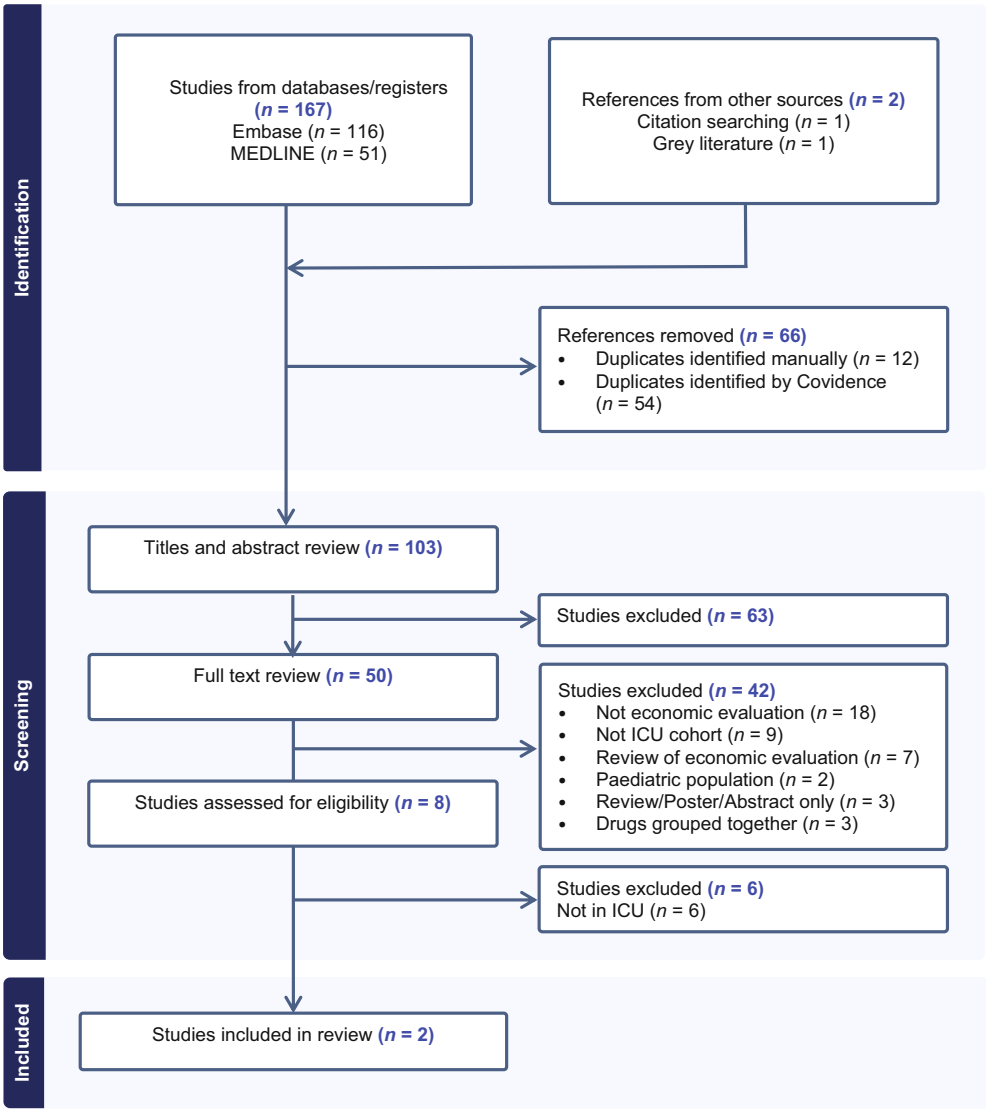


Figure 1 PRISMA Flow diagram to demonstrate study inclusions.

© 2026 The Author(s). *Internal Medicine Journal* published by John Wiley & Sons Australia, Ltd on behalf of Royal Australasian College of Physicians.

14455994, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/imj.70632 by IMJ Editorial Office - National Health And Medical Research Council , Wiley Online Library on [19/10/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

criteria as health economic evaluations (Table 3). Results of the search strategy are illustrated in Figure 1.

The Dutch study by Al *et al.*[11] conducted a cost-consequence analysis comparing ICU length of stay between remifentanil-based and conventional analgo-sedation. It used data from the UltiSAFE trial[11] and a separate micro-costing study,[17] focusing on ICU patients requiring 2–3 days of IMV, from a hospital perspective using 2006 cost data. The analysis used a Markov model to estimate costs and outcomes beyond the 10-day remifentanil treatment studied clinically. It suggested that remifentanil-based analgo-sedation may reduce ICU length of stay and generate cost savings, despite a 79% uncertainty. Additionally, the study did not measure morbidity or mortality outcomes; it assumed an equal survival/mortality rate between groups. This assumption was based on the absence of differences observed in the clinical study, even though mortality had not been an outcome in the economic evaluation, which had focused solely on costs.

Using the Drummond Checklist (Table S2), Al *et al.* demonstrated moderate to high methodological quality, with the main limitation being the absence of an incremental cost-effectiveness analysis (ICER/QALY).[11] Muellejans *et al.* were judged to be of moderate methodological quality, with limitations including a less comprehensive costing methodology, no incremental economic analysis, a small sample size and single-centre design.[12]

The German study by Muellejans *et al.*[12] was a cost analysis that used modelling to explore deviations from protocol, particularly the high remifentanil dosage and its cost implications. This study did not directly compare the differences in costs to the differences in length of stay. Although the study perspective was not explicitly stated, it likely reflected a healthcare or hospital resource use perspective. The remifentanil/propofol regimen had significantly shorter weaning (2.2 vs 5.7 h; $P < 0.05$) and extubation times (20.7 vs 24.2 h; $P < 0.05$) when compared to the midazolam/fentanyl regimen. Despite higher remifentanil drug costs, total costs were similar. Sensitivity analysis supported these findings, and modelling suggested potential cost savings with adjusted remifentanil dosing in real-world practice.

Table 4 Consolidated health economic evaluation reporting standards (CHEERS) assessment of economic evaluation analysis studies of remifentanil with usual care, fentanyl, or other control ($n = 2$)

Section/Topic	Author	Al 2011	Muellejans 2006
	Title	1	½
	Abstract	1	1
	Background and objectives	1	1
Methods	Study population	1	1
	Setting and location	1	½
	Perspective	1	1
	Comparators	1	1
	Time horizon	0	0
	Discount rate	N/A	N/A
	Choice of health outcomes	1	1
	Measurement of effectiveness	1	1
	Measurement of preference-based outcomes	N/A	0
	Resources and costs	1	1
	Currency, price date and conversion	0	0
	Choice of model	1	N/A
	Characterising uncertainty	1	0
	Characterising heterogeneity	1	N/A
	Analytics and assumptions	N/A	1
Results	Study parameters	1	1
	Summary of main results: Incremental costs and outcomes	1	½
	Effect of uncertainty	1	½
Discussion	Study findings, limitations, generalisability and current knowledge	1	1
Other relevant information	Source of funding	0	0
	Conflicts of interest	0	0
	Total	**17/21**	**13/22**
	% score	**81**	**59**

0 = not reported or insufficiently reported; ½ = reporting unclear or components not reported; 1 = sufficient reporting.

© 2026 The Author(s). *Internal Medicine Journal* published by John Wiley & Sons Australia, Ltd on behalf of Royal Australasian College of Physicians.

14455994, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/imj.70632 by IMJ Editorial Office - National Health And Medical Research Council , Wiley Online Library on [19/10/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Quality assessment

The CHEERS assessment of economic evaluation analysis is summarised in Table 4. The reporting quality of the two studies varied significantly: Al *et al.*'s[11] was rated as a very good quality study (81%), whereas Muellejans *et al.*'s[12] study was only rated as good quality (59%).

Discussion

This systematic review identified only two economic evaluations of remifentanil use in ICU settings. The studies varied significantly in methodology, including outcomes measured, cost components, time horizons and perspectives. This heterogeneity precluded meta-analysis and limits the certainty of conclusions. These findings highlight important gaps in the economic evidence base for remifentanil in critical care.

Economic evidence for remifentanil use in ICU settings is limited. Many initially relevant studies were excluded due to a lack of primary cost data (i.e. were not an economic evaluation) or initiation of sedation outside the ICU (i.e. surgery or anaesthesia). Given the ICU's unique resource demands, only studies conducted specifically within this setting were deemed suitable. Ultimately, just two studies met inclusion criteria, both comparing remifentanil to fentanyl. Each supported reduced duration of IMV and ICU stay with remifentanil use. The Dutch study[11] reported a significant reduction in ICU costs with remifentanil, while the German study[12] found overall costs comparable between agents. Clinical outcomes beyond length of stay were either not assessed or assumed equal. Both studies were conducted more than 15 years ago, limiting their applicability to contemporary ICU practice. Since then, remifentanil acquisition costs, ICU resource utilisation, sedation practices and healthcare funding models have evolved substantially. Consequently, the reported economic findings may not be directly generalisable to the current Australian healthcare setting or other modern critical care systems.

The scope of economic evaluations has been limited due to the scarce availability of evidence from high-quality RCTs and a lack of long-term outcomes data, including QALYs. While RCTs offer strong internal validity, they often fail to capture comprehensive resource use or extended follow-up.[21] As a result, most economic assessments rely on modelling to estimate long-term costs and effects. Both studies included in this review[11,12] used modelling to project outcomes and assess cost-effectiveness. Robust data are needed to better inform healthcare decision-makers about the economic impact of opioid-based sedation in ICU settings.

Despite the high costs associated with IMV and the abundance of RCTs, few economic evaluation analyses have compared remifentanil to other opioids in ICU settings. The reviewed studies reveal substantial gaps in the economic evaluation of opioid interventions and highlight the inherent complexity of conducting such analyses in critical care. These findings underscore the urgent need for more comprehensive assessments of both costs and outcomes.

Since these economic evaluations were conducted, our group's recent pilot RCT has demonstrated the feasibility and potential clinical benefits of remifentanil-based analgo-sedation compared with fentanyl, highlighting the need for contemporary trial-based economic evaluations to determine whether these clinical improvements translate into value for money in modern ICU practice.[13,25]

The strengths of this systematic review included its comprehensive search strategy that covered multiple electronic databases to ensure all relevant economic evaluations of remifentanil and fentanyl had been considered. The reliability of this review was increased by the independent scrutiny of study selection, data extraction and the evaluation of reporting quality that was conducted by two separate reviewers. However, this review had several limitations. First, the CHEERS checklist assessed reporting quality but did not evaluate the appropriateness of the methods or the quality of underlying data. Second, due to methodological and reporting heterogeneity across studies, a qualitative synthesis was required in place of a quantitative meta-analysis. Third, although reporting quality and methodological quality were assessed using the CHEERS and Drummond checklists, respectively, these tools may not capture all potential sources of bias within the included economic evaluations. Finally, the literature search was completed in 2023 in accordance with the prospectively registered review protocol in PROSPERO. More recent studies have since been published, including a contemporary retrospective cohort study evaluating remifentanil versus fentanyl in mechanically ventilated ICU patients. Although this study did not include an economic evaluation and therefore would not have altered the findings of this review, it highlights the evolving evidence base and reinforces the need for updated systematic reviews incorporating future economic analyses.

Conclusion

This systematic review identified only two heterogeneous and largely outdated economic evaluation designs of remifentanil-based analgo-sedation in mechanically ventilated ICU patients, with inconsistent findings regarding costs. Although both studies suggested shorter

© 2026 The Author(s). *Internal Medicine Journal* published by John Wiley & Sons Australia, Ltd on behalf of Royal Australasian College of Physicians.

14455994, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/imj.70632 by IMJ Editorial Office - National Health And Medical Research Council , Wiley Online Library on [19/10/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

durations of mechanical ventilation and ICU stay with remifentanil, whether these clinical benefits translate into overall cost savings is likely to depend on contemporary drug pricing, ICU resource costs and local sedation practices. Together with recent clinical trial evidence demonstrating the feasibility and potential clinical benefits of remifentanil-based analgo-sedation, these findings highlight the need for contemporary, high-quality trial-based economic evaluations to determine its value for money in modern critical care practice and inform healthcare policy and resource allocation.

Acknowledgements

Open access publishing facilitated by Monash University, as part of the Wiley - Monash University agreement via the Council of Australasian University Librarians.

Data availability statement

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

References

1 Hodgson CL, Cooper DJ, Arabi Y, King V, Bersten A, Bihari S *et al*. Maximal recruitment open lung ventilation in acute respiratory distress syndrome (PHARLAP). A phase II, multicenter randomized controlled clinical trial. *Am J Respir Crit Care Med* 2019; **200**: 1363–72 (in English).
2 Wunsch H, Kahn JM, Kramer AA, Rubenfeld GD. Use of intravenous infusion sedation among mechanically ventilated patients in the United States. *Crit Care Med* 2009; **37**: 3031–9 (in English).
3 Casamento A, Bellomo R. Fentanyl versus morphine for analgo-sedation in mechanically ventilated adult ICU patients. *Crit Care Resusc* 2019; **21**: 76–83 (in English).
4 Murray MJ, Oyen LJ, and Browne WT. Use of sedatives, analgesics, and neuromuscular blockers. In: Parrillo LDR, ed. *Critical Care Medicine - Principles of Diagnosis and Management in the Adult*, 3rd edn. Philadelphia: ELSEVIER; 2008; 327–42.
5 Egan TD. Remifentanil pharmacokinetics and pharmacodynamics. A preliminary appraisal. *Clin Pharmacokinet* 1995; **29**: 80–94 (in English).
6 Devlin J. The pharmacology of over sedation in mechanically ventilated adults. *Curr Opin Crit Care* 2008; **14**: 403–7.
7 Devlin JW, Roberts RJ. Pharmacology of commonly used analgesics and sedatives in the ICU: benzodiazepines, propofol, and opioids. *Crit Care Clin* 2009; **25**: 431–49.
8 Foster J. Complications of sedation and critical illness. *Crit Care Nurs Clin North Am* 2005; **17**: 287–96 (in English).
9 Kapila A, Glass PS, Jacobs JR, Glass PSA, Muir KT, Hermann DJ *et al*. Measured context-sensitive half-times of remifentanil and alfentanil. *Anesthesiology* 1995; **83**: 968–75 (in English).
10 Dahaba AA, Grabner T, Rehak PH, List WF, Metzler H. Remifentanil versus morphine analgesia and sedation for mechanically ventilated critically ill patients: a randomized double blind study. *Anesthesiology* 2004; **101**: 640–6 (in English).
11 Al MJ, Hakkaart L, Tan SS, Bakker J. Cost-consequence analysis of remifentanil-based analgo-sedation vs. conventional analgesia and sedation for patients on mechanical ventilation in the Netherlands. *Crit Care* 2010; **14**: R195.
12 Muellejans B, Matthey T, Scholpp J, Schill M. Sedation in the intensive care unit with remifentanil/propofol versus midazolam/fentanyl: a randomised, open-label, pharmacoeconomic trial. *Crit Care* 2006; **10**: R91.
13 Rajamani A, Subramaniam A, Lung B, Masters K, Gresham R, Whitehead C *et al*. Remi-fent 1-a pragmatic randomised controlled study to evaluate the feasibility of using remifentanil or fentanyl as sedation adjuncts in mechanically ventilated patients. *Crit Care Resusc* 2023; **25**: 216–22.
14 Bravata DM, Perkins AJ, Myers LJ, Arling G, Zhang Y, Zillich AJ *et al*. Association of intensive care unit patient load and demand with mortality rates in US Department of Veterans Affairs Hospitals during the COVID-19 pandemic. *JAMA Netw Open* 2021; **4**: e2034266 (in English).
15 Richards-Belle A, Orzechowska I, Gould DW, Thomas K, Doidge JC, Mouncey PR *et al*. COVID-19 in critical care: epidemiology of the first epidemic wave across England, Wales and Northern Ireland. *Intensive Care Med* 2020; **46**: 2035–47 (in English).
16 Gusmão Vicente F, Polito Lomar F, Mélot C, Vincent JL. Can the experienced ICU physician predict ICU length of stay and outcome better than less experienced colleagues? *Intensive Care Med* 2004; **30**: 655–9.(in English).
17 Rozendaal FW, Spronk PE, Snellen FF, Schoen A, Zanten ARH, Foudraine NA *et al*. Remifentanil-propofol analgo-sedation shortens duration of ventilation and length of ICU stay compared to a conventional regimen: a centre randomised, cross-over, open-label study in The Netherlands. *Intensive Care Med* 2009; **35**: 291–8 (in English).
18 Westmoreland CL, Hoke JF, Sebel PS, Hug CC Jr, Muir KT. Pharmacokinetics of remifentanil (GI87084B) and its major metabolite (GI90291) in patients undergoing elective inpatient surgery. *Anesthesiology* 1993; **79**: 893–903 (in English).
19 Shehabi Y, Bellomo R, Kadiman S, Ti LK, Howe B, Reade MC *et al*. Sedation intensity in the first 48 hours of mechanical ventilation and 180-day mortality: a multinational prospective longitudinal cohort study. *Crit Care Med* 2018; **46**: 850–9 (in English).
20 MacLaren R, Sullivan PW. Economic evaluation of sustained sedation/analgesia in the intensive care unit. *Expert Opin Pharmacother* 2006; **7**: 2047–68 (in English).
21 Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. *Methods for the Economic Evaluation of Health Care Programmes*, 4th edn. Oxford: Oxford University Press; 2015.
22 Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009; **6**: e1000097 (in English).
23 Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D *et al*.

© 2026 The Author(s). *Internal Medicine Journal* published by John Wiley & Sons Australia, Ltd on behalf of Royal Australasian College of Physicians.

14455994, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/imj.70632 by IMJ Editorial Office - National Health And Medical Research Council , Wiley Online Library on [19/10/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Consolidated health economic evaluation reporting standards (CHEERS)–explanation and elaboration: a report of the ISPOR health economic evaluation publication guidelines good reporting practices task force. *Value Health* 2013; **16**: 231–50 (in English).

24 Hope SF, Webster J, Trieu K, Pillay A, Ieremia M, Bell C *et al*. A systematic review of economic evaluations of population-based sodium reduction interventions. *PLoS One* 2017; **12**: e0173600 (in English).

25 Ashwin S, Gold L, Rajamani A, Masters K, Gresham R, Lowrie J *et al*. The cost analysis of remifentanil and fentanyl for analgosedation in mechanically ventilated patients in intensive care: post hoc analysis of an open-labelled pilot randomised controlled study. *Crit Care Resusc* 2026; **28**: 100189 (in English).

Supporting Information

Additional supporting information may be found in the online version of this article at the publisher's web-site:

Table S1: Keyword searches in the different databases.
Table S2: Drummond Assessment of the quality of the economic evaluations.

© 2026 The Author(s). *Internal Medicine Journal* published by John Wiley & Sons Australia, Ltd on behalf of Royal Australasian College of Physicians.

14455994, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/imj.70632 by JMJ Editorial Office - National Health And Medical Research Council , Wiley Online Library on [19/10/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License