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SYSTEMATIC REVIEW

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Pain management of adults in the prehospital setting: a scoping review

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Abstract

Background The most effective treatment for pain in prehospital adults remains uncertain. This scoping review aimed to descriptively synthesize the evidence and identify research gaps regarding pain interventions for adults in prehospital settings.

Methods We searched MEDLINE, EMBASE, CINAHL, the Cochrane Library, and TRIP on 11 April 2025. Systematic reviews of adults receiving a pain intervention in the prehospital setting were included. We defined prehospital pain in this review as adults (18 years or >) treated for pain by a healthcare professional in the out-of-hospital setting from the time of first contact at the scene until emergency department admission. AMSTAR 2 was used to assess quality.

Results There were 22 systematic reviews ($n=193$ primary studies, $n=93{,}092$ adults) included that assessed 24 interventions including fentanyl ($n=9$ reviews, 41%), ketamine ($n=9$, 41%), morphine ($n=7$, 32%), ketamine plus morphine ($n=7$, 32%), fascia iliaca nerve block ($n=5$, 23%), methoxyflurane ($n=5$, 23%), nitrous oxide ($n=5$, 23%), sufentanil ($n=4$, 18%), tramadol ($n=4$, 18%), paracetamol ($n=3$, 14%), alfentanil ($n=2$, 9%), femoral nerve block ($n=2$, 9%), ibuprofen ($n=2$, 9%), pentazocine ($n=2$, 9%), transcutaneous electrical nerve stimulation ($n=2$, 9%), auricular acupressure ($n=1$, 5%), butorphanol ($n=1$, 5%), hydromorphone ($n=1$, 5%), ketamine plus nitrous oxide ($n=1$, 5%), meperidine ($n=1$, 5%), metamizole ($n=1$, 5%), papaveretum ($n=1$, 5%), and traction/splinting ($n=1$, 5%). A third (38%; $n=8$) of reviews conducted meta-analyses; median = 876 participants (IQR: 320–1538). However, no meta-analyses met the threshold of 5126 participants deemed necessary following trial sequence analysis. The quality of reviews was high ($n=8$, 36%), moderate ($n=9$, 41%), low ($n=2$, 9%), and critically low ($n=3$, 14%).

Conclusions Larger pragmatic trials using a single validated pain scale with interventions administered at standardized time intervals are required to facilitate evidence synthesis and evidence-based decision-making for pain management in prehospital settings.

Study protocol pre-registration https://doi.org/10.17605/OSF.IO/MH7Q9 .

Keywords Analgesia, Out-of-hospital, Systematic review, Fentanyl, Ketamine, Trauma

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Background

Between one-third and two-thirds of adults report pain in the prehospital setting before admission to the emergency department [1, 3, 13, 16]. However, prehospital pain is often undertreated [4, 13, 16, 28]. The causes of undertreated prehospital pain include limited understanding of the most effective interventions or limited training in the use of analgesics among prehospital clinicians [16]. Other reported causes are inconsistent or absent pain assessment [4, 14, 16], and reluctance to administer analgesics because of the possibility of inducing physiologic instability or sedation compromising clinical assessment [14, 16].

The undertreatment of prehospital pain contributes to physiological instability by increasing circulating catecholamine levels, exacerbating acute injury or illness resulting in disability, delayed healing, and prolonged hospital admissions [27, 30]. Undertreated prehospital pain may also result in the development of chronic pain, post-traumatic stress disorder, or addiction to prescribed and illicitly obtained opioid drugs [4, 30]. Therefore, understanding the most effective treatments for managing pain in the prehospital setting is essential.

Reviews have investigated both pharmacological and nonpharmacological interventions for pain in the prehospital settings [31, 33, 48]. However, a scoping review of systematic reviews of interventions used to manage adult prehospital pain management has not yet been performed. Further, no previous scoping reviews have assessed the quality of the evidence, nor have they conducted a trial sequence analysis to determine the optimal information size required to facilitate a meaningful meta-analysis of interventional effectiveness.

Considering the range of clinical presentations and causes of pain encountered in the prehospital setting, we included a broad adult population with heterogeneous causes of pain, consistent with the objectives of a scoping review, to identify the breadth of existing evidence, methodological limitations, and identify knowledge gaps. Therefore, this scoping review was designed to descriptively synthesize the evidence on pain management for adults in the prehospital setting by identifying the types of interventions used and evidence gaps, while also assessing the quality of the evidence.

Methods

Study design

A scoping review of systematic reviews was designed, and the study protocol was pre-registered on an open repository [7].

Eligibility criteria

We included systematic reviews of randomized controlled trials (RCTs), observational studies, and quasi-experiments (including interrupted time-series and before-and-after studies), published with or without meta-analysis. All evidence sources were required to be available in full-text form. Reviews included adults aged 18 years or greater who were treated for pain by a healthcare professional during the prehospital period. We defined the prehospital period as the time from first contact with a person requiring pain treatment by a healthcare professional in the out-of-hospital setting until admission to the emergency department. Any pharmacological or nonpharmacological prehospital pain management intervention(s) were considered for inclusion. Reviews conducted in any country were included.

We excluded reviews published before 1995, as this was the inception of the Cochrane Database of Systematic Reviews when formal methods for systematic reviews were established. Reviews not published in English were excluded as professional translation resources were unavailable.

Search strategy

We searched MEDLINE (Ovid), EMBASE (Ovid), the Cumulative Index to Nursing and Allied Health Literature (CINAHL), the Cochrane Library, and the Trip database on April 11, 2025. The first 10 pages of PROSPERO, the Open Science Framework (OSF), and the International Platform of Registered Systematic Review and Meta-analysis Protocols (INPLASY) registries were also searched to identify any planned systematic reviews. The first two pages (20 results) of medRxiv using the 'best match' function were searched to identify any unpublished reviews. The reference lists of included systematic reviews were screened to identify additional eligible reviews following full-text screening. The searches were designed using keywords from the research question, including "prehospital", "analgesia", and "pain" (Appendix 1), which were developed in consultation with an information specialist.

Screening

Two reviewers (JMB, DV) independently performed title and abstract, and full-text screening using Covidence. A third reviewer (GCR, CH) resolved disagreements.

Data extraction

A single reviewer (JMB) extracted data into a pre-developed data extraction form using Google Sheets. The draft data extraction form was piloted using two included reviews to validate data items and identify new data items (Appendix 2). An iterative process was used throughout data extraction, and the data extraction form was modified as data emerged. If data were missing, review authors were contacted.

Quality assessment

One reviewer (JMB) assessed the quality of the included reviews using the AMSTAR 2 (A MeaSurement Tool to Assess systematic Reviews 2) tool [41]. The AMSTAR 2 tool is a 16-item checklist used to critically appraise the methodological quality of systematic reviews that include randomized and non-randomized intervention studies. Among the 16 items are seven critical domains, including protocol registration (Item 2), comprehensive search strategy (Item 4), list and justification of excluded studies (Item 7), risk of bias assessment (Item 9), appropriate use of meta-analytic methods (Item 11), accounting for risk of bias when interpreting review results (Item 13), and investigation of publication bias (Item 15). A low score in a critical domain reduces confidence in review results. Following completion of the appraisal checklist, an overall confidence rating for each review (high, moderate, low, or critically low) was assigned based on the review results. We also extracted whether the reviews analysed the funding sources of included primary studies (Item 10). The overall quality assessment reported in each review was synthesized.

Data synthesis and analysis

We synthesized extracted data descriptively and narratively. Medians with interquartile ranges (IQR) were used for continuous variables and frequencies (%) for categorical variables. Knowledge gaps were summarized narratively. Figures were created to illustrate the body of evidence by treatments used and grouped by drug class, target population, and evidence certainty. When reviews included studies of pediatric populations or emergency department settings among studies of prehospital adults, only data from prehospital adults were extracted. When a review investigated more than one pairwise comparison, each intervention was analyzed individually to determine its frequency.

For each review, we synthesised its general characteristics, including data on populations, interventions, comparators, and outcomes measured, and identified the World Bank income status based on the first author's nationality [51]. We analyzed the date of the last literature search and year of publication for each review and examined the progression of review quality over time.

We performed a trial sequence analysis using the meta-analytic data reported by Sobieraj [46] to calculate the optimal information size of a meta-analysis that would detect a 30% change in pain score (mean difference) at 30 minutes post-administration between opioids and ketamine. We used the data from the Sobieraj meta-analysis [46] as this was the largest meta-analysis included in our scoping review. We maintained the original 30% change in pain score at 30 minutes post-administration parameters of the Sobieraj meta-analysis in our trial sequence analysis to ensure consistency. The Trial Sequence Analysis Viewer (v 0.9.5.10 Beta) [49] was used to perform the analysis using the methods described by Garcia-Alamino et al. [18]. A two-sided test with an α of 0.05, power of 0.20 and heterogeneity correction for the I^2 of 74% from the original meta-analysis was applied.

Software and reporting

Covidence was used to screen studies for eligibility, remove duplicates, and produce a PRISMA flow diagram [10]. Data was extracted and analyzed using Google Sheets. Figures were created using Microsoft Excel. All study material is openly available on the Open Science Framework, including the study protocol [7].

Results

Study selection

Twenty-two systematic reviews were included (Fig. 1; Table 1) [2, 11, 12, 17, 20–22, 25, 26, 29, 34, 36–40, 44–46, 50, 52, 53], which included 192,872 participants across 289 primary studies. After removing 96 duplicates, 193 unique primary studies involving 102,495 participants were identified, of which 91% (n = 93,092) were adults and 9% (n = 9,403) were children (< 18 years).

Characteristics of included systematic reviews

The reviews were published between 2010 and 2024 (Fig. 2), with two-thirds published since 2018. Literature searches were conducted by the reviewers between 2009 and 2024, with 82% of the reviews published within one year of searches. Review first authors were from Europe (n = 13, 59%), followed by Australia (n = 4, 18%), North America (n = 3, 14%), and Asia (n = 2, 9%). Twenty-one reviews (96%) were conducted in countries with high World Bank income status, and one (4%) was performed in Iran, a lower-middle-income country. Seven reviews (32%) reported receiving internal or external funding to produce their reviews (Appendix 3).

Median sample size of systematic reviews and meta-analyses

The median number of study participants was 2541 (IQR = 511–9,284) across the reviews. The three largest reviews, Hansen et al. [20], Hyldmo et al. [26] and Haske et al. [26] included data from a single retrospective observational study [32] that enrolled 47,984 adults, representing almost half the study participants in this scoping review.

There were a median of 876 (IQR = 320–1,538) study participants across the eight (38%) reviews that conducted meta-analyses [22, 37, 39, 44–46, 52, 53]. The largest meta-analysis by Sobieraj et al. [46]. compared the effectiveness of ketamine to opioids at 15-, 30-, and 60-minutes post-administration.

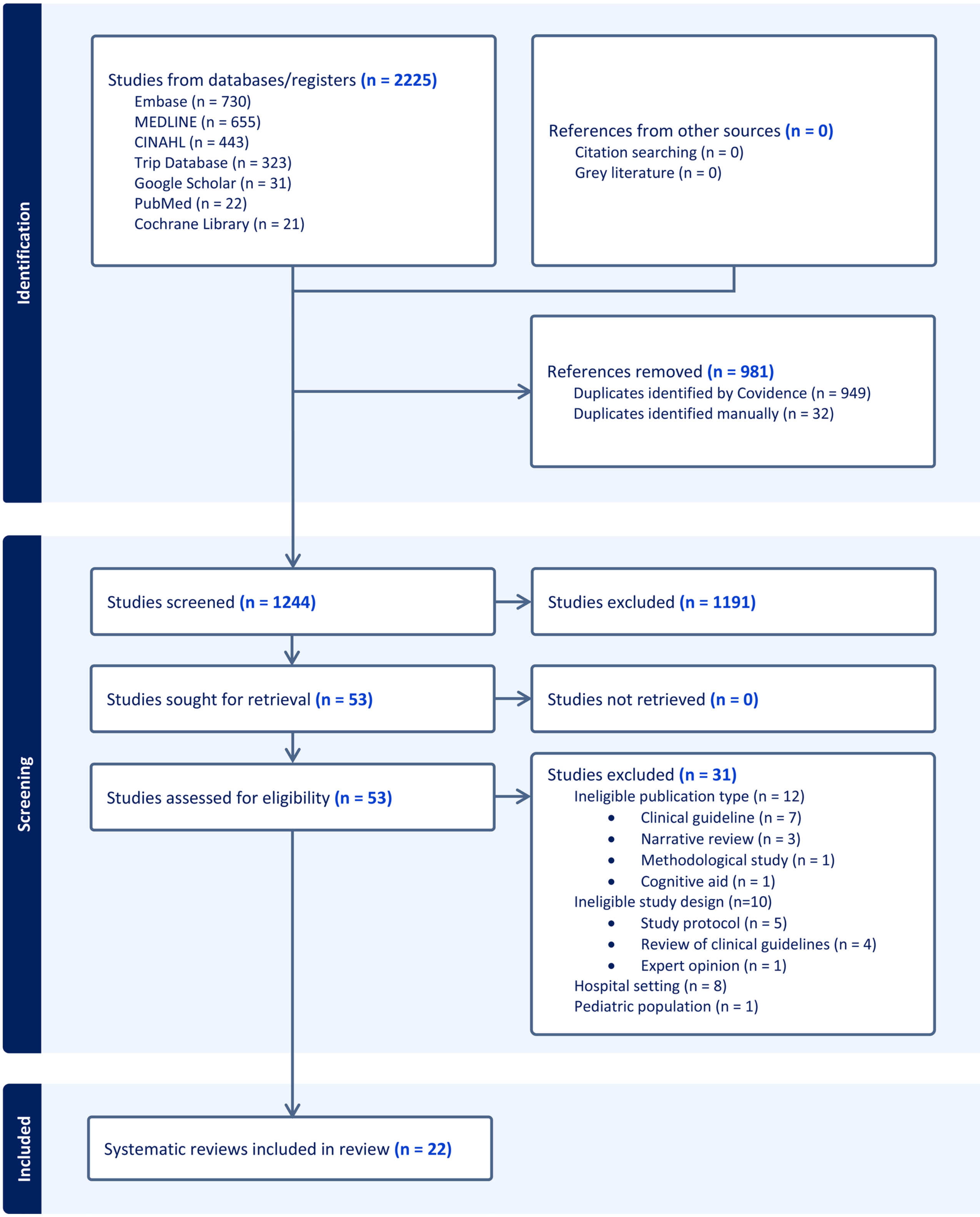

Fig. 1 PRISMA flow diagram of the screening and selection of systematic reviews included in this review

Table 1 Summary table of the 22 included systematic reviews of prehospital pain control interventions used in adults

Author, year (citation)	Date of search	No. of studies	Type of studies (n)	Population	Intervention(s)	Comparator(s)	Risk of bias (RoB) tool	Reported risk of bias	Quality assessment Tool	Quality assessment outcome	AMSTAR 2 overall grade
Opioids and non-opioid interventions											
Sobieraj, et al. 2020 [48]	09 May 2019	65	RCTs (52) and OSs (13)	6296 adults or children in the PHS or ED being treated for trauma or acute pain	fentanyl, morphine, ketamine, ketamine + morphine	ketamine, morphine, ibuprofen, ketorolac, paracetamol, nitrous oxide, placebo	Cochrane RoB Tool	High RoB (2), Medium RoB (6), Low RoB (30), Unclear RoB (3)	Evidence Based Practice Center of the U.S. Agency for Healthcare Research and Quality Method	Insufficient data to make conclusions	High quality SR
Haske, et al. 2017 [23]	28 Feb 2016	41	RCTs (17) and OSs (24)	69154 adults or children in the PHS or ED being treated for trauma pain	fentanyl, morphine, ketamine, ketamine + morphine, sufentanil, pentazocine, paracetamol, ibuprofen, methoxyflurane, nitrous oxide	fentanyl, fentanyl + midazolam, morphine, ketamine, codeine + APAP, methoxyflurane	Cochrane RoB tool	High RoB (2), Unclear RoB (8). (RoB assessment conducted only in RCTs included in meta-analysis)	Oxford Centre for Evidence Based Medicine Levels of Evidence Tool	Level 2b (19), Level 3 (1), Level 3b (7), Level 4 (14)	Moderate quality SR
Dijkstra, et al. 2014[13]	31 Dec 2011	25	RCTs (17), OSs (7), Qualitative (1)	1780 PHS or ED adults treated for trauma pain	morphine, sufentanil, metamizole, paracetamol, fentanyl, ketamine, ketamine + morphine, ibuprofen, tramadol nitrous oxide	morphine, diclofenac, tramadol, fentanyl, morphine + placebo, piritramide, oxycodone/ APAP, placebo, indomethacin	Dutch Institute of Health care Improvement	Mentioned in Methods but not reported in publication or supplementary materials	Australian National Health and Medical Research Council	Level A2 (4), Level B (10), Level C (11)	Critically low-quality SR
Park, et al. 2010[37]	28 Nov 2009	21	RCTs (5), OSs (16)	6212 adults in the PHS being treated for acute pain	morphine, fentanyl, alfentanil, tramadol, pentazocine, ketamine, fascia iliaca block, nitrous oxide, methoxyflurane	morphine	N/A	No RoB assessment reported	Not performed	N/A	Critically low-quality SR
Opioids only											
Serra, et al. 2023[41]	31 Dec 2022	23	RCTs (10), OSs (13)	10280 adults in the PHS being treated for moderate to severe trauma or acute pain	fentanyl	fentanyl	RCTs RoB-2, OSs MINORS	RCTs: High RoB (3), Low RoB (7). OSs: High RoB (3), Moderate RoB (8), Low RoB (11)	Not performed	N/A	Moderate quality SR
Hutchings, et al. 2023[26]	01 Feb 2022	4	RCTs	448 adults in the PHS or ED being treated for acute pain	sufentanil	morphine, placebo	RoB-2	Some concerns (1), Low RoB (3),	Not performed	N/A	Moderate quality SR
Friesgaard, et al. 2022 [18]	04 Jan 2021	12	RCTs	21,317 adults in the PHS, being treated for trauma or acute pain.	fentanyl, morphine, sufentanil, tramadol, alfentanil	morphine, placebo	RoB-2	High RoB (10), Some concerns (1), Low RoB (1)	GRADE	Very low to low quality evidence	High quality SR
Hansen, et al. 2013[21]	09 Feb 2012	12	RCTs (9), OSs (3)	47984 adults or children in the PHS or ED being treated for acute pain	fentanyl	morphine, methoxyflurane, fentanyl + methoxyflurane	Cochrane RoB Tool	High RoB (11), Moderate RoB (2), Low RoB (1)	Not performed	N/A	High quality SR

Table 1 (continued)

Niemi-Murola, et al. 2011[35]	30 Sep 2010	20	RCTs	2322 adults in the PHS or ED being treated for acute pain	papaveretum IM, fentanyl + saline NEB, morphine, paracetamol, hydromorphone, tramadol, butorphanol, pethidine	fentanyl + saline NEB, morphine, pethidine, placebo	N/A	No RoB assessment reported	Not performed	N/A	Low quality SR
Ketamine											
Bansal, et al. 2020[2]	30 Oct 2018	10	RCTs (4), OSs (6)	4778 adults in the PHS being treated for acute pain	ketamine, ketamine + morphine	pentazocine, morphine, morphine + placebo, placebo,	Scottish Intercollegiate Guidelines Network	High RoB (2), Low RoB (5), Very low RoB (3)	GRADE	Low to moderate quality evidence	High quality SR
de Rocuigny, et al. 2020[39]	31 Jan 2019	8	OSs	11338 adults in the PHS being treated for military trauma	ketamine	ketamine + morphine, ketamine + fentanyl	Not performed	N/A	Not performed	N/A	Critically low-quality SR
Sandberg, et al. 2020[40]	15 Feb 2020	8	RCTs (5), OSs (3)	2760 adults in the PHS being treated for trauma or acute pain	ketamine, ketamine + morphine, ketamine + nitrous oxide	morphine, fentanyl, pentazocine, ketamine, nitrous oxide, placebo	Cochrane RoB-1, ROBINS-1	High RoB (6), Unclear RoB (2)	GRADE	Very low to moderate quality evidence	High quality SR
Yousefifard, et al. 2020[54]	31 Dec 2018	7	RCTs (4), OSs (3)	857 adults in the PHS being treated for moderate to severe trauma pain	ketamine, ketamine + morphine	morphine, fentanyl, no treatment	Cochrane RoB-1	High RoB (6), Low RoB (1)	Not performed	N/A	Moderate quality SR
Jennings, et al. 2011[30]	30 May 2010	6	RCTs (2), OSs (4)	340 adults or children in the PHS being treated for acute pain	ketamine, ketamine + morphine	morphine	Scottish Intercollegiate Guidelines Network	High RoB (1), Moderate RoB (2), Low RoB (3)	International Liaison Committee on Resuscitation Method	Level 1 (1), Level 4 (4)	Moderate quality SR
Methoxyflurane											
Hyldmo, et al. 2024[27]	Mar 2024	7	RCT (1), QRCT (2), ROS (3), POS (1)	56,535 adults in the PHS being treated for acute pain	methoxyflurane, nitrous oxide	fentanyl, paracetamol, tramadol, morphine, ibuprofen, placebo	Cochrane Effective Practice and Organization of Care	High RoB (4), Moderate RoB (2), Low RoB (1)	GRADE	Very low to low quality evidence	High quality SR
Zaki, et al. 2023[55]	08 Oct 2022	4	RCTs	1130 adults in the PHS being treated for moderate to severe trauma pain	methoxyflurane	morphine, fentanyl, paracetamol, NSAIDs, placebo	Cochrane RoB-2	High RoB (4)	Not performed	N/A	Low quality SR
Peripheral nerve blocks											
Slade, et al. 2023[47]	01 July 2022	5	RCTs (2), OSs (3)	340 adults in the PHS being treated for femoral fracture pain	Fascia iliaca compartment block (FICB)	Standard of care	Cochrane RoB-2, ROBINS-2	High RoB (3), Low (2)	GRADE mentioned in Methods but not reported in publication or supplementary materials	N/A	Moderate quality SR
Raatiniemi, et al. 2020[38]	30 Sep 2019	4	RCTs (3), OSs (1)	252 adults in the PHS being treated for acute pain	Femoral nerve block (FNB), FNB with epinephrine + magnesium	metamizole, FNB with epinephrine, no treatment	Cochrane RoB-1, Murad, et al. Case Report Tool	High RoB (2), Low RoB (2)	GRADE	Very low quality of evidence	High quality SR
Williams, et al. 2019[52]	24 Apr 2018	4	RCT (1), OSs (3)	152 adults or children in the PHS	FICB	morphine	BestBets Tool	High RoB (4)	Oxford Centre for Evidence Based	Level 2 (1), Level 5 (3)	Moderate quality SR

Table 1 (continued)

				being treated for femoral fracture pain					Medicine Levels of Evidence Tool		
Hards, et al. 2018[22]	01 Feb 2017	7	RCT (1), OSs (6)	699 adults or children in the PHS being treated for femoral fracture pain	FICB, FNB	morphine, FNB, no treatment	Cochrane RoB Tool	No RoB assessment reported in article or supplementary material	Oxford Centre for Evidence Based Medicine Levels of Evidence Tool	Level 1b (1), Level 2b (3), Level 4(1), Level 5 (1), Not reported (1)	Moderate quality SR
Nonpharmacological interventions											
Davis, et al. 2021[12]	23 Mar 2020	19	RCTs (4), OSs (12), Qualitative (3)	4172 adults or children in the PHS with femoral fracture	Traction/splinting, auricular acupressure, Transcutaneous electrical nerve stimulation, FICB, morphine, fentanyl, methoxyflurane, nitrous oxide	Sham procedure, standard of care analgesics	National Heart, Lung, and Blood Institute Tool, JBI Qualitative Research Appraisal Tool	Good quality (11), Fair quality (3), Poor quality (2), QS: Include (3)	Not performed	N/A	Moderate quality SR
Simpson, et al. 2014[45]	15 Dec 2012	4	RCTs	261 adults in the PHS being treated for acute pain	Transcutaneous electrical nerve stimulation	Sham procedure	Cochrane RoB Tool	Moderate RoB (4)	Not performed	N/A	High quality SR

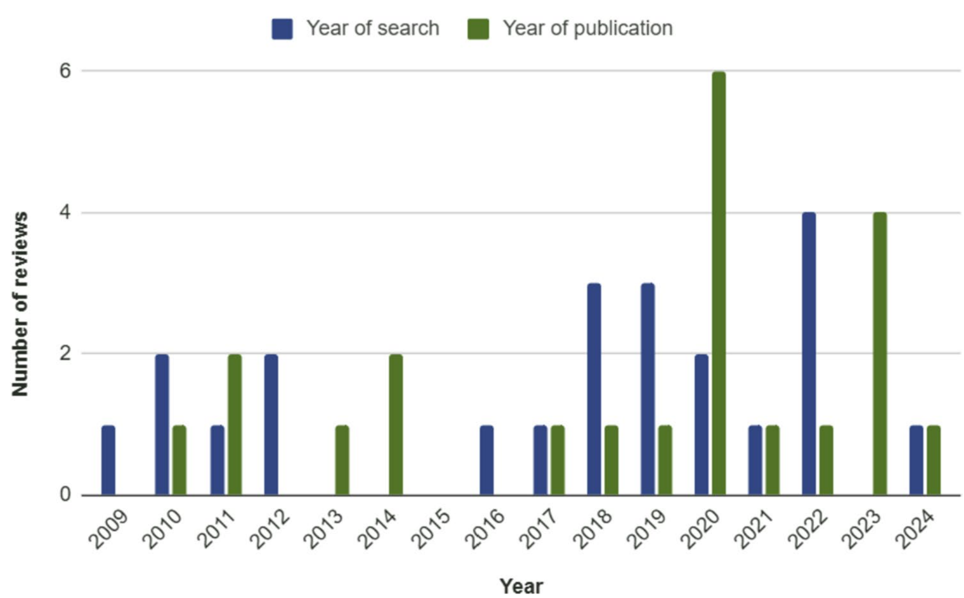

Fig. 2 Trends over time for years of literature search and review publication

Populations

Trauma-related pain management was investigated in five reviews (23%) [12, 22, 38, 52, 53], while the remaining 17 reviews (77%) investigated the management of acute prehospital pain from any cause. Nine reviews (41%) did not apply age restrictions in their inclusion criteria [11, 12, 20– 22, 29, 40, 46, 50]. Fifteen reviews (68%) included emergency department/hospital and/or pediatric studies, where six (27%) exclusively focused on the emergency department [12, 20, 22, 25, 34, 46].

Interventions

Among the 22 reviews, 20 (91%) assessed pharmacological interventions and two (9%) assessed non-pharmacological interventions. The reviews investigated 24 unique interventions across seven classes and nine routes of administration (Table 2).

Outcomes measured

All reviews reported pain reduction and adverse effects as outcomes. Most reviews ($n = 17$, 77%) recorded

Table 2 Interventions by category, number of systematic reviews investigating the intervention, and routes of administration assessed

Intervention	Number of systematic reviews	Routes of administration
Opioids		
Fentanyl	9	IV, IO, IN, TM
Morphine	7	IV, IM
Sufentanil	4	IV, IN
Tramadol	4	IV
Alfentanil	2	IV
Pentazocine	2	IV
Papaveretum	1	IV
Hydromorphone	1	IV
Butorphanol	1	IV
Meperidine	1	IV
NMDA inhibitor		
Ketamine	9	IV, IO, IN, IM
Ketamine + Morphine	7	IV
Ketamine + Nitrous oxide	1	IV/INH
Non-NSAID		
Paracetamol	3	IV, PO
Metamizole	1	IV
NSAID		
Ibuprofen	2	PO
Inhaled agents		
Methoxyflurane	5	INH
Nitrous oxide	5	INH
Peripheral nerve block		
Fascia iliaca compartment block	5	Percutaneous
Femoral nerve block	2	Percutaneous
Non-pharmacologic		
Transcutaneous electrical nerve stimulation	2	Transcutaneous
Traction/splinting	1	N/A
Auricular acupressure	1	Transcutaneous

Legend: IM, Intramuscular, IN; Intranasal, INH; Inhaled, INJ, Injection, IO; Intraosseous,IV; Intravenous, PO; Oral, TM; Transmucosal

single pre- and post-intervention pain scores, while others recorded pain scores at specified intervals (*n* = 5, 23%). Other outcomes reported by reviews included the success rate of peripheral nerve block placement (*n* = 4, 18%), onset speed of intervention (*n* = 4, 18%), duration of intervention effect (*n* = 3, 14%), the memory of pain (*n* = 1, 5%), on-scene time (*n* = 1, 5%), and rescue analgesia use (*n* = 1, 5%).

All studies measured pain using validated tools, but this varied with a total of seven different tools used, including the Visual Analog Scale (*n* = 12, 55%), Numeric Rating Scale (*n* = 11, 50%), Visual Rating Scale (*n* = 5, 23%), Nonverbal Pain Score (*n* = 1, 5%), Objective Pain Scale (*n* = 1, 5%), Verbal Numerical Pain Score (*n* = 1, 5%) and the Wong-Baker Faces Score (*n* = 1, 5%). Surveys, when used by qualitative studies included in the reviews, were patient and staff satisfaction (*n* = 3, 14%), patient satisfaction (*n* = 2, 9%) and staff observation (*n* = 1, 5%).

Optimal information size of meta-analysis comparing ketamine with opioids

The results of our trial sequential analysis indicated an optimum information size of 5126 participants was needed to detect a 30% mean difference in pain score post-administration between ketamine and opioids (Fig. 3). The cumulative Z-score line did not cross the futility plot, indicating further studies are likely to demonstrate a meaningful effect.

Quality assessment of systematic reviews

Among the reviews, eight (36%) were high quality, nine (41%) were moderate quality, two (9%) were low, and three (14%) were critically low (Table 3). Two-thirds (*n* = 15, 68%) of reviews met the criteria for all seven AMSTAR 2 critical domains described in the quality assessment section of the Methods.

The most common AMSTAR 2 critical domain exceptions were explicitly accounting for the risk of bias in the included primary studies when interpreting and discussing review results (Item 13) (*n* = 6, 27%) and using a satisfactory technique for assessing the risk of bias in the individual primary studies included in the review (Item 9) (*n* = 3, 14%). Among non-critical AMSTAR 2 domains, the most common exception was reporting on sources of funding for primary studies included in their reviews (Item 10) (*n* = 0) and not explaining their selection of the study designs included in their review (Item 3) (*n* = 8, 36%).

All reviews that conducted meta-analysis (*n* = 8) used appropriate methods for the statistical combination of results. Seven reviews (86%) explicitly described the impact of risk of bias on their results and provided explanations and discussions of heterogeneity. Publication bias investigation was not conducted in seven (86%) meta-analyses. However, these seven justified the absence of publication bias investigation as they did not include 10 or more studies in the meta-analysis and were marked as meeting the criteria.

Quality of evidence reported by reviews

Risk of bias assessment of primary studies was performed by 19 of 22 reviews (86%). Three reviews did not perform a risk of bias assessment [34, 36, 38]. There were 183 primary studies assessed within the 19 reviews evaluating risk of bias. Risk of bias was deemed high in 63 studies (34%), moderate in 28 (15%), low in 82 (45%) studies, and unclear in 10 (6%). Allocation bias from lack of randomization, performance bias from lack of blinding of participants and those administering treatment, and detection bias from failure to blind outcome

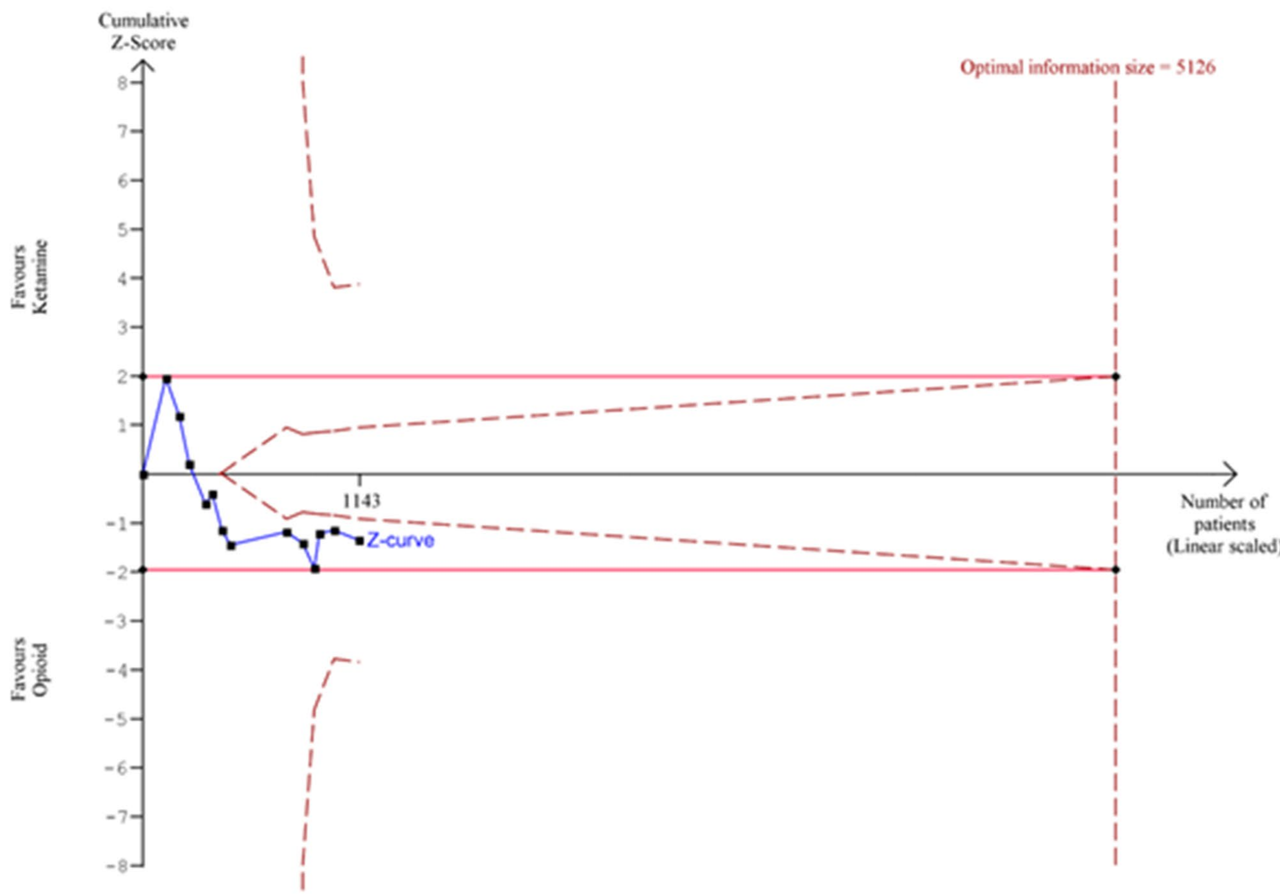

Fig. 3 Results of the trial sequential analysis of the largest included meta-analysis comparing opioids to ketamine the trial sequential analysis (TSA) plot displays cumulative evidence from trials (black points, $n = 14$) included in the meta-analysis in chronological order of publication. The cumulative Z-curve (solid blue line) represents the pooled effect estimate as each trial is added. The red horizontal lines denote the conventional thresholds for statistical significance ($Z = \pm 1.96$). The sloped inner boundaries (orange dashed lines) represent the monitoring boundaries for treatment benefit. The arrow-shaped orange dashed lines between the statistical significance thresholds represent the futility boundary. The dashed orange vertical line (right side of figure) indicates the optimal information size (OIS), analogous to the sample size needed for a single adequately powered trial. The number of patients included in the meta-analysis ($N = 1143$) is represented by a point on the right-facing arrow between the statistical significance thresholds. In this plot, the cumulative Z-curve has not crossed the statistical significance lines before reaching the OIS indicating the evidence is insufficient to determine a meaningful effect difference between opioids and ketamine and that further studies are needed. Likewise, the cumulative Z-score line did not cross the futility boundary, indicating further studies are likely to demonstrate a meaningful effect

assessors were reported by reviewers as sources of bias within RCTs. Confounding and observer bias were noted by reviewers as sources of bias in observational studies.

Assessment of the certainty or level of evidence was performed by 11 of 22 reviews (50%). The GRADE method, or a GRADE-based method, was used by six of the 11 reviews (55%) [2, 17, 26, 37, 39, 46]. One review stated that GRADE was to be used, but did not report results in the publication or supplementary material [45]. The Oxford Centre for Evidence-Based Medicine Levels of Evidence Tool was used by three reviews (27%) [21, 22, 50]. Other evidence-leveling methods were used by two reviews (18%) [12, 29].

Quality of reviews over time and by intervention category

Analysis of review quality from 2010 to 2024 showed no pattern of improvement over time (Fig. 4). The quality of pharmacological reviews ($n = 20$) was high in seven (35%), moderate in eight (40%), low in two (10%), and critically low in three (15%). The quality of nonpharmacological reviews ($n = 2$) was high in one (50%) review and moderate in one (50%).

The quality of opioid reviews ($n = 10$) was high in three (30%), moderate in four (40%), low in one (10%), and critically low in two (20%). The quality of non-opioid reviews ($n = 12$) was high in five (42%), moderate in five (42%), low in one (8%), and critically low in one (8%).

Table 3 Quality assessment of included systematic review using the AMSTAR 2 tool (*= Critical domain)

Authors	Year	1 PICO elements?	2* *a priori* Protocol?	3 Explanation study design selection?	4* Comprehensive search strategy?	5 Duplicate study selection?	6 Duplicate data extraction?	7* List and justification of excluded studies?	8 Detailed description of included studies?	9* Risk of bias (RoB) assessment?	10 Funding sources of included studies?	11* Appropriate meta-analysis methods?	12 Assessment of RoB impact on results?	13* Accounted for RoB when interpreting & discussing results?	14 Explanation and discussion of heterogeneity?	15* Publication bias investigation?	16 Conflict of interest and funding disclosure?	Confidence in review results by AMSTAR2 rating scale
Hyldmo, et al.	2024	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	NA	NA	Y	Y	NA	Y	High
Hutchings, et al.	2023	Y	Y	N	Y	Y	Y	Y	Y	Y	N	NA	NA	Y	Y	NA	Y	Moderate
Serra, et al.	2023	Y	PY	N	Y	Y	Y	Y	Y	Y	N	NA	NA	Y	Y	NA	Y	Moderate
Slade, et al.†	2023	Y	PY	N	PY	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Moderate
Zaki, et al.†	2023	Y	Y	Y	PY	Y	Y	Y	Y	Y	N	Y	N	N	Y	Y	Y	Low
Friesgaard, et al.	2022	Y	Y	Y	PY	Y	Y	Y	Y	Y	N	NA	NA	Y	Y	NA	Y	High
Davis, et al.	2021	Y	Y	N	PY	Y	Y	Y	Y	Y	N	NA	NA	Y	Y	NA	Y	Moderate
Bansal, et al.	2020	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	NA	NA	Y	Y	NA	Y	High
De Rocuigny, et al.	2020	Y	Y	N	PY	Y	N	N	Y	N	N	NA	NA	N	Y	NA	Y	Critically low
Raatiniemi, et al.	2020	Y	Y	Y	PY	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y	High
Sandberg, et al.†	2020	Y	PY	Y	PY	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	NA	Y	High
Sobieraj, et al. †	2020	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	NA	Y	High
Yousefifard, et al.†	2020	Y	PY	N	PY	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Moderate
Williams, et al.	2019	Y	PY	Y	PY	N	N	Y	Y	Y	N	NA	NA	Y	N	NA	Y	Moderate
Hards, et al.	2018	Y	PY	N	PY	Y	Y	Y	Y	PY	N	NA	NA	N	Y	NA	Y	Moderate
Haske, et al.†	2017	Y	Y	Y	PY	Y	Y	Y	Y	Y	N	Y	Y	N	Y	N	Y	Moderate
Dijkstra, et al.	2014	Y	PY	Y	N	Y	Y	Y	Y	PY	N	NA	NA	N	Y	NA	Y	Critically low
Simpson, et al.†	2014	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	High
Hansen, et al.	2013	Y	PY	Y	PY	Y	Y	Y	Y	Y	N	NA	NA	Y	Y	NA	Y	High
Jennings, et al.	2011	Y	PY	Y	Y	N	N	Y	Y	Y	N	NA	NA	Y	Y	NA	N	Moderate
Niemi-Murola, et al.	2011	Y	PY	N	PY	Y	Y	Y	Y	N	N	NA	NA	Y	Y	NA	N	Low
Park, et al.	2010	Y	PY	Y	PY	Y	Y	Y	Y	N	N	NA	NA	N	Y	NA	Y	Critically low
Met criteria		100%	50% Y 50% PY	64%	32% Y 64% PY	91%	86%	95%	100%	77% Y 9% PY	0%	100%	88%	73%	95%	100%	91%	

Discussion

This scoping review identified 22 systematic reviews that included 93,092 adults requiring pain management in the prehospital setting who were treated with 24 different interventions. Opioids and ketamine were the most common interventions synthesized in reviews, with only 10% of reviews examining nonpharmacological interventions. However, the number of participants included in meta-analyses did not meet the optimal information size we identified, which was 5126 participants required to detect a meaningful interventional effect. In contrast, the meta-analyses had a median of 876 participants, with the largest including 1153 [46]. Pain was measured using seven different validated tools, and adverse effects were reported across all 22 reviews. Three-quarters of the included reviews were of moderate to high quality, but evidence certainty was very low to low in half of the reviews. Notably, none of the included reviews reported the funding sources of the primary studies they included.

Comparison with previous scoping reviews

Three scoping reviews on prehospital pain management have explored both pharmacological and nonpharmacological interventions [31, 33, 48]. Mota et al. focused on identifying nonpharmacological interventions used to treat adult trauma patients in the prehospital, emergency department, and hospital settings [33]. Similar to our review, they identified limited evidence for nonpharmacological interventions. Lourens et al. reviewed prehospital pain management in Africa [31], but found few primary studies in this region. Similarly, we did not identify any reviews conducted in Africa and only one conducted in a low- to middle-income country, which is a persistent issue across pain research [19], Teoh et

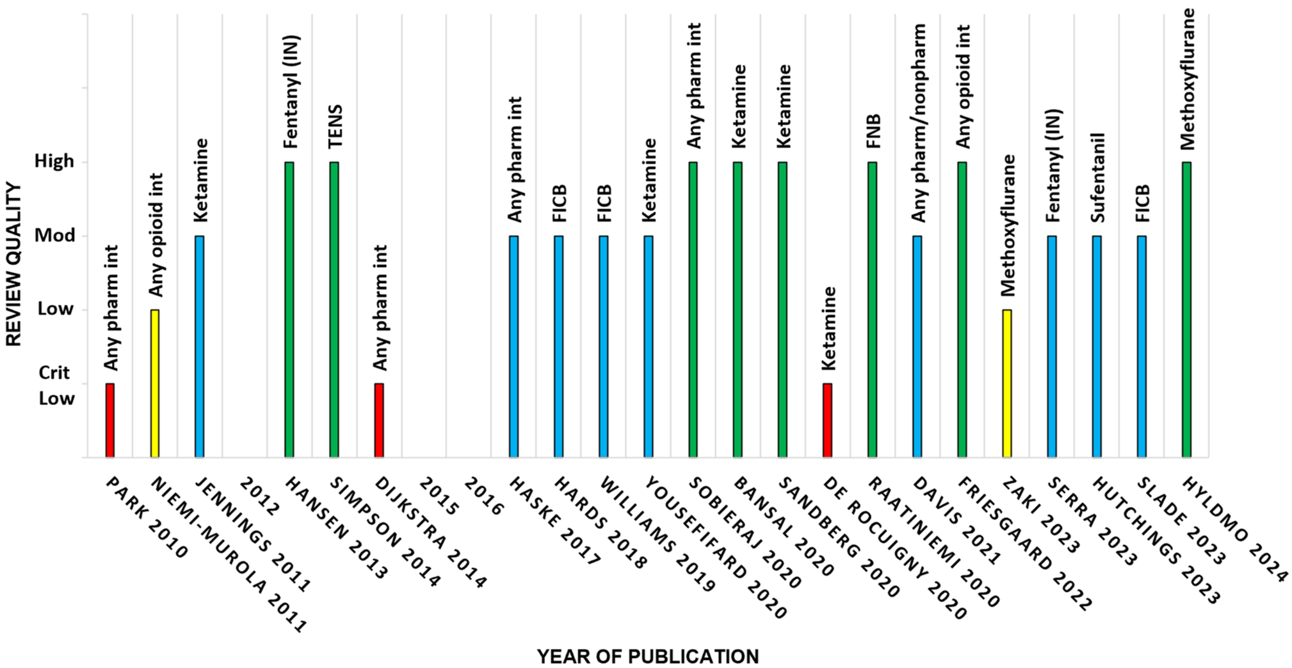

Fig. 4 Review quality over time and main intervention investigated

al. reviewed the barriers and facilitators of providing prehospital pain management [48], which further highlighted the issues of applying research findings from high-income countries to middle and low-income countries. However, these studies did not conduct a quality appraisal and were narrow in their focus of included studies. In contrast, our systematic scoping review incorporated reviews from across all regions, addressing geographic gaps and assessing methodological limitations.

Strengths and limitations

This is the first scoping review of systematic reviews, aimed at identifying both pharmacological and non-pharmacological interventions to treat pain in adults in the prehospital setting and identifying global knowledge gaps. We intentionally chose broad inclusion criteria to avoid unintentional exclusion of relevant systematic reviews which demonstrated the fragmented nature of the evidence and facilitated the identification of knowledge gaps. Our search was conducted in consultation with an information specialist, and we performed a quality assessment using AMSTAR 2. We also performed a trial sequence analysis to quantify the optimal information size required for meaningful meta-analyses of interventions for adults with prehospital pain.

Across the 22 reviews, duplicate entries were found in both the reviews and their primary studies. This was accounted for by individually removing duplicates and by examining participants' ages and study settings to exclude pediatric studies and those conducted in the emergency department. Most reviews were authored and performed in high-income nations, indicating that their results may not be generalizable to resource-limited countries. Lastly, we did not investigate the effectiveness of individual interventions, as this was not an aim of our review; instead, we aimed to identify the types of interventions and knowledge gaps.

Implications

Our review, particularly the finding that no meta-analyses met the threshold of 5126 participants needed to detect a meaningful interventional effect, demonstrates the need for more high-quality trials of prehospital analgesics across the range of populations and settings where prehospital pain management is administered. Key subgroups, including the military, older adults, pregnant individuals, rural populations, and those injured or ill in austere environments where prolonged transport time may be involved, are scant. This knowledge gap indicates some uncertainty regarding what analgesics are effective, safe, and available for use in these contexts. To generate translatable evidence, pragmatic trials should be funded and designed [24] to inform the development of clinical practice guidelines, aid implementation and increase acceptance among prehospital healthcare professionals.

Although pragmatic trials may provide valuable translatable evidence, the often chaotic prehospital setting poses substantial barriers to large-scale randomized studies. These barriers include variability in EMS staffing models, scope of practice, governance, time constraints, and informed consent issues [8]. To overcome these barriers, researchers could consider incorporating methodologies within pragmatic trials such as cluster randomization, stepped-wedge designs, registry-embedded trials, or international collaborative networks.

Cluster randomization assigns interventions at the EMS unit or station level reducing contamination between treatment arms and aligning with routine workflows [15]. Stepped-wedge designs use phased implementation across clusters so that all units eventually receive the intervention, improving acceptability and enables comparisons over time as each cluster serves as its own control [23]. Registry-embedded trials use existing registries for recruitment and randomization which increases enrollment speed, reduces costs, and facilitates data collection applicable to real-world settings [42]. Lastly, international collaborative networks increase sample size and diversity, speed of data collection, and generalizability across different EMS systems and geographic regions by pooling expertise and infrastructure across study sites [35]. Together, these methodologies support the conduct of pragmatic trials that can produce findings applicable to prehospital pain management.

Although intervention-related adverse events were reported across all reviews, only six primary qualitative studies of patient or staff satisfaction with treatment were identified within our review. This finding indicates the existence of a knowledge gap regarding patient preferences, particularly regarding trade-offs between analgesic efficacy, side effects (e.g., dissociation, nausea, respiratory depression), and functional outcomes. This gap is a significant limitation, as patient-centered outcomes are increasingly recognized as essential for informing guideline development and shared decision-making [5, 47], even in time-critical prehospital environments. More preference-sensitive qualitative research alongside trials is needed to address this knowledge gap.

The methodological limitations identified in our review could be addressed by establishing a core outcome set [9] for measuring prehospital pain and the adverse effects of interventions, as well as by establishing global standards for reporting, including separating outcomes for prehospital and emergency department settings and for pediatric and adult populations. This would reduce inconsistencies and variations across studies, increase generalizability and support evidence synthesize. PRISMA could be updated to require reporting of primary study funding sources in reviews [6] due to the impact that industry sponsorship can have on the outcomes of systematic reviews and meta-analyses [43].

Conclusions

Despite there being extensive reviews on the use of opioids and ketamine for prehospital pain management, we found that populations included in meta-analyses were below the required threshold to determine a meaningful interventional effect. Evidence on nonpharmacological interventions, key subgroups, and regional locations where pain management is often required was limited. Larger pragmatic trials, a core outcome set, and global reporting standards would facilitate the synthesis of translatable evidence and support evidence-based decision-making for pain management in prehospital settings.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12873-026-01491-1.

Supplementary material 1

Supplementary material 2

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Author contributions

JMB: Conceptualization, Methodology, Investigation, Formal analysis, Writing-Original Draft, Visualization. DV: Investigation, Validation, Writing- Review and Editing. CJH: Conceptualization, Methodology, Writing- Review and Editing, Supervision. GCR: Conceptualization, Methodology, Visualization, Writing-Review and Editing, Supervision. All authors reviewed and approved the manuscript.

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Data availability

Data extraction and analyses files are available at Open Science Framework: https://doi.org/10.17605/OSF.IO/MH7Q9 .

Declarations

Human ethics and Consent to participate

An ethics statement is not applicable because this study is based exclusively on published literature. The scoping review protocol was preregistered on the Open Science Framework platform (https://doi.org/10.17605/OSF.IO/MH7Q9) .

Consent to participate

Not applicable.

Consent for publication

All authors consented to participate in the study and its publication.

Competing interest

The authors declare no competing interests.

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