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Gender Bias in Pharmacological Pain Management in Emergency Medicine – Protocol for a Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202540067

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 April 2025 and was last updated on 21 April 2025.

INTRODUCTION

Review question / Objective Do healthcare professionals' pharmacological pain management decisions differ by patient gender among individuals presenting with pain in emergency care settings (prehospital and hospital)?

Rationale Gender-related disparities in healthcare have gained increasing attention in recent years, particularly in the context of pain management. Research indicates that biological, psychological, and social factors influence both the experience and expression of pain, as well as healthcare providers' responses to it. Gender stereotypes—such as women being more expressive or men being more stoic—may unconsciously shape clinical decisions, potentially resulting in unequal treatment. In emergency care, where decisions are often made under pressure and with limited information, reliance on cognitive shortcuts and heuristics may amplify such biases. Despite growing awareness of these dynamics, findings in the literature remain inconsistent. A systematic review and meta-analysis can help synthesize the evidence to clarify whether gender bias exists in pharmacological pain management in emergency medicine and under what conditions it manifests. The findings could guide future training, clinical practice, and policy to promote equity in emergency healthcare delivery.

Condition being studied The condition under investigation is acute pain as experienced by patients presenting to emergency medicine settings, including both prehospital care and emergency departments. Pain is one of the most common complaints in these environments and represents a complex, subjective experience influenced by physiological, psychological, and social factors. In the high-stakes and fast-paced setting of emergency care, timely and effective pain management is critical for patient outcomes and satisfaction. However, disparities in how pain is assessed and treated—particularly based on

patient gender—may contribute to inequities in care. This review focuses on pharmacological strategies used to manage pain in this context, aiming to determine whether there are systematic differences in the administration of analgesics between male and female patients.

METHODS

Search strategy Primary Search
The search strategy consists of three key concepts 'pharmacological pain management', 'emergency care and 'gender bias'. The concept of 'gender bias' was designed to identify all studies that included gender differences in their primary or secondary research question.
Furthermore, bibliographies of included studies will be searched in accordance with the AMSAR rating criteria.

Comparative Methodological Analysis (Secondary Search)
Since the search strategy includes a gender-related concept, studies that do not explicitly focus on gender bias or gender-based comparisons may not be identified. Consequently, the results may be influenced by the framing and reporting of research questions in the included literature. To investigate whether the use of an explicit gender bias focus affects the estimation of gender differences in pain management, we will conduct a secondary, simplified search limited to the concepts of 'emergency medicine' and 'analgesia'. This approach aims to assess how effect estimates vary when gender bias is not a predefined research question. The search will be conducted in a single database (MEDLINE via PubMed). One author (GF) will screen titles and abstracts in reverse chronological order, beginning with the most recent ones. If necessary, full texts will be reviewed to determine eligibility. Screening will continue until 50 eligible studies are identified. For each study, one single effect size will be extracted based on a predefined hierarchy (see below). Continuous variables will be converted to OR according to 'Additional outcomes'. All extracted data will be pooled and analyzed according to the methods described in 'Strategy of data synthesis'. The variable 'Gender issues as primary/secondary research question' will be evaluated to be an effect modifier using metaregression.

Outcome Hierarchy for the Secondary Search
1. Any analgesic given
2. Any opioid given
a. Strong Opioid +/- baseline Analgesic given (Morphine, Fentanyl, Oxycodon, Buprenorphine) (OR)
b. Weak Opioid +/- baseline analgesic given (Tramadol, Codein)
3. Any non-opioid analgesic given
a. NSAR given
b. Paracetamol given
c. Metamizole given
d. Ketamine given
4. Time to analgesia administration
5. Pain score reduction post-treatment
6. Dosage of opioid analgesic given
7. Dosage of non-opioid analgesic given
8. Receiving sedatives instead of pain medications
9. Triage category
10. Patient-reported satisfaction with pain management.

Participant or population The population studied will focus on patients 16 years or older reporting pain in an emergency medicine setting. Prehospital care will be considered as part of emergency medicine and will be included. Mixed study populations regarding the setting, consisting of emergency medicine patients and non-emergency medicine patients, will be excluded. Studies involving mixed-age populations, i.e., including children and younger adults, will be considered for inclusion if the focus are not pediatric patients.

Intervention The focus are pharmacological pain management practices conducted by any type of health care professional operating within the setting of emergency medicine (attending / resident physicians, paramedics, nurses, students, etc.). All pain relief medications (opioid and non-opioid) are included. Studies examining medications with multiple indications (e.g., acetylsalicylic acid as an analgetic and as a platelet aggregation inhibitor) are only considered for inclusion when specifically used for analgesic purposes. Interventional pain management strategies (e.g., nerve blockage) are considered as pharmacological pain management and will be included. Studies focusing on differences in pain assessment between genders such as pain reporting by patients or pain evaluation and interpretation by physicians will not be included.

Comparator The primary interest of this study are direct comparisons of pharmacological pain management between gender, assessing disparities based on gender specific stereotypes and norms perceived by the health-care professional involved in care. Due to the focus on a binary gender system (men and women / male and female) in most studies and reported patient data, this review is limited to these two gender categories only. However, we acknowledge that

sex and gender exist along a spectrum and should be considered accordingly in clinical practice.

Study designs to be included Original research articles, including randomized controlled trials (RCT), case-control studies, cross-sectional studies, cohort studies, avatar-based studies, and vignette studies published prior to the search in January 2025, will be included. Qualitative studies, case reports (defined as less than 20 cases), expert opinions and commentaries will be excluded.

Eligibility criteria The review will include: i) studies involving adult (16 years or older) patients and mixed-age populations with any kind of pain presenting in the ED or prehospital setting, ii) studies focusing on pharmacological interventions for pain management, iii) studies involving any kind of health-care professional as provider, iv) studies analyzing the comparison between male and female patients and men and women respectively, v) studies published in English and/or German, vi) studies with an objective to study gender disparities.
The following studies will be excluded: i) studies focusing on pediatric patients (less than 16 years old), ii) studies not conducted in the emergency medicine setting, iii) studies not including gender/sex differences in research question, iv) studies on gender stereotypes not involving medical personnel, v) studies without pharmacological pain intervention, vi) qualitative studies, case reports, commentaries and expert opinions, vii) studies published in other languages than English and German.

Information sources In line with the approach proposed by Bramer et al. 6, we will perform a systematic literature search across i) Embase, ii) MEDLINE, iii) the Web of Science Core Collection, and iv) Google Scholar to ensure optimal recall. Google Scholar will be limited to the first 200 hits and will be listed separately as “hand search” in the study flowchart and will be classified as gray literature search. To incorporate studies relevant to all healthcare professionals, including nurses, we will also search CINAHL database. For better identification of RCT and clinical trials, we will further extend our search to Cochrane CENTRAL and ClinicalTrial.gov.

Main outcome(s) The primary outcome will be the difference in pharmacological pain interventions between men and women in the ED or prehospital. This includes the type of analgesic (e.g., opioids, non-opioid analgesics), and timing (e.g., time to first analgesic dose), where reported.

Additional outcome(s) Secondary outcomes include gender differences for specific analgesics administered (acetaminophen, NSAID, metamizole, weak opiates, strong opiates, ketamine), dosage administered, pain relief effectiveness (when reported with validated scales), receiving sedatives instead of pain medications, patient-reported satisfaction with pain management.
Data will be extracted as (adjusted) odds ratio (OR) including 95% confidence interval (CI) where possible. For continuous variables, standardized mean difference (SMD) will be extracted and converted to OR according to Hasselblad and Hedges’ method .
Outcomes will be prioritized based on frequency of reporting across included studies, with meta-analyses conducted on outcomes reported in at least two studies using compatible metrics.

Data management
Data Management
All records retrieved in the literature search will be uploaded to Covidence, in which the records will be deduplicated prior to screening. The number of duplicates identified will be reported in the PRISMA flowchart. Duplicates identified during the screening process will be categorized as "manually deduplicated" to ensure transparency in deduplication methodology.

Selection Process
Two of the authors (GF, RI) will independently and blindly screen titles and abstracts for eligibility for full-text review using Covidence, in accordance with predefined eligibility criteria. In cases of disagreement, a third author (RB) will independently apply the eligibility criteria and participate in the discussion to reach consensus.
Subsequently, the remaining articles will undergo a full-text screening by the same two reviewers (GF, RI). If full text is not available, this will be documented and reported in the PRISMA flow diagram.

Data Collection Process
Full-text analysis and data extraction will then be performed by the same two reviewers independently (GF, RI) using Microsoft Excel.
If data are missing or unclear, we will contact the corresponding author via email twice, within a 14-day interval between attempts. Authors will be considered unresponsive if no reply is received within 14 days after the second email.

Quality assessment / Risk of bias analysis The blinded, independent quality assessment will be conducted by the same two reviewers (GF, RI) applying the “Quality Assessment Tool for

Quantitative Studies" criteria developed by the Effective Public Health Practice Project (EPHPP) Canada for included studies. The tool has been validated for interrater-agreement content and construct validity and can be used for various study designs such as RCTs, case-control studies etc. The tool evaluates six different domains: selection bias, study design, confounders, blinding, data collection methods and withdrawals / dropouts and will be applied at study level. Each domain will be rated individually as 'strong', 'moderate' or 'weak' and an overall rating will be given by combining the domains using the provided algorithm. The results of each domain and the overall score will be presented in a table. Discrepancies in ratings between GF and RI will be resolved by discussion with a third author (RB).

Strategy of data synthesis Due to the expected heterogeneity of outcomes, we will firstly give a descriptive overview of the characteristics of each study in table.
A quantitative synthesis will be conducted when an outcome is reported by at least two studies. We will use OR and where available adjusted OR for dichotomous outcomes, continuous outcomes will be converted to OR according to Hasselblad and Hedges' method for consistency. Statistical heterogeneity will be assessed using the I^2 statistic and the between-study variance (τ^2). An I^2 value above 50% will be considered substantial heterogeneity. τ^2 will be estimated as part of the random-effects model and used for study weighting and exploration of heterogeneity. Meta-analyses will be conducted using a random-effects model (DerSimonian and Laird), as clinical and methodological heterogeneity across studies is expected. Furthermore, if heterogeneity is substantial and more than ten studies report a common outcome, we will conduct meta-regression analyses to explore whether study-level characteristics (e.g., setting, provider type, publication year, risk of bias, age > 18y, gender of corresponding author) explain variability in effect sizes.

Subgroup analysis None planned.

Sensitivity analysis None planned.

Language restriction English and german.

Country(ies) involved Switzerland, Germany.

Keywords gender, pain, emergency care, pain management, women, men.

Contributions of each author

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