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Does a history of sickle cell disease affect the prescription of morphine? An international, randomised study based on clinical vignettes conducted among emergency physicians

Fabien Coisy ,[1,2] Alexandre Simon,[3] Céline Occelli,[4,5] Florence Dupriez,[6] François-Xavier Ageron,[7] Lorie N'Diaye,[2] Anne-Laure Feral-Pierssens,[8,9] Gregory Yates,[10] Xavier Bobbia[1,4]

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For numbered affiliations see end of article.

Correspondence to
Dr Fabien Coisy;
fabien.coisy@gmail.com

ABSTRACT

Objectives To assess whether emergency physicians prescribe morphine differently for patients with or without sickle cell disease (SCD). Given the difficulty of comparing strictly homogeneous patients in real clinical settings, we used a standardised clinical vignette to ensure that all clinical information was identical except for SCD status and sex.

Design International, randomised controlled, vignette-based study conducted online. The four vignette versions differed only in patient sex and SCD status, with all other clinical information fully standardised. Vignettes were validated by an expert panel and randomly allocated using a computer-generated sequence.

Setting Emergency physicians practising in France, the UK, Belgium and Switzerland were invited to complete an online survey between 17 February and 17 March 2025.

Participants A total of 1060 physicians responded, of whom 953 (90%) met eligibility criteria and were included in the analysis. Respondents were practising emergency department (ED) physicians without exclusion based on seniority or training level.

Primary and secondary outcome measures The primary outcome was the proportion of simulated patients for whom morphine was prescribed. Secondary outcomes included the number and type of analgesics prescribed and the proportion of cases meeting predefined criteria for maximal level of care (urgent triage category, lactate sampling, CT imaging and morphine administration).

Results Morphine was prescribed in 444 of 492 (90%) SCD vignettes and 389 of 461 (84%) non-SCD vignettes (absolute difference: 6% (95% CI 1% to 10%)). Morphine monotherapy was used in 41% of SCD cases and combined analgesia in 50%. No significant differences were observed according to patient sex or physician characteristics. Maximal level of care was recommended in 22% of SCD cases.

Conclusion In this randomised vignette study, emergency physicians prescribed morphine more frequently for simulated patients with SCD than for those without SCD, despite identical clinical presentations. These findings contrast with real-world reports of inadequate analgesia in SCD and suggest that the absence of perceptual cues—such as skin colour or names—may reduce implicit bias in opioid prescribing.

Trial registration number NCT06835335. IRB CHU Nîmes No 25.02.01.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Standardised vignettes ensured that all clinical information was identical across scenarios, isolating the effect of sickle cell disease status on prescribing decisions.
⇒ Randomised design reduced allocation bias and allowed comparison of physician responses across four vignette versions.
⇒ An international sample of emergency physicians provided perspectives from multiple healthcare systems, although the use of convenience sampling may limit representativeness.
⇒ Expert-informed vignette development followed Guideline for Reporting Vignette Experiments (GROVE) and Consolidated Standards of Reporting Trials 2025 recommendations, enhancing methodological transparency.
⇒ Ecological validity is limited, as vignette-based responses may differ from real clinical encounters, and poststratification was not feasible due to a lack of denominator data.

INTRODUCTION

There are disparities in the way patients are treated in emergency departments (EDs) based on their gender and ethnicity.[1] These disparities significantly impact morbidity and mortality in the ED,[2] although research on this topic has been obstructed by European legislation.[3] One such disparity is inadequate pain relief ('oligo-analgesia'), which is commonly experienced by marginalised individuals.[4 5] Indeed, pain management is

an effective way to evaluate the quality of care provided to these patients.

Patients with sickle cell disease (SCD) are almost exclusively of sub-Saharan origin[6] and frequently present to the ED with vaso-occlusive crises (VOC). These episodes can be life-threatening[7] and high-strength opioids (eg, morphine) are generally recommended to control severe pain.[8 9] Across national guidelines—including those from France, the UK and the USA—morphine is consistently recommended as first-line treatment for severe acute pain in SCD, particularly during VOC. Analgesia for these patients is often inadequate due to staff suspicions of opioid misuse, which may be influenced by racial bias.[10–12]

To our knowledge, no controlled study exists that compares analgesic prescribing in the ED between patients with and without SCD. To address this gap, we conducted a prospective, international, randomised vignette study involving a simulated case of severe abdominal pain. Because it is difficult to compare strictly homogeneous patients in real clinical practice, we used a standardised clinical vignette to simulate identical scenarios differing only by sex and SCD status. The vignette methodology has been used in prior studies to explore racial and gender biases in clinical decision-making.[13–15] We aimed to establish whether, in a case with no visual or verbal cues about ethnicity, ED physicians would be more or less likely to prescribe morphine for patients with SCD compared with those without.

METHODS

Legal statement

This prospective, randomised, parallel-group vignette-based study was approved by the ethical committee of Nîmes University Hospital, France (IRB 25.02.01) and was prospectively registered on clinicaltrial.gov (NCT06835335). The Consolidated Standards of Reporting Trials guidelines were followed in the design and conduct of this research.[16] The development of clinical vignettes followed Guideline for Reporting Vignette Experiments recommendations.[17]

Recruitment

To be eligible to participate, respondents had to be emergency physicians who were actively practising in ED. No specific exclusion criteria were applied for this study, including level of training and years of experience. Participants were recruited from France, Switzerland, Belgium and the UK through the study investigators' personal mailing lists and professional networks between 17 February and 17 March 2025. Due to this sampling method, the exact number of subjects who had access to the questionnaire was not known. Respondents outside of Europe were excluded.

Study materials

The study materials consisted of variations of a single vignette accompanied by a questionnaire on a Google Form (Google LLC, Mountain View, CA, USA). The form was available in French or English, depending on respondents' preference. To ensure realism and clinical relevance, vignette content was designed to reflect authentic ED presentations and was reviewed in detail by an expert panel in emergency medicine and discrimination in healthcare (LN'D, A-LF-P, CO and XB). The scenario was intentionally constructed to align with common ED practice patterns and to elicit valid clinical decision-making. The four vignettes were developed iteratively with input from the experts. Before dissemination, the questionnaire and vignettes underwent internal pilot testing by the investigators to verify clarity, clinical plausibility and consistency across the four versions.

All vignettes included the following basic text: *"You are an emergency physician, working in an adult emergency department. You are assessing the following patient: The patient is a 39-year-old male/female with ***. He/she is allergic to co-trimoxazole. He/she is a non-smoker. The patient has presented with sudden-onset abdominal pain that started two hours ago and has been constant since onset, despite taking a painkiller (co-codamol in the English version or Nefopam in the French version) forty-five min ago. He/she rates the pain as 8/10 in severity and there are no relieving factors. He has not had any diarrhea or vomiting. Observations are as follows: BP 140/66, HR 91, SpO2 97% on room air, RR 22, T 36.8°C. On examination, he has tenderness with localized guarding in the epigastrium. The rest of the abdomen is soft and non-tender. Bowel sounds are present. No other abnormalities are found on examination."*

Variations of this vignette were generated by manipulating the described sex and pronouns of the patient, in addition to their medical history: the asterisked section of the first sentence above could read *"a history of Meniere's disease and SS monozygotic sickle cell disease and an allergy to Bactrim"* or *"a history of Meniere's disease and an allergy to Bactrim."* This created four study groups: (1) a man with SCD, (2) a man without SCD, (3) a woman with SCD and (4) a woman without SCD, all vignettes were otherwise identical to the text above. We selected abdominal pain rather than musculoskeletal pain to avoid implying trauma in non-SCD scenarios, which would have introduced an additional confounder unrelated to SCD status. Although abdominal VOC cannot be fully excluded, the vignette was not designed to suggest a typical VOC presentation.

Respondents were randomised to one of these four groups through the use of a computer-generated random sequence. They were asked to choose the first symbol in a sequence of symbols on the initial page of the Google Form. The order of the symbols was prerandomised for each participant to ensure allocation was concealed. This randomisation method has already been used in a previous study.[14 15]

The questionnaire was comprised of two parts. In the first part, respondents were asked to state their age, graduation date, hospital type and location. In the second part, respondents were asked to answer the following four questions about the case:

- How urgently the patient needs to be investigated and managed: from 1 (immediately) to 5 (≥ 4 hours)?
- Which of the following medications would be prescribed for analgesia: codeine, ketamine, methoxyflurane, morphine, nitrous oxide, non-steroidal anti-inflammatory, paracetamol and tramadol? Respondents were allowed to select more than one analgesic option, reflecting real-life multimodal analgesia practices.
- Which of the following blood tests would be taken: full blood count, urea and electrolytes, liver function tests, lipase, bone profile, procalcitonin and lactate?
- Would a CT scan of the abdomen and pelvis be ordered?

Outcomes

The primary outcome for this study was the proportion of patients with and without SCD who were prescribed morphine. Secondary outcomes included the number and type of analgesic medications prescribed, in addition to the proportion of patients in each group whose recommended management met all the following criteria for maximal level of care: (1) categorised as life threatening emergency (urgency level 1 or 2), (2) lactate taken, (3) CT ordered and (4) morphine prescribed.

Sample size calculation

The sample size was calculated to detect a minimum absolute difference of 10% points in morphine administration between groups (90% in the non-SCD group versus 80% in the SCD group), with a two-sided alpha level of 0.05 and a power of 90%. This required at least 266 subjects per group.

Statistical analysis

Data analyses were conducted between March and May 2025 using R software V.4.4.2 (R Foundation for Statistical Computing, Vienna, Austria). There were no missing data in the dataset. Data were analysed between March and June 2025. The statistical analysis plan is provided in online supplemental file 1.

Categorical variables were described using frequencies and percentages, while continuous variables were expressed as means with SD. Comparisons between categorical variables were performed using the χ^2 test or Fisher's exact test when the expected cell count was <5. Student's t-test was used to compare continuous variables.

For the primary outcome, the absolute difference between groups was calculated with its corresponding 95% CI. Analyses were repeated using a two-sided significance threshold of $p<0.05$ to evaluate differences in the prescription of morphine, no morphine and mixed analgesia according to patient's sex, respondent's sex, respondent's seniority and respondent's country. The same approach was used for recommendations regarding maximal versus non-maximal levels of care. For categorical variables, absolute differences in proportions and their 95% CIs were estimated using the Newcombe-Wilson method without continuity correction, implemented in R (PropCIs package).

Logistic regression models were then used to estimate ORs and 95% CIs for the prescription of various analgesics, including morphine, between the SCD and non-SCD groups. A multivariable logistic regression was initially planned to assess whether respondent sex, age, professional status, country and hospital type were associated with maximal care decisions in SCD cases. However, no variables met the predefined inclusion threshold ($p<0.20$) in univariate analysis.

Patients and public involvement

None.

RESULTS

From 17 February 2025 to 17 March 2025, we received a total of 1060 responses, of which 953 (90%) were analysed. The study's flow chart is presented in figure 1. 485 (51%) of participants were women, and the mean age was 36 (±10) years old. Participants were randomised to the four study groups as follows: SCD man (n=246; 26%), non-SCD man (n=258; 27%), SCD woman (n=246; 26%) and non-SCD woman (n=203; 21%). The study's flow chart is provided in figure 1. Responses came from France (n=700; 73%), the UK (n=179; 19%), Belgium

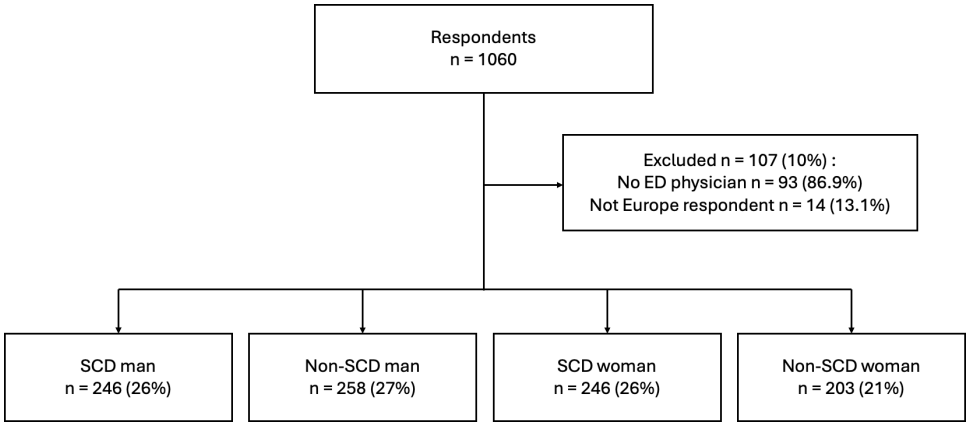

Figure 1 Study's flow chart. ED, emergency department; SCD, sickle cell disease.

Table 1 Participant characteristics and responses

Variables	Responses n=953
Responders' characteristics	
Sex, woman, n (%)	485 (51)
Age, mean (SD)	36 (10)
Hospital type, n (%)	
University hospital	500 (52)
Non-university hospital	379 (40)
Private hospital	36 (4)
Other hospital	38 (4)
Status, n (%)	
Graduated physician	674 (71)
Resident	279 (29)
Language, n (%)	
French-speaking	771 (81)
English-speaking	182 (19)
Cases responses	
Life-threatening emergency, n (%)	458 (48)
Treatments prescribed, n (%)	
Morphine	833 (87)
Paracetamol	554 (58)
Nitrous oxide	48 (5)
Tramadol	64 (7)
Codeine	19 (2)
Ketamine	10 (1)
Lactate prescription	665 (70)
CT-scan ordered, n (%)	522 (55)

CT-scan, computed tomography scan; SCD, sickle cell disease.

(n=44; 5%) and Switzerland (n=22; 2%). The respondents' characteristics are summarised in table 1. A full breakdown of responses by city and country is provided in online supplemental table S1 and figure S1.

Morphine was prescribed by respondents in 833 (87%) cases overall: 444 (90%) for the SCD group and 389 (84%) for the non-SCD group. The observed difference in morphine administration was 6% (95% CI 1% to 10%) in favour of SCD patients. Within the SCD group, morphine alone was prescribed for 200 (41%) patients and in combination with another drug for 244 (50%) patients: paracetamol (n=226; 93%), nitrous oxide (n=39; 16%), ketamine (n=8; 3.2%), codeine (n=4; 1.6%) and tramadol (n=3; 1.2%). Most (n=236; 48%) SCD patients received two analgesic drugs, with 34 (6.9%) receiving more than two and 222 (45%) receiving just one. Prescription of individual analgesic medications varied between SCD groups (table 2) and within the sex and SCD group (figure 2). Prescription according to patients' sex is provided in online supplemental figure S2. Repartition of antalgic type regarding the prescription of one, two or more than two antalgics for vignettes with SCD patients is provided in online supplemental table S3. Analgesic prescribing for SCD patients did not vary by patient sex, respondent sex or respondent seniority—but did vary by country (table 3).

Table 2 Antalgics prescription OR for patients with a history of SCD compared with patients without a history of SCD

	SCD patients n=492	Non-SCD patients n=461	OR (95% CI)
Codeine	10 (2.0)	9 (2.0)	1.04 (0.42 to 2.65)
Ketamine	8 (1.7)	2 (0.4)	3.79 (0.94 to 25.22)
Morphine	444 (90)	389 (84)	1.71 (1.16 to 2.54)
Paracetamol	265 (54)	289 (63)	0.69 (0.54 to 0.90)
Nitrous oxide	44 (8.9)	4 (0.8)	11.22 (4.50 to 37.50)
Tramadol	26 (5.3)	38 (7.8)	0.62 (0.37 to 1.04)

SCD, sickle cell disease.

The full criteria for maximal level of care were met in 110 patients (22%) in the SCD group and this did not vary by respondent characteristics (table 4). Individual criteria were met within the SCD group in the non-maximal level of care group as follows: morphine prescribed (n=334; 87%), lactate taken (n=256;

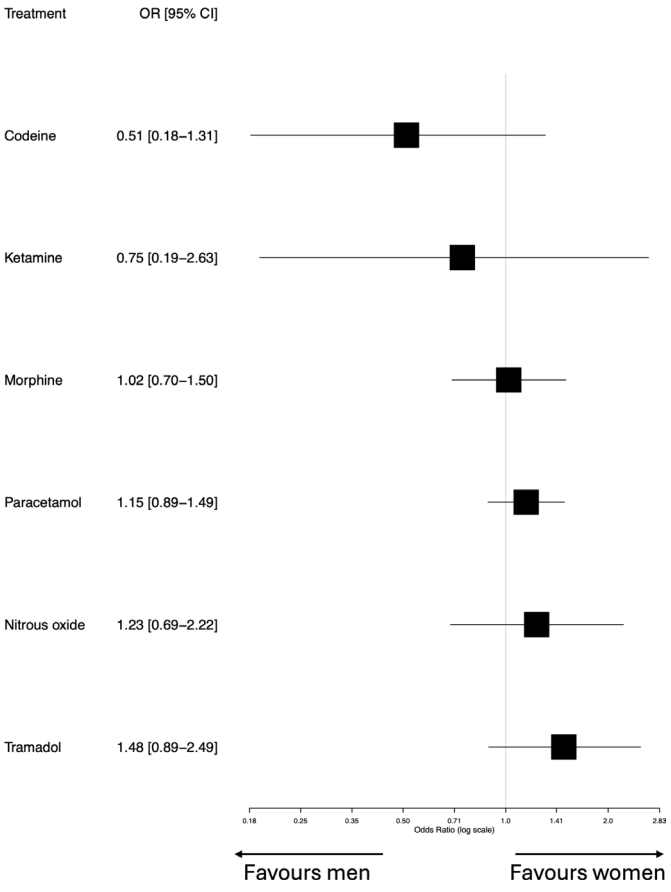

Figure 2 Treatment prescribed according to the patient's sex and history of SCD. Reference: man without a history of SCD. SCD, sickle cell disease.

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Table 3 Proportion of patients with a history of sickle cell disease, regarding the prescription of morphine alone, morphine and other antalgic and morphine

Variable	Morphine only n=200	Morphine+other drug n=244	No morphine n=48	Absolute difference Morphine+other versus morphine only	Absolute difference No morphine versus morphine only
Patients' sex					
Woman	97 (48.5)	122 (50.0)	21 (43.8)	1.5% (–10.8% to 7.8%)	–4.7% (–10.9% to 20.4%)
Man	103 (51.5)	122 (50.0)	2è (56.3)	–1.5% (–7.8% to 10.8%)	4.7% (–20.4% to 10.9%)
Respondents' sex					
Woman	95 (47.5)	134 (54.9)	20 (41.7)	7.4% (–16.7% to 1.9%)	–5.8% (–9.7% to 21.4%)
Man	105 (52.5)	110 (45.1)	28 (58.3)	–7.4% (–1.9% to 16.7%)	5.8% (–21.4% to 9.7%)
Respondent's status					
Resident	45 (22.5)	73 (29.9)	17 (35.4)	7.4% (–15.6% to 0.7%)	12.9% (–27.6% to 1.8%)
Senior	155 (77.5)	171 (70.1)	31 (64.6)	–7.4% (–0.7% to 15.6%)	–12.9% (–1.8% to 27.6%)
Country					
France	111 (55.5)	217 (88.9)	33 (68.8)	33.4% (–41.4% to –25.5%)	13.2% (–28.1% to 1.6%)
UK	76 (38.0)	18 (7.4)	6 (12.5)	–30.6% (23.1% to 38.1%)	–25.5% (14.0% to 37.0%)
Belgium	4 (2.0)	6 (2.5)	7 (14.6)	0.5% (–3.2% to 2.3%)	12.6% (–22.8% to –2.4%)
Switzerland	7 (3.5)	3 (1.2)	2 (4.2)	–2.3% (–0.6% to 5.2%)	0.7% (–6.9% to 5.5%)
Others	2 (1.0)	0 (0.0)	0 (0.0)	–1.0% (–0.4% to 2.4%)	–1.0% (–0.4% to 2.4%)

Group comparisons were exploratory and used χ^2 or the Fisher exact test. Absolute differences and 95% CIs are provided when appropriate.

67%), CT ordered (n=169; 44%), categorised as life-threatening emergency (n=154; 40%). Further details on this outcome are provided in online supplemental table S4.

Half of the respondents reported that they were the same sex as the simulated patient: 243 (52%) of men and 221 (48%) of women (online supplemental table S5). There was no significant relationship between sex concordance and morphine prescription (OR 0.87 [95 CI% 0.59 to 1.28]).

DISCUSSION

In this randomised, international vignette study in a simulated case of abdominal pain, patients with a history of SCD were prescribed morphine more often than non-SCD patients (difference: 6% [95% CI 1% to 10%]). None of the secondary outcomes, including maximal level of care, appeared to be influenced by respondents' characteristics—except for country of practice.

Table 4 Comparison of rater's characteristics regarding maximal level of care in patients with sickle cell disease

	Non-maximal level of care n=382	Maximal level of care n=110	Absolute difference (%, 95% CI)
Responder's sex, woman, n (%)	197 (52)	60 (55)	3.0% (–13.3% to 7.6%)
Responder's age, mean (SD)	37 (10)	37 (10)	
Status, graduated physician, n (%)	279 (73)	78 (71)	–2.1% (–6.8% to 12.1%)
Country, n (%)			
France	274 (71)	87 (79)	7.4% (–15.4% to 2.2%)
UK	82 (21)	18 (16)	–5.1% (–3.8% to 12.3%)
Switzerland	10 (2.6)	2 (1.8)	–0.8% (–3.9% to 3.3%)
Belgium	15 (3.9)	2 (1.8)	–2.1% (–2.7% to 4.9%)
Others	1 (0.3)	1 (0.9)	0.6% (–4.7% to 0.8%)
Hospital type, n (%)			
University hospital	190 (50)	48 (43)	–6.1% (–4.5% to 16.3%)
Non-university hospital	165 (43)	49 (45)	1.4% (–11.9% to 8.9%)
Private hospital	8 (2.1)	6 (5.5)	3.4% (–9.4% to 0.2%)
Other hospital	19 (5.0)	7 (6.4)	1.4% (–7.8% to 2.8%)

Morphine prescribing was higher (90%) for the patients with SCD in our study. This contrasts with the findings of recent studies, which suggest inadequate opioid provision for SCD patients[18 19] in line with general trends observed in racial minorities with painful conditions.[4 20] Thus, higher morphine use in SCD cases may reflect guideline adherence rather than an absence of discriminatory mechanisms in routine care. A related point may be made about the triage decisions made by emergency physicians in our study. American Society of Hematology guidelines recommend pain management within the first hour for patients with VOC.[21] This level of urgency was supported by 88% of our respondents, with similar findings noted in the non-SCD group. Again, this is different from triage decisions observed in everyday practice. Patients with SCD frequently experience longer waiting times in the ED,[22] as do racial/ethnic minorities generally.[23] Indeed, a similar vignette study conducted by our research team in 2023 demonstrated sharp discrepancies in prioritisation for patients of Black appearance.[15] Most previous studies evaluating disparities in SCD primarily examined time-based outcomes (time to triage, time to first opioid dose and cumulative analgesia). In contrast, our study isolated the very first analgesic choice in strictly identical clinical conditions. This methodological difference limits direct comparison with prior work but provides novel insight into prescribing behaviour independently of delays or workflow constraints.

Surprisingly, our study found no association between clinician or patient characteristics and prescribing patterns, including sex concordance. This contrasts with findings from surgical and cardiology settings, where sex discordance has been associated with worse clinical outcomes.[24 25] Interestingly, sex concordance does not appear to influence opioid prescribing in hospital medicine.[26] Although female patients reportedly prefer female emergency physicians, this does not translate into greater satisfaction—in fact, female patients tend to be less satisfied with their care, and this gender dynamic may introduce bias into satisfaction-based physician ratings.[27] These findings highlight the complexity of sex dynamics in emergency care.

Discriminatory bias is largely driven by perception, and the absence of visual or auditory cues such as skin colour, family name, accent or a photograph of the patient can significantly improve the equity of care provided.[28] This suggests that clinical decisions based solely on factual clinical information—without visual or auditory cues related to perceived ethnicity—may reduce discriminatory bias.[29]

We used abdominal pain rather than the more typical musculoskeletal VOC pain to avoid anchoring the non-SCD vignette in a traumatic mechanism. This allowed us to isolate SCD status as the single meaningful difference between scenarios. We found that adjuvant or alternative analgesics were underused, even though they are specified in the recommendations for managing VOC.[30] For example, ketamine has been shown to reduce morphine requirements in VOC,[31] but was rarely prescribed. Notably, NSAIDs were absent from prescriptions in our study, despite being recommended in American guidelines for the management of acute SCD pain.[21]

Limitations

This study has several limitations. First, using clinical vignettes instead of real patients may have influenced participants' responses. However, this methodology offered strong internal validity by controlling several key sources of bias that are difficult to eliminate in real-world studies.[15] Specifically, the clinical information was standardised across all cases, which eliminated variability in patient behaviour, communication style and physical appearance. Thus, our design reduced biases related to nonverbal cues, perceived race, gender, accent and emotional responses to patient interactions. Although clinical vignettes provide strong internal validity, they lack some of the ecological cues present in real encounters—including tone of voice, patient discomfort and nonverbal communication—that may influence decision-making in everyday practice.[32] Post-stratification weighting, commonly used to correct selection and non-response bias in survey research, could not be applied because no sufficiently detailed denominator data describing the age, sex and hospital-type distribution of ED physicians existed for the participating countries.

The epidemiology of SCD in Europe is heterogeneous, with the highest patient concentrations in France, the UK, Belgium and Switzerland. Although centre-level SCD volumes were unavailable due to anonymised sampling, large urban academic hospitals—over-represented in our sample—are likely to manage more SCD cases and may have greater familiarity with SCD-specific guidance. In contrast, the USA hosts larger SCD populations and more established sickle cell centres, yet Global burden of disease 2021 estimates indicate persistent under-recognition of SCD-related mortality, underscoring that even highly resourced systems continue to face challenges in acute SCD care.[33]

Furthermore, our participants were aware that they were participating in a research study and may have exhibited the Hawthorne effect[34 35]—responding in what they perceived to be a socially desirable manner rather than recreating their typical clinical practice. It is possible that some participants did this because they guessed the purpose of the study, either from communication with other participants or recognition of the authors' names from prior, related publications.

Finally, although our recruitment process—convenience sampling from peer networks—was able to generate a large amount of data, it is likely to have skewed our final sample. The individuals who respond to open surveys are generally unrepresentative of their wider professional groups, and in this case, they may have reflected a more engaged or academic subgroup of emergency physicians with distinct prescribing practices.

CONCLUSION

In this randomised vignette-based study, ED patients with SCD were more likely to receive morphine than non-SCD patients. Our findings differ from what has been described in the literature, suggesting that the absence of visual cues, such as skin colour or names, may reduce implicit bias in pain management.

Author affiliations
[1]IMAGINE UR UM 103, Montpellier University, Montpellier, France
[2]Emergency Department, Nîmes University Hospital, Nîmes, France
[3]Montpellier University, Montpellier, Occitanie, France
[4]Emergency Department, Montpellier University Hospital, Montpellier, Occitanie, France
[5]Emergency Department, Nice University Hospital, Nice, France
[6]Cliniques universitaires Saint-Luc, Brussels, Belgium
[7]Emergency Department, Lausanne University Hospital, Lausanne, Switzerland
[8]LEPS UR3412, Sorbonne Paris Nord University, Paris, France
[9]Avicenne Hospital, Paris, France
[10]Emergency Department, Manchester Royal Infirmary, Manchester, UK

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Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Consent obtained directly from patient(s).

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Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Data are available upon reasonable request. Because this study is based on randomised clinical vignettes and involves healthcare professionals rather than patients, anonymised data can be shared upon reasonable request to the corresponding author, in accordance with institutional and ethical data protection requirements.

ORCID iD
Fabien Coisy https://orcid.org/0000-0002-2812-3534

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