

## Knowledge, perceived barriers, and practices of oncology nurses regarding cancer pain management

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### ABSTRACT

**Purpose:** Effective cancer pain management involves significant knowledge and proficiency in pain assessment and recording. This study sought to assess nurses' knowledge, behaviors, and perceived impediments to managing cancer-related pain.

**Methods:** A descriptive, cross-sectional design was used. A convenience sample of 502 nurses working in three primary health care sectors in Jordan was selected to ensure national representation. To collect data, an English-language online Google Electronic Form was employed.

**Results:** Nurses were 86.4% male and 51.4% between 21 and 35. Additionally, 578.8% of nurses were employed in the private sector. The mean knowledge score for cancer pain management was 6.48/14, indicating a knowledge gap in opioid rescue dose deficiency among nurses. According to 68.1% of nurses, the most frequently encountered patient-related hurdle was insufficient expertise in pain control. 75.3%, on the other hand, named insufficient staffing, and 74.7%, opioid regulations as significant health care system impediments. Private hospital nurses score significantly higher than nurses in other hospitals. The degree of expertise varied according to age and pain management training. For 56.8% of nurses, contacting a physician for an opioid prescription is the most delayed action.

**Conclusion:** Knowledge gaps and impediments to successful cancer pain management were assessed. Additional training in cancer pain treatment is crucial, increasing coordination and communication between doctors and nurses. The survey data assist educators in developing educational techniques, and the least correctly answered answers might aid educators in identifying knowledge gaps.

**Keywords:** cancer pain, nurses, knowledge, practices, perceived barriers

### INTRODUCTION

Cancer-related pain is one of the most feared side effects of the disease and remains a significant issue for cancer patients [1]. Cancer patients frequently experience pain as a result of the disease or treatment. [2]. However, up to 95% of cancer pain can be successfully treated. Inadequate treatment may slow healing, increased complication rates, and have a lower quality of life [1]. Pain management is one of the most commonly implemented interventions by nurses; they play an essential role in pain management through practical pain assessment, proper implementation, and evaluation of pain management interventions [3]. However, inadequate education among healthcare professionals, according to Onsongo, is a significant and persistent barrier to safe and effective pain management [4].

Furthermore, healthcare providers' inadequate knowledge, negative attitudes, lack of specialty, and poor behavior performance when dealing with cancer pain are significant barriers [5]. Specific barriers – related to nurses' actions – have been identified as obstacles to providing

adequate pain management, including workload, time constraints, patients' unwillingness to cooperate, inadequate pain assessment, a lack of knowledge about pain medications, and other pain management approaches [6]. In addition, nurses have identified additional barriers in a clinical setting: a lack of physician orders, particularly before procedures, and a lack of time to premedicate patients [7]. Although nurses play an essential role in cancer pain management, the nursing education curriculum lacks basic pain management principles [8]. To the best of the researchers' knowledge, few studies have been on cancer pain management in Jordan, specifically knowledge, practices, and perceived barriers among Jordanian nurses. As a result, this study examines the knowledge, practices, and perceived barriers to managing cancer-related pain among Jordanian nurses who work with cancer patients. Also, identify areas for improvement in clinical practice, education, and policy and investigate barriers to adequate pain control in cancer patients.

## METHODS

### Design

A non-experimental, descriptive, cross-sectional approach was used to assess a sample of Jordanian nurses' knowledge of perceived nurses' barriers to cancer pain management.

### Setting

The data were obtained from various institutions around Jordan, including three key health care sectors (public, university-affiliated, and private) chosen to reflect the country. Additionally, these facilities care for cancer patients. Al-Basher Hospital was a public hospital; the University of Jordan and King Abdullah Hospital are affiliated universities, while King Hussein Cancer Center, Medical Center, Istishari Hospital, and Specialty Hospital are private hospitals.

### Sampling

We recruited a convenient sample of Jordanian registered nurses working at oncology care hospitals. First, a sample size of 200 was determined using the Raosoft sample size calculator; the indicator percentage was then set to 0.50, the margin of error to 5%, and the confidence interval to 95%. The target sample size was then increased to 250 nurses to minimize erroneous results and avoid drop-out. The total sample size, however, is 502 nurses.

### Inclusion and Exclusion Criteria

Inclusion criteria require that the hospital where the participant works admit and treat cancer patients, that the participant is employed (full or part-time), and that the participant is an active participant in the treatment process for such patients. In addition, exclude those who are not working or treating cancer patients, nursing students, and those in training. Those who did not complete all of the questionnaire items were also barred from participating.

### Instruments

Toba and colleagues developed the Knowledge of Nurses, Perceived Impediments, and Practice Relating to Cancer Pain Management Tool [9] to gather data on nurses' knowledge and behaviors related to cancer pain management and to identify barriers to effective pain control in cancer patients. Five sections comprised the questionnaire. The first featured demographic data about the participants and technical questions on the nature and duration of their interactions with cancer patients during work hours. The second section included 14 true or false questions that tested the participant's understanding of cancer management principles. The third portion examined perceived barriers to care for cancer patients, the fourth piece examined pain evaluation and documentation, and the last section examined perceptions of the most time-consuming process in opioid administration. Cronbach's coefficient of 0.771 suggested that the knowledge scale has a high degree of internal consistency reliability. To obtain data, an English-language online Google Electronic Form survey was employed. Zyoud obtained permission to use the questionnaire instrument for this study via a personal email from Sa'ed.

### Ethical Consideration

Permission was obtained from our academic institution's Institutional Review Boards (IRB), and all participants were

given a description of the study's purpose and acknowledged that their participation was entirely voluntary, with no expectation of payment or risk. Intended informed consent was granted to the nurses who completed and returned the questionnaire. The nurses' voluntary participation, anonymity, and confidentiality were ensured by designing the survey so that they could leave it before submitting it, coding data, and storing data in a password-protected Google Drive and computer, respectively. In addition, Cookie-Based Duplicate Protection was chosen to prevent duplicate survey responses. Permission was obtained from the (Nursing Education and Training Department) in target hospitals, and permission to use the questionnaire from the researcher who developed the instrument via personal emails.

### Data Analysis Plan

The data was screened, cleaned, and examined for missing value patterns. SPSS for Windows, version 25.0, was used to compute descriptive statistics. For example, data such as frequencies, percentages, mean, and standard deviation (SD) were used to answer research questions about knowledge, practices, and the perception of barriers.

Furthermore, one-way ANOVA and an independent t-test were used to investigate the relationship between the mean score of the nurses' level of knowledge and various demographic characteristics.

## RESULTS

### Sample Characteristics

Five hundred three questionnaires were distributed, and 502 were completed. **Table 1** shows the demographic information and participant characteristics. The majority of nurses (88.4%) were between 21 and 35 years old, 51.4% were male, 99.6% were educated in Jordan, and 47.7% had one to three years of experience. Additionally, 57.8% of nurses worked in the private sector, 30.5% in the public sector, and 11.8% in education.

**Table 1.** The demographic data and characteristics of participants (N = 502)

Characteristics	Frequency (N)	Percentage (%)
<b>Age</b>		
21-35 years old	319	(63.4%)
36-41 years	128	(25.4%)
More than 41 years	55	(11%)
<b>Gender</b>		
Male	258	(51.4%)
Female	244	(48.6%)
<b>Country of Education</b>		
Jordan	500	(99.6%)
Broad	2	(0.4%)
<b>Type of work</b>		
Public	153	(30.5%)
Private	290	(57.8%)
educational	59	(11.8%)
<b>Cancer experience</b>		
Non cancer experience	99	(19.7%)
Less than 1 year	49	(9.8%)
1-3 years	240	(47.7%)
4-8 years	71	(14.1%)
9-13 years	32	(6.4%)
14-18 years	9	(1.8%)
More than 18 years	2	(0.8%)

**Table 2.** The percentage (%) of correct answers of knowledge of cancer pain management (N = 502)

Correct Response	Frequency (n)	Percentage (%)
Question		
1. "You should not trust patient's subjective reports of pain" (F)	412	(82.1%)
2. "You should differentiate certain cause of pain which needs specific treatment (i.e., cord compression)" (T)	415	(82.7%)
3. "Prescribing a few different types of NSAIDs will increase the analgesic efficacy and decreased adverse effect" (F)	135	(26.9%)
4. "Pethidine can be prescribed for chronic cancer pain safely" (F)	280	(55.8%)
5. "Opioid analgesics have a high risk of addiction" (F)	113	(22.5%)
6. "The effect of immediate release oral opioid can be assessed at 1 h after administration" (T)	348	(69.3%)
7. "Opioid analgesics do not have a ceiling effect" (T)	134	(26.7%)
8. "Tolerance for opioid-induced sedation develops within a few days" (T)	222	(44.2%)
9. "For painful bone metastasis, radiotherapy can alleviate the pain or help to reduce the amount of analgesics" (T)	253	(50.4%)
10. "Opioid-induced respiratory suppression is common" (F)	94	(18.7%)
11. "Celiac plexus block is effective for treating cancer pain at upper abdomen" (T)	179	(35.7%)
12. "Opioid rescue dose equals 25% of the basal daily requirement of opioid" (F)	80	(15.9%)
13. "The IV route for opioid administration has the fastest onset of action" (T)	428	(85.3%)
14. "Refractory cancer pain rarely occurs with a percent that does not exceed 5% of cancer patients" (F)	163	(32.5%)
<b>Mean score, Mean (SD)</b>		<b>6.48 (1.97)</b>

**Table 3.** Perceived barriers for cancer pain management (N = 502)

Barriers	Frequency (n)	Percentage (%)
<b>Barriers related to medical staff</b>		
Inadequate pain assessment	342	(68.1%)
Inadequate experience on pain control	338	(67.3%)
Insufficient knowledge of pain control	330	(65.7%)
Insufficient communication with patient	316	(62.9%)
Reluctance to prescribe opioid	291	(58%)
<b>Total</b>	<b>323.4</b>	<b>(64%)</b>
<b>Barriers related to patient</b>		
Reluctance to report pain	251	(50%)
Reluctance to take opioid	258	(51.4%)
Insufficient communication with medical staff	315	(62.7%)
Financial constraints	282	(56.2%)
Insufficient knowledge of pain control	381	(75.9%)
<b>Total</b>	<b>297.4</b>	<b>(59%)</b>
<b>Barriers related to the health care system</b>		
Strict regulation of opioids	375	(74.7%)
Inadequate staffing	378	(75.3%)
Limited stock of different types of opioids	247	(49.2%)
Cancer pain management is not considered as important	89	(17.7%)
Medication and intervention costs	282	(56.2%)
<b>Total</b>	<b>274.2</b>	<b>(54%)</b>

### Knowledge of Cancer Pain Management

The rate of correct responses to questions assessing CPM knowledge was measured in **Table 2**; the mean knowledge score was 6.48, with a standard deviation of 1.97, which is insensitive to nurses having a knowledge gap in cancer pain management (CPM). Also, the analysis revealed the most significant knowledge deficit in the question about opioid rescue dose (Opioid rescue dose equals 25% of the basal daily requirement of opioid) with a correct response rate of 15.9%, and in the question about the opioid risk of addiction with a correct response rate of 18.7%. Furthermore, an 85.3% correct response rate was observed for the query regarding the quickest route of action for opioids (The intravenous (IV) route for opioid administration has the quickest onset of action), and

an 82.7% correct response rate was observed for the query regarding the differentiation of certain types of pain that require specific treatment. **Table 2** summarizes the percentage of correct answers to cancer pain management questions.

### Perceived Barriers to Cancer Pain Management

Nurses' perceived cancer pain management barriers were divided into three categories: medical staff-related, patient-related, and healthcare-system-related. Nurses reported insufficient pain assessment for patients (68.1%) and negative pain management experiences (67.3%). Regarding patient-related factors, the most frequently encountered barriers were a lack of knowledge of pain control (75.9%) and a lack of communication with medical staff (62.7%). Finally, participants identified that the most common healthcare system-related barriers (75.3%) were inadequate staffing and strict opioid regulation (74.7%). **Table 3** depicts nurses' perceptions of cancer pain management barriers (N = 502).

### Pain Assessment Practices and Documentation

Participants rated their CPM training as excellent (9.9%), good (37%), very good (29.2%), poor (16.3%), and very poor (7.4%) in terms of effectiveness; the majority of sampled nurses would assess the pain on every round (61.8%). Furthermore, nurses reported that the most frequently assessed item (87.8%) was checking all aspects of pain during assessment. Furthermore, 81.7% of nurses stated that they document pain assessments. Pain assessment and documentation practices are shown in **Table 4** (N = 502).

### Perceptions of the Most Time-Consuming Step in the Administration of Opioids

**Table 5** shows the perception of delays in cancer pain management at 56.8%. According to many nurses, the most delaying process during cancer pain management is contacting a physician for an opioid prescription. At the same time, 18.9% believe that getting opioids from a pharmacy will delay CPM. **Table 5** depicts cancer pain management delays (N = 502).

**Table 4.** Pain assessment and documentation practices (N = 502)

Type of practice	Number of nurses
<b>Training adequacy in CPM</b>	
Very poor	37 (7.4%)
Poor	82 (16.3%)
Good	186 (37%)
Very good	147 (29.2%)
Excellent	50 (9.9%)
<b>The occasion of pain assessment</b>	
Every round	310 (61.8%)
On selected occasions	153 (30.5%)
On rare occasions	39 (7.8%)
<b>Items checked during pain assessment</b>	
Location & Quality	27 (5.4%)
Related factor & Severity	26 (5.2%)
Timing	8 (1.6%)
All items	441 (87.8%)
<b>Documentation of pain assessment</b>	
	410 (81.7%)

**Table 5.** The most common perceptions of delays in cancer pain management (N = 502)

Causes of delay	Frequency (n)	Percentage (%)
Administration of opioid to patient	86	(17.1%)
Obtaining opioid from pharmacy	95	(18.9%)
Contacting physician for prescription of opioid	285	(56.8%)
The delaying process is difficult to recognize	36	(7.2%)

#### Relationship between the Mean Score of the Nurses' Level of Knowledge and Demographic Characteristics

One-way ANOVA analysis revealed a significant difference in knowledge scores among nurses from different types of hospitals; F (3.77), P 0.05, nurses experience significant F (7.49), P 0.00, employment duration in the clinical setting F (3.74) P 0.011, and age of participants F (4.60), P.010. **Table 6** shows the results of a one-way ANOVA test that looked at the difference in total nurses' knowledge mean score based on age, experience, place of work, and time spent with patients. The analysis of variance revealed that nurses employed at private hospitals had significantly higher knowledge scores than nurses employed at public and educational hospitals, F (3.77), P 0.05, nurses had significant F (7.49), P 0.00, employment duration in the clinical setting F (3.74) P 0.011, and the analysis revealed that high knowledge varied according to the age of participants, F (4.60), P.010. Pain management training is comparable to not receiving training (95% CI = 1.82–8.99; p = 0.003). There were no significant differences in knowledge and attitude among the nurses for the other demographic characteristics. The p-value exceeded or was equal to 0.05. The

**Table 6.** One way ANOVA test results analyzing the difference in mean total nurse knowledge score based on age, experience, place of work, and time duration with patients

Variable	Mean (SD)	F statistic (df)	P-Value
<b>Age</b>	21-35 years old (n=319)	6.31 (1.86)	4.60(2) .010
	36-41 years (n=128)	6.93 (2.17)	
	More than 41 years (n=55)	6.4 (2.01)	
<b>Place of work</b>			
Private (n=290)	6.66 (1.84)	3.77 (2) .024	
Governmental (n=152)	6.34 (1.99)		
Educational (n=59)	5.94 (2.43)		
<b>Cancer experience</b>			
None (n=99)	5.46 (2.18)	7.49(6) 0.00	
Less than one year (n=49)	6.24 (1.73)		
1-3 years (n=240)	6.64 (1.80)		
4-8 year (n=71)	7.07 (1.93)		
9-13 year (n=32)	7.15 (2.00)		
14-18 years (n=8)	7.62 (1.30)		
More than 18 (n=2)	7.50 (2.12)		
Total (501)	6.48 (1.97)		
<b>Time attend with patients</b>			
33% (61)	5.78 (1.98)	3.74(3) .011	
34-66% (256)	6.46 (1.95)		
67-100% (183)	6.73 (1.96)		
Total (501)	6.48 (1.97)		

results of the independent t-test are shown in **Table 6**. Gender, Education, and Opioid Analgesic Warrant Differences in Mean Total Nurse Knowledge Score. An independent t-test revealed that nurses who had previously received pain management training had a significantly higher mean score.

Additionally, an independent t-test was used to compare dichotomous demographics (gender, education, and opioid analgesic warrant). **Table 7** contains the means and standard deviations. An independent t-test revealed that nurses who had previous pain training had a significantly higher mean score.

## DISCUSSION

The nurse's role in assessing and treating pain cannot be overstated. They frequently serve as a liaison between doctors and patients and the primary observer of the patient's pain and discomfort [10]. As a result, identifying the barriers nurses perceive to CPM is critical. This study aimed to assess nurses' knowledge and practice and identify potential barriers to CPM in Jordan. Furthermore, this study is required to evaluate nurses' pain management practices to improve hospital quality of care outcomes. It is worth noting that, despite the intended sample size being 250, the final number of nurses

**Table 7.** Independent t-test results analyzing the difference in mean total nurse knowledge score based on gender, education, and opioid analgesic warrant

Variable	Mean (SD)	t statistic (df)	95% CI of difference	P-value
<b>Gender</b>				
Male (n=257)	6.6(1.90)	2.10(499)	(.024, .716)	(.355)
Female (n=244)	6.3(2.03)			
<b>Education</b>				
Bachelor (n=456)	6.4(1.95)	-2.71(499)	(-1.43, -.230)	(.007)
Master (n=45)	7.2(2.04)			
<b>Opioid analgesic warrant</b>				
Yes (n=295)	6.5(1.83)	0.86 (498)	(-1.96, -.508)	(.048)
No (n=205)	-6.4(2.15)			

enrolled was 502. This figure could be attributed to various factors, including the relatively short time required to complete the questionnaire, and nurses can complete the survey at their leisure using a Google Electronic Form questionnaire. Aside from that, the researcher has a strong rapport with the nurses. The findings indicate that most participating nurses have deficits in cancer pain knowledge, particularly regarding opioid rescue dose calculation, with only 15.9% correctly answering, opioid risk of addiction, opioid ceiling effect, opioid-induced respiratory suppression, and the use of alternative sources modalities such as celiac plexus block. These findings corroborated previous research indicating that nurses possessed the fewest correct responses to questions about opioid administration and physical dependence and knowledge gaps in the pharmacology and physiology of pain [5,9]. This, however, may be a result of a lack of knowledge regarding pharmacological pain management.

Moreover, continuing medical education (CME) classes that focus on pain management are difficult to find, and nursing curricula do not include pain management in their training. As a result, the study's findings emphasize the significance of additional pain management training and education [11, 12]. In terms of perceived CPM barriers, a high percentage of participating nurses perceived numerous barriers that had a negative impact on the CPM process in their experiences. Most notably, most participants (around 70%) reported barriers related to medical staff, including inadequate pain assessment and insufficient experience in CPM. However, [10] revealed that nurses are held accountable for all nursing care; they face time constraints for symptom assessment and management of underestimated pain scores.

Furthermore, nurses who have a negative impact on cancer pain management have a negative impact on cancer pain assessment [13]. In contrast, pain is associated with emotional issues linked to other symptoms [14]. As a result, it is recommended that nurses and other health professionals participate in pain assessment and pain assessment tool continuing professional development programs [11,15]. The majority of participating nurses (76%) reported insufficient knowledge of patient pain control as the main barriers in this study, which was supported by a previous study [16] that showed the majority of patients experienced difficulties in reporting their pain severity, reluctance to take pain medication, and fear of an addiction or side effect. The second barrier identified by nurses was a lack of communication between patients and medical staff, which is consistent with previous research findings [17,18], which revealed that ineffective communication has a negative impact on patients' quality of care. However, [19] clarified that inadequate patient communication referred to a nurse shortage and increased workload during their shift, resulting in ineffective communication and negatively impacting patient quality of care. Likewise, it may result in nurses having insufficient time to communicate with clients and negative interactions between nurses and patients. Barriers to the healthcare system are also significant impediments to effective pain management. For example, the highest score was given to strict opioid regulation (74.7%) and insufficient nursing staff (75.3%); these results were consistent with a previous study in Nebal [20], which explains that much strict regulation will result in the formulary restriction; prescription barriers result in unnecessary suffering to those who need it. For cancer patients, WHO and the International Narcotics Control Board

recommend that opioids be made available in hospitals and communities and that physicians prescribe them based on each patient's specific needs [21,22]. The inadequate nursing staff is also considered a dual system-related barrier, consistent with a previous Saudi Arabian study that found inadequate nursing staff leads to a high workload, causes failure to deliver pain medication on time and according to demand, and improper pain assessment and documentation [16]. Another study was conducted among Indonesian nurses to assess perceived barriers to pain management, with the main barrier identified as insufficient staffing [23]. Participants demonstrated good CPM practice in general—nearly two-thirds of nurses (61.8%) reported assessing pain every round. Furthermore, it was stated that all items related to the nature of pain were checked regularly.

Surprisingly, individual nurses' results of this self-evaluated pain assessment practice appear to be at odds with the findings of the section on perceived barriers, where inadequate pain assessment was identified as the most critical barrier to adequate pain control. This observation could be due to an individual nurse overestimating self-evaluated pain assessment practice rather than pain assessment as a barrier to CPM, simply because of the subjective nature of both queries in the barriers and practices sections. The nurse is more likely to overestimate his or her abilities than to assume the presence of a problem that does not exist. Nevertheless, most nurses (81.7%) demonstrated excellent adherence to documentation practices, indicating a positive attitude toward CPM among Jordanian nurses, consistent with findings from a previous study that found nurses to be more skilled at pain assessment than doctors or doctors pharmacists [24,25]. The institutional accreditation standard for our hospitals, which recommends assessing pain using assessment tools for inpatients, could have influenced nurses' pain assessment and documentation practice in our survey.

In contrast, when it comes to the causes of delaying steps in CPM, more than half of the participants (56%) reported that contacting physicians for prescriptions is the most common source of delay; this is similar to the findings of Amudha [26], who found that nurses had difficulty contacting or communicating with physicians to discuss pain treatment. Again, this result is explained by nurses' professional responsibility. Doctors and nurses must collaborate to provide the best possible care to patients.

Both professions, however, are mutually exclusive, and neither can function effectively without effective communication and collaboration with the other [27]. As a result, effective pain management in hospitals requires collaboration. As a result, it is critical to foster a supportive team spirit among doctors and nurses; thus, meetings to facilitate the discussion of pain management and emphasize clear and effective communication between all healthcare team members, respectively, are possible interventions to reduce the delay caused by these processes [28]. In addition, the workplace environment was discovered to impact pain management knowledge. For example, nurses in private-sector hospitals demonstrated significantly more knowledge about cancer pain management than others. This result could be explained by well-developed private hospital policies and regulations regarding patients and quality of care [29]. It is also worth noting that the patient-nurse ratio in private hospitals is acceptable, giving nurses more time to care for their patients. In addition, nurses' experience providing care for cancer

patients scored higher than general nurses' experience; this was supported by a study conducted in China [25]. According to Valério et al., nurses' knowledge scores increased significantly with increased work experience [28]. These findings may be related to nurses' work areas, as those nurses have sufficient experience in caring for cancer patients. At the same time, nurses who spent more time with their patients scored relatively high and significantly, similar to a Brazilian study that found that when healthcare professionals spent more time with their patients, they learned more about CPM [29].

### Recommendations and Implications

These CPM recommendations are based on findings from this study. They are meant to raise the awareness of health care policymakers and nurse managers about the need to keep nurses' knowledge about cancer pain management up to date. It also emphasizes the importance of adequately training nurses and evaluating their practice based on scientific guidelines. As a result, the researchers recommend that nurses participate in a training program to assess and manage cancer pain in accordance with pain guidelines and evidence-based practice.

Furthermore, the existing nursing curriculum should be reviewed; a comprehensive program and culturally sensitive components of cancer pain management (including topics on opioid addiction, pharmacologic and non-pharmacologic cancer pain management) should be included. Finally, nurses in the oncology ward should be familiar with the most recent information on cancer pain management from the WHO and cancer societies. The importance of assessing pain knowledge among Jordanian nursing faculty and clinical tutors is highlighted by our findings. The survey results can be used to develop educational strategies, and the items with the fewest correct answers can be used to guide educators. A more in-depth investigation is needed to look into how nurses learn about pain and pain management, assess pain, and use techniques to relieve pain. Consider how much pain is covered in Jordanian undergrad nursing curricula.

### Strength and Limitation

Verifying the knowledge deficit in pain management among participating nurses necessitates further research. However, the study's strengths are a relatively larger sample size and a multicenter design. Furthermore, the data were gathered from a convenience sample, which severely limits the generalizability of the findings.

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**Declaration of interest:** No conflict of interest is declared by authors.

**Data sharing statement:** Data supporting the findings and conclusions are available upon request from the corresponding author.

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