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## An international multicentre validation study of a pain classification system for cancer patients ☆

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### ABSTRACT

**Purpose:** The study's primary objective was to assess predictive validity of the Edmonton Classification System for Cancer Pain (ECS-CP) in a diverse international sample of advanced cancer patients. We hypothesised that patients with problematic pain syndromes would require more time to achieve stable pain control, more complicated analgesic regimens and higher opioid doses than patients with less complex pain syndromes.

**Methods:** Patients with advanced cancer ( $n = 1100$ ) were recruited from 11 palliative care sites in Canada, USA, Ireland, Israel, Australia and New Zealand (100 per site). Palliative care specialists completed the ECS-CP for each patient. Daily patient pain ratings, number of breakthrough pain doses, types of pain adjuvants and opioid consumption were recorded until study end-point (i.e. stable pain control, discharge and death).

**Results:** A pain syndrome was present in 944/1100 (86%). In univariate analysis, younger age, neuropathic pain, incident pain, psychological distress, addictive behaviour and initial pain intensity were significantly associated with more days to achieve stable pain control. In multivariate analysis, younger age, neuropathic pain, incident pain, psychological distress and pain intensity were independently associated with days to achieve stable pain control. Patients with neuropathic pain, incident pain, psychological distress or higher pain intensity required more adjuvants and higher final opioid doses; those with addictive behaviour required only higher final opioid doses. Cognitive deficit was associated with fewer days to stable pain control, lower final opioid doses and fewer pain adjuvants.

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Conclusion: The replication of previous findings suggests that the ECS-CP can predict pain complexity in a range of practice settings and countries.

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## 1. Introduction

Pain is one of the most prevalent and distressing symptoms in patients with advanced cancer. Approximately 70% of these patients will experience pain at some point during the progression of their disease.<sup>1</sup> Although most patients achieve adequate pain control,<sup>2,3</sup> some – particularly patients with more complex pain syndromes – fail to obtain satisfactory analgesia. For these patients, clinicians may need to adopt a more intense and complex programme of therapeutic intervention, and as a result, more time is often required to achieve adequate pain control.<sup>4</sup>

Standardised approaches for assessing and classifying cancer pain need to be developed to identify and treat patients with complex pain syndromes. However, the complex, multidimensional nature of cancer pain presents unique challenges for pain classification. A review of the cancer pain literature has revealed the difficulty in comparing research results of analgesic management for cancer pain, due to the lack of a standardised approach.<sup>5</sup> Diverse interpretations of the pain experience, as well as many factors that may contribute to it, have impeded the development of a standardised classification system. Although better characterisation and classification of pain syndromes would allow for more valid clinical and research comparisons, there is no universally accepted pain classification tool.<sup>6,7</sup>

The development of a standardised classification system that is comprehensive, predictive of difficulty in achieving analgesia and simple to use could provide a common language for the clinical management and research of cancer pain. Bruera and colleagues recognised the need for such a system, prompting the development of the Edmonton Staging System (ESS).<sup>8,9</sup> The ESS has been used in a number of reports where it was found useful in describing the underlying cancer pain syndrome.<sup>10–16</sup> Interpretational difficulties with analgesic prognosis and feature definitions have limited the international acceptance of the ESS. To overcome these limitations, an expert panel, consisting of physicians and researchers in the Edmonton Regional Palliative Care Program, developed the revised Edmonton Staging System (rESS). We have subsequently conducted five validation studies: a pilot study, a regional multicentre study,<sup>17</sup> secondary analysis looking at pain intensity,<sup>18</sup> opioid escalation<sup>19</sup> and a construct validation study for validating definitions using an expert panel.<sup>20</sup> Based on feedback generated by the latter study and to reflect the intended use as a classification system, the amended instrument was renamed the Edmonton Classification System for Cancer Pain (ECS-CP).<sup>21</sup> The ECS-CP includes five features – pain mechanism, incident pain, psychological distress, addictive behaviour and cognitive function (Appendix A). These features and the definitions and guidelines for use are the basis of the ECS-CP (Appendix B).

Using the revised definitions for the ECS-CP pain features,<sup>21</sup> the primary objective of this study was to assess the predictive validity of the ECS-CP as a tool for classifying cancer pain in a diverse international sample of patients, who were referred to palliative care services. Our hypothesis was that patients with more problematic pain features, as classified by the ECS-CP, would require a longer time to achieve stable pain control, require more complicated analgesic regimens and use higher opioid doses than patients with less complex pain syndromes.

## 2. Methods

A total of 1100 consecutive patients were recruited from 11 palliative care sites in Canada, the United States, Ireland, Israel, Australia and New Zealand (100 patients per site). The selection of these sites was purposeful, being limited to locations providing specialist palliative care services, such as a palliative consult service (inpatient and outpatient), tertiary palliative care unit or hospice setting. At study entry, a palliative care specialist (physician or nurse consultant) completed the ECS-CP for each patient with cancer who was referred to the service. The following additional information was recorded until the study end-point: daily patient pain ratings; daily number of breakthrough pain doses; initial and final opioid consumption and types of adjuvant pain treatments.

The primary inclusion criteria were patients with cancer, 18 years of age or older, who had been referred to a palliative care service. Cancer patients who did not have a pain syndrome resulting from their cancer diagnosis were included in the cohort description of patient demographics, but excluded from further analysis.

An initial ECS-CP assessment is recommended prior to pain management by specialist palliative care services (e.g. on admission to an inpatient unit or referral to a care consultation service). Subsequent assessments may be conducted if the patient's condition changes or as additional information regarding the five pain features is obtained. For the purposes of this study, only an initial assessment was conducted. If the patient did not have a cancer pain syndrome on initial referral or admission, then no further data were collected for the study.

Patients rated their current level of pain intensity on the day of initial assessment and then daily until study termination, using the Pain-Numerical Rating Scale (NRS), ranging from 0 (no pain) to 10 (worst possible pain). This assessment is a routine clinical practice in the designated data collection sites. A secure website was specially created to facilitate investigator training at multiple study sites. All study materials, including background information about the ECS-CP, the ECS-CP Administration Manual,<sup>21</sup> other assessment tools and password-protected data collection forms were posted

on this website. Once formal ethics board approval was obtained at a designated study site, an individual teleconference training meeting was organised between the principal investigators, the site-specific collaborator and research support staff.

Patient demographics were recorded. The following information was reviewed and recorded on initial assessment and then as required until study termination (i.e. stable pain control, discharge and death): patient rated daily pain intensity (at the moment of rating), using a numerical rating scale (0–10) in those who were cognitively intact, in the opinion of the investigator; daily number of opioid doses given for breakthrough pain; initial total morphine equivalent daily dose (MEDD) of opioid on the initial assessment day, final MEDD on the day of study termination; number and type of adjuvant analgesics and/or other treatments used to manage pain; date of and reason for study termination (achievement of stable pain control, death or discharge resulting in loss of follow-up).

For the purposes of this study, stable pain control was defined as receiving less than three breakthrough analgesic doses per day and a patient self-reported pain score of less than or equal to 3/10 for three consecutive days.<sup>17,18</sup> If the patient was unable to self-report pain, then stable pain control was defined solely as receiving less than three breakthrough opioid analgesic doses per day for 3 consecutive days.

Palliative care physicians at all sites were required to treat cancer pain according to the National Cancer Institute of Health Physician Data Query (PDQ) Pain Guidelines.<sup>22</sup> Adjuvant analgesics and non-pharmacological treatments (e.g. radiotherapy, chemotherapy, anaesthetic or surgical procedures, acupuncture and transcutaneous nerve stimulation) were used as required.

Data were recorded on the ECS-CP Teleform. The Teleform® is an optical recognition-based technology that scans and exports data from data collection forms directly to a computer database, which is particularly useful with multiple data collection sites. We have successfully implemented this data collection process in previous research.<sup>17,23</sup>

Pooled data from all 11 sites were analysed using descriptive and inferential statistics. Kaplan–Meier survival curves were constructed to estimate the probabilities of achieving stable pain control over time for the eight explanatory variables identified in our previous validation studies (i.e. age, gender, mechanism of pain, incident pain, psychological distress, addictive behaviour, cognitive function and pain intensity).<sup>17,18</sup> Univariate and multivariate Cox regression analyses were performed, for identifying the associations between the eight explanatory variables and the outcome variable, time to stable pain control.<sup>24</sup> A Chi-square test was used to determine the differences in the use of adjuvant analgesics and non-pharmacological treatments for pain control. The non-parametric Kruskal–Wallis One-Way ANOVA by ranks and Mann–Whitney tests were used to examine differences in final median opioid doses, as the sample distribution was not normal. Statistical significance was set at  $p < 0.05$  (2-tailed). The univariate and multivariate Cox regression analyses were performed using the SAS procedure PHREG (SAS 9.1 TSIM3; SAS Institute, Cary, NC).

### 3. Results

Demographic and clinical characteristics of the 1100 patients included in the study are listed in Table 1. Of these, 944 (86%) had a pain syndrome. The patients with a pain syndrome were significantly younger ( $p < .001$ ), less likely to have lung

**Table 1 – Patient demographics and clinical characteristics (n = 1100).**

Characteristics	Patients with a pain syndrome n (%) (n = 944) <sup>a</sup>	Patients without a pain syndrome n (%) (n = 156)	p-Value Chi-square test
<i>Age, years</i>			
Mean	61	69	<.001
Standard deviation	15	13	
<i>Sex</i>			
Female	472 (50)	74 (47)	.55
<i>Diagnosis</i>			
Gastrointestinal	228 (24)	41 (26)	.77
Lung	208 (22)	49 (31)	.03
Genitourinary	146 (15)	12 (8)	.01
Breast	125 (13)	17 (11)	.33
Head and Neck	52 (6)	5 (3)	.19
Other	59 (6)	16 (11)	.09
Unknown origin	41 (4)	7 (4)	.98
Haematological	47 (5)	9 (6)	.76
<i>Disposition</i>			
Stable pain	478 (51)		
Death	160 (17)		
Discharge	306 (32)		
<i>Mechanism of pain</i>			
Nociceptive (Nc)	636 (67)		
Neuropathic pain (Ne)	257 (27)		
Unknown (Nx)	51 (5)		
<i>Incident pain</i>			
Absent (Io)	408 (43)		
Present (Ii)	457 (48)		
Unknown (Ix)	79 (8)		
<i>Psychological distress</i>			
Absent (Po)	417 (44)		
Present (Pp)	413 (44)		
Unknown (Px)	114 (12)		
<i>Addictive behaviour</i>			
Absent (Ao)	743 (79)		
Present (Aa)	107 (11)		
Unknown (Ax)	94 (10)		
<i>Cognition</i>			
Unimpaired (Co)	653 (69)		
Impairment (Ci)	200 (21)		
Unresponsive (Cu)	78 (8)		
Unknown (Cx)	13 (1)		

Note: Percentages do not always add up to 100% due to rounding.

<sup>a</sup> Frequencies do not always add up to 944 due to missing values.

cancer ( $p = .03$ ) and more likely to have genito-urinary cancer ( $p = .01$ ) than the patients with no pain syndromes. Fifty per cent of patients with a pain syndrome ( $n = 478$ ) achieved stable pain control. The remaining patients had either died ( $n = 160$ , 17%) or had been discharged and lost to follow-up ( $n = 306$ , 32%). Most patients had nociceptive pain (67%), and neuropathic pain was present in 27%; 48% had incident pain; psychological distress was present and absent in similar numbers (44%); addictive behaviour was present in 11% and 69% were cognitively intact. The ‘unknown’ classification option was used to varying degrees for all features, ranging from 1% (cognition) to 12% (psychological distress).

The associations between time to achieve stable pain control and age, gender, pain mechanism, incident pain, psycho-

logical distress, addictive behaviour, cognition and pain intensity are summarised in Table 2. As shown in this table, the median time to achieve stable pain control ranged from 3 d (unknown cognitive function and unknown pain mechanism) to 16 d (neuropathic pain and unknown psychological distress). Based on the univariate Cox regression analyses, age less than 60 years ( $HR = 0.68$ ,  $p < .0001$ ), neuropathic pain ( $HR = 0.55$ ,  $p < .0001$ ), incident pain ( $HR = 0.57$ ,  $p < .0001$ ), psychological distress present ( $HR = 0.74$ ,  $p = .002$ ) and unknown ( $HR = 0.63$ ,  $p = .006$ ), addictive behaviour ( $HR = 0.71$ ,  $p = .029$ ) and pain intensity moderate (4–6) ( $HR = 0.65$ ,  $p < .0001$ ) and severe (7–10) ( $HR = 0.52$ ,  $p < .0001$ ) were significantly associated with longer time to achieve stable pain control. Unknown pain mechanism ( $HR = 1.58$ ,  $p = .031$ ) and unresponsive cogni-

**Table 2 – Association between time to achieve stable pain control and age, gender, ECS-CP features and baseline pain intensity ratings.**

	Kaplan–Meier		Cox regression <sup>b</sup>				
	No. of patients <sup>a</sup>	Median time (days) to stable pain control (95% confidence interval (CI))	Univariate ( $n = 944$ )		Multivariate ( $n = 860$ )		
			Chi-square	$p$	HR (95% CI)	$p$	HR (95% CI)
<b>Age</b>							
≥60	518	7 (6–8)			1		1
<60	426	11 (9–14)	17.34	<.0001	0.68 (0.56–0.81)	.049	0.82 (0.67–1.00)
<b>Sex</b>							
Female	472	8 (7–9)			1		1
Male	472	9 (7–11)	0.76	.382	0.92 (0.77–1.11)	.866	0.98 (0.81–1.20)
<b>Pain mechanism</b>							
Nociceptive	636	7 (6–8)			1		1
Neuropathic	257	16 (11–25)	27.54	<.0001	0.55 (0.45–0.69)	<.0001	0.62 (0.49–0.79)
Unknown	51	3 (3–6)	4.68	.031	1.58 (1.04–2.39)	.837	0.93 (0.48–1.80)
<b>Incident pain</b>							
Absent	408	7 (5–7)			1		1
Present	457	11 (10–15)	33.20	<.0001	0.57 (0.48–0.69)	.001	0.72 (0.59–0.88)
Unknown	79	6 (4–9)	0.05	.828	1.04 (0.73–1.49)	.886	1.04 (0.60–1.81)
<b>Psych distress</b>							
Absent	417	7 (6–8)			1		1
Present	413	9 (8–11)	10.01	.002	0.74 (0.61–0.89)	.018	0.79 (0.64–0.96)
Unknown	114	16 (9–28)	7.65	.006	0.63 (0.46–0.88)	<.0001	0.37 (0.22–0.60)
<b>Addict behaviour</b>							
Absent	743	8 (7–9)			1		1
Present	107	14 (8–26)	4.75	.029	0.71 (0.52–0.97)	.199	0.81 (0.58–1.12)
Unknown	94	10 (5–16)	0.12	.728	0.94 (0.67–1.32)	.671	0.90 (0.55–1.47)
<b>Cognition</b>							
Normal	653	9 (7–10)			1		1
Impaired	200	9 (7–12)	0.09	.760	0.97 (0.77–1.21)	.614	0.94 (0.73–1.20)
Unresponsive	78	5 (3–8)	6.71	.010	1.55 (1.11–2.16)	.366	1.25 (0.77–2.01)
Unknown	13	3 (3 to –)	2.06	.152	1.81 (0.81–4.06)	.218	1.92 (0.68–5.39)
<b>Pain intensity</b>							
Mild (0–3)	310	5 (4–6)			1		1
Mod (4–6)	267	10 (8–11)	13.91	<.0001	0.65 (0.52–0.82)	.005	0.72 (0.57–0.91)
Severe (7–10)	283	13 (9–17)	30.64	<.0001	0.52 (0.41–0.66)	.001	0.65 (0.51–0.83)
Missing	84						

Abbreviations: HR – hazard ratio; n.s. – non-significant; PD – psychological distress; AB – addictive behaviour.

<sup>a</sup> Total number of patients may vary due to missing values.

<sup>b</sup> Forced entry model.

tive status ( $HR = 1.55$ ,  $p = .01$ ) were significantly associated with shorter time to stable pain control. In the multivariate Cox regression analysis, only younger age ( $HR = 0.82$ ,  $p = .049$ ), neuropathic pain ( $HR = 0.62$ ,  $p < .0001$ ), incident pain ( $HR = 0.72$ ,  $p = .001$ ), psychological distress present ( $HR = 0.79$ ,  $p = .018$ ) and unknown ( $HR = 0.37$ ,  $p < .0001$ ) and pain intensity (moderate,  $HR = 0.72$ ,  $p = .005$ ; severe,  $HR = 0.65$ ,  $p = .001$ ), were significantly associated with longer time to achieve stable pain control.

The number of adjuvant treatments used for pain control was calculated for each individual. These were further classified into three groups, according to the number required to achieve stable pain control: no adjuvant treatments required; one adjuvant treatment required and two or more adjuvant treatments required (Table 3). Patients with neuropathic pain, incident pain and moderate to severe pain intensity used significantly more modalities to achieve stable pain control ( $p < .001$ ). Patients with psychological distress also required a greater variety of management options ( $p = .041$ ). Patients reported as having an unknown pain mechanism ( $p = .019$ ), unknown addictive behaviour status ( $p < .001$ ) or a cognitively unresponsive status ( $p < .001$ ) required significantly less treatment options.

Analysis of the final morphine equivalent daily dose (MEDD) demonstrated significantly higher opioid doses for patients with neuropathic pain ( $p < .001$ ); incident pain ( $p < .001$ ); psychological distress ( $p = .002$ ); addictive behaviour

( $p = .038$ ) and moderate to severe pain intensity ( $p < .001$ ). Unknown cognition or unresponsive patients required a significantly lower final MEDD ( $p = .01$  and  $p < .001$ , respectively), as did patients with unknown pain mechanism ( $p = .002$ ) and unknown addictive behaviour ( $p < .001$ ) (Table 4).

#### 4. Discussion

The results of this international multicentre study confirm the findings of our previous research: neuropathic pain, incident pain, psychological distress, addictive behaviour and moderate to severe pain intensity are significant predictors of complexity of pain management as measured by the outcomes of longer duration (days) to achieve stable pain control, the use of more adjuvant treatments and the use of higher opioid doses. As noted previously<sup>17</sup> these findings reflect clinical practice, in which patients with more complex pain syndromes, such as neuropathic and incident pain, psychological distress, addictive behaviour and moderate or severe pain intensity, can still achieve stable pain control, but may require more time and more complex management strategies involving more adjuvant approaches and higher opioid doses, in comparison with patients with less complex pain syndromes. Conversely, declining cognition and the proxy measure of the 'unknown' option for the other features (perhaps in some cases due to difficulty obtaining a history in cognitively impaired patients) were associated with less complexity in pain

**Table 3 – Use of adjuvant analgesics and non-pharmacological management for pain control (n = 944).**

ECS-CP features	# of adjuvants used n (%)			p value Chi-square test
	0	1	2+	
<i>Pain mechanism</i>				<.001
Nociceptive (n = 636)	247 (39)	246 (39)	143 (22)	
Neuropathic (n = 257)	28 (11)	87 (34)	142 (55)	<.001
Unknown (n = 51)	30 (59)	14 (27)	7 (14)	.019
<i>Incident pain</i>				<.001
Absent (n = 408)	177 (43)	139 (34)	92 (23)	
Present (n = 457)	89 (19)	182 (40)	186 (41)	<.001
Unknown (n = 79)	39 (49)	26 (33)	14 (18)	0.53
<i>Psychological distress</i>				0.11
Absent (n = 417)	149 (36)	147 (35)	121 (29)	
Present (n = 413)	114 (28)	161 (39)	138 (33)	.041
Unknown (n = 114)	42 (37)	39 (34)	33 (29)	0.97
<i>Addictive behaviour</i>				.004
Absent (n = 743)	224 (30)	279 (38)	240 (32)	
Present (n = 107)	34 (32)	40 (37)	33 (31)	0.93
Unknown (n = 94)	47 (50)	28 (30)	19 (20)	<.001
<i>Cognition</i>				<.001
Normal (n = 653)	188 (29)	238 (36)	227 (35)	
Impaired (n = 200)	68 (34)	79 (40)	53 (27)	0.083
Unresponsive (n = 78)	43 (55)	26 (33)	9 (12)	<.001
Unknown (n = 13)	6 (46)	4 (31)	3 (23)	0.38
<i>Pain intensity</i>				<.001
0–3 (n = 310)	136 (44)	101 (33)	73 (24)	
4–6 (n = 267)	64 (24)	111 (42)	92 (34)	<.001
7+ (n = 283)	54 (19)	114 (40)	115 (41)	<.001
Missing (n = 84)				

n.s. – non-significant ( $p$  value > 0.05).

**Table 4 – Final MEDD\* by ECS-CP features (n = 944).**

ECS-CP features	Median final MEDD (25–75% quartile range)	p value Kruskal–Wallis	p value Mann–Whitney
<i>Pain mechanism</i>		<.001	
Nociceptive pain	32 (12–100)		
Neuropathic pain	100 (36–235)		<.001
Unknown pain syndrome	15 (4–60)		.002
<i>Incident pain</i>			
Absent	32 (10–110)	<.001	
Present	60 (20–170)		<.001
Unknown	27 (10–60)		0.17
<i>Psychological distress</i>		.009	
Absent	37 (12–104)		
Present	50 (16–150)		.002
Unknown	49 (12–137)		0.22
<i>Addictive behaviour</i>		<.001	
Absent	48 (14–135)		
Present	65 (18–192)		.038
Unknown	24 (10–68)		<.001
<i>Cognition</i>		<.001	
Normal	50 (15–138)		
Impaired	45 (15–154)		0.91
Unresponsive	20 (10–60)		<.001
Unknown	12 (4–50)		.012
<i>Pain intensity</i>		<.001	
0–3	25 (8–80)		
4–6	64 (16–169)		<.001
7+	68 (20–200)		<.001

\* Morphine equivalent daily dose; n.s. – non-significant (p value > 0.05).

management. The surprise finding of increased time to achieve stable pain control in those with unknown psychological distress status requires further explanation. This may be explained by the investigator's difficulty in applying the definition for this feature on initial assessment or difficulties in relation to patients' cognitive status. We cannot exclude the possibility that many of these patients could have met the definition on reassessment.

The magnitude of the association between pain intensity and time to achieve stable pain control in the multivariate analysis is not as strong as in our previous study (i.e.  $p = .001$  versus  $p < .0001$ ).<sup>18</sup> However, the robust multivariate findings suggest that the association of initial pain intensity with time to stable pain control is truly independent, and needs to be incorporated into the classification system. A simple and practical suggestion proposed at a recent workshop on 'Pain classification and assessment' at the Mari Negri Institute in Milan was to add the pain intensity number to the other ECS-CP features. For example, a patient with neuropathic pain (Ne), incident pain (Ii), psychological distress (Pp) and addictive behaviour (Aa), with normal cognition (Co) and a pain intensity of 7, could be classified as 7-NeliPPA-aCo. There are a number of items captured by the ECS-CP, but there are likely other confounding issues for some individuals such as age, chronic pain, true analgesic tolerance or genetic

factors. Further research and mathematical modelling may provide a mechanism to attribute a numerical value (e.g. weighting system) to the items included in the ECS-CP as we work towards developing a comprehensive, prognostic, standardised classification system for cancer pain.

A standardised, comprehensive and simple classification of cancer pain would support physicians to better manage patients' cancer pain and inform resource allocation decisions within cancer programmes, through earlier identification of patients with more difficult to manage pain. This type of classification would also enable researchers to compare results of outcome surveys and clinical trials in cancer pain management. Currently, it is possible that large discrepancies in the efficacy of a given treatment between groups can simply result from different characteristics in the population under study. It is our hope that, in the future, the ECS-CP could play a significant role in treatment planning, evaluating and reporting research results in the assessment and management of cancer pain. One positive development arising from site participation in this study is the potential establishment of an international working group for further development and validation of this pain classification system. This study involving diverse palliative populations strengthens the potential use of the ECS-CP as the base for ongoing development and evolution of an internationally recognised classification system.

At a European Palliative Care Research Collaborative (EPCRC) Research forum in the Lofoten Islands prior to the European Association of Palliative Care Conference in Trondheim, Norway in May 2008, the discussion of a Classification system for Cancer Pain was informed and guided by a Systematic Literature review on the topic.<sup>6,25</sup> As there is no single accepted framework on how to classify cancer pain, one of the aims of the EPCRC is to develop a classification system for advanced cancer patients with pain, based on international consensus. A pivotal issue of the discussion was whether to go ahead and gain experience with introducing and applying the items included in the ECS-CP and continue to develop this system or to develop a new consensus tool. There was agreement that the ECS-CP offered the best starting point for evolution of an international classification system for cancer pain and would be used in multi-site research initiatives being planned by the EPCRC.<sup>25</sup>

The current study has several limitations. The patient population was heterogeneous by design due to the multiple sites and centres. Further research on more homogeneous patient populations may improve understanding of how the different features of the ECS-CP influence the achievement of stable pain control and complexity of management in different settings. We cannot exclude a selection bias due to referral of patients with more difficult pain problems to the respective palliative care services at the multiple study sites. Despite the intent to have patients report current pain intensity, the possibility that some patients reported worst or average pain intensity cannot be excluded. We did not systematically record the degree of chronicity of the cancer pain presentation. It is possible that some patients had pain for a longer period before referral to the different sites, and neurophysiological changes due to chronicity of pain could have resulted in a longer time to achieve stable pain control.

## 5. Conclusion

The ECS-CP is a simple, comprehensive categorical classification system for meaningfully assessing cancer pain. While many factors have been proposed as prognostic for pain control, the ECS-CP is the first pain classification system to simultaneously integrate these factors within a cohesive framework. The items included in the ECS-CP represent only initial efforts to define a standard core of variables, and additional items such as analgesic tolerance, genetic variations and age would be worthy of further research. This international validation study confirms its predictive validity, reproducibility and generalisability in diverse palliative care settings and advances the process of development towards an internationally recognised pain classification system. The ECS-CP and future modifications could play a significant role in routine clinical assessment and management of cancer pain, as well as providing a standard for describing the patient population in reporting research results.

## 6. Conflict of interest statement

None declared.

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## Appendix A

### Edmonton Classification System for Cancer Pain

For each of the following features, circle the response that is most appropriate, based on your clinical assessment of the patient.

### 1. Mechanism of Pain

- No – No pain syndrome
- Nc – Any nociceptive combination of visceral and/or bone or soft tissue pain
- Ne – Neuropathic pain syndrome with or without any combination of nociceptive pain
- Nx – Insufficient information to classify

### 2. Incident Pain

- Io – No incident pain
- Ii – Incident pain present
- Ix – Insufficient information to classify

### 3. Psychological Distress

- Po – No psychological distress
- Pp – Psychological distress present
- Px – Insufficient information to classify

### 4. Addictive Behaviour

- Ao – No addictive behaviour
- Aa – Addictive behaviour present
- Ax – Insufficient information to classify

### 5. Cognitive function

- Co – No impairment. Patient able to provide accurate present and past pain history unimpaired
- Ci – Partial impairment. Sufficient impairment to affect patient's ability to provide accurate present and/or past pain history
- Cu – Total impairment. Patient unresponsive, delirious or demented to the stage of being unable to provide any present and past pain history
- Cx – Insufficient information to classify.

ECS-CP profile: (combination of the five circled responses, one for each category)

Assessed by: \_\_\_\_\_ Date: \_\_\_\_\_

## Appendix B

### Definitions of Terms

#### Incident Pain

Pain can be defined as incident pain when a patient has background pain of no more than moderate intensity with intermittent episodes of moderate to severe pain, usually having a rapid onset and often a known trigger.

- Io – No incident pain
- Ii – Incident pain present
- Ix – Insufficient information to classify<sup>j</sup>

#### Guidelines for use

There are six key characteristics of *incident pain*, as defined in the ECS:

**Relationship with background pain:** The intensity of incident pain is significantly greater than background pain.

**Severity:** The intensity of incident pain is moderate to severe.

**Predictability:** The trigger is often known such as movement, defecation, urination, swallowing and dressing change. However, clinically significant episodic pain (i.e. no predictable trigger) can be included (e.g. bladder or bowel spasm).

**Onset:** Its onset is rapid, with intensity often peaking within 5 minutes.

**Transiency:** Incident pain is transient, and may return to baseline shortly after the trigger is stopped or removed.

<sup>j</sup> (Insufficient information to classify due to factors such as questionable/unknown diagnosis, patient's unwillingness to participate or physical impairments (e.g. aphasia)).

**Recurrence:** It is intermittent, recurring when the trigger is reinitiated or reapplied.

### Psychological Distress

Po – No psychological distress present  
 Pp – Psychological distress present  
 Px – Insufficient information to classify<sup>j</sup>

Psychological distress, within the context of the pain experience, is defined as a patient's inner state of suffering resulting from physical, psychological, social, spiritual and/or practical factors that may compromise the patient's coping ability and complicate the expression of pain and/or other symptoms.

#### Guidelines for use

There are five key characteristics of *psychological distress*, as defined in the ECS:

**Relationship with pain:** The definition of psychological distress is limited to patients who are experiencing psychological distress within the context of the pain experience and who appear to express their suffering through physical symptoms.

**Relationship with suffering:** It is an expression of suffering, often referred to as *total pain*.

**Multidimensional:** It is multidimensional in nature, influencing many spheres of a patient's experience, including but not necessarily limited to physical, psychological, social and spiritual factors.

**Relationship with coping:** It may impair a patient's ability to cope with his/her illness.

**Physical symptom expression:** It is often expressed as an exacerbation of pain and/or other symptoms, which may be conceptualised as a form of somatisation.

#### Assessment

Assessment of psychological distress may include, but is not necessarily limited to, the following:

Assessment of patient's experience in multidimensional domains  
 Patient's behavioural presentation and symptom reporting profile  
 Collateral history from primary caregivers

### Addictive behaviour

Ao – Addictive behaviour not present  
 Aa – Addictive behaviour present  
 Ax – Insufficient information to classify<sup>j</sup>

Addiction is a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterised by behaviours that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm and craving.

#### Guidelines for use

There are five key characteristics of *addictive behaviour*, as defined in the ECS:

**chronicity:** It is a chronic disorder, which may have periods of relapse and remission.

**Multidimensional:** It is multidimensional in its development and expression, including genetic, psychosocial and environmental factors.

**Compulsivity**  
*persistent use despite harm*  
*craving*

This definition is limited to the following:

A remote history of prior alcohol/substance use **may not** be considered relevant as a complicating factor in ongoing pain assessment and management.

Substances of abuse include alcohol, prescription/non prescription medications, and illicit drugs.

It does not include chronic tobacco use.

#### Assessment

Assessment of *addictive behaviour* may include, but is not necessarily limited to, the following:

Use of CAGE as screening tool for possible alcohol abuse  
 Patient's behavioural presentation over a series of visits  
 A strong clinical history of substance abuse provided by patient  
 Collateral history from primary caregivers

**Reference:** Nekolaichuk C, Fainsinger R, Lawlor P. A validation study of a pain classification system for advanced cancer patients using content experts: The Edmonton classification system for cancer pain. *Palliat Med* 2005; 19(6):466–476.

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