Classification of pain in cancer patients – a systematic literature review

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One of the aims of the European Palliative Care Research Collaborative (EPCRC) is to achieve consensus on a classification system for cancer pain. We performed a systematic literature review to identify existing classification systems and domains/items used to classify cancer patients with pain. In a systematic search in the databases Medline and Embase, covering 1986–2006, 692 hits were obtained. 92 papers were evaluated to address pain classification. Six standardised classification systems were identified; three of them systematically developed and partially validated. Both pain characteristics and patient characteristics relevant for cancer pain classification were included in the classification systems. All but one of the standardised systems aim at predicting treatment response or adequacy of treatment. Several domains and items used to describe cancer pain but not formally described as part of a classification system were also identified and systematised. The existing approaches to pain classification in cancer patients are different, mostly not thoroughly validated, and none is widely applied. An internationally accepted classification system for cancer pain could improve research and cancer pain management. This systematic review suggests a need for developing an international consensus on how to classify pain in cancer patients. Palliative Medicine (2009); 23: 295–308

Key words: cancer; classification; pain; palliative care; symptoms; systematic review

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Introduction

Pain due to cancer is a complex symptom that affects most aspects of a person’s life: physical functioning, daily activity, psychological and emotional status and social life. The palliative care population is heterogeneous in many different aspects, also in how pain is experienced and how it appears.1-3 The heterogeneity and complexity represent challenges of how to describe the individual patients in a common language; a classification system.

Taxonomy is the practice and science of classification. ‘To classify’ means to arrange groups of conditions. When a condition or a patient is classified, the physician or researcher can compare the cases and communicate the results easier and more accurately. Stringent definitions of patient characteristics and observations are required to identify to which class or subclass the patient belongs.4-6

In a classification system, all relevant information from the patient’s medical history, the clinical examination and different supplementary examinations is summarised into a short, common and useful description. The ‘International Classification of Diseases’ (ICD-10)7 and the ‘TNM Classification of Malignant Tumours’8,9 are well-known examples of widely used classification systems within medicine.

A common language to describe cancer pain in palliative care patients would improve the translation of results from clinical trials into clinical practice, improve the quality of meta-analyses and make the direct comparison of effects between studies more adequate.10-12 A classification system may guide what information to assess, the clinical decision-making and the interpretation of research results. Inadequate assessment and a lack of common descriptors of pain are stated as main reasons for under treatment of cancer pain.13,14 To achieve consensus would represent a major improvement of research and management of pain in cancer patients.15-17

After the initial pioneering work done by Foley18 and others19 about the relevance of pain diagnosis and mechanism for treatment, several attempts to develop criteria on how to classify cancer pain patients according to clinically relevant characteristics are known.20 However, the description of palliative care patients included in clinical studies is still not standardised; classification and assessment methods vary across studies.10 The need for an internationally accepted classification system for use both in research and in clinical practice has been recognised in reviews, studies and editorials.20-24

The European Palliative Care Research Collaborative (EPCRC) was funded by the European Unions 6th framework in 2006.25 One of the tasks of this international research network is development of a classification system for pain in patients with advanced cancer. To identify existing approaches to classification of cancer, pain is considered to be an important first step of this work. Thus, the present systematic review of the existing literature about cancer pain classification was conducted. The aims were to identify and describe systems for classification of pain in cancer patients, their development and validation, domains and relevant items, methods of assessment and their impact on clinical studies as well as factors predictive for response to pain treatment.

Material and methods

The medical literature published from 1986 to 2006 was searched in the Medline and EmBase databases with OVID as the search engine. The following search terms were used to specifically identify papers primarily concerned about classification:

- Medline: Search terms ((classif$ adj5 pain) OR (Cut point$ adj5 pain) OR (Staging adj5 pain) OR (Categor$ adj5 pain) OR (character$ pain adj5) OR (grad$ adj5 pain)) AND (cancer OR Neoplasms). ‘pain adj5’ means that the word pain should be adjacent to the other term with a maximum of five words between them.
- EmBase: The same searching terms were applied with minor adaptations to suit the EmBase library.

The titles and abstracts of all hits were independently screened by four of the authors of the present review (AKK, NAa, MJ, MJH) to identify possibly relevant papers for our aim. The search was performed to investigate pain in cancer patients in all phases of the disease. Papers of all methodological categories were included. Predefined criteria for exclusion of papers were: papers published before 1986, non-English papers, papers on non-malignant pain, papers addressing children or adolescents and papers exclusively addressing development or validation of pain-scoring instruments. When at least two of the authors identified a title and/or an abstract containing information of some aspect of cancer pain classification, the papers were included for further evaluation. Papers identified as relevant by only one of the reviewers were discussed to reach consensus about whether to include or exclude.

All included papers were reviewed by three of the authors (AKK, NAa, MJ) according to a checklist that was developed prior to the reading and mainly based on expert opinions within the EPCRC. For each paper, the reviewers registered domains, sub-domains and items of cancer pain applied in the papers such as pain intensity, pain mechanism, temporal variations, pain sites, aetiology, pain syndromes and pain treatment. Furthermore, the information provided on other subjective symptoms and signs such as psychological distress, physical functioning and interference were assessed. In addition, the following variables
were registered: methodology, country of origin of the study, assessment methods, patients’ demographics, primary cancer disease, stage and location of disease and tumour directed treatment. A systematic approach was applied for the evaluation of the papers. The main findings were categorised by the authors as 1) formal classification systems; systematically developed and partially validated, or not validated, and 2) characteristics not formally described as part of a classification system (informal approaches).

- A formal classification system means a set of domains and items that are used to describe and separate groups with a potential clinical impact. It is a standardised system to be applied across studies or populations. The formal classification systems were further divided into formal systematically developed and partially validated systems, and formal, although not validated systems. A classification system may be taxonomic (descriptive) or prognostic (Section ‘Formal, systematically developed and partially validated, classification systems’), or mainly a treatment evaluation tool (Section ‘Formal, although not validated classification systems’).

- Characteristics not formally described as part of a classification system (informal approaches, Section ‘Characteristics not formally described as part of a classification system’), were defined as a various set of domains and items used in papers identified by the literature search using the terms ‘classifying’/‘categorising’/‘staging’/‘grading’ to assess cancer pain and the cancer patients having pain. These informal approaches to classification were divided into two categories: 1) ‘pain characteristics’ (Section ‘Pain’) and 2) ‘patient characteristics relevant for cancer pain classification’ (Section ‘Patient characteristics relevant for cancer pain classification’). Domains, sub-domains and items were identified for each category (Figure 1). Pain intensity, pain mechanism and incident pain are examples of domains that describe different aspects of cancer pain. A domain, for example, pain mechanism, is described by sub-domains, such as neuropathic pain, and/or by one or several items, for example, a neuro-physiological examination. Pain intensity can be measured by one simple question ranked on a numerical rating scale (NRS), verbal rating scale (VRS) or visual analogue scale (VAS), whereas incident pain is often considered to be more complex and therefore a combination of different items is needed.

Results

The search resulted in 692 hits, 442 papers in Medline and 250 in EmBase. After screening of the titles and the domains and items used in papers identified by the literature search using the terms ‘classifying’/‘categorising’/‘staging’/‘grading’ to assess cancer pain and the cancer patients having pain. These informal approaches to classification were divided into two categories: 1) ‘pain characteristics’ (Section ‘Pain’) and 2) ‘patient characteristics relevant for cancer pain classification’ (Section ‘Patient characteristics relevant for cancer pain classification’). Domains, sub-domains and items were identified for each category (Figure 1). Pain intensity, pain mechanism and incident pain are examples of domains that describe different aspects of cancer pain. A domain, for example, pain mechanism, is described by sub-domains, such as neuropathic pain, and/or by one or several items, for example, a neuro-physiological examination. Pain intensity can be measured by one simple question ranked on a numerical rating scale (NRS), verbal rating scale (VRS) or visual analogue scale (VAS), whereas incident pain is often considered to be more complex and therefore a combination of different items is needed.

Results

The search resulted in 692 hits, 442 papers in Medline and 250 in EmBase. After screening of the titles and the

Figure 1 Cancer pain classification – methods and main results (numbers correlate with the subtitles in the manuscript).
abstracts, 92 papers were identified as papers including any form of pain classification (Figure 2).

### Educational papers

37 papers were defined as educational papers. These included two systematic reviews, 31 regular reviews, three editorials, and one short comment. Two of the educational papers each focused on one primary cancer diagnosis, genitourinary cancer and breast cancer, whereas one focused on pancoast tumours. A total of 13 of the educational papers reviewed cancer pain in patients with advanced cancer or metastatic disease, whereas one of these focused on patients with terminal disease. Five educational papers reviewed breakthrough pain, three papers focused on neuropathic pain in general, one on muscle pain and one on pain caused by bone metastases. Nine papers focused on different treatment strategies of cancer pain and response to treatment and two papers dealt with treatment-induced pain.

The educational papers did not add any additional domains, sub-domains or items related to the categories ‘pain characteristics’ and ‘patient characteristics relevant for cancer pain classification’ not already identified in the clinical studies (vide infra).

### Clinical studies

A total of 55 of the reviewed papers were clinical studies; 29 prospective, 23 cross-sectional and 3 retrospective studies. None of these were randomised controlled studies, but two studies compared patients with and without symptoms and one compared psychosocial adaptation to pain in cancer and non-cancer patients. Most of the clinical studies included patients with different types of primary cancer diagnosis, whereas nine studies included patients with one or two predefined primary cancer diagnoses, for example, only patients with lung or prostate cancer. The majority of the included patients had metastatic disease, described as advanced, metastatic or incurable disease or as a palliative care population or patients in hospice. Two studies focused on patients with terminal disease.

The clinical studies were performed in the following countries: United States (n = 24), Italy (n = 8), Canada (n = 6), Sweden (n = 3), Denmark (n = 2), Germany
The International Association for the Study of Pain (IASP) established a subcommittee on taxonomy in 1975 to achieve consensus on classification of chronic pain syndromes. A list of pain terms was first published in 1979. Based upon these terms, expert opinions and clinical experience, the IASP Classification of Chronic Pain was developed and first presented in 1986. This is a descriptive coding system for chronic pain syndromes, both non-malignant and malignant, without any prognostic indication. The classification consists of five axes considered relevant to the diagnosis of chronic pain: I, anatomical region or site affected by pain; II, organ systems whose abnormal functioning produces pain; III, temporal characteristics of pain; IV, pain intensity and time since pain onset; V, aetiology. Except for the patient’s self-report on pain intensity and duration, the assessment is physician-based and consists of medical history, clinical examination and supplementary investigations. In this system, a code number is given to every clinical pain syndrome. A second edition of the IASP Classification of Chronic Pain was published in 1994 after experts’ evaluations. The changes made after this process were mainly additional descriptions of existing syndromes and some new conditions were added.

Three formal, systematically developed and partially validated, pain classification systems were used in six of the clinical studies: the Classification of Chronic Pain of the International Association for the Study of Pain (IASP), the Edmonton Classification System for Cancer Pain (ECS-CP), and the Cancer Pain Prognostic Scale (CPPS) (Table 1). Three formal, although not validated systems were identified in six clinical studies, systems to be defined as treatment evaluation tools relevant for cancer pain classification. In addition, several domains and items not formally described as part of a classification system (informal approaches) were recognised in the remaining 43 cancer pain studies (Figure 1).

### Table 1 Main content of the formal, systematically developed and partially validated classification systems

<table>
<thead>
<tr>
<th>Classification of Chronic Pain of the International Association for the Study of Pain</th>
<th>The Edmonton Classification System for Cancer Pain</th>
<th>The Cancer Pain Prognostic Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regions involved (axis I)</td>
<td>Pain mechanism</td>
<td>Mixed pain</td>
</tr>
<tr>
<td>Systems involved (axis II)</td>
<td>Incident pain</td>
<td>Worst pain severity</td>
</tr>
<tr>
<td>Temporal characteristics (axis III)</td>
<td>Psychological distress</td>
<td>Daily opioid dose</td>
</tr>
<tr>
<td>Pain intensity/time since onset of pain (axis IV)</td>
<td>Addictive behaviour</td>
<td>Emotional well-being</td>
</tr>
<tr>
<td>Aetiology (axis V)</td>
<td>Cognitive function</td>
<td></td>
</tr>
</tbody>
</table>

(\(n = 2\)), United Kingdom, Australia, Spain, Japan, the Netherlands, Turkey (\(n = 1\)) and multinational studies (\(n = 4\)).

Only one clinical study was identified that systematically applied the IASP Classification for Chronic Pain in cancer patients. Grond, et al. recorded up to three anatomically distinct pain syndromes in 2266 cancer patients, focusing on intensity, pathophysiology, location and aetiology of pain. Using this approach, they were able to show that patients’ pain could be categorised by the IASP system. To our knowledge, no attempts to evaluate the impact of this classification system on clinically significant outcomes are available. Three of the educational papers described the IASP classification system.

### The Edmonton Classification System for Cancer Pain (ECS-CP)

The Edmonton Classification System for Cancer Pain (ECS-CP) is an instrument developed with the primary aim to predict response to treatment in patients with advanced cancer. The first version of the instrument from 1989, at that time named the Edmonton Staging System for Cancer Pain (ESS), contained seven domains (called ‘features’ in the original work) considered to have prognostic value for treatment response: mechanism of pain, incident pain, previous narcotic exposure, cognitive function, psychological distress, opioid tolerance and history of drug or alcohol abuse. The patients were categorised into three groups according to probability of response to analgesic treatment: good, intermediate and poor prognosis. This pilot study on 56 patients suggested a good predictive value of the ESS. In a study in 1995, 277 patients were dichotomised to good and poor prognosis for pain control as very few patients belonged to the group of intermediate prognosis. The predictive value could be confirmed for the good prognosis group (0.93), but about 50% of the patients with poor prognosis also achieved good pain control. The two domains, cognitive function and daily opioid consumption, were not found to be independent predictors for achieving pain control and were removed from the staging system.

In the revised ESS from 2005 (rESS), cognitive function was reintroduced based upon literature review and
expert opinion. Tolerance was excluded from the rESS because of difficulty of clinical interpretation. In this study, including 746 patients, it was demonstrated that the time to achieve pain control was shorter (median = 4 days) in patients in the good prognosis group than in those belonging to the poor prognosis group (median = 6 days). In multivariate analysis, only the presence of neuropathic pain, incident pain and age were associated with the outcome measure. Based on clinical experience and expert consensus following a Delphi method consensus on construct validity, the authors decided to rename the rESS as a classification system (ECS-CP).16,75 Thus, at present, the ECS-CP consists of five domains: pain mechanism, incident pain, psychological distress, addictive behaviour and cognitive function. The assessment includes clinical interview with the patient, patient’s medical record, the CAGE questionnaire for screening for alcohol addiction, the Mini Mental Status Exam (MMSE) for the assessment of cognitive function as well as consultation with family members and other health care team members. The assessment should be completed by a physician or nurse practitioner/consultant using the definitions and guidelines for use described in the Administration Manual. All clinical studies, except the pilot study referred to above, as well as two educational papers32 and one short comment regarding the ECS-CP, were included in the present review. At present an ongoing international multicentre validation study on more than 1000 patients is close to completion.16

The Cancer Pain Prognostic Scale (CPPS)

The Cancer Pain Prognostic Scale (CPPS) was developed as a prognostic tool for prediction of pain relief in cancer patients. One prospective study describing the development of the CPPS was identified. Four assessment instruments were applied in this study, all mainly based on patients’ self-report: Brief Pain Inventory (BPI), Functional Assessment Cancer Therapy (FACT-G), Memorial Symptom Assessment Short Form (MSAS-SF) and Mental Health Inventory (MHI). In addition, the MMSE was completed at study entry. Items related to the cancer disease and patient demographics were assessed as well. The patients were divided into two prognostic groups: good or poor prognosis of achieving pain relief within two weeks when treated with analgesics. After identifying predictors of pain relief, the CPPS constituted four domains: worst pain severity (BPI: NRS 0–10), emotional well-being (FACT-G score >17), daily oral opioid dose >60 mg and the presence of mixed pain, for which the results were summarised into a sum score ranging from 0 to 17. Higher scores corresponded to a higher probability of pain relief one and two weeks after primary assessment. No further clinical studies or educational papers applying the CPPS were identified in this review.

Formal, although not validated classification systems

Three other formal systems used for cancer pain classification were identified, although they have not been validated. These systems are mainly tools for prognostication and/or evaluation of pain treatment.

Opioid Escalation Index (OEI)

Classification of opioid responsiveness using the OEI as a measure of the patient’s opioid requirement combined with the level of pain intensity was applied in five clinical studies, all published by Mercadante, et al. The assessment was performed by doctors and nurses in a palliative care team. By using the OEI as a treatment evaluation tool, the patients in two of the reviewed studies were divided into three groups: good, partial and no response to treatment.

Prognostic tool for pain treatment

In 1992 Mercadante, et al. presented a prognostic tool for pain treatment that aimed to predict the success of pain control by pharmacological pain treatment [nonsteroidal anti-inflammatory drug (NSAIDs) and opioids]. Six prognostic groups were established depending on the following items: number of days until achieving pain relief, the presence of incident pain and required dose of opioids. Doctors and nurses in a palliative care team were responsible for the evaluation; a VRS was used for assessment of pain intensity. No other studies applying this prognostic tool were identified.

The Pain Management Index (PMI)

The Pain Management Index was introduced by Cleeland in 1994. It compared the most potent analgesic drug prescribed for a patient with the patient’s reported level of worst pain by use of NRS in the BPI. The index ranged from –3 (severe pain, no analgesic drug) to +3 (patient on a strong opioid and reporting no pain) and aimed to assess adequacy of pain treatment. This study was not among the papers found by the predefined search criteria because neither the title nor the abstract focused on classification, but on response to analgesic treatment. However, the PMI was described as a classification system in one of the reviewed educational papers. In a recent review, the PMI was considered to be a relatively rough method for evaluating the appropriateness of cancer pain treatment and as a potential indicator to compare
different populations and pain practices at the national and international level.85

Characteristics not formally described as part of a classification system

The literature search identified 43 clinical studies concerning classification of pain in cancer patients not applying a formal or standardised classification system. These studies were investigated to identify and systematisate domains, sub-domains and items belonging to the categories ‘pain characteristics’ and ‘patient characteristics’ relevant for cancer pain classification’. The main findings are summarised in Table 2.

Pain

Several domains of the category of pain were identified in the cancer pain classification studies.

Pain intensity

Pain intensity was the most frequently applied domain; reported in 34 clinical studies. Various methods were applied to measure intensity. VAS (n = 15)2,13,63,64,73,73,86,94 and NRS (n = 11)95-105 were the most commonly used assessment methods. Verbal rating scales were also common (n = 10)61-63,65,72,89,102,106-108. Some studies made use of two different scales. Different time frames were applied, such as pain intensity during the last 24 h or the last week. Furthermore, average pain intensity and worst pain intensity were assessed.

Temporal pattern

The domain temporal variation of pain was identified in 13 of the clinical studies using sub-domains such as acute/chronic pain, continuous/intermittent pain and breakthrough pain.2,13,63,64,90,94,99,104,108-111 The terminology applied for breakthrough pain varied across studies, for example, incident, incidental, episodic or transitory pain. Eight of the clinical studies were designed to investigate aspects of breakthrough pain.60,94,99,104,108-111 Items used to assess breakthrough pain were mainly intensity scales, frequency, onset and duration of the pain episodes as well as location, predictability, precipitating and relieving factors.48 The assessment was mainly based on patients’ self-report. Two studies used the Breakthrough Pain Questionnaire.99,111 Study specific questionnaires were developed in two studies94,108 and standardised screening questions about the presence of breakthrough pain were in use in four studies. 60,104,109,110

Pain mechanism/pathophysiology

Pain mechanism was described in 17 of the 43 clinical studies.13,63,73,86,90-92,96,99,104,105,108,111-113 The terms ‘pain mechanism’ and ‘pathophysiology’ were used in different papers to describe the same construct. Sub-domains of pain mechanism included nociceptive, somatic, visceral, neuropathic and idiopathic or psychogenic as well as mixed pain. The allocation to a certain pain mechanism in the clinical studies was mainly based on items such as patients’ self-report of symptoms, medical history, clinical examination and further examinations such as CT scan and MRI. Six studies reported definitions and/or checklists for the items to be assessed to allocate pain to the proper pain mechanism.13,63,86,93,99,112 ‘Nociceptive’ pain (n = 6)63,86,95,105,108,111 ‘Somatic’ pain (n = 8)13,90,93,96,99,104,112,113 ‘Visceral’ pain (n = 9)13,73,90,93,96,99,104,112,113 Traditionally ‘neuropathic’ pain (n = 14).13,63,86,92,93,95,96,99,104,105,108,111-113 The term ‘neurogenic’ pain was used in two studies to describe the same phenomenon.93,95 Most studies did not define the pain mechanisms explicitly. However, a set of items for neuropathic pain was presented in one study,112 and a detailed list of items for both nociceptive and neuropathic pain was presented in another study.63

If no organic lesion was found as explanation of pain, this was often considered an item of ‘idiopathic’ pain, which appeared to be similar in some articles to the use of the term ‘psychogenic’ pain (n = 4).95,96,104,105 If the patient had more than one type of pain or the pain was difficult to categorise, ‘mixed’ or ‘unknown’ (n = 5)13,63,86,96,112 and ‘others’ (n = 1)108 were used as further sub-domains. In addition, the sub-domains ‘radiating’ pain (n = 2),90,95 ‘central’ pain (n = 1)114 and ‘non-neuropathic’ pain (n = 1)92 were applied.

Aetiology

Nine clinical studies recorded the domain causal factors of pain.13,63,66,87,96,104,108,109,112 It was most common to distinguish between the following items: pain caused by direct cancer involvement (e.g., nerve root compression), treatment-related pain (e.g., chemotherapy-induced paresthesia) and pain unrelated to cancer (e.g., arthritis).74,96,112

Location

Site of pain was a domain in focus in nine studies.13,63,69,88,94,99,106,112,115 A body map was used to assess the location of pain in three of these studies.63,69,106 In the remaining studies, the location of pain was described as a part of the clinical examination.

Treatment

A total of 18 studies focused on pain treatment. Of these, 13 mainly investigated treatment with opioids and other analgesics,13,69,71,86-90,92,93,96,98,99 three looked at...
Table 2  Summary of content of formal classification systems and characteristics not formally described as part of a classification system applied in the clinical studies

<table>
<thead>
<tr>
<th>Category</th>
<th>Domain</th>
<th>Formal classification systems (Clinical studies n = 6)</th>
<th>Formal, not validated classification systems (n = 6)</th>
<th>Characteristics not formally described as part of a classification system (n = 43)</th>
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<tr>
<td></td>
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<td>IASP</td>
<td>ECS-CP</td>
<td>CPPS</td>
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<td>Temporal variation/ breakthrough pain</td>
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<td>Location of metastases</td>
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<td>Tumour-directed treatment</td>
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<td>Demographics</td>
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<td>Age, gender, occupation, education, marital status, medical history</td>
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IASP, The International Association for the Study of Pain: Classification of Chronic Pain; ECS-CP, Edmonton Classification System for Cancer Pain; CPPS, Cancer Pain Prognostic Scale; OEI, Opioid Escalation Index; PMI, Pain Management Index.

*Not focus in the studies, but recorded as part of several background variables.
radiotherapy, one at ganglia block and one study evaluated a biophysical treatment method. Twelve studies focused on treatment response, mainly assessed as decrease of the self-reported pain intensity.

**Pain syndromes**

Caraceni and Weinstein described pain syndromes in a review article as ‘repeated recognition of a cluster of symptoms and signs, including pain, which combined with other relevant information from the history and examination, identify a clinical entity that can be used to define that specific situation’. The assessment of pain syndromes was based on clinical findings and supplementary examinations as well as the physician’s clinical experience. Three clinical studies focused on pain syndromes. In a cross-sectional study published by the IASP Task Force on Cancer Pain, 51 cancer pain specialists evaluated 1095 cancer patients with severe cancer pain. Three main domains were assessed: pain intensity, pain mechanism and pain syndromes. A checklist of 51 pain syndromes was used for assessment; 22 of these were most prevalent. Some clustering of pain syndromes with different cancer diagnoses and pain characteristics could be suggested.

**Patient characteristics relevant for cancer pain classification**

*Other subjective symptoms*

Domains belonging to the category ‘other subjective symptoms’ were regularly assessed in the pain classification studies as a significant component of the complexity of cancer pain. Performance status or physical functioning was recorded as background variable in 17 studies by using different methods of reporting. Weight changes were registered in three studies, also as background variable. Functional interference caused by pain in the areas of daily activity, physical functioning, sleep, mood, anxiety, depression and relationship with others were used as items to describe consequences of pain in 12 studies. The assessment was mainly based on the seven interference items from the BPI, that is, self-report.

Different aspects of the patient’s emotional or psychological status such as depression, anxiety, mood and history of psychological symptoms were recorded in 10 studies. Among the methods used for assessment of this domain were different questionnaires, for example, EORTC-QLQ-C30, Hospital Anxiety and Depression Scale (HADS), the FACT-G and Mental Health Inventory (MHI). One of the studies used the ‘Symptom Checklist 90-R’, a 90-item self-report tool. One study evaluated patients’ satisfaction.

**Cancer disease**

Information concerning the underlying cancer disease was regularly reported in the identified clinical studies, mainly as background variables. Primary diagnosis, extent or stage of disease, specified site(s) of metastases and prior/ongoing tumour-directed treatment were common domains. Seven of the 43 studies applying an informal approach investigated patients with a specified primary cancer diagnosis. Six studies did not record the primary cancer diagnosis. Stage of disease was not reported in four studies. Six studies assessed patients with pain caused mainly by bone metastases. Survival was recorded in three studies as background variable. The influence of cancer diagnosis in the development of different pain conditions was not proven in any studies although suggested in one study.

**Patient demographics**

Patient demographics such as age and gender were reported as background information in all reviewed studies except two. In addition, some studies also recorded ethnicity, educational level, employment, marital status and religious affiliation. Co-morbidity and medication were also regularly recorded. Sex differences and age were domains investigated in one study each.

**Discussion**

Classification of patients with cancer pain includes information on the patient, the cancer disease and the pain. There are different approaches to summarise this in a formal description of the cancer pain population. This description has been accomplished in different ways according to our literature analysis.

The present systematic literature review identified six formal cancer pain classification systems. Three of them were systematically developed and partially validated according to our interpretation, while three were not validated and mainly to define as tools for prognostication and evaluation of pain treatment. In addition, several other domains and items not formally described as part of a classification system were identified. Categories and domains relevant for classification of pain in cancer patients applied and described in the reviewed papers are summarised in Table 2.
None of the systems identified have been widely applied in international empirical clinical studies even though the systems have been developed by researchers of outstanding reputation in palliative care and published in peer reviewed journals.

The lack of a systematic and widespread use of the identified classification systems may have several explanations. It may be related to limited knowledge of the classification systems. A lack of face and content validity and a lack of a consensus-based development procedure may be further reasons. The need for a classification system may not be recognised by researchers or clinicians. Furthermore, it is not mandatory to apply a given set of domains and items when publishing in international journals.

The content of any assessment or classification system need to be clinically valid, meaning that it measures what it is intended to measure. For a cancer pain classification system, ‘why’, ‘what’ and ‘how’ to classify needs to be specified. If possible, a common understanding among clinicians as well as researchers need to be reached on the ‘why’, ‘what’ and ‘how’ at an early stage of the instrument development phase: ideally based upon empirical data from clinical practice, research as well as from patients’ input. Only one of the six formal classification systems has followed a stepwise procedure, which may build the basis for a broad consensus, namely the ECS-CP. It has been developed over 20 years, first locally, then nationally and internationally, but the impact on clinical outcomes has yet to be proven. However, a significant agreement about the relevance of the underlying constructs has been demonstrated.

A common and valid description of the palliative care population is crucial when publishing on cancer pain in international journals. A step forward could be to challenge the editors of the main journals within palliative care to develop common recommendations for publications on patient classification generally and pain classification specifically.

Information on the category ‘pain characteristics’ were included in all identified systems. The category ‘patient characteristics relevant for cancer pain classification’ was included in two of the formal systems as well as in the informal approaches. Domains describing the cancer disease and patient demographics were widely applied as background descriptors. Such domains and items are frequently a part of the patient characteristics reported in clinical studies. One may argue that some of these domains and items need to be included in a future classification system for cancer pain.

Five domains were identified in two or more of the formal systems: intensity, temporal variations, pain mechanism, response to treatment and psychological distress. The ECS-CP is the only formal system not including pain intensity. However, the Edmonton group has shown the importance of pain intensity and the need to consider including this domain in future versions of the ECS-CP. Breakthrough pain is a sub-domain included in three of the formal systems; none of them are using the same terminology. A common language would improve this important part of cancer pain management. Pain mechanism is included in two of the formal systems. It is of importance in a future system as neuropathic pain or mixed pain is considered to be more difficult to treat than, for example, pure nociceptive pain. Furthermore, pain mechanism is relevant regarding choice of therapy. To agree upon how to define and report treatment response is also important. All formal systems, except the IASP Classification of Chronic Pain, are aiming at predicting treatment response or adequacy of treatment, but define this differently.

The domains cognitive function, addictive behaviour and pain syndromes were applied in one of the formal systems each. One may therefore question whether these three domains need to be included in a future classification system. However, cognitive impairment is considered to have clinical implications for assessment and management of patients with cancer pain as well as for participation in studies and is therefore still one domain of the ECS-CP. In the initial work of Bruera et al., a history of drug or alcohol abuse was considered to increase the risk of opioid addiction and would make the assessment of symptoms and treatment response less reliable. The role of previous misuse of alcohol or drugs for an ongoing treatment of cancer pain still remains unclear. The cancer pain syndromes mainly consist of three domains: aetiology, location and pain mechanism. An argument for the application of syndromes when describing cancer patients is that it may increase the understanding of the causes of the pain and improve the pain treatment. In recent publications, more than 20 cancer pain syndromes have been identified. Taking the complexity of the syndrome approach into consideration, one may question its usefulness and place in a future, simple and standardised classification system. However, this approach might be useful in clinical practice, specifically in the treatment of complex cancer patients. Additionally, the educational role of this approach in clinical training and in integrating formal specialist assessment of pain is supported by experts’ opinion and clinical practice.

One may question whether all relevant papers and relevant domains, sub-domains and items for cancer pain classification were identified in the present review. A large number of clinical studies and reviews have been published about cancer pain. It would, however, not be possible to explore all the existing papers published about cancer pain to address the question of pain classification. By use of the relatively narrow search terms in the present literature search, we may have missed some
relevant papers. This is confirmed by the identification of additional papers on, for example, pathophysiological classification of pain,19,118,119 reviews on pathophysiology120 as well as pain syndromes121 by hand searching. However, except from an assessment tool used for identifying patients with neuropathic pain (The Leeds Assessment of Neuropathic Symptoms and Signs Scale),118 these papers do not add any other classification system or clearly any domains, sub-domains or items. During the evaluation of the papers identified in this review, a saturation point of domains, sub-domains and items was already reached as the six formal systems were examined. The remaining clinical studies only added the domain interference. This indicates that little relevant information was missed.

The present systematic literature review describes the use of pain classification in cancer patients during the last 20 years. Most of the classification systems identified have not been extensively validated beyond the primary publications. This knowledge may contribute to the development of an international classification system for cancer pain within the EPCRC. The methodology on how to reach this goal and future plans of the EPCRC-project were presented in a recent paper.122 It describes a nine-step process consisting of systematic literature reviews, repeatable input from clinical experts and patients as well as empirical data collections. The next steps of the tool development procedure will be to collect empirical data to test each domain, sub-domain and item as well as receive systematic input from clinical experts and patients. All steps will be carried out and validated in an international collaborative consisting of clinical researchers and clinical experts. Through this process, we will hopefully end up with a shorter, more convenient, thoroughly validated, and consensus-based classification tool that may have the potential to become a standard for pain classification in the future. In the development of a new cancer pain classification system, it is important to agree upon the aim of such a system. Both descriptive and prognostic as well as evaluative information may be considered as part of such a future system. Additionally, a new international system needs to be cross culturally robust and to prove to have an impact on significant clinical outcomes such as better control of cancer pain.123

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