

# Assessment and classification of cancer pain

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## Purpose of review

Pain is probably the most feared symptom in cancer, and pain control has received considerable attention. Adequate pain management requires precise and thorough assessment including universally accepted definitions; an area with a great potential for improvement. There is still little consensus on how to categorize or classify cancer pain. The recent literature was reviewed in order to evaluate the development in cancer pain classification and assessment, respectively.

## Recent findings

At present, only three standardized, systematically developed but not fully validated pain classification systems exist. However, their use in clinical practice is relatively limited, with one exception; the Edmonton Classification System for Cancer Pain, which is now subject to a large, international validation study. The findings from the cancer pain assessment literature reveal a plethora of instruments indicating that tool development is a continuous process, which does not follow systematic guidelines. The driving force is most often specific research interests in a limited number of issues related to cancer pain.

## Summary

There is still no universally accepted tool for cancer pain assessment or general agreement on which domains to include in a classification system. In order to improve cancer pain management and research, we need to agree internationally on how to classify and assess cancer pain. Consensus can only be achieved through worldwide research collaborative work employing a systematic, stepwise process based on the existing body of knowledge, patient and expert opinions and clinical validation studies.

## Keywords

cancer pain, pain assessment, pain classification, pain management

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## Introduction

About 90% of cancer patients experience pain at some point during their illness [1]. A recent review on cancer pain presented pooled prevalence rates from 33% after curative treatment to 64% in patients having advanced disease, with one-third overall rating their pain as moderate or severe [2<sup>\*</sup>]. These unacceptably high prevalence rates exist in spite of great medical, pharmacological and technological advances, supplemented by the increased interest in pain assessment methods. However, the plethora of assessment tools developed through the last 2 decades does not seem to overcome the single most important barrier to optimal pain management – inadequate pain assessment [3<sup>\*</sup>,4].

## The need for a common language

Cancer pain is a complex multifactorial symptom in patients with malignant disease. The overall concept of cancer pain does not suffice to classify or describe

the different pain characteristics that are due to different tumor related, etiologic, pathophysiologic, anatomic, treatment-related and temporal factors. Furthermore, psychological and patient-related factors strongly influence the individual pain experience that guides the basis for pain treatment with the WHO pain ladder as the most common approach combined with various other treatment modalities as necessary [5]. Ideally, all of the factors above should be systematically assessed and classified in order to optimize pain management and predict treatment success in the individual patient.

However, there is little consensus with respect to definitions, framework, format and content related to these two related yet distinct concepts; pain assessment and pain classification in relation to cancer [3<sup>\*</sup>].

## The concept of classification

Originally, classification was a method originating from biology for the grouping or categorization of living

organisms, most often based on a hierarchical structure [6]. The concept 'taxonomy' however, which is by definition the practice and science of classification, has attained a wider use and now also refers to a classification of things, as well as to the principles underlying such a classification. The International Classification of Diseases (ICD)-10 [7] is an example of a taxonomic scheme, corresponding to the Tumour, Nodes, Metastases (TNM) classification, a common language in oncology [8]. A similar standardized, consensus-based approach for pain classification is not in wide-spread use, despite the development of the International Association for the Study of Pain (IASP) [9] pain list and the Edmonton Classification System for Cancer Pain (ECS-CP) [10–12,13\*,14].

The intention of a cancer pain classification system is to improve pain management. Through a standardized and systematic description, it is possible to perform a grouping of patients according to agreed-upon characteristics of the disease, the pain and the patient. These groups may help in predicting the likelihood of successful pain treatment or in the identification of approximately 20% of cancer patients who are less likely to respond to standard treatment.

Consensus-based definitions are of the utmost importance for description of patient cohorts in clinical studies, in clinical practice and in order to understand which specific guidelines are developed for whom. This is also necessary for making comparisons across studies and for drawing conclusions about medication or other treatment options. Stringent definitions of patient characteristics and observations are required to identify to which class or subclass the patient belongs [15,16]. It is a major problem that study populations vary considerably in several characteristics associated with the complexity of pain management [13\*,17\*\*,18–20].

The IASP taxonomy of cancer pain is a list of diseases and lesions which produce pain and provides important information about difficult malignant and chronic pain syndromes primarily based on physician's examinations [9]. Pain intensity and duration are the only factors based on the patient's own report.

The need for an internationally accepted classification system with a common language for use both in research and in clinical practice has been recognized in reviews, studies and editorials [1,21\*,22\*,23]. In order to succeed in being a frequently used tool in clinical practice, the system must be regarded as relevant, short and applicable according to the given situation, that is, prediction of pain relief. However, a major challenge is that the system needs to be brief and sufficiently comprehensive. Items to consider include the clinical characteristics of pain, relationship to underlying pathological processes and

pain mechanisms (i.e. visceral, neuropathic, idiopathic), other domains such as location, as well as patient-related factors (i.e. sociodemographic, cognitive, history of addiction). These need to be elicited directly from the patient where possible [24], and then combined with clinical findings and supplementary examinations.

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### Classification of cancer pain

A recent review on cancer pain classification identified three classification systems labelled as formal systems by the authors as they encompass a set of domains and items which constitute a defined or standardized classification system intended for use across studies (Knudsen *et al.*, in preparation). This comprehensive review of the literature on classification of cancer pain provides an important overview of the existing validation systems, their content and factors that limit their clinical usefulness. Additionally, three tools judged to be relevant for pain classification were identified as treatment evaluation tools, but these were not systematically developed or validated: The Opioid Escalation Index (OEI) is a classification system of opioid responsiveness reported in 1994 [25], as well as in subsequent studies by Mercadante *et al.* [26–29]. This index is a measure of the patient's opioid requirement combined with the level of pain intensity. Another system by the same author presented six prognostic groups for the likelihood of pain relief after pain treatment with NSAIDs and opioids [30]. The factors included were number of days until achieving pain relief, the presence of incident pain and required dose of opioids. It should be noted, however, that both of these classification systems were retrospective classifications or grouping of patients after specific treatment regimens and as such do not provide a universal framework for cancer pain classification. The third of the nonvalidated systems, developed in 1994, could be viewed as a treatment appropriateness evaluation tool, rather than a classification system. It compared the patient's self-reported peak pain intensity to the most potent analgesic drug that was prescribed to the patient [31].

Three standardized classification systems were systematically developed and partially validated; the IASP Classification of Chronic Pain [9,32], the ECS-CP [10–12,13\*,14] and the Cancer Pain Prognostic Scale (CPPS) [33].

The IASP list of pain terms was first published in 1979 [32], later revised and extended twice [9] as a result of expert opinions and clinical experience. In the IASP Classification of Chronic Pain for malignant and non-malignant chronic pain syndromes, each clinical pain syndrome is assigned a code number based on five areas: anatomical site, organ systems whose abnormal functioning produces pain, temporal characteristics, pain intensity

and time since debut, pain etiology. The recent review by Knudsen *et al.* (in preparation) identified only one clinical study in which the IASP system was used [34]. This comprehensive review of the literature on classification of cancer pain provides an important overview of the existing validation systems, their content and factors that limit their clinical usefulness.

The same review identified only one study employing the CPPS: the original one describing its development [33]. The CPPS is basically an index score, primarily based on self-report, that is used to dichotomize patients into good or poor prognosis for pain relief. It consists of four domains: worst pain severity on an 11-point numerical rating scale (NRS) scale (0–10), emotional well-being from the Functional Assessment of Cancer Therapy (FACT-G) [35], daily oral opioid dose of more than 60 mg and the presence of mixed pain.

The ECS-CP, however, has gone through several stepwise and systematic validation studies, though clinical use so far is mainly restricted to Canada. In the first version of the ECS-CP, called the Edmonton Staging System (ESS), patients with advanced cancer were classified as having a good, intermediate or poor prognosis for successful pain treatment, based on their scores on seven domains: mechanism of pain, incident pain, previous opioid exposure, cognitive function, psychological distress, opioid tolerance and past history of drug or alcohol abuse [10]. A subsequent study led to a dichotomization of the groups, good or bad prognosis for pain control [36], whereas two of the factors, cognitive function and previous opioid consumption, were removed as they were not found to be independent predictors for achieving pain control.

In a later, regional multicentre study, aiming to test interrater reliability and predictive validity evidence, cognitive function was reintroduced based on expert opinions and literature reviews whereas tolerance was excluded because of interpretational difficulties [12]. The next validation study [14] was performed to gather construct validity evidence to develop consensus definitions and to develop and evaluate the administration manual [37]. Input from national and international expert reviews by means of the Delphi techniques [38] led to some revisions, with five domains (mechanism of pain, incident pain, addictive behaviour, psychological distress, cognitive status) being included in the renamed ECS-CP.

As can be inferred from the above, only one of the classification tools, the ECS-CP, has been used in more than one study, has been subject to several revisions based on validation studies, expert opinions and formal construct validation and is now subject to a large international validation study that includes 1100 patients.

The fact that no standardized systems are widely used in clinical studies underlines the necessity to reach expert consensus on the purpose of a classification system and what to include through stepwise, iterative, international processes preferably also including patients' views as end-users.

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### The concept of assessment

Assessment is the process of documenting, usually in measurable terms, knowledge, skills, attitudes and beliefs in various disciplines, that is, education, economy and health [39]. In relation to health, this may include clinical examinations, blood tests and patients' self-report of symptoms and problems.

Measurement of health-related quality of life (HRQoL), a multidimensional construct that encompasses physical, psychological and social function and disease and treatment-related symptoms, has gained wide attention in oncology over the past 20 years [40]. In palliative care, in particular, subjective assessment of symptoms may serve as the primary outcome for clinical practice and in research, as the fluctuation of symptoms and consequences for the individual may be viewed differently by patients and physicians [41•].

Despite numerous publications on quality of life-related issues and the widespread use of the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 [42] and FACT-G [35], there is still little international consensus on how to measure HRQoL and the key symptoms in cancer. This is particularly related to poorly defined concepts and ambiguity in the interpretation which in turn creates confusion. In order to improve instruments, clear definitions and conceptualization of relevant domains to include are necessary [43].

A symptom by definition [39] indicates an accident, misfortune that is a departure from normal function or feeling which is noticed by a patient, indicating the presence of disease or abnormality.

A domain is the distinguished part of an abstract or physical space where something exists, is performed or is valid [39]. This concept is used in every branch/sector/field of human activity. In relation to cancer pain, pain intensity and breakthrough pain are domains of the pain symptom. For example, pain assessment has been recommended by professional experts and patients to comprise at least five key domains, often also called dimensions that are intensity, temporal pattern, exacerbation/relieving factors, localization and interference [44••].

An item is an entry in a list, or one object in a collection of objects [39]. In relation to measurement theory, it is

based on the idea that the probability of getting an item correct is a function of a latent trait or ability. Thus, items for assessment of the various pain domains must be selected on the basis of their ability to serve as indicators of the specific pain domain, that is, intensity, pain quality, breakthrough pain, etc. An example of this framework from the work of the European Palliative Care Research Collaborative (EPCRC), a pan-European, European Union-funded translational research program [45] is displayed in Fig. 1.

### Assessment of cancer pain

Ideally, pain assessment should be brief, precise, multi-dimensional and specifically targeted to the patient population. It is generally recommended that pain intensity should be assessed by a simple 11-point NRS), whereas well validated instruments such as the Brief Pain Inventory (BPI) [46] or the McGill Short Form questionnaire [47] are recommended for a more comprehensive, multi-dimensional pain assessment [48].

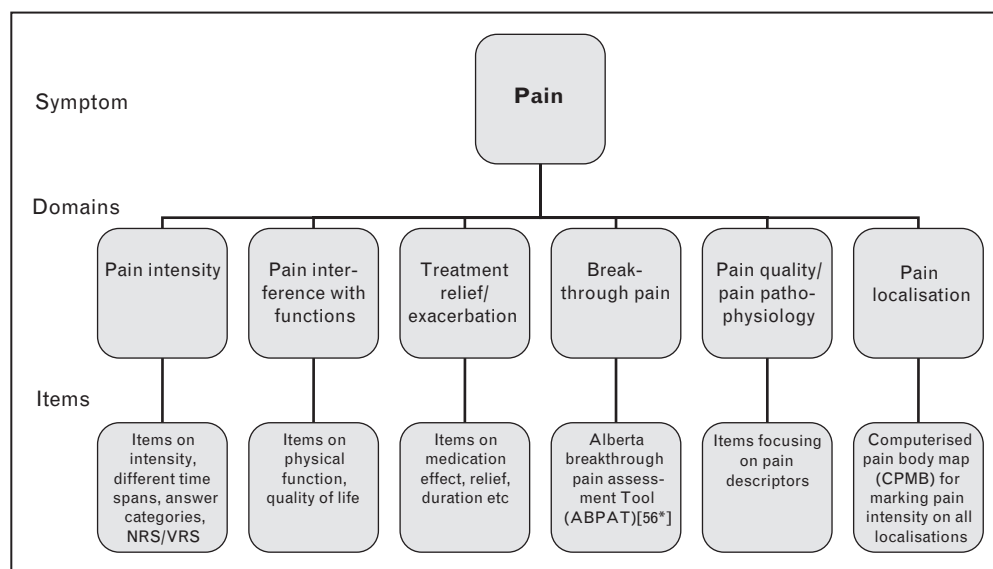
Despite these recommendations, pain is still not routinely measured in cancer clinical practice [49,50,51]. This may be because most tools are too long and cumbersome for patients and clinicians to use [3,52,53].

A recent review [52] examined the content (domains and items) of pain assessment tools in palliative care as well as their development and validation procedures according

to the internationally accepted EORTC methodology ([www.eortc.be/home/qol/Manuals.htm](http://www.eortc.be/home/qol/Manuals.htm)) [54]. Out of 11 tools developed after 2003, nine were multidimensional and three of the five highest-ranked domains in Holen's review [44]: intensity (rank 1), treatment/relief/exacerbation (rank 3) and location (rank 4) were included in seven, six and five of the tools, respectively. One tool, however, an ad hoc inventory for clinical practice, included all five dimensions [55]. Only two of 11 instruments were extensively validated or cross-culturally tested.

The overall impression from the review was that there is a continuous flow of new instruments, and only a minority is developed according to standardized development procedures [44,52]. Furthermore, the development of new tools is driven by specific research interests and as such focus on one or a few domains only, such as pain beliefs, information and prescription routines [52]. One exception, however, was the Alberta Breakthrough Pain Assessment Tool [56], specifically developed for assessment of breakthrough pain, a prevalent pain syndrome. This is one of two newer tools [52] that has been subject to systematic development by means of a Delphi process with expert panel reviews followed by a think-aloud process involving patients with cancer-related breakthrough pain and clinical validity testing. The tool was primarily developed for research purposes, but may as well be an important contribution to specific pain assessment in the clinical setting, though further testing is necessary.

**Figure 1** The conceptual framework used for assessment of pain in the European Palliative Care Research Collaborative data collection study



The figure displays the structural framework used by the EPCRC [45], with the overall symptom pain, being divided into different domains such as intensity, breakthrough pain which are assessed by several items. CPMB, computerized pain body map; NRS, numerical rating scale; VRS, verbal rating scale.

A major problem with the narrow-focused, specific tools is the need for additional instruments in clinical studies to obtain a multidimensional pain assessment. This increases the burden on patient and staff, the instrument package is perceived as cumbersome by both parties, which in turn reduces the compliance and use, and the vicious circle of unsystematic symptom assessment is complete.

We believe that the tremendous interest in symptom assessment in general and in pain measurement in particular has been to the benefit of patients and science. However, we have now reached a point when we should seriously consider if it is wise to continue in the same direction. Sometimes 'perfect is the enemy of good', and the plethora of new tools with different definitions and nomenclature is unlikely to improve the standard of pain assessment.

We strongly believe that a scientific, systematic approach to any assessment is necessary, regardless of whether the symptom is easily observable, based on self-report or measured by variables anticipated or postulated to describe an unobservable symptom such as anxiety. In relation to cancer pain, we need international consensus that can only be obtained through collaborative work. This should include systematic work with extensive literature searches, expert and user involvement, rigorous translation procedures, cross-cultural validation and psychometric testing in clinical studies [22\*].

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### Directions for the future

A recent report examining the status of research in palliative care in which symptom alleviation is the major goal concluded that notable progress has been achieved in Europe with respect to quantity and quality, though palliative care research could still be regarded as being in its infancy [19].

Several well funded palliative care research initiatives have been established in Canada, the United States, Australia and Europe during the past 5–6 years [21\*,57\*]. In Canada, a palliative end-of-life care initiative through the Canadian Institute of Health Research (CIHR) was granted 16.5 million Canadian dollars to build research capacity and create interdisciplinary research focusing on topics such as symptom control, communication, care-giver research, end-of-life care, symptom assessment and classification [21\*]. In the United States, the National Palliative Care Research Center (NPCRC) [58] was established in 2005 and has allocated several research grants to promote palliative care research for the improvement of evidence-based treatment. The Palliative Care Clinical Studies Collaborative in Australia was funded with some of the objectives being to provide registration of palliative medicines,

perform clinical comparison trials, develop national partnerships and provide capacity for future clinical and nonclinical research in palliative care [59].

The European community has funded several palliative care and cancer research initiatives through the 6th and 7th framework programs for research. The EPCRC translational research collaborative with members from eight European countries and collaborators from Canada and Australia aims to develop novel genetic methods for the prediction of opioid responses and individual variation in cachexia, in addition to developing consensus and evidence-based methodology for assessment and classification of pain, cachexia and depression [45]. The development of European evidence-based guidelines for treatment and assessment will be based on the results from research. The European Commission's Executive Agency for the Public Health Program (PHEA) received funding for the development of mechanisms for reporting and analyses of health issues and producing public health reports, focusing on best practices and models in palliative care, that is, the provision of specialist against basic palliative care as dependent and integrated approaches. Two other initiatives, the PRISMA (Optimizing Cancer Patient Care through the Advancement of Research and Education) and a European Collaboration to optimize research for the care of cancer patients in the last days of life (OPCARE9) were also recently funded by the European Union [60].

All these new initiatives focus on clinical practice and call for a standardization in the assessment of subjective symptoms, particularly so in pain. The need to standardize patient-reported outcomes has also been acknowledged by the National Cancer Institute (NIH, USA) which has funded a patient-reported outcome measurement system (PROMIS) aiming to develop a widely available set of standardized instruments to measure subjective outcomes in many chronic illnesses, including cancer [61,62]. Furthermore, it is important to take advantage of the rapid development in computer technology and the increased use of digital communication channels. Computers enhance the precision of the assessment, provide rapid calculation of scale scores, allow for tailored assessments by omitting irrelevant items for the individual patient and may be automatically linked to data from the medical charts, if in accordance with the institutional policy. This, in turn, reduces respondent burden and provides a head-start for doctor–patient communication [63,64]. A recent study showed that the vast majority of patients in palliative care were able to complete a computer-based assessment precisely and reported high satisfaction with this methodology [Fyllingen *et al.* Computer-based assessment of symptoms and mobility in palliative care: benefits and challenges (in preparation)].

To further develop and improve the assessment and classification of cancer pain, in general, the initiatives taken within the palliative care community should be continued [21<sup>\*</sup>,57<sup>\*</sup>]. The patient's perspective on symptoms and health should be central and supplemented with medical and clinical data for thorough classification of patients and symptoms in order to allow for comparisons across studies.

## Conclusion

Consensus on what to measure, when to measure and how to measure is of the utmost importance in relation to the current stage of pain assessment and classification. Decisions on this can only be reached through international collaboration and consensus processes. Nevertheless, the new initiatives in pain and palliative care represent major steps towards the goals of better symptom management and hopefully preventing patients from suffering from unnecessary pain.

## References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

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Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 81).

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