The IASP classification of chronic pain for ICD-11: chronic cancer-related pain

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Abstract
Worldwide, the prevalence of cancer is rising and so too is the number of patients who survive their cancer for many years thanks to the therapeutic successes of modern oncology. One of the most frequent and disabling symptoms of cancer is pain. In addition to the pain caused by the cancer, cancer treatment may also lead to chronic pain. Despite its importance, chronic cancer-related pain is not represented in the current International Classification of Diseases (ICD-10). This article describes the new classification of chronic cancer-related pain for ICD-11. Chronic cancer-related pain is defined as chronic pain caused by the primary cancer itself or its metastases (chronic cancer pain) or its treatment (chronic postcancer treatment pain). It should be distinguished from pain caused by comorbid disease. Pain management regimens for terminally ill cancer patients have been elaborated by the World Health Organization and other international bodies. An important clinical challenge is the longer term pain management in cancer patients and cancer survivors, where chronic pain from cancer, its treatment, and unrelated causes may be concurrent. This article describes how a new classification of chronic cancer-related pain in ICD-11 is intended to help develop more individualized management plans for these patients and to stimulate research into these pain syndromes.

Keywords: Classification, Chronic pain, ICD-11, Cancer, Radiotherapy, Chemotherapy, Diagnosis

1. Background on cancer-related pain
Worldwide, many people are affected by cancer, and the prevalence is rising. Estimates for 2020 suggest that, of 17 million new cases, 66% will survive for at least 5 years, and 40% will be alive more than 10 years after the diagnosis. Every year, 8.5 million people die from cancer. Pain is the commonest symptom of cancer at diagnosis and rises in prevalence throughout and beyond cancer treatment. Between 33% and 40% of cancer survivors, that is persons with cancer whose curative treatment was completed, suffer from chronic pain. By contrast, for those patients with advanced disease approaching death, at least 66% will experience pain and 55% of all patients will experience pain of moderate to severe intensity.

The term “cancer pain” is often poorly defined and is not synonymous with pain in a cancer patient or pain in a cancer survivor. Causes of cancer-related pain include the tumour itself or its metastases inflaming or eroding bone, viscerum or nerves, or pain related to tissue or nerve damage induced by cancer treatments (surgery, chemotheraphy, and radiation). Patients who are diagnosed with cancer are frequently older and may have comorbid diseases unrelated to their cancer. The aetiology of pain in some patients may therefore not be cancer-related but may instead arise from osteoarthritis, diabetic neuropathy, or a range of other diseases. The situation is made even more difficult by the fact that it is common for patients to experience pain from more than one of these sources; one systematic review found that there was a mean of 2 pains reported per patient with cancer.

Correctly identifying the nature and cause of pain in a cancer patient or cancer survivor is important to achieve optimal pain control. Accurate diagnosis and classification are more likely to lead to important benefits for patients: (1) tailored treatment incorporating analgesic medicine, anticancer therapies (including modification of the cancer treatment regimen if a chronic cancer treatment pain syndrome already exists), surgery, or non-drug interventions such as physiotherapy or cognitive behavioral therapy; (2) triggering support for patients to promote their own self-management through educational interventions, resources, and coping strategies; and (3) more specialist referrals for some patients, eg, multimodal pain treatment, interventional nerve blocks, or intraspinal analgesic procedures.

Current treatment guidelines created by the World Health Organization (WHO) and other national or international bodies are broad and do not relate treatment approaches to pain classification. Even with these guidelines and the availability...
of analgesia, barriers to management exist\textsuperscript{57} and undertreatment of cancer-related pain is common, in part related to lack of access or late access to opioids.\textsuperscript{19,21,55}

2. The need for a classification system

The Edmonton Staging System for Cancer Pain has been developed as a consensus for assessment and classification tools for cancer-related pain.\textsuperscript{15,26,29} Important domains that should be included in an assessment system were identified.\textsuperscript{30} These were a standardized assessment of pain characteristics (intensity, time course, and location), pathological processes and mechanisms, and patient-related factors (psychosocial factors and addictive behaviours). Classification and assessment are related, but not identical, concepts. Assessment typically aims at quantifying certain parameters, whereas a classification strives to provide distinct categories that are mutually exclusive and jointly exhaustive; both endeavours can be seen as complementary.

There is no widely recognized standardized taxonomy for the classification of cancer-related pain. The European Palliative Care Research Collaborative recommendations emphasized the need for such a taxonomy and an agreed classification system.\textsuperscript{4,23} Despite the ICD-10 containing a dedicated chapter with detailed codes C00-D48 for various types of cancer,\textsuperscript{52} there is only one code (G89.3) that denotes neoplasm-related pain, but this does not differentiate acute vs chronic pain. There are no detailed codes in the ICD-10 that systematically distinguish between cancer patients with and without various types of chronic cancer-related pain. This shortcoming impedes the acquisition of accurate epidemiological data for chronic cancer-related pain. Because ICD codes are also used for the reporting of target diseases and patients’ comorbidities in clinical research, the lack of such codes hinders the development and implementation of new therapies and may prevent adequate billing for health care expenses related to pain treatment. Moreover, this also renders chronic cancer-related pain statistically invisible and is detrimental to its recognition in public policy decisions.

3. The IASP Task Force ICD initiative

To remedy the lack of accurate classification of chronic pain in general and chronic cancer-related pain in particular, the International Association for the Study of Pain (IASP) established a task force that worked in close co-operation with WHO representatives in generating a systematic and improved classification of chronic pain.\textsuperscript{48} The classification is dedicated exclusively to chronic pain syndromes and excludes acute pain. Chronic pain was defined as persistent or recurrent pain lasting longer than 3 months. This definition was chosen because it provides a clear operationalization that is in line with widely used criteria\textsuperscript{52} and includes most relevant conditions.

The IASP task force recognizes that while the 3-month definition is important for distinguishing chronic pain from acute pain, the criterion might be more challenging to apply in the context of pain from progressive cancer. First, in the face of continuous and progressive tumour-related tissue destruction, the distinction between acute and chronic pain is blurred. Second, many patients with painful progressive tumour-related pain may not survive more than 3 months from onset of continuous pain; median duration of strong opioid treatment before death in one cohort study was 9 weeks.\textsuperscript{53} Thus, the proposed taxonomy could also be relevant in the context of continuous tumour-related pain before the 3-month mark, particularly when no further anticancer treatments are indicated.

In the proposed classification, optional specifiers will allow for recording the time course and severity of the pain as well as the presence of psychosocial factors.\textsuperscript{48} Pain severity will take into account the pain intensity, pain-related distress, and functional impairment assessed with the help of standardized rating scales (numerical rating scales [NRS] or visual analogue scales [VAS]) (see general companion paper\textsuperscript{57} and supplementary material for details on coding the specifiers; available at http://links.lww.com/PAIN/A658); functioning will in addition be specified according to the International Classification of Functioning (ICF).\textsuperscript{36,54} As such, the specifiers tie in well with the recommendations regarding the measurement of cancer-related pain.\textsuperscript{23,27,30}

4. The classification of chronic cancer-related pain

As in ICD-10, the codes for the cancer itself will be collected in their own chapter in the ICD-11 (foundation ID: 1630407678). The diagnosis of chronic cancer-related pain should be given in addition to these codes when appropriate (foundation ID: 785363034). For a complete overview of all codes for chronic cancer-related pain as implemented in the ICD-11 foundation layer, please refer to the supplementary material (available at http://links.lww.com/PAIN/A658). The foundation is the set of all entities represented in the ICD-11 and is continually updated and expanded. Coherent subsets of the foundation, called “linearizations,” are prepared for actual diagnostic coding by the WHO. At certain intervals, so-called “frozen versions” are prepared by the WHO. They are “snapshots” of the linearization at a particular point to establish a common reference version during the developmental process. The frozen version for implementation is from June 18, 2018. Another novel feature in ICD-11 is the so-called “multiple parenting” that allows one and the same definition to be subsumed under (and be accessed from) more than one higher level category (the so-called “parent”). As will become apparent below, it allows for (eg,) greater systematic clarity by listing neuropathic cancer pain both as cancer pain and neuropathic pain.

4.1. The general structure of the classification

The main sources for chronic pain in relation to cancer are the cancer itself and the treatments used to combat it. The classification reflects this structure: The top-level entity chronic cancer-related pain describes pain from both these sources. At the levels below, pain caused by the cancer itself and pain caused by its treatment are distinguished (Fig. 1).

4.2. The diagnostic codes in the classification of chronic cancer-related pain

In the following, the codes that will be available in ICD-11 are described briefly.

4.2.1. Chronic cancer-related pain

Chronic cancer-related pain is chronic pain caused by the primary cancer itself or metastases (chronic cancer pain) or its treatment (chronic postcancer treatment pain). It is distinct from pain caused by comorbid disease. Pain in cancer survivors must be monitored carefully because a change in pain quality or intensity can indicate recurrence of the initial malignancy. Careful assessment is required to distinguish pain caused by cancer from pain caused by cancer treatment or comorbid conditions. It is common for these pains to be concurrent, eg, thoracic surgery for a lung cancer might cause postsurgical pain, which can be
exacerbated by cancer recurrence in the same area. In these situations, the clinician must decide the predominant cause of the pain and prioritize the approach to pain treatment. The proposed classification of chronic cancer-related pain provides specific codes to cover these aspects (see below). The general diagnostic code “cancer-related pain” only demands that the pain arose in relation to cancer; it does not require a decision on the exact aetiology (cancer itself or its treatment). This allows for coding the cancer-related pain syndrome in situations in which the individual contributions of the various factors are not separable. The availability of this diagnosis helps to distinguish these patients from cancer patients without chronic pain.

4.2.1.1. Chronic cancer pain

Chronic cancer pain is defined as chronic pain caused by the primary cancer or metastases. Chronic cancer pain consists of inflammatory and neuropathic mechanisms as a direct effect of tissue response to the primary tumour or metastases. These are caused by tumour expansion, which induces tissue damage and release of various inflammatory mediators. In addition, the cancer can also compress and destroy a sensory nerve, which denervates the target tissue resulting in neuropathic changes. Cancer pain can be considered a type of mixed nociceptive and neuropathic pain, but increasing amounts of evidence suggest additional unique features indicating that it should be regarded as a separate pain state.\(^\text{16}\)

The temporal characteristics of cancer pain will be described as continuous (background pain) or intermittent (episodic pain). Intermittent pains can be predictable (incident pain), eg, an exacerbation of pain caused by weight bearing or activity (including swallowing, defaecation, coughing, or repeated dressing changes), or unpredictable (spontaneous pain) unrelated to movement or activity, eg, colic, stabbing pain associated with nerve injury. Intermittent pains such as those related to single clinical procedures (injections or biopsies) are regarded as acute pains and not included within the chronic pain classification. Chronic cancer pain is subdivided into 4 categories: 3 with distinct aetiologies: visceral, bone and neuropathic,\(^\text{11,22,45}\) and the final category as “other.”

4.2.1.1.1. Chronic visceral cancer pain

Chronic visceral cancer pain is chronic pain caused by the primary tumour or metastases damaging or injuring visceral organs in the head and neck region or within thoracic, abdominal, or pelvic cavities. Examples include painful liver metastases, coeliac plexus invasion by a pancreatic tumour,\(^\text{17}\) and retrosternal pain from locally progressive oesophageal or lung tumours. Chronic visceral cancer pain is often poorly localized and indeed may present as

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Figure 1. Organisation of cancer-related pain ICD-11 diagnoses. Levels 1 and 2 are part of the 2018 frozen version of the ICD-11; level 3 was entered into the foundation layer. According to the new concept of multiple parenting in ICD-11, an entity may belong to more than one group of diagnoses. “Chronic postcancer surgery pain is coded with all other chronic postsurgical pain according to the type of surgery in the respective chapter.”
referred pain (eg, shoulder tip pain from liver metastases is to be coded as chronic visceral cancer pain); pain mechanisms include compression, distension, inflammation, and ischaemia. The pain can be continuous or may be episodic, particularly if associated with organ distension (for an illustration of this type of pain see case vignette 1). Chronic secondary visceral pain is a secondary parent for this diagnosis.\(^5\)

4.2.1.1.2. Chronic bone cancer pain

Chronic bone cancer pain is chronic pain caused by the primary tumour or metastases damaging or injuring bone skeleton, and it is the most common type of chronic cancer pain.\(^33\) Metastases from other cancer sites are the most common form of chronic bone cancer pain as primary bone tumours are rare. Examples include an isolated metastasis to femoral shaft from colon cancer, or multiple metastases from breast or prostate cancer, or multiple myeloma. The most common sites of metastases are vertebrae, pelvis, long bones, and ribs.\(^28\) A bone metastasis can weaken bone sufficiently such that an innocuous movement, bump, or fall may result in a pathological fracture.

4.2.1.1.3. Chronic neuropathic cancer pain

Chronic neuropathic cancer pain is chronic pain caused by a primary tumour or metastases damaging or injuring the peripheral or central nervous system.\(^42\) Examples of chronic peripheral neuropathic cancer pain include thoracic tumour or metastases damaging the brachial plexus or abdominal or pelvic cancers damaging the lumbosacral plexus. Spinal cord compression (from collapsed vertebral boney metastases) can result in chronic central neuropathic cancer pain. Chronic neuropathic cancer pain may be associated with distinct symptom descriptors.\(^34\) and the pain is typically perceived in the distribution of affected nerves. Neuropathic mechanisms are associated with poorer outcomes in cancer pain.\(^39\) It is important to identify correctly the neuropathic mechanisms to guide the use of additional analgesic treatment.\(^25\)

4.2.1.1.4. Other chronic cancer pain

This code applies to chronic pain caused by the primary cancer or metastases that is not visceral, neuropathic, or bone in origin, and where the aetiology is known. For example, this code may be assigned to painful soft-tissue invasion by tumour, skin pain in T-cell lymphoma or painful lymph node metastases. If the aetiology is not known, or if the pain is a mix of known aetiologies caused by primary cancer or metastases, then the parent code “chronic cancer pain” will apply.

4.2.2. Chronic postcancer treatment pain

In addition to the cancer itself, the treatments for cancer also may cause pain. Typical treatments for cancer are surgery, chemotherapy, and radiotherapy, all of which may result in chronic pain.\(^38\) In patients who have received extensive anticancer treatment, eg, pelvic surgery, systemic chemotherapy, and radical pelvic radiotherapy, it can be difficult to isolate the exact aetiology of the chronic postcancer treatment pain. For these instances, the general diagnosis of chronic postcancer treatment pain will be appropriate. If the cause of the pain is known, or only one treatment was given, specific subdiagnoses as detailed below can be used.

4.2.2.1. Chronic postcancer medicine pain

Chronic postcancer medicine pain is chronic pain caused by any disease-modifying anticancer medicine, including systemic chemotherapy, hormonal treatment, and biological therapies. The most common form of anticancer medicine is systemic chemotherapy given orally or intravenously. However, hormonal treatments such as anti-oestrogens (tamoxifen), anti-androgens (bicalutamide and abiraterone), aromatase inhibitors (arimidex and letrozole), and luteinizing hormone inhibitors (goserelin) are commonly used and are associated with different chronic pain syndromes. Newer biological therapies such as monoclonal antibodies and protein kinase inhibitors are increasingly used as targeted therapies. Other examples include bisphosphonates used to manage bone metastases, which may cause painful osteonecrosis of the jaw, and corticosteroids leading to painful avascular necrosis of the femoral head.

Painful chemotherapy-induced polyneuropathy (CIPN) is described as a specific ICD-11 diagnosis (below). Chronic artralgia presenting as symmetrical joint pains, most commonly affecting the wrists, hands, and knees, is reported in 45% of women receiving hormonal treatment for breast cancer.\(^7\) This side effect is the most common reason for treatment discontinuation.\(^31\) Anecdotal case reports have suggested associations between some newer biological therapies and chronic pain syndromes such as chronic abdominal and musculoskeletal pain, but clinical experience is not yet sufficiently established to determine causality.

4.2.2.2. Chronic postradiotherapy pain

Chronic postradiotherapy pain is chronic pain caused by oral or intravenous chemotherapy given to treat the primary tumour or metastases. Common chemotherapy agents that cause peripheral neuropathy include taxanes (paclitaxel and docetaxel), platinum-based drugs (cisplatin and oxaliplatin), vinca alkaloids (vincristine), thalidomide, and proteasome inhibitors (bortezomib). Painful CIPN can begin after the first dose of chemotherapy and is often related to cumulative dose. Chemotherapy-induced polyneuropathy affects 60% of patients 3 months after treatment with chemotherapy and some protein kinase inhibitors, and 30% at 6 months or more.\(^44\) Pre-existing neuropathy is a risk factor for developing CIPN.\(^24\) Painful CIPN manifests in hands, feet, and sometimes face and can extend in a glove and stocking distribution to affect lower arms and lower legs. The pain is typically of pricking or burning character and may be described as an “electric sensation” (For an illustration of this type of pain see case vignette 2). Chronic painful polyneuropathy is a secondary parent for this diagnosis.\(^42\)

4.2.2.2. Chronic postradiotherapy pain

Chronic postradiotherapy pain is chronic pain caused by delayed local damage to the nervous system, bones, or other soft tissues in the field of radiotherapy given to treat the primary tumour or metastases. Chronic postradiotherapy pain is rare, but its occurrence is better recognized with improved long-term cancer survival.\(^12,25\) Onset can be within a few months of the end of radiotherapy or up to several years later. Risk factors include large overall treatment dose, large dose per radiotherapy treatment, and combined treatment with surgery or chemotherapy. Although overall the incidence is falling, nevertheless, about 2% of breast cancer survivors and up to 15% of head and neck cancer survivors can experience this type of pain.\(^12\) Pain from cancer recurrence should be excluded before making this diagnosis. The most recognized form of postradiotherapy pain is chronic radiation-induced neuropathy, which is described in a separate ICD-11 diagnosis (below).\(^12\) Other forms include
chronic pelvic pain and chronic head and neck pain. Chronic pelvic and low back pain are likely to be caused by insufficiency fractures of bone.25

4.2.2.2.1. Chronic painful radiation-induced neuropathy

Chronic painful radiation-induced neuropathy is chronic pain caused by delayed local damage to the nervous system in the field of radiotherapy given to treat the primary tumour or metastases. It is probably caused by nerve compression as a consequence of radiation-induced fibrosis, but direct injury to nerves and blood vessels is also likely after microvascular ischaemia.12,13 It usually occurs several years after radiotherapy and is often progressive and irreversible. The most frequent and best-known form of radiation-induced neuropathy is brachial plexopathy,18 which may follow irradiation for breast cancer or apical lung cancer. However, painful lumbosacral plexopathy after pelvic radiotherapy and axial neuropathy of the spinal cord after cervical radiotherapy have also been described.14 Chronic painful polyneuropathy is a secondary parent for this diagnosis.42

4.2.2.3. Chronic postcancer surgery pain

A first line treatment for many cancers is surgery to remove the cancer or the metastases. Because surgery-related chronic pain will be the same regardless whether the surgery is related to cancer or to some other condition, chronic postcancer surgery pain will be coded alongside other chronic postsurgical pain according to the type of surgery in the section on postsurgical pain. This will also include chronic pain after biopsy or from a chest or abdominal drain insertion for pleural effusion or peritoneal ascites.43 Chronic postcancer surgery pain is particularly common after treatment for breast (postmastectomy pain) or lung cancer (post-thoracotomy pain) but can follow any cancer surgery or surgical procedure (eg, a tissue biopsy or insertion of a thoracic drain). At 9 months after mastectomy, 63% of women reported persistent pain that was moderate to severe in 25% of the whole sample.8 After thoracotomy for lung cancer, 33% reported pain at 3 years after surgery, which was moderate to severe in 11% to 18% of the whole sample.51 The predominant mechanism of postsurgical pain is likely to be neuropathic but not exclusively so.50

4.2.2.4. Other chronic postcancer treatment pain

This code will apply to chronic pain caused by cancer treatment that is not related to cancer medicine, radiotherapy, or surgery, and where the aetiology is known. Currently, there are very few cancer treatments that would fulfill these criteria but they might include, eg, pain after insertion of oesophageal or rectal stent. If the aetiology is not known, or the pain is a mix of known cancer treatment aetiologies, then the parent code “chronic postcancer treatment pain” should be allocated.

5. Discussion

As codes for chronic secondary pain syndromes, the cancer-related chronic pain codes are intended to be given as codiagnoses of the underlying oncological conditions. The case vignettes provide contains examples of how such chronic pain may be coded including use of the optional specifiers for temporal course and for severity (pain intensity, distress, and disability). This will flag the need for medical care in its own right for this type of pain, despite the pain being considered a symptom. For patients with more advanced disease nearing the end of life, pain treatment pathways directed by palliative care specialists will apply. For patients living with and beyond cancer (cancer survivors), chronic pain treatment pathways directed by pain specialists will apply. This treatment may outlast the initial oncological treatment, and hence, the code for chronic postcancer treatment pain may become the leading code for these patients over time (as in case vignette 2). In the pilot field testing of the classification, the inclusion of chronic cancer-related pain codes was welcomed very strongly.2

6. Summary and conclusions

Including a distinct cancer-related pain classification within the ICD-11 will lead to multiple benefits, stimulate research into these pain syndromes, their treatment and prevention, including multimodal and behavioral interventions, and further promote a standardized assessment for cancer-related pain. For the individual patient, it may contribute to improved access to treatments. Further refinements to this classification can be made in the light of new data from epidemiological, translational, and clinical studies.

Case vignette 1: Chronic visceral cancer pain; continuous; overall severity code 3.3.3

A 78-year-old woman with pancreatic cancer experiences upper abdominal pain with occasional radiation into her upper back between the scapulae. The patient underwent surgery followed by 3 cycles of chemotherapy, but the tumour has progressed despite treatment. The pain is always present (extension code for the temporal course: “continuous” applies) and is described as dull, aching, gnawing, and nauseating. The pain intensity is rated 8/10 by the patient (extension code 3 = severe) and prevents her from doing much activity (interference of pain with daily activity 9/10, extension code 3 = severe). She reports pain-related emotional distress of 7/10 (extension code 3 = severe). The pain can sometimes be worse after meals or lying supine. On examination, there is tenderness in the epigastrium but no tenderness over the back. She has been treated with oral sustained release morphine 80 mg twice daily with some improvement.

Case vignette 2: Chronic painful chemotherapy-induced polyneuropathy; continuous; overall severity code 2.1.1

A 56-year-old man with colon cancer complains of painful feet 3 months after completing 6 cycles of platinum-based chemotherapy. The pain is constant but worse at night and on standing. It is described as numb, tingling, and pricking and sometimes radiates into the lower leg. The pain intensity is rated 4/10 by the patient (extension code 2 = moderate), and he is able to carry on most of his usual activities (interference rating 1 = mild). He reports pain-related emotional distress of 3/10 (extension code 1 = mild). On examination, there is loss of sensation to soft touch and pin prick over both feet to just above the ankles, and reduced discrimination between hold and cold sensations. He has been treated with pregabalin 75 mg twice daily but with no benefit.
Conflict of interest statement

The authors have no conflict of interest to declare.

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Appendix A. Supplemental digital content

Supplemental digital content associated with this article can be found online at http://links.lww.com/PAIN/A658. SDC includes a complete reference list of the diagnoses entered into the foundation with the foundation IDs as well as the extension codes (specifier). Since the complete list is contained, the material is identical for all papers of the series.

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