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## Chronic pain as a symptom or a disease

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# PAIN

# Chronic Pain as a symptom or a disease: The IASP Classification of Chronic Pain for the International Classification of Diseases ICD-11 --Manuscript Draft--

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# Chronic Pain as a symptom or a disease: The IASP Classification of Chronic Pain for the International Classification of Diseases ICD-11

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#### Abstract

Chronic pain is a major source of suffering. It interferes with daily functioning, and often is accompanied by distress. Yet, in the International Classification of Diseases (ICD), chronic pain diagnoses are not represented systematically. The lack of appropriate codes renders accurate epidemiological investigations difficult and impedes health policy decisions regarding chronic pain. This hinders adequate financing of treatments for chronic pain patients, limiting access to multimodal care. In cooperation with the WHO, an IASP Working Group has developed a classification system that is applicable in a wide range of contexts, including pain medicine, primary care, and low-resource environments. Chronic pain is defined as pain that persists or recurs for more than three months. In chronic pain syndromes, pain can be the sole or a leading complaint and requires special treatment and care. In conditions such as fibromyalgia or nonspecific low back pain, chronic pain may be conceived as a disease in its own right; in our proposal, we call this subgroup 'chronic primary pain'. In six other subgroups, pain is secondary to an underlying disease: chronic cancer-related pain, chronic neuropathic pain, chronic secondary visceral pain, chronic posttraumatic and postsurgical pain, chronic secondary headache and orofacial pain, and chronic secondary musculoskeletal pain. These conditions are summarized as 'chronic secondary pain' where pain may at least initially be conceived as a symptom. Implementation of these codes in the upcoming 11<sup>th</sup> edition of ICD will lead to improved classification and diagnostic coding, thereby advancing the recognition of chronic pain as a health condition in its own right.

Keywords: Classification; ICD-11; Chronic Pain; Symptom; Disease; Chronic Primary Pain; Chronic Secondary Pain; Functioning; Diagnoses; Coding;

1. Introduction

Pain is one of the most frequent causes for patients to seek medical.<sup>27</sup> While mortality rates are highest for cardiac infarction and stroke, infectious diseases, cancers and diabetes, chronic pain is a leading source of human suffering and disability (Goldberg and McGee 2011).<sup>17</sup> Pain itself and many diseases associated with chronic pain are not immediately life threatening; people continue to live with their pain and hence these conditions are common in both developed and developing countries.<sup>8,11</sup> The Global Burden of Disease Study 2013 evaluated 'years lived with disability' (YLDs: the prevalence multiplied by a disability-weighting factor) for a broad range of diseases and injuries in 188 countries.<sup>33</sup> The single greatest cause of YLDs around the world was chronic low back pain, followed by major depressive disorder. Other frequent causes of YLDs include chronic neck pain, migraine, osteoarthritis, other musculoskeletal disorders, and medication overuse headache. Chronic back pain and chronic neck pain featured in the top 10 causes of YLDs in every country examined.

Yet, in the International Classification of Diseases (ICD), chronic pain diagnoses are not represented systematically.<sup>14,34</sup> In many modern health care systems, referral for specific treatment such as multimodal pain management is dependent upon suitable ICD codes as indications. The lack of appropriate codes contributes to the paucity of clearly defined treatment pathways for patients with chronic pain. Some pain specialists have argued for recognition of chronic pain as a disease in its own right (for a review see <sup>32</sup>), while others have argued against this. Recognition of migraine as a primary headache disorder has been a crucial step towards including the International Headache Classification of the International Headache Society into ICD.<sup>20</sup> Similarly, conditions such as fibromyalgia or complex regional pain syndrome may qualify for classification as primary pain disorders in ICD. On the other hand, chronic pain may be secondary to osteoarthritis or diabetic polyneuropathy, where it

may at least initially be considered as a symptom. In either case, chronic pain is a long-term condition that requires special treatment and care.

Pain management should be guided by some measure of patient reported severity of this longterm condition. In acute pain management, a level of 'no more than mild pain' was established as treatment goal.<sup>28</sup> Comparison of the epidemiology of 'any', 'significant' and 'severe' chronic pain indicated progressively more marked adverse associations with employment status, interference with daily activities and general health.<sup>39</sup> Thus, a future classification of chronic pain should also include an option to code pain severity, which refers not just to pain intensity, but also to distress and disability.

A systematic classification of chronic pain was developed by a task force of the *International Association for the Study of Pain* (IASP).<sup>42</sup> This classification distinguishes chronic primary and chronic secondary pain syndromes, integrates existing pain diagnoses including headaches, provides precise definitions and further characteristic features of the respective diagnoses according to the content model of the WHO for ICD-11, including the severity of pain, its temporal course and evidence for psychological and social factors. It also aims to harmonize definitions and descriptions of chronic pain syndromes, and to use similar classification rationales as far as possible. These pain diagnoses have been implemented in the 11<sup>th</sup> version of ICD that was released by WHO in June 2018.

#### 2. Methods

The IASP, an NGO in official relationship with the WHO, contacted the WHO in 2012 with respect to developing a new and pragmatic classification of chronic pain for the upcoming 11<sup>th</sup> revision of the ICD. The goal was to create a classification system that is applicable in clinical

settings for specialized pain management as well as in primary care. A Task Force for the Classification of Chronic Pain was formed by recruiting pain experts from around the globe http://www.iasp-pain.org/Advocacy/icd.aspx?ItemNumber=5234&navItemNumber=5236], soliciting recommendations from IASP special interest groups and topical advisory groups of other ICD-11 sections. The co-chairs of the Task Force (WR and RDT) were in regular contact with WHO representatives. The overall structure of the chronic pain classification was developed by group consensus at the first face-to-face meeting and by plenary phone conferences. Subsequently, the subtopics were assigned to seven smaller author teams moderated by AB; overlaps between subtopics (e.g. chronic neuropathic pain after cancer treatment) were resolved via e-mail and phone conferences and definitions established by consensus among the teams concerned, and guidelines for classification in overlapping fields were specified.

The ICD-11 development process requires the generation of content models for each diagnostic entity, which contain definitions, diagnostic criteria and synonyms as well as state of the art scientific information about the respective entity. The content models were developed by the seven author teams, and were then entered as children of the appropriate parent entities via the WHO proposal platform. Preliminary versions of the classification were published (Treede et al. 2015),<sup>42</sup> presented at international conferences (World Congress on Pain 2016, European Pain Congress 2017) and were open to public comment via the IASP website and the WHO proposal platform. An early version of the classification underwent pilot ecological field testing in five countries in 2016.<sup>3</sup> The prefinal version was further subjected to the official international field testing of the WHO via the IASP website.

#### 3. Results

Chronic pain was defined previously as pain that persists past normal healing time<sup>7</sup> and hence lacks the acute warning function of physiological nociception. The concept of persistence beyond normal healing may apply to pain after surgery and the concept of lack of warning function to migraine headaches; but these concepts are difficult to verify in other conditions such as chronic musculoskeletal or neuropathic pains. Hence, a purely temporal criterion was chosen: chronic pain is pain that lasts or recurs for longer than 3 months.<sup>42</sup>

The chronic pain definition was cast into the format of the 'content models' as required by WHO for ICD-11 and was entered into what is called the 'foundation layer of ICD-11'. The foundation layer is the set of all entities represented in the ICD-11, which is continually updated and expanded, and where each is assigned a unique identifier (chronic pain: http://id.who.int/icd/entity/1581976053). Chronic pain is the 'parent code' for seven other codes that comprise the most common clinically relevant groups of chronic pain conditions (Figure 1): (i) chronic primary pain; (ii) chronic cancer-related pain; (iii) chronic postsurgical and posttraumatic pain; (iv) chronic neuropathic pain; (v) chronic secondary headache and orofacial pain; (vi) chronic secondary visceral pain; (vii) chronic secondary musculoskeletal pain.

### Insert Figure 1 about here

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There is some overlap between these groups of chronic pain conditions (e.g. neuropathic pain caused by cancer or its treatment) and between the pain codes and other existing codes in ICD-11 (e.g. chronic headaches). The ICD-11 solves the problem of entities that belong to several fields (e.g. stroke as both a cardiovascular and a neurological disorder) by so-called

'multiple parenting'. Multiple parenting allows that one definition (the child) may be accessed from more than one higher level category (parent). This feature allows more flexibility than in previous versions of ICD; for an example see Figure 2.

#### Insert Figure 2 about here

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So-called 'linearizations' are subsets of the foundation layer that are used for statistical and coding purposes. The most important linearization is the 'Mortality and Morbidity Linearization'. The new ICD category for 'Chronic Pain' and its seven sub-categories are part of this linearization, where they are listed in the chapter that describes 'certain symptoms, for which supplementary information is provided, that represent important problems in medical care in their own right' (Chapter 21). A 'frozen version' of the Mortality and Morbidity Linearization for quality control through field testing was made available in April 2017 and was updated in April 2018; the codes in linearizations may change over time as ICD-11 evolves and is maintained by the WHO (Chronic pain was MJ60 in 2017 and MG30 in 2018 frozen versions). A 'frozen version for implementation' has been published on June 18, 2018, and is scheduled for voting by the World Health Assembly in May 2019. Following endorsement, countries around the world are expected to report their health statistics using ICD-11 from 2022 onward.

3.1 Chronic primary pain syndromes

Chronic primary pain is defined as pain in one or more anatomic regions that persists or recurs for longer than 3 months and is associated with significant emotional distress or functional disability (interference with activities of daily life and participation in social roles) and that cannot be better explained by another chronic pain condition.<sup>29</sup> This is a new phenomenological definition, which applies to chronic pain syndromes that are best conceived as health conditions in their own right.<sup>32</sup> Examples include chronic widespread pain, complex regional pain syndromes, and irritable bowel syndrome. Chronic primary headaches are cross-referenced in this section making use of the 'multiple parenting' option of ICD-11, which means that chronic migraine is listed in both the headache section and the chronic pain section. The term 'chronic primary pain' may sound unusual, but is consistent with language used in other parts of ICD-11. The recently proposed definition of 'nociplastic pain' may describe some of the underlying mechanisms.<sup>25</sup>

#### 3.2. Chronic secondary pain syndromes

Chronic secondary pain syndromes are linked to other diseases as the underlying cause, for which pain may initially be regarded as a symptom. The proposed new ICD-11 codes become relevant as a co-diagnosis, when this symptom requires specific care for the patient. This marks the stage when the chronic pain becomes a problem in its own right. In many cases, the chronic pain may continue beyond successful treatment of the initial cause; in such cases the pain diagnosis will remain, even after the diagnosis of the underlying disease is no longer relevant. We expect that this new coding will facilitate treatment pathways for patients with these painful conditions by recognizing the chronic pain problem early in the course of the disease. This is also important if the underlying disease is painful in only some of the patients; disease diagnosis alone does not identify these patients without the co-diagnosis of chronic pain.

#### 3.2.1. Chronic cancer-related pain

Chronic cancer-related pain is defined as pain caused by the cancer itself (by the primary tumor or by metastases) or by its treatment (surgery, chemotherapy, radiotherapy).<sup>4</sup> Pain is a frequent and debilitating accompaniment of cancer and its treatment.<sup>10</sup> It becomes more and more apparent that chronic pain syndromes are prevalent in long-term survivors of cancer and that these chronic secondary pain syndromes include neuropathic and musculoskeletal pains.<sup>15</sup> Chronic pain caused by the cancer or by chemotherapy or radiation therapy is coded in this section. Pain that is caused by surgical cancer treatment is coded in the section of chronic postsurgical pain.

#### 3.2.2. Chronic postsurgical and posttraumatic pain

Whether or not pain persists past normal healing time<sup>7</sup> is operationalized most naturally for chronic pain after surgery or other trauma, where the initiating events and normal healing times are known. To be consistent with the definition of the parent entity 'chronic pain', the temporal criterion of three months is also used as cutoff here, even though aspects of chronicity may be detectable earlier.<sup>26</sup> Diagnostic entities within this category are divided according to the initiating event being either surgical or nonsurgical trauma.<sup>37</sup> Chronic postsurgical pain is a prime candidate for prevention programs to be combined with the usual preparation of a patient for surgery. Chronic posttraumatic pain is a major problem in rehabilitation and return-to-work programs. In both cases, pain often is neuropathic in nature (on average 30% of cases with a range from 6 to 54% and more).<sup>18</sup> In such cases 'chronic peripheral neuropathic pain' may be given as a codiagnosis.

#### 3.2.3. Chronic neuropathic pain

Neuropathic pain is defined as pain caused by a lesion or disease of the somatosensory nervous system.<sup>22,41</sup> This pain is typically perceived within the innervation territory that is somatotopically represented within the lesioned nervous system structure (projected pain). Neuropathic pain may be spontaneous or evoked by sensory stimuli (hyperalgesia, allodynia). This category is divided into chronic peripheral or chronic central neuropathic pain.<sup>36</sup> Algorithms for grading the diagnostic certainty have been published.<sup>13,41</sup> The diagnosis of neuropathic pain requires a history of nervous system injury, for example, by a stroke, nerve trauma or diabetic neuropathy, and a neuro-anatomically plausible distribution of the pain. Negative (loss of sensory function) or positive sensory signs (pain, paresthesia) must be compatible with the innervation territory of the lesioned nervous structure. For the identification of *definite* neuropathic pain, it is necessary to additionally demonstrate the lesion or disease involving the nervous system, for example, by imaging, biopsy, or neurophysiological tests. Questionnaires may be useful as screening tools to support the clinical hypothesis of neuropathic pain but are not diagnostic.<sup>1</sup>

#### 3.2.4. Chronic secondary headache or orofacial pain

This section is largely cross-referenced to the headache classification of the International Headache Society (IHS) that is implemented in full in the chapter on neurology.<sup>20</sup> The IHS classification differentiates between primary (idiopathic) headaches, secondary (symptomatic) headaches and orofacial pains including cranial neuralgias. Chronic headache and orofacial pain is defined as headaches or orofacial pains that occur for more than two

hours per day on at least 50% of the days during at least 3 months. Only chronic secondary headaches and chronic orofacial pains are included here;<sup>6</sup> chronic primary headaches are listed under chronic primary pain syndromes. The subdivisions of chronic orofacial pain are more elaborate than in the IHS classification, thanks to contributions from the IASP SIG on orofacial pain and include chronic dental pains and temporomandibular disorders.<sup>5</sup>

#### 3.2.5. Chronic secondary visceral pain

Chronic secondary visceral pain is defined as persistent or recurrent pain that originates from internal organs of the head/neck region and the thoracic, abdominal and pelvic cavities (Schwartz and Gebhart 2014).<sup>38</sup> The pain is usually perceived in somatic tissues of the body wall (skin, subcutis, muscle) in areas that receive the same sensory innervation as the internal organ at the origin of the symptom (referred visceral pain) (Giamberardino et al. 2006).<sup>16</sup> Diagnostic entities within this category are subdivided according to the major underlying mechanisms, i.e. mechanical factors (e.g., traction, obstruction), vascular mechanisms (ischemia, thrombosis), or persistent inflammation.<sup>2</sup> Pain due to cancer or metastasis in internal organs is coded in the chapter chronic cancer-related pain, whereas pain due to functional or unexplained mechanisms is listed under chronic primary pain.

#### 3.2.6 Chronic secondary musculoskeletal pain

Chronic secondary musculoskeletal pain is defined as persistent or recurrent pain that arises as part of a disease process directly affecting bone(s), joint(s), muscle(s) or related soft tissue(s).<sup>31</sup> Pain may be spontaneous or movement-induced. This category is limited to *nociceptive* pain and does not include pain that may be perceived in musculoskeletal tissues

but does not arise therefrom, such as the pain of compression neuropathy or somatic referred pain. Diagnostic entities within this category are subdivided according to the major underlying mechanisms, i.e. persistent inflammation of infectious, auto-immune or metabolic etiology (e.g. rheumatoid arthritis), structural changes affecting bones, joints, tendons or muscles (e.g. symptomatic osteoarthrosis) or chronic musculoskeletal pain secondary to diseases of the motor nervous system (e.g. spasticity after spinal cord injury or rigidity in Parkinson's disease). Well-described apparent musculoskeletal conditions for which the causes are incompletely understood, such as non-specific back pain or chronic widespread pain, are included in the section on chronic primary pain.

#### 3.3 Severity and other extension codes in ICD-11

Optional specifiers (called 'extension codes' in WHO terminology) are available for all chronic pain diagnoses and allow recording pain severity, its temporal course and evidence of psychological and social factors. The severity of chronic pain is proposed to be determined as a compound measure of pain intensity, and pain-related distress and task interference. Pain intensity denotes the strength of the subjective pain experience ('how much does it hurt?'). Pain-related distress is the multifactorial unpleasant emotional experience of a psychological (cognitive, behavioral, emotional), social or spiritual nature due to the persistent or recurrent experience of pain ('how distressed are you by the pain?').<sup>21</sup> Pain-related interference describes how much the pain interferes with daily activities and participation ('how much does the pain interfere with your life?'). Each of the severity determinants (intensity, pain-related distress, interference) is rated by the patient on a numerical rating scale from 0 - 10 and then transformed into WHO severity stages of 'mild', 'moderate' and severe' (see <u>Box 1</u>). Temporal

characteristics can be coded as continuous pain, episodic recurrent pain and continuous pain with pain attacks.

The presence of significant psychological and social factors can also be documented with an extension code. Psychological factors in this sense are cognitive (such as catastrophizing or worry and rumination;<sup>12,40</sup>), behavioral (such as avoidance or endurance;<sup>19,44</sup>), emotional (such as fear or anger;<sup>35,43</sup>). Social factors refer to the impact of chronic pain on the relationship with others and vice versa.<sup>9,23</sup> This extension code should be used when psychological and social factors are judged to contribute to the onset, the maintenance or exacerbations of pain or are regarded as relevant consequences of the pain. Assigning this extension code does not require a judgement regarding causal priorities or etiological contributions. Since all chronic pain is regarded as a multifactorial, biopsychosocial phenomenon, this extension code is available for *all* chronic pain diagnoses and *is not limited* to the chronic primary pain syndromes.

ICD-11 will be coordinated within the *WHO Family of International Classifications* that also includes the *International Code of Functioning* (ICF) and the *International Code of Health Interventions* (ICHI). Each ICD-11 code will refer to the relevant section of ICF as 'functional properties# of the ICD code. A harmonization with ICF is particularly relevant for chronic pain conditions, because both systems address pain and pain-associated disability. The ICF was developed by the *International Society for Physical and Rehabilitation Medicine* (ISPRM) with the WHO. A draft of the functioning properties for chronic pain on the basis of the ICF domains was developed jointly by IASP and ISPRM.<sup>30</sup>

4. Discussion

The classification system for chronic pain conditions submitted by IASP to WHO is compatible with ICD-principles and aims to improve pain research, health policy decisions, and patient care. The temporal cut-off of three months for defining chronic pain has the advantage that clinicians, at a reasonable point in time, will be alerted to the possibility that pain may be the leading or sole medical problem of a given patient. This clearly operationalized and easily measurable criterion will help to use uniform criteria in healthcare statistics, clinical trials, publications, and medical textbooks. The question whether pain can become chronic at an earlier stage is a research question that can also be addressed by contrasting patient histories with this definition.

In the field of headache, precise and operationalized criteria for diagnosis (e.g. a strict temporal criterion for migraine) have greatly facilitated research in all areas ranging from basic to epidemiological science, which in turn informed the refinement of diagnostic criteria at a later stage. One of the aims of the new classification of chronic pain is to improve reporting for health statistics and research by clearly operationalized criteria. The organizing principle is the same as that used throughout ICD: give first priority to pain etiology (primary pain syndromes, cancer-related pain, postsurgical and posttraumatic pain), followed by underlying pathophysiological mechanisms (neuropathic pain), and finally body site or affected organ system (headache and orofacial pains, visceral pain, musculoskeletal pain).

Integrating existing diagnoses into this multilayered classification was greatly facilitated by the principle of 'multiple parenting': it allows the same diagnosis to be referenced in more than one category. In this regard, ICD-11 transcends the discipline-specific structure of previous versions. It allows different angles from which to approach a diagnosis: A cancer-specialist will

be able to look up chronic neuropathic chemotherapy-induced pain among the cancer-related pain diagnoses, whereas a neurologist will be able to find exactly the same diagnosis from the perspective of chronic neuropathic pain. Especially, for a phenomenon such as chronic pain, which – by its very nature – may be part of many different conditions and important to many medical specialties, this is a great advancement that facilitated inclusion of the current classification of chronic pain into ICD-11 itself.

Chronic pain may be a symptom of an underlying chronic condition, but it frequently outlasts the normal healing process and often no other underlying disease can be identified. The proposed classification of chronic pain distinguishes between chronic primary pain syndromes (long-term conditions in their own right) and chronic secondary pain syndromes (symptoms of another non-pain problem). If the chronic pain condition persists, clinicians should continue to use a diagnosis of chronic secondary pain even after the causing medical condition has been treated successfully or remitted. After longer periods of obvious dissociation between the medical causes and chronic pain, and with clear evidence for other factors determining the chronic pain condition, a change of the chronic pain diagnosis (e.g., to chronic primary pain, or to another chronic secondary pain diagnosis) should be considered.

With the introduction of chronic primary pain as a new diagnostic entity, the classification recognizes conditions that affect a broad group of pain patients who are not adequately represented in categories defined strictly according to either somatic or psychological etiology (Rief et al. 2008). Due to the success of the behavioral neurosciences, even mental disorders can nowadays no longer be considered purely non-somatic. Of note, all chronic pain, including chronic primary pain, will be coded outside the realm of psychiatric diagnosis: This accords more with the current scientific understanding of chronic pain and often aligns better with patients' own views. In addition, it will help avoid stigma in many cultures.<sup>24</sup>

All clinically relevant chronic pain is conceptualized within the biopsychosocial model. The seven major categories of chronic pain represent a compromise between comprehensiveness and practical applicability of the classification system. Several clinically important conditions that were neglected or inadequately represented in previous ICD revisions are now included as diagnoses, e.g. chronic cancer-related pain, chronic postsurgical pain or chronic neuropathic pain. Etiological factors, temporal factors, pain severity and functional properties are reflected. Assessment of pain intensity and severity should become part of all routine medical examinations. Underlying causes and mechanisms should then be identified and lead to a personalized pain management plan. Joint efforts by IASP and WHO have resulted in the WHO analgesic ladder for treatment of cancer pain in 1986. Now is the time for a similar coordinated effort to promote improved diagnostic classification and multimodal management approaches for pain around the world.

#### 5. Conclusion

This is the first systematic classification of chronic pain that is also part of the ICD. We hope that this classification strengthens the representation of chronic pain conditions in clinical practice and research. The introduction of appropriate codes for chronic primary and secondary pain syndromes is expected to promote access to multimodal care for all chronic pain patients. It will facilitate accurate epidemiological investigations and health policy decisions regarding chronic pain, including adequate financing of treatments. Acknowledgements

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- [1] Attal N, Bouhassira D, Baron R. Diagnosis and assessment of neuropathic pain through questionnaires. Lancet Neurol 2018;17:456-466.
- [2] Aziz\* Q, Giamberardino\* MA, Barke\* A, Korwisi B, Rief W, Treede R-D, The IASP Taskforce for the Classification of Chronic Pain. The IASP Classification of Chronic Pain for ICD-11: Chronic secondary visceral pain. Pain 2018.
- [3] Barke A, Korwisi B, Casser H-R, Fors EI, Geber C, Schug S, Stubhaug A, Ushida T, Wetterling T, Rief W, Treede R-D. Pilot Field Testing of the Chronic Pain Classification for ICD-11: The Results of Ecological Coding. BMC Public Health (revision stage).
- [4] Bennett\* MI, Kaasa\* S, Barke\* A, Korwisi B, Rief W, Treede R-D, The IASP Taskforce for the Classification of Chronic Pain. The IASP Classification of Chronic Pain for ICD-11: Chronic cancer-related pain. Pain 2018.
- [5] Benoliel R, Birman N, Eliav E, Sharav Y. The International Classification of Headache Disorders: accurate diagnosis of orofacial pain? Cephalalgia 2008;28:752-762.
- [6] Benoliel\* R, Svensson\* P, Evers\* S, Wang\* S-J, Barke\* A, Korwisi B, Rief W, Treede R-D. The IASP-Classification of chronic pain for ICD-11: Chronic secondary headache and orofacial pain. Pain 2018.

[7] Bonica JJ. The Management of Pain. Philadelphia: Lea & Febiger, 1953.

- [8] Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. Survey of chronic pain in
   Europe: prevalence, impact on daily life, and treatment. Europ J Pain 2006;10:287 333.
- [9] Campbell P, Wynne-Jones G, Dunn KM. The influence of informal social support on risk and prognosis in spinal pain: A systematic review. Europ J Pain 2011;15:1-14.

- [10] Caraceni A, Portenoy RK, Working Group of the IASP Task Force on Cancer Pain. An international survey of cancer pain characteristics and syndromes. Pain 1999;82:263-274.
- [11] Dureja GP, Jain PN, Shetty N, Mandal SP, Prabhoo R, Joshi M, Goswami S, Natarajan KB, Iyer R, Tanna DD, Ghosh P, Saxena A, Kadhe G, Phansalkar AA. Prevalence of chronic pain, impact on daily life, and treatment practices in India. Pain Pract 2014;14:E51-62.
- [12] Eccleston C, Crombez G. Worry and chronic pain. A misdirected problem solving model.Pain 2007;132:233-236.
- [13] Finnerup NB, Haroutounian S, Kamerman P, Baron R, Bennett DL, Bouhassira D, Cruccu G, Freeman R, Hansson P, Nurmikko T, Raja SN, Rice AS, Serra J, Smith BH, Treede RD, Jensen TS. Neuropathic pain: An updated grading system for research and clinical practice. Pain 2016;157:1599-1606.
- [14] Finnerup NB, Scholz J, Attal N, Baron R, Haanpaa M, Hansson P, Raja SN, Rice ASC, Rief W, Rowbotham MC, Simpson DM, Treede R-D. Neuropathic pain needs systematic classification. Europ J Pain 2013;17:953-956.
- [15] Geber C, Breimhorst M, Burbach B, Egenolf C, Baier B, Fechir M, Koerber J, Treede R-D, Vogt T, Birklein F. Pain in chemotherapy-induced neuropathy - more than neuropathic? Pain 2013;154:2877-2887.
- [16] Giamberardino MA, Affaitati G, Costantini R. Referred pain from internal organs. In: F
   Cervero, TS Jensen, editors. Handbook of Clinical Neurology. Amsterdam: Elsevier,
   2006. pp. 343-360.
- [17] Goldberg DS, Summer JM. Pain as a global public health priority. BMC Public Health 2011:770.

- [18] Haroutiunian S, Nikolajsen L, Finnerup NB, Jensen TS. The neuropathic component in persistent postsurgical pain: a systematic literature review. Pain 2013;154:95-102.
- [19] Hasenbring MI, Hallner D, Klasen B, Streitlein-Böhme I, Willburger R, Rusche H. Painrelated avoidance versus endurance in primary care patients with subacute back pain: psychological characteristics and outcome at a 6-month follow-up. Pain 2012;153:211-217.
- [20] Headache Classification Committee. The International Classification of Headache Disorders, 3rd Edition. Cephalalgia 2018;38:1-211.
- [21] Jensen MP, Chodroff MJ, Dworkin RH. The impact of neuropathic pain on health-related quality of life: Review and implications. Neurol 2007;68:1178-1182.
- [22] Jensen TS, Baron R, Haanpaa M, Kalso E, Loeser JD, Rice ASC, Treede R-D. A new definition of neuropathic pain. Pain 2011;152:2204-2205.
- [23] Karos K, de Williams AC, Meulders A, Vlaeyen JWS. Pain as a threat to the social self: A motivational account. Pain 2018.
- [24] Katz J, Rosenbloom BN, Fashler S. Chronic Pain, Psychopathology, and DSM-5 Somatic Symptom Disorder. Can J Psychiatry 2015;60:160-167.
- [25] Kosek E, Cohen M, Baron R, Gebhart GF, Mico JA, Rice ASC, Rief W, Sluka AK. Do we need a third mechanistic descriptor for chronic pain states? Pain 2016;157:1382-1386.
- [26] Macrae WA. Chronic post-surgical pain: 10 years on. Br J Anaesth 2008;101:77-86.
- [27] Mäntyselkä P, Kumpusalo E, Ahonen R, Kumpusalo A, Kauhanen J, Viinamäki H, Halonen P, Takala J. Pain as a reason to visit the doctor: A study in Finnish primary health care.
   Pain 2001;89:175–180.

- [28] Moore RA, Straube S, Aldington D. Pain measures and cut-offs 'no worse than mild pain' as a simple, universal outcome. Anaesthesia 2013;68:400-412.
- [29] Nicholas\* M, Vlaeyen\* JWS, Rief\* W, Barke\* A, Aziz Q, Benoliel R, Cohen M, Evers S, Giamberardino MA, Göbel A, Korwisi B, Perrot S, Svensson P, Wang S-J, Treede R-D, The IASP Taskforce for the Classification of Chronic Pain. The IASP classification of chronic pain for ICD-11: Chronic Primary Pain. 2018.
- [30] Nugraha\* B, Gutenbrunner\* C, Barke\* A, Jakob R, Karst M, Korwisi B, Schiller J, Rief W, Treede R-D, The IASP Taskforce for the Classification of Chronic Pain. The IASP classification of chronic pain for ICD-11: Functioning properties of chronic pain. Pain 2018.
- [31] Perrot\* S, Cohen\* M, Barke\* A, Korwisi B, Rief W, Treede R-D, The IASP Taskforce for the Classification of Chronic Pain. The IASP classification of chronic pain for ICD-11: Chronic secondary musculoskeletal pain. Pain 2018.

[32] Raffaeli W, Arnaudo E. Pain as a disease: An overview. J Pain Res 2017;10:2003-2008.

- [33] Rice ASC, Smith BH, Blyth FM. Pain and the global burden of disease. Pain 2016;157:791-796.
- [34] Rief W, Kaasa S, Jensen R, Perrot S, Vlaeyen JWS, Treede RD, Vissers KC. The need to revise pain diagnoses in ICD-11. Pain 2010:169-170.
- [35] Roelofs J, Sluiter JK, Frings-Dresen MH, Goossens M, Thibault P, Boersma K, Vlaeyen JWS. Fear of movement and (re) injury in chronic musculoskeletal pain: Evidence for an invariant two-factor model of the Tampa Scale for Kinesiophobia across pain diagnoses and Dutch, Swedish, and Canadian samples. Pain 2007;131:181-190.
- [36] Scholz\* J, Finnerup\* NB, Barke A, Rief W, Treede R-D, Classification Committee of the Neuropathic Pain Special Interest Group (NeuPSIG), The IASP Taskforce for the

Classification of Chronic Pain. The IASP Classification of Chronic Pain for ICD-11: Chronic neuropathic pain. 2018.

- [37] Schug\* SA, Lavand'homme\* P, Barke\* A, Korwisi B, Rief W, Treede R-D, The IASP Taskforce for the Classification of Chronic Pain. The IASP Classification of Chronic Pain for ICD-11: Chronic postsurgical and posttraumatic pain. 2018.
- [38] Schwartz ES, Gebhart GF. Visceral Pain. In: BK Taylor, DP Finn, editors. Behavioral Neurobiology of Chronic Pain. Heidelberg: Springer, 2014. pp. 171-197.
- [39] Smith BH, Elliott AM, Chambers WA, Smith WC, Hannaford PC, Penny K. The impact of chronic pain in the community. Fam Pract 2001;18:292-299.
- [40] Sullivan MJL, Thorn B, Haythornthwaite JA, Keefe F, Martin M, Bradley LA, Lefebvre JC. Theoretical perspectives on the relation between catastrophizing and pain. Clin J Pain 2001;17:52-64.
- [41] Treede R-D, Jensen TS, Campbell JN, Cruccu G, Dostrovsky JO, Griffin JW, Hansson P, Hughes R, Nurmikko T, Serra J. Neuropathic pain: Redefinition and a grading system for clinical and research purposes. Neurol 2008;70:1630-1635.
- [42] Treede\* R-D, Rief\* W, Barke\* A, Aziz Q, Bennett MI, Benoliel R, Cohen M, Evers S,
   Finnerup NB, First MB, Giamberardino MA, Kaasa S, Kosek E, Lavand'homme P,
   Nicholas M, Perrot S, Scholz J, Schug S, Smith BH, Svensson P, Vlaeyen JW, Wang S-J.
   A classification of chronic pain for ICD-11. Pain 2015;156:1003-1007.
- [43] Trost Z, Vangronsveld K, Linton SJ, Quartana PJ, Sullivan MJL. Cognitive dimensions of anger in chronic pain. Pain 2012;153:515-517.
- [44] Vlaeyen JWS, Linton SJ. Fear-avoidance model of chronic musculoskeletal pain: 12 years on. Pain 2012;153:1144-1147.

Box 1: Specifiers or 'extension codes' in ICD-11

<u>Pain intensity</u> may be assessed verbally or on a numerical or visual rating scale. For the severity coding the patient should be asked to rate the average pain intensity for the last week on an 11-point NRS rating scale (ranging from from 0 'no pain' to 10 'worst pain imaginable') or a 100 mm VAS scale:

mild pain	(NRS: 1-3; VAS: <31mm)
moderate pain	(NRS: 4-6; VAS: 31-54mm)
severe pain	(NRS: 7-10; VAS: 55-100mm)

<u>Pain-related distress</u> may be assessed by asking the person to rate the pain-related distress they experienced in the last week (multifactorial unpleasant emotional experience of a cognitive, behavioral, emotional, social or spiritual nature due to the persistent or recurrent experience of paint) on an 11-point numerical rating scale or a VAS scale from 'no pain-related distress' to 'extreme pain-related distress' ('Distress Thermometer').

mild distress	(NRS: 1-3; VAS: <31mm)
moderate distress	(NRS: 4-6; VAS: 31-54mm)
severe distress	(NRS: 7-10; VAS: 55-100mm)

<u>Pain-related interference</u> last week as rated by the patient on an 11-point numerical rating scale (NRS: from 0 'no interference' to 10 'unable to carry on activities') or Visual Analog Scale (VAS: 0mm 'no interference' to 100mm 'unable to carry on activities').

Code 0: no interference

Code 1: mild interference	(NRS: 1-3; VAS: <31mm)
Code 2: moderate interference	(NRS: 4-6; VAS: 31-54mm)
Code 3: severe interference	(NRS: 7-10; VAS: 55-100mm)

<u>Overall severity</u> combines the ratings of intensity, distress and disability using a three-digit code: Example: A patient with a moderate pain intensity, severe distress and mild disability will receive the code '231'. The severity code is optional.

<u>Other extension codes</u> are temporal characteristics (continuous, episodic recurrent, continuous pain with attacks) and psychosocial cofactors (cognitive, behavioral, emotional, social).

Figure Legends:

# Fig. 1: Structure of the IASP Classification of Chronic Pain

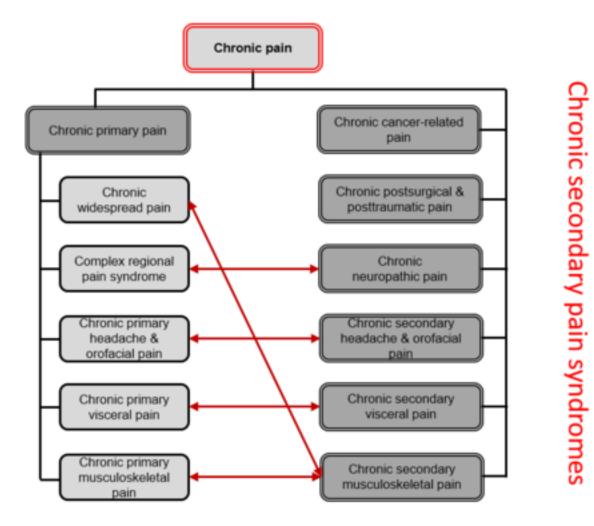
## Notes to Figure 1

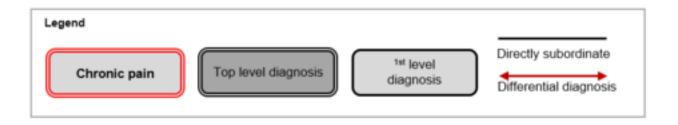
In chronic primary pain syndromes (left) pain can be conceived as a disease, while in chronic secondary pain syndromes (right) pain initially manifests itself as a symptom of another disease such as breast cancer, a work accident, diabetic neuropathy, chronic caries, inflammatory bowel disease or rheumatoid arthritis. Differential diagnosis between primary and secondary pain conditions may sometimes be challenging (arrows), but in either case the patient's pain needs special care when it is moderate or severe. After spontaneous healing or successful management of the underlying disease, chronic pain may sometimes continue and hence the chronic secondary pain diagnoses may remain and continue to guide treatment as well as health care statistics.

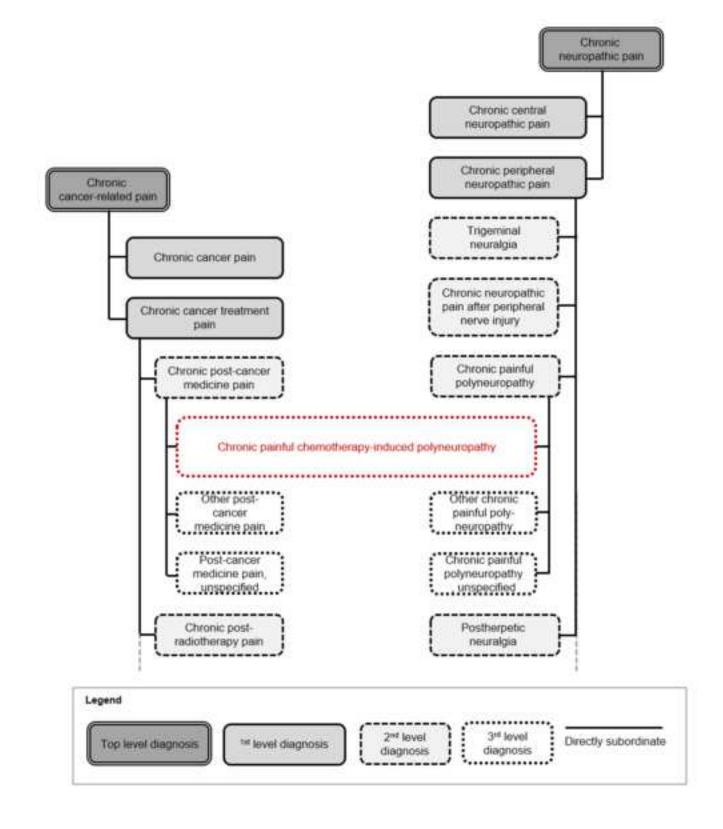
# Fig. 2: Multiple parenting concept of WHO for ICD-11

# Notes to Figure 2

In contrast to the strictly linear structure of all previous versions of ICD, ICD-11 allows for any given disease ('child') to belong to more than one section ('parent'). This is called 'multiple parenting'. 'Chronic painful chemotherapy-induced polyneuropathy' is illustrated here as one example.







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