<table>
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<tr>
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<td>Taxonomies for chronic visceral pain</td>
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</tbody>
</table>
| **Corresponding Author:** | Winfried Häuser, MD  
Klinikum Saarbrücken  
Saarbrücken, GERMANY |
| **Corresponding Author's Institution:** | Klinikum Saarbrücken |
| **First Author:**      | Winfried Häuser, MD |
| **Order of Authors:**  | Winfried Häuser, MD  
Andrew Baranowski, Professor  
Bert Messelink, Dr  
Ursula Wesselmann, Professor |
| **Question**           | Have you posted this manuscript on a preprint server (e.g., arXiv.org, BioXiv, PeerJ Preprints)? |
| **Response**           | No |
Saarbrücken and Baltimore, January 3, 2020

Title: Taxonomies for chronic visceral pain
ID: PAIN-D-19-00563R1

Dear Dr Keefe,

We thank the reviewer for her/his comments. Please see our point-by-point reply below. The revisions in the manuscript are marked with the track change function of WORD.

Sincerely

Winfried Häuser

Ursula Wesselmann
Reviewer #2: The authors have addressed some of the reviewer comments, but not all:

1. Composition of EAU guideline committee was not clarified in the MS.
   **Reply:** The composition of the EAU guideline committee has been detailed in table 1. "Multidisciplinary and multispeciality group with clinical and research experience". In detail: The EAU guideline committee was composed of the following disciplines (number of representatives): urology (4), pain medicine (2), gynecology (1), gastro-enterology (1), pelvic floor physiotherapy (1), psychology (1), sexology (1).

2. The methods reports from ref 1 and 25 were not included in Table 1.
   **Reply:** We have added the methods reports from 25 in Table 1 in this second revision: "Group consensus; guidelines for classification in overlapping fields were specified". We assume that the reviewer refers to reference 3 (Aziz et al.). We checked the paper again and found no reports on the methods used to develop this classification.

3. The erroneous statement on coding of chronic pancreatitis was not revised. The authors seem to think that ICD-11 allows only one diagnosis per patient. This is explicitly not the case, and a combination of codes may well fulfill the stated needs. So the authors should give it a try.
   **Reply:** We are aware that ICD-11 allows several diagnoses per patient. However, to our best knowledge it does not allow to code more than one mechanism for a given pain syndrome, and we have changed the paragraph in the review to reflect this more clearly.

The revised MS was submitted with changes tracked in WORD; that is nice within WORD, but terrible when converted to a PDF, when there are many changes. For this reason I found it impossible to review the modified Tables 1 and 2. The author response sounds promising, but I could not verify the statements. I suggest resubmitting tables with all changes shown in addition to a clean (i.e. no track changes) set of tables with next requested revision.

**Reply:** We have submitted a clean copy of the revised tables.
Taxonomies for chronic visceral pain

Winfried Häuser ¹, Andrew Baranowski ², Bert Messelink ³, Ursula Wesselmann ⁴

¹ Department Internal Medicine 1 (Gastroenterology, Hepatology, Oncology, Infectious Diseases), Klinikum Saarbrücken and Department Psychosomatic Medicine and Psychotherapy, Technische Universität München, Germany

² The National Hospital for Neurology and Neurosurgery, University College London Hospitals Foundation Trust, London, UK

³ Department of Urology and Sexology, Medical Centre Leeuwarden, Netherlands

⁴ Departments of Anesthesiology/Division of Pain Medicine, Neurology and Psychology, University of Alabama at Birmingham, USA

Number of text pages of the entire manuscript (including pages containing figures and tables): 26

Actual number of tables: 3

Adress for correspondence:

Winfried Häuser
Internal Medicine 1, Klinikum Saarbrücken, Germany
Tel: +49-681-9632020
Fax: +49-681-9632020
Email: whaeuser@klinikum-saarbruecken.de
URL: https://www.klinikum-saarbruecken.de
1. Background

In the past, pain associated with the viscera has typically been considered as a symptom of visceral disease. It is only more recently that the medical specialties of gynecology, gastroenterology and urology have recognized that visceral pain can be a pain syndrome in its own right. As visceral pain has been recognized as a chronic pain syndrome, which often occurs as a co-morbid condition together with other chronic pain syndromes [5,23,27], several medical and scientific associations have developed taxonomies for specific visceral pain conditions.

Taxonomies in general are defined as hierarchical arrangements of terms that describe a particular branch of science or field of knowledge. Ideally, terms are selected and arranged to be mutually exclusive, thus creating an ordered universe with a place for everything and everything in its place. However, medicine does not lend itself well to such pure rationalism [20]. The open conceptual question remains whether taxonomies should use a ‘lumping’ or ‘splitting’ approach. Specifically the question has been raised if different diagnostic manifestations of a basic pathological process have been divided into multiple diagnostic silos by taxonomies, creating artifactual comorbidity in certain circumstances [15].

2. Scope of the review

The scope of this Topical Review is to highlight the strengths and limitations of different taxonomies for visceral pain and to initiate collaborations between the different scientific associations, who have developed different classification systems. Ultimately, a unified and evidenced-based pain classification system will have to be widely adopted by patients and both the clinical and the research communities, as well as regulatory agencies and pharmaceutical companies to advance diagnosis, clinical pain management, clinical trial design and pain research in the field of visceral pain.

3. Methods

We searched PubMed and GoogleScholar with the terms „taxonomy“, „chronic visceral pain“ and „chronic abdominal pain“. We included overarching taxonomies for
chronic visceral pain syndromes and excluded taxonomies for single diseases such as chronic pancreatitis. We included taxonomies developed by international and interdisciplinary working groups and excluded taxonomies from national and / or monodisciplinary committees.

4. Results (alphabetical order) (for details see tables 1 and 2)

4.1 European Association of Urology (EAU)

In 2004 the multidisciplinary guideline panel of the EAU guideline on Chronic Pelvic Pain built the concept of Chronic Pelvic Pain Syndromes (CPPS), which is now referred to as “pain as a disease process” [11]. In 2013 they published an article illustrating the paradigms in the new approach of chronic pelvic pain [CPP] [9]. The terminology of the EAU guideline has always been in close relationship with the taxonomy of the IASP SIG visceral pain Taxonomy (see below 4.4.), most recently published in 2012 [16]. The dichotomy between pain as a symptom of a well known disease and pain as a disease in its own rights has been the basis. In 2016, the guideline was rewritten in such a way that it is centred around pain instead of being organ-centered [10]. CPP may be sub-divided into conditions with well-defined classical pathology named „specific disease-associated pelvic pain” and those with no obvious pathology named “chronic pelvic pain syndrome”. CPPS is seen as a subdivision of CPP.

4.2 International Continence Society (ICS)

The ICS published in 2016 a standard for terminology in CPSS. It was written by the Chronic Pelvic Pain Working group [7]. Its aims are to: 1. describe the nine clinical domains involved in CPPS; 2. define terminology; 3. develop an evaluation guideline for each domain; 4. establish a process for evolving terminology in response to scientific and clinical development and patient need. The working group identified the following nine domains: Lower Urinary Tract Domain; Female Genital Domain; Male Genital Domain; Gastro-Intestinal Domain; Musculoskeletal Domain; Neurological Domain; Psychological Domain; Sexual Domain; Comorbidities.
In this document there is a mix of definitions and descriptions of terms, clinical situations, signs and symptoms and evaluation aspects.

4.3 IASP - ICD 11 Taxonomy

In 2012, IASP contacted the WHO with respect to developing a new and pragmatic classification of chronic pain for the upcoming 11th revision of the ICD. 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 goal of the IASP-ICD-11 task force was to create a classification system that is applicable in clinical settings for specialised pain management and in primary care [24].

A diagnosis of chronic primary visceral pain should be given if the chronic pain condition is considered to have a multifactorial etiology and is believed to be associated with the internal organs for which no underlying pathology/cause can be identified, and hence, symptoms are not better explained by any of the other chronic visceral pain diagnoses in the secondary domain. These syndromes are summarized under chronic primary visceral pain: Chronic primary chest pain syndrome, chronic primary epigastric pain syndrome, irritable bowel syndrome, chronic primary abdominal pain syndrome, chronic primary bladder pain syndrome, chronic primary pelvic pain syndrome, chronic pelvic pain in females, chronic pelvic pain in males [21].

Chronic secondary visceral pain is persistent or recurrent pain originating from internal organs of the head or neck region or of the thoracic, abdominal, and pelvic cavities. Three main mechanisms may account for chronic secondary visceral pain, and they also structure the classification of chronic secondary visceral pain: 1. persistent inflammation; 2. vascular mechanisms; 3. mechanical factors. At every level of the classification, the WHO adds residual categories “other specified” and “unspecified.” The category “other” is used for specific diagnoses that fall in the same category but are not represented individually. On this level of the classification of chronic visceral pain, the category “other chronic secondary visceral pain” would be the umbrella term for chronic secondary visceral pain diagnoses that are due to neither persistent inflammation, vascular mechanisms, nor mechanical factors.

Within each of the three the subdivisions are structured anatomically into four areas: head or neck region; thoracic region; abdominal region; pelvic region [3].
4.4 Pain of Urogenital Origin Special Interest Group (SIG) of IASP (PUGO)

PUGO is the acronym for the SIG of IASP that represents those involved in the clinical management and research of abdominal and pelvic pain. PUGO was founded in 1998 and later renamed SIG on Abdominal and Pelvic Pain. In 2004 a working group was set up by PUGO members to look at the taxonomy, classification and terminology for pain perceived in the pelvis. Their recommendations were incorporated in 2012 into the IASP Classification of Chronic Pain, Second Edition (Revised) that had been updated in 2011 by the IASP Terminology Working Group with the main emphasis on pelvic pain being a condition in its own right in many circumstances. We refer to this terminology here as the 2012 IASP SIG visceral pain taxonomy [16]. The terminology of „pain syndrome“ was a key innovation on the pathway to accepting that many pelvic pain conditions are primary pain conditions and are often associated with bladder, bowel and systemic changes as well as psychological, behavioural and sexual connotations.

4.5 Rome Foundation

The Rome Foundation is an independent not-for-profit organization that provides support for activities designed to create scientific data and educational information to assist in the diagnosis and treatment of functional gastrointestinal disorders (FGID). The Advisory Council consists of representatives of all Rome Foundation sponsors, Rome Board members, the American Gastroenterological Association the International Foundation for Functional Gastrointestinal Disorders and representatives of interested scientific and regulatory agencies. The Rome Foundation has its origins in the late 1980s, where an expert group, produced the first diagnostic criteria for irritable bowel syndrome. Diagnostic criteria for an increasing number of FGID were produced by a growing number of experts (Rome I in 1994, Rome II in 1999/2000, Rome III in 2006, Rome IV in 2016) [8]. The Rome symptom-based categoric criteria are of particular value for clinical research and pharmaceutical trials. They provide a clear strategy for selecting study subjects, they are endorsed by regulatory agencies, and are used by clinical investigators and industry for clinical trials around the world. The definition of FGIDs changed with Rome III from the prior absence of structural disease to disorders of gut-brain interaction. The Rome IV criteria of FGID include 33
adult and 20 pediatric FGIDs. The classification of the disorders into anatomic regions (ie, esophageal, gastroduodenal, bowel, biliary, and anorectal) presumes unifying features underlying diagnosis and management that relate to these organ locations. The classification of FGIDs is based primarily on symptoms rather than physiological criteria. This has been favored because of its utility in clinical care, limited evidence that physiological disturbance (ie, motility) fully explained patient symptoms, and the fact that symptoms are what bring patients to health care providers.

4.6 Mental health care groups

It is estimated, that about 50% of somatic symptoms including abdominal pain presented in primary care, cannot be explained by a defined somatic disease. These symptoms are labelled „medically unexplained somatic symptoms“ in family medicine. In general medicine and partially in psychosomatic medicine, the terms „functional disorders“ or „functional somatic syndromes“ are used, too. These terms have been applied to several related syndromes characterized more by defined symptoms, suffering, and disability than by consistently demonstrable tissue abnormality such as IBS. The term does not assume psychogenesis but only a disturbance in bodily functioning [26]. In addition, some chronic pain syndromes were coded by mental health care specialists in the ICD-10 as somatoform pain disorder if the predominant complaint is of persistent, severe, and distressing pain, which cannot be explained fully by a physiological process or a physical disorder, and which occurs in association with emotional conflicts or psychosocial problems that are sufficient to allow the conclusion that they are the main causative influences. The debates on the underlying concept of somatization and the uncertainties about excluding a physiological process or a physical disorder which fully explains the pain, led to the decision of mental health care associations, to delete the category „somatoform pain disorder“, e.g. in the ICD-11 and in the Diagnostic and Statistical Manual of Psychiatric 5th edition diseases of the American Psychiatric Association [2,14]. However, there are substantial differences between the different new taxonomies (see table 3).

5. Discussion

The IASP - ICD 11 Taxonomy entails the most comprehensive classification system covering all visceral pain locations. IASP’s pretention to account the already widely
established taxonomies for the chronic visceral pain syndromes such as the ROME criteria for primary visceral pain syndromes as well as criteria for interstitial cystitis and bladder pain syndromes can partially be confirmed. The IASP - ICD 11 classification comprises only a minority – yet the most prevalent – functional gastrointestinal disorders with the major symptom pain.

Some issues of the IASP - ICD 11 classification need further discussion:

a) A critical limitation of the IASP - ICD 11 taxonomy for clinical practice and research as well as for epidemiological studies is the concept to classify visceral pain based on the 'major pathophysiological mechanisms', since in the majority of chronic visceral pain syndromes these pathophysiological mechanisms have actually not been identified yet. For these diseases, the code „unspecified“ would have to be used according to the new IASP - ICD 11 taxonomy. A classification of visceral pain related to organ (systems) as proposed by the previous 2012 IASP SIG visceral pain taxonomy [16] seems to be more useful for classification and coding in clinical practice at this time.

b) Multiple pathophysiological mechanisms may play a role in the development and persistence of a visceral pain syndrome (e.g. mechanical factors and persistent inflammation in a duodenal stenosis by Crohn’s disease). However, there is no possibility to code more than one mechanism for a given pain syndrome. In addition, some other pain mechanisms in chronic visceral pain are not covered by the new IASP – ICD 11 proposal such as neuropathic pain mechanisms and neuroplastic changes in the central pain pathways in chronic pancreatitis [22]. These mechanisms have to be coded as „other specified“ according to the IASP - ICD 11 taxonomy. Because of the uncertainties mentioned above, 2nd level diagnoses will be a challenge to use in a consistant manner even by specialists in chronic abdominal pain.

c) The challenge from a clinical perspective is, that this separation into primary and secondary pain is not straightforward for chronic visceral pain conditions, since many chronic visceral pain conditions share a poorly defined pathophysiology, and the correlation between the underlying disease and the pain complaint is unclear. In several cases ‘organic pathologies’ that were initially thought to be correlated to the pain complaint, have been found to be a spurious finding, and are no longer required for the taxonomy of the chronic pain condition. An example are glomerulations in interstitial cystitis [28]. In contrast, abdominal pain due to peptic ulcers and chronic
gastritis, which has been considered a psychosomatic disease in the past, has been linked to Helicobacter Pylori infections and can be successfully treated with appropriate antibiotics in a subgroup of patients. However, the brain-gut axis may also play a role in the susceptibility to Helicobacter Pylori infections [19]. Some visceral disease, such as endometriosis, can be associated with chronic pelvic pain, but there is no correlation between the extent of the endometriotic lesions and the severity of the pain complaint [17], and the chronic pain complaint might persist although the endometriotic lesions have been successfully treated from an organic/pathology standpoint. In the current classification it is unclear how to proceed in case a secondary pain condition becomes primary when the underlying cause has gone, but the pain persists.

d) The term primary visceral pain might be a challenging term for insurance reimbursements regarding diagnostic work-up in some countries. Should a patient with vulvodynia first be coded for billing as secondary visceral pain, until the diagnostic work-up is completed and other diseases with similar symptoms have been excluded? This will be an important question to be addressed by health insurance systems to insure that adequate diagnostic work-up of patients with presumed primary chronic visceral pain can be pursued and reimbursed. An additional aspect is that this issue will have consequences for interpreting ICD codes on visceral pain for epidemiological studies.

6. Conclusions

The IASP aims that its ICD 11 taxonomy will provide an umbrella classification system for all chronic pain syndromes. A collaboration with international scientific societies of gynecology, gastroenterology, urology, psychosomatic medicine and psychiatry will be necessary to identify pathways to link the established visceral taxonomies with the new ICD-11 codes proposed by IASP and to be implemented worldwide as a uniform pain taxonomy.

The ICD diagnostic and coding manual that unifies medical and psychiatric practice across the globe, determines how conditions in medicine and mental health are organized and how they are conceived. At present, there is a mess of terms and criteria around bodily distress disorders. A collaboration of the different working groups of the WHO (IASP, WHO Somatic Distress and Dissociative Disorders Working Group, WHO Working Group consisting of primary care physicians with a
special interest in mental illness) is urgently needed to achieve a consistent terminology by overcoming boundaries of subspecialties.
Acknowledgments: Ursula Wesselmann’s research program on chronic pain in women at the University of Alabama at Birmingham is supported by the William A. Lell, M.D. – Paul N. Samuelson, M.D. Endowed Professorship in Anesthesiology.

Conflicts of interest: APB, BM and WH have no financial conflicts of interest to declare.

- BM is a member of the EAU taxonomy group.
- APB was Chair of the PUGO taxonomy group from 2004-2012, which developed the 2012 IASP SIG visceral pain taxonomy. He was a member of the EAU, and he has contributed to the IASP - ICD 11 Taxonomy process and has authored on the subject.
- UW serves on the External Consultant Board for the “NIH Preclinical Screening Platform for Pain”, a novel pre-clinical pain therapy screening platform that has been launched at the National Institute for Neurological Disorders and Stroke in the U.S. as part of the NIH Helping to End Addiction Long-term Initiative. In her capacity as a special government employee of the U.S. Food and Drug Administration (FDA), she has served as a voting member of the FDA Anesthetic and Analgesic Drug Products Advisory Committee. She has served as a consultant for Grünenthal GmbH and Ironwood Pharmaceuticals Inc. UW is a member of the Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks (ACTTION) public-private partnership with the United States Food and Drug Administration (FDA) http://www.acttion.org since 2012. As a member of ACTTION she is an inaugural committee member of the working group Addressing Disparities in the Distribution and Assessment of Pain and its Treatments (ADDAPT) since 2017 and a committee member of the ACTTION-American Pain Society Pain Taxonomy (AAPT) collaboration, where she serves as the co-chair for the taxonomy working group developing the AAPT Diagnostic Criteria for Chronic Abdominal, Pelvic, and Urogenital Pain since 2014. She was member of the PUGO taxonomy group of IASP from 2004-2012, which developed the 2012 IASP SIG visceral pain taxonomy, and served as the elected chair of PUGO during that time from 2005-2008. She served as a consulting member of the International Continence Society guideline panel for the Standardization of Terminology for Chronic Pelvic Pain from 2011 to 2016. She has
contributed to the IASP - ICD 11 Taxonomy process and has authored on the subject.
References


Institute of Medicine Report (Committee on Advancing Pain Research, Care, and Education, Board on Health Sciences Policy), The National Academies Press, 2011.


Table 1: Comparison of key features of taxonomies of chronic visceral pain

<table>
<thead>
<tr>
<th>Organisation [References]</th>
<th>Target audience</th>
<th>Scope of the taxonomy</th>
<th>Basement of taxonomy</th>
<th>Selection of developers</th>
<th>Number of working groups and experts</th>
<th>Methods used to develop criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>European Association of Urology (EAU) [9-11]</td>
<td>Primarily urologists, other clinicians</td>
<td>Guidance in clinical practice for clinicians treating patients with CPP</td>
<td>Pain mechanisms and anatomic regions. Partially based on medical specialties</td>
<td>Clinical expertise in the field from different disciplines and no conflict of interests</td>
<td>About 10</td>
<td>Based on 2012 IASP visceral pain Taxonomy report [16]</td>
</tr>
<tr>
<td>International Association for the Study of Pain (IASP) and World Health Organization (WHO) collaboration</td>
<td>Clinicians and researchers</td>
<td>To create a classification system for chronic pain that is applicable in clinical settings for specialized pain</td>
<td>Pathophysiology and anatomic regions</td>
<td>Clinical expertise in the field, different disciplines, one patient advocate</td>
<td>A Task Force of 20 members</td>
<td>Group consensus; guidelines for classification in overlapping fields were specified</td>
</tr>
<tr>
<td>Group</td>
<td>Clinicians and researchers</td>
<td>Facilitation of research, enhancement of therapy development, support of healthcare delivery.</td>
<td>Nine domains, mostly organ based, and psychological and sexual aspects.</td>
<td>The ICS Standardisation Steering Committee selected the members and 2 mentors and 5 consultants (including a patient advocate)</td>
<td>15 members</td>
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<tr>
<td>International Continence Society (ICS) [7]</td>
<td>Clinicians and researchers</td>
<td>Facilitation of research, enhancement of therapy development, support of healthcare delivery.</td>
<td>Nine domains, mostly organ based, and psychological and sexual aspects.</td>
<td>The ICS Standardisation Steering Committee selected the members and 2 mentors and 5 consultants (including a patient advocate)</td>
<td>15 members</td>
<td></td>
</tr>
<tr>
<td>Special interest Group on abdominal and pelvic pain of IASP (PUGO) [16]</td>
<td>Clinicians and Clinician Scientists</td>
<td>Clinical based taxonomy to be incorporated into the IASP taxonomy</td>
<td>Clinical pain presentation and pain mechanisms</td>
<td>Multidisciplinary and multispeciality group with clinical and research experience</td>
<td>16 members</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>Other guidelines, consensus documents, scientific publications</td>
<td></td>
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</table>
pain mechanisms; specific details are not reported; the recommendations were incorporated in 2012 into the IASP Classification of Chronic Pain, revised Second Edition referred here as the 2012 IASP visceral pain Taxonomy [16]
<table>
<thead>
<tr>
<th>Rome Foundation [8]</th>
<th>Clinical scientists to make recommendations for diagnosis and treatment that can be applied in research and clinical practice</th>
<th>Functional gastrointestinal disorders</th>
<th>Anatomic regions</th>
<th>Scientific and clinical expertise</th>
<th>18 committees (117 authors from 23 countries)</th>
<th>Systematic search of literature, non-structured consensus, external review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mental health care groups of the World Health Organisation (WHO) [1,2,18,26]</td>
<td>Clinicians and researchers</td>
<td>Mental disorders with predominant somatic symptoms</td>
<td>Not known</td>
<td>Scientific and clinical expertise</td>
<td>17 mental health care specialists</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

Abbreviations: IBS= Irritable bowel syndrome; ICD= International Classification of Diseases; IPPS= International Pelvic Pain Society ISSVD: International Society for the Study of Vulvovaginal Disease ISSWHSH= International Society for the Study of Women’s Sexual Health; PUGO=Pain of Urogenital Origin (Special Interest Group of IASP)
Table 2: Comparison of key features of taxonomies of chronic visceral pain II (alphabetical order)

<table>
<thead>
<tr>
<th>Organisation [References]</th>
<th>Definition chronic visceral (abdominal) pain</th>
<th>Validation studies</th>
<th>Overlap of IASP with other taxonomies</th>
<th>Pain, 'symptom' or 'disease in its own right'?</th>
</tr>
</thead>
<tbody>
<tr>
<td>European Association of Urology (EAU) [9-11]</td>
<td>Chronic pelvic pain is chronic or persistent pain perceived in structures related to the pelvis of either men or women. It is often associated with negative cognitive, behavioural, sexual and emotional consequences as well as with symptoms suggestive of lower urinary tract, sexual, bowel, pelvic floor or gynaecological dysfunction</td>
<td>Not known</td>
<td>The terminology is based on the 2012 IASP visceral pain Taxonomy The Rome III criteria for IBS were adapted.</td>
<td>Disease</td>
</tr>
<tr>
<td>International Association for the Study of Pain (IASP) and World Health Organization (WHO) collaboration for ICD -11 Taxonomy</td>
<td>Pain originating from internal organs. Chronic primary and secondary visceral pains are often associated with significant emotional distress (such as anger, anxiety, and</td>
<td>One study [4]</td>
<td>Rome foundation criteria for IBS and abdominal/epigastric pain syndrome were adapted</td>
<td>Disease</td>
</tr>
<tr>
<td>Source</td>
<td>Description</td>
<td>Adapted Criteria</td>
<td>Notes</td>
<td></td>
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<tr>
<td>[3,21,24,25]</td>
<td>depression) and functional disability (interference in everyday life, reduced participation, and effect on cognition).</td>
<td>EAU criteria for interstitial cystitis and pain bladder syndrome were adapted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>International Continence Society (ICS) [6]</td>
<td>Chronic visceral pain arises from visceral organs, with involvement of the organ capsule with aching, and is localized. Chronic pelvic pain is characterized by persistent pain lasting longer than 6 months or recurrent episodes of abdominal/pelvic pain, hypersensitivity or discomfort often associated with elimination changes, and sexual dysfunction often in the absence of organic etiology</td>
<td>None</td>
<td>This guideline is described as complementary to the 2012 IASP visceral pain Taxonomy and the EAU guideline. The Rome III criteria for IBS were adapted.</td>
<td></td>
</tr>
<tr>
<td>Special Interest Group on abdominal and pelvic pain [7]</td>
<td>Built on the concept of Complex Regional Pain Syndromes and the mechanisms of pain as a primary condition including the</td>
<td>None</td>
<td>Informed the IASP 2012 and the EAU classifications</td>
<td></td>
</tr>
<tr>
<td>Pelvic pain of IASP (PUGO) [16]</td>
<td>Psychosocial, sexual and behavioural aspects</td>
<td>The Rome III criteria for IBS were adapted</td>
<td>Rome Foundation [7]</td>
<td>None</td>
</tr>
</tbody>
</table>

Abbreviations: IASP=International Association for the Study of Pain; IBS= Irritable bowel syndrome; ICD= International Classification of Diseases; PUGO=Pain of Urogenital Origin (Special Interest Group of IASP)
Table 3: Comparison of key features of classification systems of mental health care associations (modified from [1])

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Developed for</td>
<td>Clinical research and practice</td>
<td>DSM-5</td>
<td>ICD-11</td>
<td>ICD-11 PHC</td>
</tr>
<tr>
<td>Developed by</td>
<td>Danish working group of mental health care specialists for functional disorders</td>
<td>Working group of American Psychiatric Association</td>
<td>Working group of WHO</td>
<td>Working group of WHO</td>
</tr>
<tr>
<td>Defined as a mental disorder</td>
<td>No: Intends to challenge the mental-physical dichotomy (psychosocial and physiological)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Key features</td>
<td>Physical symptom patterns or clusters of cardiopulmonary, gastrointestinal, musculoskeletal or general symptoms that result in significant distress or impairment</td>
<td>Excessive, disproportionate or maladaptive responses to one or more physical symptoms or sensations of any aetiology that</td>
<td>Excessive, disproportionate or maladaptive responses to one or more physical symptoms or sensations of any aetiology that result in significant distress or impairment</td>
<td>At least three persistent symptoms over time of cardio-respiratory, gastrointestinal, musculoskeletal or general symptoms of tiredness</td>
</tr>
<tr>
<td>Emotional or behavioural responses required</td>
<td>Not required for diagnosis, but considered common and may be important for treatment</td>
<td>Yes (see above)</td>
<td>Yes (see above)</td>
<td>Yes (see above)</td>
</tr>
<tr>
<td>--------------------------------------------</td>
<td>---------------------------------------------------------------------------------</td>
<td>----------------</td>
<td>----------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Symptoms medically explained or not</td>
<td>Medically unexplained physical symptoms</td>
<td>Both medically unexplained and medically explained physical symptoms</td>
<td>Both medically unexplained and medically explained physical symptoms</td>
<td>Medically unexplained physical symptoms</td>
</tr>
<tr>
<td>Exclusion /differential diagnoses</td>
<td>Psychiatric and general medical diagnoses have to be excluded; IBS and FM are not excluded</td>
<td>Certain psychiatric disorders have to be excluded; general medical diagnoses are not excluded</td>
<td>Does not exclude presence of depression or anxiety; general medical diagnoses are not excluded. If a medical condition is causing or contributing to the symptoms, the</td>
<td>Psychiatric and general medical diagnoses have to be excluded IBS; FM are not excluded</td>
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<td>Hypothesized aetiology</td>
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<td>No assumptions about aetiology</td>
<td>No assumptions about aetiology</td>
<td>Hyperarousal of the autonomic nervous system;</td>
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Abbreviations: DSM= Diagnostic and Statistical Manual; FM= Fibromyalgia; IBS= Irritable bowel syndrome; ICD= International Classification of Diseases; WHO= World Health Organisation
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1. Given Name (First Name) Ursula
2. Surname (Last Name) Wesselmann
3. Date 06-November-2019

4. Are you the corresponding author?  Yes ☑ No

5. Manuscript Title Taxonomies for chronic visceral pain

6. Manuscript Identifying Number (if you know it) PAIN-D-19-00563

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<th>Non-Financial Support?</th>
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