EAU Guidelines on

Chronic Pelvic Pain

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1. INTRODUCTION

1.1 Aim

This guideline plays an important role in the process of consolidation and improvement of care for patients with abdominal and pelvic pain. From both literature and daily practice it has become clear that abdominal and pelvic pain are areas still under development. This guideline has been recognised as a cornerstone for important developments that have taken place in the past 10 years.

This guideline aims to expand the awareness of caregivers in the field of abdominal and pelvic pain and to assist those who treat patients with abdominal and pelvic pain in their daily practice. The guideline is a useful instrument not only for urologists, but also for gynaecologists, surgeons, physiotherapists, psychologists and pain doctors.

It must be emphasised that clinical guidelines present the best evidence available to the experts. However following guideline recommendations will not necessarily result in the best outcome. Guidelines can never replace clinical expertise when making treatment decisions for individual patients, but rather help to focus decisions - also taking personal values and preferences/individual circumstances of patients into account.

Structure and scope

The panel wishes to take advantage of modern methods of delivering guideline information to clinicians dealing with these patients. We therefore plan to make a stepped information structure, in alignment with stepped care protocols. It is the vision of the panel to use new digital information sources like websites and apps to aid this process. Furthermore, the panel wishes to change the guideline according to the template used in all other non-oncology guidelines of the EAU. It has been recognised that structuring a guideline on chronic pain is quite different from structuring one on another subject. A multi-disciplinary approach is of utmost importance and demands a broad view.

Summary of Changes

For the 2016 version the panel has made updates focusing on two important changes to the guideline. The first one was to rewrite the guideline in such a way that it is centred around pain instead of being organ centred. Chapters in previous editions were named after the organ or after the specialist that is consulted by the patient. For the 2016 edition of this guideline, pain is the centre and all other information is built around this central theme. The guideline is partly theoretical to show the importance of using this pain centred approach. The biggest part, however, deals with the practical approach in diagnostics, treatment and management of patients with abdominal and pelvic pain. In this version the panel can only provide data on incidence, costs and quality of life issues in selected sub-chapters.

The second change the panel worked on is the way of presenting the practical aspects of pain. The guideline, based on pain in the centre, leads the healthcare professional through the different steps in the process of dealing with abdominal and pelvic pain patients. One could say that it is patient centred instead of complaint centred. Theoretical information will serve as background and can be read when needed.

This second focus of updating is of great importance for developing modern ways to make information available for the general clinicians who see the patient in their office. It contains red flags, associated conditions and available first line treatments. It is available for the medical specialist who sees a patient with chronic pain. The guideline highlights necessary investigations and phenotyping, treatment options, decision making on whether a treatment is rational or not, and how and when to refer to a specialised pelvic pain centre. Caregivers who treat patients for pain related problems like myofascial and sexological dysfunctions will find help in making treatment plans and in the timing of referring back to specialised pain care. The guideline will also aid those involved in coaching self-management and shared care.

1.2 Publication history

The EAU Guidelines on Chronic Pelvic Pain were first published in 2003 [1] which formed the basis of a scientific publication in European Urology in 2004 [2]. Also, in the 2003 edition the concept of Chronic Pelvic Pain Syndromes (CPPS) was introduced, which is now referred to as “pain as a disease process”. Partial updates of the CPP Guidelines were published in 2008 and formed the basis for another scientific publication in European Urology in the year 2010 [3, 4].

Two chapters were added at that time: Chapter 5 ‘Gastrointestinal aspects of chronic pelvic pain’ and Chapter 7 ‘Sexological aspects of chronic pelvic pain’.

In the 2014 edition minor revisions were made in the Chapters 5 ‘Gastrointestinal aspects of chronic pelvic pain’ and 8 ‘Psychological aspects of chronic pelvic pain’.

For the 2015 edition the Panel critically reviewed the sub-chapter on bladder pain syndrome which is now a comprehensive part of the guidelines [5].

1.3 Available Publications

Alongside the full text version, a quick reference document (Pocket Guidelines) is available, presenting key findings of the Chronic Pelvic Pain Guidelines. These reference documents follow the updating cycle of the underlying large texts. All available material can be viewed and downloaded for personal use at the EAU website. The EAU website also includes a selection of EAU Guidelines articles as well as translations produced by national urological associations: http://www.uroweb.org/guidelines/online-guidelines/.

1.4 Panel composition

The panel of experts responsible for this document include three urologists, a neuro-urologist, two consultants in pain medicine, a gynaecologist, a psychologist, a gastroenterologist and one sexologist.

The Panel is most grateful for the expertise and support given by Dr. A. Cottrell (Guidelines Associate) in the process of transforming the document into the 2016 guideline structure, according to the template used in all other non-oncology guidelines of the EAU.

The Panel is also grateful to Dr. N. Wood for his expertise, time and diligence in undertaking a review of these Guidelines from a patient perspective.

1.5 Terminology

Definitions of CPP terminology

Classification

Much debate over the classification of CPP has occurred, is ongoing and will continue in the future. Classification involves three aspects of defining a condition: phenotyping, terminology and taxonomy.

Phenotyping

Phenotyping is describing the condition. For example, chronic bladder pain may be associated with the presence of Hunner’s ulcers and glomerulation on cystoscopy, whereas other bladder pain conditions may have a normal appearance on cystoscopy. These are two different phenotypes. The same is true for irritable bowel syndrome (IBS), which may be subdivided into that with primarily diarrhoea or that with constipation. Phenotyping is based upon mechanisms when they are known (e.g., infection, ischaemic, autoimmune, or neuropathic). In the absence of well-defined mechanisms, describing the condition by its symptoms, signs and, where possible, by investigations, has been demonstrated to have clinical and research validity in many situations. When pain is the main symptom and pain as a disease process is considered the cause, the condition is often referred to as a pain syndrome - a well-defined collection of symptoms, signs and investigation results associated with pain mechanisms and pain perception as the primary complaint.

Terminology

Terminology is the words that are used within classification, both to name the phenotype and within the definition of the phenotype. Examples of names for phenotypes associated with the bladder include interstitial cystitis, painful bladder syndrome or bladder pain syndrome (BPS). The EAU, the International Society for the study of BPS (ESSIC), the International Association for the Study of Pain (IASP) and several other groups now prefer the term bladder pain syndrome. In the pain syndromes, the role of the nervous system in generating the sensations is thought to be pivotal, but the term syndrome is also comprehensive and takes into account the emotional, cognitive, behavioural, sexual and functional consequences of the chronic pain.

When defining the phenotype, the terminology used in that definition must also be clear and if necessary defined. One of the most important guiding principles is that spurious terminology should be avoided. Terms that end in “itis” in particular should be avoided unless infection and or inflammation is proven and considered to be the cause of the pain [6]. It must be appreciated that end-organ inflammation may be secondary and neurogenic in origin and not a primary cause of the pain.

Taxonomy

Taxonomy places the phenotypes into a relationship hierarchy. The EAU approach subdivides CPP into

conditions that are pain syndromes and those that are non-pain syndromes. The latter are conditions that have well-recognised pathology (e.g., infection, neuropathy or inflammation), whereas the former syndromes do not and pain as a disease process is the mechanism. Other terms for the non-pain syndromes include “classical conditions”, “well-defined conditions” and “confusable diseases”. Although the EAU approach deals primarily with urological conditions, this approach to classification can be applied to all conditions associated with pain perception within the pelvis; the classification has been developed to include non-urological pain and was accepted by the IASP for publication in January 2012.

Classification of CPP syndromes

Importance of classification

It should be obvious to all that a condition cannot be treated unless it is defined. However, the reasons for classifying CPP go far beyond that.

Clues to the mechanism

As a result of systematic phenotypic and taxonomic classification, similarities and differences between conditions become clear. Drawing comparisons between the phenotypes of different disorders allows one to compare disorders such as bladder and bowel pain syndromes, thus facilitating research and treatment.

Guidelines for best treatment options

As conditions become better defined, more specific treatment approaches can be adopted. In particular, there will be a move away from treatments based upon spurious terms (e.g., antibiotics and non-steroidal anti-inflammatory drugs for the “-itis” conditions). Generic treatments aimed at groups of conditions will be more commonplace and based upon research evidence.

Research platform

Only by clearly defining the phenotype being investigated can research be valued or applied in the clinical situation.

Patient needs

A diagnosis, or name, for a set of symptoms can provide patients with a sense of being understood, as well as hope for relief. It may therefore help in acceptance of the problem as chronic, resolution of unfounded fears about its implications (if not life-threatening), and engagement in therapeutic endeavours, as well as in self-management. However, it may also lead to accessing information of variable quality associated with the diagnosis or name, and the possibility of generating new concerns about long-term consequences or about appropriateness of treatment.

IASP definitions

Subdividing pain syndromes

There is much debate on the subdivisions of the pain syndromes within the hierarchical taxonomy. The EAU has led the way in this regard and the guiding principles are as follows [2]:

1. The pain syndromes are defined by a process of exclusion. In particular, there should be no evidence of infection or inflammation. Investigations by end-organ specialists should thus be aimed at obtaining a differential diagnosis; repeated, unnecessary investigations are detrimental in the management of chronic pain syndromes.
2. A subdivision phenotype should only be used if there is adequate evidence to support its use. For instance, in non-specific, poorly localised pelvic pain without obvious pathology, only the term chronic pelvic pain syndrome (CPPS) should be used. If the pain can be localised to an organ, then a more specific term, such as rectal pain syndrome, may be used. If the pain is localised to multiple organs, then the syndrome is a regional pain syndrome and the term CPPS should once again be considered. As well as defining the patient by a specific end-organ phenotype, there are several other more general descriptors that need to be considered. These are primarily psychological (e.g., cognitive or emotional), sexual, behavioural and functional. Psychological and behavioural factors are well established factors which relate to quality of life (QoL) issues and prognosis. In North America a research programme, the MAPP program (Multi-disciplinary Approach to the study of Chronic Pelvic Pain research) has been devised to investigate the importance of these factors and looks at all types of pelvic pain irrespective of the end-organ where the pain is perceived. It also looks at systemic disorder associations, such as the co-occurrence of fibromyalgia, facial pain, or autoimmune disorders.
3. In 2004 this expert panel introduced the concept of managing the polysymptomatic nature of CPP, since

then others have developed their own schemes, such as Nickel's UPOINT [7], modified by Magri *et al.* [8]. In the light of these and other publications, the symptom classification table has been updated (Table 1).

The debate in relation to subdividing the pain syndromes remains ongoing. As more information is collected suggesting that the central nervous system (CNS) is involved, and indeed may be the main cause of many CPP conditions (e.g., bladder, genitalia, colorectal or myofascial), there is a general tendency to move away from end-organ nomenclature. Whether this is appropriate, only time and good research will tell. To enable such research, it is essential to have a framework of classification within which to work. Any hierarchical taxonomy must be flexible to allow change.

In Table 1 the classification has been set up according to the axis system used by IASP.

Table 1: EAU classification of chronic pelvic pain syndromes

Axis I Region		Axis II System	Axis III End-organ as pain syndrome as identified from Hx, Ex and Ix		Axis IV Referral characteristics	Axis V Temporal characteristics	Axis VI Character	Axis VII Associated symptoms	Axis VIII Psychological symptoms
Chronic pelvic pain	Specific disease associated pelvic pain OR Pelvic pain syndrome	Urological	Prostate		Suprapubic Inguinal Urethral Penile/clitoral Perineal Rectal Back Buttocks Thighs	ONSET Acute Chronic ONGOING Sporadic Cyclical Continuous TIME Filling Emptying Immediate post Late post TRIGGER Provoked Spontaneous	Aching Burning Stabbing Electric	UROLOGICAL Frequency Nocturia Hesitance Dysfunctional flow Urge Incontinence GYNAECOLOGICAL Menstrual Menopause GASTROINTESTINAL Constipation Diarrhoea Bloatedness Urge Incontinence NEUROLOGICAL Dysaesthesia Hyperaesthesia Allodynia Hyperalegesie SEXUOLOGICAL Satisfaction Female dyspareunia Sexual avoidance Erectile dysfunction Medication MUSCLE Function impairment Fasciculation CUTANEOUS Trophic changes Sensory changes	ANXIETY About pain or putative cause of pain Catastrophic thinking about pain DEPRESSION Attributed to pain or impact of pain Attributed to other causes Unattributed PTSD SYMPTOMS Re-experiencing Avoidance
				Bladder					
				Scrotal Testicular Epididymal					
				Penile Urethral					
				Postvasectomy					
		Gynaecological	Vulvar Vestibular Clitoral						
			Endometriosis associated						
			CPPS with cyclical exacerbations						
			Dysmenorrhoea						
		Gastrointestinal	Irritable bowel						
			Chronic anal						
			Intermittent chronic anal						
		Peripheral nerves	Pudendal pain syndrome						
		Sexological	Dyspareunia						
			Pelvic pain with sexual dysfunction						
		Psychological	Any pelvic organ						
		Musculo-skeletal	Pelvic floor muscle Abdominal muscle Spinal						
			Coccyx						

Hx = History; Ex = Examination; Ix = Investigation; PTSD = post-traumatic stress disorder.

Pain syndromes

The original EAU classification [2] was inspired by the IASP classification [9] and much work around what has become known as "pain as a disease" and its associated psychological, behavioural, sexual and functional correlates. After 10 years work developing the initial ideas, an updated version was accepted by IASP Council for publication in January 2012.

Definition of chronic pelvic pain (CPP)

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. [*Perceived indicates that the patient and clinician, to the best of their ability from the history, examination and investigations (where appropriate) has localised the pain as being perceived in the specified anatomical pelvic area.]

In the case of documented nociceptive pain that becomes chronic/persistent through time, pain must have been continuous or recurrent for at least 6 months. That is, it can be cyclical over a 6-month period, such as the cyclical pain of dysmenorrhoea. Six months is arbitrary, however, it was chosen because 3 months was not considered long enough if we include cyclical pain conditions. If non-acute and central sensitisation pain mechanisms are well documented, then the pain may be regarded as chronic, irrespective of the time period. Cyclical pain is included in the classification and hence dysmenorrhoea needs to be considered as a chronic pain syndrome if it is persistent and associated with negative cognitive, behavioural, sexual, or emotional consequences.

Chronic pelvic pain may be subdivided into conditions with well-defined classical pathology (such as infection or cancer) and those with no obvious pathology. For the purpose of this classification, the term "specific disease-associated pelvic pain" is proposed for the former, and "chronic pelvic pain syndrome" for the latter. The following classification only deals with CPPS.

Definition of chronic pelvic pain syndrome (CPPS)

Chronic pelvic pain syndrome is the occurrence of CPP when there is no proven infection or other obvious local pathology that may account for the pain. It is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. CPPS is a subdivision of CPP.

Further subdivision of CPPS

Pain perception in CPPS may be focused within a single organ, more than one pelvic organ and even associated with systemic symptoms such as chronic fatigue syndrome (CFS), fibromyalgia (FM) or Sjögren's syndrome. When the pain is localised to a single organ, some specialists may wish to consider using an end organ term such as BPS. The use of such a phrase with the terminology "syndrome" indicates that, although peripheral mechanisms may exist, CNS neuromodulation may be more important and systemic associations may occur. When the pain is localised to more than one organ site, the term CPPS should be used. Many, including some of the authors of this text, never subdivide by anatomy and prefer to refer to patients with pain perceived within the pelvis and no specific disease process as suffering from CPPS, subdivided by psychological and functional symptoms.

Psychological considerations for classification

Many CPPSs are associated with a range of concurrent negative psychological, behavioural and sexual consequences that must be described and assessed. Examples that need to be considered are depression, anxiety, fears about pain or its implications, unhelpful coping strategies, and distress in relationships. Both anxiety and depression can be significant important concomitant symptoms that are relevant to pain, disability and poor QoL. Catastrophic interpretation of pain has been shown to be a particularly salient variable, predicting patients' report of pain, disability, and poor QoL, over and above psychosocial variables such as depression or behavioural factors such as self-reported sexual dysfunction. It is suggested that CPPS sometimes creates a sense of helplessness that can be reported as overwhelming, and may be associated with the refractory nature of the patients' symptoms. It is important to note that many of these biopsychosocial consequences are common to other persistent pain problems but may show varying degrees of importance for any one individual suffering from CPPS. In all patients with CPPS, these consequences must be clearly described as part of the phenotype (where the term phenotype is used to indicate the observable characteristics of the syndrome).

Functional considerations for classification

Functional disorders, for the purpose of this document, are pathologies that have arisen secondary to changes

in the control mechanisms of an organ or system. That is, they are disorders characterised by disturbance of function. As an example, slow colonic transit is a functional disorder of the bowel - the normal function of the bowel is not occurring as a result of changes in the mechanisms that produce defecation, and hence the bowel control is abnormal. The term is not used in the sense of a psychiatric functional disorder. Many CPPSs are associated with functional abnormalities at a local and even systemic level. These also need to be defined as a part of the phenotype.

Functional pain disorders may not express significant pathology in the organs that appear responsible for the primary symptoms, but they are associated with substantial neurobiological, physiological and sometimes anatomical changes in the CNS.

Multi-system subdivision

It is recognised that the end-organ where the pain is perceived may not be the centre of pain generation. This classification is based upon the most effective accepted method of classifying and identifying different pain syndromes, that is, by site of presentation. It is argued that keeping the end-organ name in the classification is inappropriate because, in most cases, there are multi-systemic causes and effects, with the result that symptoms are perceived in several areas. This is an area in which discussions are ongoing, and despite there being strong arguments for both keeping and dispensing with end-organ classification, the authors have not taken the umbrella approach of referring to all pain perceived in the pelvis as CPPS.

Dyspareunia

Dyspareunia is defined as pain perceived within the pelvis associated with penetrative sex. It tells us nothing about the mechanism and may be applied to women and men. It is usually applied to penile penetration, but is often associated with pain during insertion of any object. It may apply to anal as well as vaginal intercourse. It is classically subdivided into superficial and deep.

Perineal pain syndrome

Perineal pain syndrome is a neuropathic-type pain that is perceived in the distribution area of the pudendal nerve, and may be associated with symptoms and signs of rectal, urinary tract or sexual dysfunction. There is no proven obvious pathology. It is often associated with negative cognitive, behavioural, sexual and emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. Perineal pain syndrome should be distinguished from pudendal neuralgia, which is a specific disease associated with pelvic pain that is caused by nerve damage.

Table 2: Urological pain syndromes

Urological Pain Syndromes	
Abdominal and Pelvic Pain Syndromes	
Prostate pain syndrome	Prostate pain syndrome (PPS) is the occurrence of persistent or recurrent episodic pain (which is convincingly reproduced by prostate palpation). There is no proven infection or other obvious local pathology. PPS is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction. The term "chronic prostatitis" continues to be equated with that of PPS. In the authors' and others' opinion, this is an inappropriate term, although it is recognised that it has a long history of use. The National Institutes of Health (NIH) consensus [10] includes infection (types I and II), which the authors feel should not be considered under PPS, but as specific disease-associated pelvic pain. The term prostadynia has also been used in the past but is no longer recommended by the expert panel. Please note that some of the authors of the IASP document disagree with this term and suggest that CPPS of the male is used instead of PPS, which has been agreed by the majority.
Bladder pain syndrome	Bladder pain syndrome (BPS) is the occurrence of persistent or recurrent pain perceived in the urinary bladder region, accompanied by at least one other symptom, such as pain worsening with bladder filling and day-time and/or night-time urinary frequency. There is no proven infection or other obvious local pathology. BPS is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction. BPS is believed to represent a heterogeneous spectrum of disorders. There may be specific types of inflammation as a feature in subsets of patients. Localisation of the pain can be difficult by examination, and consequently, another localising symptom is required. Cystoscopy with hydrodistension and biopsy may be indicated to define phenotypes. Recently, ESSIC has suggested a standardised scheme of subclassifications [11] to acknowledge differences and make it easier to compare various studies. Other terms that have been used include "interstitial cystitis", "painful bladder syndrome", and "PBS/IC" or "BPS/IC". These terms are no longer recommended.
Scrotal pain syndrome	Scrotal pain syndrome is the occurrence of persistent or recurrent episodic pain localised within the organs of the scrotum, and may be associated with symptoms suggestive of urinary tract or sexual dysfunction. There is no proven infection or other obvious local pathology. Scrotal pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction. Scrotal pain syndrome is a generic term and is used when the site of the pain is not clearly testicular or epididymal. The pain is not in the skin of the scrotum as such, but perceived within its contents, in a similar way to idiopathic chest pain.
Testicular pain syndrome	Testicular pain syndrome is the occurrence of persistent or recurrent episodic pain perceived in the testes, and may be associated with symptoms suggestive of urinary tract or sexual dysfunction. There is no proven infection or other obvious local pathology. Testicular pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction. Previous terms have included orchitis, orchialgia and orchiodynia. These terms are no longer recommended.
Epididymal pain syndrome	Epididymal pain syndrome is the occurrence of persistent or recurrent episodic pain perceived in the epididymis, and may be associated with symptoms suggestive of urinary tract or sexual dysfunction. There is no proven infection or other obvious local pathology. Epididymal pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction.
Penile pain syndrome	Penile pain syndrome is the occurrence of pain within the penis that is not primarily in the urethra, in the absence of proven infection or other obvious local pathology. Penile pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction.

Urethral pain syndrome	Urethral pain syndrome is the occurrence of chronic or recurrent episodic pain perceived in the urethra, in the absence of proven infection or other obvious local pathology. Urethral pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. Urethral pain syndrome may occur in men and women.
Post-vasectomy scrotal pain syndrome	Post-vasectomy scrotal pain syndrome is a scrotal pain syndrome that follows vasectomy. Post-vasectomy scrotal pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction. Post-vasectomy pain may be as frequent as 1% following vasectomy, possibly more frequent. The mechanisms are poorly understood and it is for that reason considered a special form of scrotal pain syndrome.
Gynaecological Pain Syndromes: external genitalia	
Vulvar pain syndrome	Vulvar pain syndrome is the occurrence of persistent or recurrent episodic vulvar pain. There is no proven infection or other local obvious pathology. It is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. Although pain perceived in the vulva was included under sexual disorders in the DSM-IV-R manual for classifying psychiatric disorders, there is no scientific basis for this classification, and pain perceived in the vulva is best understood as a pain problem that usually has psychological consequences. There is no evidence for its classification as a psychiatric disorder. The International Society for the Study of Vulvovaginal Disease (ISSVD) has used the term vulvodynia, where we use the term vulvar pain syndrome. According to the ISSVD, vulvodynia is vulvar pain that is not accounted for by any physical findings. The ISSVD has defined vulvodynia as "vulvar discomfort, most often described as burning pain, occurring in the absence of relevant visible findings or a specific, clinically identifiable, neurologic disorder". If physical findings are present, the patient is said to have vulvar pain due to a specified cause. The ISSVD has subdivided vulvodynia based on pain location and temporal characteristics of the pain (e.g.,provoked or unprovoked). The following definitions are based on that approach.
Generalised vulvar pain syndrome	Generalised vulvar pain syndrome refers to a vulvar pain syndrome in which the pain/burning cannot be consistently and precisely localised by point-pressure mapping via probing with a cotton-tipped applicator or similar instrument. Rather, the pain is diffuse and affects all parts of the vulva. The vulvar vestibule (the part that lies between the labia minora into which the urethral meatus and vaginal introitus open) may be involved but the discomfort is not limited to the vestibule. This pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences. Previous terms have included "dysesthetic vulvodynia" and "essential vulvodynia", but are no longer recommended.
Localised vulvar pain syndrome	Localised vulvar pain syndrome refers to pain that can be consistently and precisely localised by point-pressure mapping to one or more portions of the vulva. Clinically, the pain usually occurs as a result of provocation (touch, pressure or friction). Localised vulvar pain syndrome can be subdivided into vestibular pain syndrome and clitoral pain syndrome.
Vestibular pain syndrome	Vestibular pain syndrome refers to pain that can be localised by point-pressure mapping to the vestibule or is well perceived in the area of the vestibule.
Clitoral pain syndrome	Clitoral pain syndrome refers to pain that can be localised by point-pressure mapping to the clitoris or is well perceived in the area of the clitoris.

Gynaecological system: internal pelvic pain syndromes	
Endometriosis-associated pain syndrome	Endometriosis-associated pain syndrome is chronic or recurrent pelvic pain in patients with laparoscopically confirmed endometriosis, and the term is used when the symptoms persist despite adequate endometriosis treatment. It is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. Many patients have pain above and beyond the endometriotic lesions; this term is used to cover that group of patients. Endometriosis may be an incidental finding, is not always painful, and the degree of disease seen laparoscopically does not correlate with severity of symptoms. As with other patients, they often have more than one end-organ involved. It has been suggested that this phenotype should be removed from the classification because the endometriosis may be irrelevant.
Chronic pelvic pain syndrome with cyclical exacerbations	Chronic pelvic pain syndrome with cyclical exacerbations covers the non-gynaecological organ pain that frequently shows cyclical exacerbations (e.g., IBS or BPS) as well as pain similar to that associated with endometriosis/adenomyosis but where no pathology is identified. This condition is different from dysmenorrhoea, in which pain is only present with menstruation.
Dysmenorrhoea	Dysmenorrhoea is pain with menstruation that is not associated with well-defined pathology. Dysmenorrhoea needs to be considered as a chronic pain syndrome if it is persistent and associated with negative cognitive, behavioural, sexual or emotional consequences.
Gastrointestinal Pelvic Pain Syndromes	
Irritable bowel Syndrome (IBS)	IBS is the occurrence of chronic or recurrent episodic pain perceived in the bowel, in the absence of proven infection or other obvious local pathology. Bowel dysfunction is frequent. IBS is often associated with worry and preoccupation about bowel function, and negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract or gynaecological dysfunction. The above classification is based upon the Rome III Criteria [12]: 3 months of continuous or recurring symptoms of abdominal pain or irritation that may be relieved with a bowel movement, may be coupled with a change in frequency, or may be related to a change in stool consistency. Two or more of the following are present at least 25% of the time: change in stool frequency (> 3 bowel movements per day or < 3 per week); noticeable difference in stool form (hard, loose, watery or poorly formed stools); passage of mucus in stools; bloating or feeling of abdominal distension; or altered stool passage (e.g., sensation of incomplete evacuation, straining, or urgency). Extra-intestinal symptoms include: nausea, fatigue, full sensation after even a small meal, and vomiting.
Chronic anal pain syndrome	Chronic anal pain syndrome is the occurrence of chronic or recurrent episodic pain perceived in the anus, in the absence of proven infection or other obvious local pathology. Chronic anal pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction.
Intermittent chronic anal pain syndrome	Intermittent chronic anal pain syndrome refers to severe, brief, episodic pain that seems to arise in the rectum or anal canal and occurs at irregular intervals. This is unrelated to the need to or the process of defecation. It may be considered a subgroup of the chronic anal pain syndromes. It was previously known as “proctalgia fugax” but this term is no longer recommended.

Musculoskeletal System	
Pelvic floor muscle pain syndrome	Pelvic floor muscle pain syndrome is the occurrence of persistent or recurrent episodic pelvic floor pain. There is no proven well-defined local pathology. It is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. This syndrome may be associated with overactivity of or trigger points within the pelvic floor muscles. Trigger points may also be found in several muscles, such as the abdominal, thigh and paraspinal muscles and even those not directly related to the pelvis.
Coccyx pain syndrome	Coccyx pain syndrome is the occurrence of chronic or recurrent episodic pain perceived in the region of the coccyx, in the absence of proven infection or other obvious local pathology. Coccyx pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. The term “coccydynia” was used but is no longer recommended.

2. METHODOLOGY

2.1 Methods

References used in this text are assessed according to their Level of Evidence (LE) and Guidelines are given a Grade of Recommendation (GR), according to a classification system modified from the Oxford Centre for Evidence-based Medicine Levels of Evidence [13]. Additional methodology information can be found in the general Methodology section of this print, and online at the EAU website: http://www.uroweb.org/guideline/. A list of Associations endorsing the EAU Guidelines can also be reviewed online at the above address.

The 2012 full text update is based on a systematic review of literature using the Embase and Medline databases, the Cochrane Central Register of controlled trials and the PsycInfo and Bandolier databases to identify the best evidence from randomised controlled trials (RCTs), Level of Evidence 1 (LE: 1), according to the rating schedule adapted from the Oxford Centre for Evidence-based Medicine Levels of Evidence [13]. Where no (LE: 1) literature could be identified the search was moved down to the next lower level on the rating scale. Extensive use of free text ensured the sensitivity of the searches, resulting in a substantial body of literature to scan. Searches covered the period January 1995 and July 2011 and were restricted to English language publications.

Further updates of Chapter 5 ’Gastrointestinal aspects of chronic pelvic pain’ and Chapter 8 ‘Psychological aspects of chronic pelvic pain in the 2014 edition were based on systematic reviews of the literature in the aforementioned databases, including PsycInfo.

2.2 Review

This document was subject to peer review prior to publication in 2015. The decision to re-review is made based on the extent of the revision. A major revision resulting in significant changes to the clinical recommendations presented in the text will warrant re-review.

3. EPIDEMIOLOGY, AETIOLOGY AND PATHOPHYSIOLOGY

3.1 Chronic visceral pain

Definition of pain

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage (IASP Taxonomy).

Introduction to chronic pelvic pain syndromes

Over the years much of the focus for CPP has been on peripheral-end-organ mechanisms, such as

inflammatory or infective conditions. However, both animal and clinical research have indicated that many of the mechanisms for the CPP syndromes are based within the CNS. Although a peripheral stimulus such as infection may initiate the start of a CPP condition, the condition may become self-perpetuating as a result of CNS modulation. As well as pain, these central mechanisms are associated with several other sensory, functional, behavioural and psychological phenomena. It is this collection of phenomena that forms the basis of the pain syndrome diagnosis and individual phenomena need to be addressed in their own right through multispecialty and multidisciplinary care. Although ongoing peripheral organ pathology can produce persistent and chronic pain, the main focus of these guidelines is on CPP syndromes in which no peripheral ongoing pathology (such as infection or neoplastic disease) is detected. The main exception is when pain is due to peripheral nerve damage.

*3.1.1 **Incidence***

No adequate data on incidence were found.

*3.1.2 **Prevalence***

In a large study in Europe done in 2004 [14] it was found that chronic pain of moderate to severe intensity occurs in 19% of adult Europeans, seriously affecting the quality of their social and working lives. There are some differences between countries but not much spread is seen.

*3.1.3 **Influence in QOL***

Assessing the quality of life in pelvic pain patients is challenging due to the multi-faceted nature of the complaints and the overlap between the different pelvic pain syndromes [15]. Assessment of quality of life is further complicated due to the complex pathology of pain itself [16].

Pelvic pain pain syndromes do have an impact on the QoL [17, 18]. This may result in depression, anxiety, impaired emotional functioning and fatigueness [18]. If these aspects are identified and targeted early in the diagnostic process, the associated pain symptoms may also improve [19]. Addressing co-morbidities will help in further improving the QoL [20]. QoL assessment is therefore important in patients with pelvic pain and should include physical, psychosocial and emotional tools, using standardised and validated instruments [17].

The impact of pain on QoL has been assessed in an extensive European study [14]. In-depth interviews with 4839 respondents with chronic pain (about 300 per country) showed: 66% had moderate pain (NRS = 5-7) and 34% had severe pain (NRS = 8-10), 46% had constant pain, 54% had intermittent pain. 59% had suffered with pain for two to 15 years, 21% had been diagnosed with depression because of their pain, 61% were less able or unable to work outside the home, 19% had lost their job and 13% had changed jobs because of their pain. 60% visited their doctor about their pain 2-9 times in the last six months. Only 2% were currently treated by a pain management specialist.

*3.1.4 **Costs***

No adequate data on costs were found.

*3.1.5 **Risk Factors and underlying causes***

3.1.5.1 Risk factors

Risk factors include many different factors from various areas, including genetic, psychological state, recurrent somatic trauma and endocrine factors.

The endocrine system is involved in visceral function. Significant life events, and in particular, early life events may alter the development of the hypothalamic-pituitary-adrenal axis and the chemicals released. Increased vulnerability to stress may occur following such events and is thought to be partly due to increased corticotrophin-releasing hormone (CRH) gene expression. Up-regulation of CRH has been implicated in several pain states such as rectal hypersensitivity to rectal distension. This model suggests an action of CRH on mast cells. A range of stress-related illnesses have been suggested, e.g. IBS and BPS. There is evidence accumulating to suggest that the sex hormones also modulate both nociception and pain perception. Stress can also produce long-term biological changes which may form the relation between chronic pain syndromes and significant early life and adverse life events [21]. Asking the patient about these events is important as they have an effect on a patient's psychological wellbeing [22-24].

Genetics also play a role in assessing the risk of developing chronic pain. An individual who has had one chronic pain syndrome is more likely to develop another. Family clusters of pain conditions are also observed and animals can be bred that are more prone to an apparent chronic pain state. A whole range of genetic variations have been described that may explain the pain in certain cases; many of these are to do with subtle changes in transmitters and their receptors. However, the picture is more complicated in that development, environment and social factors also influence the situation. Evidence that BPS may have a

genetic component has been presented in several studies, but genetics may contribute to less than one third of total variation in susceptibility to BPS.

Studies about integrating the psychological factors are few but the quality is high. Psychological factors are consistently found to be relevant in the maintenance of persistent pelvic and urogenital pain with current neurobiological understanding of pain. Symptom-related anxiety and central pain amplification may be measurably linked, as in IBS [25]. Central sensitisation has been demonstrated in symptomatic endometriosis [26]. Central changes are evident in association with dysmenorrhea and increasingly recognised as a risk for female pelvic pain [27]. The various mechanisms of CNS facilitation, amplification and failure of inhibition, mean that there is no simple relationship between physical findings, pain experienced and resulting distress and restriction of activities. Women experiencing diagnoses which assign their pain to psychological origin, is common in primary care [28], due to scepticism about the reality or severity of their pain [29], thereby undermining any therapeutic relationship [30]. Division of aetiology into organic vs. psychogenic is unscientific. Pelvic pain and distress may be related [31]; the same is true of painful bladder and distress [32]. The only systematic review [33] of risk factors for chronic non-cyclical pelvic pain in women included, as well as medical variables: sexual or physical abuse (OR from 1.51 to 3.49); psychological problems such as anxiety (OR: 2.28, 95% CI: 1.41- 3.70) and depression (OR: 2.69, 95% CI: 1.86-3.88); multiple somatic problems (OR: 4.83, 95% CI: 2.50-9.33); and psychosomatic symptoms (OR: 8.01, 95% CI: 5.16-12.44).

Many studies have reported high rates of childhood sexual abuse in adults with persistent pain, particularly in women with pelvic pain [34, 35]. In these studies it is suggested that there is increased frequency of sexual abuse or trauma history, anxiety and depression in women with CPP [36-40]. The only prospective investigation into the relationship between childhood sexual abuse, physical abuse, or neglect, and “medically unexplained pain”, including pelvic pain, used court records to compare women with a definite history with matched classmates [24] and concluded that physically and sexually abused individuals were not at risk for increased pain, although women with pain problems as adults were more likely to report earlier sexual or physical abuse or neglect. The correlation between childhood victimisation and pain may concern retrospective explanations for pain; controlling for depression significantly weakens the relationship between childhood abuse and adult pain [41]. Disentangling the influences and inferences requires further prospective studies or careful comparisons [21]. There is some evidence for a specific relationship between rape and CPP (and with fibromyalgia and functional gastrointestinal disorders) [42], recent sexual assault may prompt presentation of pelvic pain [34, 43]. Few studies have been found of sexual or physical abuse in childhood and pelvic pain in men, although it has known adverse effects on health [42, 44]. In the BACH study, it was found that men who reported having experienced sexual, physical, or emotional abuse had increased odds (3.3 compared to 1.7) for symptoms suggestive of CPP. The authors suggested that clinicians may wish to screen for abuse in men presenting with symptoms suggestive of CPP. Conversely, clinicians may wish to inquire about pelvic pain in patients who have experienced abuse [45].

3.1.5.2 Underlying causes

The mechanisms that serve as an underlying cause for chronic pelvic pain are:

1. Ongoing acute pain mechanisms [46] (such as those associated with inflammation or infection), which may involve somatic or visceral tissue.
2. Chronic pain mechanisms, which especially involve the CNS [6].
3. Emotional, cognitive, behavioural and sexual responses and mechanisms [47-49].

Table 3 illustrates some of the differences between the somatic and visceral pain mechanisms. These underlie some of the mechanisms that may produce the classical features of visceral pain; in particular, referred pain and hyperalgesia.

Table 3: Comparison between visceral and somatic pain

	Visceral pain	Somatic pain
Effective painful stimuli	Stretching and distension, producing poorly localised pain.	Mechanical, thermal, chemical and electrical stimuli, producing well localised pain.
Summation	Widespread stimulation produces significantly magnified pain.	Widespread stimulation produces a modest increase in pain.
Autonomic involvement	Autonomic features (e.g., nausea and sweating) frequently present.	Autonomic features less frequent.
Referred pain	Pain perceived at a site distant to the cause of the pain is common.	Pain is relatively well localised but well recognised.
Referred hyperalgesia	Referred cutaneous and muscle hyperalgesia is common, as is involvement of other visceral organs.	Hyperalgesia tends to be localised.
Innervation	Low density, unmyelinated C fibres and thinly myelinated A∂ fibres.	Dense innervation with a wide range of nerve fibres.
Primary afferent physiology	Intensity coding. As stimulation increases, afferent firing increases with an increase in sensation and ultimately pain.	Two fibre coding. Separate fibres for pain and normal sensation.
Silent afferents	50-90% of visceral afferents are silent until the time they are switched on.	These fibres are very important in the central sensitisation process. Silent afferents present, but form a lower percentage.
Central mechanisms	Play an important part in the hyperalgesia, viscero-visceral, visceromuscular and musculovisceral hyperalgesia.	Sensations not normally perceived become perceived and non-noxious sensations become painful. Responsible for the allodynia and hyperalgesia of chronic somatic pain.
Abnormalities of function	Central mechanisms associated with visceral pain may be responsible for organ dysfunction.	Somatic pain associated with somatic dysfunction, e.g., muscle spasm
Central pathways and representation	As well as classical pathways, there is evidence for a separate dorsal horn pathway and central representation.	Classical pain pathways.

Ongoing peripheral pain mechanisms in visceral pain

In most cases of CPP, ongoing tissue trauma, inflammation or infection is absent [50-53]. However, conditions that produce recurrent trauma, infection or ongoing inflammation may result in CPP in a small proportion of cases. It is for this reason that the early stages of assessment include looking for these pathologies [11]. Once excluded, ongoing investigations for these causes are rarely helpful and indeed may be detrimental.

When acute pain mechanisms are activated by a nociceptive event, as well as direct activation of the peripheral nociceptor transducers, sensitisation of those transducers may also occur, thus magnifying the afferent signalling. Afferents that are not normally active may also become activated by the change, that is, there may be activation of the so-called silent afferents. Although these are mechanisms of acute pain, the increased afferent signalling is often a trigger for the chronic pain mechanisms that maintain the perception of pain in the absence of ongoing peripheral pathology (see below) [54, 55].

There are a number of mechanisms by which the peripheral transducers may exhibit an increase in sensibility.

1. Modification of the peripheral tissue, which may result in the transducers being more exposed to peripheral stimulation.
2. There may be an increase in the chemicals that stimulates the receptors of the transducers [56].
3. There are many modifications in the receptors that result in them being more sensitive.

In general, the effect of 1 and 2 is to lower the threshold and the effect of 3 is to increase responsiveness to

external stimuli. Some of the chemicals responsible for the above changes may be released from those cells associated with inflammation, but the peripheral nervous system may also release chemicals in the positive and inhibitory loops [57].

Central sensitisation as a mechanism in visceral pain

It is important to appreciate that nociception is the process of transmitting information to centres involved in perception of a stimulus that has the potential to cause tissue damage. Pain is far more complex and involves activation of the nociceptive pathways but also the emotional response. The brain may affect the modulation of pain pathways at the spinal cord level.

Central sensitisation [58] is responsible for a decrease in threshold and an increase in response duration and magnitude of dorsal horn neurons. It is associated with an expansion of the receptive field. As a result, sensitisation increases signalling to the CNS and amplifies what we perceive from a peripheral stimulus. As an example, for cutaneous stimuli, light touch would not normally produce pain, however, when central sensitisation is present, light touch may be perceived as painful (allodynia). In visceral hyperalgesia (so called because the afferents are primarily small fibres), visceral stimuli that are normally subthreshold and not usually perceived may be perceived. For instance, with central sensitisation, stimuli that are normally subthreshold may result in a sensation of fullness and a need to void or to defecate. Stimuli normally perceived may be interpreted as pain and stimuli that are normally noxious may be magnified (true hyperalgesia) with an increased perception of pain. As a consequence, one can see that many of the symptoms of BPS and IBS may be explained by central sensitisation. A similar explanation exists for the muscle pain in fibromyalgia.

It is now well accepted that there are both descending pain-inhibitory and descending pain-facilitatory pathways that originate from the brain [59]. Several neurotransmitters and neuromodulators are involved in descending pain-inhibitory pathways. The main contenders are the opioids, 5-hydroxytryptamine and noradrenaline.

The autonomic nervous system also plays a role in sensitisation. There is good evidence that damaged afferent fibres may develop a sensitivity to sympathetic stimulation, both at the site of injury and more centrally, particularly in the dorsal horns. In visceral pain, the efferent output of the CNS may be influenced by central changes (again, those changes may be throughout the neuraxis), and such modification of the efferent message may produce significant end-organ dysfunction. These functional abnormalities can have a significant effect on QoL and must be managed as appropriate.

Psychological mechanisms in visceral pain

Psychological processes of emotions, thought and behaviour involve networks rather than distinct centres. Some of these processes are sophisticated and others fundamental in evolutionary terms, and their interaction with pain processing is complex.

Various psychological processes affect pain neuromodulation at a higher level. Inhibiting or facilitating both the nociceptive signal reaching the consciousness and appraisal and interpretation of that signal, will also modulate the response to the nociceptive message and hence the pain experience. Further, descending pathways represent cognitive, emotional and behavioural states at spinal and peripheral levels. Functional Magnetic Resonance Imaging (fMRI) has indicated that the psychological modulation of visceral pain probably involves multiple pathways. For instance, mood and attentional focus probably act through different areas of the brain when involved in reducing pain [60].

This psychological modulation may act to reduce nociception within a rapid time frame but may also result in long-term vulnerability to chronic visceral pain, through long-term potentiation. This involvement of higher centre learning may be at both a conscious and subconscious level, and is clearly significant in the supratentorial neuroprocessing of nociception and pain. Long-term potentiation [61] may occur at any level within the nervous system, so that pathways for specific or combinations of stimuli may become established, resulting in an individual being vulnerable to perceiving sensations that would not normally be experienced as painful.

An important review [21] of CPP in women identifies the notion that women without physical findings to which pain can be causally attributed differ in psychological characteristics from women with physical findings. It argues for better methodology, and for greater use of idiographic methods. In summary, women with pelvic pain often have other 'medically unexplained' symptoms, and current or lifetime anxiety and depression disorder; they may have a history of physical or sexual abuse in childhood of unclear significance. Studies that invoke 'medically unexplained' or 'psychosomatic' or 'somatoform' disorders are entirely inconsistent with current pain science, ignoring phenomena such as viscerovisceral cross sensitisation in relation to multiple pain sites [62], and interpreting absence of physical findings to indicate psychological origins of the complaint [63, 64]. Some pain problems which affect sexual activity are diagnosed as sexual problems (e.g. 'dyspareunia') when pain is the central problem and not contingent on sexual activity alone [65]. Better integration of sexology and mainstream psychology for pelvic pain in both men and women is needed [66], building on a

biopsychosocial formulation [67, 68].

The term psychosomatic symptoms can best be understood as multiple somatic symptoms not associated with or indicative of any serious disease process. Medical and surgical history may also be important [69]. There have been a few studies of maintenance of or recovery from pelvic pain in relation to psychological factors of importance in pain. Those that that described pelvic pain as medically unexplained or psychosomatic, due to the lack of physical findings, have been discarded, because such a distinction is inconsistent with known pain mechanisms [63].

Understanding the psychological components of pain

Psychological processes of emotions, thought and behaviour involve networks rather than distinct centres, and their interaction with pain processing is complex, producing inhibition and facilitation of signal processing, appraisal, and response. Models that integrate the psychological factors consistently found to be relevant in the maintenance of persistent pelvic and urogenital pain with current neurobiological understanding of pain are few but the quality is high (see 3.1.5.1).

There is no evidence that women with CPP without physical findings are primarily presenting a psychological problem [21]. Anxiety and post-traumatic stress symptoms are common in some women with CPP [28, 70], and may account for substantial variance in health status and treatment use. Negative investigative findings do not necessarily resolve women's anxieties about the cause of pain [71, 72], and anxiety often focuses on what might be 'wrong' [73]. Depression may be related to pain in various ways, as described above. Until measures are available that are adequately standardised in patients with pain, anxiety and distress may be best assessed by questions about concerns about the cause of pain, its implications, and its consequences for everyday life [74]. Reference to the studies of the IMMPACT group [75] is recommended for guidance on outcome measures suitable for pain trials.

Stress can modify the nervous system to produce long-term biological changes. These structural changes may be responsible for significant early life and adverse life events which are associated with chronic pain syndromes [26]. The patient should be asked about adverse life events that may produce these biological responses and affect a patient's general psychological wellbeing [23, 24, 76].

3.1.5.3 Clinical paradigms in visceral pain

Referred pain

Referred pain is frequently observed and its identification is important for diagnosis and treatment. Referral is usually somatic to somatic, or visceral to somatic. However, there is no reason why pain cannot also be perceived within the area of an organ with the nociceptive signal having arisen from a somatic area. Referred pain may occur as a result of several mechanisms but the main theory is one of convergence-projection. In the onvergence-projection theory, as an example, afferent fibres from the viscera and the somatic site of referred pain converge onto the same second order projection neurons. The higher centres receiving messages from these projection neurons are unable to separate the two possible sites from the origin of the nociceptive signal [51, 54, 77].

Hyperalgesia refers to an increased sensitivity to normally painful stimuli. In patients that have passed a renal stone, somatic muscle hyperalgesia is frequently present, even a year after expulsion of the stone. Pain to non-painful stimuli (allodynia) may also be present in certain individuals. Somatic tissue hyperaesthesia is associated with urinary and bilary colic, IBS, endometriosis, dysmenorrhoea, and recurrent bladder infection. Vulvar pain syndromes are examples of cutaneous allodynia that, in certain cases, may be associated with visceral pain syndromes, such as BPS. Referred pain with hyperalgesia is thought to be due to central sensitisation of the converging viscero-somatic neurones. Central sensitisation also stimulates efferent activity that could explain the trophic changes that are often found in the somatic tissues.

Muscles and pelvic pain

In the urogenital pain syndromes, muscle tenderness and trigger points may be implicated as a source of pain. Central mechanisms are of great importance in the pathogenesis of this muscle hyperalgesia. The muscles involved may be a part of the spinal, abdominal or pelvic complex of muscles. It is not unknown for adjacent muscles of the lower limbs and the thorax to become involved. Pain may be localised to the trigger points but it is more often associated with classical referral patterns. As well as trigger points, inflammation of the attachments to the bones (enthesitis) and of the bursa (bursitis) may be found [78]. Certain postures affect the different muscles in different ways, and as a consequence, may exacerbate or reduce the pain. Stress has been implicated as both an initiator of pelvic myalgia and as a maintenance factor. As a result, negative sexual encounters may also have a precipitating effect [21].

Visceral hyperalgesia

The increased perception of stimuli in the viscera is known as visceral hyperalgesia, and the underlying

mechanisms are thought to be responsible for IBS, BPS and dysmenorrhoea. The mechanisms involved are often acute afferent input (e.g., due to infection) followed by long-term central sensitisation. Viscero-visceral hyperalgesia is thought to be due to two or more organs with converging sensory projections and central sensitisation. For instance, overlap of bladder and uterine afferents or uterine and colon afferents.

3.2 Pelvic Pain

*3.2.1 **Incidence***

No adequate data on incidence were found.

*3.2.2 **Prevalence***

3.2.2.1 Prostate Pain syndrome

There is only limited information on the true prevalence of PPS in the population. As a result of significant overlap of symptoms with other conditions (e.g. benign prostatic enlargement and BPS), purely symptom-based case definitions may not reflect the true prevalence of PPS [79, 80]. In the literature, numbers of the population-based prevalence of prostatitis symptoms range from 1 - 14.2% [81, 82]. The risk of prostatitis increases with age (men aged 50-59 years have a 3.1-fold greater risk than those aged 20-39 years).

3.2.2.2 Bladder Pain syndrome

Reports of Bladder Pain Syndrome (BPS) prevalence have varied greatly, along with the diagnostic criteria and populations studied. Recent reports range from 0.06% to 30% [83-92]. There is a female predominance of about 10:1 [89, 93-95] but possibly no difference in race or ethnicity [79, 96, 97]. The relative proportions of classic and non-lesion disease are unclear. Incidence in studies has ranged from 5 to 50% [98-102]. There is increasing evidence that children under 18 may also be affected, although prevalence figures are low thus, BPS cannot be excluded on the basis of age [103].

3.2.2.3 Sexual pain syndrome

In the 1980s an association between CPP and sexual dysfunction was postulated. In two reviews the relationship between PPS and health status, with influence on sexual activity, was addressed [104, 105]. In a Chinese study of men with CPP 1,768 males completed the questionnaires. The overall prevalence of sexual dysfunction was 49%. Erectile dysfunction (ED) is the most investigated sexual dysfunction in PPS patients. The reported prevalence of ED ranges from 15.1% to 48%, varying with the evaluation tools and populations [106, 107]. ED was prevalent in 27.4% of Italian men aged 25-50 [108], 15.2% among Turkish men (significantly higher than in the control group) [109] and 43% among Finnish men with PPS [110]. The prevalence of ED was found to be higher in young men with PPS than in the general population. According to other studies men with pelvic pain had a higher chance of suffering from ED [111, 112]. Recently, a significant correlation between “chronic prostatitis”, CPP symptoms (measured by NIH-CPSI) and ED (measured by IIEF) was confirmed [113], while other studies using the same questionnaires were not able to confirm such a correlation [68, 114]. Some studies also report ejaculatory dysfunction, mainly premature ejaculation [106, 107, 115, 116].

In community-based studies in the UK [117], New Zealand [118] and Australia [119], a substantially larger proportion of the women with CPP reported dyspareunia (varying between 29% and 42%) than women without CPP (varying between 11% and 14%). Only a few studies have investigated sexual problems within clinical populations [120, 121]. Another study showed that all of the sexual function domains (desire, arousal, lubrication, orgasm, satisfaction, and pain) were significantly lower in women with CPP than in women without CPP [120]. In line with the results of the community based studies, patients with CPP reported more sexual problems such as dyspareunia, problems with desire or arousal and lubrication than women without CPP [120, 122, 123]. One study of patients enrolled in chronic pain treatment programs in England has reported that 73% had pain-related sexual problems [124].

3.2.2.4 Myofascial pain syndromes

The relationship between muscular dysfunction (especially overactivity) and pelvic pain has been found in several studies. Rectal pain treated with pelvic floor muscle therapy is only relieved when patients learn to relax their pelvic floor muscles [125]. The vast majority (92.2%) of men visiting a tertiary centre for pelvic pain had dysfunction of the pelvic floor muscles. This finding was true regardless of evidence of inflammation (prostatitis or cystitis) [126]. This relationship has been found in chronic prostatitis [127] BPS [128] and vulvar pain [129]. Dysfunction of the pelvic floor directly affects function of the pelvic viscera and vice versa. Both systems can act as the primary signal to the spinal cord, with a cascade of reactions ascending to the CNS as a result. The muscle itself ends up with a diminished length, leading to restrictions even when it is in a relaxed state.

*3.2.3 **Influence in QoL***

Data on the influence in QoL will be included in the next version of the guidelines.

*3.2.4 **Costs***

No adequate data on costs were found.

*3.2.5 **Risk factors and underlying causes***

The risk factors are unspecific for most of the pain syndromes in the pelvic area. They are described in 3.1.5.1. The underlying causes, including the mechanisms are described here for the different clinical pain syndromes.

3.2.5.1 Prostate Pain Syndrome

Pain is the main symptom in PPS. As a common feature of chronic pain syndromes, no single aetiological explanation has been found. One explanation [130] is that the condition probably occurs in susceptible men exposed to one or more initiating factor, which may be single, repetitive or continuous. Several of these potential initiating factors have been proposed, including infectious, genetic, anatomical, neuromuscular, endocrine, immune (including autoimmune), or psychological mechanisms. These factors may then lead to a peripheral self-perpetuating immunological inflammatory state and/or neurogenic injury, creating acute and then chronic pain. Based on the peripheral and the central nervous system, sensitisation involving neuroplasticity may lead to a centralised neuropathic pain state [130]. This could also explain why tissue damage is not usually found in PPS. There is growing evidence for a neuropathic origin and association with CNS changes of pain in PPS.

3.2.5.2 Bladder Pain syndrome

An initial unidentified insult to the bladder, leading to urothelial damage, neurogenic inflammation and pain is thought to be the cause of BPS. However, BPS might be a local manifestation of a systemic disorder. No infection has as yet been implicated. Nevertheless, urinary infection is significantly more frequent during childhood and adolescence, in patients with BPS in adulthood [131]. Experimental induction of CPP by O-antigen deficient bacterial strains reinstates the bacterial hypothesis [132]. Pancystitis, with associated perineural inflammatory infiltrates, and mast cell count increase is an essential part of BPS type 3 C [133], but is scant in non-lesion BPS [24, 60, 134, 135]. Cystoscopic and biopsy findings in both lesion and non-lesion BPS are consistent with defects in the urothelial glycosaminoglycan (GAG) layer, which might expose submucosal structures to noxious urine components [136-143] and a consequent cytotoxic effect [144, 145].

An association has been reported between BPS and non-bladder syndromes such as FM, chronic fatigue syndrome (CFS), IBS, vulvodynia, depression, panic disorders, migraine, sicca syndrome, temporomandibular joint disorder, allergy, asthma and systemic lupus erythematosus [146-152].

Risk of BPS correlates with a number of non-bladder syndromes in each patient [153]. Recent work showing non-lesion BPS to have significantly more FM, migraine, temporomandibular joint disorder and depression than BPS type 3C patients, emphasises the need for subtyping [154].

3.2.5.3 Scrotal Pain Syndrome

Often scrotal pain is not associated with any specific pathology. Pain is perceived in the testes, epididymis, or the vas deferens. The ilioinguinal, genitofemoral and the pundendal nerves innervate the scrotum [155]. Any pathology or intervention at the origin or along the course of the nerves may result in pain perceived in the scrotum [156].

Two special forms of scrotal pain syndrome can be described. The first one is the post-vasectomy scrotal pain syndrome which occurs following vasectomy. The mechanisms are poorly understood and it is for that reason considered a special form of scrotal pain syndrome.

Incidence of post-vasectomy pain is 2-20% among all men who have undergone a vasectomy [157]. In men with post-vasectomy pain, 2-6% have a VAS score > 5 [158]. In a large cohort study of 625 men, the likelihood of scrotal pain after 6 months was 14.7%. The mean pain severity on a VAS score was 3.4/10. In the pain group, 0.9% had quite severe pain, noticeably affecting their daily life. In this cohort, different techniques were used to perform the vasectomy. The risk of post-vasectomy pain was significantly lower in the no-scalpel vasectomy group (11.7% vs. the scalpel group 18.8%) [159].

The second form of scrotal pain is post-inguinal hernia repair pain. It is seen as a complication of hernia repair, but in trials it is seldom reported or it is put under the term chronic pain (not specified). In studies that have explicitly mentioned scrotal pain, there was a difference in incidence between laparoscopic and open hernia repair. In almost all studies, the frequency of scrotal pain was significantly higher in the laparoscopic than in the open group [156, 160]. In one particular study, there was no difference at 1 year but after 5 years, the open group had far fewer patients with scrotal pain [161].

3.2.5.4 Urethral Pain Syndrome

Some mechanisms for the development of urethral pain syndrome have been proposed. The intimate relation of the urethra with the bladder (both covered with urothelium) suggests that urethral pain syndrome may be a form of BPS. Mechanisms thought to be basic for BPS may also apply to the urethra. This means that the specific testing with potassium is used to support the theory of epithelial leakage [162, 163]. Another possible mechanism is neuropathic hypersensitivity following urinary tract infection [164]. The relationship with gynaecological and obstetric aspects is unclear. In a small group of patients with urethral pain, it has been found that grand multiparity and delivery without episiotomy were more often seen in patients with urethral syndrome, using univariate analysis [165].

3.2.5.5 Vaginal and vulvar pain syndromes

Pain in the vagina or the female external genital organs is often due to infection or trauma, as a consequence of childbirth or surgery. Pain is usually a precedent to dyspareunia. When the pain persists for > 6 months, it can be diagnosed as vulvar pain syndrome previously known as “vulvodynia” or “chronic vaginal” with no known cause. It is still a poorly understood condition, and thus difficult to treat.

There are two main subtypes of vulvar pain syndrome: generalised, where the pain occurs in different areas of the vulva at different times; and focal, where the pain is at the entrance of the vagina. In generalised vulvar pain syndrome, the pain may be constant or occur occasionally, but touch or pressure does not initiate it, although it may make the pain worse. In focal vulvar pain syndrome, the pain is described as a burning sensation that comes on only after touch or pressure, such as during intercourse.

The possible causes of vulvodynia are many and include:

- History of sexual abuse
- History of chronic antibiotic use
- Hypersensitivity to yeast infections, allergies to chemicals or other substances
- Abnormal inflammatory response (genetic and non-genetic) to infection and trauma
- Nerve or muscle injury or irritation
- Hormonal changes

3.2.5.6 Associated conditions in pelvic pain syndromes

Nerve damage

Spinal pathology and any pathology along the course of the nerve involved may result in neuropathic pain in the distribution of these nerves. Neoplastic disease, infection and trauma, surgical incisions and postoperative scarring may result in nerve injury [166].

Pudendal neuralgia is the most often mentioned form of nerve damage in the literature. Anatomical variations may predispose the patient to developing pudendal neuralgia over time or with repeated low-grade trauma (such as sitting for prolonged periods of time or cycling) [167, 168].

The pudendal nerve may be damaged at the level of:

1. The piriformis muscle. For example, as part of a piriformis syndrome: in some cases, the nerve may pass through the muscle and hence be trapped; or in other cases, muscle hypertrophy or spasm is implicated.
2. The sacrospinal/sacrotuberous ligaments, possibly accounting for 42% of cases.
3. Within Alcock’s canal (medial to the obturator internus muscle, within the fascia of the muscle), possibly accounting for 26% of cases.
4. Multiple levels in 17% of cases.

The site of injury determines the site of perceived pain and the nature of associated symptoms (e.g., the more distal the damage, the less likely the anal region will be involved).

The clinical presentation depends on different factors. There is a wide age range, as one would expect with a condition that has so many potential causes. There is a suggestion that, the younger the patient, the better the prognosis. Essentially, the sooner the diagnosis is made, as with any compression nerve injury, the better the prognosis, and older patients may have a more protracted problem [169-171]. Six out of ten cases are observed in women. Some special situations can be listed:

- In orthopaedic hip surgery, pressure from the positioning of the patient, where the perineum is placed hard against the brace, can result in pudendal nerve damage [172, 173]. The surgery itself may also directly damage the nerve. Pelvic surgery such as sacrospinous colpopexy is clearly associated with pudendal nerve damage in some cases [174, 175]. In many types of surgery, including colorectal, urological and gynaecological, pudendal nerve injury may be implicated.
- Fractures of the sacrum or pelvis may result in pudendal nerve/root damage and pain. Falls and trauma to the gluteal region may also produce pudendal nerve damage if associated with significant tissue injury or prolonged pressure.

- Tumours in the presacral space must be considered. Tumours invading the pudendal nerve may occur and there may also be damage from surgery for pelvic cancer [176].
- The pudendal neuralgia of birth trauma is thought to resolve in most cases over a period of months. However, rarely, it appears to continue as painful neuropathy. Multiple pregnancies and births may predispose to stretch neuropathy in later life. This is more difficult to be certain about [177].
- Child birth and repeated abdominal straining associated with chronic constipation [178] are thought to predispose elderly women to post-menopausal pelvic floor descent and stretching of the pudendal nerve with associated pain. Changes in the hormone status may also be a factor. In the Urogenital Pain Management Centre, the commonest associations with pudendal neuralgia appear to be: history of pelvic surgery; prolonged sitting (especially young men working with computer technology); and post-menopausal older women.

Sexual dysfunction

Chronic pelvic pain is a clinical condition that results from the complex interactions of physiological and psychological factors and has a direct impact on the social, marital, and professional lives of men and women.

Men

Chronic pain and its treatment can impair our ability to express sexuality. In a study in England 73% of patients with chronic pain had some degree of sexual problems as result of the pain [124]. These problems can occur because of several factors. Psychological factors like decrease in self-esteem, depression and anxiety can contribute to loss of libido. Physiological factors like fatigue, nausea and pain itself can cause sexual dysfunction. Pain medications (opioids, and the selective serotonin re-uptake inhibitors (SSRI) can also decrease libido [179] and delay ejaculation. The number of studies on the effects of CPP on sexual function is limited. Sexual dysfunction is often ignored because of a lack of standardised measurements. At the present, the most commonly used tool is the International Index of Erectile Function (IIEF) questionnaire [114].

The presence of pelvic pain may increase the risk for ED independent of age [180, 181]. On the other hand, cross-sectional data suggest no improvement of lower urinary tract symptoms (LUTS) by an increased frequency of ejaculation [105]. Although mental distress and impaired QoL related to illness could contribute to sexual dysfunction observed in patients with PPS, the presence of erectile and ejaculatory disorders is more frequently related to symptoms suggestive of a more severe inflammatory condition [116]. These arguments are important for the understanding of the close relationship between CPP symptoms, disturbed sexuality, impact on QoL, and psychological implications including depression [104-107, 182]. Sexual dysfunction heightens anger, frustration and depression, all of which place a strain on the patients' relationships. The female partners of men with sexual dysfunction and depression often present with similar symptoms including pain upon intercourse and depressive symptoms. Men with CPP have reported a high frequency of sexual relationship dissolution and psychological symptoms, such as depression and suicidal thinking [104, 181]. PPS patients reported greater sexual and relationship problems [104, 181, 183]. On the other hand, it was found that men with PPS did not report significantly decreased sexual satisfaction compared to controls [184]. There is consensus that therapeutic strategies reducing symptoms of pelvic pain, are of relevance in relation to changes of sexuality. Also intimacy and having sex can yield positive experiences that will reduce the pain. The CNS plays an important role in this mechanism.

Women

Chronic pelvic pain leads to substantial impairment in QoL and several sexual dysfunctions [118, 185-187]. It seems reasonable to expect that pain, extreme fatigue, depressive mood and pain drugs will affect women's sexuality. Women with CPP reported significantly more pain, depression, and anxiety symptoms and were physically more impaired than women in the control group. In comparison with controls, women with CPP reported significantly more sexual avoidance behaviour, non-sensuality, and complaints of "vaginismus" [188]. In one study of CPP patients' feelings and beliefs about their pain or illness, 40 out of 64 participants cited sexual dysfunction as one of the main problems the illness had caused, making it the most frequent complaint [189]. Patients with CPP reported more sexual problems than women with any other type of chronic pain problem [190]. The quality of intimate relationships is closely connected with sexual function [191]. Satisfaction with sexual relationships appears to be associated with higher marital functioning [192]. In addition sexual dissatisfaction is related to sexual dysfunction. When one partner suffers from chronic pain, the ability of both partners to cope with the pain and the extent to which partners are supportive of the chronic pain sufferer have been found to be a predictor of sexual functioning [192].

Approximately two-thirds of patients in another study have reported reduced frequency in their sexual

relations as a result of CPP [193]. One study demonstrated that CPP patients reported worse sexual function with regard to desire, arousal, lubrication, orgasm, satisfaction, and more frequent and severe pain with vaginal penetration than women without sexual dysfunction [194]. In an interview with 50 chronic pain sufferers and their spouses, 78% of the pain sufferers and 84% of partners described deterioration, including cessation of their sex life [180]. In a study in patients with back pain, half reported decreased frequency of sex since the onset of chronic pain [124]. The Female Sexual Function Index (FSFI) has been developed as a brief, multidimensional self-report instrument for assessing the key dimensions of sexual function in women, which includes desire, subjective arousal, lubrication, orgasm, satisfaction, and pain. Using the FSFI, women with CPP reported worse sexual function in all subscales and total score than did women without CPP. The largest differences between women with CPP and without CPP were seen for the domains of pain and arousal. The total score and the subscales of the FSFI had high levels of internal consistency and test-retest reliability when assessed in a sample of women with CPP. The FSFI also showed good ability to discriminate between women with and without CPP [36].

Myofascial pain

Chronic pelvic pain can simply be a form of myalgia, due to the muscles being used in an abnormal way, in this case, the pelvic floor muscles. Studies in the field of chronic prostatitis support the idea that patients with CPP have more muscle spasm and increased muscle tone and report pain when the pelvic floor muscles are palpated [195]. Muscle relaxation can diminish spasm and pain [196]. Repeated or chronic muscular overload can activate trigger points in the muscle. A report from the Chronic Prostatitis Cohort Study showed that 51% of patients with prostatitis and only 7% of controls had any muscle tenderness. Tenderness in the pelvic floor muscles was only found in the CPP group [127].

In 1999, the first ideas about the neurological aspects of the pelvic floor muscles in relation to CPP were published. The probability of CNS breakdown in the regulation of pelvic floor function was suggested as a mechanism for development of CPP. Of the patients presenting with pelvic pain, 88% had poor to absent pelvic floor function [470]. Basic studies on the role of neurogenic inflammation have also elucidated some important phenomena. Irritation of the prostate, bladder and pelvic floor muscles results in expression of C-fos-positive cells in the CNS. There appears to be convergence of afferent information onto central pathways. Once the central changes have become established, they become independent of the peripheral input that initiated them [197].

Repeated or chronic muscular overload can activate trigger points in the muscle. Trigger points are defined as hyperirritable spots within a taut band. Other criteria for trigger points are: recognition of the pain as ‘familiar’, and pain on stretching the muscle. Apart from pain, trigger points prevent full lengthening of the muscle, thereby restricting the range of movement. Pain as a result of these trigger points is aggravated by specific movements and alleviated by certain positions. Positions and movements in which the shortened muscle is stretched are painful. Patients know which activities and postures influence pain. Trigger points can be located within the pelvic floor muscles and in adjacent muscles such as the abdominal, gluteal and ileopsoas muscles. Pain is aggravated by pressure on the trigger point (e.g., pain related to sexual intercourse). Pain also worsens after sustained or repeated contractions (e.g., pain related to voiding or defecation).

3.3 Abdominal aspects of pelvic pain

3.3.1 ***Incidence***

Epidemiological data on IBS and CPP are scarce. CPP has been shown to be one of the most common functional disorders in women of reproductive age. The monthly incidence rate of CPP published by Zondovan was 1.58/1000.

3.3.2 ***Prevalence***

Using a vague definition of continuous or episodic pain over 6 months situated below the umbilicus one study reported that CPP was the one of most common diagnosis in primary care units in Great Britain [198]. The monthly prevalence rate of CPP in this study was 21.5/1000, with an annual prevalence of 38.3/1000. They increase significantly with older age and vary significantly between regions in the UK. The overall prevalence of anorectal pain in a sample of US householders was 6.6% and was more common in women [199]. IBS is associated with common gynaecologic problems (endometriosis, dyspareunia, and dysmenorrhea) [200]. 50% of women who presented with abdominal pain to the gynaecologic clinic or were scheduled for laparoscopy due to CPP had symptoms of IBS [201]. In a survey from Olmsted county 20 % of women reported CPP and 40% of those met criteria for IBS [202]. This overlap of CPP and IBS was associated with an increased incidence of somatisation. Not gynaecological surgical procedures but only psychosocial variables predict pain

development without a different incidence of IBS in a prospective and controlled study [203]. Clinical features of pelvic floor dysfunction, gynaecological and psychological features are related to disordered anorectal function in IBS patients but do not predict physiological anorectal testing.

*3.3.3 **Influence in QOL***

There is little known on health related quality of life (HRQoL) in patients with CPP and a need to develop validated disease specific HRQoL instruments for CPP in addition to sound measurement properties. More data is available in patients with IBS treated at referral centres who have comparable HRQoL scores as patients with other common disorders such as diabetes, end-stage renal disease, and inflammatory bowel disease [204]. Subgroups of IBS with predominance of diarrhea or constipation show no difference in HRQoL. Multivariate analysis shows that HRQoL in patients with IBS is affected by sex and psychological conditions.

*3.3.4 **Costs***

Costs combine direct health-care costs and societal costs (productivity loss) such as under-performance and absenteism from work. The annual costs to society can be calculated by using the average population earnings. In Germany direct care costs are estimated € 791 and societal costs € 995 per patient with IBS per year which may be comparable to patients with CPP [205].

*3.3.5 **Risk factors & underlying causes***

Risk factors are covered in Section 3.1.5.

3.4 Summary of evidence and recommendations: CPP and mechanisms

Summary of evidence	**LE**
CPP mechanisms are well defined and involve mechanisms of neuroplasticity and neuropathic pain.	2
The mechanisms of neuroplasticity and neuropathic pain result in increased perception of afferent stimuli which may produce abnormal sensations as well as pain.	1
End-organ function can also be altered by the mechanisms of neuroplasticity so that symptoms of function can also occur.	1
The diagnosis of a CPPS as a pain syndrome is essential as it encourages a holistic approach to management with multispecialty and multidisciplinary care.	2

Recommendations	**GR**
All of those involved in the management of CPP should have knowledge of peripheral and central pain mechanisms.	A
The early assessment of patients with CPP should involve: • investigations aimed at specific disease-associated pelvic pain • assessment of functional, emotional, behavioural, sexual and other quality of life issues, such as effect on work and socialisation.	A
CPPS patients should be managed in a multispecialty and multidisciplinary environment with consideration of all their symptoms.	A

CPP = chronic pelvic pain; CPPS = chronic pelvic pain syndrome.

4. DIAGNOSTIC EVALUATION

4.1 General Evaluation

*4.1.1 **History***

History is very important for the evaluation of patients with CPP. Pain syndromes are symptomatic diagnoses, which are derived from a history of pain perceived in the region of the pelvis, and absence of other pathology, for a minimum of 3 out of the past 6 months. This implies that specific disease-associated pelvic pain caused by bacterial infection, cancer, primary anatomical or functional disease of the pelvic organs, and neurogenic disease must be ruled out.

4.1.1.1 Anxiety, depression, and overall function

Distress is best understood in the context of pain and of the meaning of pain to the individual and is best assessed ideographically rather than normatively. Almost all diagnostic measures and standardised instruments of anxiety and depression are designed for people without significant physical problems, so are hard to interpret in CPP [206-208].

Anxiety about pain often refers to fears of missed pathology (particularly cancer) as the cause of pain, or to uncertainties about treatment and prognosis. The question: “What do you believe or fear is the cause of your pain?” has been suggested [209]. Anxiety may also concern urinary urgency and frequency as a possible problem in social settings.

Depression or depressed mood are common in chronic pain [e.g [210], often related to losses consequent to chronic pain (work, leisure activities, social relationships, etc.). Because of the lack of suitable assessment instruments, it is better to ask a simple question such as “How does the pain affect you emotionally?” If the answer gives cause for concern about the patient’s emotional state, further assessment should be undertaken by an appropriately qualified colleague.

Most measures of restricted function are designed primarily for musculosketal pain and may emphasise mobility problems rather than the difficulties of the individual with pelvic or urogenital pain. A promising specific measure, UPOINT, is available [211]. Generic quality of life measures are helpful. If such an instrument is not already used in the clinic, the Brief Pain Inventory [212] provides a broad and economical assessment of interference of pain with various aspects of life in various languages. (For further suggested instruments see [213]). In a study, more pain, pain-contingent rest, and urinary symptoms were associated with poorer function [49].

4.1.1.2 Urological aspects

Pain may be associated with urological symptoms. A detailed history of lower urinary tract functions should be taken. Dysfunctions of the lower urinary tract may exacerbate symptoms, as pain may interfere with the function of the lower urinary tract. Micturition in all its aspects should be addressed. Special attention should be paid to the influence of micturition on the experience of pain.

Prostate pain syndrome

PPS is diagnosed from a history of pain perceived in the region of the prostate (convincingly reproduced by prostate palpation), and absence of other lower urinary tract pathology, for a minimum of 3 out of the past 6 months. As mentioned above, specific disease-associated pelvic pain must be ruled out.

A thorough history is an important first step in the evaluation of PPS. It should include type of pain and localisation. Pain is often reported in other pelvic areas outside the prostate such as perineum, rectum, penis, testicles and abdomen [41]. In addition, associated lower urinary tract symptoms, sexual function, psychological, social and economic factors should be addressed. Determination of the severity of disease, its progression and treatment response can be assessed only by means of a validated symptom-scoring instrument (see section 4.2.3). These subjective outcome measures are recommended for the basic evaluation and therapeutic monitoring of patients in urological practice.

Bladder pain syndrome

BPS should be diagnosed on the basis of pain, pressure or discomfort associated with the urinary bladder, accompanied by at least one other symptom, such as daytime and/or night-time increased urinary frequency, the exclusion of confusable diseases as the cause of symptoms, and if indicated, cystoscopy with hydrodistension and biopsy (Table 4) [11].

The nature of pain is key to disease definition:

1. Pain, pressure or discomfort perceived to be related to the bladder, increasing with increasing bladder content.
2. Located suprapubically, sometimes radiating to the groins, vagina, rectum or sacrum.
3. Relieved by voiding but soon returns [214-218].
4. Aggravated by food or drink [218].

BPS type 3 can lead to a small capacity fibrotic bladder with or without upper urinary tract outflow obstruction.

4.1.1.3 Gynaecological aspects

A detailed medical history outlining the nature, frequency and site of pain; its relationship to precipitating

factors and the menstrual cycle, may help define the aetiology. A menstrual and sexual history, including a history of sexually transmitted diseases, vaginal discharge, as well as previous sexual trauma is mandatory as well as up to date cervical cancer screening.

4.1.1.4 Gastrointestinal aspects

The predominant symptoms that patients are interviewed about are discomfort or pain in relation to their bowel habits, daily activities, and eating. A precise history of dysfunctional voiding or defecation should be asked, ideally applying symptom questionnaires for urinary and anorectal symptoms (e.g., Rome III criteria for anorectal pain). Excessive straining at most defecations, anal digitations in dyssynergic defecation, and a sensation of anal blockage may be found in patients with chronic anal pain. History of anxiety and depression with impaired QoL is often encountered in anorectal functional disorders and should be evaluated.

Diagnostic criteria for chronic anal pain syndrome (chronic proctalgia) according to the Rome III criteria are as follows and must include all of the following: chronic or recurrent rectal pain or aching, episodes last at least 20 min and exclusion of other causes of rectal pain such as ischaemia, inflammatory bowel disease, cryptitis, intramuscular abscess and fissure, haemorrhoids, prostatitis, and coccygodynia. These criteria should be fulfilled for the past 3 months with symptom onset at least 6 months before diagnosis [219].

The chronic anal pain syndrome includes the above diagnostic criteria and exhibits exquisite tenderness during posterior traction on the puborectalis muscle (previously called " Levator Ani Syndrome"). Pathophysiology of pain is thought to be due to overactivity of the pelvic floor muscles.

Intermittent chronic anal pain syndrome (proctalgia fugax) consists of all the following diagnostic criteria, which should be fulfilled within three months: recurrent episodes of pain localised to the anus or lower rectum, episodes last from several seconds to minutes and there is no anorectal pain between episodes.
Stressful life events or anxiety may precede the onset of the intermittent chronic anal pain syndrome. The attacks may last from a few seconds to as long as 30 min. The pain may be cramping, aching or stabbing and may become unbearable. However, most patients do not report it to their physicians and pain attacks occur less than five times a year in 51% of patients.

4.1.1.5 Peripheral nerve aspects

A proportion of patients will be able to relate the onset of pain to an acute event such as surgery, sepsis or trauma, and occasionally, cycling for a prolonged period. Chronic injury is more frequent, such as associated with sitting for prolonged periods over time. Many will be idiopathic.

The pain is classically perceived in the perineum from anus to clitoris/penis. However, less-specific pain distribution may occur, and this may be due to anatomical variation, involvement of branches of the nerve rather that the main nerve, CNS central sensitisation, and consequently, the involvement of other organs and systems in a regional pain syndrome. Other nerves in the vicinity may also be involved, for example, inferior cluneal nerve and perineal branches of the posterior femoral cutaneous nerve. The musculoskeletal system may become involved, confusing the pain picture as aches and pain developing in the muscles due to immobility and disability, possibly magnified by the CNS changes.

Burning is the most predominant adjective used to describe the pain. Crushing and electric may also be used, indicating the two components - a constant pain often associated with acute sharp episodes. Many patients may have the feeling of a swelling or foreign body in the rectum or perineum, often described as a golf or tennis ball. The term pain has different meanings to patients and some would rather use the term discomfort or numbness.

Aggravating factors include any cause of pressure being applied, either directly to the nerve or indirectly to other tissue, resulting in pudendal traction. Allodynia is pain on light touch due to involvement of the CNS, and may make sexual contact and the wearing of clothes difficult. These patients often remain standing, and as a consequence, develop a wide range of other aches and pains. Soft seats are often less well tolerated, whereas sitting on a toilet seat is said to be much better tolerated. If unilateral, sitting on one buttock is common. The pain may be exacerbated by bowel or bladder evacuation.

Pudendal nerve damage may be associated with a range of sensory phenomena. In the distribution of the nerve itself, as well as unprovoked pain; the patient may have paraesthesia (pins and needles); dysaesthesia (unpleasant sensory perceptions usually but not necessarily secondary to provocation, such as the sensation of running cold water); allodynia (pain on light touch); or hyperalgesia (increased pain perception following a

painful stimulus, including hot and cold stimuli). Similar sensory abnormalities may be found outside of the area innervated by the damaged nerve, particularly for the visceral and muscle hyperalgesia.

The cutaneous sensory dysfunction may be associated with superficial dispareunia, but also irritation and pain associated with clothes brushing the skin. There may also be a lack of sensation and pain may occur in the presence of numbness. Visceral hypersensitivity may result in an urge to defecate or urinate. This is usually associated with voiding frequency, with small amounts of urine being passed. Pain on visceral filling may occur. Anal pain and loss of motor control may result in poor bowel activity, with constipation and/or incontinence. Ejaculation and orgasm may also be painful or reduced.

Many of those suffering from pudendal neuralgia complain of fatigue and generalised muscle cramps, weakness and pain. Being unable to sit is a major disability, and over time, patients struggle to stand and they often become bedbound. The immobility produces generalised muscle wasting, and minimal activity hurts. As a consequence of the widespread pain and disability, patients often have emotional problems, and in particular, depression. Patients with CPP are also often anxious and have the tendency to catastrophise. Depression, catastrophising and disability are all poor prognostic markers. Cutaneous colour may change due to changes in innervation but also because of neurogenic oedema. The patient may describe the area as swollen due to this oedema, but also to the lack of afferent perception.

4.1.1.6 Myofascial aspects

When taking a history from a patient with pelvic pain it is important to address the function of all the organs in the pelvic area.The following items certainly should be addressed: lower urinary tract function, anorectal function, sexual function, gynaecological items, presence of pain and psycho-social aspects. One cannot state that there is a pelvic floor dysfunction based only on the history. But there is a suspicion of pelvic floor muscle dysfunction when two or more pelvic organs show dysfunction, for instance a combination of micturition and defecation problems.

4.1.2 ***Physical Evaluation***

The clinical examination often serves to confirm or refute the initial impressions gained from a good history. The examination should be aimed at specific questions where the outcome of the examination may change management. Prior to an examination, best practice requires the medical practitioner to explain what will happen and what the aims of the examination are to the patient. Consent to the examination should occur during that discussion and should cover an explanation around the aim to maintain modesty as appropriate and if necessary why there is a need for rectal and/or vaginal examination. Finally, the risk of exacerbating the pain should form a part of that request. A record of the discussion should be noted. The possibility of the presence of a chaperone should be discussed with the patient. As well as a local examination, a general musculoskeletal and neurological examination should be considered an integral part of the assessment and undertaken if appropriate. Following the examination, it is good practice to ask the patient if they had any concerns relating to the conduct of the examination and that discussion should be noted.

There is no specific diagnostic test for chronic pelvic pain syndromes, therefore, procedures are on the one hand directed towards identification and exclusion of specific diseases associated with pelvic pain, and on the other hand may be used for phenotypic description. Abdominal and pelvic examination to exclude gross pelvic pathology, as well as to demonstrate the site of tenderness is essential. Abnormalities in muscle function should also be sought. Examination of the external genitalia is a part of the evaluation. In patients with scrotal pain, gentle palpation of each component of the scrotum is performed to search for masses and painful spots. The penis and urethra may be palpated in a similar way. Many authors recommend that one should assess cutaneous allodynia along the dermatomes of the abdomen (T11-L1) and the perineum (S3), and the degree of tenderness should be recorded. The bulbocavernosa reflex in the male may also provide useful information concerning the intactness of the pudendal nerves. Clinical pelvic examination should be a single digit examination if possible. The usual bimanual examination can generate severe pain so the examiner must proceed with caution. A rectal examination is done to look for prostate abnormalities in male patients including pain on palpation and to examine the rectum and the pelvic floor muscles regarding muscle tenderness and trigger points.

At clinical examination, perianal dermatitis may be found as a sign of faecal incontinence or diarrhoea. Fissures may be easily overlooked and should be search for thoroughly in patients with anal pain. Rectal digital examination findings may show high or low anal sphincter resting pressure, a tender puborectalis muscle in patients with the Levator Ani Syndrome, and occasionally increased perineal descent. The tenderness during posterior traction on the puborectalis muscle differentiates between Levator Ani Syndrome and Unspecified

Functional Anorectal Pain and is used in most studies as the main inclusion criterion. Dyssynergic (paradoxical) contraction of the pelvic muscles when instructed to strain during defecation is a frequent finding in patients with pelvic pain. Attention should be paid to anal or rectal prolapse at straining, and ideally during combined rectal and vaginal examination to diagnose pelvic organ prolapse.

A full clinical examination of the spinal, muscular, nervous and urogenital systems is necessary to aid in diagnosis of pudendal neuralgia, especially to detect signs indicating another pathology. Often, there is little to find in pudendal neuralgia and frequently findings are non-specific. The main pathognomonic features are the signs of nerve injury in the appropriate neurological distribution, for example, allodynia or numbness. Tenderness in response to pressure over the pudendal nerve may aid the clinical diagnosis. This may be elicited by per rectal or per vaginal examination and palpation in the region of the ischeal spine and/or Alcock's canal. Muscle tenderness and the presence of trigger points in the muscles may confuse the picture. Trigger points may be present in a range of muscles, both within the pelvis (levator ani and obturator internus muscles) or externally (e.g., the piriformis, adductors, rectus abdominus or paraspinal muscles).

4.2 Supplemental evaluation

If history is suggestive of lower urinary tract, gynaecological, anorectal or other known etiology disease diagnostic workup should follow respective guidelines.

*4.2.1 **Assessing pain and related symptoms***

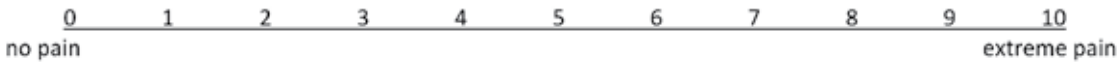
Determination of the severity of disease, its progression and treatment response can be assessed only by means of a reliable symptom-scoring instrument. These subjective outcome measures are recommended for the basic evaluation and therapeutic monitoring of patients. Pain should always be assessed (see below) to identify progression and treatment response. As well as doing this in the clinic, the patient can keep a daily record (pain diary). This may need to include other relevant variables such as voiding, sexual activity, activity levels, or analgesic use.

Increased attention to patient reported outcomes gives prominence to patients' views on their disease and pain diaries, in patients' own environments, improve data quality.

QoL should also be measured because it can be very poor compared to other chronic diseases [42, 43]. In a study [49] more pain, pain-contingent rest, and urinary symptoms were associated with greater disability (also measured by self-report), and pain was predicted by depression and by catastrophising (helplessness subscale).

Where the primary outcome of treatment is pain relief, it is useful before starting treatment to agree a clinically useful level of relief (see [220]). The most reliable methods are:

A 5 point verbal scale: none, mild, moderate, severe, very severe pain
A VAS score from 1 to 10



Pain assessment ratings are not independent of cognitive and emotional variables [10]. Target outcomes of pain severity, distress and disability co-vary only partly, and improvement in one does not necessarily imply improvement in the others. When the primary outcome is pain its meaning should be anchored in discussion of clinically important difference (e.g. see [220].

Prostate pain syndrome
Reliable, valid indices of symptoms and QoL are the NIH-CPSI [221] and the International Prostate Symptom Score (I-PSS) [222].

Bladder pain syndrome
Symptom scores may help to assess the patient and act as outcome measures. The O'Leary-Sant Symptom Index, also known as the Interstitial Cystitis Symptom Index (ICSI) was validated in a large study [223].

Gastrointestinal questionnaire
The functional anorectal pain disorders (anorectal pelvic pain) are defined and characterised by duration,

frequency, and quality of pain. More complex questionnaires are used in the setting of IBS. The validated IBS-Symptom Severity Scale (IBS-SSS) includes the broadest measurement of pain-related aspects [224, 225]. However, as different instruments measure different endpoints of chronic abdominal pain in IBS, a comparison of published studies is often impossible.

Sexual function assessment
In males most frequent effects on sexual function are erectile disfunction and premature ejaculation. These can be evaluated by proper questionnaires namely IIEF (international index of erectile function) and PEDT (premature ejaculation diagnostic tool). In comparison with controls, women with CPP reported significantly more sexual avoidance behaviour, non-sensuality, and complaints of "vaginismus" [188]. The female sexual function index (FSFI) has been developed as a brief, multidimensional self-report instrument for assessing the key dimensions of sexual function in women, which includes desire, subjective arousal, lubrication, orgasm, satisfaction, and pain.

4.2.2 Focused myofascial evaluation
Pelvic floor muscle testing can be done by the medical doctor but a consultation of the pelvic floor physiotherapist is a good alternative. A vaginal or rectal examination is performed to assess the function of the pelvic floor muscles, according to the International Continence Society (ICS) report. This assessment has been tested and shows satisfactory face validity and intra-observer reliability. It can therefore be considered suitable for use in clinical practice [226]. Rectal examination is a good way to test the pelvic floor function in men [227]. In a cohort study of 72 men with CPP, the relationship between the locations of the trigger point and the referred pain was examined. Ninety percent of the patients showed tenderness in the puborectalis muscle and 55% in the abdominal wall muscles. Of the patients in whom trigger points were found in the puborectalis, 93% reported pain in the penis and 57% in the suprapubic region. Patients with trigger points in the abdominal muscles reported pain in the penis (74%), perineum (65%) and rectum (46%) [228].

4.2.3 Neurological

Injections
An injection of local anaesthetic and steroid at the sight of nerve injury may be diagnostic. Differential block of the pudendal nerve helps to provide information in relation to the site where the nerve may be trapped [229-239]. Infiltration at the ischeal spine requires the use of a nerve stimulator/locator. Both motor (anal contraction) and sensory endpoints may be noted. The anatomical endpoint may be localised by fluoroscopy, computed tomography (CT) guidance, or the use of ultrasound (US). Ultrasound avoids any form of radiation, whereas CT guidance involves a significant amount of radiation. Currently, fluoroscopy is probably the imaging technique most frequently used because it is readily available to most anaesthetists that perform the block. Currently, infiltration of the pudendal nerve within Alcock's canal is primarily undertaken with the use of CT. As well as injecting around the pudendal nerve, specific blocks of other nerves arising from the pelvis may be performed.

Electrophysiological studies
These may reveal signs of perineal denervation, increased pudendal nerve latency, or impaired bulbocavernosal reflex [305, 312, 317-319]. However, for an abnormality to be detected, significant nerve damage is probably necessary. Pain may be associated with limited nerve damage, therefore, these investigations are often normal.

4.2.4 Imaging
Ancillary studies should be performed according to appropriate guidelines for exclusion of diseases with known aetiology presenting with symptoms identical to those of CPP. Once the latter diagnosis is established studies can be useful to assess functional abnormalities and phenotype conditions such as BPS, and chronic anal pain syndrome.

Ultrasound
Has limited value but may reassure patients. However, over-investigating may be detrimental.

MRI
MR neurography has been increasingly used in specialised centers for the diagnosis of location (proximal versus peripheral) and degree (total versus partial) of nerve injury in the peripheral nervous system, earlier and with higher specificity than conduction studies.

MR defecating proctogram
MRI in conjunction with MR defecography has become the most valuable imaging technique to assess

anorectal function dynamically. MRI studies outline simultaneously the anatomy of the pelvic floor and visualise different structural and functional pathologies, by applying dynamic sequences after filling of the rectum with a viscous contrast medium (e.g., US gel). The following pathologies can be visualised: pelvic floor descent, an abnormal anorectal angle while squeezing and straining, rectal intussusception, rectocele, enterocele and cystocele. However, limitations of MR defecography are the left lateral position and the limited space for the patient, which may reduce the ability to strain and hereby reduce the sensitivity of the method, underestimating the size of entero- and rectoceles as well as the amount of interception.

4.2.5 Laboratory Tests

Microbiology tests

Prostate pain syndrome

Laboratory diagnosis has been classically based on the four-glass test for bacterial localisation [240]. Besides sterile pre-massage urine (voided bladder urine-2), PPS shows < 10,000 cfu of uropathogenic bacteria in expressed prostatic secretions and insignificant numbers of leukocytes or bacterial growth in ejaculates. However, this test is too complex for use by practising urologists. Diagnostic efficiency may be enhanced cost-effectively by a simple screening procedure, that is, the two-glass test or pre-post-massage test (PPMT) [241-243]. Overall, these tests help only a little in the diagnosis of PPS, because 8% of patients with suggested PPS have been found to have positive prostatic localisation cultures, similar to the percentage of asymptomatic men [244].

Bladder pain syndrome

Urine dipstick and urine culture (including culture for TB if sterile pyuria) are recommended in all patients suspected of having BPS. Urine cytology is also recommended in risk groups.

Gynaecological aspects of chronic pelvic pain

Vaginal and endocervical swabs to exclude infection are recommended.

4.2.6 Invasive tests

Anorectal pain

Anorectal manometry with sensory testing (pressure volume meaurement: barostat) may be useful to diagnose dyssynergic defaecation and hypersensitivity of the rectum which are typical for patients with chronic pelvic pain and IBS. Flexible rectosigmoidoscopy or colonoscopy should be considered in patients with anorectal pain according to performed to rule out coincidental colorectal pathology.

Laparoscopy for females

Laparoscopy is perhaps the most useful invasive investigation to exclude gynaecological pathology [245, 246] and to assist in the differential diagnosis of CPP in women [247]. Often, it is combined with cystoscopy [248, 249] and/or proctoscopy to help identify the site of multi-compartment pain.

Psychological considerations around laparoscopy

Three very different studies of laparoscopy suggest that it can improve pain through resolving concerns about serious disease [250], although showing women the photograph of their pelvic contents did not improve on explanation alone [251]; and integrating somatic and psychological assessment from the start rather than dealing with psychological concerns only after excluding organic causes of pelvic pain [252].

Cystoscopy and bladder biopsy

Despite controversy on the diagnostic and follow-up value of cystoscopy in BPS [253-257], this panel believes that objective findings are important for diagnosis, prognosis and ruling out other treatable conditions (a standardised scheme of diagnostic criteria will also contribute to uniformity and comparability of different studies [258]). Endoscopically, BPS type 3 displays reddened mucosal areas often associated with small vessels radiating towards a central scar, sometimes covered by a small clot or fibrin deposit - the Hunner lesion [217]. The scar ruptures with increasing bladder distension, producing a characteristic water fall type of bleeding. There is a strong association between BPS type 3 and reduced bladder capacity under anaesthesia [259]. Non-lesion disease displays a normal bladder mucosa at initial cystoscopy. The development of glomerulations after hydrodistension is considered to be a positive diagnostic sign although they can be observed without BPS [260]. Biopsies are helpful in establishing or supporting the clinical diagnosis of both classic and non-lesion types of the disease [137, 162, 258, 261, 262]. Important differential diagnoses to exclude, by histological examination, are carcinoma in situ and tuberculous cystitis.

Table 4: ESSIC classification of BPS types according to results of cystoscopy with hydrodistension and biopsies [11]

	Cystoscopy with hydrodistension			
	Not done	**Normal**	**Glomerulations[a]**	**Hunner's lesion[b]**
Biopsy				
Not done	XX	1X	2X	3X
Normal	XA	1A	2A	3A
Inconclusive	XB	1B	2B	3B
Positive[c]	XC	1C	2C	3C

[a]*Cystoscopy: glomerulations grade 2-3*
[b]*Lesion per Fall's definition with/without glomerulations*
[c]*Histology showing inflammatory infiltrates and/or detrusor mastocytosis and/or granulation tissue and/or intrafascicular fibrosis.*

4.3 Diagnostic algorithm

Figure 1: Diagnosing chronic pelvic pain

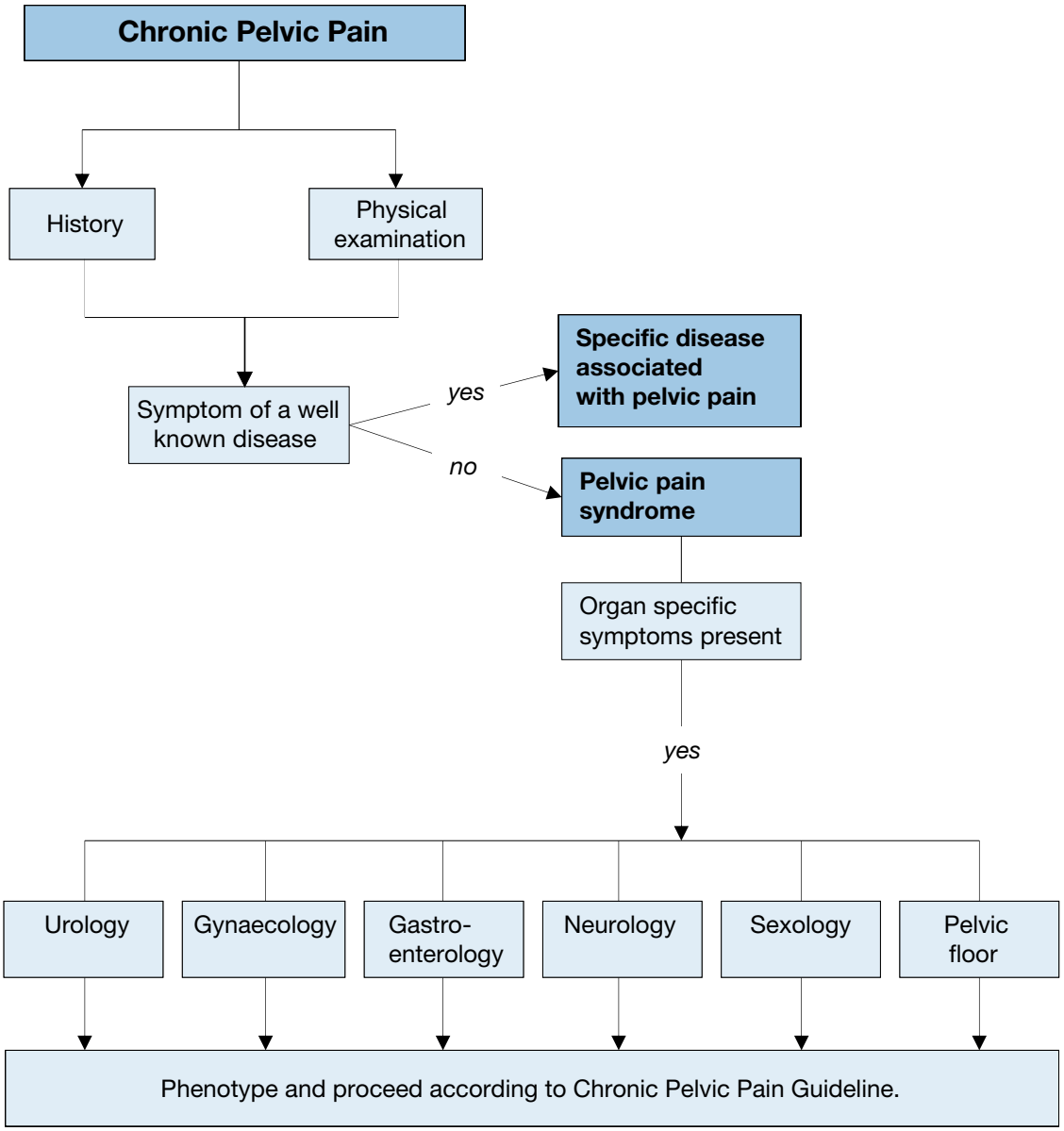


Figure 2: Phenotyping of pelvic pain - UPOINT classification

Phenotyping	Assessment
Urology	Urinary flow, micturition diary, cystoscopy, ultrasound, uroflowmetry,
Psychology	Anxiety about pain, depression and loss of function, history of negative sexual experiences
Organ specific	Ask for gynaecological, gastro-intestinal, ano-rectal, sexological complaints Gynaecological examination, rectal examination
Infection	Semen culture and urine culture, vaginal swab, stool culture
Neurological	Ask for neurological complaints (sensory loss, dysaesthesia). Neurological testing during physical examination: sensory problems, sacral reflexes and muscular function.
Tender muscle	Palpation of the pelvic floor muscles, the abdominal muscles and the gluteal muscles

4.4 Other painful conditions without a urological cause

Dysmenorrhoea
Menstrual pain or 'dysmenorrhoea' may be primary or secondary. Primary dysmenorrhoea classically begins at the onset of ovulatory menstrual cycles and tends to decrease following childbirth [247]. Secondary dysmenorrhoea suggests the development of a pathological process, such as endometriosis [246], adenomyosis [263] or pelvic infection, which need to be excluded.

Infection
In premenopausal women, a history of pelvic inflammatory disease (PID) must be excluded. A patient's sexual history should be taken along with swabs to exclude chlamydia and gonorrhoea infection. Bacterial and viral genital tract pathogens should also be excluded [264], as they can cause severe pelvic/vaginal/vulvar pain [265] and are associated with ulcerating lesions and inflammation, which may lead to urinary retention [266]. If there is any doubt about the diagnosis, laparoscopy may be helpful, as one of the differential diagnosis is endometriosis.

Endometriosis and adenomyosis
The incidence of endometriosis is rising in the developed world. The precise aetiology is unknown, but an association with nulliparity is well known. A diagnosis is usually made when a history of secondary dysmenorrhoea and/or dyspareunia exists. On examination, there is often tenderness in the lateral vaginal fornices, reduced uterine mobility, tenderness in the recto-vaginal septum, and on occasion, adnexal masses. Laparoscopy is the most useful diagnostic tool [267-269].
Endometriotic lesions affecting the urinary bladder or causing ureteric obstructions can occur, as well as lesions affecting the bowel, which may lead to rectal bleeding in association with menstruation. Adenomyosis is associated with augmented pain during menses. It is diagnosed by an US scan of the uterus, which often shows cystic dilatation of the myometrium [270].

Gynaecological malignancy
The spread of gynaecological malignancy of the cervix, uterine body or ovary will cause pelvic pain depending on the site of spread

Injuries related to childbirth
Trauma occurring at the time of childbirth may lead to CPP related to the site of injury. Female sexual dysfunction is perhaps the commonest presenting problem [271]. There is often a transient problem with oestrogen deficiency in the postpartum period and during breastfeeding, which can compound this situation. Denervation of the pelvic floor with re-innervation may also lead to dysfunction and pain.

Pain associated with pelvic organ prolapse and prolapse surgery
Pelvic organ prolapse is often asymptomatic, unless it is so marked that it causes back strain, vaginal pain

and skin excoriation [272]. Prolapse is often a disease of older women, and it is often associated with post-menopausal oestrogen deficiency, which may lead to pain associated with intercourse. Prolapse surgery may entail the use of non-absorbable mesh (usually in the form of "mesh kits") [273-275]. Although they may have a role in supporting the vagina, they are also associated with several complications including bladder, bowel and vaginal trauma [274]. In a subset of these patients, chronic pain may ensue, because mesh insertion may cause nerve and muscle irritation [271]. Patients should be fully evaluated clinically and may need specialised imaging, using contrast mediums if necessary, to make a diagnosis.

Haemorrhoids

Chronic pelvic pain is rare in haemorrhoidal disease because endoscopic and surgical treatment is mostly effective in acute disease. The most frequent aetiology of pain without significant bleeding is thrombosed external haemorrhoids or an anal fissure. Haemorrhoidal pain on defecation associated with bleeding is usually due to prolapse or ulceration of internal haemorrhoids. Anaemia from haemorrhoidal bleeding is rare but may arise in patients on anticoagulation therapy, or those with clotting disorders

Anal fissure

Anal fissures are tears in the distal anal canal and induce pain during and after defecation. The pain can last for several minutes to hours. Persistence of symptoms beyond 6 weeks or visible transversal anal sphincter fibres define chronicity. Fissures located off the midline are often associated with specific diseases such as Crohn's disease or anal cancer. Internal anal sphincter spasms and ischaemia are associated with chronic fissures.

Proctitis

Abdominal and pelvic pain in patients with inflammatory bowel disease and proctitis are often difficult to interpret. Faecal calprotectin may help to differentiate between inflammation and functional pain, to spare steroids.

Irritable bowel syndrome

Although IBS can be associated with pelvic pain, the authors of these guidelines consider a full discussion of this topic beyond the scope of these guidelines. A number of high quality clinical guidelines address this topic [276, 277].

4.5 Summary of evidence and recommendations: diagnostic evaluation

4.5.1 Diagnostic evaluation of PPS

Summary of evidence	LE
PPS is associated with negative cognitive, behavioural, sexual, or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction.	2b
PPS has no known single aetiology.	3
Pain in PPS involves mechanisms of neuroplasticity and neuropathic pain.	2a
PPS has a high impact on QoL.	2b
Depression and catastrophic thinking are associated with more pain and poorer adjustment.	3
The prevalence of PPS-like symptoms is high in population-based studies (> 2%).	2b
Reliable instruments assessing symptom severity as well as phenotypic differences exist.	2b

Recommendations	GR
Adapt diagnostic procedures to the patient. Specific diseases with similar symptoms must be excluded.	A
Use a validated symptom and quality of life scoring instrument, such as the NIH-CPSI, for initial assessment and follow-up.	B
Assess prostate pain syndrome associated negative cognitive, behavioural, sexual, or emotional consequences, as well as symptoms of lower urinary tract and sexual dysfunctions.	B

4.5.2 *Diagnostic evaluation of BPS*

Summary of evidence	LE
BPS has no known single aetiology.	3
Pain in BPS does not correlate with bladder cystoscopic or histologic findings.	2a
BPS Type 3 C can only be confirmed by cystoscopy and histology.	2a
Lesion/non-lesion disease ratios of BPS are highly variable between studies.	2a
The prevalence of BPS-like symptoms is high in population-based studies.	2a
BPS occurs at a level higher than chance with other pain syndromes	2a
BPS has an adverse impact on quality of life.	2a
Reliable instruments assessing symptom severity as well as phenotypical differences exist.	2a

Recommendations	GR
Patients with bladder pain should undergo general anaesthetic rigid cystoscopy in accordance with ESSIC guidelines	A
After primary exclusion of specific diseases, patients with symptoms according to the above definition should be diagnosed with BPS by subtype and phenotype.	A
Assess BPS associated non-bladder diseases systematically.	A
Assess BPS associated negative cognitive, behavioural, sexual, or emotional consequences.	A
Use a validated symptom and quality of life scoring instrument for initial assessment and follow-up.	B

BPS = Bladder pain syndrome.

4.5.3 *Diagnostic evaluation of scrotal pain syndrome*

Summary of evidence	LE
The nerves in the spermatic cord play an important role in scrotal pain.	2b
Ultrasound of the scrotal content does not aid in diagnostics or treatment of scrotal pain.	2b
Post-vasectomy pain is seen in a substantial number of men undergoing vasectomy.	2b
Scrotal pain is more often noticed after laparoscopic than after open inguinal hernia repair.	1b

4.5.4 *Diagnostic evaluation of urethral pain syndrome*

Summary of evidence	LE
Urethral pain syndrome may be a part of BPS.	2a
Urethral pain involves mechanisms of neuroplasticity and neuropathic pain.	2b

4.5.5 *Diagnostic evaluation of gynaecological aspects chronic pelvic pain*

Summary of evidence	LE
Clinical history and examination are mandatory to making a diagnosis.	2a
Laparoscopy is well tolerated and does not appear to have negative psychological effects	1b

Recommendations	GR
All women with pelvic pain should have a full gynaecological history and evaluation, including laparoscopy to rule out a treatable cause (e.g. endometriosis).	A

4.5.6 *Diagnostic evaluation of anorectal pain syndrome*

Summary of evidence	LE
Tenderness on traction is the main criterion of the chronic anal pain syndrome.	1a

Recommendations	GR
Functional testing is recommended in patients with anorectal pain.	A

4.5.7 Diagnostic evaluation of pudendal neuralgia

Summary of evidence	LE
Multiple sensory and functional disorders within the region of the pelvis/urogenital system may occur as a result of injury to one or more of many nerves. The anatomy is complex.	2
There is no single aetiology for the nerve damage and the symptoms and signs may be few or multiple.	1
Investigations are often normal.	2
The peripheral nerve pain syndromes are frequently associated with negative cognitive, behavioural, sexual, or emotional consequences.	1

Recommendations	GR
Rule rule out confusable diseases.	A
If a peripheral nerve pain syndrome is suspected, early referral should occur to an expert in the field, working within a multidisciplinary team environment.	B
Imaging and neurophysiology helps diagnosis but image and nerve locator guided local anaesthetic injection is preferable.	B

4.5.8 Diagnostic evaluation of sexological aspects in CPP

Summary of evidence	LE
Chronic pain can lead to decline in sexual activity and satisfaction and may reduce relationship satisfaction.	2a
Patients who reported having sexual, physical or emotional abuse show a higher rate of reporting symptoms of PPS.	2b
Sexual dysfunctions are prevalent in patients with PPS.	2b
In men with PPS the most prevalent sexual complaints are erectile dysfunction and ejaculatory dysfunction.	3
In females with CPPS all sexual function domains are lower. The most reported dysfunctions are sexual avoidance, dyspareunia and “vaginismus”.	2a
Vulvar pain syndrome is associated with BPS.	3
Women with BPS suffer significantly more from fear of pain, dyspareunia and decreased desire.	2a
Pelvic floor muscle function is involved in the excitement and orgasm phases of sexual response.	3
Chronic pain can cause disturbances in each of the sexual response cycle phases.	2b

Recommendations	GR
Patients presenting with symptoms suggestive for chronic pelvic pain syndrome, should be screened for abuse, without suggesting a causal relation with the pain.	B
The biopsychosocial model should be applied in the evaluation of the effect of chronic pelvic pain syndrome on the sexual function of the patient.	B
The biopsychosocial model should be incorporated in research in the role of chronic pelvic pain in sexual dysfunction.	B

4.5.9 Diagnostic evaluation of psychological aspects of CPP

Summary of evidence	LE
There is no evidence that distress generates complaints of pelvic pain, or that multiple symptoms suggest unreality of pain.	2b
Current or recent sexual abuse are possible contributory factors in pelvic pain.	2a

Recommendations	GR
Psychological distress is common in pelvic pain in women, but should be interpreted in the context of pain.	A
Ask patients what they think is the cause of their pain to allow the opportunity to inform and reassure as appropriate.	B

*4.5.10 **Diagnostic evaluation of pelvic floor function***

Summary of evidence	LE
The ICS classification is suitable for clinical practice.	2a
Overactivity of the pelvic floor muscles is related to chronic pelvic pain, prostate, bladder and vulvar pain.	2a
Overactivity of the pelvic floor muscles is an input to the central nervous system causing central sensitisation.	2b
There is no accepted standard for diagnosing myofascial trigger points.	2a
There is a relation between the location of trigger point and the region where the pain is perceived.	3

Recommendations	GR
Use ICS classification on pelvic floor muscle function and dysfunction.	A
In patients with chronic pelvic pain syndrome it is recommended to actively look for the presence of myofascial trigger points.	B

5. MANAGEMENT

The philosophy for the management of chronic pelvic pain is based on a biopsychosocial model. This is a holistic approach with the patients' active involvement. Single interventions rarely work in isolation and need to be considered within a broader personalised management strategy.

The management strategy may well have elements of self-management. Pharmacological and non-pharmacological interventions should be considered with a clear understanding of the potential outcomes and end points. These may well include: psychology, physiotherapy, drugs and more invasive interventions.

Treatment philosophy
Providing information that is personalised and responsive to the patient's problems, conveying belief and concern, is a powerful way to allay anxiety [278]. Additional written information or direction to reliable sources of information is useful; practitioners tend to rely on locally produced material or pharmaceutical products of variable quality while endorsing the need for independent materials for patients [279].

5.1 Conservative management

*5.1.1 **Pain education***
It is always valuable to include education about the causes of pain, including eliciting from patients their anxieties about undiscovered pathology and addressing them. Information improves adherence to treatment and underpins self-management, as shown in many other painful and nonpainful disorders but not specifically in pelvic and abdominal pain.

*5.1.2 **Physical therapy***
The physiotherapist is part of the pain management team, together with the pain doctor and the psychologist. The therapeutic options for physiotherapists may not be the same in every country. Physiotherapists can either specifically treat the pathology of the pelvic floor muscles, or more generally treat myofascial pain if it is part of the pelvic pain syndrome. In most studies that have been done looking at the effect of physiotherapy in pelvic pain the treatment of the pelvic floor is only part of the pain management. In a review about physiotherapy in women with pelvic pain, it was concluded that recommendations for physiotherapy should be given with caution [280]. They found 6 RCT's of which three showed level 1b evidence with low risk of bias. One of these three found that Mensendieck somatocognitive therapy showed a pain reduction after 1 year follow-up of 64%.

This approach consists of myofascial relaxation and tension, improving posture and movement in combination with CBT [281].

Pelvic floor muscle pain

Treating pelvic floor overactivity and myofascial trigger points should be considered in the management of CPP. Treatment should be done by specialised physiotherapists who are trained not only in the musculoskeletal aspects of pain, but also in the psychological mechanisms and the role of the CNS in chronic pain.

For patients with CPP and dysfunction of the pelvic floor muscles, it is very helpful to learn how to relax the muscles when the pain starts. By doing this, the circle of pain-spasm-pain can be interrupted. In the case of shortened muscles, relaxation alone is not enough. Stretching of the muscle is mandatory to regain length and function. Studies on physical therapy for pelvic floor pain syndrome have been sparse. A single blinded RCT with myofascial physical therapy and general massage was carried out in patients with prostate or bladder pain. The global response rate to treatment with massage was significantly better in the prostate than in the bladder pain group (57% vs. 21%). In the prostate pain group, there was no difference between the two treatment arms. In the bladder pain group, myofascial treatment did significantly better than the massage. Massage only improved complaints in the prostate pain group. The fact that the prostate pain group consisted of only men is mentioned as a possible confounding factor [282].

Myofacial trigger point release (MTrP's)

Treatment of MTrP's can be done by manual therapy, dry needling and wet needling. The evidence for all the different treatments is weak, with most studies showing no significant difference between these techniques, though most studies were small and heterogeneous with regards to the patients and methods. There is no evidence that manual techniques are more effective than no treatment [283]. Most studies of dry needling have compared with wet needling. Different systematic reviews have come to the conclusion that, although there is an effect of needling on pain, it is neither supported nor refuted that this effect is better than placebo [284]. Other reviews have concluded that the same is true for the difference between dry and wet needling [285, 286].

Physiotherapy in BPS

General muscular exercise may be beneficial in some BPS patients [287]. Transvaginal manual therapy of the pelvic floor musculature (Thiele massage) in BPS patients with high-tone dysfunction of the pelvic floor significantly improved several assessment scales [288]. The role of specific levator ani trigger point injections in women with CPP has been studied [289]. Each trigger point was identified by intravaginal palpation and injected with bupivacaine, lidocaine and triamcinolone. Seventy-two percent of women improved with the first trigger point injection, with 33% being completely pain-free. Efficacy and safety of pelvic floor myofascial physical therapy has been compared with global therapeutic massage in women with BPS; GRA rate was 59% and 26%, respectively. Pain, urgency and frequency ratings, and O'Leary-Sant IC Symptom and Problem Index decreased in both groups during follow-up, and did not differ significantly between the groups. This suggests that myofascial physical therapy is beneficial in women with BPS [290a].

Anal Pain Syndrome

In a recently published RCT, it is demonstrated that biofeedback treatment was superior to electrogalvanic stimulation and massage for treating chronic anal pain syndrome [290b]. One hundred and fifty-seven patients who had at least weekly rectal pain were investigated, but only patients with tenderness on traction of the pelvic floor showed a significant treatment benefit. In patients with tenderness of the puborectalis muscle (Rome II: Highly likely Levator Ani Syndrome), 87% reported adequate relief after one month of biofeedback vs. 45% for electrogalvanic stimulation, and 22% for massage. These results were maintained at 12 months with adequate relief after nine sessions of biofeedback in 58% of the whole group (Rome II: Highly likely and Possible Levator Ani Syndrome), after galvanic stimulation in 27% and massage in 21% of patients. As previously described in dyssynergic defecation, the ability to expel a 50 mL water filled balloon and to relax pelvic floor muscles after biofeedback treatment were predictive of a favourable therapeutic outcome [125]. The pathophysiology of the chronic anal pain syndrome is therefore similar to that of dyssynergic defecation, and this favours the role of the pelvic floor muscles in the pathophysiology of both conditions. Other treatment modalities have been less successful.

Treatment of sexual dysfunctions and CPP

Couples often benefit from early referral for relationship and sexual counselling during their treatment course [291]. Specific behavioural strategies for women who have urogenital complaints and female sexual dysfunction often include exploring alternatives to sexual intercourse (manual or oral pleasuring), different coital positions (female superior or side lying), and pacing, such as limiting thrusting to less than that causes pain. Planning

for the time of intercourse is important, and scheduling a clinic visit after intercourse might be useful to identify specific sites and causes of postcoital flares.

Other behavioural changes involve pre- and postcoital voiding, application of ice packs to the genital or suprapubic area [291, 292], and use of vaginal dilators before penile penetration. An alternative is to use natural dilators such as different fingers or sex toys. Hypoallergenic non-irritating lubricants can be used to reduce vulvar, urethra, and vaginal friction, and women with signs of vulvovaginal atrophy may benefit from introital application of minimally absorbed locally applied oestrogen cream [293]. In patients with an overactive pelvic floor, referral for physical therapy, myofascial release, and internal pelvic floor muscle massage may offer relief [294].

Other physical therapy interventions

Electromagnetic therapy in a small, sham-controlled, double-blind study of four weeks showed a significant, sustained effect over a 1-year period for CPPS [295].

In uncontrolled studies significant symptomatic improvement has been reported from heat therapy, for example, transrectal and transurethral thermotherapy [296, 297].

A small sham-controlled double-blind study of four times weekly perineal extracorporeal shock wave therapy (n = 30) in men with chronic pelvic pain syndrome showed significant improvement in pain, QoL, and voiding compared to the control group (n = 30) over 12 weeks [298]. Confirmatory studies are awaited because of an absent placebo-effect, which is very unusual in PPS trials.

In a small three-arm randomised trial of CPPS in men, electroacupuncture was superior to sham treatment and advice and exercise alone [299]. In a recent prospective case series of six weeks of weekly electro-acupuncture of 97 patients with PPS, 92% showed significant improvement in total NIH-CPSI score. Based on these studies, no definitive conclusion can be drawn.

One sham-controlled medium-sized study (n = 89) demonstrated significant improvement in total NIH-CPSI score and visual analogue scale for pain in men with category IIIB chronic prostatitis / CPP [300]. Despite the popularity of transcutaneous electrical nerve stimulation (TENS) and the number of trials undertaken, a systematic review has been unable to provide good evidence for or against its use in the management of chronic pain [509]. Furthermore, rigorous trials should be undertaken to provide some clarity for a commonly used intervention.

5.1.3 Psychological therapy

Psychological interventions may be directed at pain itself or at adjustment to pain as shown by improved function and mood and reduced health care use with or without pain reduction. Ideally, treatment follows general principles and practice in the field of chronic pain [301, 302], but these have been neglected in pelvic pain. A recent Cochrane systematic review and meta-analysis of non-surgical treatments for pelvic pain [303], excluding endometriosis, IBS, and chronic PID [304] found five eligible trials of psychologically-based treatment, but they were diverse and not combined for analysis. Surprisingly, the single component treatments for chronic pelvic pain, counselling about ultrasound results [305], and emotional disclosure [306], showed improvements in pain, while three more standard multicomponent (including psychological) treatments for pain [252, 281, 307] did not. Pain relief, of around 50%, is comparable to that from pharmacotherapy, but follow-up is lacking. Only two of the five RCTs measured mood improvement, and found no effects of psychological and physiotherapeutic treatment over gynaecological consultation [281], or for writing with vs. without disclosure of distress [306]. The importance of multidisciplinary treatment is emphasised by several reviews [308, 309], and the need for high quality psychological treatment evaluation is underlined [308]. For less disabled and distressed patients, this can be delivered in part over the internet [310]. Several other reviews make positive comments on psychological involvement [311], and recommend addressing psychological concerns from the outset, directed at the pain itself, with the intended outcome of reducing its impact on life [25], or at adjustment to pain, with improved mood and function and reduced health care use, with or without pain reduction [26].

5.1.4 Dietary treatment

Scientific data are limited and dietary restriction alone does not produce significant symptomatic relief however consider the involvement of a dietician.

5.2 Pharmacological management

5.2.1 Drugs for chronic pelvic pain syndrome

In this section the evidence available for specific CPPSs is presented. Where there is no evidence the reader is directed to the section on analgesics below (5.2.3) where more generic use is discussed. There is a large discrepancy in the treatment effects reported in case series and controlled trials that results from a large placebo effect or publication bias. As a result of the multifactorial origin of for example PPS, one reason

for treatment failure in some large randomised placebo-controlled trials may be the heterogeneity of the patient population. One strategy for improving treatment effects may be stratification of patient phenotypes. A prospective series of phenotypically directed treatment for PPS has shown significant improvement of symptoms and QoL [316]. Monotherapeutic strategies for the treatment of PPS may fail [317], therefore, most patients require multimodal treatment aimed at the main symptoms, and taking comorbidity into account. In the past 10 years, results from RCTs have led to advances in standard and novel treatment options.

5.2.1.1 Mechanisms of action

Mechanisms of action are discussed as appropriate under the drugs headings below.

5.2.1.2 Comparisons of agents used in pelvic pain syndromes

Prostate Pain Syndrome (PPS)

Anti-inflammatory drugs

For NSAIDs, a trial with celecoxib reported that the pain subscore, QoL subscore, and total NIH-CPSI score were in favour of the treatment arm vs. placebo, but effects were limited to the duration of therapy [318]. In a recent meta-analysis, two studies of NSAIDs [244, 318] and one with prednisolone [319] were pooled. Anti-inflammatory drugs were 80% more likely to have a favourable response than placebo. An updated network meta-analysis with more restrictive inclusion criteria regarding documented outcome measures but a wider spectrum of drugs (including glycosaminoglycans, phytotherapy and tanezumab) a significant effect on total NIH-CPSI scores and treatment response rates could be demonstrated. Overall, a moderate treatment effect has been shown for anti-inflammatory drugs, but larger studies are needed for confirmation, and long-term side-effects have to be taken into account.

Alpha-blockers

Positive results from RCTs of alpha-blockers, i.e. terazosin [320, 321], alfuzosin [322], doxazosin [323, 324], tamsulosin [325, 326], and silodosin [327] have led to widespread use of alpha-antagonists in the treatment of PPS in recent years. The most recent systematic review and network meta-analyses of alpha-blockers [328] have shown significant improvement in total symptoms, pain, voiding, and QoL scores. In addition, they had a higher rate of favourable response compared to placebo [relative risk (RR) 1.4, 95% confidence interval (CI) 1.1-1.8, P=0.013]. However, treatment responsiveness, i.e. clinically perceptive or significant improvement, may be lower than expected from the change in mean symptom scores. Overall, alpha-blockers seem to have moderate but significant beneficial effects. This probably is not the case for long-standing PPS patients [329]. Future studies should show if longer duration of therapy or some sort of phenotypically directed (e.g. patients with PPS and relevant voiding dysfunction) treatment strategies will improve treatment outcomes.

Antibiotic therapy.

Empirical antibiotic therapy is widely used because some patients have improved with antimicrobial therapy. Patients responding to antibiotics should be maintained on medication for 4-6 weeks or even longer. Unfortunately, culture, leukocyte and antibody status of prostate-specific specimens does not predict antibiotic response in patients with PPS [330], and prostate biopsy culture findings do not differ from those of healthy controls [331]. The only randomised placebo-controlled trials of sufficient quality have been done for oral antibiotic treatment with ciprofloxacin (6 weeks) [130], levofloxacin (6 weeks) [332], and tetracycline hydrochloride (12 weeks) [333]. The studies have been analysed in a recently published meta-analyses [328, 334]. Although direct meta-analysis has not shown significant differences in outcome measures, network meta-analysis has suggested significant effects in decreasing total symptom, pain, voiding, and QoL scores compared with placebo. Combination therapy of antibiotics with alpha-blockers has shown even better outcomes in network meta-analysis. Despite significant improvement in symptom scores, antibiotic therapy did not lead to statistically significant higher response rates [334]. In addition, the sample sizes of the studies were relatively small and treatment effects only modest and most of the time below clinical significance. It may be speculated that patients profiting from treatment have had some unrecognised uropathogens. If antibiotics are used, other therapeutic options should be offered after one unsuccessful course of a quinolone or tetracycline antibiotic over 6 weeks.

5-alpha-reductase inhibitors

Although a few small pilot studies with 5-alpha-reductase inhibitors supported the view that finasteride may improve voiding and pain, the first RCT published in a peer-reviewed journal did not support this, but the study did lack power [335]. In another RCT, finasteride provided better amelioration of symptoms compared to saw palmetto over a 1-year period, but lacked a placebo-control arm [336]. A 6-month placebo-controlled study showed a non-significant tendency towards better outcome in favour of finasteride, possibly because

of a lack of statistical power [337]. In a recently published study, NIH-CPSI scores decreased significantly in a subgroup of men enrolled in a prostate cancer risk reduction study treated with dutasteride compared to placebo [338]. Patients (n=427, age 50 to 75, elevated prostate-specific antigen) were included if they had significant "prostatitis-like" symptoms at baseline. Based on the evidence, 5-alpha-reductase inhibitors cannot be recommended for use in PPS in general, but symptom scores may be reduced in a restricted group of older men with an elevated PSA [338].

Phytotherapy
Phytotherapy applies scientific research to the practice of herbal medicine. An adequately powered placebo-controlled RCT of Cernilton, showed clinically significant symptom improvement over a 12-week period in inflammatory PPS patients (NIH Cat. IIIA) [339]. The effect was mainly based on a significant effect on pain. Quercetin, a polyphenolic bioflavonoid with documented antioxidant and anti-inflammatory properties, improved NIH-CPSI scores significantly in a small RCT [340]. In contrast, treatment with saw palmetto, most commonly used for benign prostatic hyperplasia, did not improve symptoms over a 1-year period [336]. In a systematic review and meta-analysis, patients treated with phytotherapy were found to have significantly lower pain scores than those treated with placebo [328]. In addition, overall response rate in network analysis was in favour of phytotherapy (RR: 1.6; 95% CI: 1.1-1.6).

Pregabalin is an antiepileptic drug that has been approved for use in neuropathic pain. In an adequately powered randomised placebo-controlled study, which was the only report included in a recently published Cochrane review [341], a 6-week course of pregabalin (n = 218) compared to placebo (n = 106) did not result in a significant reduction of NIH-CPSI total score [342].

Pentosan polysulphate is a semi-synthetic drug manufactured from beech-wood hemicellulose. One study using oral high-dose (3x 300 mg/day) demonstrates a significant improvement in clinical global assessment and QoL over placebo in men with PPS, suggesting a possible common aetiology [343].

Muscle relaxants (diazepam, baclofen) are claimed to be helpful in sphincter dysfunction or pelvic floor/perineal muscle spasm, but there have been few prospective clinical trials to support these claims. In one RCT, a triple combination of a muscle relaxant (tiocolchicoside), an anti-inflammatory drug (ibuprofen) and an alpha-blocker (doxazosin) was effective in treatment-naïve patients, but not superior to an alpha-blocker alone [324].

Botulinum toxin in a small randomised placebo-controlled study of perineal skeletal muscle injection (100 U) showed some effect in the global response assessment and the NIH-CPSI pain subdomain score. However, patient numbers were low (13 in the botulinum toxin type A (BTX-A) group and 16 in the placebo group), and follow-up too short to draw definitive conclusions. Side-effects are unclear.

Zafirlukast, a leukotriene antagonist, and prednisone in two low-power placebo-controlled studies failed to show a benefit [319, 344]. More recently, a placebo-controlled phase IIa study of tanezumab, a humanised monoclonal antibody against the pain mediating neurotrophin, nerve growth factor, failed to demonstrate significant effect [345].

Tanezumab is a humanised monoclonal antibody that specifically inhibits nerve growth factor (NGF), and should only be used in clinical trials.

Allopurinol
There is insufficient evidence for the use of allopurinol in PPS [346, 347].

Bladder Pain Syndrome

Treatments of significant value for BPS

Anti-histamines
Mast cells may play a role in BPS. Histamine is one of the substances released by mast cells. Histamine receptor antagonists have been used to block the H1 [348] and H2 [349] receptor subtypes, with variable results. A prospective placebo-controlled RCT of hydroxyzine or sodium pentosan polysulphate did not show a significant effect [350].

Amitriptyline
Amitriptyline is a tricyclic antidepressant. Several reports have indicated improvement of BPS symptoms after

oral amitriptyline [94, 351, 352]. Amitriptyline has been shown to be beneficial when compared with placebo plus behavioural modification [353]. Drowsiness is a limiting factor with amitriptyline, nortriptyline is sometimes considered instead.

Pentosan polysulphate sodium Is a semi-synthetic drug manufactured from beech-wood hemicellulose. Subjective improvement of pain, urgency, frequency, but not nocturia, has been reported [354, 355]. Pentosan polysulphate sodium had a more favourable effect in BPS type 3C than in non-lesion disease [356]. Response was not dose dependent but related more to treatment duration. At 32 weeks, about half the patients responded. Combination therapy showed a response rate of 40% compared to 13% with placebo. For patients with an initial minor response to pentosan polysulphate sodium, additional subcutaneous heparin was helpful [357].

Immunosuppressants
Azathioprine treatment has resulted in disappearance of pain and urinary frequency [358]. Initial evaluation of cyclosporin A (CyA) [359] and methotrexate [360] showed good analgesic effect but limited efficacy for urgency and frequency. Corticosteroids are not recommended in the management of patients with BPS because of a lack of evidence. Intravesical drugs are administered due to poor oral bioavailability establishing high drug concentrations within the bladder, with few systemic side-effects. Disadvantages include the need for intermittent catheterisation, which can be painful in BPS patients, cost and risk of infection.

Local anaesthetics
There are sporadic reports of successful treatment of BPS with intravesical lidocaine [361, 362]. Alkalisation of lidocaine improves its pharmacokinetics [363]. Combination of heparin, lidocaine and sodium bicarbonate gave immediate symptom relief in 94% of patients and sustained relief after 2 weeks in 80% [364]. Intravesical instillation of alkalinised lidocaine or placebo for five consecutive days resulted in significantly sustained symptom relief for up to 1 month [365].

Hyaluronic acid and chondroitin sulphate are described to repair defects in the GAG layer. Despite the fact that intravesical GAG replenishment has been in use for about 20 years for BPS/IC, most of the studies are uncontrolled and with a small number of patients. Based on the studies available there are differences by virtue of substance classes, whether they are natural GAG layer components, dosage formulations, and concentrations. More important, there are differences in proven efficacy. Only for chondroitin sulphate, a combination containing chondroitin sulfate and hyaluronic acid and pentosan polysulphate RCTs are published. It is well documented that intravesical instillations are a valuable and beneficial therapy, but distinct patient groups need to be confirmed by definite diagnostic findings [366].

Intravesical heparin
BPS patients were treated with heparin for three months, and over half had control of symptoms, with continued improvement after 1 year of therapy [367]. Kuo reported another trial of intravesical heparin for three months in women with frequency-urgency syndrome and a positive potassium test. Symptomatic improvement was reported in 80% of BPS patients [368]. Intravesical heparin plus dorsal tibial nerve stimulation in patients with refractory BPS was studied and it was shown that voiding frequency, pain score and maximum cystometric capacity were significantly better after 2 and 12 months [369].

Hyperbaric oxygen (HBO) has a moderate effect on a small subgroup of BPS patients. Disadvantages include high cost, limited availability of treatment sites, and time-consuming treatment [370].

Treatments of limited value for BPS

Cimetidine
There is limited data to suggest that Cimetidine improves symptoms of BPS in the short-term [371]. Compared with placebo for 3 months, cimetidine significantly improved symptom scores, pain and nocturia, although the bladder mucosa showed no histological changes in either group [372].

Prostaglandins
Misoprostol is a prostaglandin that regulates various immunological cascades. After three months of treatment with misoprostol, 14/25 patients had significantly improved, with 12 showing a sustained response after a further six months [373]. The incidence of adverse drug effects was 64%.

L-Arginine
Oral treatment with the nitric oxide (NO) synthase substrate l-arginine decreases BPS-related symptoms [121, 374, 375]. NO is elevated in patients with BPS [376]. However, others have not demonstrated symptomatic relief or changes in NO production after treatment [377, 378].

Oxybutynin is an anticholinergic drug used in overactive detrusor dysfunction. Intravesical oxybutynin combined with bladder training improves functional bladder capacity, volume at first sensation, and cystometric bladder capacity [379]. However, an effect on pain has not been reported.

Duloxetine (a serotonin-norepinephrine reuptake inhibitor antidepressant with a licence for the management of neuropathic pain) did not significantly improve symptoms of BPS [380]. Administration was safe, but tolerability was poor due to nausea. Based on these preliminary data, duloxetine cannot be recommended for treatment of BPS.

Clorpactin is a derivative of hypochloric acid previously used to treat BPS [381-385]. Due to high complication rates, clorpactin instillations can no longer be recommended [381, 382, 384, 386, 387].

Dimethyl sulphoxide (DMSO) and **Bacillus Calmette Guérin** (BCG) have been used in the past. There is insufficient evidence to recommend the use of either.

Scrotal Pain Syndrome
Treatment of chronic scrotal pain is based on the principles of treating chronic pain syndromes, as described throughout these guidelines [388]

Chronic gynaecological pain
It is difficult to compare the wide variation of drugs from an efficacy and safety perspective as they have such diverse uses/indications.

In those gynaecological patients where CPP is unrelated to any of the well-defined conditions, it is often difficult to determine a therapeutic pathway other than a multi-disciplinary chronic abdomino-pelvic pain management plan. A Cochrane review suggests there may be some evidence (moderate) supporting the use of progestogens. Though efficacious, physicians need to be conversant with progestogenic side effects (e.g. weight gain, bloatedness-the most common adverse effects) which can stop some patients from accepting such medication. Gonadotrophins, such as goserelin, are also thought to help such pain. However, when compared with progestogens, their efficacy remains limited, as is the case when comparing gabapentin with amitriptyline. The quality of evidence is generally low and is drawn from single studies [303].

Current hormonal contraceptives (e.g. the combined oral contraceptive pill and the progesterone-only pill), and intrauterine contraceptive devices (Mirena IUS™) have multiple biologic effects. Their mechanism of action my be via a primary or secondary contraceptive action. For combined oral contraceptives and progestin-only methods, the main mechanisms are ovulation inhibition and changes in the cervical mucus that inhibit sperm penetration. The hormonal methods, particularly the low-dose progestin-only products and emergency contraceptive pills, have effects on the endometrium that, theoretically, could affect implantation. Thier effectiveness as contraceptives range from 92-99.9% [312]. The precise mechanism of intrauterine contraceptive devices is unclear. Current evidence indicates they exert their primary effect before fertilization, reducing the opportunity of sperm to fertilize an ovum.Thier efficacy approaches 99% [313].

Gonadotropin-releasing hormone (GnRH) bind to specific receptors on pituitary gonadotrophs. Prolonged activation of GnRH receptors by GnRH leads to desensitization and consequently to suppressed gonadotrophin secretion. By contrast, GnRH antagonists compete with GnRH for receptors on gonadotroph cell membranes, inhibit GnRH-induced signal transduction and consequently gonadotrophin secretion. These compounds are free of agonistic actions, which might be beneficial in certain clinical applications, such as redcuing the size of fibroids, endometrial bleeding and endometriosis [314].

Pelvic Floor and Chronic Anal Pain
Botulinum A toxin (pelvic floor)
Botulinum A toxin (BTX-A) has been injected into trigger points. It is more expensive than lidocaine and has not been proven to be more effective [389]. Reviews do not support the injection of BTX-A into trigger points [390]. Pelvic floor muscle overactivity plays a role in CPP. BTX-A, as a muscle relaxant, can be used to reduce the resting pressure in the pelvic floor muscles. In women with high resting pressure in the pelvic floor muscles,

it has been found that BTX-A lowers this pressure significantly. The magnitude of reduction was significantly higher than that in the placebo group. On the pain score (VAS), no intergroup differences were found in this relatively small randomised study [391]. BTX-A can also be injected at the sphincter level to improve urination or defecation. Relaxation of the urethral sphincter alleviates the bladder problems and secondarily the spasm. In a cohort study of 13 patients with CPP, BTX-A was injected into the external urethral sphincter. Subjectively, 11 patients reported a substantial change in pain symptoms, from 7.2 to 1.6 on a VAS [392].

Botulinum A toxin (chronic anal pain syndrome)
CPP associated with spasm of the levator ani muscles and treatment of the puborectalis and pubococcygeus muscle by BTX-A appears to be promising in some women, as shown in a pilot study (n = 12). The inclusion criteria were dependent only on vaginal manometry with overactivity of the pelvic floor muscles, defined as a vaginal resting pressure > 40 cm H_2O. Although dyspareunia and dysmenorrhea improved, non-menstrual pelvic pain scores were not significantly altered [393]. In the following double-blinded, randomised, placebo-controlled trial, the same group defined pelvic floor myalgia according to the two criteria of tenderness on contraction and hypertension (> 40 cm H_2O) and included 60 women. In this larger study, non-menstrual pelvic pain was significantly improved compared to those treated with placebo (VAS score 51 vs. 22; P = 0.009). It was concluded therefore that BTX-A is effective for reducing pelvic floor-muscle associated pain with acceptable adverse effects such as occasional urinary and faecal stress incontinence [391]. However, recently, a small RCT failed to show any benefit of BTX-A [394].

Intermittent chronic anal pain syndrome
Due to the short duration of the episodes, medical treatment and prevention is often not feasible. Inhaled beta-2 adrenergic agonist salbutamol was effective in an RCT in patients with frequent symptoms and shortened pain duration [395]. Other treatment options are topic diltiazem and BTX-A [396]. However, there is still some controversy as regards the duration of pain of intermittent chronic and chronic anal pain syndrome. RCTs often use different definitions, extending the pain duration (with a shift to chronic pain) in order to include more patients and to better evaluate the study-drug action.

*5.2.2 **Analgesics***

If the use of simple analgesics fails to provide adequate benefit, then consider using the neuropathic agents, if there is no improvement, consider involving a specialist pain management centre with an interest in pelvic pain. CPP is well defined and involves multiple mechanisms as described in previous chapters. The management requires a holistic approach with biological, psychological and social components. Few studies have specifically looked at medications used in CPP [304], therefore, a wider look at the literature has been undertaken, further specific research is required. The agents concerned are divided for ease of description. Combinations often provide a greater benefit than individual agents. They may also allow lower individual dosages and thus minimise side-effects. The aim of using these drugs is to allow patients to improve their QoL. This is best measured by assessing their function as well as pain severity. If the use of these agents does not allow this, then they should be withdrawn. Unfortunately, the failure of one agent to provide benefit does not mean that there is an alternative. If the benefit is limited by side-effects, then the lowest effective dose should be found (by dose titration). Sometimes, patients will prefer a higher level of pain and have fewer side-effects.

5.2.2.1 Mechanisms of action

Mechanisms of action are discussed as appropriate under the drugs headings below.

5.2.2.2 Comparisons within and between groups in terms of efficacy and safety

Paracetamol (acetaminophen)
Paracetamol is a well-tolerated analgesic in a class of its own. This is an antipyretic analgesic with a central mechanism of action [397]. It is often available over the counter without prescription. There is evidence that paracetamol is beneficial in managing somatic and arthritic pain [398]

Non-steroidal anti-inflammatory agents (NSAIDs)
These agents are anti-inflammatory, antipyretic analgesics that act by inhibiting the enzyme cyclooxygenase (COX). They have a peripheral effect, hence their use in conditions involving peripheral or inflammatory mechanisms. They are commonly used for pelvic pain, many are available over the counter and usually well tolerated. There is no good evidence to suggest one NSAID over another for pelvic pain. Guidelines for use of NSAIDs and COX-2 selective agents have been developed. They have more side-effects than paracetamol, including indigestion, headaches and drowsiness.

The evidence for their benefit in CPP is weak or non-existent and are often limited by side-effects.

For pelvic pain in which inflammatory processes are considered important, such as dysmenorrhoea [399], NSAIDs are more effective than placebo and paracetamol, but with a higher incidence of side-effects. For pelvic pain in which central mechanisms may be incriminated, such as endometriosis [315], then the evidence is lacking for NSAIDs despite their common use.

At a practical level, if NSAIDs are considered for use, they should be tried (having regard for the cautions and contraindications) and the patient reviewed for improvement in function as well as analgesia. If this is not achieved, or side-effects are limiting, then they should be withdrawn.

Neuromodulators

These are agents that are not simple analgesics but used to modulate neuropathic or centrally mediated pain. There are several classes commonly used with recognised benefits in pain medicine. They are taken on a regular basis, all have side-effects that may limit use in some patients. In the UK, the National Institute for Health and Clinical Excellence (NICE) has reviewed the pharmacological management of neuropathic pain [400]. Not all the agents are licensed for use in pain management but there is a history and evidence to demonstrate their benefit. The evidence for treatment of CPP is lacking but is present for other painful conditions. For this chapter, most of the evidence is from non-pelvic pain sources. The general method for using these agents is by titrating the dose against benefit and side-effects. The aim is for patients to have an improvement in their QoL, which is often best assessed by alterations in their function. It is common to use these agents in combination but studies comparing different agents against each other, or in combination, are lacking. Some of these agents are also used for specific conditions.

Antidepressants

Tricyclic antidepressants

The tricyclic antidepressants (TCA's) have multiple mechanisms of action including, blockade of acetylcholine receptors, inhibition of serotonin and noradrenalin re-uptake, and blockade of histamine H1 receptors. It also have anxiolytic affects [401] and are frequently limited by their side-effects. TCA's have a long history of use in pain medicine and have been subjected to a Cochrane review [402], suggesting that they are effective for neuropathic pain. Amitriptyline is the most commonly used member at doses from 10 to 75 mg/day (sometimes rising to 150 mg/day). This is titrated against benefit or side-effects and can be taken at night [493]. Nortriptyline and imipramine are used as alternatives.

Other Antidepressants

Duloxetine is a serotonin-norepinephrine re-uptake inhibitor (SNRI) antidepressant licensed for use in, depression, urinary stress incontinence and neuropathic pain. There is moderately strong evidence of benefit in diabetic neuropathy and fibromyalgia at a dose of 60 mg/day [403]. Side-effects are common and may result in its discontinuation.

Selective serotonin reuptake inhibitors (SSRIs) are antidepressants with fewer side-effects. They are effective for depression, but there have been insufficient studies to demonstrate their benefit in pelvic or neuropathic pain [402-404].

Anticonvulsants

Anticonvulsants are commonly used in the management of neuropathic pain. There are general studies and some looking more particularly at pelvic pain. Individual agents have been systematically reviewed. Their use is suggested in the NICE Neuropathic Guidelines [400].

Carbamazepine has a long history of use in neuropathic pain. Evidence exists for its benefit [405]. Trials have tended to be of short duration, showing only moderate benefit. There are side-effects; some of which may be serious. It is no longer a first-choice agent. Other anticonvulsant agents are available with fewer serious side-effects.

Gabapentin is commonly used for neuropathic pain and has been systematically reviewed [406]. It provides good quality relief with NNT of approximately six. Side-effects are common, notably drowsiness, dizziness and peripheral oedema. For upper dose levels, reference should be made to local formularies, and many clinicians do not routinely exceed 2.4 g/day in divided doses (most commonly three times daily). One study of women with CPP has suggested that gabapentin alone or in combination with amitriptyline provides better analgesia then amitriptyline alone [407].

Pregabalin is a commonly used neuromodulator with good evidence of efficacy in some neuropathic conditions but the NNT varies depending on the condition [408]. The dose for benefit is in the range of 300 to 600 mg/day. The same systematic review found that doses less than 150 mg/day are unlikely to provide benefit. As with gabapentin, side-effects are relatively common and may not be tolerated by patients. Other anticonvulsants are available but not commonly used for managing pain.

Other agents can be used in the management of neuropathic pain but they are best administered

only by specialists in the management of pain and familiar with their use. They tend to be considered after the standard options have been exhausted. As with all good pain management, they are used as part of a comprehensive multidimensional management plan.

Opioids

Opioids are used for chronic non-malignant pain and may be beneficial for a small number of patients. Often patients will stop taking oral opioids due to side-effects or insufficient analgesia [409]. They should only be used in conjunction with a management plan with consultation between clinicians experienced in their use. It is suggested that a pain management unit should be involved along with the patient and their primary care physician.

There are well established guidelines for the use of opioids in pain management as well as considering the potential risks [410]. There is also information available online for patients [411, 412]. There are several agents available in the group. They can be divided into weak (e.g., codeine, dihydrocodeine and tramadol) or strong opioids (e.g., morphine, oxycodone, fentanyl and hydromorphone). Oral administration is preferable, but if poorly tolerated, a percutaneous (patch) route may have advantages. More invasive approaches are less commonly used and within the realms of specialist units. Side-effects are common, including constipation, nausea, reduced QoL, opioid tolerance, hormonal and immunological effects along with psychological changes and require active management.

There is a growing understanding of opioid-induced hyperalgesia; a situation in which patients taking opioids, paradoxically, become more sensitive to painful stimuli [413, 414]. This is another reason for these drugs to be used in a controlled fashion for long-term management of non-malignant pain.

Morphine is the standard opioid with which many physicians are familiar. The aim is to use a slow or sustained release preparation starting with a low dose and titrating the dose every 3 days to 1 week against improvement in both function and pain. Side-effects should also be monitored and managed accordingly. Particular attention should be paid to the management of constipation.

There are a variety of other agents available and some are mentioned below:

Transdermal fentanyl may be considered when oral preparations are restricted (e.g., iliostomy). It may also be beneficial when there are intolerable side-effects from other opioids.

Methadone has a long record of use as an opioid. There is a theoretical advantage of benefit with its N-methyl-D-aspartate receptor (NMDA) antagonist activity. This may be relevant in neuropathic pain [415].

Oxycodone may have greater efficacy than morphine in some situations, such as hyperalgesic states including visceral pain [416].

Tramadol is an established analgesic with dual effects on opioid receptors and serotonin release. More recently, tapentadol, has been released with opioid action and noradrenalin re-uptake inhibition. It is too early to assess its real value in the armamentarium for pain management.

5.3 Surgical management

5.3.1 ***Surgery***

<u>Bladder Pain Syndrome (BPS)</u>

Bladder distension

Although bladder hydrodistension is a common treatment for BPS, the scientific justification is scarce. It can be part of the diagnostic evaluation, but has limited therapeutic role.

Hydrodistension and Botulinum toxin A (BTX-A)

BTX-A may have an antinociceptive effect on bladder afferent pathways, producing symptomatic and urodynamic improvements [102]. Treatment with hydrodistension and hydrodistension plus intravesical BTX-A has been compared [417]. There was symptomatic improvement in all patients. However, in the hydrodistension only group, 70% returned to their previous symptoms after 1 month, while in the BTX-A-treated patients, VAS score, and functional and cystometric bladder capacity improved at 3 months.

BTX-A trigonal-only injection seems effective and long-lasting as 87% of patients reported improvement after 3 months follow-up [418]. Over 50% reported continued benefit 9 months after the first treatment. When retreatment was needed, similar results were obtained. The authors concluded that this treatment is safe, effective and can be repeated.

Transurethral resection (TUR), coagulation and laser

Endourological destruction of bladder tissue aims to eliminate urothelial, mostly Hunner lesions. Since the 1970s resection and fulguration have been reported to achieve symptom relief, often for more than 3 years [419, 420]. Prolonged amelioration of pain and urgency has been described for transurethral laser ablation as well [421].

Open Surgery for BPS

BPS is benign and does not shorten life, thus operative procedures rank last in the therapeutic algorithm. There is no evidence it relieves pain. Surgery for refractory BPS is only appropriate as a last resort for patients with refractory end-stage disease. Major surgery should be preceded by thorough preoperative evaluation, with an emphasis on determining the relevant disease location and subtype. If surgery is considered, our advice is to refer the patient to a specialist center experienced in managing CPP with a multidisciplinary team approach.

Four major techniques are common:

1. Urinary diversion without cystectomy. As early as 1967, it was reported that bladder augmentation without removal of the diseased tissue was not appropriate [422]. Reports that unresected BPS bladders cease to induce symptoms after loss of contact with urine are scarce [99, 423].

2. Supratrigonal cystectomy with subsequent bladder augmentation represents the most favoured continence-preserving surgical technique. Various intestinal segments have been used for trigonal augmentation [424-426].

3. Subtrigonal cystectomy. Subtrigonal resection has the potential of removing the trigone as a possible disease site, but at the cost of requiring ureteral reimplantation. Trigonal disease is reported in in 50% of patients and blamed surgical failure on the trigone left in place [427]. In contrast, Another study [428] reported six out of 17 patients being completely cured by supratrigonal resection [427]. A recent study on female sexuality after cystectomy and orthotopic ileal neobladder showed pain relief in all patients, but only one regained normal sexual activity [429].

4. Cystectomy with formation of an ileal conduit still ranks first in current USA practice trends for BPS surgery [430]. For cosmetic reasons, continent diversion is preferred, particularly in younger patients. After orthotopic bladder augmentation, particularly when removing the trigone, voiding may be incomplete and require intermittent self-catheterisation. Patients considering these procedures must be capable of performing, accepting and tolerating self-catheterisation. For patients with BPS who develop recurrent pain in the augmented bladder or continent pouch after enterocystoplasty or continent urinary diversion, Retubularisation of a previously used bowel segment to form a urinary conduit has been recommended [431]. It is important to note that pregnancies with subsequent lower-segment Caesarean section have been reported after ileocystoplasty [431, 432].

Prostate Pain Syndrome (PPS)

There is no evidence for surgical management, including transurethral incision of the bladder neck, radical transurethral resection of the prostate, or in particular, radical prostatectomy in the management of chronic pain in patients with PPS.

Urethral Pain Syndrome

There is no specific treatment that can be advised. Management should be multidisciplinary and multimodal [433]. Laser therapy of the trigonal region may be a specific treatment. One trial comparing two forms of laser reported good results, but did not compare with sham treatment [434]. The majority of publications on treatment of urethral pain syndrome have come from psychologists [164].

Presumed intra-abdominal adhesions

In gynaecological patients with CPP and presumed adhesions, there is no consensus as to whether adhesiolysis should be performed to improve pain [435, 436].

Extensive surgery for endometriosis is challenging and is still considered to be controversial, as there is at least one RCT showing no benefit in pain relief in the removal of early extensive endometriosis compared to sham surgery [437, 438].

In patients with adenomyosis, the only curative surgery is hysterectomy but patients can benefit from hormonal therapy and analgesics (see 5.2.1)

Pudendal Neuralgia and surgery

Decompression of an entrapped or injured nerve is a routine approach and probably should apply to the pudendal nerve as it applies to all other nerves. There are several approaches and the approach of choice probably depends upon the nature of the pathology. The most traditional approach is transgluteal; however, a transperineal approach may be an alternative, particularly if the nerve damage is thought to be related to previous pelvic surgery [171, 231, 439-443]. Currently, there has been only one prospective randomised study [441]. This study suggests that, if the patient has had the pain for < 6 years, 66% of patients will see some improvement with surgery (compared to 40% if the pain has been present for > 6 years). Surgery is not the answer for all patients. On talking to patients that have undergone surgery, providing the diagnosis was clear-cut, most patients are grateful to have undergone surgery but many still have symptoms that need management.

*5.3.2 **Neuromodulation***

The role of neuromodulation in the management of pelvic pain should only be considered by specialists in pelvic pain management. These techniques are only used as part of a broader management plan and require regular follow-up. The research base is developing and the techniques broadening (e.g., spinal cord stimulation (SCS), sacral root stimulation, dorsal root ganglion stimulation or peripheral nerve stimulation). These are expensive interventional techniques for patients refractory to other therapies. Therefore, it is inappropriate to provide a detailed review in this publication. In the UK, guidance has been published for SCS in neuropathic pain [444]. This emphasises the comments above. This guidance suggests a trial period of stimulation before full implementation. Neuromodulation is still finding its role in pelvic pain management. There has been growing evidence in small case series or pilot studies, but more detailed research is required [445]. Its role in overactive bladder and faecal incontinence is more robust but is limited for pain.

Bladder Pain Syndrome

A comparison of sacral neuromodulation (SNM) vs. pudendal nerve stimulation (PNS), showed an overall 59% improvement in symptoms with PNS vs. 44% with SNM. Most patients who tested both a sacral and pudendal electrode chose PNS as the better site. Follow-up showed marked improvements in voiding variables and validated BPS symptom questionnaires. Over 90% of patients treated with neuromodulation stated that they would undergo implantation again [446]. Long-term results were verified in a retrospective study of patients from 1994 to 2008 [447]. Permanent SNM implantation was performed in patients who showed at least 50% improvement in symptoms with a temporary peripheral nerve evaluation test [447]. Median follow-up was 61.5 months. Good long-term success of SNM was seen in 72%, with a 28% explantation rate. The most frequent reason for explantation was poor outcome (54% of the failed patients). The revision rate was 50%. In a study of women who underwent permanent device implantation from 2002 to 2004 [448], mean pre-/postoperative pelvic pain and urgency/frequency scores were 21.61 ± 8.6/9.22 ± 6.6, and mean pre-/postoperative visual analogue pain scale (VAPS) scores were 6.5 ± 2.9/2.4 ± 1.1. Mean follow-up was 86 ± 9.8 months. Sacral neuromodulation showed adequate improvement for the symptoms of refractory BPS. The re-operation rate was 25%.

Pudendal Neuralgia

Pudendal neuralgia represents a peripheral nerve injury and as such should respond to neuromodulation by implanted pulse generators. However, it is important that the stimulation is perceived in the same site as the perceived pain. Spinal cord stimulation (SCS) may be effective for thoraco-lumbar afferents. However, it is difficult to obtain appropriate stimulation from SCS for the sacral nerves including pudendal. There is limited experience with sacral root stimulation and as a result stimulation for pudendal neuralgia should only be undertaken in specialised centres and in centres that can provide multidisciplinary care [449-452].

Chronic Anal Pain Syndrome

Sacral neuromodulation and percutaneous tibial nerve stimulation in pelvic pain. In a large cohort of 170 patients with functional anorectal pain from the St. Mark's Hospital (Harrow, Middlesex, United Kingdom) sacral nerve stimulation was used in 3 patients (2 improved) while biofeedback was the most used modality with the greatest treatment effect in patients with defecatory dysfunction (29 patients, 17 improved) [396]. Sacral neuromodulation has been reported to be somewhat beneficial in two uncontrolled studies, showing improvement in about half the patients [453, 454]. Sacral neuromodulation may be a choice in patients with CPP who failed to respond to biofeedback and drug therapy. The less invasive percutaneous tibial nerve stimulation (PTNS) was tested in 12 women with CPP lasting for at least 6 months and showed an improvement in pain, QoL and sexual life [455]. No "sham" SNM or PTNS control group were used in either cited studies, which limits their value as an important placebo effect cannot be ruled out.

*5.3.3 **Nerve blocks***

Nerve blocks for pain management are usually carried out by specialists in pain medicine as part of a broader management plan [51]. They may have a diagnostic or therapeutic role. Textbooks have been written on the subject and practitioners using them should be trained in appropriate patient selection, indications, risks and benefits. Many such interventions also require understanding and expertise in using imaging techniques to perform the blocks accurately. Diagnostic blocks can be difficult to interpret due to the complex mechanisms underlying the painful condition or syndrome. Sustained but limited benefit may lead to more permanent procedures (e.g., radiofrequency procedures). There is a weak evidence base for these interventions for chronic non-malignant pain.

Pudendal Neuralgia

The role of injections may be divided into two. First, an injection of local anaesthetic and steroid at the sight of nerve injury may produce a therapeutic action. The possible reasons for this are related to the fact that steroids may reduce any inflammation and swelling at the site of nerve irritation, but also because steroids may block sodium channels and reduce irritable firing from the nerve [456]. The second possible benefit is diagnostic. It has already been indicated that when the pudendal nerve is injured there are several sites where this may occur. Differential block of the pudendal nerve helps to provide information in relation to the site where the nerve may be trapped [229-239].

Infiltration at the ischeal spine requires the use of a nerve stimulator/locator. Both motor (anal contraction) and sensory endpoints may be noted. The anatomical endpoint may be localised by fluoroscopy, CT guidance, or the use of US. US avoids any radiation, whereas CT guidance involves a significant amount of radiation. Currently, fluoroscopy is probably the imaging technique most frequently used because it is readily available to most anaesthetists that perform the block. Currently, infiltration of the pudendal nerve within Alcock's canal is primarily undertaken with the use of CT. As well as injecting around the pudendal nerve, specific blocks of other nerves arising from the pelvis may be performed. Pulsed radiofrequency stimulation has also been suggested as a treatment [457].

5.4 Summary of evidence and recommendations: management

*5.4.1 **Management of PPS***

Summary of evidence	**LE**
Phenotypically directed treatment may improve treatment success.	3
Alpha-blockers have moderate treatment effect regarding total pain-, voiding-, and QoL scores in PPS.	1a
Antimicrobial therapy has a moderate effect on total pain-, voiding-, and QoL scores in PPS.	1a
NSAIDs have moderate overall treatment effects on PPS.	1a
Phytotherapy has some beneficial effect on pain and overall favourable treatment response in PPS.	1a
Pentosan polysulphate improves global assessment and QoL score in PPS.	1b
There are insufficient data on the effectiveness of muscle relaxants in PPS.	2b
Pregabalin is not effective for the treatment of PPS.	1b
BTX-A injection into the pelvic floor may have a modest effect in PPS.	2b
Posterior tibial nerve stimulation is probably effective for the treatment of PPS.	1b
There are insufficient data supporting the use of other surgical treatments, such as transurethral incision of the bladder neck, transurethral resection of the prostate, or radical prostatectomy in patients with PPS.	3
Cognitive behavioural therapy designed for PPS may improve pain, and QoL.	3

Recommendations	**GR**
Offer multimodal and phenotypically directed treatment options for PPS.	A
Single use of antimicrobial therapy (quinolones or tetracyclines) is recommended in treatment-naïve patients over a minimum of 6 weeks with a duration of PPS < 1 year.	A
Alpha-blockers are recommended for patients with a duration of PPS < 1 year.	A
High-dose pentosan polysulphate is recommended in PPS.	A
NSAIDs are recommended for use in PPS, but long-term side-effects have to be considered.	B
For PPS with significant psychological distress, psychological treatment focused on PPS is recommended.	B

PPS = prostate pain syndrome; NSAIDs = non-steroidal anti-inflammatory drugs.

5.4.2 *Management of BPS*

Summary of evidence	LE
There is insufficient data for the long-term use of corticosteroids.	3
Limited data exist on effectiveness of cimetidine in BPS.	2b
Amitriptyline is effective for pain and related symptoms of BPS.	1b
Oral pentosanpolysulphate sodium is effective for pain and related symptoms of BPS.	1a
Oral pentosanpolysulphate sodium plus subcutaneous heparin is effective for pain and related symptoms of BPS, especially in initially low responders to pentosanpolysulphate sodium alone.	1b
Intravesical lidocaine plus sodium bicarbonate is effective in the short term.	1b
Intravesical pentosanpolysulphate sodium is effective, based on limited data, and may enhance oral treatment.	1b
There are limited data on the effectiveness of intravesical heparin.	3
Intravesical chondroitin sulphate may be effective.	2b
There is insufficient data for the use of bladder distension as a therapeutic intervention.	3
Hydrodistension plus BTX-A is superior to hydrodistension alone.	1b
Intravesical BCG is not effective in BPS.	1b
Transurethral resection (coagulation and laser) may be effective in BPS type 3C.	3
Sacral neuromodulation may be effective in BPS.	3
Pudendal nerve stimulation (PNS) is superior to SNM for treatment of BPS.	1b
Avoidance of some food and drink may reduce symptoms.	3
Outcome for cystectomy for BPS is variable.	3

Recommendations	GR
Offer subtype and phenotype-oriented therapy for the treatment of BPS.	A
Multimodal behavioural, physical and psychological techniques should always be considered alongside oral or invasive treatments of BPS.	A
Administer amitriptyline for use in BPS.	A
Offer oral pentosanpolysulphate sodium for the treatment of BPS.	A
Treatment with oral pentosanpolysulphate sodium plus subcutaneous heparin is recommended especially in low responders to pentosanpolysulphate sodium alone.	A
Administer intravesical lidocaine plus sodium bicarbonate prior to more invasive methods.	A
Administer intravesical pentosanpolysulphate sodium before more invasive treatment alone or combined with oral pentosanpolysulphate sodium.	A
Administer submucosal injection of BTX-A plus hydrodistension if intravesical instillation therapies have failed.	A
All ablative organ surgery should be the last resort for experienced and BPS knowledgeable surgeons only.	A
Offer intravesical hyaluronic acid before more invasive measures.	B
Offer intravesical chondroitin sulphate before more invasive measures.	B
Offer transurethral resection (or coagulation or laser) of bladder lesions, but in BPS type 3 C only.	B
Offer neuromodulation before more invasive interventions.	B
Offer dietary advice.	C
Offer intravesical heparin before more invasive measures alone or in combination treatment.	C
Offer intravesical bladder wall and trigonal injection of BTX-A if intravesical instillation therapies have failed.	C
Corticosteroids are not recommended for long-term treatment.	C
Bladder distension is not recommended as a treatment of BPS.	C

DMSO = dimethyl sulphoxide; BPS = bladder pain syndrome; BTX-A = Botulinum A toxin; BCG = Bacillus Calmette Guérin.

5.4.3 *Management of scrotal pain syndrome*

Summary of evidence	LE
Microsurgical denervation of the spermatic cord is an effective therapy for scrotal pain syndrome.	2b
Vasovasostomy is effective in post-vasectomy pain,	2b
Orchiectomy is the last resort in treating scrotal pain syndrome.	4

Recommendations	GR
Start with general treatment options for chronic pelvic pain.	A
Inform about the risk of post-vasectomy pain when counselling patients planned for vasectomy.	A
To reduce the risk of scrotal pain, open instead of laparoscopic inguinal hernia repair is recommended.	A
It is recommended that during inguinal hernia repair all the nerves in the spermatic cord are identified.	A
For patients who are treated surgically, microsurgical denervation of the spermatic cord is recommended.	A
We recommend that orchiectomy should not be done, unless all other therapies, including pain management assessment, have failed.	C

5.4.4 *Management of urethral pain syndrome*

Summary of evidence	LE
There is no specific treatment for urethral pain syndrome.	4
In patients with significant distress associated with bladder or urethral symptoms, psychological treatment may be worth using to reduce distress and thereby improve function and QoL.	4

Recommendations	GR
Start with general treatment options for chronic pelvic pain.	A
It is recommended that patients with urethral pain syndrome are treated in a multidisciplinary and multimodal programme.	B
When patients are distressed, it is recommended to refer them for pain-relevant psychological treatment to improve function and quality of life.	B

5.4.5 *Management of gynaecological aspects of chronic pelvic pain*

Summary of evidence	LE
Therapeutic options, including pharmacotherapy and surgery, can treat endometriosis effectively.	1b
Psychological treatment (CBT or supportive psychotherapy) can improve pain and sexual and emotional function in vaginal and vulvar pain syndrome.	1b
All other gynaecological conditions (including dysmenorrhea, obstetric injury, pelvic organ prolapse and gynaecological malignancy) can be treated effectively using pharmacotherapy.	3

Recommendations	GR
Provide therapeutic options such as hormonal therapy or surgery in well-defined disease states.	B
Provide a multidisciplinary approach to pain management in persistent disease states.	B

5.4.6 *Management of anorectal pain syndrome*

Summary of evidence on functional anorectal pain	LE
Biofeedback is the preferred treatment for the chronic anal pain syndrome.	1a
Electrogalvanic stimulation is less effective than biofeedback.	1b
Botulinum toxin is effective.	1b
Percutaneous tibial nerve stimulation is effective in anal pain.	1b
Sacral neuromodulation is effective in anal pain.	3
Inhaled salbutamol is effective in intermittent chronic anal pain syndrome.	3

Recommendations for functional anorectal pain	GR
Biofeedback treatment is recommended in patients with pelvic pain and dyssynergic defecation.	A
Offer botulinum toxin A and electrogalvanic stimulation in chronic anal pain syndrome.	B
Offer percutaneous tibial nerve stimulation in chronic anal pain syndrome.	B
Offer sacral neuromodulation in chronic anal pain syndrome.	C
Offer inhaled salbutamol in intermittent chronic anal pain syndrome.	C

5.4.7 *Management of pudendal neuralgia*

Summary of evidence	LE
There are multiple treatment options with varying levels of evidence.	3

Recommendations	GR
Neuropathic pain guidelines are well established. Standard approaches to management of neuropathic pain should be utilised.	A

5.4.8 *Management of sexological aspects in CPP*

Summary of evidence	LE
Pelvic floor muscle physical therapy may offer relief of pain and reduction in sexual complaints.	2b

Recommendations	GR
Offer behavioural strategies to the patient and his/her partner to cope with sexual dysfunctions.	B
Training of the pelvic floor muscles is recommended to improve quality of life and sexual function.	B

5.4.9 *Management of pelvic floor dysfunction*

Summary of evidence	LE
Myofascial treatment is effective.	1b
Biofeedback improves the outcome of myofascial therapy.	1a
Trigger point release is effective in treating muscle and referred pain.	1a

Recommendations	GR
Apply myofascial treatment as first line treatment.	A
In patients with an overactive pelvic floor, biofeedback is recommended as therapy adjuvant to muscle exercises.	A
When myofascial trigger points are found, treatment by pressure or needling is recommended.	A

5.4.10 *Management of chronic/non-acute urogenital pain by opioids*

Recommendations	GR
All other reasonable treatments must have been tried and failed.	A
The decision to instigate long-term opioid therapy should be made by an appropriately trained specialist in consultation with another physician (including the patient and their family doctor).	A
Where there is a history or suspicion of drug abuse, a psychiatrist or psychologist with an interest in pain management and drug addiction should be involved.	A

6. EVALUATION OF TREATMENT RESULTS

6.1 Evaluation of treatment

For patients with chronic visceral pain, a visit to the clinician is important because they can ask questions, talk about how the process is going and have some time with the caregiver who understands the nature of their pain. First evaluation should take place after about six weeks to see if the treatment has been successful or not. When necessary adaptations are made and a next evaluation is planned.

*6.1.1 **Treatment has not been effective***

6.1.1.1 Alternative treatment

In cases where the treatment initiated did not have enough effect, an alternative approach is advised. First thing to do is a thorough evaluation of the patients or care providers adherence to the treatment that was initiated. Ask the patient if they have taken the medication according to the prescription, if there were any side-effects and if there where any changes in pain and function. Adjustment of medication or dose schemes might help. Another important thing to do is to read the reports of other caregivers like the physiotherapist and the psychologist. Has the therapy been followed until the end, what was the opinion of the therapist about the changes that were observed. In cases where the sessions had been ended by the patients, ask the patient why they made that decision. Check if the patient has understood the idea behind the therapy that was prematurely stopped.

6.1.1.2 Referral to next envelope of care

If patients and doctors come to the conclusion that none of the therapies given showed enough effect, then referral to a next envelope of care is advised. Unfortunately the terminology used to describe the nature and specialisation level of centres providing specialised care for visceral pain patients is not standardised country based. This does not facilitate easy referral schemes. It is advised that patients are referred to a centre that is working with a multidisciplinary team and nationally recognised as specialised in pelvic pain. Such a centre will re-evaluate what has been done and when available, provide specialised care.

6.1.1.3 Self-management and shared care

Patients who find themselves confronted with CPP for which there is no specific treatment option available, will have to live with their pain. They will need to manage their pain, meaning that they will have to find a way to deal with the impact of their pain on daily life activities in all domains of life. Self-help programs maybe advised and can be of help. This patient may also benefit from shared care, which means that a caregiver is available for supporting the self-management strategies. Together with this caregiver the patient can optimise and use the management strategies.

*6.1.2 **Treatment has been effective***

In cases where treatment has been effective the caregiver may pay attention to fallback prevention. If the patients feels the same pain again it helps to start at an early stage with the self-management strategies that he has learned during the former treatment. By doing so they will have the best chance of preventing the development of pelvic pain syndromes again.

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8. CONFLICT OF INTEREST

All members of the EAU Chronic Pelvic Pain Guidelines working panel have provided disclosure statements on all relationships that they have that might be perceived to be a potential source of conflict of interest. This information is publically accessible through the European Association of Urology website http://www.uroweb.org. This document was developed with the financial support of the European Association of Urology. No external sources of funding and support have been involved. The EAU is a non-profit organisation and funding is limited to administrative assistance and travel and meeting expenses. No honoraria or other reimbursements have been provided.