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.

1.1.1 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. Multidisciplinarity is of utmost importance and demands a broad view.

For the 2016 version the panel has made plans focussing on two important changes to the guideline. The first one is to rewrite the guideline in such a way that it is centred around pain instead of being organ centred. Chapters are now named after the organ or after the specialist that is consulted by the patient. For the 2016 edition of this guideline, pain will be the centre and every other information will be build around this central theme. The guideline will be partly theoretical to elucidate the importance of using a pain centred approach. The biggest part however, will deal with the practical approach in diagnostics, treatment and management of patients with abdominal and pelvic pain.

The second change the panel is working on is the way of presenting those practical aspects of pain. The guideline will, based on pain in the centre, lead the healthcare professional through the different steps in the process of dealing with abdominal and pelvic pain patients. One could say that it will be patient centred instead of complaint centred. Theoretical information will serve as background and can be read when needed. This second focus of updating will be of great importance for developing modern ways to make information available for the general practitioner who sees the patient in their office. It will contain red flags, associated conditions and available first line treatments. It should also be available for the medical specialist who gets a patient with chronic pain referred. The guideline will highlight 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 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].

For the update in 2012 the Panel focussed on:

1. restructuring the text to emphasise the significance of holistic management of CPP;
2. addressing the changes in the management of CPPS based on the concept of pain as a disease process.

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 has worked on reduction of the text (about 35%). This was carried out to improve the readability of the document. We did a major reduction especially in Chapter 3 “Urological aspects of chronic pelvic pain”. The subchapter on bladder pain syndrome was very critically revised and is now a comprehensive part of the guidelines. The fact that this part was so extensive shows that the roots of talking about abdominal and pelvic pain lies in the bladder, where Interstitial Cystitis was one of the first subjects addressed talking about pain in urology. The Panel has illustrated this in the publication in European Urology in 2013 [5].

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/.

This document was peer-reviewed prior to publication.

1.3 Panel composition

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

1.4 Methods

References used in this text are graded according to their Level of Evidence (LE) and Guidelines are given a Grade of Recommendation (GR). In this 2015 EAU Guidelines compilation, all standard information on LE and GR has been taken out of the individual Guidelines topics for the sake of brevity. The methodology section (see the introduction chapter of the complete book) outlines the LE and GR criteria which are used throughout the Guidelines, according to a classification system modified from the Oxford Centre for Evidence-based Medicine Levels of Evidence.

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 RCTs, Level of Evidence 1 (LE: 1), according to the rating schedule adapted from the Oxford Centre for Evidence-based Medicine Levels of Evidence (5). 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.

Initial list of abstracts	
Chapter	*Latest ‘cut-off’ date for search*
2 Chronic pelvic pain	16 May 2011
3 Urological aspects of chronic pelvic pain	
- Protate pain syndrome	04 June 2011
- Bladder pain syndrome diagnosis	08 June 2011
- Bladder pain syndrome treatment	08 June 2011
- Scrotal pain syndrome 09 June 2011	
- Urethral pain syndrome	09 June 2011
4 Gynaecological aspects of chronic pelvic pain	03 June 2011
5 Gastrointestinal aspect of chronic pelvic pain	14 January 2013
6 Peripheral nerve pain syndrome	17 May 2011
7 Sexological aspects of chronic pelvic pain	29 July 2011
8 Psychological aspects of chronic pelvic pain	16 January 2013
9 Pelvic floor function and chronic pelvic pain	08 June 2011
10 General treatment of chronic pelvic pain	29 June 2011

2. CHRONIC PELVIC PAIN

2.1 Introduction to chronic urogenital 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 central nervous system (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, independent of the original cause. 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, which will be discussed in Chapter 6.

2.2 Pain mechanisms - pain as a disease process

Chronic pelvic pain mechanisms may involve:

1. Ongoing acute pain mechanisms [6] (such as those associated with inflammation or infection), which may involve somatic or visceral tissue.
2. Chronic pain mechanisms, which especially involve the CNS [7].
3. Emotional, cognitive, behavioural and sexual responses and mechanisms [8-10]. These are covered in Chapters 7 and 8.

Table 1 illustrates some of the differences between the somatic and visceral pain mechanisms. They underlie some of the mechanisms that may produce the classical features of visceral pain; in particular, referred pain and hyperalgesia.

Table 1: 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 musculo-visceral 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.

2.2.1 Ongoing peripheral visceral pain mechanisms as a cause of CPP

In most cases of CPP, ongoing tissue trauma, inflammation or infection is not present [11-14]. 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 [15]. 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) [16, 17].

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 [18].
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 form of positive and inhibitory loops [19].

2.2.2 Central sensitisation - spinal and higher mechanisms of visceral pain

There are essentially three processes at the spinal cord level that are involved in central sensitisation [20]. Changes in existing protein activity (post-translational processing) are the earliest (within minutes); however, changes in genetic transcription of proteins and even structural changes in neuron connectivity may also have roles to play. These latter changes may occur within days [21].

2.2.3 Spinal mechanisms and visceral hyperalgesia

Central sensitisation [21] is responsible for a decrease in threshold and 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 the bladder 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 the bladder pain syndrome (BPS) and irritable bowel syndrome (IBS) may be explained by central sensitisation. A similar explanation exists for the muscle pain of fibromyalgia.

2.2.4 ***Supraspinal modulation of pain perception***

It is important to appreciate that nociception is the process of transmitting to centres involved in perception of information about 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. Pain is defined by the International Association for the Study of Pain (IASP) as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" [22]. The brain may affect the modulation of pain pathways at the spinal cord level.

2.2.5 ***Higher centre modulation of spinal nociceptive pathways***

It is now well accepted that there are both descending pain-inhibitory and descending pain-facilitatory pathways that originate from the brain [23].

Several neurotransmitters and neuromodulators are involved in descending pain-inhibitory pathways. The main contenders are the opioids, 5-hydroxytryptamine and noradrenaline.

2.2.6 ***Neuromodulation and psychology***

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 the higher level. Inhibiting or facilitating both the nociceptive signal reaching the consciousness and appraisal and interpretation of that signal; they 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 [24].

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 [25] may also 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.

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 significant adverse life events, which may produce these biological responses, and also have an effect on a patient's psychological wellbeing [27-29].

2.2.7 ***Autonomic nervous system***

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 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 quality of life (QoL) and must be managed as appropriate.

2.2.8 ***Endocrine system***

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. Upregulation 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 also evidence accumulating to suggest that the sex hormones also modulate both nociception and pain perception.

2.2.9 ***Genetics and 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.

2.3 Clinical paradigms and CPP

2.3.1 ***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 convergence-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 [12, 16, 30].

2.3.2 ***Referred pain to somatic tissues with hyperalgesia in the somatic tissues***

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.

2.3.3 ***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 [31].

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 [26].

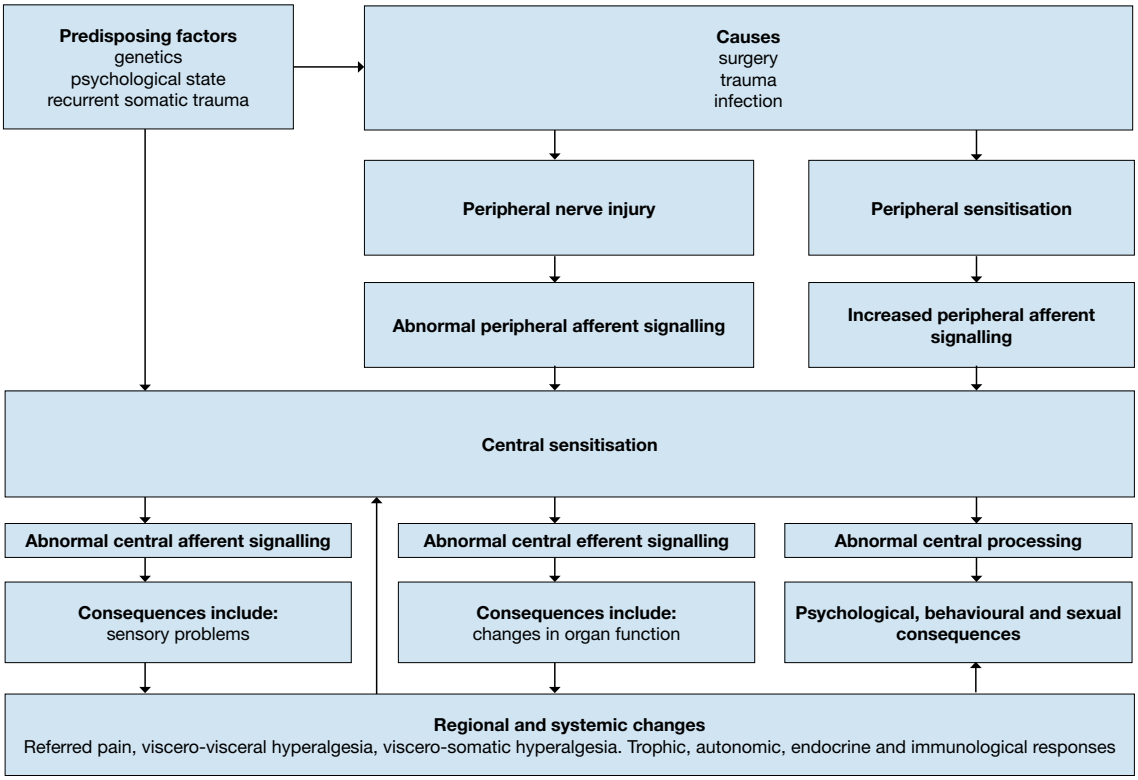
2.3.4 ***Visceral hyperalgesia***

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.

2.3.5 ***Viscero-visceral hyperalgesia***

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.

Figure 1: Predisposing factors and causes associated with central and peripheral mechanisms



2.4 Classification of CPP syndromes

*2.4.1 **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.

Phenotyping

Phenotyping is describing the condition. For example, chronic bladder pain may be associated with the presence of Hunner's lesions 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 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.

EAU classification of chronic pelvic pain syndromes is described in Table 2.

International Association for the Study of Pain (IASP) definitions, see: http://www.iasp-pain.org

Table 2: 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.

2.4.2 ***Pain syndromes***

The original EAU classification [2] was inspired by the IASP classification [22] 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.

2.4.2.1 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 cyclical pain conditions are included. 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.

2.4.2.2 Definition of chronic pelvic pain syndrome

Chronic pelvic pain syndrome (CPPS) 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.

2.4.2.2.1 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 endorgan 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.

2.4.2.2.2 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 salience 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).

2.4.2.2.3 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.

2.5.2.2.4 Multisystem 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 multisystemic 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.

2.4.2.2.5 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.

2.4.2.2.6 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.

Specific pain syndromes are defined in the relevant chapters.

2.5 Conclusions and recommendations: CPP and mechanisms

Conclusions	**LE**
CPPS 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 and neuropathic pain, so that symptoms of function can also occur.	1
CPP is associated with a high impact on QoL.	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 an understanding and training in CPPS pain mechanisms.	A
The early assessment of patients should involve not only investigations aimed at specific disease-associated pelvic pain but also 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
Future classification should involve consideration of all three recommendations above.	A

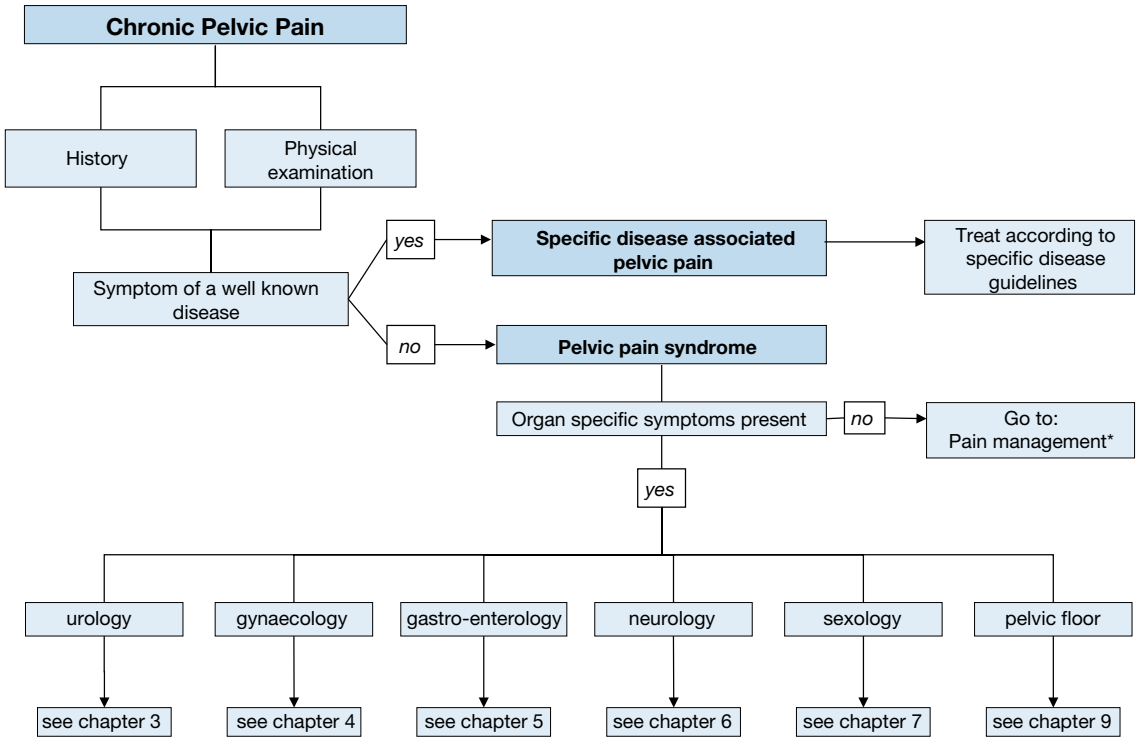
CPP = chronic pelvic pain; CPPS = chronic pelvic pain syndrome.

* Instruments for assessment see Chapter 8.

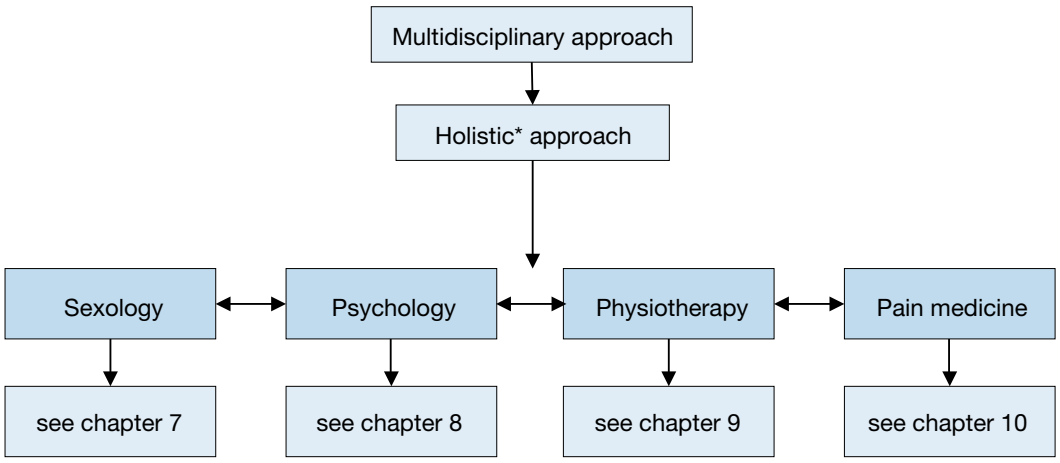
2.6 An algorithm for CPP diagnosis and treatment

The algorithm for diagnosing and treating CPP (Algorithm 1) has been developed to guide a physician through the process from diagnosis to management. A physician should follow the lines by answering the appropriate questions with yes or no. By doing this the clinician will end up at a box that refers to the chapter in this guideline that contains all the information needed. Because CPP is pain perceived in structures related to the pelvis, it is necessary to approach a patient diagnosed with CPP as a chronic pain patient. Confining the diagnosis to a specific organ may overlook multisystem functional abnormalities requiring individual treatment and general aspects of pain in planning investigation and treatment. This idea is easily recognised in the algorithm where the division in specific disease associated pain is made on one hand and pelvic pain syndrome on the other. The algorithm also illustrates that the authors advocate early involvement of a multidisciplinary pain team. In practice, this should mean that well-known diseases, e.g. 'true' cystitis and endometriosis, will be diagnosed and treated early. If treating such conditions does not reduce symptoms, or such well-defined conditions are not found, then further investigation may be necessary, depending on where the pain is localised. Every chapter of this guideline shows specific algorithms that assist the clinician in decisionmaking. It should be noted, however, that over-investigation may be as harmful as not performing appropriate investigations. The EAU algorithms introduce the concept of the 'minimum investigations' required to exclude a well-defined condition.

Algorithm 1: Diagnosing and treating CPP



Pain management*



**The term 'holistic' means consideration of the complete person, physically, psychologically, socially, and spiritually, in the management and prevention of disease.*

Figure 2: Phenotyping and assessment of CPP

Phenotyping	Assessment
Urology	Urinary flow, micturition diary, cystoscopy, ultrasound, uroflowmetry
Psychology	History of negative experiences, important loss, coping mechanism, depression
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

3. UROLOGICAL ASPECTS OF CHRONIC PELVIC PAIN

3.1 Introduction

In many of the patients with CPPS, pain is perceived predominantly in urological organs. Besides the known association of urological pelvic pain syndromes with negative psychological consequences [10] they are most frequently linked to functional disturbances of the lower urinary tract and sexuality. Multisystemic causes and effects lead to significant overlap of the different urological pain syndromes and they might be barely clinically distinguishable. Therefore, it has to be considered that some aspects of diagnosis and treatment addressed in the following subchapters may apply to all of them.

3.2 Prostate pain syndrome

*3.2.1 **Introduction***

Chronic pain in the region of the prostate has been linked to the term “prostatitis” in the past, although there is a proven bacterial infection in only 10% of the cases [32]. The remaining 90% should be classified as prostate pain syndrome (PPS), based on the fact that there is no proven infection or other obvious pathology. If CPP cannot be clearly ascribed to the prostate or another organ of the pelvis, the condition is defined more generally as CPPS, as outlined in Chapter 2.

*3.2.2 **Definition***

PPS is the occurrence of persistent or recurrent episodic pain over at least 3 out of the past 6 months (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 [10], as well as with symptoms suggestive of lower urinary tract and sexual dysfunction [33, 34].

According to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) classification, this correlates to CP/CPPS (Cat. III). Laboratory diagnosis goes along with sterile specimen cultures and either significant, or insignificant, white blood cell counts in prostate-specific specimens (i.e. semen, expressed prostatic secretions and urine collected after prostate massage) [35]. At present, there are no clinically relevant diagnostic or therapeutic consequences arising from differentiating inflammatory from non-inflammatory PPS (according to NIH definition), therefore, they are considered here as one entity.

3.2.3 ***Pathogenesis***

Pain is the main symptom in PPS. As a common feature of chronic pain syndromes, no single aetiological explanation has been found. One explanation [36] 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 CNS, sensitisation involving neuroplasticity may lead to a centralised neuropathic pain state (see Chapter 2) [36]. 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.

3.2.4 ***Epidemiology***

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 prostate syndrome and BPS), purely symptom-based case definitions may not reflect the true prevalence of PPS [37, 38]. In the literature, numbers of the population-based prevalence of prostatitis symptoms are reported ranging from 1 – 14.2% [39, 40]. 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).

3.2.5 ***Diagnosis***

Prostate pain syndrome is a symptomatic diagnosis, which 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. This implies that specific disease-associated pelvic pain caused by bacterial infection, urogenital cancer, urinary tract disease, urethral stricture, and neurogenic disease of the bladder 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 (LUTS), 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. QoL should also be measured because it can be very poor compared to other chronic diseases [42, 43]. In a study by Tripp et al. [10] 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). Reliable, valid indexes of symptoms and QoL are the NIH-CPSI [41] and the International Prostate Symptom Score (I-PSS) [44]. These subjective outcome measures are recommended for the basic evaluation and therapeutic monitoring of patients in urological practice.

There is no diagnostic test for PPS, 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. Physical examination including digital rectal examination should be carried out. Muscle tenderness and trigger points in the pelvic floor should be noted. A post-void residual should be done. Prostate-specific antigen testing does not help to diagnose PPS but can exclude prostate cancer in patients at risk.

Laboratory diagnosis has been classically based on the four-glass test for bacterial localisation [45]. 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) [46, 47]. 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 [48]. A general algorithm for assessment and treatment of PPS is shown in Figure 3.

3.2.6 *Conclusions and recommendations: assessment/diagnosis PPS*

Conclusions	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
Specific diseases with similar symptoms must be excluded. It is therefore recommended to adapt diagnostic procedures to the patient and to aim at identifying them.	A
After primary exclusion of specific diseases, patients with symptoms according to the above definition should be diagnosed with prostate pain syndrome.	A
A validated symptom and quality of life scoring instrument, such as the NIH-CPSI, should be considered for initial assessment as well as for follow-up.	B
It is recommended to assess prostate pain syndrome associated negative cognitive, behavioural, sexual, or emotional consequences, as well as symptoms of lower urinary tract and sexual dysfunctions.	B

3.2.7 *Treatment*

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 PPS, one reason for treatment failure in some large randomised placebo-controlled trials may be the heterogeneity of the patient population. Thus, 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 [49]. Monotherapeutic strategies for the treatment of PPS may fail [50], 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.

3.2.7.1 *Alpha-blockers*

Positive results from RCTs of alpha-blockers, i.e. terazosin [51, 52], alfuzosin [53], doxazosin [54, 55], tamsulosin [56, 57], and silodosin [58] have led to widespread use of alpha-antagonists in the treatment of PPS in recent years. The most recent in-depth systematic review and network meta-analyses of alpha-blockers [59] have shown significant improvement in total symptom, 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 [60]. 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.

3.2.7.2 *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 [61], and prostate biopsy culture findings do not differ from those of healthy controls [62]. The only randomised placebo-controlled trials of sufficient quality have been done for oral antibiotic treatment with ciprofloxacin (6 weeks) (36), levofloxacin (6 weeks) [63], and tetracycline hydrochloride (12 weeks) [64]. The studies have been analysed in recently published meta-analyses [59, 65]. 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 [65]. In addition, sample sizes of the studies were relatively small and treatment effects were 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.

3.2.7.3 Anti-inflammatory drugs

For non-steroidal anti-inflammatory drugs, a trial with celecoxib 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 [66].

Two low-power placebo-controlled studies for zafirlukast, a leukotriene antagonist, and prednisone failed to show a benefit [67, 68] . 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 [69].

In a recent meta-analysis, two studies of NSAIDs [48, 66] and one with prednisolone [67] were pooled. Anti-inflammatory drugs were 80% more likely to have a favourable response than placebo. In 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.

3.2.7.4 Opioids

Opioids produce modest pain relief in some patients with refractory PPS, although there are limited data on the long-term efficacy of opioids in non-cancer pain. Opioid treatment carries the risk of side-effects, reduced QoL, addiction, opioid tolerance and opioid-induced hyperalgesia [70]. Urologists should use opioids for PPS only in collaboration with pain clinics and with other treatments.

3.2.7.5 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 placebo-controlled randomised trial published in a peer-reviewed journal did not support this, but the study did lack power [71]. In another RCT, finasteride provided better amelioration of symptoms compared to saw palmetto over a 1-year period, but lacked a placebo-control arm [72]. 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 [73]. 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 [74]. 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 [74].

3.2.7.6 Allopurinol

There is insufficient evidence for the use of allopurinol in PPS [75, 76].

3.2.7.7 Phytotherapy

An adequately powered randomised placebo-controlled study of Cernilton, showed clinically significant symptom improvement over a 12-week period in inflammatory PPS patients (NIH Cat. IIIA) [77]. 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 [78]. In contrast, treatment with saw palmetto, most commonly used for benign prostatic hyperplasia, did not improve symptoms over a 1-year period [72]. In a systematic review and meta-analysis, patients treated with phytotherapy were found to have significantly lower pain scores than those treated with placebo [59]. In addition, overall response rate in network analysis was in favour of phytotherapy (RR: 1.6; 95% CI: 1.1-1.6).

3.2.7.8 Pentosan polysulphate

High-dose oral pentosan polysulphate (3x 300 mg/day), as for BPS, is able to improve clinical global assessment and QoL significantly over placebo in men with PPS, suggesting a possible common aetiology [79].

3.2.7.9 Muscle relaxants

Muscle relaxants (diazepam, baclofen) are claimed to be helpful in sphincter dysfunction or pelvic floor/perineal muscle spasm, but there have been only a few prospective clinical trials to support these claims. In a recent 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 [55].

3.2.7.10 Pregabalin

Pregabalin is an antiepileptic drug that has been approved for use in chronic postherpetic neuralgia, fibromyalgia, and diabetic neuropathy. In an adequately powered randomised placebo-controlled study, which was the only report included in a recently published Cochrane review [80], 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 by at least 6 points [81].

3.2.7.11 Botulinum toxin A

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 number was too low (13 in the BTX-A group and 16 in the placebo group), and follow-up was too short to draw definitive conclusions. Side-effects are unclear and it is advised to only use BTA within the context of a clinical trial.

3.2.7.12 Physical treatments

- *Electromagnetic therapy*. In a small, sham-controlled, double-blind study, 4 weeks electromagnetic therapy showed a significant, sustained effect over a 1-year period [82].
- *Microwave thermotherapy*. In uncontrolled studies significant symptomatic improvement has been reported from heat therapy, for example, transrectal and transurethral thermotherapy [83, 84]
- *Extracorporeal shock wave therapy*. A recent sham-controlled double-blind study of four times weekly perineal extracorporeal shock wave therapy (n = 30) showed significant improvement in pain, QoL, and voiding compared to the control group (n = 30) over 12 weeks [85]. Confirmatory studies are awaited because of an absent placebo-effect, which is very unusual in PPS trials.
- *Electroacupuncture*. In a small three-arm randomised trial, electroacupuncture was superior to sham treatment and advice and exercise alone [86]. In a recent prospective case series of 6 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.
- *Posterior tibial nerve stimulation*. One sham-controlled medium-sized study (n = 89) demonstrated significant improvement in total NIH-CPSI score and visual analogue scale for pain [87].
- *Myofascial physical therapy*. A randomised feasibility trial of myofascial physical therapy including PPS (n = 21) and patients with BPS showed a clinical benefit compared to global therapeutic massage [88]. In the PPS group alone, there was no difference in the effect between the two treatment arms.

3.2.7.13 Surgical management

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

3.2.7.14 Psychological treatment

The evidence for psychological treatment is lacking, there is weak evidence for improvement of pain and QoL but not for some urinary symptoms. Details concerning appropriate treatment content and delivery are covered in Chapter 8.

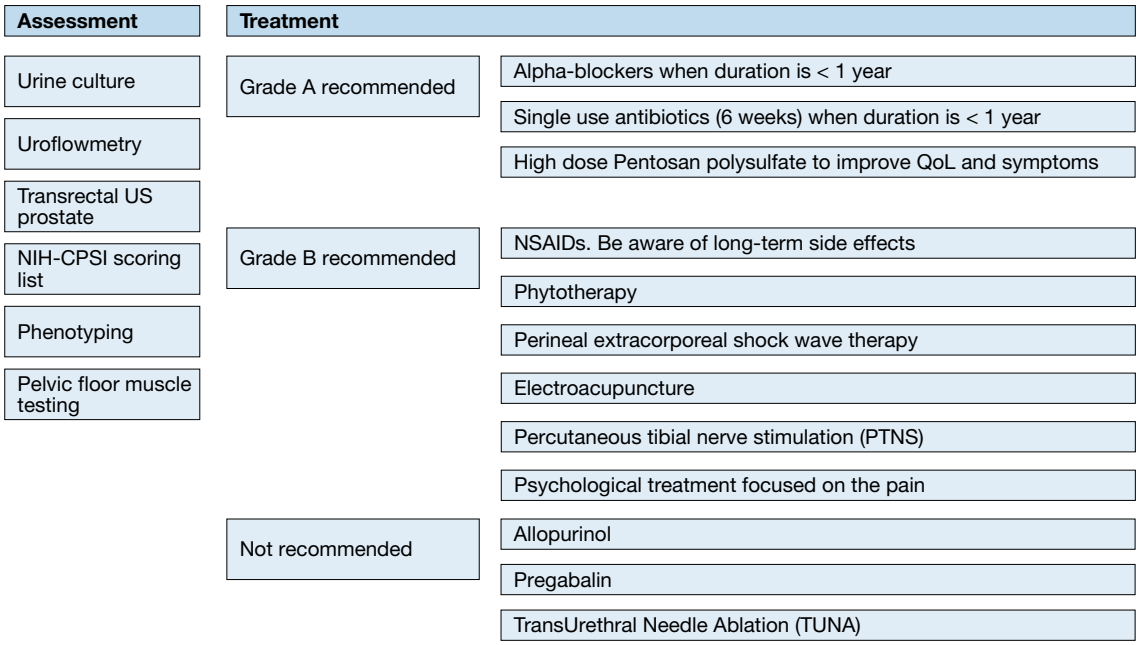
3.2.8 *Conclusions and recommendations: treatment of PPS*

Conclusions	LE
Monotherapeutic treatment regimens in PPS may fail.	3
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
There are insufficient data on the effectiveness of steroids in PPS.	2b
There are insufficient data on the effectiveness of opioids in PPS.	4
There are insufficient data on the effectiveness of 5-alpha-reductase inhibitors in PPS.	2b
There are insufficient data on the effectiveness of allopurinol in PPS.	2b
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
There are only limited data on the effectiveness of electromagnetic therapy in PPS.	2b
There are only limited data on the effectiveness of microwave thermotherapy in PPS.	3
Perineal extracorporeal shock wave therapy probably is effective for the treatment of PPS.	1b
There are limited data on the effectiveness of electro-acupuncture for the treatment of PPS.	2b
Posterior tibial nerve stimulation is probably effective for the treatment of PPS.	1b
There are insufficient data on the effectiveness of myofascial physical therapy for the treatment of PPS.	2b
There are limited data on lack of effectiveness of TUNA of the prostate for PPS.	2b
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
Consider multimodal and phenotypically directed treatment options for PPS.	B
Alpha-blockers are recommended for patients with a duration of PPS < 1 year.	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
NSAIDs are recommended for use in PPS, but long-term side-effects have to be considered.	B
Allopurinol is not recommended for use in PPS.	B
Phytotherapy might be used in patients with PPS.	B
Consider high-dose pentosan polysulphate to improve symptoms and quality of life in PPS.	A
Pregabalin is not recommended for use in PPS.	A
Perineal extracorporeal shock wave therapy might be considered for the treatment of PPS.	B
Electro-acupuncture might be considered for the treatment of PPS.	B
Posterior tibial nerve stimulation might be considered for the treatment of PPS.	B
TUNA of the prostate is not recommended for the treatment of PPS.	B
For PPS with significant psychological distress, psychological treatment focussed on PPS should be attempted.	B

PPS = prostate pain syndrome; TUNA = transurethral needle ablation; NSAIDs = non-steroidal anti-inflammatory drugs.

Figure 3: Assessment and treatment of PPS



US = ultrasound.

3.3 Bladder pain syndrome

*3.3.1 **Introduction***

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. The term BPS rather than interstitial cystitis (IC) was put forward by the International Society for the Study of BPS (ESSIC) and will be used in these guidelines. In accordance Classic IC (Hunner's lesion and inflammation) will be referred to as BPS type 3 C (See Chapter 2, section 2.4 'Definitions of CPP terminology').

*3.3.2 **Pathogenesis***

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 [89]. Experimental induction of chronic pelvic pain by O-antigen deficient bacterial strains reinstates the bacterial hypothesis [90].

Pancystitis, with associated perineural inflammatory infiltrates, and mast cell count increase is an essential part of BPS type 3 C [91], but is scant in non-lesion BPS [92, 93] (24, 29).

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 [94-101] and a consequent cytotoxic effect [102-104].

*3.3.3 **Epidemiology***

Reports of BPS prevalence have varied greatly, along with the diagnostic criteria and populations studied. Recent reports range from 0.06% to 30% [105-114]. There is a female predominance of about 10:1 [111, 115-117] but possibly no difference in race or ethnicity [37, 118, 119]. The relative proportions of classic and non-lesion disease are unclear. Incidence in studies has ranged from 5 to 50% [120-124]. Evidence that BPS may have a genetic component has been presented in several studies, but may contribute to less than one third of total variation in susceptibility for BPS.

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 [125].

Bladder pain syndrome has significant economic costs. Direct annual costs in the USA have been estimated to be $750 million [126].

*3.3.4 **Association with other diseases***

An association has been reported between BPS and non-bladder syndromes such as fibromyalgia (FM), chronic fatigue syndrome (CFS), irritable bowel syndrome (IBS), vulvodynia, depression, panic disorders, migraine, sicca syndrome, temporomandibular joint disorder, allergy, asthma and systemic lupus erythematosus [127-133].

Risk of BPS correlates with a number of non-bladder syndromes in each patient [134]. 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 [135].

*3.3.5 **Diagnosis***

Bladder pain syndrome 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 3, Algorithm 3) [15].

The nature of pain is key to disease definition:

- Pain, pressure or discomfort perceived to be related to the bladder, increasing with increasing bladder content.
- Located suprapubically, sometimes radiating to the groins, vagina, rectum or sacrum.
- Relieved by voiding but soon returns [136-140].
- Aggravated by food or drink [140].

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

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 [141].

Cystoscopy

Despite controversy on diagnostic or follow-up value of cystoscopy [142-146]. this panel believes 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 [147]). 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 [139]. The scar ruptures with increasing bladder distension, producing a characteristic water fall type of bleeding. There is a strong association between BPS type 3 C and reduced bladder capacity under anaesthesia [123, 139, 148]. 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 [149].

Biopsies are helpful in establishing or supporting the clinical diagnosis of both classic and non-lesion types of the disease [95, 147, 150-152]. Important differential diagnoses to exclude by histological examination are carcinoma in situ and tuberculous cystitis.

Table 3: ESSIC classification of BPS types according to results of cystoscopy with hydrodistension and biopsies [15]

	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.*

Potassium chloride bladder permeability tests are no longer advised in current practice based on lack of evidence in the literature.

Phenotyping and biological markers
All putative biological markers to date have yet to be validated [97].

Recent work has indicated the need to phenotype BPS patients. UPOINT (Urinary, Psychosocial, Organ Specific, Inflammation, Neurological/Systemic, Tenderness) is an example of phenotyping which supports individualised therapy [153].

3.3.6 ***Conclusions and recommendations: assessment and diagnosis BPS***

Conclusions	**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 cannot be confirmed by non-invasive means.	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 associated non-bladder diseases are extremely prevalent, differ in BPS subtypes and correlate with BPS risk.	2a
BPS has a high impact on quality of life.	2a
There is significant overlap of symptoms with other conditions.	2a
Reliable instruments assessing symptom severity as well as phenotypical differences exist.	2a

Recommendations	**GR**
Specific diseases with similar symptoms must be excluded. It is therefore recommended to adapt diagnostic procedures to each patient and aim at identifying them.	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
A validated symptom and quality of life scoring instrument should be considered for initial assessment as well as for follow-up.	B
BPS associated non-bladder diseases should be assessed systematically.	A
BPS associated negative cognitive, behavioural, sexual, or emotional consequences should be assessed.	A

BPS = Bladder pain syndrome.

3.3.7 ***Medical treatment***
Analgesics. Urologists should preferably use analgesics in collaboration with pain clinics. For further information see Chapter 10. [70].

Corticosteroids are not recommended in the management of patients with BPS because of a lack of evidence.

Anti-allergics. 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 [154] and H2 [155] receptor subtypes, with variable results. A prospective placebo-controlled RCT of hydroxyzine or sodium pentosan polysulphate did not show a significant effect [156].

Amitriptyline. The tricyclic antidepressant amitriptyline alleviates symptoms in BPS, probably via blockade of acetylcholine receptors, inhibition of serotonin and noradrenalin reuptake, and blockade of histamine H1 receptors. It is also an anxiolytic agent [157]. Several reports have indicated amelioration after oral amitriptyline [116, 158, 159]. Amitriptyline has been shown to be beneficial when compared with placebo plus behavioural modification [160]. Drowsiness is a limiting factor with amitriptyline, and thus, nortriptyline is sometimes considered instead.

Pentosan polysulphate sodium (Elmiron) is thought to repair defects in the GAG layer. Subjective improvement of pain, urgency, frequency, but not nocturia, has been reported [161, 162]. Pentosan polysulphate sodium had a more favourable effect in BPS type 3C than in non-lesion disease [163]. 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 [164].

Antibiotics have no role in BPS due to the lack of evidence.

Immunosuppressants. Azathioprine treatment has resulted in disappearance of pain and urinary frequency [165]. Initial evaluation of cyclosporin A (CyA) [166] and methotrexate [167] showed good analgesic effect but limited efficacy for urgency and frequency.

Gabapentin and Pregabalin are used in neuropathic pain as part of a broad multimodal management plan (see Chapter 10 General Treatment)

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

3.3.8 ***Intravesical treatment***

Intravesical drugs are administered due to poor oral bioavailability establishing high drug concentrations at the target, 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 [168, 169]. Alkalisation of lidocaine improves its pharmacokinetics [170]. Combination of heparin, lidocaine and sodium bicarbonate gave immediate symptom relief in 94% of patients and sustained relief after 2 weeks in 80% [171]. Intravesical instillation of alkalinised lidocaine or placebo for five consecutive days resulted in significantly sustained symptom relief for up to 1 month [172].

Hyaluronic acid (hyaluronan) and Chondroitin sulphate are described to repair defects in the GAG layer. Despite the fact that intravesical GAG replenishment is 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, or concentrations. More important, there are differences in proved 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 [173].

Intravesical heparin. BPS patients were treated with heparin for 3 months, and over half had control of symptoms, with continued improvement after 1 year of therapy [174]. Kuo reported another trial of intravesical heparin for 3 months in women with frequency-urgency syndrome and a positive potassium test. Symptomatic improvement was reported in 80% of BPS patients [175]. Baykal et al. evaluated intravesical heparin plus dorsal tibial nerve stimulation in patients with refractory BPS. Voiding frequency, pain score and maximum cystometric capacity were significantly better after 2 and 12 months [176].

Dimethyl sulphoxide (DMSO) has been used in the past. There is insufficient current evidence to recommend its use.

Bacillus Calmette Guérin (BCG) has been used in the past but there is insufficient current evidence to recommend its use.

Vanilloids. There is little evidence to support their routine use and they should only be considered in a research environment.

3.3.9 ***Interventional treatments***

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

Electromotive drug administration (EMDA) which enhances tissue penetration of ionised drugs by iontophoresis has been used in the research setting.

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 [177, 178]. Prolonged amelioration of pain and urgency has been described for transurethral laser ablation as well [179].

Botulinum toxin A (BTX-A) may have an antinociceptive effect on bladder afferent pathways, producing symptomatic and urodynamic improvements [124]. Treatment with hydrodistension and hydrodistension plus intravesical BTX-A (onabotulinumtoxin A) has been compared [180]. 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.

Trigonal-only injection seems effective and long-lasting because 87% of patients reported improvement after 3 months follow-up [181]. 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.

Hyperbaric oxygen (HBO) is a safe and feasible therapeutic approach, with moderate effects on a small subgroup of BPS patients. Disadvantages include high cost, limited availability of treatment sites, and time-consuming treatment [182].

Neuromodulation. 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 [183]. Long-term results were verified in a retrospective study of patients from 1994 to 2008 [184]. Permanent SNM implantation was performed in patients who showed at least 50% improvement in symptoms with a temporary peripheral nerve evaluation test [184]. 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 [185], 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. Reoperation rate was 25%.

3.3.10 ***Treatments of limited efficacy and absence of recent publications***

Cimetidine. There is limited data to suggest that Cimetidine improves symptoms of BPS in the short-term [186]. 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 [187].

Prostaglandins. Misoprostol is a prostaglandin that regulates various immunological cascades. After 3 months of treatment with misoprostol, 14/25 patients had significantly improved, with 12 showing a sustained response after a further 6 months [188]. The incidence of adverse drug effects was 64%.

L-Arginine. Oral treatment with the NO synthase substrate l-arginine decreases BPS-related symptoms [189-191]. NO is elevated in patients with BPS [192]. However, others have not demonstrated symptomatic relief or changes in NO production after treatment [193, 194].

Anticholinergics. 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 [195]. However, the effect on pain has not been reported.

Duloxetine inhibits both serotonin and noradrenaline reuptake. Duloxetine did not significantly improve symptoms of BPS [196]. 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 [197-201]. Due to high complication rates, clorpactin instillations can no longer be recommended [197, 198, 200, 202].

3.3.11 ***Other treatments***

Diet. Scientific data are limited and dietary restriction alone does not produce complete symptomatic relief.

Acupuncture. Scientific evidence for acupuncture is often poor, with contradictory results from a few low evidence reports, with effects being limited and temporary.

3.3.12 ***Surgical treatment***

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 in a MDT.
Four major techniques are common:

- Urinary diversion without cystectomy
- supratrigonal (i.e., trigone-sparing) cystectomy
- subtrigonal cystectomy
- radical cystectomy including excision of the urethra.

Urinary diversion without cystectomy. As early as 1967, Turner-Warwick reported that bladder augmentation without removal of the diseased tissue was not appropriate [203]. Reports that unresected BPS bladders cease to induce symptoms after loss of contact with urine are scarce [121, 204].

Supratrigonal cystectomy with subsequent bladder augmentation represents the most favoured continence-preserving surgical technique. Various intestinal segments have been used for trigonal augmentation [205-207].

Subtrigonal cystectomy. Subtrigonal resection has the potential of removing the trigone as a possible disease site, but at the cost of requiring ureteral reimplantation. Nurse et al. reported trigonal disease in 50% of their patients and blamed surgical failure on the trigone left in place [208]. In contrast, Linn et al. reported [209] six out of 17 patients being completely cured by supratrigonal resection [208]. 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 [210].

Cystectomy with formation of an ileal conduit still ranks first in current US practice trends for BPS surgery [211]. 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, Elzawahri recommended retubularisation of a previously used bowel segment to form a urinary conduit [212]. It is important to note that pregnancies with subsequent lower-segment Caesarean section have been reported after ileocystoplasty [212, 213].

3.3.13 Conclusions and recommendations: treatment of BPS

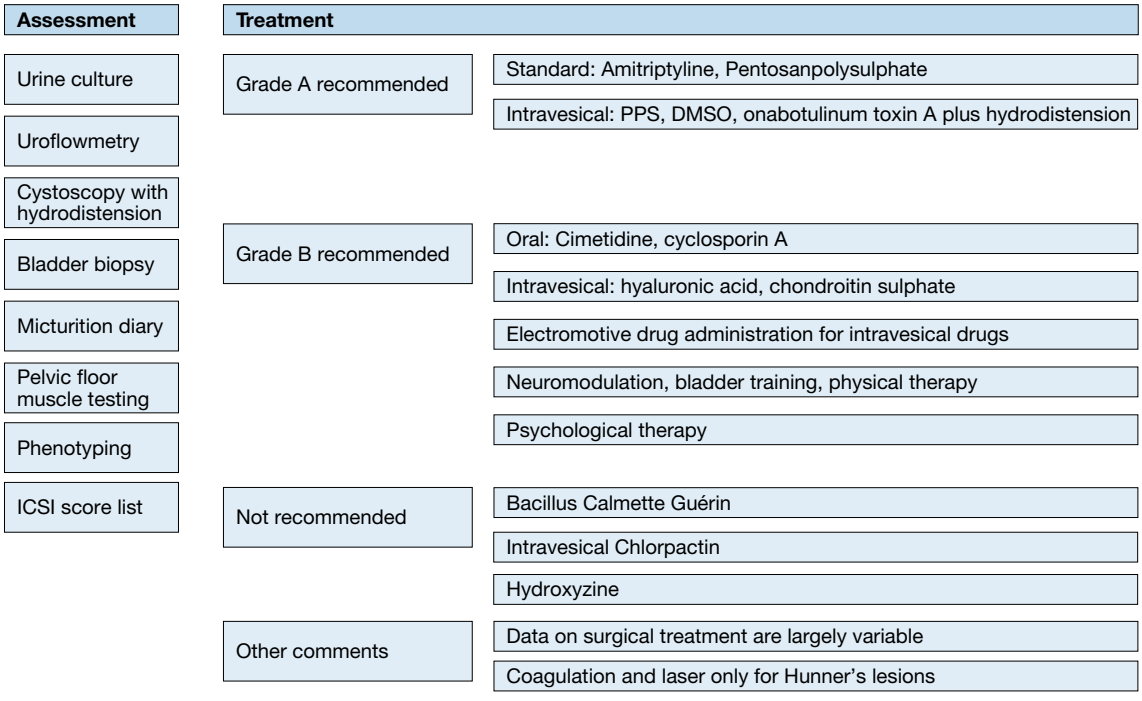
Conclusions	**LE**
None of the present treatments affect all BPS subtypes or phenotypes.	4
Corticosteroids are not recommended for long-term treatment.	3
Hydroxyzine has limited efficacy in BPS.	3
Limited data exist on effectiveness of cimetidine in BPS.	2b
Amitriptyline is effective for pain and related 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
Insufficient data exist for the effectiveness of prostaglandins in BPS. Adverse effects are frequent.	3
Global response to cyclosporin A is superior to that of pentosanpolysulphate sodium, but associated with more adverse effects.	1b
Duloxetin shows no efficacy and tolerability is poor.	2b
Oxybutynin has limited effect on BPS pain, but data are scant.	3
Preliminary data showed effectiveness of quercetin alone and in multimodal uncontrolled studies.	3
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 hyaluronic acid may have long-term effects in BPS patients with positive intravesical modified KCl test.	2b
Intravesical chondroitin sulphate may be effective according to non-randomised studies. Published RCTs are underpowered.	2b
There is insufficient current evidence for Intravesical DMSO.	1b
Intravesical submucosal BTX-A injection plus hydrodistension are significantly superior to hydrodistension alone.	1b
Only limited data exist on the effectiveness of BTX-A injection into the detrusor or trigone.	3
Intravesical BCG is not effective in BPS.	1b
Intravesical clorpactin has insufficient data to support effectiveness, and high complication rates.	3
Bladder distension should only be used as diagnostic.	3
Scarce data indicate electromotive drug administration may have a beneficial effect in some patients.	3
Transurethral resection (coagulation and laser) may be effective in BPS type 3C.	3
Sacral neuromodulation may be effective in BPS.	3
PNS is superior to SNM for treatment of BPS.	1b
Avoidance of some food and drink avoids pain triggering.	3
Acupuncture data are contradictory.	3
No definitive conclusion on the effectiveness of organ removal for BPS can be drawn based on the large variability of results.	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
Analgesics should be used preferably in collaboration with a pain clinic.	C
Corticosteroids are not recommended for long-term treatment.	C
Do not offer hydroxyzine for the treatment of BPS.	C
Consider cimetidine as a valid oral option before invasive treatments.	B
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
Prostaglandins are not recommended. Insufficient data on BPS, adverse effects are considerable.	C
Cyclosporin A might be used in BPS but adverse effects are significant and should be carefully considered.	B
Duloxetin is not recommended for BPS treatment.	C

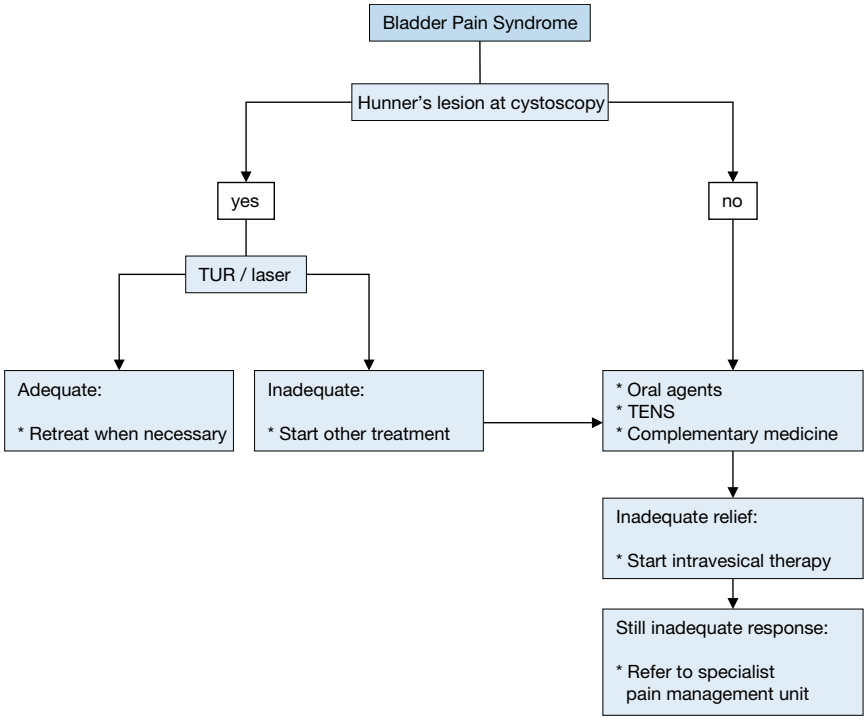
Oxybutynin might be considered for the treatment of BPS.	C
Gabapentin might be considered for oral treatment of BPS.	C
Administer intravesical lidocaine plus sodium bicarbonate prior to more invasive methods.	A
Administer intravesical pentosanpolysulphate sodium before more invasive treatment alone or combined with oral pentosanpolysulphate sodium.	A
Consider intravesical heparin before more invasive measures alone or in combination treatment.	C
Consider intravesical hyaluronic acid before more invasive measures.	B
Consider intravesical chondroitin sulphate before more invasive measures.	B
Consider intravesical bladder wall and trigonal injection of BTX-A if intravesical instillation therapies have failed.	C
Administer submucosal injection of BTX-A plus hydrodistension if intravesical instillation therapies have failed.	A
Intravesical therapy with BCG is not recommended in BPS.	A
Intravesical therapy with clorpactin is not recommended in BPS.	A
Bladder distension is not recommended as a treatment of BPS.	C
Consider transurethral resection (or coagulation or laser) of bladder lesions, but in BPS type 3 C only.	B
Neuromodulation might be considered before more invasive interventions.	B
Consider diet avoidance of triggering substances.	C
Acupuncture is not recommended.	C
All ablative organ surgery should be the last resort for experienced and BPS knowledgeable surgeons only.	A

DMSO = dimethyl sulphoxide; BPS = bladder pain syndrome.

Figure 4: Diagnosis and therapy of BPS



Algorithm 3: Treatment of BPS Type 3 C



3.4 Genital pain syndrome

*3.4.1 **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.

*3.4.2 **Definitions***

3.4.2.1 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, and with symptoms suggestive of lower urinary tract and sexual dysfunction. Previous terms have included orchitis, orchialgia and orchiodynia. These terms are no longer recommended.

3.4.2.2 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, and with symptoms suggestive of lower urinary tract and sexual dysfunction.

*3.4.3 **Pathogenesis***

Often scrotal pain is not associated with any specific pathology. Pain is perceived in the testes, epididymis, or the vas deferens.

3.4.3.1 Nerves

The ilioinguinal and genitofemoral and pundendal nerves innervate the scrotum [214]. Any pathology or intervention at the origin or along the course of the nerves may result in pain perceived in the scrotum [215].

3.4.3.2 Postvasectomy pain syndrome

Postvasectomy scrotal pain syndrome occurs following vasectomy and is often associated with negative cognitive, behavioural, sexual or emotional consequences, and with symptoms suggestive of lower urinary tract and sexual dysfunction. Postvasectomy 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.

Incidence of postvasectomy pain is 2-20% among all men who have undergone a vasectomy [216]. In men with postvasectomy pain, 2-6% have a VAS score > 5 [217]. 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 postvasectomy pain was significantly lower in the no-scalpel vasectomy group (11.7% vs. the scalpel group 18.8%) [218].

3.4.3.3 Post-inguinal hernia repair

Chronic scrotal pain is 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 [215, 219]. 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 [220].

*3.4.4 **Diagnosis***

A physical examination is mandatory in patients with scrotal pain. Gentle palpation of each component of the scrotum is performed to search for masses and painful spots. A rectal examination is done to look for prostate abnormalities and to examine the pelvic floor muscles. Scrotal ultrasound (US) has limited value in finding the cause of the pain. In > 80% of patients, US does not show abnormalities that have clinical implications [221, 222]. If physical examination is normal, US can be performed to reassure the patient that there is no pathology that needs therapy (mainly surgery). Ultrasound can be used to diagnose hydroceles, spermatoceles, cysts and varicoceles. When abnormalities such as cysts are seen, this may play a role in therapeutic decision making.

*3.4.5 **Treatment***

Treatment of chronic scrotal pain is based on the principles of treating chronic pain syndromes, described throughout these guidelines [223].

3.4.5.1 Conservative treatment

Conservative treatment should be in accordance with the principles described within this guideline (Chapters 9 and 10).

3.4.5.2 Surgery

The only surgical treatment that seems to be effective is microsurgical denervation which is for specific indications (see below). Epididymectomy may also be a choice in selected cases and orchiectomy is the last resort.

3.4.5.2.1 Microsurgical denervation

The three studies that have been carried out were cohort studies but their success rates were high. All studies are comparable on indication criteria, diagnostic methods and the surgical approach used. All had a follow-up of at least 20 months. Ultrasound showed no abnormalities and a spermatic cord block showed pain relief of > 50%.

Complete relief of pain is achieved in 71-96% and partial relief in 9-17%. Testicular atrophy was seen in 3-7% of the operated patients [224-226].

3.4.5.2.2 Epididymectomy

Evidence is conflicting around epididymectomy for scrotal pain and this should only be done as a part of a clinical trial.

3.4.5.2.3 Orchiectomy

There is no evidence to support orchiectomy and this should only be done within a clinical trial.

3.4.5.2.4 Vasovasostomy

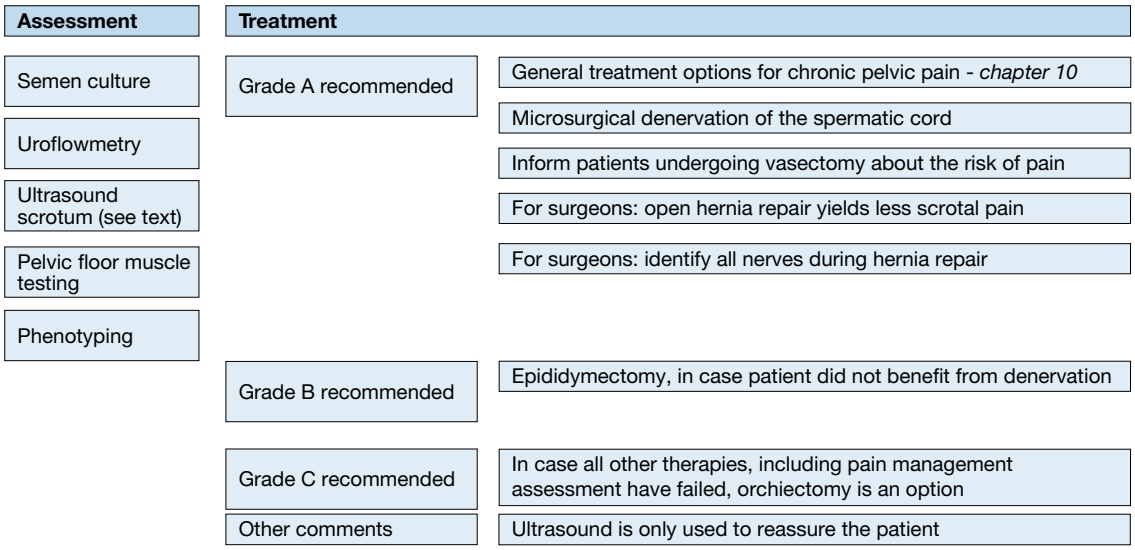
In postvasectomy pain syndrome, a vasovasostomy might help to overcome the obstruction and thereby improve the pain. Some studies have shown good results but the quality of these studies was limited [227, 228].

*3.4.6 **Conclusions and recommendations: scrotal pain syndrome***

Conclusions	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 nor treatment of scrotal pain.	2b
Postvasectomy 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
Microsurgical denervation of the spermatic cord is an effective therapy for scrotal pain syndrome.	2b
Vasovasostomy is effective in postvasectomy pain.	2b
Orchiectomy is the last resort in treating scrotal pain syndrome.	4

Recommendations	GR
Start with general treatment options for chronic pelvic pain (see chapter 10).	A
Inform about the risk of postvasectomy 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
For patients who do not benefit from denervation it is recommended to perform epididymectomy.	B
We recommend that orchiectomy should not be done, unless all other therapies, including pain management assessment, have failed.	C

Figure 5: Assessment and treatment of scrotal pain syndrome



3.5 Urethral pain syndrome

*3.5.1 **Definition***

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.

*3.5.2 **Pathogenesis***

Based on the definition, there is no well-known pathogenetic mechanism responsible for urethral pain syndrome. There are no data available to answer the question: “how common is dysuria in the presence of

negative rigorous investigation of the bladder and urethra?". Some suggestions have been proposed. The intimate relation of the urethra with the bladder (both covered with urothelium) makes it plausible that pathology seen in the bladder is also found in the urethra and causes the same symptoms. This is the case in classifying urethral pain syndrome as a form of BPS. It is obvious that what might cause pain in the bladder could be responsible for urethral pain. Mechanisms thought to be basic for BPS also apply to the urethra. This means that the specific testing with potassium is used to support the theory of epithelial leakage [152, 229]. Urethral syndrome is supposed to be the same as BPS in that the epithelium is leaking, thereby causing pain. Another possible mechanism is the neuropathic hypersensitivity following urinary tract infection [230].

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 [231].

*3.5.3 **Treatment***

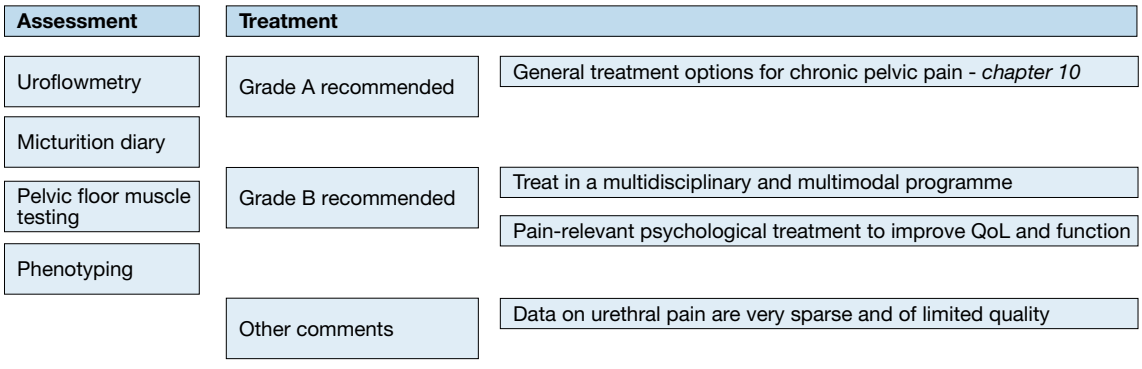
There is no specific treatment that can be advised. Management should be multidisciplinary and multimodal [232]. Laser therapy of the trigonal region may be a specific treatment. One trial comparing two forms of laser reported good results, but did not compare with sham treatment [233]. The majority of publications on treatment of urethral pain syndrome have come from psychologists [230].

*3.5.4 **Conclusions and recommendations: urethral pain syndrome***

Conclusions	**LE**
Urethral pain syndrome may be a part of BPS.	2a
Urethral pain may be neuropathic hypersensitivity following urinary tract infection.	2b
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 quality of life.	4

Recommendations	**GR**
Start with general treatment options for chronic pelvic pain (see chapter 10).	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

Figure 6: Assessment and treatment of urethral pain syndrome



4. GYNAECOLOGICAL ASPECTS OF CHRONIC PELVIC PAIN

4.1 Introduction

Chronic pelvic pain in urological and gynaecological practice is complex and difficult to treat. The aim is to define the aetiology and treat it appropriately. However, in 30% of cases, there is no definable cause and this poses a challenge [234].

4.2 Clinical history

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.

4.3 Clinical examination

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. 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. Examining a woman with CPP is difficult, and 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).

*4.3.1 **Investigations***

Vaginal and endocervical swabs to exclude infection are recommended, and cervical cytology screening is advisable. Pelvic imaging can provide useful information about pelvic anatomy and pathology. Areas of tenderness detected during a transvaginal scan can help determine the possible presence of current or pre-existing visceral disease [235, 236]. Laparoscopy is perhaps the most useful invasive investigation to exclude gynaecological pathology [237, 238] and to assist in the differential diagnosis of CPP in women [239]. Often, it is combined with cystoscopy [240, 241] and/or proctoscopy to help identify the site of multi-compartment pain.

Psychological considerations around laparoscopy

There have been three diverse studies of laparoscopy. Elcombe et al. have shown that there was a distinct and lasting improvement in pain consequent of laparoscopy. Improvement was related to beliefs about pain and its meaning in terms of serious disease, and not to medical variables [242]. In another study, showing women a photograph of their pelvic contents taken during laparoscopy did not improve pain ratings/ beliefs about pain, than those who did not see a photograph [243]. Peters et al. compared standard clinical care of patients with CPP, where organic causes of pelvic pain were excluded first and diagnostic laparoscopy was routinely performed, with a second group, where an integrated approach was chosen from the beginning, with equal attention being given to somatic and psychological factors and laparoscopy was not routinely performed [244]. Both patient groups were similar in their characteristics. Evaluation of pain and function one year after therapy commenced revealed that the integrated approach improved pelvic pain parameters significantly more often than the standard approach, suggesting that equal attention to both organic and other causative factors is the best way forward [244].

4.4 Pain associated with well-defined conditions

*4.4.1 **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 [239]. Secondary dysmenorrhoea suggests the development of a pathological process, such as endometriosis [238], adenomyosis [245] or pelvic infection, which need to be excluded.

Treatment

Simple analgesics and/or non-steroidal anti-inflammatory drugs (NSAIDs) [246], can be helpful if they are started before the onset of each menstrual cycle. Suppression of ovulation using combined or progesterone-only contraceptive tablets or the use of a levo-norgestrol intra-uterine device also reduces dysmenorrhoea. Dysmenorrhoea is a chronic condition and should be managed within a multidisciplinary pain management setting.

*4.4.2 **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 [247], as they can cause severe pelvic/vaginal/vulvar pain [248] and are associated with ulcerating lesions and inflammation, which may lead to urinary retention [249]. If there is any doubt about the diagnosis, laparoscopy may be helpful, as one of the differential diagnosis is endometriosis.

Treatment
Treatment of infection depends on the causative organisms. Subclinical chlamydial infection may lead to tubal pathology, and thus subfertility. Thus, screening for this organism in sexually active young women is essential to prevent this complication. Standard broad-spectrum antibiotics targeting Grampositive and negative organisms are normally recommended. Chronic PID is no longer common in developed countries, but still poses a significant problem for women in developing countries. Hospitalisation and opiates may be needed to achieve adequate analgesia.

4.4.3 ***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 [250-252].

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 ultrasound scan of the uterus, which often shows cystic dilatation of the myometrium [253].

Treatment
Analgesics and NSAIDs are also helpful in easing pain during menses, along with the use of hormonal therapies. They modify the disease but do no cure it. Suppression with GnRH analogues may create an artificial menopause, although the resulting oestrogen deficiency can have marked long-term side-effects, such as reduced bone density and osteoporosis. Thus, these drugs are normally only used before surgery to improve surgical outcome. 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 [254, 255].

A multidisciplinary surgical and pain management team should be integrated into the management pathway of women with endometriosis and pain. Pain in women with endometriosis is often not proportionate to the disease seen and has complex psycho-bio-social components. In patients with adenomyosis, the only curative surgery is hysterectomy but patients can benefit from hormonal therapy and analgesics.

4.4.4 ***Gynaecological malignancy***
The spread of gynaecological malignancy of the cervix, uterine body or ovary will cause pelvic pain depending on the site of spread. Treatment is of the primary condition, but all physicians dealing with pelvic pain must be fully aware of the possibility of gynaecological malignancy.

4.4.5 ***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 [256]. 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.

Treatment
Treatment with a short course of hormone replacement cream can be beneficial. However, reassurance that the situation will improve on the cessation of breastfeeding is also helpful.

4.4.6 ***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 [257]. Prolapse is often a disease of older women, and it is often associated with postmenopausal oestrogen deficiency, which may lead to pain associated with intercourse. Hormone replacement therapy is usually helpful. Specially designed supportive plastic vaginal devices or surgery may

also be helpful. Prolapse surgery may entail the use of non-absorbable mesh (usually in the form of “mesh kits”) [258-260]. Although they may have a role in supporting the vagina, they are also associated with several complications including bladder, bowel and vaginal trauma [259]. In a subset of these patients, chronic pain may ensue, because mesh insertion may cause nerve and muscle irritation [256].

Clinical evaluation
Patients should be fully evaluated clinically and may need specialised imaging, using contrast mediums if necessary, to make a diagnosis. Most patients can be treated by multidisciplinary pain management strategies, including psychology, or mesh-excisional surgery [261, 262], if appropriate.

4.5 Vaginal and vulvar pain syndromes

Pain in the vagina or the female external genital organs is most commonly 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 “vulvodynia” or “chronic vaginal/vulvar pain syndrome” with no known cause. It is still a poorly understood condition, and thus difficult to treat.

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

The 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

Although therapeutic options remain limited and require a multidisciplinary pain management approach, with psychological and physiotherapy input, they can be treated effectively with physiotherapy, stretching exercises and even botulinum toxin, though in the case of the latter the evidence is variable.

4.6 Managing chronic gynaecological pain in ill-defined conditions

In those where CPP is unrelated to any of the above 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 that there may be some evidence (moderate in nature) which supports the use of progestogens in such cases. 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 gabapetin with amitriptyline. The quality of evidence is generally low and is drawn from single studies [263].

In patients with presumed adhesions, there is no consensus as to whether adhesiolysis should be performed to improve pain [264, 265].

4.7 Summary

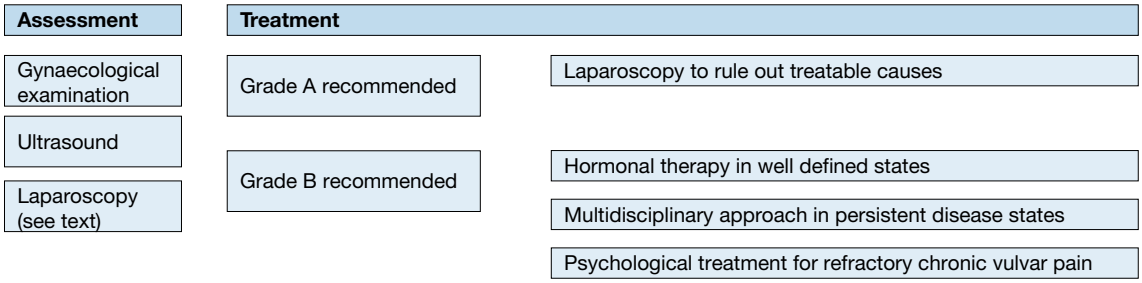
Pain in association with urinary and gastrointestinal symptoms must be considered carefully. For example, patients with bladder pain quite often present with dyspareunia due to bladder base tenderness, so despite the dyspareunia being the focus it is the bladder component that is the main problem. Similarly, in those with anal pain it may be the evacuatory dysfunction that is the main culprit. Conditions, such as pelvic congestion have been cited as a cause of pelvic pain of unknown aetiology, but this diagnosis is not universally recognised [248, 249]. It is only when all the above conditions have been excluded that the physician may declare that the patient has ‘unexplained’ pelvic pain. Treating these patients remains a challenge for all physicians, but quite clearly the best results are obtained from a multidisciplinary approach that considers all possible causes.

4.7.1 *Conclusions and recommendations: gynaecological aspects of chronic pelvic pain*

Clinical state		LE
Clinical history and examination	Mandatory to making a diagnosis	2a
Investigations	Mandatory to making a diagnosis	2a
	Laparoscopy is well tolerated and does not appear to have negative psychological effects	1b
Pain associated with well-defined conditions	Dysmenorrhoea: effective therapeutic options	3
	Infection: effective therapeutic option	3
	Endometriosis: effective therapeutic options including medical and surgical care	1b
	Gynaecological malignancy: effective therapeutic options	3
	Injuries related to childbirth: effective therapeutic options	3
	Pain associated with pelvic organ prolapse: effective therapeutic options	3
Vaginal and vulvar pain syndrome	Diagnosis and therapeutic interventions	3
	Psychological treatment (CBT or supportive psychotherapy) can improve pain and sexual and emotional function	1b

Recommendations	GR
All women with pelvic pain should have a full gynaecological history and evaluation, and including laparoscopy is recommended to rule out a treatable cause (e.g. endometriosis).	A
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
Recommend psychological treatment for refractory chronic vulvar pain.	B
Use alternative therapies in the treatment of chronic gynaecological pelvic pain.	C

Figure 7: Assessment and treatment of gynaecological aspects in chronic pelvic pain



5. GASTROINTESTINAL ASPECTS OF CHRONIC PELVIC PAIN

5.1 Introduction

This chapter describes CPP perceived to be associated with the gastrointestinal tract, which is mainly due to functional disorders and cannot be explained by structural or specific well-defined diseases of the pelvis. Some points to note:

- There may be a considerable overlap of the gastrointestinal with other pelvic pain syndromes.
- Defined gastrointestinal conditions with specific structural defects and diseases may coexist.
- Behavioural changes such as straining can lead to organic diseases such as rectal prolapse, solitary rectal lesion syndrome, or pudendal nerve injury with consecutive faecal incontinence. Some structural gastrointestinal abnormalities (e.g., postpartum anal sphincter defects, or small rectoceles) are often observed in asymptomatic individuals and may be coincidental with the

gastrointestinal pelvic pain syndrome.

- Different diseases can aggravate previously asymptomatic functional disorders which may become symptomatic such as faecal incontinence in patients with diarrhoea of different origins or anal fissure in patients with dyssynergic defecation.
- Finally, we need to consider that all functional disorders such as anorectal pain are defined on the basis of retrospectively evaluated longstanding symptoms, which ideally would have been registered prospectively with symptom diaries [266, 267].

5.2 Clinical history

Functional anorectal disorders are diagnosed by symptoms, supplemented by objective findings. 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 questionnaire 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.

*5.2.1 **Clinical examination and investigations***

At clinical examination, perianal dermatitis may be found as a sign of faecal incontinence or diarrhoea. Fissures may be easily overlooked and should be searched 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 bimanual examination by the gynaecologist to diagnose an enterocele or cystocele.

*5.2.2 **Diagnostic assessment***

The Rome III criteria for diagnosis of functional anorectal diseases include symptoms for each specific functional disorder as listed below. The gastrointestinal diagnostic assessment should be performed in an interdisciplinary manner, preferably at a pelvic floor centre by a dedicated team, and appropriate testing. The most frequently performed investigations are flexible rectosigmoidoscopy or colonoscopy, pelvic ultrasound, anorectal endosonography and anorectal manometry combined with anal electromyography (EMG) and balloon expulsion test. Three-dimensional anorectal ultrasound has become an indispensable readily available tool for the specialised proctologist. Perineal ultrasound offers the advantage of sphincter imaging without insertion of the transducer into the rectum.

Magnetic resonance imaging in conjunction with MR defecography has become the most valuable imaging technique to assess anorectal function dynamically. Magnetic resonance imaging 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., ultrasound 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.

Surgical consultations should be available for all patients, plus referral to a urogynaecologist or urologist when indicated. Biofeedback treatment, botulinum toxin A injection, and percutaneous tibial nerve stimulation (PTNS) and sacral neuromodulation (SNM) should be available as a complementary therapeutic option to medical and surgical treatment.

5.3 Pain associated with well-defined conditions

*5.3.1 **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. Different treatments of

haemorrhoids have been evaluated by two Cochrane reviews. Excisional haemorrhoidectomy (EH) has been compared to the less-invasive technique of rubber band ligation (RBL), and has been shown to increase pain, with more complications and time off work. However, despite these disadvantages of EH, complete long-term cure of symptoms is increased by surgery, and minor complications are accepted by patients [268]. Rubber band ligation is the choice of treatment for grade II haemorrhoids, whereas EH should be reserved for grade III haemorrhoids or recurrence after RBL [268]. New stapler techniques of haemorrhoidopexy are associated with a higher long-term risk of recurrence and prolapse compared to conventional EH. Further studies are needed [269].

*5.3.2 **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. Medical therapy with nitrates and calcium channel blockers resulting in anal sphincter relaxation is more effective in children than in adults [270]. Recently, 2% diltiazem ointment has been shown to be superior to glyceryl trinitrate in terms of time to healing and recurrence rate in children with anal fissure [271]. In adults, 75 RCTs with 17 agents were analysed by a Cochrane review [270]. Nitroglycerin ointment (GTN), isosorbide mono & dinitrate, botulinum toxin A, diltiazem and nifedipine (calcium channel blockers) were found to be marginally better than placebo, but less efficacious than surgical sphincterotomy. Botulinum toxin A injection represents an alternative treatment option with a fissure healing rate which is comparable to topical diltiazem after 3 months [272]. Surgery with lateral-internal sphincterotomy is the most studied procedure but carries the risk of postoperative faecal incontinence, and may be replaced by fissure excision combined with botulinum toxin A or anal advancement flap [273].

*5.3.3 **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. Tricyclic antidepressants at low dose can be effective in this situation when acute exacerbation has been ruled out [274, 275].

*5.3.4 **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].

5.4. Chronic anal pain syndrome

*5.4.1 **Diagnostic criteria***

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:

1. Chronic or recurrent rectal pain or aching.
2. Episodes last at least 20 min.
3. 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 [266].

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"). This common and debilitating condition is frustrating to treat. Pathophysiology of pain is thought to be due to overactivity of the pelvic floor muscles. Chiarioni et al. have recently published an RCT demonstrating that biofeedback treatment was superior to electrogalvanic stimulation and massage for treatment of the chronic anal pain syndrome. 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 [278]. 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.

*5.4.2 **Botulinum toxin A in pelvic pain***

Chronic pelvic pain associated with spasm of the levator ani muscles and treatment of the puborectalis and pubococcygeus muscle by botulinum toxin 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 H2O. Although dyspareunia and dysmenorrhea improved, non-menstrual pelvic pain scores were not significantly ameliorated [279]. 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 H2O) and included 60 women. In this larger study, non-menstrual pelvic pain was significantly improved compared to that treated with placebo (VAS score 51 vs. 22; P = 0.009). It was concluded therefore that botulinum toxin A is effective for reducing pelvic floor-muscle associated pain with acceptable adverse effects such as occasional urinary and faecal stress incontinence [280]. However, recently, a small RCT failed to show any benefit of botulinum toxin A [281].

*5.4.3 **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) [282]. Sacral neuromodulation has been reported to be somewhat beneficial in two uncontrolled studies, showing improvement in about half the patients [283, 284]. 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, quality of life and sexual life [285]. No "sham" SNM or PTNS control group were used in neither cited studies, which limits their value as an important placebo effect cannot be ruled out.

*5.4.4 **Intermittent chronic anal pain syndrome***

Intermittent chronic anal pain syndrome (proctalgia fugax) consists of all the following diagnostic criteria, which should be fulfilled for 3 months and before 3 months:

1. Recurrent episodes of pain localised to the anus or lower rectum.
2. Episodes last from several seconds to minutes.
3. 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. 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 [286]. Other treatment options are topic diltiazem and botulinum toxin A [282]. 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.

5.5 Summary

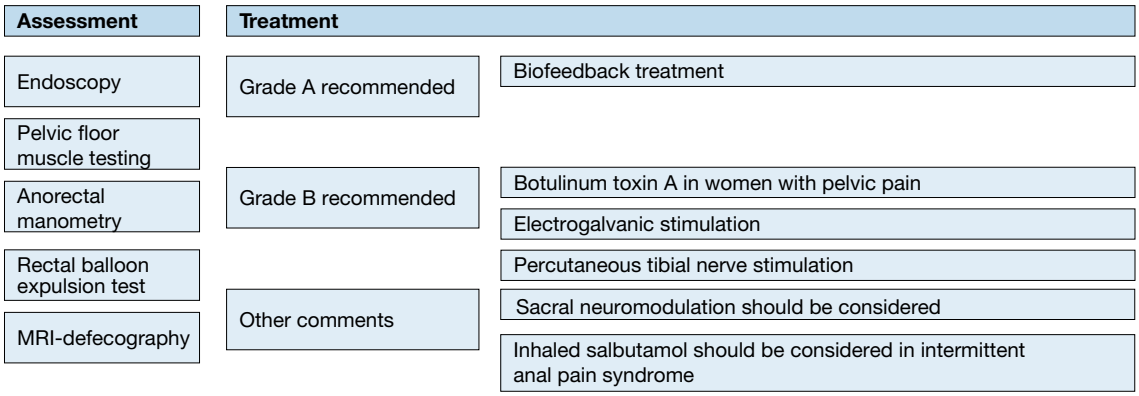
Chronic pelvic pain is an interdisciplinary entity needing multispeciality and multidisciplinary diagnostic assessment by a gastroenterologist, urologist, gynaecologist and pain teams as appropriate, with the input of physicians, psychologists and physiotherapists amongst others. Anorectal pain is investigated best by endoscopic and functional testing to rule out structural disease that can be treated specifically. Chronic pelvic pain due to functional disorders remains a therapeutic challenge that may respond to biofeedback therapy, electrogalvanic stimulation and botulinum toxin A in the case of Levator Ani Syndrome and defecatory disorders associated with pelvic pain.

5.5.1 *Conclusions and recommendations: anorectal pain syndrome*

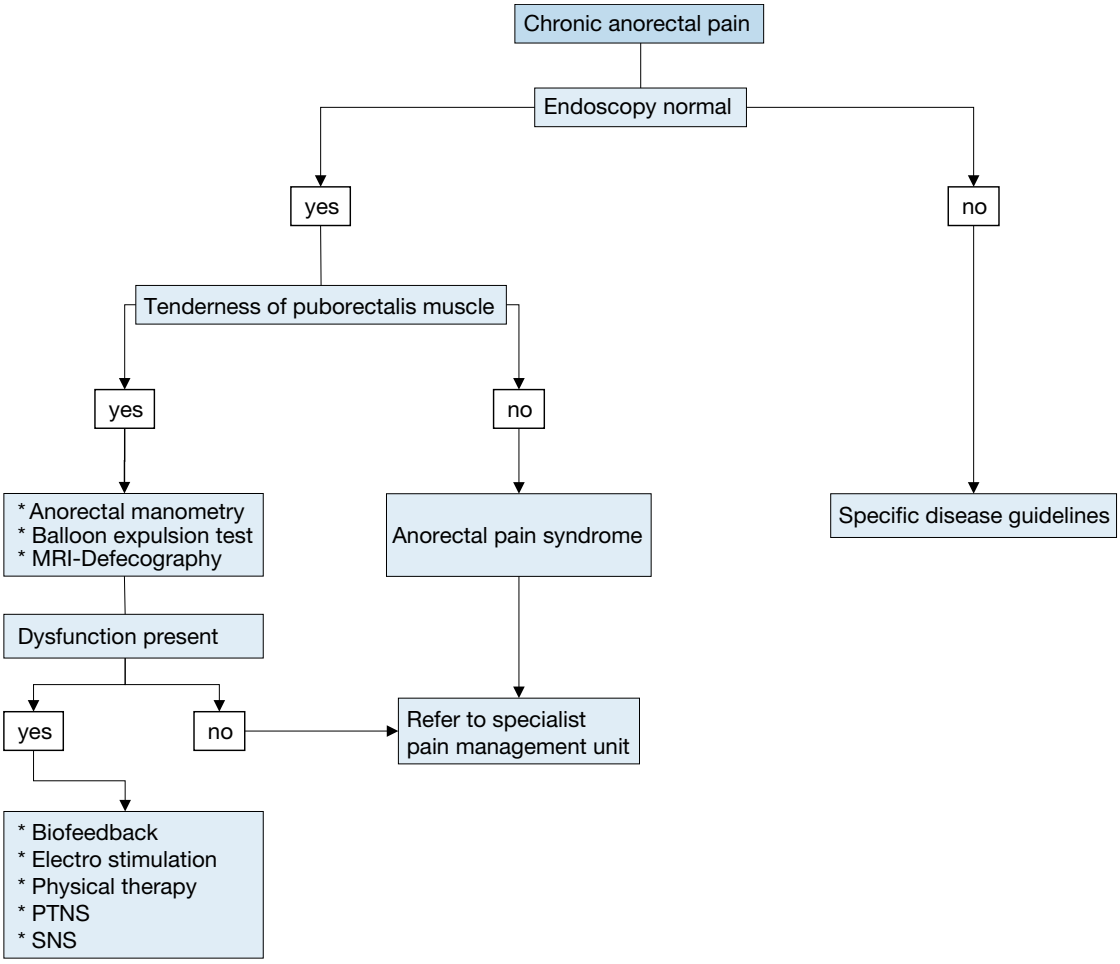
Conclusions on functional anorectal pain	**LE**
Tenderness on traction is the main criterion of the chronic anal pain syndrome.	1a
Biofeedback is the preferred treatment for the chronic anal pain syndrome.	1a
Electrogalvanic stimulation is less effective than biofeedback.	1b
Botulinum toxin is efficient in CPP with spasms.	1b
Percutaneous tibial nerve stimulation is effective in pelvic pain.	1b
Sacral neuromodulation is effective in pelvic pain.	3
Inhaled salbutamol is effective in intermittent chronic anal pain syndrome.	3

Recommendations for functional anorectal pain	**GR**
Functional testing is recommended in patients with anorectal pain.	A
Biofeedback treatment is recommended in patients with pelvic pain and dyssynergic defecation.	A
Botulinum toxin A and electrogalvanic stimulation can be considered in the chronic anal pain syndrome.	B
Percutaneous tibial nerve stimulation can be considered in the chronic anal pain syndrome.	B
Sacral neuromodulation should be considered in the chronic anal pain syndrome.	C
Inhaled salbutamol should be considered in the intermittent chronic anal pain syndrome.	C

Figure 8: Assessment and treatment of anorectal pain syndrome



Algorithm 4: Diagnosis of chronic anorectal pain



6. PERIPHERAL NERVE PAIN SYNDROMES

6.1 Neuropathic pain

Much has been written on the subject of peripheral neuropathic pain [287-290] including its diagnosis and treatment. There are some fundamental principles that are worth considering:

1. Nerve injury is associated with changes both within the peripheral nervous system (PNS) and the central neural axis including the higher centres. These changes serve to produce an increasing disparity between stimulus and response (Chapter 2).
2. In the PNS, nerve damage may produce a neuroma that can provide a source of ongoing afferent central activity. The neuroma may be discreet and palpable to touch or en-passage and not palpable. Neuromas are sensitive and respond to: compression (e.g., by the surrounding tissue or digital pressure), temperature change and adrenergic stimulation. Sympathetic nerve fibres can grow into neuromas as well as the associated dorsal root ganglia, which may result in sensitivity to body adrenaline changes such as through mood and environment with subsequent changes in pain.
3. Windup is a progressive increase in centrally elicited action potentials per unit peripheral stimulus. A severe acute insult or a chronic repeated stimulus may result in a transient windup phenomenon becoming permanent. These long-term changes in central sensitisation are associated with dysfunction of the afferent sensory nervous system and perception, as well as efferent motor, vasomotor and pseudomotor activity within the pathways of the injured nerve [291].
4. These central changes may result in abnormal afferent processing for nerves other than those originally damaged, so that increased perception (pain, allodynia and hyperaesthesia) from an area greater than the expected pattern may occur. In the case of tissues with innervation that overlaps with an injured nerve, somatic and visceral hypersensitivity (e.g., sensory urge with increased

frequency of voiding/evacuation) may be perceived from those tissues.

Essentially, what may be considered a simple nerve injury may be magnified by the CNS so that a whole region may be involved and a non-specific regional pain syndrome may arise. There is also a suggestion that involvement of both the peripheral and CNS in the control of the endocrine and immunological system may also become abnormal. Certainly, there is a complex interaction between nerve injury, emotional well being, disability and widespread pain. A proportion of patients go on to develop CFS, FM and immunological disorders [134, 292, 293].

6.2 Anatomy

When considering pelvic pain mechanisms, nerves associated with the pelvis/genitalia are generally divided into thoraco-lumbar and sacral root afferents. The hypogastric plexus is mixed autonomic (sympathetic and parasympathetic) and may contain afferents associated with pain.

*6.2.1 **The posterior subgluteal triangle nerves***

The posterior triangle area is the area defined superiorly by the upper border of the piriformis, inferiorly by the lower border of quadratus femoris, laterally by the greater trochanter and medially by the lateral border of the sacrum, the lateral borders of the sacrotuberal ligament and ischeal tuberosity. This region contains the sciatic nerve, posterior femoral cutaneous nerve (which branches into the posterior cutaneous perineal branch and the cluneal nerves), the nerve to the obturator internus muscle, and the pudendal nerve. These nerves pass deep to the piriformis muscle and superficial to the superiour gemellus and obturator internus muscles. Injury in this area may damage one or more of these nerves (Figure 9) [294-300].

*6.2.2 **Branches of the pudendal nerve***

The pudendal nerve has its origins at the S2-S4 levels. S2 and S3 also contribute to the sciatic nerve and S4 to the coccygeal plexus and the annoccoccygeal nerves. The pudendal nerve has three main branches: the inferior anorectal nerve, the superficial perineal nerve (which terminates as cutaneous branches in the perineum and posterior aspect of the scrotum), and the deep perineal nerve, which is distributed to the pelvic structures (innervating parts of the bladder, prostate and urethra). This branch terminates as the dorsal nerve of the penis/clitoris, which innervates the glans. In addition to sensory branches, the pudendal nerve provides motor innervation to anal and urethral sphincters, as well as to the bulbospongiosus and ischiocavernous muscles (involved in the bulbocavernosal response, orgasm and ejaculation). Autonomic fibres also pass with the pudendal nerve and are derived from the presacral parasympathetic as well as sympathetic fibres via the hypogastric plexi.

*6.2.3 **Anatomical relations of the pudendal nerve***

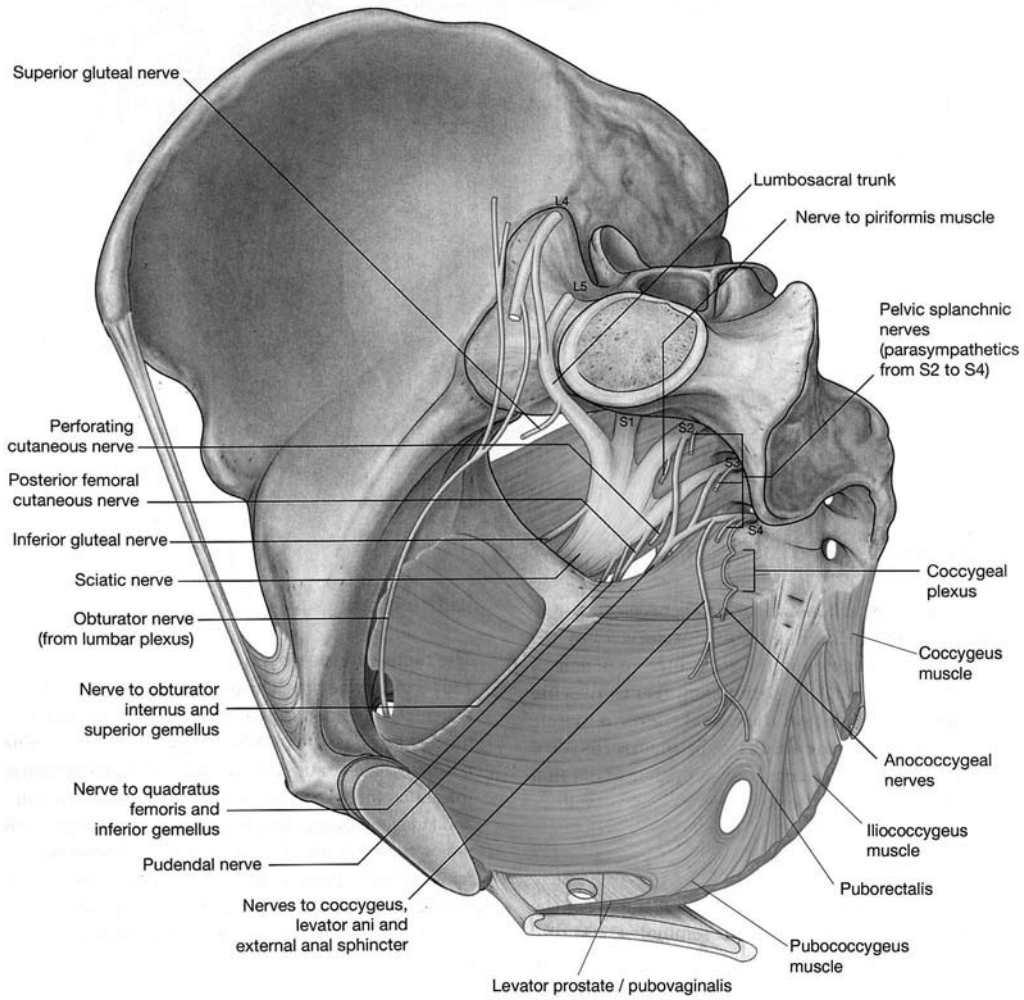
The anatomy may be variable, however, the three roots that form the pudendal nerve usually merge anterior to the sacrum and inferior to the piriformis muscle (Figure 9). The pudendal nerve leaves the pelvis via the greater sciatic notch to enter the subgluteal region. In the posterior subgluteal triangle (the area bordered by the inferior edge of the piriformis muscle, the sarotuberous ligament medially and the upper border of the rectus femoris muscle inferiorly), the nerve emerges from under the inferior border of the piriformis muscle with its associated pudendal artery and veins; it is medial to the nerve innervating the obturator internus muscle, which is medial to the posterior femoral cutaneous nerve (which divides into its cutaneous branch but also the inferior cluneal nerves and perineal nerves), which is medial to the sciatic nerve. These anatomical relations are important for neurotracing techniques used for nerve blocks and because symptoms in those nerve territories also help with diagnosis [301-303].

The pudendal nerve leaves the subgluteal region as it wraps around the superficial surface of the ischeal spine/sacrospinal ligament to re-enter the pelvis via the lesser sciatic notch (between the more ventral sacrospinal ligament and the more dorsal sacrotuberal ligaments) [294, 297]. This occurs 15% of the time at the enthesis of the spine and the ligament; in 75% of the time, it is more medial, and in 10% it wraps around the spine. The sacrotuberal ligament may have a sharp superior border, be wide, and as a result, close to the spinosacral ligament, or be divided with the pudendal nerve passing through it. All of these features may predispose to nerve injury. As the pudendal nerve re-enters the pelvis below the levator muscles, it runs within a fascial canal medial to the internal obturator muscle (Alcock's canal).

The inferior anorectal branch may never be a true branch of the pudendal nerve, and may have its origins directly from the sacral roots. As a consequence, pain associated with pudendal nerve injury may not involve the anorectal area. Similarly, pain may only be perceived in the anorectal area if the main pudendal nerve is not involved. In 11% of cases, the inferior anorectal nerve pierces the sacrospinal ligament, possibly increasing the

risk of entrapment. Other variations of the anorectal branch exist with the nerve branching off from the main pudendal nerve at any point in the gluteal region or within the pelvis. In 56% of cases, the pudendal nerve is a single trunk as it re-enters the pelvis. Some people have two or three pudendal nerve trunks.

Figure 9: Anatomical relations of the pudendal nerve



Source: Drake, Vogel, & Mitchell: GRAY's ANATOMY FOR STUDENTS, 2004 Elsevier Inc.

6.2.4 ***Afferent nerves and the genitalia***

- The afferents from the skin of the genitals pass via a complex of multiple sensory nerves and this makes the anatomical diagnosis of nerve injury as a cause of pain difficult.
- The anterolateral part of the scrotum/labia majora has afferents associated with the genitofemoral nerve primarily; there may also be some involvement of the ilioinguinal and iliohypogastric nerves.
- The posterior scrotal/labia branches of the pudendal nerve transmit sensation from the posterior scrotum/labia majora.
- The penis shaft is innervated on its dorsal surface by the genitofemoral, ilioinguinal and iliohypogastric nerves, and the ventral surface by the perineal branches of the posterior femoral cutaneous nerve and cutaneous branches of the pudendal nerve.
- The glans penis/clitoris is associated with the dorsal nerve of the penis/clitoris, the terminal branch of the pudendal nerve.
- All the nerves that are associated with the scrotum may also receive afferents from the testes, although classically, the nerves from the testes are usually associated with the genitofemoral nerve (thoracolumbar as opposed to sacral roots).
- The superficial branches of the pudendal's superficial perineal nerve and the perineal branch of the posterior femoral cutaneous nerve receive afferents from the perineal skin.
- Deeper afferents from the perineum and from some of the pelvic organs pass to the pudendal nerve via its deep perineal branch.

6.2.5 *Afferents in the autonomic plexus*

The pelvic plexus is associated with both the parasympathetic and sympathetic nerves, and as well as afferents associated with these pathways, afferents may travel back to the sacral and thoracolumbar roots with these autonomic nerves. Sites for injury and possible intervention may thus include: the ganglion impar, superior hypogastric plexus, inferior hypogastric plexus, and lumbar sympathetic trunk, as well as more central spinal root areas.

6.3 Aetiology of nerve damage

6.3.1 *Anterior groin nerves - aetiology of nerve damage*

The primary afferents of the anterior groin nerves enter the spinal cord at the thoracolumbar level (T10 to L3). Thoracolumbar spinal pathology and any pathology along the course of the nerve may result in neuropathic pain in the distribution of these nerves. As well as neoplastic disease, infection and trauma, surgical incisions and postoperative scarring may result in nerve injury [304].

6.3.2 *Pudendal neuralgia - aetiology of nerve damage*

Anatomical variations

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) [294, 297].

The pudendal nerve may be damaged due to local anatomical variation 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).

6.3.3 *Surgery*

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 [305, 306]. 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 [307, 308]. In many types of surgery, including colorectal, urological and gynaecological, pudendal nerve injury may be implicated.

6.3.4 *Trauma*

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.

6.3.5 *Cancer*

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 [298].

6.3.6 *Birth trauma*

This is more difficult to be certain about [295]. 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.

6.3.7 *Elderly women*

Child birth and repeated abdominal straining associated with chronic constipation [309] are thought to predispose elderly women to postmenopausal 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 postmenopausal older women.

6.4 Diagnosis for pudendal neuralgia

*6.4.1 **Differential diagnosis of other disorders***

Other forms of neuropathic pain [310, 311].

As well as the pudendal nerve, there are several other nerves that may mimic the symptoms of pudendal neuralgia if they are damaged.

Inferior cluneal nerve. This is a branch of the posterior femoral cutaneous nerve. This nerve is prone to injury in the ischial region. Cluneal nerve injury produces a sensation of pain perceived more laterally than that for pudendal neuralgia.

Sacral nerve roots. The S2-S4 nerve roots may be involved. This is an important differential diagnosis as tumours must be excluded.

Cauda equina syndrome. Lumbar spinal pathology involving the cauda equina may result in an intractable neuropathic pain.

Ilioinguinal, iliohypogastric and genitofemoral nerves. Injury to these nerves or their roots may occur from thoracolumbar pathology, abdominal posterior wall conditions, surgery, and entrapment in the groin. The pain may extend into the groin, anterior perineum and scrotum/labia majorum. If the femoral branch of the genitofemoral nerve is involved, pain may extend into the inner thigh.

Referred spinal pain

Pain from thoracolumbar pathology may refer to the groin. Spinal pain may become associated with muscle hyperalgesia and trigger points. The muscle associated pain may spread to involve a range of muscles, including the pelvic floor muscles with resultant pelvic pain.

Musculoskeletal disorders

Trigger points associated with localised tenderness and pain may be detected in the piriformis, obturator internus, levator ani, bulbocavernosal and ischeocavernosal muscles, as well as the gluteal, adductor, rectus abdominus and spinal muscles. All of these may refer the pain to or close to the pelvis.

Pathology of the joints (sacroiliac, pubic symphysis, hip and spinal) may also refer into the pelvis.

Coccyx pain syndrome, a painful coccyx may occur for a number of reasons (Chapter 2).

*6.4.2 **Clinical presentation of pudendal neuralgia***

6.4.2.1 Age

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 [312-314].

6.4.2.2 Sex

Six out of ten cases are observed in women.

6.4.2.3 History

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 pains develop 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.

6.4.2.4 Associated features

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.

6.4.2.5 Clinical examination

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).

6.4.2.6 Investigations

Magnetic resonance imaging scans of the pelvis are usually normal although some practitioners claim them to be useful [315, 316]. However, MRI scans of the pelvis and spine (mid thoracic to coccyx) are considered essential to help with the differential diagnosis of pudendal neuralgia. Electrophysiological studies 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 in patients thought to have pudendal neuralgia.

6.5 Management of pain associated with nerve damage

The approach to managing a patient with pain following nerve damage is similar irrespective of the nerve involved. There is a suggestion that early treatment has a better prognosis. The general principles are covered in chapter 10 of this document.

*6.5.1 **Pudendal neuralgia and injections***

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 [320]. The second possible benefit of local infiltration 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 [301-303, 315, 321-327].

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 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. Similarly, trigger point injections into tender areas within muscles may also be considered. Pulsed radiofrequency stimulation has also been suggested as a treatment [328].

*6.5.2 **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 the transgluteal approach; however, a transperineal approach may be an alternative, particularly if the nerve damage is thought to be related to previous pelvic surgery [299, 300, 314, 315, 329-331].

Currently, there has been only one prospective randomised study [299]. This 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 by no means 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.

*6.5.3 **Pudendal neuralgia and neuromodulation***

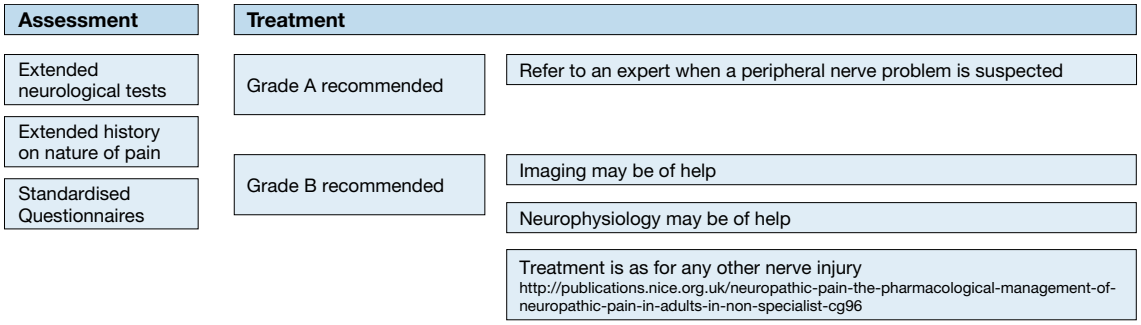
Pudendal neuralgia represents a peripheral nerve injury and as such should respond to neuromodulation by implanted pulse generators. However, it is important that the stimulation is perceived in the same site as the perceived pain. Spinal cord stimulation (SCS) may be effective for thoraco-lumbar afferents. 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 [332-335].

6.6 Conclusions and recommendations: pudendal neuralgia

Conclusions	**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
There are multiple treatment options with varying levels of evidence.	1

Recommendations	**GR**
It is important to 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 may help with the diagnosis, but the gold standard investigation is an image and nerve locator guided local anaesthetic injection.	B
Neuropathic pain guidelines are well established. Standard approaches to management of neuropathic pain should be utilised.	A

Figure 10: Assessment and treatment of peripheral nerve pain [317, 333, 336].



7. SEXOLOGICAL ASPECTS OF CHRONIC PELVIC PAIN

7.1 Introduction

In general, human sexuality has three aspects - sexual function, sexual self-concept, and sexual relationships. Pain can affect self-esteem, one's ability to enjoy sex and relationships. Healthy sexuality is a positive and life-affirming part of being human. The capacity to experience optimal comfort and satisfaction in sexual expression also requires basic physical abilities. Essentially, these include intact sensory and motor processes, and the ability to move with ease.

Chronic pain may hinder the ability to move freely, and thus, may limit the positions one can get into to have sex. Second, chronic pain may affect the ability to respond sexually and conversely; in Chronic Pelvic Pain (CPP) the sex act can be associated with pain that can be inhibiting. Research on male sexual dysfunction highlights the importance of considering partners and the impact that male sexual problems have on their partners. Sexual dysfunction occurs in an interpersonal context and has implications for both partners in a relationship. Chronic pain also impacts the sexual and interpersonal functioning of couples; declines in sexual activity and reduced relationship satisfaction have been noted among patients with chronic pain and their partners [337, 338]. It is recommended that a biopsychosocial model of CPP should be incorporated into future research, and that research considers the role that sexual and relationship variables may play in couples' adjustment. The sexual-response cycle is divided into five phases: desire, arousal (excitement), plateau, orgasm and resolution. They are actually all part of a continuous process of sexual response. There is much variation among individuals, as well as between different sexual events and there are different models to describe the sexual responses [339].

During the sexual response cycle, the different phases are controlled by a different part of the brain and spinal cord. In each of these phases chronic pain and CPP in particular can cause disturbances [340].

- The Desire Phase begins in the "pleasure centres" of the brain and controls a person's sexual appetite or drive. Pain or even the fear of pain can decrease desire, making the person uninterested in sex. In some cases, however, having sex may actually help to relieve pain.
- The Arousal Phase is associated with the swelling of the blood vessels in a man's penis and in a woman's labia, vagina, and clitoris. This swelling causes an erection in the penis and in the clitoris and release of lubricating fluids. If a person experiences pain at the time of becoming excited, the excitement may be reversed, in a man the penis will become limp and in a woman the lubrication will stop, leading to dryness.
- The Orgasm Phase describes a genital reflex controlled by the spinal cord, which causes the genital muscles to contract, involuntarily releasing sexual tension and swelling that build up during the excitement phase. In some cases, pain prevents people from reaching this phase.

7.2 General considerations

Pelvic pain in women [341] and in men [342] is associated with significant sexual dysfunction. While chronic pain impacts all aspects of functioning, including work, family relationships, and social activities, the most frequent complaint cited by patients with CPP is sexual dysfunction [343]. Factors contributing to sexual

dysfunction in patients with chronic pain are multifactorial and contextual [344], and may be related to comorbidity with depression [345, 346], use of antidepressant medications [347], and relationship satisfaction [348], among many other factors. There are reports of increased rates of past sexual abuse which may have negative impact on sexual function [349, 350]. Chronic pelvic pain may have a higher association with sexual dysfunction than other types of chronic pain. CPP specifically involves areas intimately connected to sexuality, which may negatively impact one's body image and sexual self-esteem [351], and also affects both partners in the relationship [352].

7.3 Pelvic floor involvement in sexual function and dysfunction

The pelvic floor of the male appears to have some impact on sexual function, although its exact role is unclear. Erection is a neurovascular event in which the smooth and striated musculature of the corpora cavernosa and pelvic floor play a role in facilitating and maintaining the erection [353]. In ejaculation and orgasm the rhythmic contraction of the bulbocavernous and ischiocavernous muscles is perceived as pleasurable. Ejaculation is controlled by the sympathetic nervous system and performed with help of the pelvic floor muscles. Controlling the pelvic floor muscles may delay the onset of ejaculation through an active relaxation of the pelvic floor muscles. This is a learned technique, which may be mastered using pelvic floor biofeedback. Pelvic floor exercise and biofeedback for the treatment of both erectile dysfunction (ED) and premature ejaculation (PE) have been reported on in the literature. The effectiveness of physical therapy in treating sexual pain disorders has been reported upon in the literature also. Retrospective studies have reported a success rate of 77% [354, 355]. Goetsch recently reported her findings that physical therapy may serve as important adjunct to surgery for "vulvar vestibulitis" (vulvar pain syndrome) [356].

7.4 Chronic pelvic pain and sexual dysfunction in men

In the BACH study, Hu et al. found that men who reported having experienced sexual, physical, or emotional abuse had increased odds (1.7 compared to 3.3) 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 [357]. A key feature of CPP is chronic pain. 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 [344]. 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 reuptake inhibitors, SSRI) can also decrease libido [358] 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 [359]. Post-ejaculation pain is not mentioned in this questionnaire.

In the 1980s an association between CPP and sexual dysfunction was postulated. In 2 reviews the relation between PPS and health status, with influence on sexual activity, were addressed [360, 361]. In a Chinese study of men with CPP 1768 males completed the questionnaires. The overall prevalence of sexual dysfunction was 49%. Erectile dysfunction 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 [362, 363]. Erectile dysfunction was prevalent in 27.4% of Italian men aged 25-50 [364], 15.2% among Turkish men (significantly higher than control group) [365] and 43% among Finnish men with PPS [366]. 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 [367, 368]. Recently, a significant correlation between "chronic prostatitis", CPP symptoms (measured by NIH-CPSI) and ED (measured by IIEF) was confirmed [369], while other studies using the same questionnaires were not able to confirm such a correlation [359, 370]. Some studies also report ejaculatory dysfunction, mainly premature ejaculation [342, 354, 362, 363].

A study from Turkey concerning the interaction between CPP and premature ejaculation (PE) according to intravaginal ejaculation latency time showed that 77% of men with PPS suffered from PE [365]. Screponi et al. reported the high incidence of prostatic inflammation symptoms in men with PE [371]. Premature ejaculation associated with CPP is hypothesised to be caused by infection or inflammation, thus treatment with antibiotics should reduce PE symptoms. In two studies antibiotic treatment has shown a significant increase in patient's IELT (intravaginal ejaculation latency time). Despite these improvements, the mean IELT was still very low and questionable. Before these results can be recommended, further placebo controlled studies are mandatory [372, 373]. Furthermore, there are reports which highlight the appearance of ejaculatory pain in patients with CPP [374] while some studies suggested CPP symptom improvement by increased ejaculatory frequency and sexual activity [375, 376].

The presence of pelvic pain may increase the risk for ED independent of age [338]. On the other hand, cross-sectional data suggest no improvement of lower urinary tract symptoms (LUTS) by an increased frequency of ejaculation [361]. In a study bridging the gap between LUTS and ED, Muller and Mulhall have speculated on the negative impact of PPS on QoL, leading to consecutive impairment of erectile function [377]. 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 and imaging suggestive of a more severe inflammatory condition [342]. These arguments are important for the understanding of the close relationship between CPP symptoms, disturbed sexuality, impact on QoL, and psychological implications including depression [360-363, 378]. Sexual dysfunction heightens anger, frustration and depression, all of which place a strain on the relationship and the partner. 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 [360, 377]. Prostate pain syndrome patients reported greater sexual and relationship problems [360, 377, 379]. On the other hand, Smith et al. found that men with PPS did not report significantly decreased sexual satisfaction compared to controls [380]. There is consensus that therapeutic strategies reducing symptoms, especially against pelvic pain, are of relevance in relation to changes of sexuality. On the other hand, having sex and intimacy can yield positive experiences that will reduce the pain. The CNS plays an important role in this mechanism.

7.5 Chronic pelvic pain and sexual dysfunction in women

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 women. Chronic pelvic pain leads to substantial impairment in QoL and several sexual dysfunctions [381-384]. It seems reasonable to expect that pain, extreme fatigue, depressive mood and pain drugs will affect women's sexuality. Ter Kuile et al. found that 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" [385]. Chronic pelvic pain is more directly associated with sexual dysfunction than chronic pain at other sites. 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 [386]. Collett and colleagues [387] also found that patients with CPP reported more sexual problems than women with any other type of chronic pain problem. The quality of intimate relationships is closely connected with sexual function [388]. Satisfaction with the sexual relationship appears to be associated with higher marital functioning [389]. In addition sexual dissatisfaction is related to sexual dysfunction. In cases in which 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 [389].

In community-based studies in the UK [343], New Zealand [381] and Australia [390], 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 [387, 391, 392]. The study of Veritt et al. shows 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 [392]. 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 [391-393]. One study of patients enrolled in chronic pain treatment programs in England has reported that 73% had pain-related sexual problems [344]. Approximately two-thirds of patients in another study have reported reduced frequency in their sexual relations as a result of CPP [394]. 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 [395]. Maruta et al. interviewed 50 chronic pain sufferers and their spouses, of whom 78% of the pain sufferers and 84% of partners described deterioration, including cessation of their sex life [338]. In another study, in patients with back pain, half reported decreased frequency of sex since the onset of chronic pain [344]. 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. The study of Veritt et al. showed that when FSFI was used, 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 correlations of FSFI corresponded well to each other; 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; and finally, that the

FSFI showed good ability to discriminate between women with and without CPP [396]. Some studies report a significant association between sexual abuse before the age of 15 years and later CPP [349]. It is suggested that there is increased frequency of sexual abuse or trauma history, anxiety and depression in women with CPP [396-400]. While the study of Fry et al. with 164 women with CPP show that child sexual abuse did not apparently differ in prevalence from that in the general population, which must throw into question previous assertions about its widespread and general role in CPP.

7.6 Treatment of sexual dysfunctions and CPP

Couples often benefit from early referral for relationship and sexual counselling during their treatment course [401]. 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 [401, 402], 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 [403]. In patients with an overactive pelvic floor, referral for physical therapy, myofascial release, and internal pelvic floor muscle massage may offer relief [340].

7.7 Summary

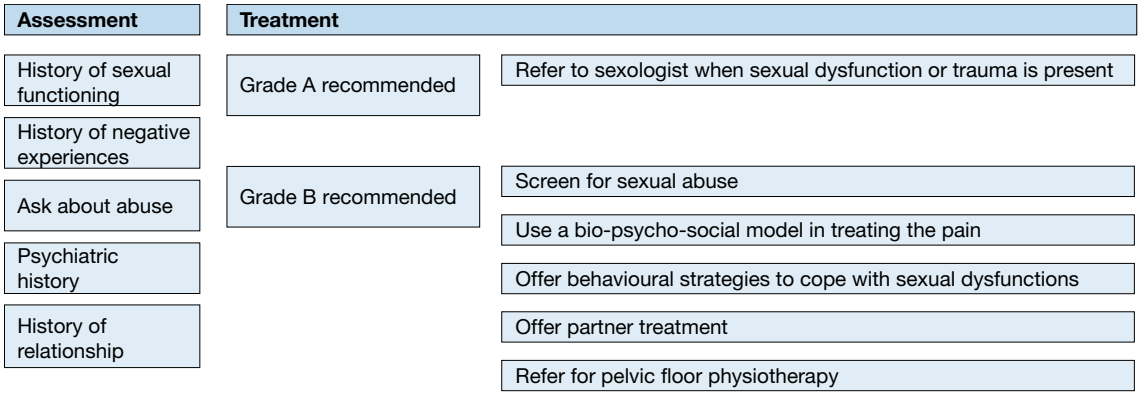
Problems with sexual function resulting from CPP have to be addressed and assessed by the healthcare professional. The attention directed toward these patients must be focused not only on the disease but also on the woman as a whole. As treatment solely of the underlying disease is not acceptable, the care of these suffering women should also address the emotional, sexual, and social problems that the disease causes.

7.8 Conclusions and recommendations: sexological aspects in CPP

Conclusions	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 patient 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 less 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
Pelvic floor muscle physical therapy may offer relief of pain and reduction in sexual complaints.	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
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

Figure 11: Assessment and treatment of sexological aspects in chronic pelvic pain



8. PSYCHOLOGICAL ASPECTS OF CHRONIC PELVIC PAIN

This chapter addresses general issues concerning the psychological contribution to pelvic pain and its presenting problems, and assessment and treatment. The same areas are also covered in relation to CPP in women, as that is where psychology has focussed.

8.1 Understanding the psychological components of pain

*8.1.1 **Neurophysiology of pain***

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. Symptom-related anxiety and central pain amplification may be measurably linked, as in IBS [404]. Bajaj et al. have demonstrated central sensitisation in symptomatic endometriosis (see Chapter 4) [405]. Decreases in gray matter (in the thalamus), characteristic of diverse chronic pains [406], has been shown in women with pelvic pain, associated with pain but not with endometriosis found in some of the sample [407]. Interestingly, central changes are evident in association with dysmenorrhea, increasingly recognised as a risk for female pelvic pain [408]. 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.

However, difficult as it is to relieve chronic pain, the pain system is plastic and treatment attempts are not entirely unsuccessful.

*8.1.2 **Sexual abuse and trauma***

Many studies have reported high rates of childhood sexual abuse in adults with persistent pain, usually in hospital samples, and particularly in women with pelvic pain [409]. However, all these studies are retrospective, and often of poor quality [410]. 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 establish a definite history, and compared with matched classmates [29]. The conclusions were that physically and sexually abused individuals were not at risk for increased pain, although those 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 be more about retrospective explanations for pain than about occurrence or extent of abuse. Controlling for depression also significantly weakens the relationship between childhood abuse and adult pain [411]. Disentangling the influences and inferences requires prospective studies or careful comparisons [26]. No studies have been found of sexual or physical abuse in childhood and pelvic pain in men, although such abuse has other adverse effects on psychological and physical health [412, 413].

*8.1.3 **Interpreting psychological differences***

An important review [26] of CPP in women identifies as problematic 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 but the significance of this for pelvic pain is unclear. Studies that invoke 'medically unexplained' or 'psychosomatic' or 'somatoform' disorders do not engage with current pain science, such as viscerovisceral cross sensitisation in relation to multiple pain sites [414], instead interpreting absence of physical findings to indicate psychological origins of the complaint [415, 416]. For instance, women with pelvic pain report more sexual and marital problems than those with migraine but are otherwise comparable (57). 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 [417]. Better integration of sexology and mainstream psychology for pelvic pain in both men and women is needed [418], building on a biopsychosocial formulation [370, 419].

8.2 Psychological assessment of pain

The report of anxiety, depression and sexual problems is sufficiently common for these to be important in assessment and in planning treatment, although they are often absent from treatment trials on the assumption that they will resolve with improvement in pain. Distress is best understood in the context of pain and of the meaning of pain to the individual. Additionally, impact on daily life and on QoL should be addressed (for suggested instruments in each of these domains see Turk et al. [420]).

Anxiety often refers to fears of missed pathology (particularly cancer) as the cause of pain, and to uncertainties about treatment and prognosis. A question such as that suggested by Howard [421], "What do you believe or fear is the cause of your pain?" is more suitable than a general anxiety questionnaire. Anticipated problems with urinary urgency and frequency when away from the home can also generate considerable anxiety of social disgrace.

Depression is also common in men and women with persistent pelvic pain [422]. A study comparing women with pelvic pain and men with urogenital pain with men and women with low back pain [351], after controlling for age and pain duration and severity, showed no differences in depression. However, there is a risk of diagnostic or standard assessment instruments attributing pain-related problems such as poor sleep to neurovegetative signs of depression [423, 424] where pain-related distress is often the cause [425]. Pain ratings themselves may be predicted by cognitive and emotional variables [10]. Furthermore, target outcomes of pain severity, distress and disability co-vary only partly, and improvement in one does not necessarily imply improvement in the others. Therefore, it is particularly important when the primary outcome is pain to anchor its meaning in a study such as that by Gerlinger et al. [426], who determined clinically important differences in pain in relation to overall satisfaction with treatment. There are many measures of restricted function, or disability, most suited to musculosketal pain and mobility problems rather than the difficulties of the individual with pelvic or urogenital pain, although specific measures such as the UPOINT are being developed [427], and generic QoL measures are useful.

8.3 Psychological issues in the treatment of pain

Providing information that is personalised and responsive to the patient's problems, conveying belief and concern, is a powerful way to allay anxiety [428]. Additional written information or direction to reliable sources 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 [429].

Ideally, treatment arises from general principles and practice in the field of chronic pain, with specific study of the population of concern and design of appropriate treatment trials [430]. Curiously, in pelvic pain, the mainstream psychologically based treatments are overlooked in trial design for often rather idiosyncratic versions, published in single, often underpowered trials. It is hard to conclude anything from these, as is evidenced in sections of several other chapters. Psychological interventions may be directed at pain itself or at adjustment to pain - improved mood and function and reduced health care use with or without pain reduction. The major psychologically based treatment, cognitive behavioural therapy (CBT), the subject of several systematic reviews [431] produces small but consistent improvement in mood, disability, and cognitive set. Maintenance in the longer term is variable. An uncontrolled feasibility trial of CBT for men with CPP produced results consistent with these effects [432]. For less disabled and distressed patients, this can be delivered in part over the internet [433]. The crucial question, of what is the best choice of components in pelvic pain, is unanswered and possibly unanswerable given the complexity of variables, outcomes, and the difficulties in standardising treatments.

8.4 Female pelvic pain

8.4.1 Psychological risk factors in development and maintenance of pelvic pain

A thorough review from nearly 15 years ago [434] argues against division of aetiology into organic vs. psychogenic, and concludes that, given the methodological problems of many studies, the evidence for sexual abuse as a risk factor is uncertain. Pelvic pain and distress may be variously related, each as the consequence of the other, or arising independently; the same is true of painful bladder and distress [435]. The only systematic review [410] of risk factors for chronic non-cyclical pelvic pain in women included as well as medical variables: sexual or physical abuse (ORs 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); hysteria, i.e., multiple somatic problems (OR: 4.83, 95% CI: 2.50-9.33); and psychosomatic symptoms (OR: 8.01, 95% CI: 5.16-12.44). The terms hysteria and psychosomatic symptoms can best be understood as multiple somatic symptoms not associated with or indicative of any serious disease process, and personality variables are not reliably associated with pelvic pain in women. A comparison of clinic-attending women with diffuse abdominal/pelvic pain against those with vulvovaginal or cyclic pain found the former to report higher rates of lifetime trauma, but they also had more pelvic surgery, more non-pelvic symptoms and were more disabled by their pain [436]. Some of these risk factors are interrelated e.g. history of sexual abuse and depression, but cannot be disentangled. The most recent Diagnostic and Statistical Manual (DSM-V) puts more emphasis on pain [419, 437], but still subsumes female genital pain under sexual disorders. Issues of early trauma such as childhood sexual or physical abuse as a risk factor are addressed in section 8.1.2, but it is important to say that better quality studies, including one prospective study [29], have reported a weaker or no relationship, or not one which is specific to pelvic pain [410, 438-440]. However, another systematic review [413] has concluded that there is some evidence for a specific relationship between rape and CPP (and with fibromyalgia and functional gastrointestinal disorders). It is also important to recognise the possible role of recent sexual assault on the presentation of pelvic pain [409, 441].

There have been fewer studies of maintenance of or recovery from pelvic pain in relation to psychological factors. Weijenborg et al. found, in 25% of women treated surgically, recovery from pelvic pain over a mean 3 years follow-up was not predicted by pain variables at baseline, nor by a general measure of psychological distress or sociodemographic variables, or reports of childhood sexual abuse [442]. Studies that have described pelvic pain as medically unexplained or psychosomatic, due to the lack of physical findings, have been discarded, because such a distinction is unhelpful and inconsistent with known pain mechanisms [415]. Women experience diagnoses which assign their pain to psychological origin as scepticism about the reality or severity of their pain [443], undermining any therapeutic relationship [444]. Ehlert et al. [445] have found that women with pelvic pain with and without laparoscopic findings do not differ from one another; only from pain-free controls, as anticipated by Savidge [26], but a large primary care study [446] showed doctors' tendency to attribute pelvic pain without obvious pathology to a psychological cause.

Anxiety and post-traumatic stress symptoms are common in some women with CPP [446, 447], 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 [448, 449], and anxiety often focuses on what might be 'wrong' [450]. 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 [451]. Reference to the studies of the IMMPACT group [351] is recommended for guidance on outcome measures suitable for pain trials.

8.4.2 Psychological factors in treatment of persistent pelvic pain

A recent Cochrane systematic review and meta-analysis of non-surgical treatments for pelvic pain [263], excluding that due to endometriosis, IBS, and chronic PID [452] found five eligible trials of psychologically-based treatment, but they were diverse and not combined for analysis. Surprisingly, the single component treatments, counselling about ultrasound results [453], and emotional disclosure [454], showed improvements in pain, while three more standard multicomponent (including psychological) treatments for pain [244, 455, 456] did not. As surprisingly, only two measured mood improvement, and found no effects of psychological and physiotherapeutic treatment over gynaecological consultation [456], or for writing with vs without disclosure of distress [454]. The importance of multidisciplinary treatment is emphasised by several reviews [457, 458], and the need for high quality psychological treatment evaluation is underlined [457]. Several other reviews make positive comments on psychological involvement [459], and recommend addressing psychological concerns from the outset, directed at the pain itself, with the intended outcome of reducing its impact on life [404], or at adjustment to pain, with improved mood and function and reduced health care use, with or without pain reduction [405].

In the first category are relaxation and biofeedback methods of controlling and decreasing pain by reducing muscle tension, applied in mainly uncontrolled trials to pelvic floor retraining both in men and women. The only RCT applied a specific type of cognitively enhanced physical therapy to overall muscle tension, not to the pelvic floor, combined with normal gynaecological treatment compared with gynaecological treatment alone [456]. Pain was reduced by 50% and motor function improved in various aspects by 10 h of physical therapy, with particular attention to tension, relaxation and to the thoughts and emotions that generate tension. In the second category, multicomponent pain management, involving education, physical retraining, behavioural change, and increasing activity, relaxation and cognitive therapy, is often applied to mixed groups of chronic pain patients, including those with pelvic pain. A systematic review and meta-analysis which shows a good outcome for mixed chronic pain or back pain groups across pain experience, mood, coping, and activity, cannot with confidence be extrapolated to women with pelvic pain alone [460] although it is probably applicable.

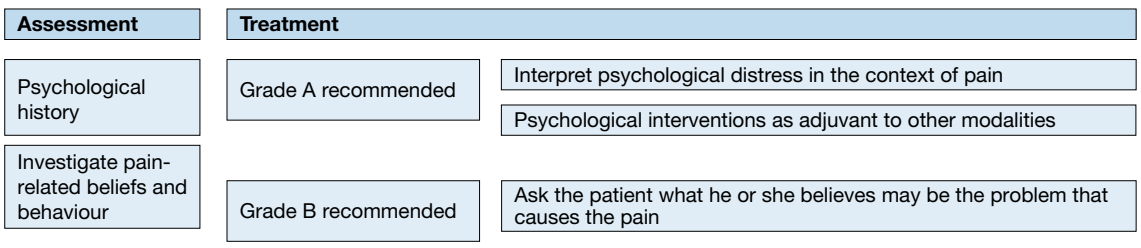
The only RCT in CPP used elements of this approach in combination with medroxyprogesterone acetate (MPA) or placebo [455]. Combination of MPA and psychological therapy outperformed other treatment methods in the long-term, with nearly three quarters of women reporting > 50% pain relief. Several single treatments with benefits in other chronic pain or chronic health problems have been tried in pelvic pain: emotional disclosure by writing about pain (with writing about positive events as a control) [454] produced small differences on one measure of pain appraisal, particularly in women with more distress at baseline. Given the extent of problems associated with pelvic pain, this intervention on its own is unlikely to produce much change, but could be combined with other components described above. Finally, a small RCT of transcranial direct current stimulation compared to sham stimulation [461] produced greater pain reduction and improvement in disability in the treatment group, in the first week only.

8.5 Conclusions and recommendations: psychological aspects of CPP

Conclusions	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 should be assessed as possible contributory factors in pelvic pain.	2a
Psychological intervention in general can produce benefits in pain, mood, and quality of life, depending on its content and focus.	1a
Psychologically informed physical therapy can improve pain and function.	1b
Combined exercise and cognitive behavioural therapy with medroxyprogesterone acetate can reduce pain in the majority of women with pelvic pain.	1b
Transcranial direct current stimulation may reduce pain in the short-term.	1b

Recommendations	GR
Psychological distress is common in pelvic pain in women, but should be interpreted in the context of pain.	A
Ask the patient what she/he thinks may be wrong to cause the pain, to allow the opportunity to inform and reassure as appropriate.	B
Try psychological interventions in combination with medical and surgical treatment, or alone.	A

Figure 12: Assessment and treatment of psychological aspects of chronic pelvic pain



9. PELVIC FLOOR FUNCTION AND CHRONIC PELVIC PAIN

9.1 Introduction

The pelvic floor is made up of muscles and fascia. The muscles usually function as a composite, although the anterior and posterior components may act in isolation. The pelvic floor has three functions: support, contraction and relaxation.

9.2 Function

In its resting state, the pelvic floor supports the bladder and the urethra in the anterior compartment, the uterus and the vagina in the middle compartment, and the rectum and the anus in the posterior compartment. When intra-abdominal pressure rises, the pelvic floor muscles respond with a contraction occurring simultaneously or before the pressure rise. Contraction of the pelvic floor muscles results in inward movement of the perineum and upward movement of the pelvic organs. There are two types of contraction that can be distinguished: a voluntary contraction and an involuntary contraction. These contractions not only maintain support of the pelvic organs, they also close the urethra, anus and vagina, thus avoiding loss of urine or stools. Contractions also form a defence against introduction of foreign objects into the anus or vagina, and in women, they can protect against sexual penetration.

Pelvic floor muscle relaxation results in a decrease or termination of the squeezing of the urethra, vagina and anus. The perineum and the pelvic organs return to their anatomical resting position. Relaxation of the pelvic floor muscles is needed for voiding, defecation and for sexual intercourse. The muscles of the pelvic floor are integrated in the total muscular girdle of the pelvis, yielding the stability needed for bearing the trunk. In turn, instability leads to compensatory pelvic floor muscle (over) activity.

9.3 Dysfunction

Pelvic floor dysfunction should be classified according to “The standardisation of terminology of pelvic floor muscle function and dysfunction” [462]. This is an international multidisciplinary report from the International Continence Society. By palpation of the pelvic floor muscles, the contraction and relaxation are qualified. Voluntary contraction can be absent, weak, normal or strong, and voluntary relaxation can be absent, partial or complete. Involuntary contraction and relaxation is absent or present.

Based on these signs, pelvic floor muscles can be classified as follows:

- non-contracting pelvic floor
- non-relaxing pelvic floor
- non-contracting, non-relaxing pelvic floor.

Based on symptoms and signs, the following conditions are possible:

- normal pelvic floor muscles
- overactive pelvic floor muscles
- underactive pelvic floor muscles
- non-functioning pelvic floor muscles.

Normal pelvic floor muscles relax during urination and contract during coughing. Overactive pelvic floor muscles do not relax during micturition, defecation or during sex and cause dysfunctional voiding, overactive bladder, constipation and dyspareunia [463]. Underactive pelvic floor muscles do not contract sufficiently to keep the patient dry. Non-functioning pelvic floor muscles do not show any activity and can cause every type of pelvic organ dysfunction. Overactivity tends to develop over a protracted period, with many causes. A psychological mechanism that is thought to play a role is that contraction of the pelvic floor muscles closes some of the exits of the body (anus and vagina), and helps to keep urine and stool inside. It gives women a defence mechanism against unwanted vaginal penetration of any type. The pelvic floor muscles also help to postpone micturition, which can be of benefit in a social or working environment. In summary, the pelvic floor muscles assist in adaptation to different situations in life.

9.4 Pelvic floor muscles and myofascial pain

Chronic pelvic pain can simply be a form of myalgia, due to misuse of muscles, 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 pain when palpating the pelvic floor muscles [464]. Muscle relaxation can diminish spasm and pain [465]. 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 [466].

*9.4.1 **Muscular aspects***

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 [278]. 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) [467]. This relationship has been found in chronic prostatitis [466], BPS [468] and vulvar pain [469]. 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.

*9.4.2 **Neurological aspects***

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 [471].

*9.4.3 **Myofascial trigger points***

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).

9.5 Diagnostics of pelvic floor muscle function

Diagnosing pelvic floor muscle function in patients with CPP starts by taking a complete functional history of the pelvic organ function. The following items certainly should be addressed: lower urinary tract function, anorectal function, sexual function, gynaecological items, presence of pain and psycho-social aspects.

*9.5.1 **Pelvic floor testing***

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 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 [472]. Rectal examination is a good way to test the pelvic floor function in men [473].

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%) [474].

9.6 Treatment of 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.

*9.6.1 **Pelvic floor muscle exercise***

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 [475].

*9.6.2 **Biofeedback and electrostimulation***

Biofeedback can be helpful in the treatment of pelvic floor pain in the process of recognising the action of the muscles. Visualising the action of the pelvic floor muscles by using biofeedback is revealing to many patients. Biofeedback should always be used in consultation with the patient. Special care should be taken when there is a history of negative physical or sexual experiences. The numbers of patients in most studies concerning biofeedback have been small but the results are promising. In a cohort study, 31 patients with CPPS participating in a pelvic floor biofeedback re-education programme were followed. The mean chronic prostatitis symptom index decreased from 23.6 to 11.4. They also measured the pelvic floor muscle activity by EMG using an anal probe. The resting amplitude was taken as a parameter for the ability to relax the pelvic floor muscles. This parameter was 4.9 μV at the start and 1.7 μV at the end of the treatment, so the relaxation improved markedly. There was also a correlation between the decline in EMG values and improvement in prostatitis symptom score [476]. In a study among patients with Levator Ani Syndrome, biofeedback was found to be the most effective therapy. Other modalities used were electrostimulation and massage. Adequate relief was reported by 87% in the biofeedback group, 45% for electrostimulation, and 22% for massage [278]. A review on biofeedback in pelvic floor dysfunction has shown that biofeedback is better than placebo or sham treatment. An odds ratio of 5.8 favouring biofeedback has been calculated based on three studies [477].

*9.6.3 **Myofascial trigger point release***

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 [478]. 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 [479]. Other reviews have concluded that the same is true for the difference between dry and wet needling [480, 481].

Physiotherapy. General muscular exercise may be beneficial in some BPS patients [482]. 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 [483]. Langford et al. examined the role of specific levator ani trigger point injections in women with CPP [484]. 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 [485].

*9.6.4 **Botulinum A toxin***

Botulinum A toxin (BTX-A) is an inhibitor of acetylcholine release at the neuromuscular junction and has a paralysing effect on striated muscles. BTX-A has been injected into trigger points. It is more expensive than lidocaine and has not been proven to be more effective [486]. Reviews do not support the injection of BTX-A into trigger points [487]. 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 [280]. 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 [488].

*9.6.5 **Pain management***

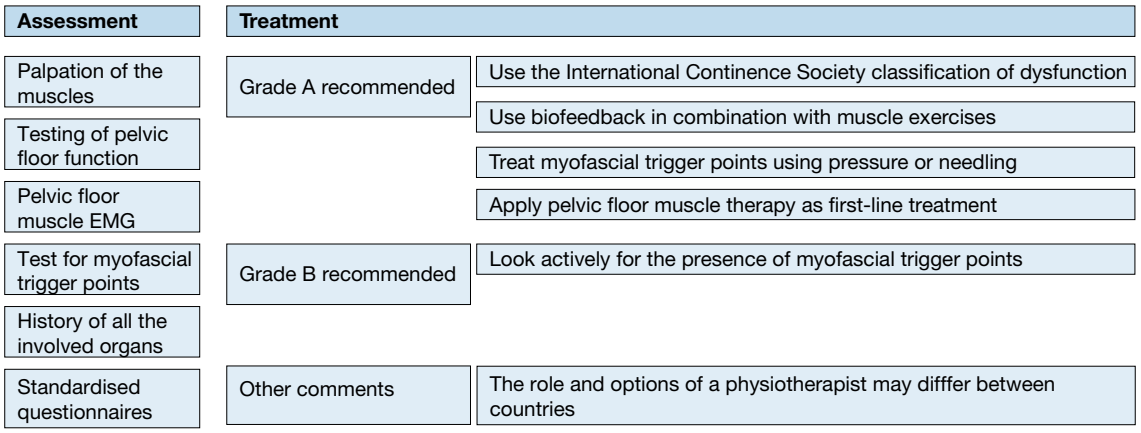
The physiotherapist is part of the pain management team, together with the pain doctor and the psychologist. The therapeutic options for physiotherapists may not be the same in every country. Physiotherapists can either specifically treat the pathology of the pelvic floor muscles, or more generally treat 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 [489]. 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 [456].

9.7 Conclusions and recommendations: pelvic floor function

Conclusions	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
Myofascial treatment is effective in prostate- and bladder pain syndrome.	1b
Biofeedback improves the outcome of myofascial therapy for pelvic floor dysfunction.	1a
Trigger point release is effective in treating muscle and referred pain, but there is no preference for this method over others.	1a

Recommendations	GR
The use of the ICS classification on pelvic floor muscle function and dysfunction is recommended.	A
In patients with chronic pelvic pain syndrome it is recommended to actively look for the presence of myofascial trigger points.	B
Apply pelvic floor muscle treatment as first line treatment in patients with chronic pelvic pain syndrome.	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

Figure 13: Assessment and treatment pelvic floor function



10. GENERAL TREATMENT OF CHRONIC PELVIC PAIN

10.1 Introduction

Chronic pelvic pain is well defined and involves multiple mechanisms as described in previous chapters. The management requires a holistic approach with biological, psychological and social components.
This chapter looks at general treatments for pain (both peripheral and central) and not the specific treatments mentioned in the Chapters 2 and 6.

Few studies have specifically looked at medications used in CPP [452], 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. 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.

10.2 Simple analgesics

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 [490]. It is often available over the counter without prescription. There is evidence that paracetamol is beneficial in managing somatic and arthritic pain [491].

Non-steroidal anti-inflammatory agents (NSAIDs)
This group of agents is anti-inflammatory, antipyretic analgesics that act by inhibiting the enzyme cyclo-oxygenase (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 are usually well tolerated. The evidence for their benefit in CPP is weak or non-existent and they do have side-effects, which may be significant. There is no good evidence to suggest one NSAID over another for pelvic pain.

For pelvic pain in which inflammatory processes are considered important, such as dysmenorrhoea [492], 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 [246], then the evidence is lacking for NSAIDs despite their common use.

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

Neuropathic analgesics
These are agents that are not simple analgesics but used to modulate neuropathic or centrally mediated pain. There are several classes commonly used with a recognised benefit in pain medicine. They are taken on a regular basis rather than as required. They all have side-effects that limit their use in some patients.

In the UK, the National Institute for Health and Clinical Excellence (NICE) has reviewed the pharmacological management of neuropathic pain [493]. Further guidance is in progress for the management of neuropathic pain in the non-specialist setting.

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. Side-effects frequently limit their use. It is common to use these agents in combination but studies comparing different agents against each other, or in combination, are lacking.

*10.2.1 **Antidepressants***

10.2.1.1 Tricyclic antidepressants

The tricyclic antidepressants have multiple mechanisms of action, a long history of use in pain medicine and have been subjected to a Cochrane review [494]. This suggests that they are effective for neuropathic pain with numbers needed to treat (NNT) of approximately three.

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.

10.2.1.2 Other antidepressants

Venlafaxine is a serotonin and noradrenalin reuptake inhibiter (SNRI). It is not licensed for managing neuropathic pain but there is evidence of its benefit in chronic pain [493]. There are cautions particularly in patients with heart disease. This is a drug best used by those familiar with its use.

Duloxetine is a newer SNRI antidepressant. It is used for depression, urinary stress incontinence and neuropathic pain. There is moderately strong evidence for a benefit in diabetic neuropathy and fibromyalgia at a dose of 60 mg/day [495]. 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 [494-496].

*10.2.2 **Anticonvulsants***

Anticonvulsants are commonly used in the management of neuropathic pain. There have been general studies as well as some looking more particularly at pelvic pain. Individual agents have been systematically reviewed. Their use is suggested in the NICE Neuropathic Guidelines [493].

Carbamazepine has a long history of use in neuropathic pain. Evidence exists for its benefit [497]. Trials have tended to be of short duration, showing only moderate benefit. There are side-effects; some of which may be serious. More recently, developed agents are available with fewer serious side-effects, carbamazepine is no longer a first-choice agent. Gabapentin is commonly used for neuropathic pain and has been systematically reviewed [498]. 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 [499].

Pregabalin is a commonly used neuromodulator with good evidence for its efficacy in some neuropathic conditions but the NNT varies depending on the condition [500]. 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.

*10.2.3 **Other agents***

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.

10.3 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 [501]. They should only be used in conjunction with a management plan and 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 [502]. There is also information available online for patients [503, 504].

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 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 [505]. This is another reason for these drugs to be used in a controlled fashion for long-term management of non-malignant pain.

*10.3.1 **Recommendations for use of opioids in chronic/non-acute urogenital pain***

Recommendations
All other reasonable treatments must have been tried and failed.
The decision to instigate long-term opioid therapy should be made by an appropriately trained specialist in consultation with another physician (including the patients and their family doctor).
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.
The patient should undergo a trial of opioids.
The dose required needs to be calculated by careful titration.
The patient should be made aware (and possibly give written consent): • Opioids are strong drugs and associated with addiction and dependency. • Opioids will normally only be prescribed from one source (preferably the family doctor). • The drugs will be prescribed for fixed periods of time and a new prescription will not be available until the end of that period. • The patient may be subjected to spot urine and possibly blood checks to ensure that the drug is being taken as prescribed, and that non-prescribed drugs are not being taken. • Inappropriate aggressive behaviour associated with demanding the drug will not be accepted. • Hospital specialist review will normally occur at least once a year. • The patient may be requested to attend a psychiatric/psychological review. Failure to comply with the above may result in the patient being referred to a drug dependency agency and the use of therapeutic, analgesic opioids being stopped
Morphine is the first-line opioid, unless there are contraindications to morphine or special indications for another drug. • The drug should be prescribed in a slow-release/modified-release form. • Short-acting preparations are undesirable and should be avoided where possible. • Parenteral dosing is undesirable and should be avoided where possible.

*10.3.2 **Morphine***

Morphine is the traditional gold standard and the opioid with which many physicians are most 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.

*10.3.3 **Other opioid agents***

There are a variety of 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 [506].

Oxycodone may have greater efficacy than morphine in some situations, such as hyperalgesic states including visceral pain [507].

Analgesics with a dual mode of action may have a role in the management of chronic pain. 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 reuptake inhibition. It is too early to assess its real value in the armamentarium for pain management.

10.4 Nerve blocks

Nerve blocks for pain management are usually carried out by specialists in pain medicine as part of a broader management plan [508]. 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.

10.5 Transcutaneous electrical nerve stimulation (TENS)

Despite the popularity of 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]. Further more, rigorous trials should be undertaken to provide some clarity for a commonly used intervention.

10.6 Neuromodulation in pelvic pain syndromes

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 interventions and thus many of the patients involved are refractory to other therapies. It is thus inappropriate to provide a detailed review of these techniques for this publication.

In the UK, guidance has been published for SCS in neuropathic pain [510]. 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 [511]. Its role in overactive bladder and faecal incontinence is more robust but is limited for pain.

10.7 Summary

Chronic pelvic pain is a common complaint that is well defined and involves multiple mechanisms. Some of the conditions have clear management pathways but many do not. In these CPP syndromes, a holistic multidisciplinary team approach is required with active patient involvement.

This chapter focuses on general treatment of CPP, mainly drug therapy, and comments on other more invasive techniques. The latter are used in combination with other modalities. Many are aimed at the management of neuropathic pain or conditions in which central mechanisms are implicated.

At this stage in management, the involvement of trained clinicians with expertise in chronic pain management should be considered. Centres with a particular interest in pelvic pain do exist and involve clinicians from several specialties along with other healthcare professionals (e.g., physiotherapy, psychology, nursing and occupational therapy).

With any of the agents above, the aim is to assess pain relief, improvement in function, and side-effects. This should be done regularly while titrating and optimising drug dose. If there is no benefit, then the drug should be withdrawn.

Neuropathic agents are frequently used and often in combination. There is significant inter-patient variability in effect. Their use is often limited by side-effects that may be worse than any pain reduction.

Opioid drugs are used in this group of patients. Their role is limited and they should only be started in

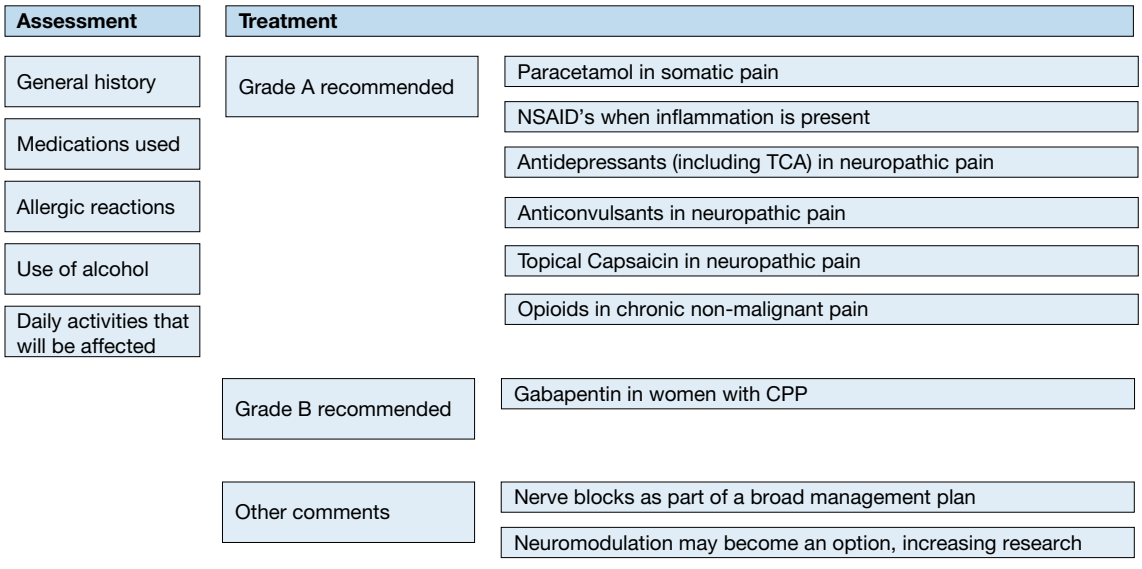
consultation with all parties involved (including the patient's family practitioner). National guidelines exist and should be followed. There is growing understanding of the limitations of opioid use, and more recently, the paradoxical situation of opioid-induced hyperalgesia.

10.8 Recommendations for the medical and interventional treatment of CPP

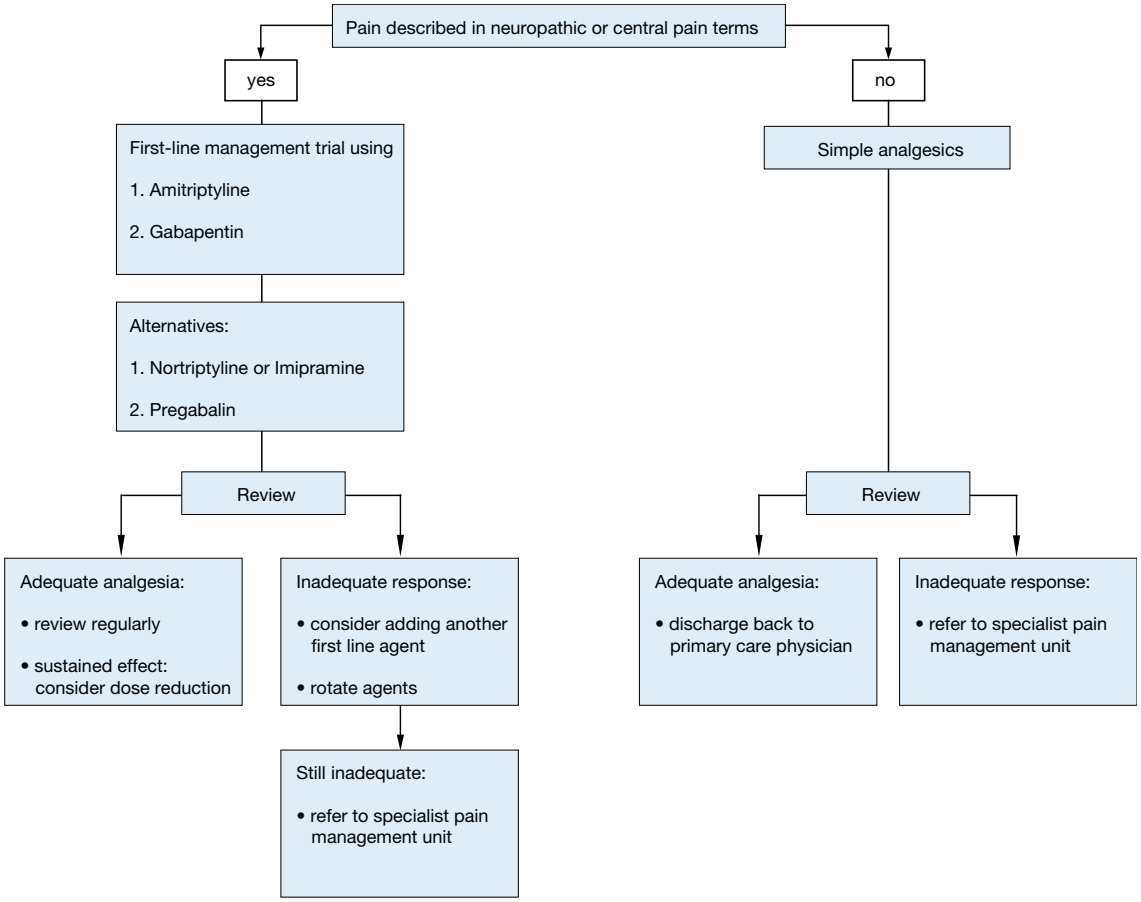
Agent	Pain Type	LE	GR	Comment
Paracetamol	Somatic pain	1a	A	Evidence based on arthritic pain with good benefit
NSAIDs	Pelvic pain with inflammatory process (e.g. dysmenorrhoea)	1a	A	Good evidence for their use
Antidepressants including tricyclic antidepressants, duloxetine and venlafaxine	Neuropathic pain	1a	A	Effective. No specific evidence for CPP
Anticonvulsants gabapentin, pregabalin	Neuropathic pain, fibromyalgia	1a	A	Effective
Gabapentin	Women with CPP	2b	B	Effective
Topical capsaicin	Neuropathic pain	1a	A	Some evidence of benefit
Opioids	Chronic non-malignant pain	1a	A	Beneficial in a small number of patients
Nerve blocks		3	C	Have a role as part of a broad management plan
TENS		1b	B	There is no good evidence for or against the use of TENS. Data covered chronic pain not just CPP and was insufficient regarding long-term reatment effects.
Neuromodulation	Pelvic pain	3	C	Role developing with increasing research

TENS = transcutaneous electrical nerve stimulation; CPP = chronic pelvic pain

Figure 14: General analgesic treatment of chronic pelvic pain



Algorithm 5: General management of CPP



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12. CONFLICT OF INTEREST

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