INTERNATIONAL CONTINENCE SOCIETY (ICS) REPORT ON THE TERMINOLOGY
FOR SEXUAL HEALTH IN MEN WITH LOWER URINARY TRACT (LUT) / PELVIC FLOOR (PF)
DYSFUNCTION - VERSION 15
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## **ABSTRACT**

**Introduction:** The terminology for sexual health in men with lower urinary tract (LUT) and pelvic floor (PF) dysfunction has not been defined and organized into a clinically based consensus Terminology Report. The aim of this Terminology Report is to provide a definitional document within this context that will assist clinical practice and research.

Methods: This Report combines the input of the members of Sexual Health in Men with LUT and PF Dysfunction working group of the International Continence Society (ICS), assisted at intervals by external referees. Appropriate core clinical categories and a sub-classification were developed to give coding to definitions. An extensive process of ... rounds of internal and external review was involved to exhaustively examine each definition, with decision-making by collective opinion (consensus). The Committee retained evidence-based definitions, identified gaps, and updated or discarded outdated definitions. Expert opinions were used when evidence was insufficient or absent.

**Results:** A Terminology Report for sexual health in men with LUT and PF dysfunction, encompassing 223 (201 *NEW*) separate definitions, has been developed. It is clinically based with the most common diagnoses defined. Clarity and user-friendliness have been key aims to make it interpretable by practitioners and trainees in all the different specialty groups involved. Conservative and surgical managements are major additions and appropriate figures have been included to supplement and clarify the text. Emerging concepts and measurements, in use in the literature and offering further research potential, but requiring further validation, have been included as an appendix. Interval (5-10 year) review is anticipated to keep the document updated.

**Conclusion:** A consensus-based Terminology Report for sexual health in men with LUT and PF dysfunction has been produced to aid clinical practice and research. The definitions that have been adopted are those that are most strongly supported by the literature at this time or are considered clinical principles or consensus of experts' opinions.

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104	Ervin Kocjancic: Neomedic (Speaker honorarium), NexHand (Patent owner), Allergan (Consultant),
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121	FIGURES: 3
122	TABLES: 7
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#### INTRODUCTION

Currently there is no comprehensive document addressing all elements required for diagnoses applicable to sexual health in men with lower urinary tract (LUT) and pelvic floor (PF) dysfunction. The term "diagnosis" is defined by "the determination of the nature of a disease" by clinical symptoms and signs and laboratory investigations. Such a specific report requires a full outline of the terminology for all symptoms, signs, diagnostic tools, and therapeutic options for sexual health in males with LUT and PF dysfunction. Sexual dysfunctions are a large group of conditions that have been classified by the International Classification of Diseases, 10th Edition (ICD-10) by the World Health Organization as organic or as non-organic even though a multifactorial etiology is often presumed.<sup>2</sup>

This Terminology Report is inherently and appropriately a definitional document, collating the definitions of terms, that is, words used to express a defined concept in a particular branch of study; sexual health in men with LUT and PF dysfunction. Emphasis has been on comprehensively including terms in current use in the relevant peer-reviewed literature. The aim is to assist clinical practice and research. Explanatory notes on definitions have been referred, where possible, to the "Footnotes section." Table 1 lists the number of definitions: (i) new; (ii) changed; (iii) total by section, compared with the previous male-inclusive reports. 3,4,5,6

As in earlier ICS Reports, qualities for a male-specific terminology report should be:

- (A) User-friendly: It should be able to be understood by all clinical and research users.
- 157 (B) Clinically-based: Symptoms, signs, validated investigations and imaging should be 158 presented for use in forming diagnoses.
- (C) Origin: Where a term's existing definition (from one of multiple sources used) is deemedappropriate, that definition will be included and duly referenced.
  - (D) Able to provide explanations: Where a specific explanation is deemed appropriate to explain a change from earlier definitions or to qualify the current definition, this will be included as an addendum to this paper (Footnote [FN] 1,2,3 . . .). Wherever possible, evidence-based medical principles will be followed.

A previous "backbone" terminology ICS paper on adult male lower urinary tract and pelvic floor symptoms and dysfunctions<sup>5</sup> has been previously published lacking the analysis of sexual male aspects. Disorders in functional urology often overlap with sexual dysfunctions,

therefore we needed to promote this update in order to focus on male sexual health features. Dysfunctions in sexual health have been defined in section 1 and their anatomical relation has been reported in section 2. Clinical and diagnostic aspects of sexual dysfunctions have been discussed in sections 3 to 6. According to diagnosis, 7 sections have been developed to define conservative and surgical treatments of male sexual dysfunctions as primary conditions or as secondarily related to benign prostatic obstruction (BPO), urethral stricture disease, overactive bladder (OAB), chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) and prostate cancer.

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Commonly accepted terminology is needed given its influence on clinician approach to clinical conditions, their studies and investigations of analyses, and for a proper communication with the patients. Thus, this Terminology Report has a crucial role as it is able to provide definitions which are critical in facilitating research, enabling clinicians to communicate accurately to each other, to their patients, and health care systems. This work also enhances the training of future clinicians.

Section Total New Changed definitions/descriptions definitions/descriptions Possible 8 46 definitions and 38 dysfunctions **Anatomical** 0 15 15 definitions Symptoms and 20 2 22 questionnaires Signs, 42 examination, and 33 9 investigations **Conservative and** pharmacological 0 17 17 treatment

Surgical	6	0	6
treatment			
BPO treatment	9	0	9
and sexual health			
Urethral stricture			
disease and	8	0	8
sexual health			
Overactive			
bladder and	11	2	13
sexual health			
Chronic	11	1	12
prostatitis /			
chronic pelvic			
pain syndrome			
and sexual health			
Prostate cancer	29	0	29
and sexual health			
Treatments that			
warrant further	4	0	4
investigation			
Total	201	22	223

**Table 1:** Total, new, and changed definitions. BPO: Benign prostatic obstruction.

# SECTION 1: OUTLINE OF POSSIBLE DEFINITIONS AND DYSFUNCTIONS IN SEXUAL HEALTH

- **1.1 Erectile function:** Complex mechanism of involuntary, neuropsychological, hormone-mediated vascular event that occurs when blood rapidly flows into the penis and becomes trapped in its spongy chambers. *(NEW)*
- **1.2 Sexual dysfunction:** Difficulty experienced by an individual or a couple during any stage of normal sexual activity; including desire, arousal, and orgasm. Sexual dysfunction requires a person to feel significant distress and interpersonal strain for at least 6 months. (NEW)
- **1.3 De-novo (postoperative) sexual dysfunction symptoms:** Symptoms related to sexual dysfunction that were not reported before surgery. (NEW)

194	1.4 Erectile function recovery: Return to baseline erectile function after treatment. (NEW)
195	1.4.1 Erectile function after treatment for prostate cancer: Ability to have successful
196	intercourse by patient self-report after any treatment for prostate cancer. (NEW)
197	1.5 Erectile dysfunction (ED): Consistent or recurrent inability to attain and/or maintain a
198	penile erection sufficient for sexual satisfaction and/or sexual intercourse.6 (CHANGED)
199	1.5.1 Vasculogenic ED: Erectile dysfunction which is secondary to a problem with
200	arterial inflow (e.g. atherosclerosis) or venous outflow (e.g. venous leak). (NEW)
201	1.5.2 Neurogenic ED: Erectile dysfunction which is secondary to pathology of the
202	central (e.g. spinal cord injury) or peripheral (e.g. diabetic neuropathy) nervous
203	system. (NEW)
204	1.5.3 End-organ ED: Erectile dysfunction which is due to pathology within the penis
205	itself (e.g. Peyronie's disease). (NEW)
206	1.5.4 Situational ED: Erectile dysfunction which only occurs in certain circumstances
207	(e.g. with a partner but not during masturbation). Generally understood to be due to
208	psychological factors. (NEW)
209	1.5.5 Endocrine ED: Erectile dysfunction secondary to an endocrine pathology, most
210	commonly hypogonadism, but may also be due to hyperprolactinemia, thyroid
211	dysfunction and diabetes mellitus. (NEW)
212	1.5.6 Mixed ED: Erectile dysfunction which has an organic cause as well psychogenic
213	factors (e.g. anxiety or depression) playing a role. (NEW)
214	1.6 Male hypoactive sexual desire disorder: Persistent or recurrent deficiency or absence of
215	sexual or erotic thoughts or fantasies and desire for sexual activity. FN1.16 (NEW)
216	1.7 Sexual aversion disorder: Persistent or recurrent extreme aversion to, and avoidance of,
217	all or almost all, genital sexual contact with a sexual partner which causes distress or
218	interpersonal difficulty.8 (NEW)
219	1.8 Hypogonadism: A term introduced to signify low testosterone levels associated with
220	infertility, sexual dysfunction, and systemic alterations (such as decreased muscle mass,
221	depressed mood, sleep disturbances, loss of body hair, lethargy). It has more recently been
222	used interchangeably with the idea of low testosterone production alone. (NEW)
223	1.8.1 Low testosterone: Serum total testosterone level being less than 300 ng/dL. FN1.2
224	<sup>9</sup> Threshold for low testosterone in the International System of Units: 11 nmol/l (US),
225	12 nmol/l (Europe). <i>(NEW)</i>

226	<b>1.8.2 Testosterone deficiency:</b> A state of low testosterone production combined with
227	symptoms and/or signs that are associated with low serum total testosterone.9,10
228	(NEW)
229	1.9 Libido: A person's overall sexual drive or desire for sexual activity. (NEW)
230	1.9.1 Altered libido: Complaint of change in interest in sexual activity. <sup>5</sup>
231	1.9.2 Decreased libido: Complaint of decreased interest in sexual activity in
232	comparison with previous experience.5
233	1.9.3 Increased libido: Complaint of increased interest in sexual activity in comparison
234	with previous experience. <sup>5</sup>
235	1.10 Ejaculatory function
236	<b>1.10.1 Ejaculation:</b> Process related to semen expulsion from the urethra. <sup>11</sup> (NEW)
237	1.10.2 Orgasm: Sensation of pleasure that accompanies sexual climax. 11 (NEW)
238	1.10.3 Emission: Process in which semen is deposited from the vas deferens in the
239	urethra. <sup>11</sup> (NEW)
240	<b>1.10.4 Ejection:</b> Synchronic contractions of the bulbospongiosus and ischiocavernosus
241	muscles and external urethral sphincter that allows semen to be expelled antegrade
242	through the urethra. <sup>11</sup> <b>(NEW)</b>
243	1.11 Ejaculatory dysfunction (EjD): Complaint of alteration of the emission or expulsion of
244	seminal fluids during ejaculation. <sup>5</sup>
245	<b>1.11.1 Anejaculation:</b> Complaint of absence of seminal fluid emission or expulsion.
246	May be associated with the absence of the sensation of orgasm or anorgasmia. <sup>5</sup>
247	1.11.2 Delayed ejaculation: Primary or acquired complaint of an increase in the time
248	taken for ejaculation to occur. <sup>5</sup> (CHANGED)
249	1.11.2.1 Primary delayed ejaculation: A lifelong experience of delayed
250	ejaculation in all or almost all (75%-100%) occasions of coital activity, which
251	causes distress. <sup>6</sup> (NEW)
252	1.11.2.2 Acquired delayed ejaculation: A distressing lengthening of
253	ejaculatory latency that occurs in most (>50%) coital experiences after a period
254	of normal ejaculatory function and/or a clinically meaningful change that
255	results in distress. <sup>6</sup> (NEW)
256	1.11.3 Premature ejaculation (PE): Complaint of a persistent or recurrent pattern of
257	too rapid achievement of ejaculation during partnered sexual activity, that is, before

258	the individual wishes it. 5 It is accompanied by negative personal consequences, such	
259	as distress, bother, frustration, and/or the avoidance of sexual intimacy. <sup>6</sup> (CHANGED	
260	1.11.3.1 Lifelong (primary) premature ejaculation: Ejaculation that always or	
261	nearly always occurs prior to or within about 1 minute of vaginal penetration	
262	from the first sexual experience. 12 (NEW)	
263	1.11.3.2 Acquired premature ejaculation: A clinically significant and	
264	bothersome reduction in latency time, often to about 3 minutes or less. 12	
265	(NEW)	
266	1.11.4 Retrograde ejaculation: Expulsion of seminal fluid into the bladder because of	
267	bladder neck dysfunction and/or disturbances involving the peri-montanal area in the	
268	presence of otherwise normal emission and expulsion. There can be no or small	
269	amounts of antegrade ejaculation. Retrograde ejaculation is defined independently	
270	from the sensation of orgasm. 6 (NEW)	
271	1.11.5 Anhedonic ejaculation: Ejaculation without the pleasurable sensation of	
272	orgasm. <sup>6</sup> (NEW)	
273	1.11.6 Hematospermia: Complaint of the appearance of visible blood in the seminal	
274	fluid. Color of the seminal fluid may be red or brown. <sup>14</sup>	
275	<b>1.12 Orgasmic disorder:</b> Presence of either of the following on all or almost all (75% - 100%)	
276	occasions of sexual activity; marked delay in, marked infrequency of, or absence of orgasm;	
277	markedly reduced intensity of orgasmic sensations. <sup>7</sup>	
278	1.12.1 Anorgasmia (male): The inability to reach orgasm despite adequate and	
279	prolonged sexual stimulation leading to adequate sexual arousal which might or might	
280	not lead to personal distress. <sup>6</sup> (NEW)	
281	1.12.2 Hypohedonic orgasm: Lifelong or acquired decreased or low level of sexual	
282	pleasure with orgasm. <sup>6</sup> (NEW)	
283	1.13.3 Dysorgasmia: Painful orgasm. (NEW)	
284	1.13 Post-orgasmic illness syndrome: Flu-like incapacitating physical and mental symptoms	
285	occurring within a few minutes to a few hours after an ejaculation, which usually lasts 3 to 7	
286	days. <sup>6</sup> (NEW)	
287	<b>1.14 Sexual arousal disorder:</b> Lack of, or significantly reduced, sexual interest or arousal. FN1.3	
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- 289 1.15 Post-5-Alpha reductase inhibitor syndrome: Persistent sexual, neurological, physical,
- and mental adverse reactions in patients who have taken 5-alpha reductase enzyme inhibitors
- 291 (finasteride and dutasteride).13 (NEW)
- 292 1.16 Benign prostatic hyperplasia (BPH): A term that is used exclusively to describe the
- 293 histologic changes related to benign prostatic growth. FN1.4, FN1.5 14 (NEW)
- 294 **1.17 Benign prostatic enlargement (BPE):** A term describing increased volume of the gland
- 295 usually secondary to BPH. The precise volume that determines the lower limit of BPE remains
- 296 to be defined; 20 mL has been suggested. <sup>14</sup> (NEW)
- 297 **1.18 Benign prostatic obstruction (BPO):** A term used to describe bladder outlet obstruction
- 298 (BOO) secondary to BPE and, therefore, usually due to BPH.<sup>14</sup> (NEW)
- 299 **1.19 Prostatitis:** An inflammatory disease of the prostate generally affecting younger men
- and causing pain and discomfort mostly in the perineal and scrotal region which can be
- 301 associated with LUTS and/or sexual dysfunction. 15 Prostatitis covers a wide range of clinical
- 302 conditions including acute bacterial prostatitis, chronic bacterial prostatitis, chronic pelvic
- 303 pain syndrome (inflammatory and noninflammatory), and asymptomatic inflammatory
- 304 prostatitis. (NEW)
- 305 **1.20 Overactive bladder (OAB) syndrome:** Urinary urgency, usually accompanied by
- 306 increased daytime frequency and/or nocturia, with urinary incontinence (OAB-wet) or
- 307 without (OAB-dry), in the absence of urinary tract infection or other detectable disease. FN1.6
- 308 16
- **1.21 Sexual activity urinary incontinence or coital urinary incontinence:** Complaint of urinary
- incontinence associated with or during sexual activity and sexual arousal.<sup>7,17</sup> (CHANGED)
- **1.22 Climacturia:** Involuntary loss of urine at the time of orgasm. *(NEW)*
- 312 1.23 Sexual arousal incontinence or foreplay incontinence: Complaint of involuntary loss of
- 313 urine during sexual arousal, foreplay and/or masturbation. (NEW)
- 314 **1.24 Penile pain with intercourse (Male dyspareunia):** Complaint of any penile discomfort
- 315 occurring during intercourse. May be caused by penile disease, vaginal anatomy (eg, vaginal
- 316 tightening, scarring, or exposed mesh) and/or may relate to various positions with
- 317 intercourse.<sup>5</sup>
- 318 **1.24.1 Hispareunia:** male partner pain with vaginal intercourse after female
- 319 reconstructive surgery. (CHANGED)

320 **1.25 Chronic sexual pain disorder:** Sexual activity may induce a central sensitization process characterized by hypersensitivity or hyperalgesia before, during or after sexual activity.<sup>20</sup> 322 (CHANGED) 323 **1.26 Pain:** A subjective phenomenon described as an unpleasant sensory and emotional 324 experience associated with actual or potential tissue damage, or described in terms of such damage. Pain should be characterized by site, type, frequency, duration, precipitating and 325 relieving factors. The word pain comes from the Latin "poena" meaning a fine or a penalty.<sup>21</sup> 326 327 **1.26.1 Acute pain:** Pain related to acute trauma, infection or other well-defined disease process.<sup>93</sup> 328 329 **1.26.2 Chronic pain:** Persistent or continuous/recurrent pain for at least 6 months. If non-acute and central sensitization pain mechanisms are well documented, then the pain may be regarded as chronic, irrespective of the time period. 93 **1.26.3 Pelvic pain syndrome:** Occurrence of persistent or recurrent episodic pelvic 332 333 pain associated with symptoms suggestive of lower urinary tract, sexual, bowel or gynecological dysfunction. There is no proven infection or other obvious disease.<sup>22</sup> 334 335 1.26.4 Perineal pain syndrome: Perineal pain syndrome is the occurrence of 336 persistent or recurrent episodic perineal pain, which is either related to the 337 micturition cycle or associated with symptoms suggestive of urinary tract or sexual 338 dysfunction. There is no proven infection or other obvious disease.<sup>22</sup> **1.26.5 Scrotal pain syndrome:** Scrotal pain syndrome is the occurrence of persistent or recurrent episodic scrotal pain which is associated with symptoms suggestive of urinary tract or sexual dysfunction. There is no proven epididymo-orchitis or other obvious disease.<sup>22</sup> 342 343 **1.26.6 Male chronic genital pain syndromes:** Male genital pain syndromes are often 344 associated with symptoms suggestive of lower urinary tract and sexual dysfunction. 345 Common complaints: genital pain, uncomfortable urination, dysuria, sensation of residual urine, increased daytime frequency, slow stream, urgency, dyspareunia. 346 Absence of infection, previous operations, or other obvious disease.<sup>21</sup> 347 1.26.6.1 Chronic (persistent or recurrent) epididymal pain syndrome: Pain is 348 specific/localized to the epididymis. i. Persistent or recurrent episodic pain. ii. 349 350 Spontaneous, or reproduced by digital pressure and physical activities. iii. Lower urinary tract symptoms or sexual dysfunction.

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352	1.26.6.2 Chronic (persistent or recurrent) penile pain syndrome: Pain within
353	the penis that is not primarily in the urethra and may be: i. Persistent or
354	recurrent. ii. Spontaneous, or reproduced by digital pressure and physical
355	activities. iii. Lower urinary tract symptoms or sexual dysfunction.
356	1.26.6.3 Chronic (persistent or recurrent) prostate pain syndrome: see 1.30.
357	1.26.6.4 Chronic (persistent or recurrent) scrotal pain syndrome: Chronic
358	scrotal pain (generic term used when the site of pain is not clearly in the testis
359	or epididymis). i. Persistent or recurrent episodic pain, unilateral or bilateral.
360	ii. Spontaneous, or reproduced by digital pressure and physical activities. iii.
361	Pain is not in the skin of the scrotum but perceived within its contents. iv.
362	Lower urinary tract symptoms or sexual dysfunction.
363	1.26.6.5 Chronic (persistent or recurrent) testicular pain syndrome: i.
364	Persistent or recurrent episodic pain. ii. Spontaneous, or reproduced by digital
365	pressure and physical activities. iii. Lower urinary tract symptoms or sexual
366	dysfunction.
367	1.26.7 Chronic prostatitis / Chronic pelvic pain syndrome (CP/CPPS): Persistent or
368	recurrent prostate and/or pelvic pain, associated with symptoms suggestive of urinary
369	tract and/or sexual dysfunction. No proven infection or other obvious pathology is
370	present to account for the symptoms. Pain may be referred to the bladder, perineum,
371	testicles, penis and/or groin. <sup>21</sup> (CHANGED)
372	1.26.7.1 Symptoms of CP/CPPS: Intermittent pain. Persistent or recurrent
373	pain. Dyspareunia and/or erectile dysfunction. Voiding and post micturition
374	symptoms (for example: hesitancy, intermittency, feeling of incomplete
375	emptying, dysuria). <i>(CHANGED)</i>
376	1.26.7.2 National Institutes of Health (NIH) prostatitis classification system.
377	Prostatitis is classified as acute bacterial prostatitis (category I), chronic
378	bacterial prostatitis (category II), chronic prostatitis (CP)/chronic pelvic pain
379	syndrome (CPPS, category III) and asymptomatic inflammatory prostatitis
380	(category IV). <sub>FN1.7</sub> , <sub>FN1.8</sub> <sup>23,24</sup>
381	1.26.7.2.1 Acute bacterial prostatitis: Characterized by severe

symptoms of prostatitis, systemic infection and acute bacterial urinary

tract infection, requires hospitalization and parenteral fluid-antibiotic therapy. 15

**1.26.7.2.2 Chronic bacterial prostatitis:** Caused by chronic bacterial infection of the prostate with or without symptoms of prostatitis. It is usually associated with recurrent urinary tract infections caused by the same bacterial strain. <sup>15</sup>

**1.26.7.2.3 Chronic pelvic pain syndrome:** Characterized by chronic pelvic pain and lower urinary tract symptoms in the absence of urinary tract infection. It is subdivided into inflammatory (3A) and noninflammatory (3B) categories depending on the presence/absence of leukocytes in expressed prostatic secretion.<sup>15</sup>

**1.26.7.2.4 Asymptomatic inflammatory prostatitis:** Characterized by histopathological evidence of prostatic inflammation in the absence of genitourinary symptoms. This is usually an incidental finding during evaluation for other conditions such as elevated PSA.<sup>9</sup>

#### Footnotes for section 1

- 1.1: History should include duration of symptoms, identification of disorder, impact on quality of life, and partner relationship. Partner interviews may be very helpful as erectile dysfunction, delayed or premature ejaculation in males with hypoactive sexual desire disorder result in a 4–30 times increased risk of female partner desire, arousal or orgasmic disorder.
- 1.2: The diagnosis of low testosterone should be made only after two total testosterone measurements taken on separate occasions with both conducted in the morning (until 10 am).9
  - 1.3: This disorder should include 3 of the following: (i) Absent/reduced interest in sexual activity; (ii) Absent/reduced sexual/erotic thoughts or fantasies; (iii) No/reduced initiation of sexual activity and unreceptive to partner's attempts to initiate; (iv) Absent/reduced sexual excitement/pleasure during sexual activity in almost all or all (75% 100%) sexual encounters; (v) Absent/reduced sexual interest/arousal in response to any internal or external sexual/erotic cues (written, verbal, visual); (vi) Absent/reduced genital or non-genital sensations during sexual activity in almost all or all (75% -100%) sexual encounters.

1.4: Epidemiological studies have demonstrated consistent evidence for an association between lower urinary tract symptoms (LUTS)/benign prostatic hyperplasia (BPH) and sexual dysfunction, regardless of age, other comorbidities and various lifestyle factors.<sup>25</sup> 1.5: Several possible pathophysiological mechanisms exist, including NOS/NO (the nitric oxide synthase) and the Rho-kinase activation pathways, autonomic hyperactivity, pelvic ischemia and microvascular dysfunction, inflammatory pathways, sex hormones, iatrogenic and psychological factors.26 1.6: According to the EpiLUTS study, patients with ED had 3 times more storage LUTS, 2.6 times more voiding LUTS and 4 times more voiding and storage LUTS. <sup>27,28</sup> In this study, both OAB wet and OAB dry were associated with worse sexual health, reduced sexual activity, and diminished enjoyment of sex (P < 0.0001) when compared with patients without OAB. 27,28 Coyne et al. conclude that the impact of OAB in sexual health is evident in both men and women, and sexual health should be assessed in patients presenting with OAB.<sup>29</sup> This was also shown by a nested case-control study, where not only was ED more frequent in OAB patients, but this group had significantly reduced sexual activity and sexual enjoyment because of urinary symptoms<sup>30</sup> (including first void after waking up from sleep and last void before sleep).5 1.7: Several factors have been proposed to establish a connection between chronic pelvic pain and sexual dysfunction, including vasculogenic, endocrine, neurogenic and psychological determinants. Shoskes et al. established that patients with chronic pelvic pain are more likely to have nitric oxidemediated vascular endothelial dysfunction compared to asymptomatic controls, which could contribute to sexual dysfunction.<sup>31</sup> Psychological factors including anxiety have been described by Mo et al. and Cortes et al. 32,33, and depression is more frequent in men with chronic pelvic pain and SD. 32,34 1.8: CP/CPPS patients are more likely to present with sexual dysfunction or depression.<sup>35</sup> Lee et al. found that SD was present in 72% of patients with CP/CPPS and most of them (42%) had both ED and ejaculatory dysfunction.<sup>36</sup> Also, patients with SD and CP/CPPS had significantly worse symptoms and quality of life. Another study designed to estimate the prevalence of CP/CPPS in Austria found that IIEF-5 was significantly worse in patients with moderate or severe symptoms, thus showing a negative impact of CP/CPPS on sexual function.<sup>37</sup> These patients are also more likely to present with erectile dysfunction and premature ejaculation.<sup>23</sup>

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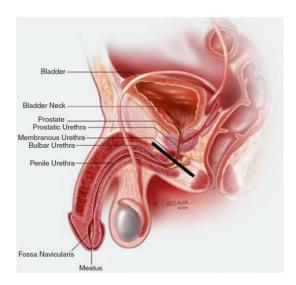
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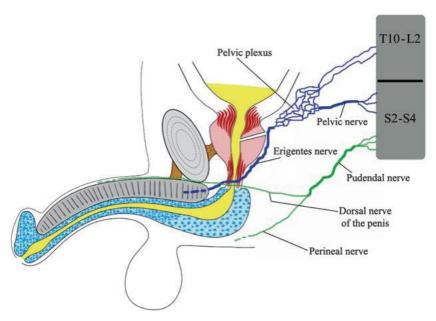
### 446 SECTION 2: ANATOMICAL DEFINITIONS RELATED TO SEXUAL DYSFUNCTION



- Figure 1: Sagittal view of the male urethra. The bold line delineates the anterior from posterior urethra. Furr J., Gelman J. (2020) Functional Anatomy of the Male Urethra for the Reconstructive Surgeon. In: Martins F., Kulkarni S., Köhler T. (eds) Textbook of Male Genitourethral Reconstruction.
- **2.1 Urethral meatus:** The distal termination of the urethra. An orthotopic urethral meatus is a vertically-oriented slit-like opening located on the glans penis.<sup>38</sup> (NEW)
- 2.2 Fossa navicularis: The distal portion of the penile urethra, located within the glans penis,
   just proximal to the urethral meatus. FN2.1 38 (NEW)
- **2.3 Penile urethra:** The portion of the urethra extending from the urethral meatus to the distal part of the bulbocavernosus muscle. The lumen is centered in and completely invested by the corpus spongiosum. FN2.2, FN2.3 38 (NEW)
- 2.4 Bulbar urethra: The portion of the urethra between the distal membranous urethra until the conjunction of the left and right corpus cavernosum. The lumen is surrounded by and sits eccentrically toward the dorsal portion of the bulbospongiosus of the corpus spongiosum.<sup>38</sup>

  (NEW)
- **2.5 Membranous urethra:** The portion of the urethra which traverses the perineal membrane
- and is surrounded by the striated external urethral sphincter.<sup>38</sup> (NEW)
- 2.6 Prostatic urethra: The portion of the urethra extending from the bladder neck to the proximal edge of the membranous urethra. (NEW)

465 2.7 Bladder neck: The most proximal part of the urethra, creating its connection with the 466 bladder. (NEW) 467 **2.8 Cavernous nerves ("Nervi Erigentes"):** These nerves are formed from the distal end of the 468 pelvic plexus and supply sympathetic and parasympathetic innervation to the corpora 469 cavernosa. The cavernous nerves are located at 3 and 9 o'clock positions at the level of the 470 membranous urethra and at 2 and 10 o'clock positions at the level of the proximal bulbar 471 urethra. These nerves are at risk during PFUI (and its repair) as well as bulbar urethroplasty.<sup>39</sup> 472 (NEW) 473 2.9 Pudendal nerves: These nerves arise from the S2-S4 spinal nerves and provide somatic 474 innervation to the pelvis and perineum. The pudendal nerve travels with the pudendal vessels 475 in Alcock's canal, before giving off the inferior rectal nerve and perineal nerve, and then terminating as the dorsal nerve of the penis. 39,40(chap109) (NEW) 476 477 **2.10 Perineal nerves:** Branches of the pudendal nerves (7.14), the perineal nerves supply 478 motor innervation to the bulbocavernosus and ischiocavernosus muscles as well as sensory innervation via the posterior scrotal and bulbourethral nerves. 39,41(chap5) (NEW) 479 480 **2.11 Dorsal nerves of the penis:** These nerves are the terminal branches of the pudendal 481 nerves. They travel through the deep perineal pouch, exiting just inferior to the pubic 482 symphysis and then run along the dorsal surface of the corpora to reach the glans. The supply sensory innervation to the penis and in particular the glans. 39,41(chap5) (NEW) 483



**Figure 2:** Relationship of the nerves to the urethra. From: Palminteri E, Lumen N, Preto M, Waterloos M. Impact of Urethral Reconstruction on Sexual Function. In: Martins FE, Kulkarni SB, Köhler TS, eds. *Textbook of Male Genitourethral Reconstruction*. Cham: Springer International Publishing; 2020:427-435.

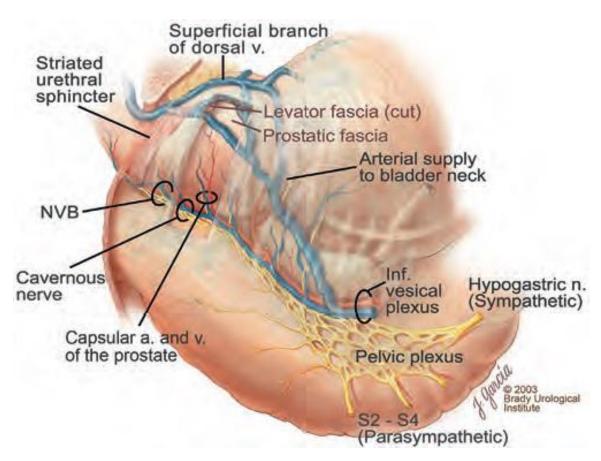


Figure 3: Anatomical landmarks related to prostatic neurovascular bundle (NVB).40

- **2.14 Neurovascular bundle (NVB):** Concentration of nerves that are situated posterolaterally
- and symmetrically to the prostate that are important in preservation of erectile function. The
- 496 nerves running through the NVB travel outside the capsule of the prostate and Denovilliers
- 497 fascia until branches perforate the capsule where they enter the prostate. 42 (NEW)
- **2.15 Cavernous nerve:** Postganglionic parasympathetic nerves that facilitate penile erection.
- 499 They arise from cell bodies in the inferior hypogastric plexus where they receive the
- 500 preganglionic pelvic splanchnic nerves (S2-S4).<sup>42</sup> (NEW)

- Footnotes for section 2:
- 503 2.1: An older term "glanular urethra" should not be used. 38
- 504 2.2: The term pendulous urethra is no longer used.
- 2.3: As per the 2002 Stockholm WHO conference and according to the 2010 International Consultation
- on Urethral Strictures, the terms "anterior" and "posterior" urethra should not be used.38

- 508 **SECTION 3: SYMPTOMS AND QUESTIONNAIRES**
- 509 A-) SYMPTOMS
- **3.1 Symptom:** Any morbid phenomenon or departure from the normal in structure, function,
- or sensation, possibly indicative of a disease or health problem. Symptoms are either
- volunteered by, or elicited from the individual, or may be described by the individual's partner
- 513 or caregiver.<sup>3,4</sup>
- **3.2 Complaint:** The description of the symptom.<sup>1</sup>
- 515 **3.3 Main (Chief) Complaint:** The symptom that a patient states as the main reason for
- seeking medical advice. The degree of "bother (worry, concern)" for other symptoms can be
- 517 variable.<sup>43</sup>
- **3.4 Lower urinary tract symptom (LUTS):** A symptom related to the lower urinary tract; it
- 519 may originate from the bladder, prostate, urethra, and/or adjacent pelvic floor or pelvic
- organs, or at times be referred from similarly innervated anatomy, for example, lower ureter.
- 521 <sub>FN3.1</sub> <sup>5</sup> *(CHANGED)*
- 522 3.5 Urgency: Complaint of sudden, compelling desire to pass urine which is difficult to
- 523 defer.<sup>5,44,45</sup>
- **3.6 Urinary incontinence (UI):** Complaint of involuntary loss of urine.<sup>5</sup>

- **3.7 Urgency urinary incontinence (UUI):** Complaint of involuntary loss of urine associated
- 526 with urgency.<sup>5</sup>
- **3.8 Daytime (urinary) frequency:** Number of micturitions during daytime (awake hours).
- 528 3.9 Nocturia: The number of times urine is passed during the main sleep period. Having
- 529 woken to pass urine for the first time, each urination must be followed by sleep or the
- 530 intention to sleep. This should be quantified using a bladder diary.<sup>5</sup>
- **3.10 Ejaculatory pain:** Complaint of pain, pressure, or discomfort felt in the perineum,
- 532 suprapubic region and/or penis during ejaculation, but may continue for a time afterwards.<sup>5</sup>
- **3.11 Decreased (low) semen volume:** Complaint of smaller amount of seminal fluid than
- 534 normal or previously experienced.<sup>5</sup>
- **3.12 Increased (high) semen volume:** Complaint of higher amount of seminal fluid than
- 536 normal or previously experienced.<sup>5</sup>
- 537 **3.13 Semen sequestration:** Trapping of ejaculate in the bulbar urethra, resulting in a
- decreased force and volume of emission; often secondary to damage to the perineal nerves
- and/or bulbospongiosus muscle. Manual pressure on the perineum at the level of the bulbar
- urethra may be required to expel sequestrated semen.<sup>39</sup> (NEW)
- **3.14 Penile shortening:** A subjective or objective decrease in penile length. Well known to be
- associated with plication procedures for Peyronie's disease, it is also associated with penile
- 543 revascularization procedures, anastomotic and augmented urethroplasty, hypospadias
- repair, and prostate cancer treatment such as radical prostatectomy.<sup>39,46</sup> (NEW)
- **3.15 Intimacy and sexual avoidance:** Unwillingness or reluctance of engaging in sexual
- activity or intimacy with others. (NEW)
- **3.16 Pain:** A subjective phenomenon described as an unpleasant sensory and emotional
- 548 experience associated with actual or potential tissue damage, or described in terms of such
- 549 damage.<sup>21</sup>
- **3.17 Chronic pelvic pain:** Characterized by persistent pain lasting longer than 6 months or
- recurrent episodes of abdominal/pelvic pain, hypersensitivity or discomfort often associated
- with elimination changes, and sexual dysfunction often in the absence of organic etiology. 21,48
- **3.18 Penile sexual pain:** Penile pain that occurs prior to penetration (ie when an erection
- occurs), with penetration or post-coital.<sup>21</sup>
- **3.19 Perineal sexual pain:** may occur during intercourse or after intercourse.<sup>21</sup>

556 **3.20 Orgasmic pain (during ejaculation):** pain may be felt on the penis, ano-rectum, perineum 557 or in the whole pelvis.<sup>49</sup> (CHANGED) 558 **B-) QUESTIONNAIRES** 559 3.21 American Urological Association (AUA) Symptom Index (AUA-SI) for Benign Prostatic 560 Hyperplasia (BPH): A symptom index for BPH which was developed and validated by a 561 multidisciplinary measurement committee of the AUA. It includes 7 questions covering 562 563 frequency, nocturia, weak urinary stream, hesitancy, intermittency, incomplete emptying, and urgency.<sub>FN3.2</sub> 50 (NEW) 564 565 **3.22 International Prostate Symptom Score (IPSS):** An 8-question written screening tool used 566 to screen for, rapidly diagnose, track the symptoms of, and suggest management of the 567 symptoms of BPH. It contains the seven questions of the AUA symptom index for BPH and one question related to the patient's perceived quality of life (bother score). FN3.3 51 (NEW) 568 569 3.23 International Index of Erectile Function (IIEF): A multi-dimensional and validated self-570 report instrument for the evaluation of male sexual function. FN3.4 52 (NEW) 571 3.24 Sexual Health Inventory for Men (SHIM): The SHIM questionnaire (also known as the 572 IIEF-5) is an abridged and slightly modified 5-item version of the 15-item IIEF, to diagnose the 573 presence and severity of ED in clinical settings. FN3.5 53 (NEW) 574 **3.25 Erection Hardness Score (EHS):** A single-item instrument that asks men to rate erection 575 hardness on a scale that ranges from 0 (penis does not enlarge) to 4 (penis is completely hard 576 and fully rigid).<sup>54</sup> (NEW) 577 3.26 Male Sexual Health Questionnaire (MSHQ): A tool for assessing key domains of sexual function and satisfaction in aging men with urogenital symptoms of LUTS and sexual 578 579 dysfunction. It consists of 25 questions that constitute subscales for Erection, Ejaculation, and Satisfaction.<sub>FN3.6</sub> <sup>55</sup> (NEW) 580 581 3.27 Premature Ejaculation Profile (PEP): A self-report questionnaire used to assess 4 components of PE: satisfaction with sexual intercourse, control over ejaculation, ejaculation-582 related distress, and interpersonal difficulty. Each of the 4 individual items is assessed on a 583 5-point scale, and the scores are averaged to provide an index PE score. 56 (NEW) 584 **3.28 Index of Premature Ejaculation (IPE):** A 10-item validated tool which was developed to 585 586 evaluate sexual satisfaction, control, and distress in men with PE.<sup>57</sup> (NEW)

# C-) QUESTIONNAIRES FOR OVERACTIVE BLADDER AND CORRELATION WITH SEXUAL DYSFUNCTION (NEW)

Questionnaire	Contents	Correlation with SD
OAB-SS (OAB	Total score is a sum of four-	In patients with diabetes, the
symptom score)	item scores based on a self-	component of urge
	administered questionnaire	incontinence has the strongest
	about four symptoms: daytime	impact on ED (OR 4.06, P =
	frequency (0-2), nighttime	0.013), followed by nocturia
	frequency (0-3), urgency (0-5),	(OR 2.71, P < 0.01) and urgency
	and urgency incontinence (0–	(OR 1.87, P = 0.046). The OR of
	5). <sup>59</sup>	ED in patients with OAB or OAB
		wet compared with no OAB was
		1.82 (P = 0.056), and 3.6 (P =
		0.026), respectively. <sup>60,61</sup>
OAB-q (OAB	33 items that assess impact of	Low correlation with SD. <sup>62</sup>
Questionnaire) and	OAB bother score and its	
HRQL (Health-	impact on QOL	
Related Quality of		
Life)		
OAB-q SF (OAB-q	6 items that address urgency,	No validation for sexual QOL
Short Form)	urinary incontinence and	
	nocturia and score them from 1	
	to 6 based on bother. <sup>63</sup>	
IPSS	See 3.22	There is a strong correlation
		between IPSS and erectile
	1	1

		·
		function, intercourse
		satisfaction, orgasmic and
		sexual desire. IPSS is also
		strongly correlated with IIEF. <sup>64</sup>
CLSS (Core Lower	10 symptoms: daytime	Total score and all symptoms
Urinary	frequency, nocturia, urgency,	but daytime frequency and
Tract Symptom	urgency incontinence, stress	incomplete voiding have a
Score)	incontinence, slow stream,	significant relationship with
	straining, incomplete voiding,	total IIEF-5 score. <sup>65</sup>
	bladder pain, and urethral pain.	
BFLUTS (Bristol	Among other LUTS, this	OAB symptoms have a negative
Female Lower	questionnaire assesses	impact on sexual life, especially
Urinary Tract	frequency, urgency, nocturia	in patients with OABwet. 65,66
Symptoms	and urgency urinary	
Questionnaire)	incontinence.	
ICIQ-OAB	4 items: frequency, urgency,	The ICIQ-mLUTSsex is and add-
(International	nocturia and UUI and bother	on of 4 items to assess impact
Consultation on	scale from 0-10 of each item.	of sex life: erection, ejaculation,
Incontinence		pain during ejaculation and
Questionnaire)		impact of urinary symptoms on
		sex life.

Table 2: OAB questionnaires, and their correlation with sexual dysfunction.

# Footnotes for section 3

 ${\bf 3.1: LUTS}$  are often associated with male sexual dysfunctions.

- 3.2: History taking in a man presenting with ED should include questions about; age, comorbid medical
- 598 (endocrinopathies, cardiovascular diseases, neurological disorders) and psychological conditions,
- prior surgeries, medications, family history of vascular disease, substance use, tobacco use.<sup>67</sup>
- 3.3: The specific LUTS can be divided into storage symptoms (urgency, frequency, nocturia, and urge
- 601 incontinence) and voiding symptoms (poor stream, hesitancy, feeling of incomplete emptying).
- Patients are classified into having none or mild, moderate, or severe LUTS based on the IPSS (0-7, 8-
- 603 21, and 21–35 points, respectively).<sup>68</sup>
- 3.4: The IIEF consists of 15 questions that quantify 5 domains (sexual desire, erectile function,
- 605 intercourse satisfaction, ejaculatory/orgasmic function, overall sexual satisfaction). The erectile
- function domain quantifies ED severity on a scale of 5-30, with scores of:
- 26-30: normal erectile function
- 608 18-25: mild ED
- 609 11-17: moderate ED
- 610 ≤10: severe ED
- 3.5: The SHIM score characterizes the severity of the patient's ED in the following manner:
- 612 22-25: No ED
- 613 17-21: Mild ED
- 12-16: Mild-to-moderate ED
- 615 8-11: Moderate ED
- 616 5-7: Severe ED
- 3.6: A 4-question version of the ejaculation subscale of MSHQ is also available to measure ejaculatory
- 618 dysfunction.

- 3.7: The BMFSI originally developed by O'Leary has been adapted for use in patient with urethral
- 620 stricture disease by Erickson et al.<sup>69</sup>

622 **SECTION 4: SIGNS AND EXAMINATION** 

- 623 A-) GENERAL SIGNS AND EXAMINATION FINDINGS
- 624 **4.1 Cardiovascular examination:** Part of the physical examination that should include
- 625 assessment of vital signs (especially blood pressure and pulse) and signs of hypertensive or
- 626 ischemic heart disease as well as peripheral vascular disease. FN4.1, FN4.2 (NEW)
- **4.2 Gynecomastia:** Excessive development of male breast tissue which may or may not be a
- 628 sign of underlying endocrinological disorder. FN4.3 (NEW)
- **4.3 Sarcopenia:** A clinical condition characterized by loss of skeletal muscle and function. It
- 630 might be a sign of hypogonadism. (NEW)

632	B-) PENILE EXAMINATION
633	4.4 Peyronie's disease: A connective tissue disorder involving the growth of fibrous plaques
634	in the soft tissue of the penis. Specifically, scar tissue forms in the tunica albuginea, causing
635	pain, abnormal curvature, erectile dysfunction, indentation, loss of girth and shortening.
636	(NEW)
637	4.5 Stretched penile length: The penile length as measured by a rigid centimeter ruler, which
638	is placed along the dorsal side of the penis (flaccid, and stretched as comfortably as possible),
639	extending in a parallel fashion from the pubopenile skin junction to the tip of the glans where
640	the pre-pubic fat pad was pushed to the bone. 70 (NEW)
641	4.6 Penile curvature: Abnormal bend in the penis occurring during erection which might lead
642	to sexual dysfunction by impairing the ability to penetrate and/or causing pain in the
643	tumescent state. (NEW)
644	4.7 Buried penis: A congenital or acquired condition in which penis is partially or totally
645	embedded underneath the skin of the abdomen, thigh, or scrotum. (NEW)
646	4.8 Phimosis: Partial or complete inability to retract the prepuce due to adhesion between
647	the glans and the prepuce or a preputial ring. <sup>5</sup>
648	<b>4.9 Paraphimosis:</b> Entrapment of the prepuce behind the glans. <sup>5</sup>
649	4.10 Hypospadias: Refers to the urethral meatus sited on the ventral surface of the penis,
650	either congenital or acquired, proximal to its normal position on the tip of the glans. <sup>5</sup>
651	<b>4.11 Epispadias:</b> Refers to the urethral meatus sited on dorsal surface of the penis, either
652	congenital or acquired, proximal to its normal position on the tip of the glans. <sup>5</sup>
653	4.12 Urethral meatal stenosis: Narrowing of the distal opening of the urethra which may be
654	congenital or occur secondary to infection, inflammation, or as a result of surgical (open or
655	endoscopic) intervention. <sup>5</sup> (CHANGED)
656	4.13 Lichen sclerosus (LS): A chronic, inflammatory disease affecting genital skin that is
657	characterized by hypomelanotic and sclerotic changes, often resulting in phimosis, meatal
658	stenosis, and even pan-urethral strictures. <sup>71</sup> (NEW)
659	

C-) SCROTAL EXAMINATION FINDINGS

661	<b>4.14 Epididymitis / epididymo-orchitis:</b> The inflammatory condition involving epididymis +/-
662	testis. Affected structures may be swollen and tender, and if severe, the inflammatory process
663	may involve the whole scrotal content and the scrotal skin as well. <sup>5</sup> (CHANGED)
664	<b>4.15 Cystic dilatations of the epididymis:</b> Epididymal cysts (or spermatocele) and hydroceles
665	(fluid collections between the visceral tunica albuginea and parietal layer of the testicular
666	peritoneum) are usually benign. The examination of these structures would be generally non-
667	tender and without pain. <sup>5</sup> (CHANGED)
668	4.16 Inguinal hernia:
669	4.16.1 Indirect inguinal hernia: Protrusion of abdominal content through inguinal
670	canal down to the scrotal sac, causing swelling, discomfort and jeopardizing the
671	vascular supply of the herniated intestinal segment. (NEW)
672	4.16.2 Direct inguinal hernia: Protrusion of abdominal content through a weakness of
673	the posterior wall of the inguinal canal medial to the inferior epigastric vessels. (NEW)
674	4.17 Varicocele: Abnormal dilation of pampiniform venous plexus which drains blood from
675	each testicle. Varicocele is graded based on the degree of dilation. (NEW)
676	4.17.1 Subclinical varicocele: Seen on doppler ultrasound imaging, no varicocele on
677	exam.
678	4.17.2 Grade 1 varicocele: Palpable with valsalva maneuver. (NEW)
679	<b>4.17.3 Grade 2 varicocele:</b> Palpable when standing, without valsalva maneuver.
680	(NEW)
681	4.17.4 Grade 3 varicocele: Visible on inspection. (NEW)
682	4.18 Testicular mass: Palpation of a mass originating from testis. This might be originating
683	from the testicular parenchyma or its appendages and may be cystic or solid in nature and
684	related to a benign or malignant (more commonly) neoplastic process. (NEW)
685	<b>4.19 Nonpalpable testis:</b> Absence of testis in the hemiscrotum or inguinal canal. This can be
686	a finding related to cryptorchidism (undescended testicle), testicular atrophy or vanishing
687	testis. (NEW)
688	4.20 Testicular torsion: Torsion of the spermatic cord structures that leads to vascular
689	compromise involving the ipsilateral testicle. Physical examination might reveal a tender,
690	swollen and erythematous hemiscrotum on the affected side. (NEW)
691	<b>4.21 Absence of vas deferens</b> : Congenital absence of vas deferens in the hemiscrotum. It may
692	be either unilateral or bilateral. FN4.4 (NEW)

693 4.22 Atrophic testis: Testicular dimensions being smaller than expected. Consistency of 694 atrophic testes might be softer than usual. Diminished testicular size may be accompanied by 695 loss of function. (NEW) 696 697 D-) DIGITAL RECTAL EXAMINATION FINDINGS **4.23 Rectal and prostate examination:** Digital rectal examination (DRE) that is generally done 698 with the patient standing and bent over the examining table, or with the patient in the left 699 lateral knees bent position, or in the lithotomy position.<sup>5</sup> It provides valuable information 700 regarding prostate size, consistency, pelvic floor muscle tone, anal sphincter tone, 701 702 constipation, and rectal/anal canal masses. It might also raise suspicion for prostate 703 cancer.<sub>FN4.4</sub> (CHANGED) 704 **4.24 Anal tone:** increased or decreased anal sphincter tone might suggest similar changes in the urinary sphincter and may indicate neurologic disease. FN4.5 5 705 706 **4.25 Prostate tenderness:** DRE of the prostate is usually painless. Pain with prostatic 707 palpation may be indicative of chronic prostatitis / chronic pelvic pain syndrome. FN4.6 5 708 (CHANGED) 709 710 E-) NEUROLOGICAL SIGNS AND EXAMINATION FINDINGS 711 **4.26 Overall neurological status:** Assessment of the abnormalities of speech, gait, as well as 712 upper and lower extremity dexterity which should be noted as they may indicate a 713 neurological cause for the sexual dysfunction.<sup>5</sup> (CHANGED) 714 **4.27 Penile, scrotal, or perianal sensory deficits:** Neurological examination findings that may 715 indicate damage or injury to sacral roots or nerves.<sup>5</sup> (CHANGED) 716 **4.28 Glans hypoesthesia:** Reduced sensitivity of the glans penis. This may be associated with 717 hypospadias and its treatment, penile revascularization procedures, bulbar urethroplasty. FN4.7 <sup>39,46</sup> (NEW) 718 719 **4.29** Bulbospongiosus reflex (BSR): A reflex contraction of the striated muscle of the pelvic 720 floor (anal sphincter) and the bulbospongiosus muscle that occurs in response to various

**4.30 Cremasteric reflex:** Contraction of the ipsilateral cremaster muscle, drawing the testis

upwards, when the upper inner aspect of the thigh is stroked longitudinally.<sup>5</sup>

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723

stimuli in the perineum or genitalia.<sup>5</sup>

7	2	1

## 725 Footnotes for section 4

- 4.1: As obesity is one of the most important risk factors for ED, it should be assessed and documented
- 727 during ED work-up.
- 4.2: Abdominal or femoral artery bruits and asymmetric or absent lower extremity pulses may be
- 729 indicative of underlying vasculogenic etiology. Skin and hair pattern evidence of vascular insufficiency
- 730 should be noted.
- 4.3: General physical examination of patients with ED should include assessment for signs of
- testosterone deficiency (e.g., gynecomastia, underdeveloped facial/pubic/axillary hair), penile skin
- 733 lesions and placement/configuration of the urethral meatus, documentation of flaccid stretched
- 734 penile length (especially if the man is considering penile prosthesis implantation or surgical
- intervention), the presence/absence of a palpable plaque, general assessment of the scrotal skin and
- palpation of the testicles to assess for size, consistency, and location.
- 4.4: Congenital absence of vas deferens is commonly associated with cystic fibrosis that occurs as a
- result of a mutation in the CFTR gene. A smaller percentage of patients might have unilateral renal
- 739 agenesis.
- 4.5: Digital rectal examination (DRE) is not required for evaluation of ED; however, BPH is a common
- comorbid condition in men with ED and may merit evaluation and treatment. During DRE, prostate
- size and consistency can be estimated, although DRE tends to underestimate true prostate size. DRE
- 743 may also allow assessment of the bulbocavernosus reflex, which provides information on neural
- integrity of the pelvis. Anal tone can help in the assessment of pelvic floor muscle tone and may be
- used to teach and tailor pelvic floor muscle exercises. 67
- 4.6: Non-urological conditions such as anal fissure, abscess or hemorrhoids or other painful situations
- of the anal canal can elicit pain upon DRE.
- 4.7: Although less recognized, penile hypoesthesia may not be limited to the glans. Procedures
- requiring penile disassembly may also result in penile shaft hypoesthesia.

# 750

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# **SECTION 5: INVESTIGATIONS**

# 752 A-) LABORATORY TESTS

- 753 Blood tests are not normally included in ICS Terminology Reports. However, certain serum-based
- 754 measurements hold critical importance in the diagnosis and treatment of ED.
- 755 **5.1 Testosterone:** Total testosterone can be measured in men with ED to determine if
- 756 testosterone deficiency (TD) is present.<sub>FN5.1</sub> <sup>67</sup> (NEW)

- 757 **5.1.1 Free testosterone**: Fraction of total testosterone that is unbound plasma to proteins. 758 (NEW) 759 **5.1.2 Sex hormone binding globulin (SHBG)**: A plasma protein that is produced by the liver 760 and transports sex hormones (estradiol, testosterone, dihydrotestosterone) in the blood as 761 biologically inactive forms. (NEW) **5.1.3 Bioavailable testosterone:** Bioavailable testosterone represents an assessment of the 762 biologically active testosterone in serum. It includes the free plus weakly protein bound 763 764 fractions of testosterone and is calculated by a formula integrating serum albumin, SHBG, and 765 total testosterone. (NEW) 766 5.2 Prostate specific antigen (PSA): Serum prostate specific antigen (PSA) level is measured 767 for prostate cancer screening and to gather additional information about the size of the 768 prostate and associated inflammatory changes. FN5.2 (NEW) 769 **B-) IMAGING STUDIES** 770 771 **5.3 Retrograde urethrography (RUG):** Imaging of the urethra with serial fluoroscopic images 772 during retrograde injection of contrast material. The patient should be positioned obliquely 773 in order to adequately visualize the urethra. Used mainly to diagnose urethral strictures or 774 diverticula, it is also of use to diagnose and stage urethral trauma. 5,72 (NEW) 775 **5.4 Voiding cystourethrography (VCUG):** Imaging of the bladder, bladder neck, urethra, and 776 prostate during voiding. The principal use is determining the site of any obstruction, for 777 example, bladder neck or prostate. It can also detect vesico-ureteric reflux, vesical or urethral fistulae, vesical or urethral diverticula and strictures.<sup>5,72</sup> 778 779 **5.5 Sonourethrography:** Ultrasound examination of the urethra, providing information on the location and length of stricture as well as the degree of spongiofibrosis. 73 (NEW) 780
  - (NEW)

**5.6 Dynamic infusion cavernosometry and cavernosography (DICC):** A combined evaluation

of intracavernosal pressures and radiographic assessment of penile blood flow. It is used to

identify vasculogenic leak in patients being considered for penile vascular surgery. FN5.3 40(chap27)

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785	<b>5.7 Penile duplex ultrasonography:</b> Use of real-time ultrasound with and without vasoactive
786	medications for pharmacologically induced erection to evaluate the flow velocities in the
787	dorsal penile and cavernosal arteries. 40(chap27) (NEW)
788	5.8 Pudendal angiography: Imaging of the pudendal arteries for patency using injection of
789	intravascular contrast and fluoroscopic imaging. <sub>FN5.4</sub> 40(chap40) (NEW)
790	
791	C-) OTHER DIAGNOSTIC TESTS / PROCEDURES
792	<b>5.9 Cystourethroscopy:</b> Direct visual inspection of the urethra and bladder with a rigid or
793	flexible cystoscope. It is the gold-standard for diagnosing the presence or absence of urethral
794	stricture disease, however it is not sufficient for complete staging. <sup>72</sup> (NEW)
795	<b>5.10 Urodynamic Studies (UDS):</b> Measurement of all the physiological parameters relevant
796	to the function and any dysfunction of the lower urinary tract. Urodynamic investigations
797	generally involve an individual attending with a comfortably full bladder for free (no catheter)
798	uroflowmetry and post-void residual (PVR) measurement prior to filling cystometry and
799	pressure-flow study. <sub>FN5.5</sub> <sup>5</sup>
800	<b>5.11 Nocturnal penile tumescence (NPT) testing:</b> A diagnostic test for evaluating the penile
801	veno-occlusive mechanism. Penile rigidity is monitored using a specialized device (often the
802	Rigiscan®) for at least two consecutive nights. Three periods of penile tip rigidity of greater
803	than 70%, lasting for at least 10 minutes each, each night, defines normal nocturnal erectile
804	function. <sub>FN5.6</sub> 46,74 (NEW)
805	5.12 Pudendal somatosensory evoked potentials (SEP): A neurophysiologic test which can
806	be used to support the diagnosis of a neurogenic cause of erectile dysfunction. The test should
807	be performed as per the International Federation of Clinical Neurophysiology guidelines. A
808	latency time >48ms is considered abnormal (the mean normal latency is 37ms). <sup>74,75</sup> (NEW)
809	
810	Footnotes for section 5
811	5.1: Routine blood work-up of ED that includes the measurements of serum testosterone,

glucose/hemoglobin A1c, and in some cases serum lipids.  $^{67}$ 

813 5.2: Studies that might be appropriate in some men if recent laboratory results are not available. These 814 include; serum BUN/Cr, fasting lipids, fasting glucose or hemoglobin A1c, and morning testosterone, 815 thyroid function studies (i.e. thyroid-stimulating hormone, free T4) and PSA.67 816 5.3: DICC useful in patients with a history of pelvic trauma or those with primary (lifelong) erectile 817 dysfunction. Nevertheless, it is not commonly used within the context of ED diagnostic work-up. 818 5.4: After PFUI, if neither pudendal artery is intact, the patient may benefit from penile artery 819 revascularization before PFUI repair in order to improve erectile potency. 820 5.5: Urodynamic studies might need to be conducted if sexual dysfunction is thought to be originating 821 from lower urinary tract dysfunction. Better assessment and treatment of the underlying urinary 822 condition with the help of urodynamic studies might serve to improve the management of sexual 823 health-related problems. 824 5.6: A normal NPT rules out a veno-occlusive cause of erectile dysfunction, but other etiologies are 825 still possible. 826 827 **SECTION 6: DIAGNOSES** 828 6.1 Erectile dysfunction (ED): Consistent or recurrent inability to attain and/or maintain a penile erection sufficient for sexual satisfaction and/or sexual intercourse.<sup>6</sup> (CHANGED) 829 830 **6.2** Hypogonadism: A term introduced to signify low testosterone levels associated with 831 infertility. It has more recently been used interchangeably with the idea of low testosterone production alone.<sup>9</sup> (NEW) 832 833 **6.3 Premature ejaculation (PE):** Complaint of a persistent or recurrent pattern of too rapid 834 achievement of ejaculation during partnered sexual activity, that is, before the individual wishes it.5 It is accompanied by negative personal consequences, such as distress, bother, 835 frustration, and/or the avoidance of sexual intimacy.<sup>6</sup> (CHANGED) 836 **6.4 Retrograde ejaculation:** Expulsion of seminal fluid into the bladder because of bladder 837 838 neck dysfunction in the presence of otherwise normal emission and expulsion. There can be no or small amounts of antegrade ejaculation. Retrograde ejaculation is defined 839 840 independently from the sensation of orgasm.<sup>6</sup> (NEW) 841 **6.5 Benign prostatic obstruction (BPO):** A term used to describe bladder outlet obstruction (BOO) secondary to BPE and, therefore, usually due to BPH. Bladder outlet obstruction is an 842 843 urodynamic entity and can only be diagnosed via pressure-flow studies. <sup>14</sup> (NEW)

844	<b>6.6 Prostatitis:</b> An inflammatory disease of the prostate generally affecting younger men and
845	causing pain and discomfort mostly in the perineal and scrotal region which can be associated
846	with LUTS and/or sexual dysfunction. 15 (NEW)
847	6.7 Overactive bladder (OAB) syndrome: Urinary urgency, usually accompanied by increased
848	daytime frequency and/or nocturia, with urinary incontinence (OAB-wet) or without (OAB-
849	dry), in the absence of urinary tract infection or other detectable disease. 16
850	<b>6.8 Male chronic genital pain syndromes:</b> Male genital pain syndromes are often associated
851	with symptoms suggestive of lower urinary tract and sexual dysfunction. Common
852	complaints: genital pain, uncomfortable urination, dysuria, sensation of residual urine,
853	increased daytime frequency, slow stream, urgency, dyspareunia. Absence of infection,
854	previous operations, or other obvious pathology. <sup>21</sup>
855	6.9 Chronic prostatitis / Chronic pelvic pain syndrome (CP/CPPS): Persistent or recurrent
856	prostate and/or pelvic pain, associated with symptoms suggestive of urinary tract and/or
857	sexual dysfunction. No proven infection or other obvious pathology is present to account for
858	the symptoms. Pain may be referred to the bladder, perineum, testicles, penis and/or groin. <sup>76</sup>
859	(CHANGED)
860	<b>6.10 Urethral stenosis:</b> A narrowing of the anterior urethra, caused by spongiofibrosis of the
861	corpus spongiosum. <sup>38</sup> (NEW)
862	<b>6.11 Posterior urethral stenosis:</b> Narrowing of the membranous urethra, prostatic urethra,
863	or bladder neck, when the prostate is still in-situ. <sup>38,77</sup> (NEW)
864	<b>6.12 Vesicourethral anastomotic stenosis (VAS):</b> Narrowing of the posterior urethra after
865	radical prostatectomy. <sup>77</sup> (NEW)
866	6.13 Lichen sclerosus (LS): A chronic, inflammatory disease affecting genital skin that is
867	characterized by hypomelanotic and sclerotic changes, often resulting in phimosis, meatal
868	stenosis, and even pan-urethral strictures. FN6.1 71 (NEW)

6.14 Urethral trauma

870	<b>6.14.1 Blunt urethral trauma:</b> An injury to the urethra from a non-penetrating injury.
871	May include straddle injuries, deceleration injuries, penile fracture, and pelvic fracture
872	urethral injuries. <sup>38</sup> (NEW)
873	6.14.2 latrogenic urethral trauma: Injury to the urethra resulting from
874	instrumentation of the urethra, such as with cystoscopy or catheterization, or
875	treatment of disease in the urethra or prostate, such as urethral dilation, transurethral
876	resection of the prostate, prostate radiation, or radical prostatectomy. <sup>38</sup> (NEW)
877	6.14.3 Pelvic fracture urethral injury (PFUI): A urethral distraction injury, typically
878	involving the bulbomembranous junction. Previously known as pelvic fracture urethral
879	distraction defects, this term should be reserved for cases of PFUI with loss of urethral
880	continuity. <sup>38,78</sup> (NEW)
881	6.14.4 Penetrating urethral trauma: Injury to the urethra resulting from an object
882	passing into or through the urethra from outside the body. Gunshot wounds, stab
883	injuries, and penile amputation are examples of penetrating urethral trauma. (NEW)
884	5.14.5 Straddle Injury: Injury to the bulbar urethra resulting from a blunt trauma
885	which compresses the bulbar urethra against the inferior pubic rami. May be remote,
886	or even not recalled by the patient. 79 (NEW)
887	<b>6.15 Post-infectious stricture:</b> Urethral stricture disease developing as a result of gonococcal
888	and nongonococcal (Ureaplasma urealyticum, Mycoplasma genitalium, schistosomiasis, and
889	tuberculosis) urethritis. <sup>38,79</sup> (NEW)
890	<b>6.16 Prostate cancer (CaP):</b> Development of cancer from the prostate gland. <sub>FN6.2</sub> <sup>40</sup> (NEW)
891	<b>6.16.1 Localized:</b> Cancer confined to the gland of the prostate. FN6.3 80 (NEW)
892	6.16.2 Locally-advanced: Spread of prostate cancer outside the prostate capsule,
893	involvement of the seminal vesicles or involvement of adjacent organs without distant
894	metastasis. <i>(NEW)</i>
895	6.16.3 Metastatic: Distant spread of prostate cancer to other areas of the body
896	beyond the pelvis, most notably bone and lymph nodes. Spread can also occur to the
897	liver and lungs. (NEW)

899	Footnotes for section 6
900	6.1: Lichen sclerosus was previously known as <i>Balanitis Xerotica Obliterans (BXO)</i> , but this term is no
901	longer in widespread use.
902	6.2: The most common pathologic subtype of prostate cancer is adenocarcinoma. Other types include
903	small cell carcinoma, neuroendocrine tumor, urothelial carcinoma and sarcoma. <sup>40</sup>
904	6.3: Localized prostate cancer can be categorized based on PSA, PSA density, clinical stage digital rectal
905	exam, grade group, amount of cancer on biopsy and imaging results. This risk stratification allows for
906	better prediction of survival and appropriate counselling regarding treatment options.80
907	
908	SECTION 7: CONSERVATIVE AND PHARMACOLOGICAL TREATMENTS FOR SEXUAL
909	DYSFUNCTION (GENERAL)
910	7.1 Psychotherapy: Psychotherapy and psychosexual counseling focus on helping patients
911	and their partners improve communication about sexual concerns, reduce anxiety related to
912	entering a sexual situation and during a sexual situation, and discuss strategies for integrating
913	ED treatments into their sexual relationship. <sup>67</sup> (NEW)
914	7.2 Lifestyle recommendations: Dietary changes, weight loss, physical activity increases, and
915	smoking cessation that may improve overall health and ameliorate the comorbidities
916	associated with ED. <sup>67</sup> (NEW)
917	<b>7.3 Herbal therapy:</b> Plant-derived remedies that can provide alternatives for men to improve
918	their sexual health. <sub>FN7.1</sub> <sup>81</sup> <i>(NEW)</i>
919	7.4 Phosphodiesterase type 5 inhibitors (PDE5i): Oral medication used to block the action of
920	phosphodiesterase type 5 on cyclic guanosine monophosphate in the smooth muscle cells
921	causing a vasodilation of the arteries in the corpora cavernosa of the penis facilitating an
922	erection during sexual stimulation. FN7.2, FN7.3 (NEW)
923	7.4.1 On-demand dosing of PDE5i: PDE5i being taken prior to anticipated sexual
924	intercourse. (NEW)
925	7.4.2 Daily dosing of PDE5i: PDE5i being taken on a daily basis, irrespective of sexual
926	activity. <sub>FN7.4</sub> (NEW)
927	7.4.3 Instructions in the appropriate use of PDE5i: Instructions that include the fact
928	that sexual stimulation is necessary and that more than one trial with the medication
929	may be required to establish efficacy. It should include information regarding the

930	medications' characteristics with regard to the onset of action, duration of action, and
931	whether food intake limits efficacy. Discussion on side effects should include common
932	PDE5i side effects as well as drug-specific side effects. (NEW)
933	7.5 Vacuum erection device (VED): Negative-pressure chambers that provide passive
934	engorgement of the corpora cavernosa, together with a constrictor ring placed at the base of
935	the penis to retain blood within the corpora. 25 (NEW)
936	<b>7.6 Intraurethral alprostadil:</b> Topical application of the vasoactive agent alprostadil, which is
937	an analogue of prostaglandin E1. Herein, a specific formulation of alprostadil in a medicated
938	pellet (MUSE $^{\text{\tiny{M}}}$ ) that includes a permeation enhancer in order to facilitate absorption of
939	alprostadil is administered via the urethral meatus. <sup>25</sup> (NEW)
940	7.6.1 In-office test of intraurethral alprostadil: An in-office consultation that has to
941	be made with every patient being prescribed intraurethral alprostadil that includes
942	instructions about the method, initial dose-titration, detailed counseling regarding
943	possible adverse reactions and actions to take in response to potentially serious side
944	effects. <sup>67</sup> (NEW)
945	7.7 Intracavernous injection (ICI): Injecting vasoactive agents into the corpus cavernosa of
946	the penis to produce an erection. The four substances commonly used in clinical practice are
947	alprostadil, papaverine, phentolamine, and atropine. FN7.5 67 (NEW)
948	7.7.1 Single agent: ICI of alprostadil (NEW)
949	7.7.2 Bimix: ICI of papaverine + phentolamine (NEW)
950	7.7.3 Trimix: ICI of alprostadil + papaverine + phentolamine (NEW)
951	7.7.4 Quadmix: ICI of alprostadil + papaverine + phentolamine + atropine (NEW)
952	7.8 In-office injection test: An in-office consultation that has to be made with every patient
953	being recommended ICI of vasoactive agents which aims to determine the appropriate dose
954	and medication(s) to produce sufficient duration of response and to minimize AEs. $_{\text{FN7.6}}$ $^{67}$
955	(NEW)
956	7.9 Penile rehabilitation: Program that aims to help men regain the ability to achieve
957	erections sufficient for satisfactory sexual intercourse during rehabilitation from prostate
958	cancer treatment, and ultimately return to pretreatment erectile function. $_{\text{FN7.7}}$ 82 (NEW)
959	

Footnotes for section 7

961	7.1: Panax ginseng, Butea superba, Epimedium nerbs (icariin), Tribulus terrestris, Securidaca
962	longipedunculata, Piper guineense, and yohimbine have been investigated for ${ m ED.}^{81}$
963	7.2: The FDA-approved oral PDE5i available for management of ED in the U.S. include sildenafil,
964	tadalafil, vardenafil, and avanafil. Several other PDE5i have been approved for use in other countries. $^{67}$
965	7.3: For men with LUTS/BPH and ED, sildenafil and tadalafil appear to have similar efficacy to treat
966	ED. There are no studies of vardenafil or avanafil that focused on men with LUTS/BPH and ED. All
967	studies of men with LUTS/BPH and ED used daily dosing because of the beneficial urinary tract effects
968	of PDE5i. <sup>67</sup>
969	7.4: This approach is particularly suitable for tadalafil 5mg.
970	7.5: Only alprostadil is FDA-approved in the U.S. for ICI. <sup>67</sup>
971	7.6: This in-office test also helps the man achieve confidence with the technique and to facilitate
972	adherence. <sup>67</sup>
973	7.7: The use of any intervention or interventions whose goal is broadly thought of as being aimed at
974	restoring satisfactory erectile functioning. <sup>82</sup>
975	
976	SECTION 8: SURGICAL TREATMENTS FOR SEXUAL DYSFUNCTION (GENERAL)
977	8.1 Implantation of penile prosthesis: The surgical implantation of a penile prosthesis for
978	patients who do not respond to more conservative therapies or who prefer a permanent
979	solution to their ED. <sup>25</sup> (NEW)
980	8.1.1 Inflatable penile prosthesis (IPP): The penile prosthesis type which can be
981	inflated by the patient to create an erection on demand and deflated at other times. $^{10}$
982	(NEW)
983	8.1.1.1 3-piece IPP: The IPP type which consists of a fluid-filled reservoir
984	implanted under the abdominal wall, a pump and a release valve placed in the
985	scrotum, and two inflatable cylinders inside the penis. 10 (NEW)
986	8.1.1.2 2-piece IPP: The IPP type which works in a similar way as the 3-piece
987	IPP, but the fluid reservoir is part of the pump implanted in the scrotum. 10
988	(NEW)
989	8.1.2 Semirigid (malleable) penile prosthesis (MPP): The penile prosthesis type which
990	consists of two flexible rods that are placed inside the penis. Once implanted with the
991	malleable prosthesis, the penis can be bent away from the body for sexual intercourse
992	and toward the body for concealment. <sup>25</sup> (NEW)

993	<b>8.2 Penile artery revascularization:</b> A variety of surgical techniques that may be used to
994	reestablish arterial flow to the penis. This is generally reserved for patients with proven
995	pudendal or penile arterial anomalies secondary to post-traumatic lesions or congenital
996	disorders. <sup>46</sup> (NEW)
997	8.3 Treatments that warrant further investigation (see appendix): Low-intensity
998	extracorporeal shock-wave therapy (LI-SWT), Platelet-rich plasma (PRP) therapy,
999	Intracavernosal stem cell therapy, Nerve graft.
1000	
1001	SECTION 9: TREATMENTS FOR LUTS/BPH AND RELATED SEXUAL DYSFUNCTIONS
1002	A-) CONSERVATIVE AND PHARMACOLOGICAL TREATMENT OPTIONS FOR LUTS/BPH
1003	9.1 Watchful waiting: Recommended treatment option for patients with an IPSS score of less
1004	than 7 who feel that their symptoms are manageable and do not have signs of postrenal
1005	compromise. This treatment consists of the patient decreasing their fluid intake, minimizing
1006	caffeinated and alcoholic beverages, and avoiding cholinergic medications. 67,25 (NEW)
1007	9.2 Phytotherapy: Utilization of herbal preparation (plant extracts) to address LUTS/BPH
1008	either alone or in combination with oral pharmacotherapy. FN9.1 6 (NEW)
1009	9.3 Alpha-blockers: The first-line pharmacotherapeutic options for LUTS/BPH which are
1010	effective at relieving emptying phase symptoms via blockade of the alpha-adrenergic
1011	receptors in the prostate and the bladder neck. <sup>83</sup> (NEW)
1012	9.3.1 Alpha-blocker and ejaculatory dysfunction (EjD): Alpha-adrenergic antagonists
1013	may cause anejaculation. The effect of alpha-blockers on EjD in men with LUTS is
1014	significantly affected by two agents (tamsulosin and silodosin). The other alpha-
1015	blockers have little or no impact on EjD. <sup>6</sup> (NEW)
1016	<b>9.4 5-Alpha reductase inhibitors (5-ARI):</b> Medications that inhibit the enzyme responsible for
1017	the conversion of testosterone to dihydrotestosterone (DHT), which is a more potent
1018	androgen and is responsible for prostate growth and development. There are 2 drugs in this
1019	category; finasteride inhibits only type 2 of 5-AR, and dutasteride inhibits both types 1 and
1020	2. <sup>83</sup> (NEW)
1021	<b>9.4.1 5-ARI and sexual dysfunction:</b> The effect of 5ARI on sexual function in men with
1022	LUTS is modest with effects on penile erection, ejaculation, sexual desire, and includes
1023	a small risk of post-finasteride syndrome. FN9.2 6 (NEW)

9.5 Beta-3 agonists: A medication class which can be used to improve storage phase LUTS.
Mirabegron, a beta-3 agonist, exerts its clinical effect via relaxation of the bladder smooth muscle and increasing bladder storage capacity. (NEW)
9.6 Anticholinergics (Antimuscarinics): Medications that exert their clinical effect via blocking muscarinic (predominantly M3 type) receptors in the bladder and can be used to address storage phase LUTS.<sup>84</sup> (NEW)
9.7 Phosphodiesterase type 5 inhibitors (PDE5i): PDE5i might be used to address LUTS/BPH

by inhibition of the PDE5 in the prostate, causing smooth muscle relaxation by a mechanism similar to the one postulated for alpha blockers. *(NEW)* 

# B-) SURGICAL TREATMENT OPTIONS FOR LUTS/BPH<sup>85</sup>

Treatment	Potential sexual side effect
Alpha-blockers	Retrograde ejaculation, reversible anejaculation
5-Alpha reductase inhibitors	Erectile dysfunction, loss of libido, reduction of ejaculate volume, post-finasteride syndrome
Transurethral resection of prostate (TURP)	Retrograde ejaculation, anejaculation, erectile dysfunction
Transurethral incision of prostate (TUIP)	Retrograde ejaculation (lower risk than TURP)
Simple prostatectomy	Retrograde ejaculation, anejaculation
Laser prostatectomy	Retrograde ejaculation (lower risk than TURP)

 Table 3: Potential sexual side effects related to LUTS/BPH treatment.fng.3, fng.4

#### Footnotes for section 9

9.1: They are derived from the roots, seeds, bark, or fruits of the various plants used. Saw palmetto (serenoa repens), pygeum africanum, cucurbita pepo, secale cerelae, urtica dioica and quercetin have all been reported as possible treatments for LUTS/BPH.<sup>6</sup>

1043	to be no significant difference between the two agents that are currently available. $^{6}$
1044	9.3: Interventions for LUTS/BPH have numerous sexual side effects, including retrograde ejaculation,
1045	orgasmic dysfunction, and erectile dysfunction. Sexual side effects from surgical treatments are more
1046	likely to be permanent than those from medical treatments, which can often be reversed by stopping
1047	medical treatment or switching to an alternative treatment.
1048	9.4: Surgical interventions which involve resection and/or incision at the level of bladder neck (TURP,
1049	TUIP, open prostatectomy) increase the risk of retrograde ejaculation.
1050	
1051	SECTION 10: TREATMENTS FOR URETHRAL STRICTURE DISEASE AND RELATED SEXUAL
1052	DYSFUNCTIONS
1053	A-) NOMENCLATURE OF URETHRAL STRICTURE DISEASE
1054	10.1 Urethral stenosis: A narrowing of the anterior urethra, caused by spongiofibrosis of the
1055	corpus spongiosum. <sup>38</sup> (NEW)
1056	10.2 Posterior urethral stenosis: Narrowing of the membranous urethra, prostatic urethra,

9.2: The impact on ejaculation is likely more significant than that on erection and libido. There seems

1060

1061

1057

1058

1059

1042

# B-) SURGICAL TREATMENT OPTIONS FOR URETHRAL STRICTURE DISEASE<sup>85</sup>

or bladder neck, when the prostate is still in-situ.<sub>FN10.1,10.2</sub> <sup>38,77</sup> (NEW)

radical prostatectomy.<sub>FN10.2</sub> <sup>77</sup> (NEW)

Treatment	Potential sexual side effects
Direct visual internal urethrotomy (DVIU)	Erectile dysfunction
Penile urethroplasty	Poor penile cosmesis, erectile dysfunction (lower risk than bulbar urethroplasty)
Bulbar urethroplasty	Erectile dysfunction, penile curvature, penile shortening, glans hypoesthesia, semen sequestration

10.3 Vesicourethral anastomotic stenosis (VAS): Narrowing of the posterior urethra after

Posterior urethral reconstruction	Erectile dysfunction, penile curvature, penile shortening, glans hypoesthesia, semen sequestration, retrograde ejaculation	
Table 4: Treatment modalities addressing urethral stricture disease, and their sexual health-related side effects. FN10.3		
Footnotes for section 10:		
10.1: Commonly secondary to treatment for prostate cancer such as brachytherapy or external beam radiation. May also be secondary to treatments for BPH such as TURP.		
10.2: Posterior urethral stenosis and vesicourethral anastomotic stricture are preferred over other terms such as bladder neck stenosis or contracture, prostatic urethral stenosis, and bulbomembranous stricture.		
10.3: Other terms such as visual internal urethrotomy (VIU) and optical internal urethrotomy (OIU) are sometimes used, but DVIU is the preferred term. Erectile dysfunction after DVIU occurs at a rate between around 2-10% of cases; mechanisms include damage to the cavernous nerves, fistula creation between corpus cavernosum and spongiosum, and fibrosis from extravasation of irrigant and infectious complications. <sup>86</sup>		
SECTION 11: TREATMENTS FOR OVERADYSFUNCTION	ACTIVE BLADDER AND RELATED SEXUAL	
A-) CONSERVATIVE AND PHARMACOLOGICAL TREATMENT OPTIONS FOR OAB		
11.1 Behavioral treatments for OAB: considered first-line treatment, these therapies aim at		
symptomatic improvement by changing behavioral and environmental issues. (NEW)		
11.1.1 Bladder training: It consists of a program of patient education, along with a		
scheduled voiding regimen with gradually adjusted voiding intervals. FN 11.187		
11.1.2 Prompted voiding: is used to teach people to initiate their own toileting		

through requests for help and positive reinforcement from caregivers, often done in

combination with a scheduled voiding regimen, typically every 2h. <sup>87</sup>

1087	11.1.3 Double voiding: The patient is taught to urinate, relax, and attempt to urinate
1088	again. It is especially useful for patients with incomplete voiding and high post-void
1089	residue. <sup>87</sup> <i>(CHANGED)</i>
1090	11.1.4 Scheduled or timed voiding: A passive toileting assistance program, initiated
1091	and maintained by caregivers for patients who cannot participate in independent
1092	toileting. It is a fixed voiding schedule. $^{87}$
1093	11.1.5 Self-monitoring: This strategy is part of bladder training and consists of
1094	registering voiding habits in a bladder diary. (NEW)
1095	11.1.6 Habit training: Consists of a toileting schedule matched to the individual's
1096	voiding patterns based on their voiding diary. The toileting schedule is assigned to fit
1097	a time interval that is shorter than the person's normal voiding pattern and precedes
1098	the time period when incontinent episodes are expected. <sup>87</sup>
1099	11.1.7 Lifestyle modifications: Weight loss and smoking cessation have been shown
1100	to reduce LUTS, urgency and urinary incontinence in patients with OAB.88 (NEW)
1101	11.1.8 Dietary modifications: Consists of reducing or eliminating bladder irritants
1102	from the diet. <sub>FN 11.2</sub> <sup>87</sup> <i>(CHANGED)</i>
1103	11.2 Pelvic floor muscle training (PFMT): Exercise to improve PFM strength, endurance,
1104	power, relaxation, or a combination of these parameters. <sup>87</sup>
1105	11.3 Frequency volume chart (FVC): The recording of the time of each micturition together
1106	with the volume voided for at least 24 hours. Ideally a minimum of 3 days of recording (not
1107	necessarily consecutive) will generally provide more useful clinical data. It is relevant to
1108	discriminate between daytime and night-time micturition. <sup>5</sup>
1109	11.3.1 Bladder diary: Adds to the FVC, the fluid intake, pad usage, incontinence
1110	episodes, the degree of incontinence and the circumstances at the time of the leakage.
1111	Episodes of urgency and sensation might also be recorded, as might be the activities
1112	performed during or immediately preceding the involuntary loss of urine. Additional
1113	information obtained from the bladder diary involves: severity of incontinence in
1114	terms of leakage episodes and pad usage. <sup>5</sup>
1115	11.4 Pharmacologic treatment for OAB: considered second-line treatment, may be used in
1116	combination with first-line treatments. (NEW)
1117	11.4.1 Antimuscarinics: see 9.6.

1118	<b>11.4.2 Beta-3 agonists:</b> see 9.5.
1119	11.4.3 Combination therapy: this treatment consists of administering an
1120	antimuscarinic together with a beta-3 agonist. FN11.3 89 (NEW)
1121	11.4.4 PDE5i: This treatment reduces OAB symptoms through the phosphodiesterase
1122	- nitric oxide pathway. <sub>FN11.4</sub> <sup>90</sup> <b>(NEW)</b>
1123	
1124	B-) SURGICAL (INVASIVE) TREATMENT OPTIONS FOR OAB
1125	11.5 Third-line treatment for OAB: these therapies include intradetrusor botulinum toxin
1126	injection, peripheral tibial nerve stimulation (PTNS) and sacral neuromodulation. (NEW)
1127	11.5.1 Intradetrusor botulinum toxin injection: injection of onabotulinumtoxinA in
1128	the bladder wall to induce detrusor muscle relaxation. (NEW)
1129	11.5.2 Peripheral (or posterior tibial) nerve stimulation (PTNS): A neuromodulation
1130	technique that consists in stimulating the posterior tibial nerve with a transcutaneous
1131	or percutaneous electrode to modulate the neuronal activity of bladder nerves that
1132	share the same dorsal root as the posterior tibial nerve (S3). (NEW)
1133	11.5.3 Sacral neuromodulation (SNM): this neuromodulation technique consists in
1134	percutaneously implanting a set of electrodes in the S3 foramen connected to an
1135	external (temporary) or subcutaneous (permanent) stimulator to modulate the

**11.6 Fourth-line treatment for OAB:** considered as last resort for patients that have failed all previous treatments, these include augmentation cystoplasty and urinary diversion. *(NEW)* 

activity of bladder nerves. (NEW)

Treatment	Effect on SD
Lifestyle modifications	A healthy lifestyle has been shown to reduce OAB, SD and their risk factors. 91,92
Antimuscarinics	Transdermal oxybutinin for OAB showed an improvement in patient's sex life, a positve effect on relationships and an increase in sexual interest. <sup>93</sup>
PDE5i	A well-known treatment for SD, daily tadalafil has been shown to also improve OAB symptoms. <sup>90</sup>
Sacral neuromodulation	Some studies have shown improvement in sexual function in neurogenic patients. 94,95

1140	Table 5: Effect of OAB treatments on sexual dysfunction.	
1141		
1142	Footnotes for section 11	
1143	11.1: In the past, bladder training has also been referred to as bladder drill, bladder discipline, bladder	
1144	re-education, and bladder retraining. Specific goals are to correct faulty habit patterns of frequent	
1145	urination, improve control over bladder urgency, prolong voiding intervals, increase bladder capacity,	
1146	reduce incontinent episodes, and restore patient confidence in controlling bladder function.	
1147	11.2: Bladder irritants include oxalate-rich food (ie spinach, orange, berries, chocolate, coffee, black	
1148	tea, tofu, soya, sodas), alcoholic drinks and spicy food.	
1149	11.3 PDE5i have also been combined with $\beta$ 3-adrenoceptor agonists with good results. $^{96}$	
1150	11.4 Despite it hasn't been officially recommended in international guidelines, the effects of PDE5i	
1151	have been well established in randomized clinical trials and have a positive effect in patients with SD. $^{90}$	
1152		
1153	SECTION 12: TREATMENTS FOR CHRONIC PROSTATITIS / CHRONIC PELVIC PAIN SYNDROME	
1154	AND RELATED SEXUAL DYSFUNCTION <sup>97–99</sup> (NEW)	
1155		
1156	A-) CONSERVATIVE AND PHARMACOLOGICAL TREATMENT OPTIONS FOR CHRONIC	
1157	PROSTATITIS / CHRONIC PELVIC PAIN SYNDROME (CP / CPPS)	
1158	12.1 Non-pharmacological therapies for CP / CPPS: these therapies aim at symptomatic	
1159	improvement by changing behavioral and environmental issues and also include minimally-	
1160	invasive therapies with a low risk for adverse events. 100 (NEW)	
1161	12.1.1 Acupuncture: procedure that consists in inserting acupuncture needles in	
1162	specific anatomic locations or "acupoints". 101 (NEW)	
1163	12.1.2 Lifestyle modifications: treatment based on avoiding irritant food, having a	
1164	balanced diet, adopting certain sexual habits, avoiding perineal trauma and having a	
1165	healthy lifestyle. 102 (NEW)	
1166	12.1.3 Physical activity: treatment based on a regular exercise program. 103 (NEW)	
1167	12.1.4 Extracorporeal shockwave therapy: periodic stimulation of the perineum with	
1168	extracorporeal low-energy shockwaves. 104 (NEW)	
1169	12.1.5 Transrectal thermotherapy: application of transrectal radiofrequency	
1170	hyperthermia on the prostate. 105 (NEW)	

1171	12.1.6 Cystoscopy and bladder hydrodistention: procedure that consists in distending	
1172	the bladder during cystoscopy, at a pressure of 80 to 100 cmH2O, lasting 1 to 2	
1173	minutes and up to 2 times. 49,106 (CHANGED)	
1174	12.1.7 Neuromodulation: see 11.5.3	
1175	12.1.8 Transurethral resection: see 9.10	
1176	12.1.9 Pelvic floor muscle training (PFMT): see 11.2	
1177	12.2 Pharmacological therapies for CP / CPPS: different treatments that aim at alleviating	
1178	and controlling CP and CPPS via pharmacological pathways. 107 (NEW)	
1179	12.2.1 Alpha blockers: see 9.3	
1180	12.2.2 5-alpha reductase inhibitors (5-ARI): see 9.4	
1181	12.2.3 Antibiotics: this treatment is indicated for chronic bacterial prostatitis	
1182	(category II of the NIH, see 1.30.2). 107 (NEW)	
1183	12.2.4 Anti-inflammatories: nonsteroidal anti-inflammatory drugs (NSAIDs)	
1184	treatment is based on decreasing the pain mediated by inflammatory pathways. $^{107}$	
1185	5 <b>(NEW)</b>	
1186	12.2.5 Phytotherapy: see 9.2	
1187	12.2.6 Nerve blockade/Epidural pain pump: treatment based on the administration	
1188	of analgesics directly into the epidural space with a small catheter and a pump. (NEW)	
1189	12.1.7 Botulinum toxin injections of the prostate <sup>85</sup> and/or bladder (see 11.5.1)	
1190	12.1.8 Phosphodiesterase type 5 inhibitors (PDE5i): see 7.4. PDE5i may alleviate	
1191	Cp/CPPS symptoms by reducing oxidative stress and inflammation on the prostate and	
1192	pelvic floor. <sup>108</sup> (NEW)	

Treatment	Direct effect on SD
Tension reduction, relaxation, physical therapy, lifestyle modifications	Usually beneficial <sup>97–99</sup>
Psychotherapy and multidisciplinary pain management	Usually beneficial <sup>97–99</sup>
Nonsteroidal anti-inflammatory drugs (NSAID)	No direct effect on SD

Opioids	Chronic use is associated with worsening of SD <sup>109</sup>
Tricyclic antidepressants (TCA)	Amitriptyline may have a negative impact on arousal and libido, especially on depressive patients <sup>110</sup>
Anticonvulsants	Pregabalin may cause ED, anorgasmia and loss of libido <sup>111</sup>
PDE5i	May improve CPPS symptoms as well as SD <sup>112</sup>
Pentosan polysulfate (PPS)	No direct effect on SD
Intravesical therapy (Pentosan polysulfate, DMSO, hyaluronic acid, chondroitin sulfate)	No direct effect on SD
Bladder hydrodistention	No direct effect on SD
Nerve blockade/Epidural pain pump	No direct effect on SD
Botulinum toxin injection	No direct effect on SD
Neuromodulation	Some studies have shown improvement in sexual function in neurogenic patients <sup>94,95</sup>
Transurethral resection	Retrograde ejaculation

**Table 6:** Treatment modalities addressing CP/CPPS, and their sexual health-related side effects.

### SECTION 13: TREATMENTS FOR PROSTATE CANCER AND RELATED SEXUAL DYSFUNCTIONS

# A-) CONSERVATIVE, PHARMACOLOGICAL, AND NONSURGICAL TREATMENT OPTIONS FOR PROSTATE CANCER

13.1 Active surveillance (AS): A treatment plan that involves closely watching a patient's condition but not giving any treatment unless there are changes in test results that show the condition is getting worse. This is suitable for men with favorable-risk prostate cancer (very low to low-risk) who wish to avoid treatment associated harm. Intervention for cure is pursued in those who experience disease progression while on active surveillance. (NEW) 13.2 Watchful waiting (WW): Waiting until the disease progresses to intervene with a palliative approach. Historically the aim of watchful waiting was to avoid treatment altogether among men with a limited life expectancy and advanced disease detected in an era when screening was not routine. (NEW)

1208	13.3 Androgen deprivation therapy (ADT): An antihormone therapy used to control prostate
1209	cancer. Prostate cancer cells require androgens to grow. ADT reduces the levels of androgens
1210	in the body thereby slowing prostate cancer growth and progression. FN13.1 114 (NEW)
1211	13.4 Radiation therapy: Delivery of ionizing radiation treatments to the prostate to control
1212	or kill malignant cells. FN13.2 115 (NEW)
1213	13.4.1 Brachytherapy: Delivery of radioactive material sealed in needles, seeds, wires
1214	or catheters directly into the prostate gland for curative management of prostate
1215	cancer. <sup>115,116</sup> (NEW)
1216	13.4.1.1 Low-dose rate (LDR) brachytherapy: Utilizes radioactive seeds that
1217	are implanted based on pretreatment and intraoperative image-guidance
1218	according to a computer plan. FN13.3 115 (NEW)
1219	13.4.1.2 High-dose rate (HDR) brachytherapy: Utilizes temporary catheters
1220	implanted in the prostate to allow for the delivery of a high-activity radiation
1221	source. <sub>FN13.4</sub> 115 <i>(NEW)</i>
1222	13.4.2 External beam radiation therapy (EBRT): A form of radiation therapy that uses
1223	multiple radiation beams and/or arcs to provide a highly conformal treatment of the
1224	prostate with normal tissue sparing of adjacent organs, such as the rectum and
1225	bladder. <sup>115</sup> (NEW)
1226	13.4.3 Conformal radiation therapy: A type of 3D radiation therapy that uses
1227	computer-generated images to show the size and shape of the tumor. As a result, a
1228	higher and more effective dose of radiation can be delivered directly to cancerous
1229	cells. <sup>117</sup> (NEW)
1230	13.4.4 Intensity-modulated radiation therapy (IMRT): A type of 3D radiation therapy
1231	that uses computer-generated images to show the size and shape of the tumor. Thin
1232	beams of radiation of different intensities are aimed at the tumor from many angles.
1233	This type of radiation therapy reduces the damage to healthy tissue near the
1234	tumor. 118,119 (NEW)
1235	13.4.5 Stereotactic body radiation therapy (SBRT): A form of radiation therapy that
1236	uses photon-based IMRT to deliver hypofractionated radiation usually in five or fewer
1237	fractions of treatment to kill malignant cells.115 (NEW)
1238	13.4.6 Proton beam radiation therapy: A type of radiation therapy that uses streams
1239	of protons (tiny particles with a positive charge) to kill tumor cells. This type of

1240	treatment can reduce the amount of radiation damage to healthy tissue near a
1241	tumor. <sup>113</sup> (NEW)
1242	13.5 Focal therapy: Tissue-preserving strategy aimed to target the cancer and not the whole
1243	organ when it is morphometrically possible to do so and thus reduce damage to collateral
1244	tissues. 120 (NEW)
1245	13.5.1 Cryotherapy: Focal delivery of the cryoprobe transrectally to the prostate to
1246	induce extremely low temperatures with subsequent thawing. This process results in
1247	direct cellular injury and a delayed inflammation-mediated mechanism of cellular
1248	destruction. 120 (NEW)
1249	13.5.2 High-intensity focused ultrasound (HIFU): Focal delivery of ultrasonic waves
1250	(frequencies 0.8 to 3.5 MHz) to selectively initiate cellular damage. The energy of the
1251	ultrasonic waves is absorbed by the target tissue and converted to heat causing
1252	coagulative necrosis. Furthermore, inertial cavitation is caused by alternating cycles
1253	of compression and rarefaction. 120 (NEW)
1254	13.5.3 Irreversible electroporation: Delivery using a Nanoknife system to deploy a
1255	low-energy direct current to a targeted region within the prostate. 121 (NEW)
1256	<b>13.5.4 Laser ablation:</b> Utilization of a laser to focally ablate the tissue. (NEW)
1257	13.5.5 Photodynamic therapy: Use of pharmacological agents that become active in
1258	the presence of light (photosensitizers) to kill malignant cells. 121 (NEW)
1259	13.5.6 Radiofrequency ablation (RFA): Use of a bipolar radiofrequency ablation probe
1260	transperineally to deliver radio waves that heat and destroy abnormal cells. 121,122
1261	(NEW)
1262	
1263	B-) SURGICAL TREATMENT OPTIONS FOR PROSTATE CANCER
1264	13.6 Radical prostatectomy (RP) <sup>85</sup>
1265	13.6.1 Nerve spare: Avoidance of electrocautery and high anterior release with careful
1266	lateral dissection and gentle lateral traction preserves the neurovascular bundles
1267	(NVBs; Figure 3) as they course anterior to Denovilliers' fascia at the posterolateral
1268	edge of the prostate. FN13.5, FN13.6 123 (NEW)
1269	13.6.2 Salvage prostatectomy: Operative removal of the prostate with the goal of
1270	successfully eradicating locally recurrent cancer after definitive radiation therapy. FN13.7
1271	<sup>40</sup> (NFW)

Treatment	Potential sexual side effect
Active surveillance (AS)	Erectile dysfunction, loss of sexual
retive surveinance (7.5)	desire <sup>124,125</sup>
Androgen deprivation therapy (ADT)	Ejaculatory dysfunction, erectile
, maragemachmation merapy (no.)	dysfunction, hypogonadism, loss of sexual
	desire, orgasmic disorder, penile
	shortening <sup>126,127</sup>
Focal therapy	Erectile dysfunction <sup>120,128</sup>
Tocal merupy	5: 1: 1: 1: 1: 1: 1: 1: 1: 1: 1: 1: 1: 1:
Radiation therapy	Ejaculatory dysfunction, erectile
	dysfunction <sup>129</sup>
Radical prostatectomy (RP)	Climacturia, ejaculatory dysfunction,
	erectile dysfunction, orgasmic dysfunction,
	peyronie's, penile shortening <sup>130–132</sup>
Watchful waiting (WW)	-

**Table 7:** Potential sexual side effects of each prostate cancer treatment.

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1276

### Footnotes for section 13

- 1277 13.1: ADT is used as a radiosensitizer with radiation therapy to cure localized prostate cancer or alone
   to control locally-advanced or metastatic prostate cancer.
- 1279 13.2: Radiation therapy is used in combination with androgen deprivation therapy to treat localized prostate cancer with curative intent. 115
- 1281 13.3: Standard LDR brachytherapy is 120 Gy. 133
- 1282 13.4: Standard HDR brachytherapy is 38 Gy delivered in 4 fractions, 2 times daily for 2 days. 133
- 13.5: The sparing of nerves during radical prostatectomy is the only method to date that can
   preserve erectile function. 134,135
- 1285 13.6: A meta-analysis of studies with > 12 months follow-up post RP reported that use of bilateral
- nerve spare with associated with a 60% erectile function recovery rate (95% CI 58.0-62.0; 21 studies)
- 1287 compared to a rate of 47% (95% CI 42.0 53.0; 12 studies for use of a unilateral nerve-sparing
- 1288 technique). 123

13.7: To be a candidate the patient must have excellent health with a life expectancy of more than 15 years, no evidence of metastatic disease with prostate biopsy, histologic grade, clinical examination findings and serum PSA levels suggesting localized disease).<sup>40</sup>

### **AREAS FOR FURTHER RESEARCH**

This consultation was performed by several experts in the field of male sexual dysfunction and functional urology. The definitions have different levels of empirical support, and some are based on expert clinical opinion, rather than a strong evidence base. Further research should be conducted to determine the support for these definitions and that, where necessary, appropriate modifications will be made to reflect these research findings.

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No discussion on terminology should fail to acknowledge the fine leadership shown by the ICS over many years. The legacy of that work by many dedicated clinicians and scientists is present in all the Reports by the different Standardization Committees and Working Groups. It is pleasing that the ICS leadership has accepted this vital initiative as a means of progress in this important and most basic area of Terminology and its Standardization.



This document has involved ... rounds of full review, by coauthors, of an initial draft (OA, EK) with the collation of comments and figures. Included in the review process were as follows: (i) 6 external expert reviewers; (ii) an open ICS website review; (iii) ICS Standardisation Steering Committee review and (iv) ICS Board of Trustees review. The process was subject to live meetings in Florence (September 2017, planning), and in-person Working Group Meetings in Philadelphia (August 2018), and Gothenburg (September 2019). There were also 2 teleconferences (March and May 2019). Thereafter, we held monthly online Working Group Meetings, between February - November 2020. Versions 8 to 13 underwent comprehensive reformatting based on the comments of BH (Ex chair, ICS SSC), which included structural changes, redactions, and revisions with regard to scientific content.

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1715 Appendix: 1716 1717 Low-intensity extracorporeal shock-wave therapy (LI-SWT): Extracorporeal application of 1718 low intensity shock wave which is a kind of acoustic wave that carries energy and that, when 1719 propagating through a medium, can be targeted and focused noninvasively to affect a distant 1720 selected anatomic region. When LI-ESWT is applied to penis, the shock waves interact with 1721 the targeted tissues and induce a cascade of biological reactions which in turn triggers 1722 neovascularization with subsequent improvement of the blood supply. 136 (NEW) 1723 1724 Platelet-rich plasma (PRP) therapy: PRP is an autologous product obtained from whole blood 1725 that contains high concentrations of platelet-derived growth factors and provides 1726 a fibrin framework over platelets that has the potential to support the regenerative matrix 1727 and promote recovery in damaged tissues. PRP therapy denotes intracavernosal injection of 1728 autologous platelet-rich plasma concentrates to address erectile dysfunction. (NEW) 1729 1730 Intracavernosal stem cell therapy: Intracavernosal injection of stem cells, which are derived from multiple tissue sources (such as bone marrow, adipose tissue) and have the potential 1731 1732 for self-replication, proliferation and differentiation, to restore erectile function. 138 (NEW) 1733 1734 **Nerve graft:** Interposition of sural nerve graft at the time of RP is proposed to help recovery 1735 of erectile function in men who had both cavernous nerves resected. (NEW)