

The Prevalence and the Use of the Questionnaire's Related to the Neglected Sexual Side Effects After Prostate Cancer Treatment: A Scoping Review of the Literature

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Research

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Abstract

Background: Early prostate cancer (PCa) treatment interventions may leave men with debilitating sexual side effects. These side effects may remain permanent, often undiagnosed, and undermanaged. The objective of this study was to map the evidence pertaining to the prevalence, and use of questionnaires, related to the neglected sexual side effects (NSSE) after PCa treatment consisting of radical prostatectomy (RP) surgery or radiation treatment (RT).

Methods: This systematic scoping review's search strategy involved the search of PubMed, Science Direct, and Google Scholar databases. Following title searching, two-independent reviewers conducted screening of abstracts and full articles. The screenings were guided by the eligibility criteria. Data were extracted from the included studies and the emerging themes were analysed. The review team analysed the implications of the findings in relation to the research question and aims of the study. The Mixed Method Appraisal Tool was employed for quality appraisal of included studies.

Discussion: Twenty-three studies about the prevalence and questionnaire use for NSSE after early PCa treatment were included. Two studies investigated most of the collective group of NSSE's, and all the other studies mostly looked at a single NSSE. No single validated questionnaire was found that investigates the NSSE after early PCa treatment. Most studies incorporated some aspects of other questionnaires. Two studies used non-validated questionnaires that picked up on the majority of the collective group of NSSE.

Conclusion: NSSEs are prevalent in men after RP and RT. Peyronie's Disease, orgasmic Dysfunction and Penile Length Shortening are all similarly prevalent after RP and RT. Anejaculation was only found to be prevalent after RT*. Orgasm associated incontinence resulted from RP and RT, but the prevalence in RP patients was 6 times that of RT patients. Study participants felt inadequately informed about possible sexual side effects caused by their treatment choices. Questionnaires are effective at detecting NSSE after PCa treatment, but there is no valid and reliable questionnaire currently available to detect all the collective NSSE after PCa treatment. There is a scope to develop a validated and reliable PCa NSSE questionnaire. The NSSE questionnaire must be quick, straightforward, and effective.

Background

Prostate cancer (PCa) is a major cause of disease and morbidity among men and it is the second most common cancer affecting men on a global scale (1). Early PCa or localized PCa is cancer contained within the prostate described as being stage I or II on the tumour-node-metastasis system (2). Early PCa treatment consisting of radical prostatectomy surgery or radiotherapy, either through external beam radiotherapy or brachytherapy, results in side effects including sexual dysfunction. Other side effects could include both pain and incontinence (3) as well as less common physical deformities such as penile length shortening (PLS) and penile curvature changes (Peyronie's disease)(4, 5). Sexual dysfunction from PCa treatment is common regardless of whether the treatment modality included surgical or non-surgical interventions. Sexual dysfunction was found to increase during each year of follow-up after the initial intervention and it affects an average of 50% of patients within 5 years of receiving treatment (6).

Most men generally recover from pain and incontinence after a prostatectomy but sexual side effects often remain untreated, leaving them with long-lasting and debilitating sexual dysfunction (7). Men and their partners also suffer psychologically after prostate cancer treatment due to anxiety and depression related to sexual dysfunction(8). Specific conditions related to physical sexual dysfunction are common after PCa treatment. These conditions include orgasm-associated incontinence, (OAI) urinary incontinence during sexual stimulation (UIDSA), altered perception of orgasm, orgasm pain (OP), anejaculation, PLS, and penile deformity/Peyronie's disease (PD) (4, 5, 7, 9). These conditions are collectively referred to as the "Neglected Sexual Side Effects" (NSSE) and the symptoms are reportedly prevalent in 20–93% of post-prostatectomy patients (7).

Only a fifth of the men who had been diagnosed with PCa will ever discuss issues related to sexual dysfunction with their health care practitioners (HCP) (10). A questionnaire may be useful as a non-threatening strategy to initiate such a discussion and allow the patient to indicate their presenting symptoms. Two validated questionnaires, the Expanded Prostate Cancer Index Composite (EPIC) (11) and International Index of Erectile Function (IIEF) (12) were recommended for use in this context in 2015 (3).

Reason for this review

While the EPIC and IIEF both help to stimulate the conversation around general urinary and sexual function, they do not address the NSSE after PCa treatment. There is currently a lack of evidence about the availability of a possible questionnaire to specifically address the NSSE after PCa treatment. It was therefore important to conduct a systematic scoping review to improve our understanding of the prevalence of NSSE and to highlight knowledge gaps on the role of questionnaires in the assessment of the NSSEs.

Term	Definition
Erectile Dysfunction	Consistent or recurrent inability to attain and/or maintain penile erection sufficient for sexual satisfaction (clinical principle).
Anorgasmia	The inability to reach an orgasm despite adequate and prolonged sexual stimulation leading to adequate sexual arousal. Anorgasmia might or might not lead to personal distress
Painful Ejaculation or Orgasm	The occurrence of genital and/or pelvic pain during or shortly after ejaculation or orgasm (clinical principle).
Anejaculation	The absence of normal antegrade ejaculation during orgasm owing to the absence of the emission and expulsion phases of the ejaculation reflex (clinical principle).

Other Definitions (14)

Orgasmic dysfunction	Inability to achieve an orgasm, markedly diminished intensity of orgasmic sensations or marked delay of orgasm from any kind of sexual stimulation.
Peyronie's disease	Named after the French physician Francois de la Peyronie, is an acquired disorder of the tunica albuginea, characterized by the formation of a plaque of fibrous tissue and often accompanied by penile pain, deformity on erection, and ED. Fractured penis, intracavernosal injection, and other trauma may also cause Peyronies disease. During these injuries, the tunica albuginea is injured and heals with fibrosis and scar tissue which results in the deformity in genetically susceptible individuals. Cavernosal fibrosis can occur following low flow priapism, corporeal surgery (e.g. Insertion of a prosthesis) as well as the other causes of Peyronies disease (trauma, injections, etc).

Table 1

Definitions according to the 4th International Consultation on Sexual Medicine (13)

Methodology

A protocol for this scoping review has previously been submitted for publication; It may be accessed at: <https://dx.doi.org/10.21203/rs.3.rs-27667/v1>

A systematic scoping review was conducted to map the evidence on:

1. the prevalence of NSSE after early treatment PCa, and
2. the literature on the use of questionnaires in the assessment of NSSE after early treatment for PCa.

The scoping review followed the five steps described by (15) that included the following;

1. Identifying the research question
2. Identifying relevant studies
3. Study selection
4. Charting the data
5. Collating, summarizing and reporting on the data

Quality assessment of each of the included primary studies was be done as directed by (16)

Identifying the research question

The research question aimed to identify current academic literature on the NSSE after men have undergone early treatment for PCa.

The research sub-questions were as follows:

- What is the prevalence of NSSE after early treatment for PCa?
- Which questionnaires are being used to assess NSSE after early treatment for PCa?

Eligibility criteria

The Population Concept Context (PCC) framework was used to determine the eligibility of the research question as illustrated in Table 2.

Table 2
The PCC framework

Criteria	Determinants
Population	Men who received surgical and non-surgical treatment following early PCa diagnosis
Concept	Neglected sexual side effects (NSSE)
Context	Prevalence of NSSE Questionnaire use to assess NSSE

Identifying relevant studies

A literature search was conducted using the databases Pubmed, Science Direct and Google Scholar to search for articles matching the objectives mentioned above. A Boolean terms and MeSH (Medical Subject Heading) terms were employed using the keywords: *Orgas* OR Penil* OR Climacturia OR Dysorgasmia OR anejaculation OR Peyronie OR neglected AND [prostate cancer OR Prostatectomy]*. The search was conducted on 1 January 2020 and articles published between 1 January 2009 and 31 December 2019 were included. Other search parameters included English, original studies, about humans. Only studies that matched our aims mentioned above in their titles were selected for further processing.

Study selection

The identification of the relevant literature followed a systematic approach. The results of all three databases were combined into one Excel spreadsheet after applying the search parameters.

A total of 1369 articles were identified. After removing 207 duplicates, 1162 articles remained. The titles were screened, and after applying the including and excluding criteria (Table 3), another 1096 articles were removed with reasons. The abstracts of 66 articles were screened, and a final 23 articles were selected for full-text review. All 23 articles review matched the criteria and were selected for the final inclusion. No additional studies were included after consulting previous searches and reference lists, making the final number of articles included 23. Figure 1 explains the study selection process.

Table 3
Inclusion & Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Articles that involved the neglected sexual sides effects of after radical prostatectomy and radiation therapy treatment for PCa	Literature on sexual dysfunction not relating to the prevalence and questionnaire use after prostate cancer treatment
Published timeframe 1 January 2009-31 December 2019	Articles published outside the applicable time frame
Written in English	Articles not written in English
Original research articles published	Review articles Non-peer reviewed articles (e.g. books, magazines, policy briefs, etc.)
	Commentaries, editorials, programme evaluations and letters

Charting the data

A data extraction tool (*appendix 1*) was developed to organize information about each included study. Table 4 illustrates the information that was charted from each included study.

Table 4 *Data charting tool included information on:*

- Author, date and reference
- Aims and research questions
- Geographical setting
- Study Population
- Study design
- Number of participants
- Period post-PCa investigated
- Prevalence of NSSE
- Reported use of Questionnaire

Quality of the study

The data were organized according to the study objectives, Objective A and B. Furthermore, the data about objective A relating to the prevalence of NSSE, was further organised according to the two main approaches for treating prostate cancer, namely:

Surgical approaches/radical prostatectomy (RP)

Non-surgical approaches/radiation therapy (RT).

Table 4 explains how the data was charted.

Quality Appraisal

An electronic version of the Mixed Method Appraisal Tool (MMAT) (17) was adapted to assess the quality of the included studies. The study designs included in this scoping review included qualitative, quantitative descriptive, and mixed methods studies. The specific criteria to determine the appropriateness of each included study are outlined in appendix 2.

Two reviewers assigned a score to assess each article that assessed the appropriateness of the study's aims and its relevance for inclusion in the review. The overall quality for each included study was calculated according to the following MMAT guidelines (score = number of criteria met/total score in each domain). 1 point was to be given for each question and a total score out of 5 was calculated. This score is represented as a percentage which correlates to the quality of the included studies. (*Appendix 2*)

The results used the following descriptors.

- Very poor quality (20%) where minimal criteria are met
- Poor quality (40%) where less than half the criteria is not met
- Fair quality (60%) where just more than half the criteria is met
- Good quality (80%) where most of the criteria are being met
- Excellent quality (100%) all criteria are met

The overall quality of a combination of components cannot be more than its weakest component when it comes to mixed-methods studies, making the overall score equal to the lowest-scoring component (17).

Collating, summarizing and reporting on the data

The findings of this scoping review were analysed using a content analysis approach of the themes emerging from the extracted data. The themes were collated to answer each research question. The review team discussed findings, resolved issues, and finalised findings. The review team analysed the implications of the study findings in how they relate to the study's aims and further research in the field.

The collected data was organized into subgroups according to Fig. 2. The findings were analysed and reported concerning the research question and the objectives of the scoping review. The data relating to the prevalence of the NSSE was quantitative, and the data about the use of a questionnaire yielded either one of 3 results being i) a commonly used standardized questionnaire, ii) and informal questionnaire, or iii) no questionnaire. In addition to the above-mentioned methodologies, the Preferred Reporting Items for Systematic reviews and Meta-Analysis extension for Scoping Reviews (PRISMA-ScR) checklist (18) were used to guide the write up of the scoping review (*appendix 3*).

Results

The results were synthesised and presented according to the objectives (A or B) of the study which was to report on,

1. the prevalence of the common NSSE's following early PCa treatment through surgical interventions/RP (Fig. 2).
2. the prevalence of each of the common NSSE after PCa after non-surgical interventions/RT (Fig. 2).
3. Mapping the evidence on the role and use of questionnaires in detecting NSSE studies after early PCa treatment (Fig. 2).

A total of 23 studies were included that reported on the NSSE after PCa treatment. As indicated in Table 4, the NSSE reported after surgical interventions were collectively reported 27 times in the included studies, whereas NSSE's about non-surgical interventions were reported 12 times.

Table 4
Representation of studies reporting of specific NSSE after PCa treatment.

NSSE after early PCa treatment relating to Objective A and B				
	27*	Surgical Interventions (RP)	Non-Surgical Interventions (RT)	12*
	Studies			Studies
Reference	Number of Studies	NSSE	Number of Studies	Reference
(5, 19–23)	6	Orgasmic Dysfunction (OD)	1	(4)
(5)	1	Altered Perception of Orgasm (APO)	1	(4)
(5, 23–25)	4	Orgasm Associated Pain/Dysorgasmia (OAP)	1	(4)
(5, 26–29)	5	Orgasm Associated Incontinence (OAI)	2	(4, 26)
	0	Anejaculation	3	(4, 30, 31)
(5)	1	Penile Sensory Changes (PSC)	1	(4)
(5, 32–38)	8	Penile Length Shortening (PLS)	2	(4, 35)
(5, 39)	2	Penile Deformity/ Peyronies Disease (PD)	1	(4)

Two studies by Frey et al published in 2017 and 2014 reported on all the 8 common NSSEs of interest in our review. The 2017 study reported on NSSE following RT interventions and the 2014 study reported on the prevalence of NSSE after RP interventions (4, 5).*

All the studies included for review (n = 23) had cross-sectional study designs and specifically examined NSSEs after PCa treatment. The included studies represented data from eleven countries, with 11 of the studies having been conducted in the USA. Eleven of the remaining studies were conducted in European countries, one study was conducted in South America (Brazil), one in Asia (Japan). No African or Australasian studies matched the inclusion criteria (see Fig. 3.)

Prevalence of NSSE (Objective A)

Surgical Interventions

Prevalence of Orgasmic Dysfunction/Anorgasmia after Surgical intervention (RP):

Six studies met the inclusion criteria (5, 19–23). The 2017 study reported on 415 men with an average of 60 years, where a questionnaire had been used by participants to rate their orgasmic function (OF) on a scale. They used this scale preoperatively and described the OF as either worsening, being stable, or improving preoperatively, and were asked to repeat the rating for a period up to 36 months postoperatively (19). Only 9,4% of participants reported an improved OF after 36 months while OF worsened in 60,1% and remained stable in 30,5% of participants respectively. This study concluded that patients who were younger than age 50 at the time of surgery, patients who had undergone nerve-sparing RP, and patients who had better (higher) OF before surgery could expect a higher rate of OF postoperatively.

A study by Ostby-Deglum et al (2016) reported on the ability to reach orgasm in men (n = 609 men) of an average age of 63 years, 3 years after their robotic-assisted laparoscopic prostatectomy (RALP). They reported poor ability to reach orgasm in 73% of the participants (20). Of the 27% of participants who were able to achieve orgasm after the procedure, 34% relied on erectile aids intermittently or always. Unfortunately, no pre-operative data on the ability to reach orgasm was taken from participants.

Frey et al (2014) investigated 316 patients between 3–36 months after their RP. Participants were an average age of 64 years (5). Five percent of the sexually active participants reported anorgasmia and 57% reported having delayed orgasms.

A 2011 study investigated OF in men (n = 408) of 60 years average age who were potent preoperatively and who had underwent RALP 3 years prior (21). The report found that 88,4% of participants younger than 60 years and 82,6% of participants older than 60 years were able to achieve an orgasm. The study also reported that 90,7% of bilateral nerve sparing (BNS) procedure patients were able to achieve orgasm, compared to 82,1% of the unilateral nerve-sparing (UNS) procedure participants.

One study retrospectively reviewed previous clinical notes of patients (n = 1021) of an average age of 64 who had undergone a radical retropubic prostatectomy (RRP) for 30 years. The procedures were performed by different surgeons (22). The review specifically focussed on OF in a subgroup (n = 458) of participants. The study found that only 66,8% of the men who had an orgasmic function before the surgery also attained OF afterward. They also concluded that a normal expected age-related decline in OF was prevalent, in such a way that patients under the age of 60 years would have a 77,4% probability of maintaining their ability to orgasm.

The 2010 study by Salonia et al investigated the improvement of OF over an extended period. The study was conducted with 334 men of average age 62 years, over 48 months after a nerve-sparing surgical procedure (23). An inability to achieve orgasm was reported by 37% of the participants. The study

concluded that the OF had increased in these participants over 48 months after RP surgery. The study also reported that OF deteriorated after RP with advancing age.

Prevalence of Altered Perception of Orgasm after Surgery (RP)

Frey et al (2014) reported decreased orgasm intensity in 60% of the sexually active participants (n = 316) of 64 average years in 3–36 months after their RP. (5)

Prevalence of Orgasm Associated Pain/Dysorgasmia after Surgery (RP)

Four studies included in this review reported on decreased OF after RP (5, 23–25). The 2014-study by Frey et al, (n = 316) of 64 average years in 3–36 months after their RP, (5) reported OP in 10% of the sexually active participants in the study.

A 2013-study with participants (n = 1288) of 63 years average age who had undergone RP between 6 months and 5 years previously (24), reported OP in 11% of the participants in the previous 6 months. Of this group, the patients who had bilateral seminal vesicle sparing, 21% reported OP compared to 12% of the patients who had unilateral seminal vesicle sparing.

A similar result was reported in a 2012 study of 702 participants of an average age of 64 years, with 12% of their patients experiencing OP after RP (25). They further found that 72%, 26%, and 7% of the study participants complained of pain during orgasm at 12, 18, and 24 months respectively. Pain of 6/10 or more measured on the visual analogue scale (VAS) was experienced by 26% of their participants at 6 months, and 16% of participants at 24 months after the RP.

A 2010 study previously mentioned, reported that 14% of participants reported pain during orgasm over 28 months after their nerve-sparing RP(23).

Prevalence of Orgasm Associated Incontinence/Climacturia after Surgery (RP)

Five studies met the inclusion criteria (5, 26–29). Frey et al's study with patients (n = 316) of 64 years average age who were assessed within 3–36 months after RP reported UIDS in 38% of the participants. (5)

Another 2014-study investigated the prevalence of OAI in participants (n = 412) who had RP, RT, or both (26). The average age of the participants was 62, 2 years for the RP group, and 65 years for the RT group. The study reported a prevalence of OAI in 22.6% of the total study group and OAI prevalence of 28,3% of RP participants.

A 2012 video-urodynamic study by Manserri et al was included, as its first objective was to investigate the incidence of OAI in a group of 84 potent and continent men who had undergone a bladder neck sparing RP at least a year prior (27). Of this group, 28,6% reported experiencing OAI. The study further evaluated 7 participants with a video-urodynamic evaluation and concluded that the functional urethral length was significantly lower in the OAI group, and that this could explain OAI in RP patients.

Nilsson et al; (2011) reported from their study of 1261 participants of an average age of 63 years 2 years after their RP (28). OAI was experienced by 21% of the participants in the previous 6 months. Of the total study population, only 55% were sexually active, and of this group, 4% had OAI during every orgasm, 39% had had an incidence of OAI and 7% of the group had OAI more than half the time. They also found that patients who experienced OAI reported a decreased ability to satisfy their sexual partner, and these patients avoided sexual activity due to fear of failing, inferior orgasmic satisfaction, and a lower frequency of sexual intercourse.

The oldest study (2011) included in this review investigated 1421 men of an average age of 58,4 years over 24 months after a RP (29). The study reported on inconvenience related to UIDS. The study describes UIDS as a combination of OAI and incontinence during masturbation or foreplay. Researchers reported 44% of their participants experiencing difficulty with incontinence during sexual activity at 3 months. The study found that UIDS decreased to 36, 1% amongst the participants at 24 months. In the same group, 22, 4% of participants reported major difficulty from UIDS at 3 months and UIDS remained a problem for 12,1% of the participants at 24 months.

Prevalence of Anejaculation after Surgery (RP)

No studies in the current review reported on this issue.*

Prevalence of Penile Sensory Changes after Surgery (RP)

Only a study by Frey et al 2014 investigated patients (n = 316) at 3–36 months after their RP. Participants were an average of 64 years old (5). Twenty-five percent of the total participant group reported sensory changes in their penises.

Prevalence of Penile Shortening after Surgery (RP)

Eight studies that met the inclusion criteria were found (5, 32–38). The most recent study included for review investigated looked at 507 participants who had RP (32). The participants were grouped into a complete recovery (CR) group of an average age of 59, 3 years, and an incomplete recovery (IR) group, with an average age of 62 years. The CR group experienced a 1,9 cm (14, 13%) PLS at 7 days, compared to the 3,38 cm (23, 8%) PLS experienced by the IR group. Of the entire study population, 60, 2% regained their pre-operative penile length (PL) at 12 months after the RP. The study concluded that younger age and pre-operative erectile function are associated with complete PL recovery.

A 2017 study reported on 102 men of an average age of 64,4 years (33). They found that stretched PL was the shortest 10 days after the RP with a mean shortening of 19,9 mm. Magnetic resonance imaging (MRI) testing was done to determine a possible cause for PLS. MRI results confirmed that the distal end of the membranous urethra moved proximally at 10 days after the RP, then returned gradually to its pre-operative position at 12 months.

Frey et al; (2014) reported on 316 patients, 3–36 months after their RP with an average age of 64 (5). The study found that 47% of patients had a self-reported PLS of more than 1 cm.

Berookhim et al;(2013) reported on 118 men of an average age of 58 years, over a period of 6-months after their RP (34). At 2 months postoperatively, they reported a 2,4 mm PLS compared to baseline. At 6 months, there was no difference in PL compared to baseline.

Parekh et al; (2013) investigated a registry of 948 men who had treatment for PCa. Over 75% of the registry participants were aged between 60–80 (35). The study participants consisted of an RP group of participants making up 53,8% of the group, The results showed that 3,73% of the RP participants reported a self-perceived PLS. This study concluded that PLS is associated with treatment regret.

A 2012 study looked at self-reported PLS in 1288 patients of a mean age of 64,8 years after RP (36). They found that 55% of men had a self-reported penile shortening after RP. A subgroup of participants data reported that with an increase in the nerve-sparing operative procedures, there is a decrease in self-perceived PLS with 58% of UNS participants reporting PLS compared to 33% BNS participants.

A study by Vasconcelos et al; (2012) screened patients over 5 years after RP. They looked at 105 men of an average age of 65 years (37). The study reported a mean PLS of nearly 1 cm at 3 months, and this difference maintained up to 24 months postoperatively, after which it recovered gradually up until 48 months. The study concluded that preserved sexual function will ensure baseline PL is reached sooner.

A 2011 study reported on 127 men, 97 of which completed the 11 month follow up after RP (38). The participants had an average age of 54,5 years. Stretched PL reduced from a mean 11.77 cm to 11.13 cm at 1 month after the RP surgery, but no difference was found to the baseline measurements at 6 months postoperatively. Recovery trends started at 3 months postoperatively.

Prevalence of Penile Deformity/Peyronie's Disease (PD) after Surgery (RP):

Two studies were included (5, 39). The 2014-study of patients (n = 316) of 64 average age at 3–36 months after their RP, found abnormal curve in the penis reported by 10% of participants. (5).

A 2010 study reported on 1011 men with an average age of 60,2 years, who were treated with RP (39). PD was investigated over a period of 3 years after the RP. The study showed that 15,9% of the participants had reported PD that developed over an average period of 13,9 months. The mean penile curve reported by participants was 31 degrees. The study found PD in RP patients to be more prevalent in younger white men.

Non-Surgical Interventions

Prevalence of Orgasmic Dysfunction; Altered Perception of Orgasm and Orgasm Associated Pain/Dysorgasmia; Orgasm Associated Incontinence/Climacturia

Only one study met the inclusion criteria of interest. Frey et al 2017-study investigated the NSSE between 3 months to 5 years after RT in 109 participants of an average age of 71 years (4). The study reported a prevalence of anorgasmia in 24% of participants.

Altered Perception of Orgasm

The same study reported decreased orgasmic intensity in 44% of the participants. (4)

Orgasm Associated Pain/Dysorgasmia

Frey et al's (2017) reported OP in 15% of their participants. (3)

Orgasm Associated Incontinence/Climacturia

Frey et al's study reported UIDS in 4% of their participants. (3) A 2014 study of participants (n = 412) who had RP (279), RT (110) or both (23) (26). The mean age of the RT participants was 65 and the mean age of the RP participants was 62 years. OAI was found in 22.6% of the total study group, but in only 5.2% of the RT participants.

Prevalence of Anejaculation after RT

Ejaculation symptoms were reported in three studies. Frey et al (2017) reported anejaculation in 11% of the 2017 study. (3)

A 2013 study reported on 364 men of an average age of 64 years and had concluded that 72% of the study population lost the ability to ejaculate in an antegrade fashion after a 6 year follow up period (31). Anejaculation was experienced at 1, 3, and 5 years after RT by 16%, 69%, and 89% of the respondents respectively. The study further linked that the failure to ejaculate increases in men with a higher dose of RT, older age, and smaller prostates at the time of RT.

A 2009 study of 241 men of an average age of 65 years found that at 36 months after RT (Brachytherapy), 81,3% of the sexually active study participants were able to ejaculate (30). A total of 84.9% of participants however experienced a reduction in volume and a deterioration in their orgasm after treatment compared to 26,9% before. The number of participants with rare/no ejaculations doubled after the treatment from 7,5% before to 18,7% after treatment. A total

of 10% of the study respondents experienced no orgasms during sexual activity. Dry ejaculations increased from 0% before the RT to 18,7% of the participants after the RT.

Prevalence of Penile Sensory Changes; Penile Deformity and Penile length Shortening

The 2017 study by Frey and colleagues reported on all three of these conditions.

The study reported on the prevalence of some penile sensation changes in 27% of the participants (4)

Prevalence of Penile Deformity/Peyronie's Disease after RT :

Frey et al: (2017) reported that 12% of the participants reported an altered curvature of their penis (4)

Prevalence of Penile Shortening after RT :

The 2017 study reported that 42% of participants reported more than 1 cm subjective PLS. (4)

A 2013 study by Parekh and colleagues of men (n = 948) mostly aged between 60–80 who reported self-perceived PLS (35). The study participants consisted of 22, 5% RT participants. That study reported 0% self-perceived PLS amongst the RT participants.

Questionnaire use after early PCa treatment (Objective B)

NSSE as a combined set of symptoms:

The two studies by Frey et al; (2017) and Frey et al; (2014) both used a study-specific informal questionnaire base on other questionnaires (4, 5). The questionnaire enquired about OD, APO, OAP, OAI, PSC, PLS, PD,

Orgasmic Dysfunction

Du et al's quality of life questionnaires included the EPIC (11), American Urological Association Symptoms Index (AUASI), and Sexual Health Inventory for Men (SHIM) (19). The questionnaire enquired about OD in a study of 415 men, reporting on how the symptoms change over 36 months.

A 2016 study used the EPIC-26 questionnaire that only included one item to obtain data pertaining to orgasmic function. The question asked, "How would you rate your ability to reach orgasm" (20). The study concluded that only 23% of participants had a good ability to reach orgasm after 3 years.

A 2011 study used the EPIC-26 questionnaire, and the IIEF questionnaire preoperatively, and the EPIC questionnaire at regular intervals after surgery to investigate the orgasmic outcomes in participants 3 years after their RALP (21). In addition, patients were asked to evaluate their orgasm, and state whether they experienced any pain during orgasms.

Dubbelman et al did not use any questionnaire in their 2010 study. They rather interviewed their participants using structured questioning to explore issues regarding orgasmic function (22). Salonia et al's study used the IIEF questionnaire, particularly the IIEF-OF domain to enquire about OF in their study (23).

Both studies by Frey and colleagues conducted in 2014 and 2017 respectively enquired into OD as part of a set of NSSEs by using a study-specific questionnaire (4, 5). The RT study showed that 5% of participants reported OD (4), compared to 24% of the RP participants(5)

Altered Perception of Orgasm

No additional studies

Orgasm Associated Pain/Dysorgasmia

One study used a self-designed questionnaire of 145 questions, where 5 questions dealt with orgasmic characteristics (24), and another reported on the use of the orgasmic frequency scale (OFS) and the VAS (25).

Orgasm Associated Incontinence

A 2014 study used a non-validated author designed questionnaire (26) and a 2011 study used a study-specific questionnaire based on the Scandinavia Prostate Cancer Group 4 questionnaire (28). Manassero et al;(2012) used the IIEF 5 item questionnaire and the International Prostate Symptom Score Test as well as a telephonic interview to probe whether climacturia was present (27). The 2011 study used the UCLA Prostate cancer Index questionnaire (29). OAI after RP (28,3%) was compared to OAI in RT ((5, 2) in one study (26)

Anejaculation

A 2013 study used the IIEF and in particular question 9 (when you had sexual stimulation or intercourse, how often did you ejaculate?) and 10 (when you had sexual stimulation or intercourse, how often did you have the feeling of orgasm or climax?) (31). The participants were firstly interviewed by a sexual medicine physician and were questioned about their ejaculatory function (presence/absence, intensity and ease of achievement) and orgasm (presence/absence, intensity and ease of achievement). Those who were sexually active were asked to complete the IIEF questionnaire.

The 2009 study asked participants to complete the IIEF-5 questionnaire to assess erectile dysfunction, and a modified version (5 items not 7) of the Male Sexual Health Questionnaire (MSHQ) that specifically addressed: i) frequency ii) volume iii) dryness, iv) pleasure and v) pain during ejaculation. (30)

Penile Sensory Changes

No additional studies

Penile Length Shortening

Three studies all used a semi-rigid ruler in conjunction with the IIEF questionnaire (33, 34, 38). A 2012 study used an author designed questionnaire containing questions relating to self-perceived PLS (36). A 2018 study based their results on the physical measurement of PLS (32). Parekh et al;(2013) reported in their study that physicians completed a questionnaire based on their patients, one question noted under the complaints section referred to reduced penile size (35). No physical measurements were reported on. The last study by Vasconcelos et al; (2012) used a physical measurement using an anthropometric ruler (37).

Penile Deformity/Peyronies Disease (PD)

The single study by Tal et al; (2010) did not report any questionnaire being used, but rather that the baseline data was collected by a urologist before the RP (specifically assessing the penis for PD plaque presence), and the same procedure afterward as well as an assessment of a penile curvature with a goniometer if the patient reported a curvature (39).

Discussion

Prevalence of Combined NSSE after RP/RT (Objective A)

Two studies were the most important of all the studies, as they investigated most of the collective group of NSSE (4, 5). A similar approach was used in both studies in that they used the same set of questions to determine the presence of various NSSE from participants in the different treatment approaches, making the comparison of NSSE between the two approaches easy. These results will be discussed under each NSSE category.

Prevalence of Orgasmic Dysfunction after RP/RT

A varied range of OD was reported between studies, but OD featured in RP and RT participants. Two-thirds of men reported poor ability to orgasm at 3 years (19, 20), and no orgasm by one-third of men at 2–5 years after an RP (22, 23). Although OF improved postoperatively over time (23), it also deteriorated with age (19, 21–23). Nerve sparing RP procedures predicted better post-operative OF (19, 21). Increased time needed to reach orgasm was experienced by almost half the men, 5 years after RT (4).

Prevalence of Altered Perception of Orgasm after RP/RT

Similar results were found in an RP study and an RT study, where, the RP study (5) reported that 60% of participants vs almost 50% of the RT participants (4) reported a decrease in orgasm intensity.

Prevalence of Orgasm Associated Pain/Dysorgasmia after RP/RT

OP after an RP was reported on in 4 studies compared to 1 RT study. Similar results were found between the RP studies, in that between 10–12% reported OP in RP participant groups in all the OP studies (5, 24, 25). One study further described that the pain felt was mostly (70% of the time) felt in the penis (25), while another made the association between bilateral seminal vesicle sparing procedures as the possible cause of OP (24).

Prevalence of Orgasm Associated Incontinence/Climacturia after RP/RT

Climacturia is an NSSE in men after RP and RT. Five studies looked at OAI after RP, compared to two studies after RT. This NSSE was reported by anywhere between 21% (28) to 38% (5) of participants across the five RP studies after 12–24 months (28) (5, 26, 27, 29)

OAI in RT was reported to be much lower, affecting only 4% of participants in one study (4). This notion was concurred by the only study that compared RP and RT participants experiencing OAI. This study concluded that the OAI rates after RP were six times more than that of RT (28,3% vs 5,2%) (26). Climacturia is associated with major sexual inconvenience/bother (28).

Prevalence of Anejaculation after RP/RT

According to this review, anejaculation is a consequence of RT (30, 31). Anejaculation becomes worse over time after RT until it reaches its peak at 5 years after treatment with 89% of the study group being affected (31). An older study reported a conflicting rate of anejaculation with 81,3% of their participants having conserved their ejaculatory function (30). This study was however done on a shorter average post-RT follow up time of 3 years(30), compared to the latest study who had a population with higher stage diseases receiving higher RT doses, possibly explaining the increased anejaculation rates (31). The one

study did report that 75% of the participants had a reduction in ejaculate volume, and that 19% of the men experienced a dry ejaculation (30). Higher RT dose, older age, and smaller prostates at the time of treatment increased the likelihood of failure to ejaculate (31).

*Anejaculation is however also a given consequence of RP, as the ejaculatory apparatus (prostate, seminal vesicles, and ejaculatory ducts) are removed (7, 40), but the authors were unable to source any studies within our search parameters that met the study inclusion criteria.

Prevalence of Penile Sensory Changes after RP/RT

Similar results were seen across 2 studies, one on each intervention type. The RP study (5) reported that 25% of their participants had penile sensory changes, while the RT study reported the same for 27% of participants (4).

Prevalence of Penile Shortening after RP/RT

PLS was reported found in two RT studies (4, 35), and eight RP studies (5, 32–38). The one study reported on both RT and RP, and concluded that no RT participants had PLS (35). PLS was worst at 7–10 days postoperatively (32, 33), but started recovering at 3–6 months (38). Self-perceived PLS is however still experienced by 55% of men 2 years after RP, and a nerve-sparing procedure reduced the risk of self-perceived PLS (36). Men who eventually do not fully regain their PL, can experience up to a 24% PL loss at 7 days postoperatively(32). Younger age and better pre-operative erectile function is associated with complete PL recovery(32), and PLS is associated with treatment regret (35).

Prevalence of Penile Deformity/Peyronies Disease after RP/RT

Two studies on RP participants found that 10–15,9% of participants reported the presence of a penile curvature or PD (5, 39). The average reported curvature angle was 31 Degrees (39). A similar result was reported in the only RT study. They concluded that 12% of their participants reported an altered curve of the penis (4)

Questionnaire used in Assessing NSSE (Objective B)

It is clear from all the retrieved studies that there is no single validated questionnaire available that investigates the NSSE after early PCa treatment. Most studies incorporated some aspects of other questionnaires, or simply made their up their questionnaires. Two studies used a non-validated questionnaire that was able to pick up on the majority of the collective group of NSSE (4, 5). These two studies looked particularly and the prevalence and predicting factors of the NSSE. The Epic-26 (11) questionnaire featured in a few studies pertaining to OD (19–21), but couldn't sufficiently be used to report on OD, and thus additional orgasm rating questions were asked to participants(19, 21). One study used the Dysorgasmia Frequency Scale (25). The IIEF was used in many studies (5, 21, 23, 27, 31, 33, 34, 37, 38), but had no purpose in detecting any of the NSSE. The EHS (41) was used in a few studies (5, 33), but once again had no role to play in detecting the NSSE. The SHIM questionnaire (a modified 5 item version of the IIEF) was used in one study (19, 32), and another study (30) based their informal questionnaire on the Male Sexual Health Questionnaire (42).

Study Limitations

The inclusion and exclusion criteria only allowed original research to be considered, and many reviews that matched the study objectives could not be included. The data search was done only done on three databases, although allowance was made for appropriate articles not contained in the databases to be included.

Conclusion

NSSEs are prevalent in men after RP and RT. PD, OD, and PLS are similarly prevalent after RP and RT. Anejaculation after RP studies could not be sourced, as only RT studies met the study inclusion criteria. OAI/Climacturia was shown to be caused by RP and RT, but the prevalence found in the RP patients was 6 times that found in the RT patients. A common theme through most of the studies were that the participants felt like they were not adequately informed about these possible sexual side effects before commencing their treatment. Questionnaires are effective, but there are many modified informal non-specific questionnaires currently being used to detect NSSE after PCa treatment. There is no valid and reliable questionnaire currently available to detect all the collective NSSE after PCa treatment. There is a scope to develop a validated and reliable NSSE questionnaire to use on PCa patients after their treatment. This NSSE questionnaire must be quick, straightforward, and effective.

Abbreviations

PCa: Prostate cancer, PLS: Penile Length Shortening, OAI: Orgasm Associated Incontinence, UIDSa: Urinary Incontinence During Sexual Activity, OP: Orgasm Pain, PD: Peyronie's Disease, NSSE: Neglected Sexual Side Effects, HCP: Health Care Practitioner, NSSE: Neglected sexual side effects, EPIC: Expanded Prostate Cancer Index, IIEF: International Index of Erectile Function, PCC: Population Concept Context, MeSH: Medical Subject Heading, MMAT: Mixed Method Appraisal Tool, PRISMA-ScR: Preferred Reporting Items for Systematic Reviews and Meta-Analysis Extension for Scoping Reviews, RP: Radical Prostatectomy, RT: Radiation Therapy, OF: Orgasmic Function, RALP: Robotic Assisted Laparoscopic Prostatectomy, BNS: Bilateral Nerve Sparing, UNS: Unilateral Nerve Sparing, RRP: Radical Retropubic Prostatectomy, VAS: Visual Analogue Scale, CR: Complete Recovery, IR: Incomplete Recovery, PL: Penile Length, MRI,

Magnetic Resonance Image, AUASI: American Urological Association Symptoms Index , SHIM: Sexual Health Inventory for Men, OFS: Orgasmic Function Scale, MSHQ: Male Sexual Health Questionnaire.

Declarations

Ethics approval and consent to participate

Full ethical clearance was obtained from the University of KwaZulu-Natal, School of Health Sciences Research Committee (Biomedical Research Ethics Committee) with registration no: BREC/00000478/2019

Consent for publication

Not applicable

Availability of data and materials

Not applicable

Competing interests

The authors declare that they have no competing interests

Funding

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Authors' contributions

PR conceived the study and participated in the design involved in drafting and finalising the manuscript. RS revised the manuscript and provided clinical input and approved the manuscript for final submission. JM came up with the study idea and provided clinical input and revised the manuscript for final submission. JvW participated in the conceptual design of the study, drafting the manuscript and revising it critically providing final approval of the version to be published.

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Appendix

APPENDIX 1							
Author/Date/Study Title/Reference	Study Design	Geographical Setting	Number of Participants, Age at treatment intervention and Intervention reported	NSSE Reported	Period after treatment investigated	Aims and Objectives	NSSE Prevalence Reported
Frey et al ; (2017): Prevalence and Predicting Factors for Commonly Neglected Sexual Side Effects to External-Beam Radiation Therapy for Prostate Cancer. (4)	Quantitative: Questionnaire based investigation	Denmark (single Center)	109 men (median age 71) treated with RT-External Beam	Multiple	3 Months to 5 years	To investigate orgasmic dysfunction, urinary incontinence during sexual activity, changes in penile morphology and penile sensory changes.	Of the study participants 24% reported anorgasmia 44% reported decreased in orgasm intensity 4% reported urinary incontinence during sexual activity 40% reported and increased time needed to achieve orgasm 42% reported penile length shortening
Frey et al ; (2014): Prevalence and Predicting Factors for Commonly Neglected Sexual Side Effects to Radical Prostatectomies:Results from a Cross Sectional Questionnaire based study (5)	Quantitative: Questionnaire based investigation	Denmark	316 men (median age 64) treated with RP	Multiple	3-36 Months	Prevalence and predicting Factors for Commonly Neglected Sexual side Effects to radical prostatectomy	Of the study participants 5% of the sexually active participants had reported anorgasmia 60% of the sexually active participants had reported a decrease in orgasm intensity 57% reported delayed orgasms 10% of sexually active participants had painful orgasms 38% of the participants reported urinary incontinence during sexual activity 25% of the total participant group reported sensory changes in their penis 47% of patients had a self-reported penile length loss of more than 1 cm 10% of participants

							reported an abnormal curve in the penis.
<p>Mogorovich et al; (2013):</p> <p>Radical prostatectomy, sparing of the seminal vesicles, and painful orgasm. (24)</p>	<p>Quantitative</p> <p>Questionnaire based investigation</p>	Sweden	<p>1288 men (median age 63) treated with RP:</p> <p>RRP (33%) and RALP (67%)</p>	Orgasmic Pain	6 months to 5 years	To investigate the prevalence of painful orgasm and to identify potential risk factors	<p>11% of participants reported a painful orgasm in the previous 6 months</p> <p>21% of bilateral seminal vesicle sparing participants reported PO</p> <p>12 % of unilateral seminal vesicle sparing participants reported PO</p> <p>Other Findings:</p> <p>Bilateral seminal vesicle sparing and age below 60 significantly related to the presence of painful orgasm.</p>
<p>Matsushita et al;(2012):</p> <p>The Evolution of Orgasmic Pain (Dysorgasmia) Following Radical Prostatectomy. (25)</p>	<p>Quantitative</p> <p>Questionnaire based investigation</p>	USA	702 men (mean age 64) treated with RP	Orgasmic pain	6-24 months	To Assess the evolution of dysorgasmia in RP Patients	<p>12% of participants reported dysorgasmia</p> <p>72%, 26% and 7% of participants complained of pain during orgasm at 12, 18 and 24 Months</p> <p>An intensity of pain of 6/10 or more was experienced by 26% of participants at 6 months, and 165 of participants at 24 months.</p> <p>Other Findings:</p> <p>70% reported PO in the Penis, 22% in testes, 8% other areas.</p>
<p>Du et al; (2017):</p> <p>Orgasmic Function after Radical Prostatectomy (19)</p>	<p>Quantitative</p> <p>Questionnaire based investigation</p>	USA (Single center)	<p>415 men (median age 60) treated with RP</p> <p>(median age unavailable)</p>	Orgasmic Dysfunction	36 months	To examine OF overtime after RP	<p>60,2% of participants had OF worsening after the RP, whereas 30,5% remained stable, and 9,4% improved</p> <p>High pre-operative OF predicted high post-operative OF (15 x that of low OF pre-operative men)</p>

							Younger age (below 50) and nerve sparing procedures predicted higher post-operative OF
Ostby-Deglum et al; (2016): Ability to Reach Orgasm in Patients With Prostate Cancer Treated With Robot-assisted Laparoscopic Prostatectomy. (20)	Quantitative Questionnaire based investigation	Norway	609 men (median age 63) treated with RP: RALP	Orgasmic Dysfunction	3 years	To study the ability to reach orgasm after RALP	78% of participants had poor ability to reach orgasm 23% of participants reported good ability to reach orgasm Older age, poor physical quality of life and erectile dysfunction associated with poor orgasmic ability
Tewari et al;(2012); Nerve sparing can preserve orgasmic function in most men after robotic-assisted laparoscopic radical prostatectomy. (21)	Quantitative Questionnaire based investigation	USA	408 men (median age 60) treated with RP: RALP	Orgasmic Dysfunction	36 Months	To investigate orgasmic outcomes in patients undergoing RALP and the effects of age and nerve sparing on these outcomes	88,4% of participants under age 60 able to achieve orgasm/82,6% over 60 90,7% BNS participants able to achieve orgasm/82,1 UNS 3,2% of BNS had decreased sensation of orgasm
Dubbelman et al;(2010): Orgasmic dysfunction after open radical prostatectomy: clinical correlates and prognostic factors. (22)	Quantitative: Analysis of clinical notes	Netherlands	458 men (median age 64) treated with RP: RRP (over a 30-year period.	Orgasmic Dysfunction	Up to 2 years	To analyse sexual function and orgasmic function in men before and after RP	Of the studied men who had orgasmic function before the surgery, 66,8% had orgasmic function afterwards with an age-related decline
Salonia et al ;(2010): Postoperative orgasmic function increases over time in patients undergoing nerve-sparing radical prostatectomy. (23)	Mixed method design	Italy	334 men (median age 62) treated with RP: BNSRRP	Orgasmic Dysfunction	Over 48 months	To assess orgasmic functioning over time in men after bilateral nerve sparing-sparing radical retro pubic prostatectomy for PCa	37% of participants reported complete inability to achieve orgasm 14% of participants reported pain during orgasm Orgasmic function showed an increase over time postoperatively! Orgasmic function deteriorated

							with age postoperative!
O'Neil et al; (2014): Climacturia after definitive treatment of prostate cancer. (26)	Quantitative Questionnaire based investigation	USA	412 men (mean age 62,2 (RP), 65 (RT) and Combined approaches 63,2) RP (67,7% of which 39,1 % open procedure vs robotic, and 88,45 underwent a nerve sparing procedure) RT (26,7%, of which 45,5% Brachytherapy, 34,5 % external beam radiation and 20% combined) RP+RT (5,6%)	OAI/Climacturia	RP: 20,3 Months RT: 23,9 Months RP+RT: 10,2 Months	To examine the prevalence, causes and impact on orgasm function of climacturia after definitive treatment of PCa with surgery	Climacturia reported in 22.6% of study group Climacturia was more prevalent after surgery (28,3%) compared to radiation (5,2%). Relationship between Stres: Urinary Incontinence and Climacturia Climacturia is not necessarily associated with negative sexual satisfaction
Manassero et a; ((2012): Orgasm-associated incontinence (climacturia) after bladder neck-sparing radical prostatectomy: clinical and video-urodynamic evaluation. (27)	Quantitative	Italy	Phase 1: 84 men Phase 2: 7 men (mean age 64,1) underwent video analysis- N/A	OAI/Climacturia	1 year	To Investigate the incidence and Video-urodynamics of Climacturia in continent and potent patients after BNS RP	28,6 % Climacturia reported as baseline investigations for a N/A stud
Nilsson et al; (2011) Orgasm-associated urinary incontinence and sexual life after radical prostatectomy. (28)	Quantitative	Sweden	1261 men (median age 63) treated with RP	Orgasm Associated urinary incontinence	Mean follow up of 2 years after RP	To determine the prevalence of OAI after RP and its effect on sexual satisfaction	45% of the study participants were not sexually active 21% of the participants had experienced OAI Of the sexually active men: 4% had urinary leakag during every orgasm, 39% have had an incident of urinary leakage during orgasm and 7% of participants experienced OAI more than half the time. <i>Other findings</i> orgasm associated urinary incontinence in the previous 6 months was associated with i) decreased ability to

							<p>satisfy sexual partner,</p> <p>ii) avoiding sexual activity due to fear of failing</p> <p>iii) inferior orgasmic satisfaction</p> <p>iv) lower frequency of sexual intercourse</p>
<p>Mitchell et al; (2011): Post-prostatectomy incontinence during sexual activity: a single center prevalence study. (29)</p>	Quantitative	USA	1421 men (median age 58,4) treated with RP (82,7% BNS, 14,6 % UNS, 2,7% none)	Incontinence during sexual activity	3, 6, 14 and 24 months	To determine the time dependent prevalence and severity of incontinence during sexual activity	<p>44% of participants reported Incontinence during sexual activity at 3 months</p> <p>36,1% of participants reported Incontinence during sexual activity at 24 Months</p>
<p>Sullivan et al; (2013): Ejaculation Profiles of Men Following Radiation Therapy for Prostate Cancer. (31)</p>	Quantitative: Structured interview and questionnaire	USA	364 men (median age 64) treated with RT: (68,6% External Beam and 30,7% Brachytherapy)	Ejaculation function	6 years	To define the ejaculation profiles of men after RT for PCa.	<p>72% of the study population lost the ability to ejaculate in an anterograde fashion</p> <p>Anejaculation was experienced at 1,3 and 5 year: after RT by 16%, 69% and 89% of the respondents</p> <p><i>Other Findings</i></p> <p>The likelihood of failure to ejaculate is increased in men with a high dose of RT, older age, and smaller prostates at the time of RT.</p>
<p>Huyghe et al; (2009): Ejaculatory Function After Permanent 125I Prostate Brachytherapy for Localized Prostate Cancer. (30)</p>	Quantitative: Questionnaire based investigation	France	241 men before and 198 men after treatment (median age 65) treated with RT (brachytherapy)	Ejaculatory Function	36 months	To conduct a detailed analysis of ejaculatory function after brachytherapy for PCa	<p>· Most participants (81,3%) had conserved ejaculatory function at 36 months after prostate brachytherapy</p> <p>· ¾ of the men with conserved ejaculatory function after the treatment experienced a reduction in</p>

							<p>ejaculate volume (</p> <ul style="list-style-type: none"> · 18,7 % of the sexually active respondents experienced dry ejaculation after treatment · 12,9% had painful ejaculations before, compared to 30,3% after · 10% of respondents experience no orgasms during sexual activity after treatment compared to only 1% before
<p>Kwon et al; (2018): Longitudinal recovery patterns of penile length and the underexplored benefit of long-term phosphodiesterase-5 inhibitor use after radical prostatectomy. (32)</p>	Quantitative study	USA	507 men (median age 59,3% CR group and 62 IR group) treated with RP	Penile length shortening	7 days-12 months	To describe longitudinal patterns of PL recovery and to evaluate factors predicting complete return to baseline PL	<p>The CR group experienced an average 14,13% (1,9cm) reduction in PL at 7 days after the RD</p> <p>The IR group experienced a 23,8 % (3,38cm) reduction in PL at 7 days after the RP</p> <p>60,2 % of the participants regained their pre-op PL at 12 months</p> <p>Younger age and pre-operative Erectile function are associated with complete PL recovery.</p>
<p>Kadono et al; (2017): Changes in penile length after radical prostatectomy: investigation of the underlying anatomical mechanism. (33)</p>	Quantitative: Questionnaire based	Japan	102 men (median age 64,4) treated with RP	Penile length shortening	Before RP 7 days-24 months after RP	To measure changes in penile length over time before and after RP, and to investigate the underlying mechanisms for these changes.	<ul style="list-style-type: none"> · Stretched penile length was shortest at 10 days (mean shortening of 19,9 mm) after RP and gradually recovered thereafter · Stretched penile length at 12 months after RP was not significantly different to that of the preoperative measurement · MRI results concluded that the distal end of the

							membranous urethra moved proximally (mean proximal displacement of 3,9mm) at 10 days after RP, and then returned to the preoperative position at 12 months
Berookhim et al; (2014) Prospective analysis of penile length changes after radical prostatectomy. (34)	Qualitative	USA	118 Men (median age 58) treated with RP	Penile length shortening	Baseline, 2months, 6 months	To assess the impact of RP on penile dimensions, and the assess the impact of Phosphodiesterase-5-inhibitor use on penile length changes	<ul style="list-style-type: none"> At 2 months post operatively, there was a 2.4mm difference (shortening) in stretched flaccid penis length compared to baseline At 6 months, there was no difference compared to baseline PDE51 use preserved stretched flaccid penile length at 6 months
Parekh et al ; (2013): Reduced Penile Size and Treatment Regret in Men With Recurrent Prostate Cancer After Surgery, Radiotherapy Plus Androgen Deprivation, or Radiotherapy Alone. (35)	Quantitative	USA	948 men treated for PCa 53,8% had RP 22.5 % had RT 23,7% had RT and ADT ¾ of the participants were between 60-80 years old	Penile length shortening		To report the relative incidence of the perceived reduction in penile size across prostate cancer treatment modalities.	<ul style="list-style-type: none"> 3.73 % of Surgical Cases had reduced PL 2,67 % RT cases plus ADT had reduced PL 0% RT cases without ADT had reduced PL <p>Penile length shortening is associated increased treatment regret.</p>
Carlsson et al (2012): Self-perceived penile shortening after radical prostatectomy (36)	Quantitative: Questionnaire based investigation	Sweden (Single center)	1288 men (median age 64,8) treated with RP	Penile length shortening	24,2 months	To evaluate self-perceived penile shortening in PCa after RP	<ul style="list-style-type: none"> 55% of RP Participants had Self Perceived PLS With increasing nerve sparring operative procedure, the risk of self-perceived PLS decreased. A subgroup of participants data reported that with an increase in

							nerve sparing operative procedures, there is a decrease in self perceived PLS with 58% of UNS participants reporting PLS compared to 33% BNS participants.
Vasconcelos et al; (2012); The natural history of penile length after radical prostatectomy: a long-term prospective study. (37)	Quantitative	Brazil	105 men (median age 65) treated with RP	Penile Length Shortening	Baseline preoperatively 3-60 Months	To describe the penile length after RP in a long-term follow up	1 cm mean PL loss at 3 to 24 months Baseline PL reestablished at 48 months Preserved sexual function will ensure baseline PL is reached sooner
Engel et al; (2011): Changes in Penile Length After Robot-Assisted Laparoscopic Radical Prostatectomy (38)	Quantitative: Questionnaire based investigation and a physical assessment	USA	127 men (median age 56,5) treated with RALP RP	Penile length shortening	Baseline, preoperatively, 1-11 months after	To describe changes in penile length after robot assisted radical prostatectomy	· Stretched penile length reduced from a mean 11.77cm to 11.13cm at 1 month after the surgery · Recover trends started at 3 months and 6 months · Mean stretched penile length was not significantly different from baseline at 9, 10 and 11 months
Tal et al; (2010): Peyronie's Disease Following Radical Prostatectomy: Incidence and Predictors. (39)	Mixed method Qualitative and Quantitative	USA	1011 men (median age 60,2) treated with RP	Peyronies disease	Baseline, up to 3 years after RP	To define the incidence of PD in men who had RP and determine possible predictors of PD development after RP	PD Incidence 15,9 % in RP population PD developed on average at 13,9 Months Mean curvature magnitude was 31 Degrees PD after a RP is more prevalent in young white men

Figures

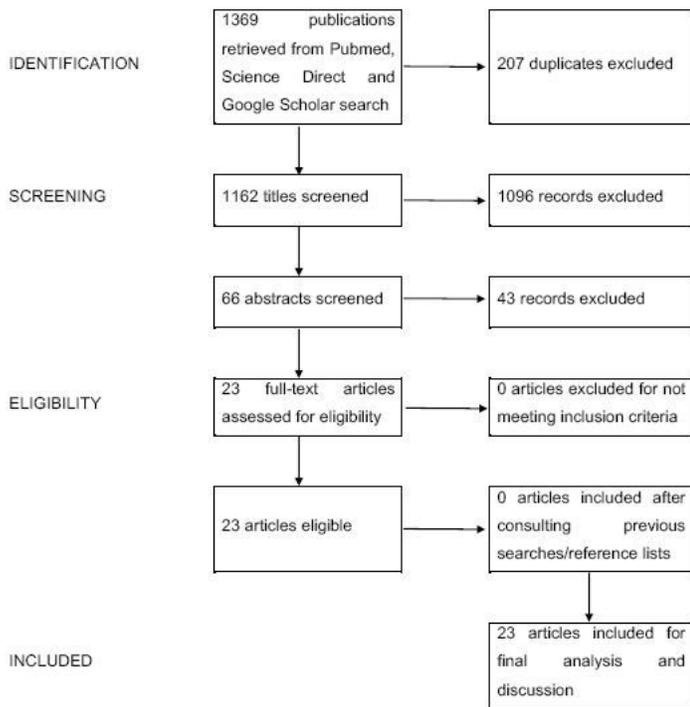
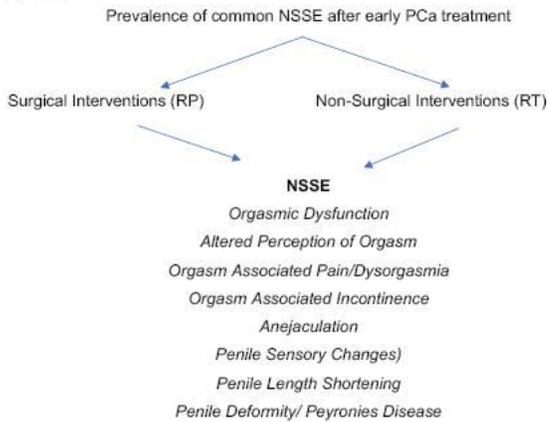


Figure 1

Study Selection Process

Objective A



Objective B

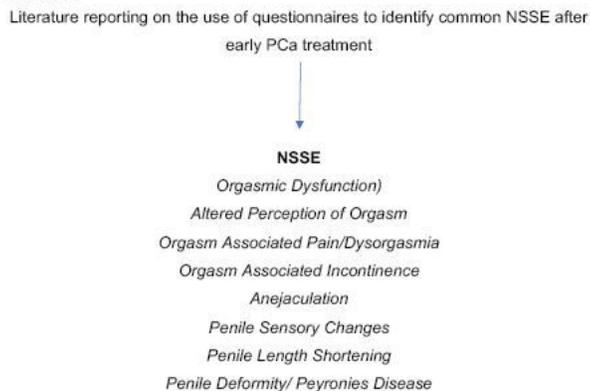


Figure 2

Study Objectives

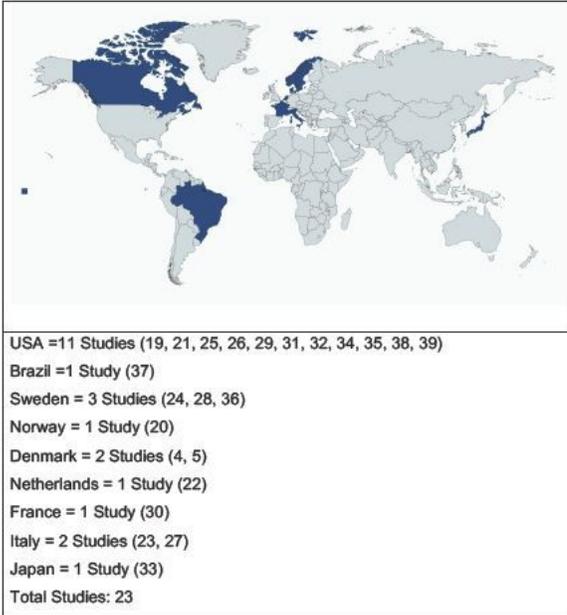


Figure 3

Distribution of Study Origin

Supplementary Files

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