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GUIDELINES FOR SEXUAL HEALTH CARE FOR PROSTATE CANCER PATIENTS

RECOMMENDATIONS OF AN INTERNATIONAL PANEL

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Table of Contents

ABSTRACT 6

PREFACE 7

STATEMENT LIST 8

SECTION 1: PURPOSE 16

SECTION 2: METHODOLOGY 18

SECTION 3: INTRODUCTION 24

SECTION 4: GUIDING PRINCIPLES 30

SECTION 5: GUIDELINE STATEMENTS SUPPORTING WITH EVIDENCE 33

I. Counseling Patients and Partners about the Impact of Prostate Cancer Therapies on the Biopsychosocial Aspects of Sexuality 34

II. Counseling Patients and Partners about the Specific Impact of Individual Prostate Cancer Therapies on Sexual Function 41

III. Assessment of Sexual Function and Sexual Distress 60

IV. Lifestyle Modification 67

V. Psychosocial Treatment 68

VI. Biomedical Treatment 77

VII. Lifestyle Modification Strategies 99

VIII. Clinician Education and Training 100

IX. Healthcare Programs and Systems 102

SECTION 6: Future Directions 106

Related Resources

Clinical Guidelines Infographic
truenorth.movember.com/images/assets/GuidelinesSummary.pdf

Guideline Publication J Sex Med 2022
academic.oup.com/jsm/article-abstract/19/11/1655/7012851

Patient Sexual Health Guidelines
truenorth.movember.com/images/assets/SexualHealthGuidelines-Patient.pdf

True North Sex and Intimacy Guide
truenorth.movember.com/sex-after-prostate-cancer

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Peer Review and Document Approval

An integral part of the guideline development process at Movember is the external peer review. The Panel conducted a thorough peer review process to ensure that the document was reviewed by multidisciplinary experts in Prostate Cancer oncological and sexual health care. A call to suggested reviewers was sent out via e-mail on April 8, 2021 to allow interested parties to request a copy of the document for review. The draft guideline document was distributed to 39 interested external reviewers; 28 external reviewers (26 peer reviewers and 2 patients) provided comments. All peer review comments were sent to the Panel leads for review. Following comment review, the Panel revised the draft as needed.

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Abstract

Purpose: This guideline informs practitioners, patients and partners about the impact of prostate cancer therapies (PCT) on sexual health of patients and partners, and on their sexual relationships, as well as about biopsychosocial rehabilitation strategies available in prostate cancer survivorship.

Methods:
An international panel of experts and a guideline methodologist participated in the development of the guideline. A systematic review of the literature using the Ovid MEDLINE, Scopus, CINAHL, PsychINFO, LGBT Life, and Embase databases (search dates 1/1/1995 through 4/30/2022) was conducted to identify peer-reviewed publications relevant to the impact of prostate cancer therapies, the assessment of prostate cancer therapy consequences for sexuality and sexual function, and treatments for the sexual sequelae of prostate cancer therapies. Search words are included in Appendix A. The reference lists from included articles and review articles were searched to identify additional potentially relevant studies and expert panel members contributed additional key citations. The review yielded an evidence base of 610 articles after application of inclusion/exclusion criteria. These publications were used to create the guideline statements. Evidence assessments and recommendations followed the nomenclature of the American Urological Association. If sufficient evidence existed, then the body of evidence for a particular treatment was assigned a strength rating of **A high certainty, B moderate certainty,** or **C low certainty**. Evidence-based statements of Strong, Moderate, or Conditional Recommendation, which can be supported by any body of evidence strength, were developed based on benefits and risks/burdens to men and their partners. Additional information is provided as Clinical Principles and Expert Opinion when insufficient evidence existed.

Results:
The guideline is contextualized within cultural, ethnic and racial diversity. The needs of individuals with diverse sexual orientations and gender identities are also recognized. Forty-seven statements were generated guided by a theoretical model of sexual recovery after PCT and by principles that promote clinician-initiated discussion of realistic expectations of sexual outcomes and mitigation of sexual side effects through biopsychosocial rehabilitation. The statements focus on counseling about the impact of PCT on sexuality and treatment of changes in the psychosexual and relationships domains (9 statements), sexual function domain (26 statements), fertility (2 statements) and lifestyle modifications (2 statements). The guideline includes statements about sexual function and sexual distress assessment (4 statements), the importance of provider sexual health education and training (1 statement), and about the challenges to providing sexual health care for PC survivors and their partners in diverse health care systems (3 statements).

Conclusions:
The guideline documents the distressing sexual sequelae of prostate cancer therapies and makes evidence-based recommendations for sexual rehabilitation in prostate cancer survivorship. Areas for future research are also outlined.

Preface

Sexual dysfunction is the most commonly reported health-related quality of life outcome following therapies for prostate cancer. The preservation of sexual function and the treatment of and recovery from sexual dysfunction, therefore, should be central to survivorship care for men with prostate cancer, as well as for their partners. This guideline is an international collaboration among sexual health clinicians and researchers, physicians (urologists, oncologists, radiation oncologists, a psychiatrist and a primary care provider), nurses, psychologists, physical therapists, social workers, and prostate cancer survivors and their partners. It critically evaluates the available literature on all aspects of sexual dysfunction and recovery.

The impact of sexual dysfunction is complex, and differentially affects patients and their partners based on age, race, sexual orientation, gender identity, personal relationships, medical comorbidities, treatment modality, and cultural environment. The available literature on sexual dysfunction following prostate cancer therapies is, accordingly, heterogeneous. The authors of this guideline have contextualized this heterogeneity as a strength in order to craft a guideline that is inclusive for all prostate cancer survivors, and their partners. The term 'biopsychosocial' will be applied throughout the guideline to imply that all domains of sexuality affected by prostate cancer and associated therapies must be understood, assessed and may need to be treated. Sexuality refers to the person's physiologic function, psychological response to the treatment-related sexual side-effects, the sexual relationship and the cultural, ethnic and racial context within which sexual expression is experienced. The authors intend that the guideline will provide information to clinicians, patients, and partners regarding the biopsychosocial impact of prostate cancer therapies on the patient's sexual function, on the partner, and on the sexual relationship; to outline a clinical strategy for the assessment of the sexual consequences of prostate cancer therapies; and, to provide an evidence-based patient- and partner-centered framework for treatment of the sexual consequences of prostate cancer therapies.



The authors also intend that the guideline will provide a tool to engage patients in taking ownership of their sexual recovery and a framework to facilitate shared decision-making between clinicians, patients and partners around this important survivorship goal.

The authors recognize that in some parts of the world, and specifically in the US, guidance for screening for prostate cancer often considers the importance of preventing over-treatment in order to protect patients' quality of life, including sexual function. It is an important aspect of the prostate cancer care continuum and there are variations in the way screening proceeds in different countries. A discussion of prostate cancer screening falls outside of the scope of this guideline. Additionally, this guideline does not specifically address sexual function amongst prostate cancer patients treated with active surveillance. While the diagnosis of prostate cancer and recurrent biopsies and imaging alone during active surveillance may have a psychogenic impact on sexual function, this effect is not yet well studied in the literature.

Guideline statements:

I. Counseling Patients and Partners about the Impact of Prostate Cancer Therapies on the Biopsychosocial Aspects of Sexuality

STATEMENT 1: A clinician-initiated discussion should be conducted with the patient and the partner (if partnered and culturally appropriate) about realistic expectations of the impact of prostate cancer therapy on the patient's sexual function, the partner's sexual experience, and the couples' sexual relationship. The clinician should promote openness and inclusivity, consider cultural context, and tailor counseling to the specific needs of patients who are heterosexual, gay, bisexual, identify as men who have sex with men, transgender women and gender non-conforming individuals. *(Strong Recommendation; Evidence Strength Grade C)*

STATEMENT 2: Patients and partners should be advised that biopsychosocial treatment for sexual problems can mitigate sexual dysfunctions and lead to the recovery of sexual intimacy. *(Strong Recommendation; Evidence Strength Grade C)*

STATEMENT 3: Patients and partners should be advised that psychological distress, including grief and mourning about sexual losses, resulting from the sexual side-effects of prostate cancer therapies, can be experienced after prostate cancer therapies, and that distress can be mitigated with appropriate biopsychosocial rehabilitation strategies. *(Strong Recommendation; Evidence Strength Grade C)*



Guideline statements:

II. Counseling Patients and Partners about the Specific Impact of Individual Prostate Cancer Therapies on Sexual Function

STATEMENT 4: Patients and partners should be counseled that all prostate cancer therapies may result in the patient's short-term and long-term erectile dysfunction. *(Strong Recommendation; Evidence Strength Grade B).*

STATEMENT 5: Patients and partners should be counseled that patients treated with radical prostatectomy have different trajectories of sexual function decline and potential recovery compared to patients treated with radiotherapy. *(Moderate Recommendation; Evidence Strength Grade C)*

STATEMENT 6: Patients and partners should be counseled that after prostate cancer therapies, most patients do not return to their pre-treatment erectile function levels. *(Strong Recommendation; Evidence Strength Grade B).*

STATEMENT 7: Patients and partners should be advised that pre-existing erectile dysfunction is associated with a higher risk of post-treatment erectile dysfunction after radical prostatectomy regardless of the surgical technique used, and after radiotherapy, regardless of the type of radiation employed. *(Strong Recommendation; Evidence Strength Grade B)*

STATEMENT 8: Patients and partners should be informed there is no clear evidence supporting an advantage of robotic, laparoscopic or open radical prostatectomy in terms of post-operative erectile function outcomes. *(Moderate Recommendation; Evidence Strength Grade C)*

STATEMENT 9: Patients and partners should be counseled that both prostatectomy and radiation therapy may be associated with orgasmic pain, decreased sexual desire, anodyspareunia during anal intercourse, and changes in ejaculatory function. Prostatectomy results in immediate and complete loss of ejaculate volume, while radiation therapy is associated with a more gradual decline and variable reduction in ejaculate volume. *(Moderate Recommendation; Evidence Strength Grade C)*

STATEMENT 10: Patients and partners should be counseled that sexual arousal incontinence and climacturia may occur after radical prostatectomy with the potential to recover with recovery of urinary control. *(Strong Recommendation, Evidence Strength Grade C)*

STATEMENT 11: Patients and partners should be counseled that penile length and girth/volume loss may occur after radical prostatectomy. *(Moderate Recommendation, Evidence Strength Grade C)*

STATEMENT 12: Patients and partners should be informed that radical prostatectomy may be associated with an increased risk of the development of penile curvature (Peyronie's disease; PD). *(Conditional Recommendation, Evidence Strength Grade C)*

STATEMENT 13: Patients and partners should be counseled regarding the diverse impacts of androgen deprivation therapy (ADT) (as a primary or as an adjuvant ADT) on sexual desire, erectile function, penile girth and length, ejaculatory function, orgasmic function and couples' intimacy. *(Strong Recommendation; Evidence Strength Grade C)*

STATEMENT 14: Patients and partners should be counseled that patients treated with combined ADT and radiotherapy are at risk for the cumulative sexual side effects associated with both ADT and radiotherapy. *(Strong Recommendation, Evidence Strength Grade C)*

STATEMENT 15: Prior to undergoing prostate cancer therapies, clinicians should routinely ask prostate cancer patients (regardless of age) and their partners if future fertility is desired. *(Moderate Recommendation, Evidence Strength Grade C)*

STATEMENT 16: Patients interested in future fertility should be counseled that prostate cancer therapies may negatively affect their fertility potential. These patients could consider pre-treatment sperm banking and referral to a reproductive specialist as availability of assisted reproductive techniques and financial and cultural considerations allow. *(Moderate Recommendation, Evidence Strength Grade C)*

Guideline statements:

III. Assessment of Sexual Function and Sexual Distress

STATEMENT 17: Clinicians should offer screening and assessment prior to prostate cancer therapy regularly throughout follow-up, tailored to cultural context, sexual orientation, and gender identity. *(Clinical Principle)*

STATEMENT 18: In both pre and post prostate cancer therapy assessments, clinicians should pay attention to the presence of erectile dysfunction, low sexual satisfaction [including orgasmic sensation, lack of orgasm (anorgasmia), painful orgasm (dysorgasmia) and orgasm-associated urinary incontinence (climacturia), sexual arousal incontinence, changes in penile shape, girth, length or size, anodyspareunia, curvature, couples' sexual concerns and avoidance or cessation of sexual activity, and couples' sexual concerns]. *(Strong Recommendation, Evidence Strength C)*

STATEMENT 19: Patients and partners should be counseled that an assessment of the partner's sexual function can help plan treatment designed to support couples' recovery of sexual intimacy. *(Clinical Principle)*

STATEMENT 20: Clinicians should use validated Patient Reported Outcome measures whenever appropriate or whenever possible, to assess patients' sexual function and possibly partners' sexual function, as well as sexual distress, based on a clinical assessment of the patients' and partners' goal for sexual recovery. *(Clinical Principle)*



Guideline statements:

IV. Lifestyle Modification

STATEMENT 21: Lifestyle modification should be recommended to patients to optimize their overall and sexual health, including avoiding smoking, engaging in physical activity, weight loss, increasing consumption of healthful plant-based foods, and reducing consumption of red and processed meat. *(Clinical Principle)*

V. Psychosocial Treatment

STATEMENT 22: Clinicians should provide education, individualized sexual rehabilitation, and psychosexual support to patients and partners across the entire to survivorship continuum, tailored to: prostate cancer therapy type; partnership status, cultural, ethnic, and racial context, sexual orientation, and gender identity. *(Strong Recommendation; Evidence Strength Grade C)*

STATEMENT 23: Clinicians should normalize grief as a typical reaction to sexual losses and encourage patients and partners to whom sexual recovery is important to pursue sexual intimacy despite sexual losses. *(Strong Recommendation; Evidence Strength Grade C)*

STATEMENT 24: Clinicians should include the partner, if both the patient and partner agree, and, provide support for couples coping with the sexual side-effects of prostate cancer therapy both directly and through referral for psychosexual treatment. *(Strong Recommendation, Evidence Strength Grade C)*

STATEMENT 25: Clinicians should support patients who are gay or bisexual, men who have sex with men, transgender women and gender non-conforming patients and their partners with information relevant to their sexual experience and guide them towards finding meaningful support resources. (*Expert Opinion)*

STATEMENT 26: Clinicians should refer patients, partners, and couples for whom education and support are insufficient for specialty psychosexual treatment. *(Clinical Principle)*

STATEMENT 27: Clinicians should make patients and partners aware of group interventions and digital health/telemedicine methodologies that can increase access to sexual health support in prostate cancer survivorship. *(Moderate Recommendation, Evidence Strength Grade C)*

Guideline statements:

VI. Biomedical Treatment

STATEMENT 28: Clinicians should consider nerve-sparing surgical treatment options, when available and oncologically safe, irrespective of baseline erectile function. *(Moderate Recommendation; Evidence Strength Grade C)*

Penile Rehabilitation

STATEMENT 29: Clinicians should define the intent and goals of penile rehabilitation strategies on an individualized basis, including preservation of penile length, maintenance of corporal tissue quality, and early patient engagement in sexual recovery. Penile rehabilitation should not be equated with treatment for the recovery of unassisted erectile function. *(Clinical Principle)*

STATEMENT 30: Clinicians should counsel patients that use of phosphodiesterase type 5 inhibitors (PDE5i) for penile rehabilitation in the early post-prostatectomy period (up to 45 days post-surgery) does not improve rates of unassisted and PDE5i-assisted erectile function recovery at 12 months compared to placebo. *(Moderate Recommendation, Evidence Strength C)*

STATEMENT 31: Clinicians should advise patients there is limited evidence to determine the benefit of non-PDE5i approaches for penile rehabilitation, in order to promote recovery of erectile dysfunction. *(Moderate Recommendation, Evidence Strength Grade C)*

STATEMENT 32: Patients and partners should be counseled that there is insufficient evidence to definitively support penile rehabilitation with PDE5 inhibitors for the prevention of penile volume loss. *(Conditional Recommendation, Evidence Strength Grade C)*

STATEMENT 33: Clinicians should counsel patients that there is insufficient evidence to determine the benefit of PDE5i use after radiation therapy as a strategy for penile rehabilitation. *(Conditional Recommendation, Evidence Strength C)*

Erectile Dysfunction Treatments

STATEMENT 34: Clinicians should support patients' use of pro-erectile aids, as well as non-penetrative sexual activity, if they wish to continue to engage in sexual activity. *(Strong Recommendation; Evidence Strength Grade C)*

STATEMENT 35: Clinicians should discuss all available erectile function treatment options with patients following all modalities of prostate cancer therapy, including PDE5i, intraurethral suppositories, intracavernosal injections (ICI), vacuum erection devices (VED), penile traction therapy, and penile implants. Clinicians should tailor recommendations based on patient preference, efficacy, and phase of sexual function recovery. This discussion should address benefits, risks, and contraindications associated with each option, as well as patient and partner goals. *(Clinical Principle)*

STATEMENT 36: Clinicians should inform patients with persistent erectile dysfunction after completion of prostate cancer therapies about the potential benefits and risks of penile implant surgery. *(Moderate Recommendation, Evidence Strength Grade C)*

Guideline statements:

VI. Biomedical Treatment (Continued)

Additional Sexual Dysfunction Treatments

STATEMENT 37: If identified, altered orgasmic sensation, difficulty reaching orgasm or anorgasmia can be managed using a biopsychosocial approach. *(Expert Opinion)*

STATEMENT 38: Persistent, bothersome dysorgasmia may be treated using alpha-adrenergic blockers. *(Moderate Recommendation, Evidence Strength Grade C)*

STATEMENT 39: Patients and partners should be counseled regarding management strategies for bothersome sexual incontinence (including sexual arousal incontinence and climacturia), including psychological reframing. *(Clinical Principle)*

STATEMENT 40: Patients should be counseled that there are insufficient data regarding the efficacy of pelvic-floor rehabilitation, penile tension loop, a male sling operation or placement of an artificial urinary sphincter for the management of sexual incontinence (including sexual arousal incontinence and climacturia). *(Conditional Recommendation, Evidence Strength Grade C)*

STATEMENT 41: Clinicians may discuss the risks and benefits of testosterone therapy to improve low sexual desire in hypogonadal men following prostate cancer treatment. (Moderate Recommendation, Evidence Strength Grade C)

STATEMENT 42: Clinicians should counsel patients that there are inadequate data to quantify the risks versus benefits regarding testosterone therapy to treat low sexual desire in men with treated, or active, non-metastatic prostate cancer. *(Conditional Recommendation, Evidence Strength Grade C)*

VII. Lifestyle Modification Strategies

STATEMENT 43: Patients and partners should be informed about the importance of and benefits of exercise for sexual health as a component of medical management related to ADT. *(Moderate Recommendation; Evidence Strength Grade C)*

Guideline statements:

VIII. Clinician Education and Training

STATEMENT 44: Clinicians should undergo sexual health education in interprofessional groups using case based/reflective learning approaches, adopting a biopsychosocial lens and incorporating attention to ethnic and racial diversity and to sexual minorities. *(Strong Recommendation; Evidence Strength Grade C)*

IX. Healthcare Programs and Systems

STATEMENT 45: Providers and healthcare systems should develop culturally appropriate materials for counseling patients and their partners regarding to the impact of prostate cancer therapies on sexual health. *(Moderate Recommendation; Evidence Strength Grade C)*

STATEMENT 46: Patient education programs about sexual recovery after prostate cancer therapies should be tailored to reflect local cultural influences, based on resources available in that region, conceptualization of sexual recovery, and of the priorities in that region. *(Expert Opinion)*

STATEMENT 47: All insurance providers should cover the treatment of sexual dysfunctions secondary to prostate cancer therapies in order to validate this clinically important aspect of prostate cancer care and to reduce disparities in access to care. *(Clinical Principle)*



01 PURPOSE

SECTION 1:
Purpose

The purpose of this international guideline is to: summarize evidence regarding the biopsychosocial impact of prostate cancer therapies on sexuality; provide an evidence-informed framework for assessing sexual dysfunction and sexual concerns of men and their partners after prostate cancer therapy; and provide practical, evidence-based guidance for the delivery of sexual rehabilitation care.

The Panel notes that there is a paucity of evidence in some important areas of care. In order to provide guidance where evidence is absent or insufficient, the Panel has leveraged its cumulative expertise and clinical experience.

The guideline was created for both primary care providers and specialists who care for prostate cancer patients and their partners. For clinicians, it provides a roadmap for assessing patients' and partners' sexual concerns before and after prostate cancer therapy, supporting patients and partners in choosing treatments for sexual recovery, and measuring outcomes important to patients and partners so that progress toward recovery of sexual function and sexual intimacy can be assessed.

The guideline is informed by the available evidence and by clinical expertise regarding the role of cultural, ethnic and racial context, sexual orientation and gender identity in patient counseling, assessment, treatment, and outcomes measurement.



02 METHODOLOGY

SECTION 2:
Methodology

Purpose of Review

The purpose of this systematic review was to support the development of a guideline to address patient and partner counseling regarding the impact of prostate cancer therapies, the assessment of prostate cancer therapies' consequences for sexuality and sexual function, and treatments for the sexual sequelae of prostate cancer therapies. An additional goal was to delineate the evidence gaps in the treatment of the physical/functional and psychosocial consequences for men and partners of prostate cancer diagnosis and treatment.

Search Strategy

Literature searches (date range 1/1/1995 to 4/30/2022) using key words and controlled vocabulary relevant to the specified questions were carried out using Ovid MEDLINE, Scopus, CINAHL, PsychINFO, LGBT Life, and Embase (See Appendix A for search words). In addition to the literature searches, the reference lists from included articles and review articles were searched to identify additional potentially relevant studies, and expert panel members contributed key citations. Titles and abstracts were imported into a bibliographic database, reviewed by the methodologist (MF) and panel members for relevance (DW and section leads), and preliminary exclusions were made. Articles that appeared to be relevant then were retrieved in full-text form for more detailed examination.

Inclusion/Exclusion Criteria

Provisionally included articles were individual studies or systematic reviews (with or without accompanying meta-analyses) that reported findings relevant to the review questions; no exclusions were made based on study design. Additional exclusions were made after full-text review. Studies were excluded for reasons including: topic not addressed in the guideline; outcomes combined across different treatments; lack of baseline or follow-up data or lack of sexual function data; inadequate sample size; article not available in English; methods dated or historical; abstract only without a full-text publication; non-systematic review or commentary. Multiple reports on the same patient group were carefully examined to prevent inclusion of redundant information.

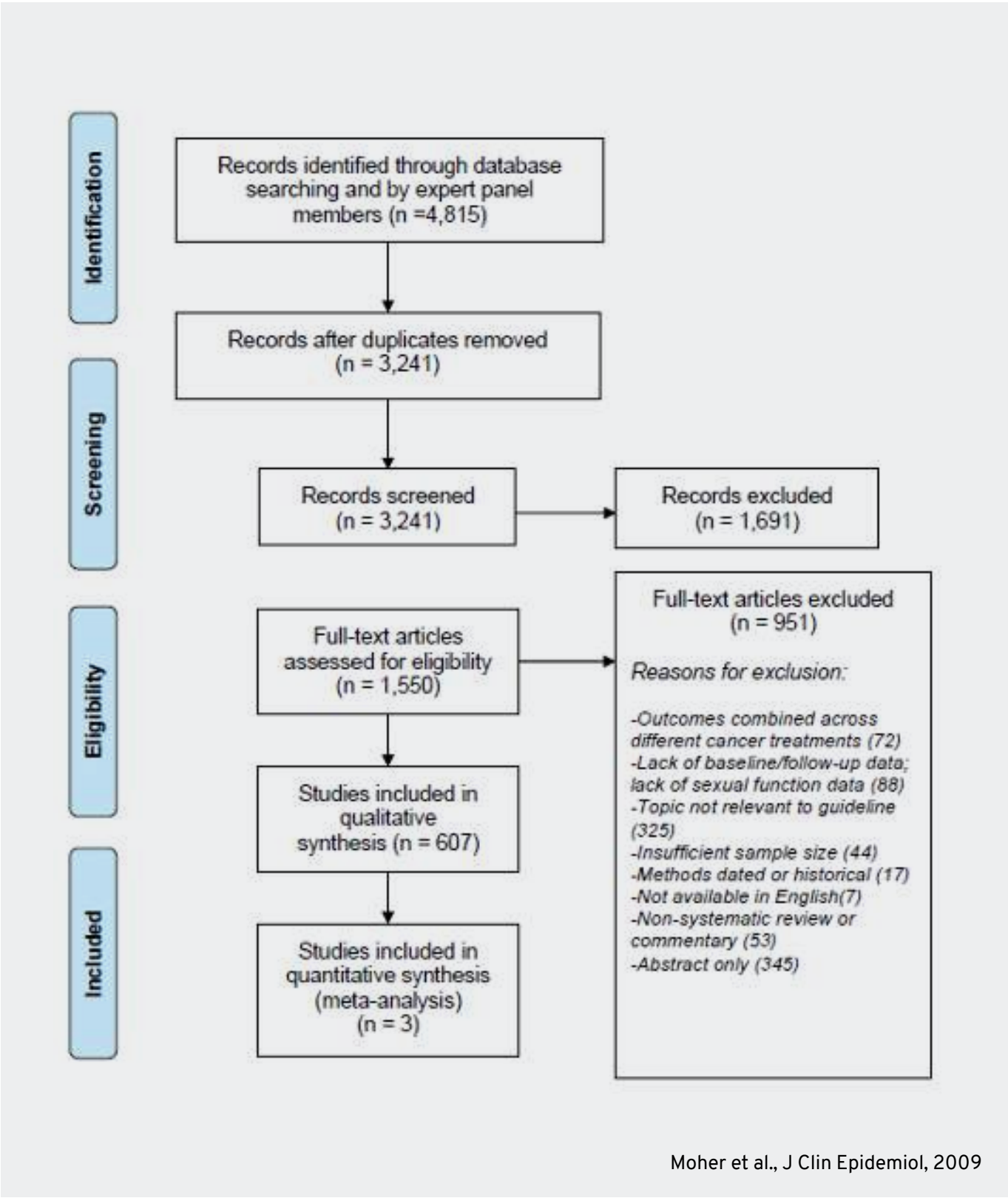
In order to focus on articles that could provide the most robust information, additional inclusion criteria were applied to studies reporting the clinical outcomes of prostate cancer therapies. Articles examining sexual function outcomes had to meet the following additional inclusion criteria:

1. Report outcomes associated with prostatectomy, external beam radiation, or brachytherapy alone or in combination with androgen deprivation therapy (ADT) or ADT alone.
2. Report baseline sexual function data as well as follow up sexual function data.
3. Have a minimum sample size of 100 men at study initiation. For studies that compared treatments, the number of men at study initiation across treatments had to be at least 100.
4. Have a minimum follow-up duration of one year to assess sexual outcomes.

Results

In our review, we followed [CE1] the Cochrane Handbook for Systematic Reviews of Interventions; we diagrammed study selection based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; see Figure 1.).[1] The search strategies and additional efforts to identify relevant citations yielded 3,213 records after removal of duplicates. Of these records, 610 met inclusion criteria.

FIGURE 1:



Moher et al., J Clin Epidemiol, 2009

SECTION 2:
Methodology

Study Quality Assessment

Systematic reviews and meta-analyses

Published systematic reviews (SRs), with or without meta-analyses, were rated using A Measurement Tool to Assessment Systematic Reviews (AMSTAR).[2] The AMSTAR instrument measures the quality of systematic reviews based on 11 domains. It generates a score from 0 to 11; the higher the score, the better the quality of the review. The AMSTAR tool focuses on the validity of the processes used to assemble the review and the appropriateness of the meta-analytic methods if a meta-analysis was performed.

Randomized Trials

Randomized trials were rated using the Cochrane Collaboration's Risk of Bias Tool.[3] The Risk of Bias tool addresses the adequacy of randomization processes, blinding procedures, whether incomplete outcome data were satisfactorily explained, whether outcomes were selectively reported, and whether other sources of bias are potentially present in the study. The tool yields a rating of low risk of bias (high quality), unclear risk of bias, or high risk of bias (low quality).

Observational Studies

Observational studies included prospective cohort designs and case series (single- and multi-institution) as well as retrospective chart reviews. There is no standardized and accepted method for assessing quality of this type of design. The design is inherently limited by the absence of randomization that can result in biases that limit causal attributions. The quality of individual observational studies, therefore, was not assessed.

Meta-analytic Methods

If appropriate and feasible, then meta-analyses were performed using RevMan 5.3 with a random effects model. Heterogeneity of pooled studies was evaluated using the I^2 statistic. Appropriate meta-analyses are those in which the choice to pool studies is valid; that is, patients and interventions across studies are similar enough that pooling is conceptually coherent and will yield a meaningful result.[4] Feasible meta-analyses are those in which all or most of the studies relevant to a given question provided sufficient information such that pooling is possible.

Data Extraction

For individual studies, data were extracted by trained extractors using a standardized electronic template and verified against the full-text article by the methodologist.

Body of Evidence Strength (ES)

Evidence-based guidelines link the quality of a body of evidence for a specific question to the strength of a particular guideline statement.

The categorization of evidence strength (ES) is conceptually distinct from the quality of individual studies. Evidence strength refers to the body of evidence available for a particular question and includes consideration of: study design; individual study quality; whether the patients, treatments and settings were similar across studies; the consistency of findings across studies; the adequacy of sample sizes and follow-up duration; and the generalizability of samples, settings, and treatments for the purposes of the guideline. It is possible to have a group of studies that individually are of high-quality but that as a group constitute poor evidence because they measured constructs that are not comparable, they did not address issues important to the guideline or because they provided contradictory findings.

There are many systems for categorizing body of evidence strength and they apply similar principles. Assessment of evidence begins with a consideration of study designs and then is adjusted based on other factors such as the integrity of methods used to conduct randomized controlled trials, the consistency of findings across studies, etc. This document uses the American Urological Association's (AUA) system *(Burnett AL, Nehra A, Breau RH et al: Erectile dysfunction: AUA guideline. J Urol 2018; 200: 633).* This system, and the way in which it links to statement type (see below) is based on the principles of GRADE and is similar to the systems used by other evidence-based guideline producing organizations (i.e., the American College of Chest Physicians) (Table 1.).

Evidence assessments and recommendations followed the nomenclature of the American Urological Association. This system categorizes body of evidence strength as Grade A (well-conducted and highly-generalizable RCTs or exceptionally strong observational studies with consistent findings), Grade B (RCTs with some weaknesses of procedure or generalizability or moderately strong observational studies with consistent findings), or Grade C (RCTs with serious deficiencies of procedure or generalizability or extremely small sample sizes or observational studies that are inconsistent, have small sample sizes, or have other problems that potentially confound interpretation of data). By definition, Grade A evidence is evidence about which there is a high level of certainty, Grade B evidence is evidence about which there is a moderate level of certainty, and Grade C evidence is evidence about which there is a low level of certainty.

SECTION 2:
Methodology

Linking Statement Type to Evidence Strength

Statement type is explicitly linked to body of evidence strength, level of certainty, magnitude of benefit or risk/burdens, and the judgment regarding the balance between benefits and risks/burdens (see Table 1. below).

- STRONG RECOMMENDATIONS are directive statements that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be undertaken because net benefit or net harm is substantial.
- MODERATE RECOMMENDATIONS are directive statements that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be undertaken because net benefit or net harm is moderate.
- CONDITIONAL RECOMMENDATIONS are non-directive statements used when the evidence indicates that there is no apparent net benefit or harm or when the balance between benefits and risks/burden is unclear.

All three statement types may be supported by any body of evidence strength grade.

- Body of evidence strength **Grade A** in support of a Strong or Moderate Recommendation indicates that the statement can be applied to most patients in most circumstances and that future research is **unlikely to change confidence.**
- Body of evidence strength **Grade B** in support of a Strong or Moderate Recommendation indicates that the statement can be applied to most patients in most circumstances, but **better evidence could change confidence.**
- Body of evidence strength **Grade C** in support of a Strong or Moderate Recommendation indicates that the statement can be applied to most patients in most circumstances but **better evidence is likely to change confidence.**
- Conditional Recommendations also can be supported by any body of evidence strength. When body of evidence strength is Grade A, the statement indicates that benefits and risks/burdens appear balanced, the best action depends on patient circumstances, and future research is **unlikely to change confidence.** When body of evidence strength Grade B is used, benefits and risks/burdens appear balanced, the best action also depends on individual patient circumstances and better evidence **could change confidence.** When body of evidence strength Grade C is used, there is uncertainty regarding the balance between benefits and risks/burdens, alternative strategies may be equally reasonable, and better evidence is **likely to change confidence**

Frequently there are areas relevant to include in the guideline for which there is little or no evidence. In these circumstances, guidance is provided based on principles widely accepted in clinical care and/or as expert opinion. In this system, these categories are referred to as Clinical Principles or Expert Opinion. Clinical Principles are statements that address a component of clinical care about which there is virtually universal agreement, such as the need to take a careful patient history; there may or may not be evidence to support Clinical Principles.

Expert Opinion statements are consensus statements based on the guideline-writing group's clinical training, experience, knowledge, and judgment; Expert Opinion statements are generally used when there is little or no relevant evidence. Panel experts reviewed these statements regularly and provided feedback. Differences of opinion were resolved by consensus.

Process

The Guideline for Sexual Health Care in Prostate Cancer Survivorship Panel was created in 2017 in the context of the Movember TrueNTH initiative that focused on prostate cancer survivorship interventions. The panel chair and co-chair (Daniela Wittmann, PhD, MSW and Eilis McCaughan, PhD, RN) identified Panel members with specific expertise. The Panel included two patients and three partners who contributed their experience and perspective. The Guideline underwent a thorough peer review process. The draft guidelines document was distributed to 39 external reviewers. Of those, 28 (26 peer reviewers, 2 patients) returned their reviews. The Panel leads reviewed and distributed comments that had been submitted and discussed to the full Panel, then revised the draft as needed. Movember funds 10% of the chair's salary for leading an international work group that develops sexual health interventions for prostate cancer survivors and their partners. Panel members received no remuneration for their work.

SECTION 2:
Methodology

TABLE 1. Nomenclature Linking Statement Type to Level of Certainty, Magnitude of Benefit or Risk/ Burden, and Body of Evidence Strength – American Urological Association.

This table is present in all the guidelines of the American Urological Association and is reproduced here with permission.

	Evidence Strength A (High Certainty)	Evidence Strength B (Moderate Certainty)	Evidence Strength C (Low Certainty)
STRONG RECOMMENDATION (Net benefit or harm substantial)	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) is substantial Applies to most patients in most circumstances and future research is unlikely to change confidence	Benefits > Risks/ Burdens (or vice versa) Net benefit (or net harm) is substantial Applies to most patients in most circumstances but better evidence could change confidence	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) appears substantial Applies to most patients in most circumstances but better evidence is likely to change confidence (rarely used to support a Strong Recommendation)
MODERATE RECOMMENDATION (Net benefit or harm moderate)	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) is substantial Applies to most patients in most circumstances and future research is unlikely to change confidence	Benefits > Risks/ Burdens (or vice versa) Net benefit (or net harm) is moderate Applies to most patients in most circumstances but better evidence could change confidence	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) appears moderate Applies to most patients in most circumstances but better evidence is likely to change confidence
CONDITIONAL RECOMMENDATION (No apparent net benefit or harm)	Benefits = Risks/Burdens Best action depends on individual patient circumstances Future research unlikely to change confidence	Benefits = Risks/ Burdens Best action appears to depend on individual patient circumstances Better evidence could change confidence	Balance between Benefits & Risks/Burdens unclear Alternative strategies may be equally reasonable Better evidence likely to change confidence
CLINICAL PRINCIPLE	A statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature		
EXPERT OPINION	A statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there is no evidence		



03 INTRODUCTION

SECTION 3:
Introduction

Background

Prostate cancer is the second most common solid tumor cancer in men worldwide.[5] In 2018, approximately 1.27 million men were estimated to be newly diagnosed.[6] Significant national and regional variation exists with regard to diagnosis timing, the most likely treatment type, and risk of dying from the disease. The highest incidence of prostate cancer occurs in Northern and Western Europe, North America, Australia, and New Zealand. Immigration patterns can result in high incidences among specific cultural and ethnic groups in other countries. For example, the higher incidences among men of Afro-Caribbean and West African descent reported in Canada can be traced to the high incidence of prostate cancer in those particular regions.[7 8] The availability of prostate-specific antigen (PSA) screening allows early diagnosis while the cancer is still localized; early treatment is associated with long-term survival in most cases. However, disparity in resources, in the availability of PSA testing, and in culture-specific health beliefs, lifestyle, and other social and environmental conditions can lead to large differences in morbidity and mortality.[9] For example, in low and middle income countries, prostate cancer is diagnosed in more advanced stages. This later diagnosis is believed to result in part from the stigma associated with cancer, as well as a lack of cultural acceptance of sexual dysfunction that may result from prostate cancer treatment.[10]

Regardless of the timing of diagnosis, most men with localized prostate cancer eventually undergo treatment with surgery, radiation alone, or radiation with hormonal therapy. Radiation, with or without hormonal therapy, is also utilized in the treatment of men with biochemical recurrence. Men with metastatic disease usually receive systemic treatment with hormonal therapy and chemotherapy.

All treatments for prostate cancer have sexual side-effects that affect men's quality of life.[11-13] Men and their partners report consistently that these side-effects cause distress and studies indicate that sexual dysfunction after prostate cancer treatment disrupts relationships.[14-23] Yet, despite recommendations in countless publications that assistance for sexual issues should be available, there is little support provided to men and their partners, even in countries with greater resource availability such as Australia, Sweden, France, the United States, Canada, the United Kingdom, Kenya, Nigeria, Japan and others.[24-30] We assume that lack of sexual dysfunction support also is present in countries where research has not yet been conducted. There is some evidence in developing countries that men search for traditional remedies for sexual dysfunction rather than for medical or psychosocial treatments.[31]

If treated early, prostate cancer is a highly survivable disease in most cases. In the US, a nearly 99% 5-year survival rate is attainable for men treated for localized disease (limited to the prostate) or regional disease (spread outside the prostate to nearby structures or lymph nodes). Once disease has spread to other body regions (distant disease), approximately 30% of men average a 5-year survival rate.[32] These survival outcomes are similar in other developed countries, but are lower in developing countries. The highest death rate following prostate cancer diagnosis is reported in Africa where men are diagnosed at a later stage.[6] The global disparity in outcomes may be attributed in part to availability of early detection via PSA testing. PSA testing has been implemented aggressively in North America, Australia, and New Zealand and less aggressively in Western European countries. PSA testing is increasing in Africa and other developing countries, although barriers to testing such as beliefs, education, lack of knowledge, and distrust of medical authorities persist.[33-35] AAccess to treatments also is limited in the developing world, resulting in shorter life spans for men with prostate cancer.[36]

Men live in prostate cancer survivorship for varying numbers of years, based on the stage and aggressiveness of the disease, access to therapies, type of therapy received, and other individual health conditions. According to the United States National Cancer Institute, "an individual is considered a cancer survivor from the time of diagnosis, through the balance of his or her life. There are many types of survivors, including those living with cancer and those free of cancer. This term is meant to capture a population of those with a history of cancer rather than to provide a label that may or may not resonate with individuals."[37] Cancer survivorship "covers the physical, psychosocial, and economic issues of cancer, beyond the diagnosis and treatment phases. Survivorship includes issues related to the ability to get health care and follow-up treatment, late effects of treatment, second cancers, and quality of life. Family members, friends, and caregivers are also considered part of the survivorship experience."[38]

To optimize men's ability to live well in prostate cancer survivorship, it is important to understand their experiences and concerns. In addition to fear of recurrence, prostate cancer survivors express the most distress about the one enduring side-effect of all treatments: sexual dysfunction.[14, 39, 40] The most salient sexual side-effect of treatment is erectile dysfunction (ED), but other sexual side-effects contribute to men's difficulty with sexual performance and satisfaction, including penile shortening, penile curvature, orgasmic changes, genital shrinkage, and changes in the appearance of the penis.[41] In addition, radiation therapy can cause degenerative changes to the anorectal area resulting in anodyspareunia (painful receptive anal sex), a relevant consequence for gay and bisexual men.[42] The American Cancer Society's Prostate Cancer Survivorship Guidelines summarized these long-term and late functional sexual effects of prostate cancer treatment (see Table 2.).

TABLE 2. Summary of common long-term and late sexual side-effects of prostate cancer and its treatment (from Skolarus et al., American Cancer Society Prostate Cancer Survivorship Guidelines, CA J Clin, 2014)[43]

TREATMENT TYPE	LONG-TERM EFFECTS	LATE EFFECTS
Surgery (radical prostatectomy; open, laparoscopic, robtic-assisted)	Urinary dysfunction • Urinary incontinence (stress) • Urinary symptoms (urgency, frequency, nocturia, dribbling) • Urethral stricture formation (scarring at the urethra) Sexual dysfunction • ED • Lack of ejaculation • Orgasm changes (without erection, associated with incontinence) • Penile shortening	Disease progression
Radiation (external beam or brachytherapy)	Urinary dysfunction • Urinary incontinence • Urinary symptoms (dysuria, urgency, frequency, nocturia, dribbling) • Hematuria • Urethral stricture Sexual dysfunction • Progessive ED • Decreased semen volume Bowel dysfunction • Fecal urgency, frequency, incontinence • Blood in stool • Rectal inflammation, pain	Urinary dysfunction • Urethral stricture • Hematuria due to small blood vessel changes Sexual dysfunction • ED can delay in onset 6 to 36 mo after therapy Bowel dysfunction • Rectal bleeding secondary to thinning/small blood vessel changes of anterior rectal wall mucosa • Disease progression
Hormone (androgen deprivation therapy)	Sexual dysfunction • Loss of libido • ED Other • Hot flashes/sweats • Weight gain, abdominal obesity • Change in body image • Excessive emotional reactions and frequent mood changes • Depression • Fatigue/decrease activity • Gynecomastia • Anemia • Body hair loss • Dry eyes	• Osteoporosis, fractures • Metabolic syndrome • Cardiovascular disease (possible increased risk of myocardial infarction) • Diabetes; decreased sensitivity to insulin and oral glycemic agents • Increased cholesterol • Increased fat mass and decreased lean muscle mass/muscle wasting • Venous thromboembolism • Vertigo • Cognitive dysfunction • Disease progression
Expectant management (active surveillance or watchful waiting)	• Stress, anxiety, worry • Risks associated with repeat biopsy (active surveillance), PSAs and DREs • Symptoms associated with disease progression	Disease progression

SECTION 3:
Introduction

Sexual dysfunctions secondary to prostate cancer therapies have far-reaching effects on men psychologically, leading to depression, anxiety, sense of loss of masculinity, lack of sexual confidence, and potential avoidance of sexual activity.[44-46] These dysfunctions also affect partners whose sexual lives are altered despite their own unchanged sexual function.[47-50] Partners are not always included in discussions with providers and couples may not communicate effectively about sexual concerns. As a result, relationships suffer.[20, 21, 51, 52] Help for sexual problems is rarely available in developed countries and even less available in developing countries. Consequently, men and their partners are left stranded, coping as best as they can.[53] In a US study of 2,499 prostate cancer survivors, men were still searching for help with sexual problems an average nine years after diagnosis.[54] Men with a high sexual symptom burden had correspondingly high needs for more information regarding prostate cancer recurrence, effects on relationships, and long-term effects of cancer therapies compared to men with a low sexual symptom burden (see Figure 2.).
Some men and partners may give up on sexual recovery completely if they give up on the use of pro-erectile aids.[55, 56] In a review of help-seeking for prostate cancer across cultures, King-Okoye and Faithful identified embarrassment, concerns about masculinity, and distrust of medical care as drivers of delayed help-seeking; Cultural, spiritual and traditional beliefs, as well as the use of herbal medicine were reported as playing an important role in Africa in terms of how men cope with the sexual side effects of prostate cancer therapies. These treatments have not been studied empirically, and their effectiveness is only known anecdotally.[57]

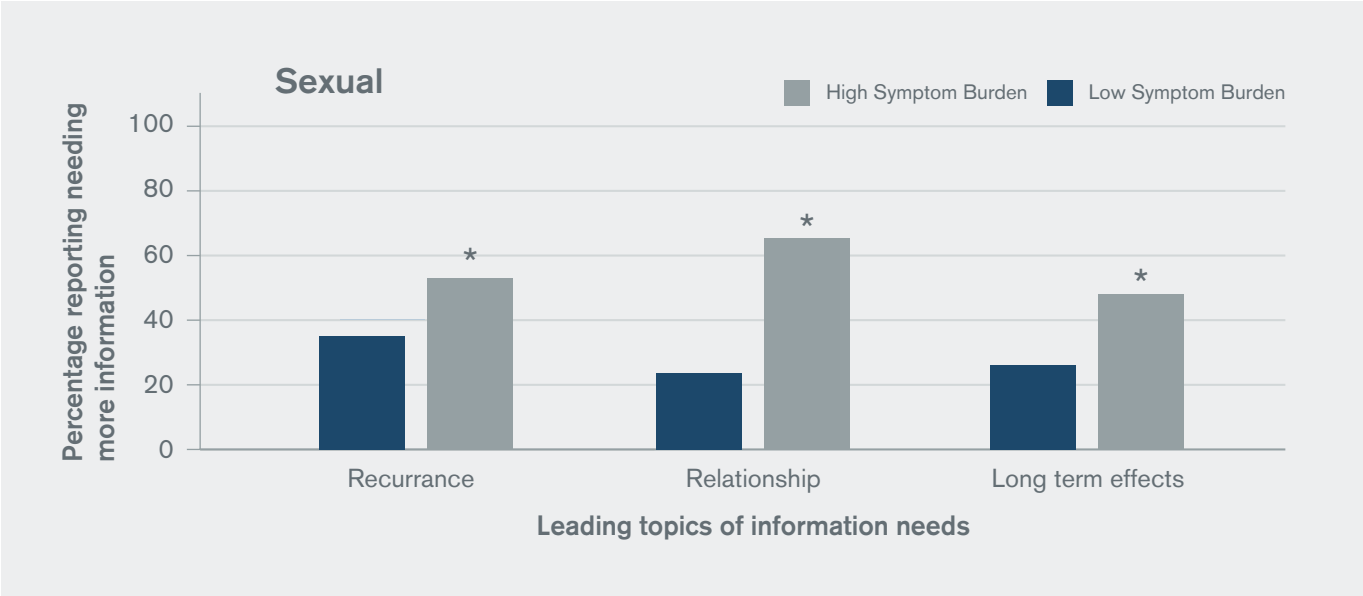


FIGURE 2. Information needs differences between prostate cancer survivors with low vs high domain-specific symptom burden[54] (from Bernat et al., BJUI, 2016)

SECTION 3: Introduction

The Role of Culture, Ethnicity and Race

Ethnicity, race, and culture affect sexual health-related quality of life associated with prostate cancer therapies. Ethnicity and culture shape sexual health outcomes after prostate cancer therapy. The conceptualization of culture, ethnicity, and race is complex. National origin, ethnicity, tribe, and race all affect perspectives on gender roles, sexual orientation, relationships, health beliefs, disparities in access to healthcare, and response to healthcare offered. The same group identities also affect beliefs about whether sexual health rightfully belongs in healthcare as an aspect of general health. An individual experiences sexuality as the intersection of these identities, so sexual health care must respect the individual's self-perception, personal history, and lived experience. This guideline is largely based on existing research that was primarily conducted in developed countries. Research in developing countries is emerging. As a result, this guideline's goal, to provide international guidance, must be regarded as only partially empirically based. It is, however, aspirational, as men with prostate cancer deserve support across the globe, based on the intersection of all relevant group identities. In this guideline, we refer to culture, ethnicity, and race to summarize the issues stated above. We discuss these concepts in more detail where relevant.

Men from different cultures, ethnic groups, and races may value sexual function differently, may experience functional impairments after prostate cancer therapies differently, and may perceive their impact on quality of life differently. Further, men of different groups may vary in their coping mechanisms in the face of functional impairments after prostate cancer therapy. This issue is important because it may inform prostate cancer clinical management decisions that dictate survival outcomes. Specifically, the presentation, acceptance, and execution of recommended prostate cancer therapies may differ in accordance with patient and provider perceptions of quality of life impact. For instance, Black-American men in the United States are disproportionately at higher risk for prostate cancer incidence and mortality among ethnic groups.[58, 59] Is it possible that worry about treatment-related sexual dysfunction affects this ethnic group more substantially than others to the extent that it influences whether someone chooses life-saving treatment? If so, then the specific priorities and ability to cope with sexual dysfunction in Black-American men may influence prostate cancer treatment decisions and survival outcomes. A review of the literature on attitudes about prostate cancer among African men and men of African descent suggests that these groups may perceive both cancer and sexual dysfunction as stigmatizing, as well as a threat to their masculine role in society. In addition, they may find diagnostic procedures such as digital rectal exam unacceptable because of the perceived resemblance to homosexual activity. Further, in viewing physical health as representative of their masculine strength, men may avoid screening for prostate cancer and treatment.[60] Finally, some men may not seek help because of culturally driven discomfort about discussing the side-effects of treatment, thinking them embarrassing, emasculating, and intensely private.[57]

The Importance of Sexual Function

Studies have shown that people acknowledge and perceive sexual dysfunction and limitations differently across cultures. Patients say that retaining sexual function is a foremost concern after prostate cancer therapy.[61-63] However, the importance of sexual function at baseline among cultural groups may vary. In comparative analyses in the United States of baseline sexual function among different groups of men undergoing clinically localized prostate cancer therapy, Black (non-Caucasian) patients rated this function and its bother as indicators of better quality of life more highly than White (Caucasian) patients.[64-66] Additional insights arise when considering cross-cultural studies between Japanese and American men (of all backgrounds and races) undergoing radical prostatectomy. Japanese men reported lower sexual function scores at baseline, and they were also less likely than American men to be concerned about their level of sexual function.[67, 68] Accordingly, those who treat patients with prostate cancer must not only understand the impact of prostate cancer therapies on sexual function and support patients in obtaining sexual dysfunction treatment, but must take into account ethnic and cultural differences in the importance of sexual function as well as the meaning of sexual dysfunction.

Cultural, Ethnic and Racial Differences in Sexual Function Outcomes

Numerous studies have documented variability in sexual function outcomes based on culture, ethnicity, or race. However, the size and direction of differences is not consistent. In the U.S., the highest quality evidence comes from population-level studies.

SECTION 3: Introduction

The Prostate Cancer Outcomes Study (PCOS), a population-based longitudinal cohort evaluation derived from the Surveillance, Epidemiology, and End Results (SEER) cancer registries representing six geographic regions of the USA, reported that at 18 or more months after radical prostatectomy, erectile function recovery status varied by race, with Black-American men experiencing a significantly better outcome: 38.4% of Black-American men reported erections firm enough for intercourse at 24 months compared with only 21.3% of Whites and 25.9% of Hispanics.[69] At 60 months after surgery, functional erections were better in Black-American men than in Whites, although this outcome was more acceptable to Whites than in Black-Americans, whereas there was equivalent acceptance at this interval between Whites and Black-Americans after radiation therapy.[70]

Data from the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE), a large, national observational database of newly diagnosed patients with prostate cancer, found that at 12 months after surgery or radiation while controlling for age, education and income, Black-American men had less decline in sexual function scores than White men (although baseline function was also higher in African-American men).[71] Similarly, the Prostate Cancer Outcomes and Satisfaction with Treatment Quality Assessment (PROSTQA), a prospective, longitudinal multicenter investigation of health-related quality of life outcomes after prostate cancer treatment, found that better functional erection preservation was observed for brachytherapy in Black-American men than in Whites. No differences were found for radical prostatectomy or external radiation in Black-American men relative to White men by 24 months post-treatment.[72] The Comparative Effectiveness Analysis of Surgery and Radiation (CEASAR) study, another prospective, population-based, observational study, also found that at 12 months post-treatment there was no difference in sexual function recovery across White, Hispanic, and Black-American men.[73]

Treatment Choices

Patient selection of prostate cancer therapy offers a proxy for appraising the importance of sexual function in the context of the patient's perceived risk of sexual function loss associated with specific therapies. In a study of primary therapy choice for men with screen-detected, clinically localized prostate cancer, White patients were more than four times more likely to select radical prostatectomy versus watchful waiting than Black-patients. Intact sexual function pre-treatment was found to be a significant factor influencing non-surgical treatment selection.[74] Researchers considered the potential role of inequitable access to treatment options by evaluating patients presenting to an "equal access," military, multidisciplinary prostate cancer clinic.[75] In this study, White patients (as well as those possessing higher income and education level) chose radical prostatectomy over external beam radiation therapy more frequently compared to Black patients, despite the association of this therapy with higher risk of health-related quality of life decline.[75]

A retrospective survey study found a similar result: Black-American men were more likely than White men to have undergone radiation therapy and to have indicated a desire to maintain sexual functioning as a determinant for their treatment choice.[76] Studies of decisional regret suggest similar patterns. A comparative assessment of treatment decisional regret following robotic-assisted laparoscopic prostatectomy using a validated questionnaire found that a significantly greater proportion of Black versus White patients regretted their treatment decision (20.6% vs. 11.2%, respectively).[77] Significantly younger age was recorded among Black-American men (56 vs. 60 years), and factors significantly associated with decisional regret included postoperative sexual dysfunction, pad usage, and length of hospital stay.[77]

Additional reports of treatment decisional regret corroborate these findings.[78-80] These studies suggest that how men weigh the possibility of sexual dysfunction may influence their prostate cancer therapy decisions toward options that afford the least adverse sexual dysfunction outcomes, particularly in groups concerned about preserving sexual function integrity. It is important to acknowledge that provider and health care system factors may also have been in play in these studies and have influenced decision making and delivery of care.

Overall, the available evidence suggests that differences based on culture, ethnicity, or race may exist in the experience and consequences of sexual dysfunction after prostate cancer treatment.

These findings may signify that cultural, racial, and ethnic factors influence the perception of sexual function outcomes in various groups. Taken together, the evidence suggests that there is a need to frame sexual health care in prostate cancer survivorship within the context of culture, race, and ethnicity.



04 GUIDING PRINCIPLES

SECTION 4:
Guiding Principles

This guideline was created based on six guiding principles. The principles were used to inform literature searches, to place the available evidence in context, to identify gaps in evidence, and to create the guideline content.

These principles are:

1. **The healthcare provider plays a key role in routinely and systematically bringing up and addressing sexual function and sexual concerns in prostate cancer survivorship.**
   The purpose of this role is to initiate and maintain communication in order to promote realistic expectations of outcomes and facilitate identification and management of sexual issues to maximize patients' and partners' sexual wellbeing. including reducing patients' and partners' experience of shame, embarrassment, and isolation.

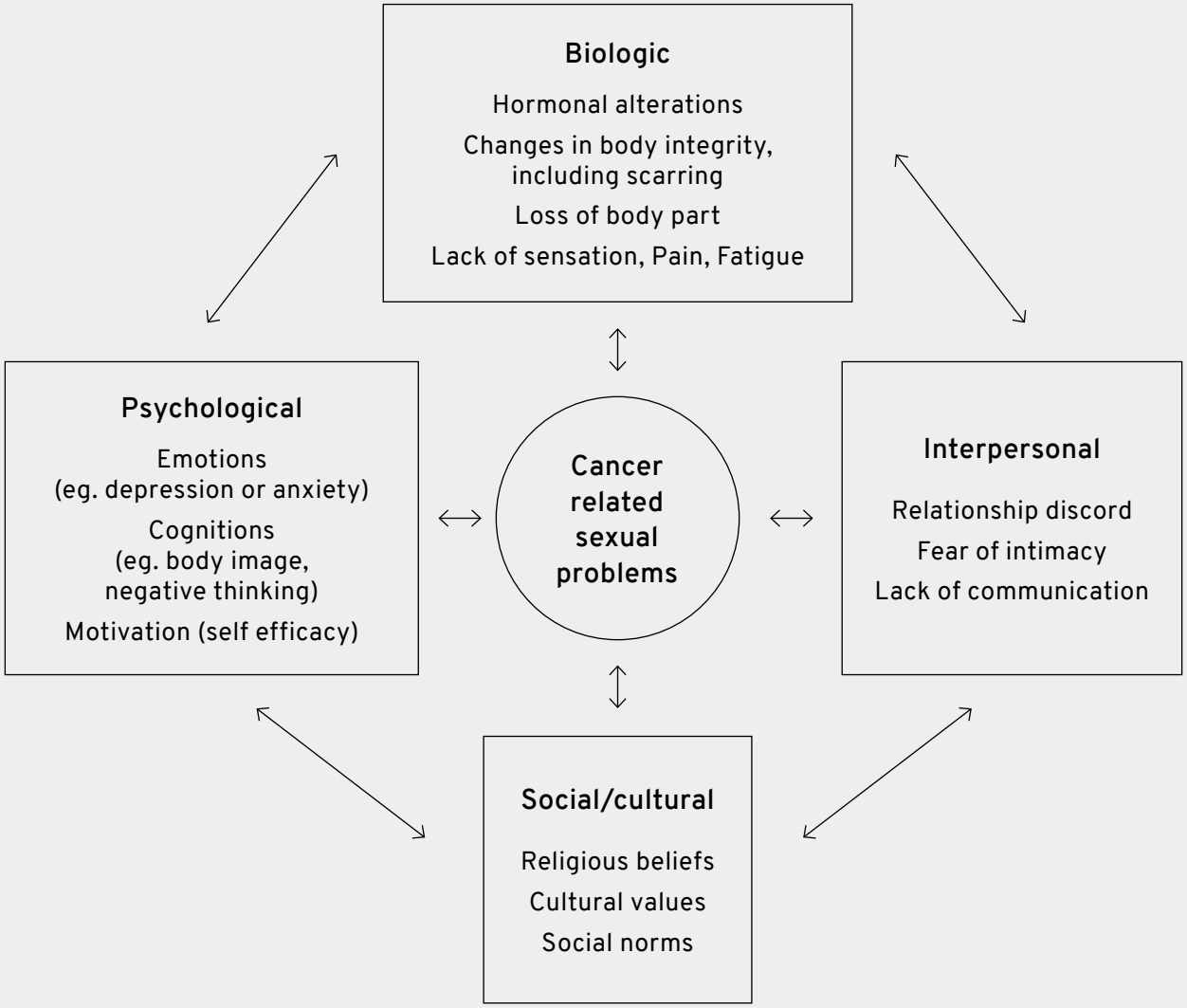
2. **Sexuality and sexual recovery are multi-dimensional, with sexual function representing only one component of that experience.**
   Sexuality also includes the individual's experience, the couple's relationship, and the impact of social and cultural factors on sexual practices and beliefs. A biopsychosocial perspective thus must inform clinician approach to assessment and treatment. All statements in this guideline that reference the biopsychosocial perspective include sexual function, a person's response to it, the sexual relationship (or potential for a relationship) and impact of culture, ethnicity and race.

3. **The role of grief and mourning in couples' recovery of sexual intimacy has emerged as a path towards achieving a new sexual paradigm despite sexual dysfunction.**
   The new sexual paradigm may include the use of sexual aids.[81, 82] Cancer therapies bring about sexual losses that are experienced in all of the functional, psychological, relationship, cultural, ethnic and racial domains (Figure 3).[81] Men and their partners must cope with these treatment-related sexual losses in survivorship. This model of sexual recovery incorporates the biopsychosocial perspective on sexuality, grief, and mourning as the path to sexual recovery, and encourages the use of sexual aids (Appendix B[83]). Included in the model is the recognition that single men, men in same sex relationships, men who have sex with men, transgender women and gender non-conforming individuals and their partners have both similar and unique needs, as compared to men and partners in heterosexual relationships, that must be assessed and attended to from the beginning of prostate cancer care.

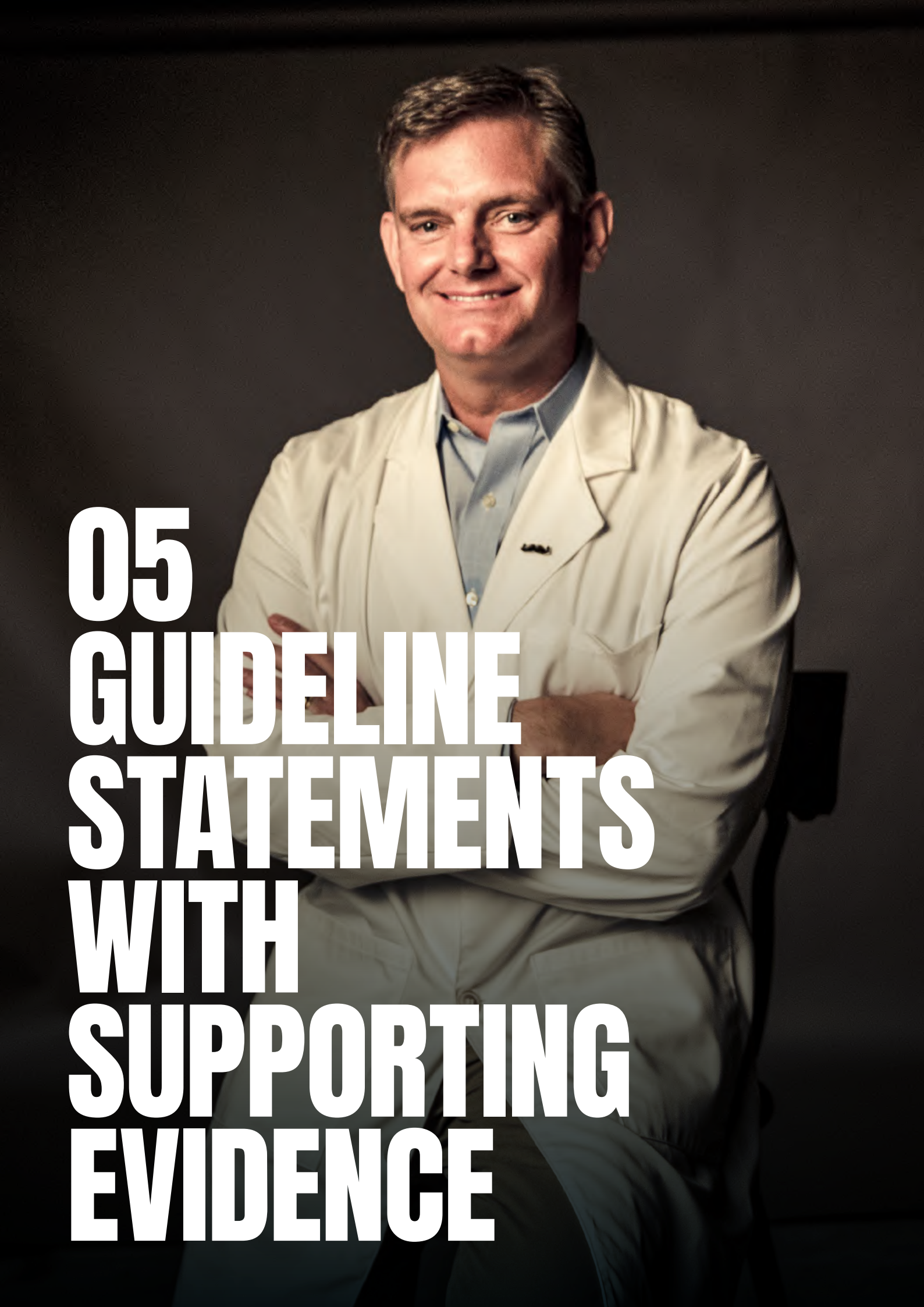
4. **Men rarely return to baseline sexual function after they undergo therapies for prostate cancer.** Research on sexual function outcomes after prostate cancer therapies clearly indicates that the vast majority of men do not return to baseline sexual function even if their therapy is local and time limited.[84] Men on ongoing hormonal therapy remain in the dysfunctional range. It is therefore important that prior to treatment men and partners understand that their sexuality will likely not return to its pre-treatment state and that sexual rehabilitation may involve the use of medications or devices or even surgical interventions to maximize their sexual experience after treatment.

5. **Including the partner in all aspects of pre- and post-treatment evaluation and counseling, whenever possible and with consent of both partners, is preferable because sexuality is experienced by most men in the context of a relationship.** Partners are significantly impacted by the prostate cancer survivor's treatment-related sexual dysfunction and require support for their own needs in sexual recovery. Patients and partners will optimize sexual recovery if they work on sexual recovery together.

FIGURE 3. A biopsychosocial model of the impact or cancer on sexuality[85]



6. **6) Support by a multidisciplinary team of healthcare providers is needed to best support men and their partners who desire to recover sexual intimacy after prostate cancer therapy.** These healthcare providers include clinicians in primary care, urology, radiation oncology, medical oncology, gynecology, physical therapy, nursing, social work, psychiatry, and psychology.



05 GUIDELINE STATEMENTS WITH SUPPORTING EVIDENCE

SECTION 5:

Guideline Statements With Supporting Evidence

I. Counseling patients and partners about the impact of prostate cancer therapies on the biopsychosocial aspects of sexuality

Introduction

Traditionally, treatment success for prostate cancer has been evaluated almost exclusively on survival rates with sparse attention given to what has been termed as 'patient and partner health-related quality of life' (HRQoL).

A contemporary paradigm shift has altered this perspective, resulting in the reconceptualization of prostate cancer as a chronic illness with long-term consequences that go far beyond oncological outcomes. This reconceptualization has led to the proliferation of research examining the short and long-term HRQoL of patients treated for prostate cancer and their partners.

These studies make clear that prostate cancer treatment-related sexual dysfunction and its biopsychosocial sequelae have far-reaching and long-term effects on the wellbeing of men and partners in prostate cancer survivorship. Men and their partners should be thoroughly counseled before beginning prostate cancer treatment regarding these consequences.

Body of evidence strength for Guideline Statements 1 to 3: The body of evidence strength for these statements is Grade C. The supporting evidence is derived from a broad body of literature that is composed primarily of observational studies that reported on relatively small samples and used a variety of methodologies.

Given the Panel's clinical experience, which is consistent with the reported findings, the Panel is confident that all patients (and partners, if partnered) should receive counseling on these issues (i.e., Strong Recommendations).

GUIDELINE STATEMENT 1:

A clinician-initiated discussion should be conducted with the patient and the partner (if partnered and culturally appropriate) about realistic expectations of the impact of prostate cancer therapy on the patient's sexual function, the partner's sexual experience, and the couples' sexual relationship. The clinician should promote openness and inclusivity, consider cultural context, and tailor counseling to the specific needs of patients who are heterosexual, gay, bisexual, identify as men who have sex with men, transgender women, and gender non-conforming individuals.

(Strong Recommendation; Evidence Strength Grade C)

SECTION 5:
Guideline Statements With Supporting Evidence

Discussion

Patients and partners are unlikely to initiate discussions about the impact of prostate cancer therapies, including the effects of these therapies on sexual function.[86] The clinician's role is to initiate the discussion about prostate cancer therapy impact and to maintain communication. The goal of this discussion is to promote realistic expectations of outcomes and facilitate identification and management of sexual issues regularly in survivorship to maximize patients' and partners' sexual health, including reducing patients' and partners' experience of embarrassment and isolation.

Prostate cancer treatment-related sexual dysfunction is ubiquitous in short-term and long-term survivorship.[16, 87-92] Given the prevalence of prostate cancer, the pervasiveness of treatment-related sexual dysfunction, and the extent of distress, it is probable that millions of people in North America are affected.[43] Approximately 81-93% of these patients report that prostate cancer therapy has negatively affected their sex lives, with 20-58% of men reporting cessation of sexual activity with their partner.[93] The sexual side-effects of prostate cancer treatment, irrespective of therapy type, are reported to be highly bothersome, and are associated with psychosocial morbidity and poor overall health status.[93-97] The extent of the negative impact on the partner's HRQoL and on overall relationship satisfaction has also been established.[98-100] Importantly, changes in sexual health and the psychosocial impact of these changes remain the most commonly reported unmet care need in prostate cancer survivorship.

Several studies have determined the presence of significant and enduring bother and psychological distress related to sexual dysfunction among prostate cancer survivors. In a recent study, 17% and 10% of prostate cancer survivors reported moderate to severe anxiety and depression respectively. This distress was associated with the presence of sexual side-effects.[97] Similarly, bother associated with sexual dysfunction was the most prevalent concern for patients one and two years after receiving a radical prostatectomy.[101, 102] The nature of the bother and psychological distress described in the literature includes fear, anxiety, worry, frustration, anger, regret, and depression associated with sexual dysfunction, as well as losses in sexual confidence and overall self-esteem.[103-106] Men's body image and sense of masculinity also are negatively affected.[107-109] Several recent studies have also described a framework that conceptualizes the impact of sexual dysfunction in terms of patient, partner and couple *loss*; namely losses in spontaneous sexual activity, sexual identity, feelings of masculinity or femininity, and losses in relationship intimacy.[21, 105, 110, 111] Under these circumstances, it becomes critical to provide psychoeducation on strategies to successfully integrate loss via the process of grieving and mourning.

Studies have also reported the adverse effects of sexual dysfunction after prostate cancer therapy on a patient's feelings of masculinity and sexual identity. Findings indicate that masculinity plays an integral role in how men frame their responses to sexual dysfunction.[112] Therapies for prostate cancer can affect many masculinity characteristics, most notably sexual prowess. Men who hold strong beliefs about masculinity or aspire to maintain traditional male traits are at elevated risk for psychological distress as a consequence of prostate cancer therapy.[113, 114] Specifically, men suffering erectile dysfunction and penile shortening as a result of prostate cancer therapy report distress related to body image concerns and poor sexual performance.[14, 114] Losses in masculinity are strongly linked to depression, decreased self-worth, fear of being stigmatized, and damage to a patient's overall sexual identity.[104, 110, 115-119] To lessen the impact of traditional masculine beliefs on mental health status and sexual identity, healthcare professionals can help patients broaden their perception of masculinity beyond sexual prowess with the goal of insulating the patient's masculine self-esteem.[120]

Recent research documents the substantive negative HRQoL impact on partners of prostate cancer survivors.[121-123] Partners are reported to have higher levels of depression than the patients themselves, and 70% of spouses report a decline in sex life quality.[124, 125] Although partners report similar experiences of psychological distress and loss to their patient counterparts, further investigation into the nature of partner distress suggests that partners particularly struggle with changes in sexual satisfaction and relationship intimacy.[105, 110, 126-128] Research has also



found that the distress experienced by female partners was most affected by the degree of psychological distress and sexual bother experienced by the patient.[115] Partners also report feeling isolated in their experience given that patients are often non-communicative and healthcare providers often fail to actively include them in consultation regarding sexual health issues.[129] Wittmann et al. reported that men were unaware of their partners' needs for support.[130] Accordingly, a review of interventions to support partners concluded that healthcare provision should target improved communication and intimacy within the couple, and provide the opportunity for partners to express and receive support for their distress.[122]

The challenges in a couple's sexual relationship after prostate cancer therapy can in turn threaten a couple's individual and mutual wellbeing. Garos et al. (2007) found that in comparison to normative samples, patient and partners had greater levels of depression and sexual dissatisfaction.[131] Additionally, research has shown that patients with poor erectile functioning were more likely to experience marital distress and avoid open spousal discussions.[132] Conversely, couples who worked as a team, and who described high levels of communication regarding sexual dysfunction after prostate cancer treatment, reported better marital adjustment. Similarly, research has shown that couples respond differently to prostate cancer related sexual dysfunction, and that healthcare providers need to consider the unique relationship and intimacy needs of men (patients and partners), women, and couples.[20, 133] Couples also reported that they felt ill-prepared to manage sexual side-effects and sexual rehabilitation after prostate cancer therapy, and that sexual dysfunction had broad effects on the couple's overall wellbeing.[100, 134] Overall, a review of the evidence advocates for individualized assistance in helping couples navigate the psychological burden of sexual dysfunction. This means addressing the sexual rehabilitation needs of patients and partners, via dyadic approaches that support healthy couple communication towards enhanced relationship satisfaction.[103, 123, 129, 135-139]

A major area of concern is the importance of patients and partners approaching sexual recovery with realistic expectations of outcomes.[140] Unrealistic expectations often result from a lack of pre-treatment information and too little education about possible changes in sexual functioning and related psychosocial impacts.[126, 141-145] Unfortunately, studies continue to find that sexual health concerns are often not discussed during consultations. When communication does occur it is often not comprehensive, and rarely involves partners even when partners were present during the consultation.[52, 99, 146] Although consultation on the pharmacologic treatment of erectile dysfunction is more commonplace, discussions on broader sexual health issues pertinent to prostate cancer therapies continue to be marginalized.[52]

SECTION 5:
Guideline Statements With Supporting Evidence

Men who are Gay, Bisexual, or Identify as Men who have Sex with Men

In the United States, an estimated 97,845-123,006 gay and bisexual prostate cancer survivors experience lack of appropriate healthcare for treatment-related sexual dysfunctions.[23] It is difficult to estimate how many gay men live with prostate cancer worldwide, given that same-sex sexual or romantic relationships are stigmatized and criminalized in almost 80 countries across the globe.[147] Available estimates of the numbers of men who have sex with men in Asia, Latin America and Eastern Europe suggest a prevalence of 6-20%.[148]

It is difficult to determine how many are prostate cancer survivors, but there clearly is a plurality of gay and bisexual men with prostate cancer worldwide whose sexual health support needs are underappreciated and unmet.

Healthcare providers generally presume that their patients are heterosexual and are not prepared to discuss sexual concerns with gay and bisexual men. This lack of perceived relevance of sexual orientation in urology and oncology settings constitutes a barrier to appropriate care. For example, in a national survey of oncologists, only 39.6% agreed that knowing a patient's sexual orientation was important.[149] Gay and bisexual men have experienced rejection when they disclosed their sexual orientation. These negative experiences in healthcare mean that gay and bisexual men are not counseled appropriately regarding prostate cancer sexual consequences and are not supported as they navigate recovery from the side-effects of prostate cancer therapy in survivorship.[17]

Gay and bisexual men have been generally overlooked in research on sexual problems after prostate cancer treatment. Until recently, research has focused on heterosexual men and couples. Compared to heterosexual men, gay and bisexual men score worse on urinary, bowel, and hormonal functioning but better on sexual functioning (although both groups have poor sexual function).[16, 91, 92] In a recent study of 21 cancer centers with a comprehensive designation from the National Cancer Institute (NCI), only three collected sexual orientation information and only four distinguished current gender identity from sex assigned at birth.[150] In addition, in a study of community-based oncology practices participating in the NCI Community Oncology Research Program, only 24% and 10% routinely collected sexual orientation and gender identity data, respectively.[151] As a result of that focus, the particular needs and sexual concerns of gay and bisexual men have remained largely unaddressed in sexual health treatment, rehabilitation and social support strategies. Access to this sexual minority population can also be difficult due to societal—and healthcare—discrimination they almost certainly have experienced in the past, making disclosure seem unsafe and trust much harder to establish.

In 2011 the United States declared LGBT people a health disparity population. An Institute of Medicine report cited untrained providers, discrimination, and the related unsafe health care environment as the root causes that needed to be remedied.[152] The National Institutes of Health in the US recommended that research be directed to understanding the healthcare needs of LGBT populations in order to provide care tailored to their needs.[153]

Emerging research, mostly conducted in Australia and the United States, has documented some of the specific sexual health issues faced by gay and bisexual men that can now be addressed to improve their care in prostate cancer survivorship. The use of online participant recruitment in research has helped overcome barriers to disclosure and inability to identify gay and bisexual men with prostate cancer in healthcare databases, greatly improving study sample sizes.[96, 154] Moreover, qualitative research has brought to light a deeper understanding of the experience of gay and bisexual men. Recurring themes across studies reinforce confidence that at least some aspects of care for gay and bisexual men can be outlined and addressed immediately.[17, 154, 155] Rosser et al. provide a conceptual model for understanding the experience of gay and bisexual men coping with the sexual side-effects of prostate cancer treatment from the qualitative results of the *Restore Study* (Appendix B).[17]

SECTION 5:
Guideline Statements With Supporting Evidence

Transgender Women and Gender Non-conforming Patients

Although there is limited research on this population of patients, it must be acknowledged that trans women and gender non-conforming patients who have a prostate should be not only be screened for prostate cancer but should also be supported for sexual recovery during survivorship. Several authors have noted that stigma, discrimination and lack of knowledge by healthcare providers can discourage trans and gender non-conforming patients from seeking care.[156, 157] Taking a sexual health history can help identify sexual health issues and concerns and inform what kind of sexual health support will be needed for a patients when the degree of transition that a patient may have undergone is uncertain, or when the non-binary identification of a gender-non-conforming patient is not known. Learning and using the language of gender identity (she/her/hers or they/them/theirs, respectively) can be welcoming and helpful.

In particular, for transgender women it is important to know where the patient is in the process of gender-affirming hormone therapy and gender-affirming surgical intervention before impacts of prostate cancer and its treatment on all biopsychosocial aspects of sexuality can be assessed. It is also important to know whether she has completed genital gender affirming surgery that includes orchiectomy (bilateral orchiectomy eliminates the majority of endogenous testosterone production) and vaginoplasty with (versus without) creation of a vaginal canal. If a transgender woman has undergone creation of a neovaginal canal already, the prostate can be palpated digitally via a transvaginal approach and should be biopsied only via a transvaginal approach (transrectal biopsies with a neovaginal canal in place risks creating a recto-vaginal fistula). Lastly, if a transgender woman has already undergone vaginoplasty with creation of a vaginal canal, then prostatectomy and/or prostate radiotherapy will likely compromise the viability of the skin lining the neovaginal canal space. Such risks should be discussed before commencing treatment. As with all other patients, the impact of prostate cancer and its treatment on transgender women and patients who are gender non-conforming will vary, based on sexual goals.

In the United States, an estimated 97,845-123,006 gay and bisexual prostate cancer survivors experience lack of appropriate healthcare for treatment-related sexual dysfunctions.



SECTION 5:

Guideline Statements With Supporting Evidence



GUIDELINE STATEMENT 2:

Patients and partners should be advised that biopsychosocial treatment for sexual problems can mitigate sexual dysfunctions and lead to the recovery of sexual intimacy.

(Strong Recommendation; Evidence Strength Grade C)

Discussion

Data suggest that distress about sexual dysfunction may be mitigated by ensuring that consultations occur over time, actively including the partner, if available and willing. Such consultations provide education and guidance specific to treatment effects on erectile function, orgasm, sexual desire, body image, sexual identity, performance anxiety, sexual satisfaction, relationship/intimacy, and guidance on navigating pro-erectile therapies.[52, 103, 111, 126, 141, 145, 146, 158-160]

SECTION 5:

Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 3:

Patients and partners should be advised that psychological distress, including grief and mourning about sexual losses, resulting from the sexual side-effects of prostate cancer therapies, can be experienced by patients after prostate cancer therapy, and that distress can be mitigated with appropriate biopsychosocial rehabilitation strategies.

(Moderate Recommendation; Evidence Strength Grade C)

Discussion

Research on sexual health interventions for couples suggests that when couples work together to grieve the loss of familiar sexual interactions and to come to terms with sexual challenges after prostate cancer treatment, they can learn to incorporate sexual aids, emotionally support one another, and move towards a new paradigm for their sexual relationship. This approach reinforces emotional intimacy. In a qualitative study of couples that compared couples who valued primarily sexual pleasure vs those who valued relational intimacy when engaged sexually, those oriented towards emotional intimacy in sex were better poised to adjust to sexual changes after prostate cancer treatment.[21, 161]

Flexibility, acceptance and persistence promotes the process of sexual recovery. Pillai-Friedman and Ashline who describe the role of grief in sexual recovery in breast cancer, similarly suggest that the ability to accept sexual changes and work to re-eroticize the body can lead to a successful adaptation after the loss of sexual function due to cancer treatment.[162]

Several studies have determined the presence of significant and enduring bother and psychological distress related to sexual dysfunction in prostate cancer survivors. In a recent study, 17% and 10% of prostate cancer survivors reported moderate to severe anxiety and depression respectively, and that this distress was associated with the presence of sexual side-effects.[97] Similarly, bother associated with sexual dysfunction was the most prevalent concern for patients 1 and 2 years after receiving a radical prostatectomy.[101, 102]

The nature of the bother and psychological distress described in the literature includes fear, anxiety, worry, frustration, anger, regret, and depression associated with sexual dysfunction, as well as losses in sexual confidence and overall self-esteem.[103, 105, 163] Under these circumstances, it becomes critical to provide psychoeducation on strategies to successfully integrate loss via the process of grieving and mourning on the path to the recovery of sexual intimacy.

SECTION 5:
Guideline Statements With Supporting Evidence

II. Counseling patients and partners about the specific impact of individual prostate cancer therapies on sexual function

Introduction

ERECTILE DYSFUNCTION (ED)

- *Post-radiation.* The etiology of post-radiation therapy (RT) erectile dysfunction is multifactorial, appearing to involve damage to neurons, vascular structures, and smooth muscle.[164] Damage to the cavernous nerves is hypothesized to occur as a result of inflammation-induced reductions in nitric oxide synthase (nNOS). Blood flow to the penis is compromised by reduction of smooth muscle volume and fibrotic changes in the blood vessels that support erection, with reduction in internal pudendal arterial tone. As a result, the corpora cavernosa begin to atrophy and erection is compromised.

  Studies that have examined the relationship between radiation dose to the neurovascular bundles, the penile bulb and the penile bodies and post-radiation ED report contradictory results, but most studies had small sample sizes and were likely underpowered.[165-171] Several studies have investigated models of the radiation dose to specific pelvic structures, and how this correlates with the risk of developing ED.[169, 172-175] In a randomized dose-escalation trial no statistically significant correlations between post-radiation ED and dose-volume parameters in the crura, the superiormost 1-cm segment of the crura, or the penile bulb were found.[168] The dose to the penile bulb and corporal bodies has been reported as low and not predictive of post-radiation ED.[176] Experimental animal studies revealed defects in the erectile tissue vascular supply and decreased cavernous smooth muscle of irradiated rats (19) as well as fibrotic changes in the arteries of the rat penis after fractionated irradiation of the prostatic area.[177] The cavernosal arteries exhibited loss of smooth muscle cells, thickening of the intima, and occlusions.[177] These data suggest that post-radiation ED might be caused by radiation damage to the arterial supply of the corpora cavernosa.[177, 178] Overall, studies to-date suggest that post-radiation ED results from radiation dose to multiple anatomical structures and the interaction over the long term of the consequences of these exposures.

- *Post-prostatectomy.* The surgical trauma from radical prostatectomy contributes to the development of erectile dysfunction. Sources of damage include nerve trauma from stretching, heating, ischemia, and local inflammation. Neuropraxia leads to penile smooth muscle apoptosis and fibrosis, which disrupts the veno-occlusive mechanism that produces an erection.[179, 180]

Body of evidence strength for Guideline Statements 4 to 16: Body of evidence strength for the impact of prostate cancer treatments on sexual function is Grade B (Statements 4, 6, 7) or Grade C (Statements 5, 8-16). The available literature is composed primarily of observational designs with findings susceptible to bias in the absence of controls for the passage of time. Sample sizes in many studies were relatively small. In a few cases an RCT contributed relevant data, but a sufficient body of evidence derived from multiple randomized trials is lacking. The major difference in evidence strengths is the magnitude of the available literature; more literature is available for statements supported by Grade B evidence than for statements supported by Grade C evidence.

The available published systematic reviews and individual studies consistently make clear that prostate cancer treatments negatively affect sexual function. However, quantification of the impact on sexual function and the extent of recovery after specific types of prostate cancer therapy remain elusive. The systematic reviews did not provide precise estimates of sexual function recovery after radical prostatectomy (RP) or radiotherapy (RT). Nor did they provide definitive answers regarding whether specific types of prostatectomies or types of RT are

associated with higher rates of sexual function recovery.[181-190] Approximately half of the reviews noted that meta-analyses were not appropriate given the variability of measures used in the included studies and the absence of sufficient information. The reviews that conducted meta-analyses reported pooled values characterized by statistically significant heterogeneity that is unexplained, raising questions about the validity, and therefore the utility, of the reported values.

Greater than 95% of the individual studies that met our inclusion criteria were observational designs. These designs lack the internal validity protections that are possible with randomization and blinding, therefore findings must be interpreted with caution. In particular, groups of men who underwent different treatments (e.g., prostatectomy vs. radiotherapy), or who underwent different versions of a treatment (e.g., open prostatectomy vs. robot-assisted laparoscopic prostatectomy; external beam radiotherapy vs. brachytherapy), may not be equivalent at pre-treatment baseline in terms of sexual functioning or in terms of other factors that could affect recovery of sexual function such as the presence of comorbidities.

Specific treatment decisions and the need for adjuvant therapies such as androgen deprivation therapies (ADT) frequently are dictated by the severity of the underlying cancer; these issues are relevant to baseline levels of sexual function as well as to sexual function recovery. Although some studies clearly state whether or not adjuvant therapies were used, a substantial subset did not clearly indicate whether adjuvant therapies (ADT or RT) were used. An additional challenging issue is that studies used different measures of sexual function, some of which may lack validity and many of which are not readily comparable.

Most studies followed men for less than two years, likely an insufficient amount of time to document recovery from surgery or the extent of sexual function decline in response to radiotherapy. Further, some studies of men with normal sexual function before cancer treatment defined sexual function at baseline more stringently than during follow-up, resulting in possibly inflated recovery estimates. Finally, many studies do not clearly indicate whether men were using erectile aids either pre-cancer treatment or during the follow-up period, or whether rehabilitation protocols were used post-cancer treatment. Overall, although it is clear that prostate cancer therapies have a substantial negative impact on the sexual functioning of the overwhelming majority of patients, these issues make it difficult to generate precise estimates of the impact of specific types of prostate cancer treatment on sexual function.

SECTION 5:
Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 4:

Patients and partners should be counseled that all prostate cancer therapies may result in the patient's short-term and long-term erectile dysfunction.

(Strong Recommendation; Evidence Strength Grade B)

Discussion

Numerous studies indicate that all therapies for prostate cancer can result in erectile dysfunction. This dysfunction can occur regardless of the man's pre-treatment function level.

Radical Prostatectomy

Men with normal sexual function at pre-treatment baseline.

Thirty-two studies reported findings regarding 63 groups of men (some studies reported on multiple groups) with normal sexual function (variously defined) before undergoing prostatectomy for prostate cancer treatment.[191-222] A minority of studies used validated sexual function questionnaires at baseline and during follow-up. In most studies sexual function scores at the end of follow-up did not return to baseline values.

Fifty-nine study arms reported findings in terms of the percentage of men who met the study sexual recovery definition at the end of follow-up, but these definitions varied considerably. They included: the ability to maintain an erection sufficient for intercourse without erectile aids, the ability to have successful intercourse with or without PDE5i, return to baseline values on questionnaires, and patient report of having engaged in sexual intercourse. Sexual function recovery rates ranged from 7.6% to 92.4% at follow-up at durations ranging from 12 to approximately 100 months, with the majority of studies reporting findings at 12 months. In 22 study arms, recovery rates were less than 50%. Twenty-seven study arms reported recovery rates from 50 to 80%. Ten study arms reported rates of 80% or higher. The mean recovery rate across all study arms was 56.2%.

Men with varied levels of sexual function at baseline. Fifty-nine studies reported findings for 84 groups of men (some studies evaluated multiple groups) regarding men with varied levels of sexual function before undergoing prostatectomy for prostate cancer treatment.[63, 69, 75, 84, 94, 102, 223-275] Of the 84 study arms, 69 arms evaluated men who had RP only, the remaining study arms included men who had ADT, and one study arm reported on men who had RP and may also have had ADT and/or RT. A subset of studies used sexual function questionnaires at baseline and during follow-up. The most commonly used measures were: ULCA PCI sexual function and bother scores; the EPIC-50 or EPIC-26 sexual summary, function, and bother scores; IIEF-5 scores; and the IIEF Total and EF subscale scores.

Twenty-four studies reported findings in terms of the UCLA PCI measures. In this population of men who entered studies with varied levels of sexual function, baseline sexual function scores ranged from 23.2 to 81.8 with mean score across studies of 53.4. Post-RP scores exhibited a range shifted to lower values, from 3.9 to 54.7, with a drop in mean score to 26.7. Baseline sexual bother scores ranged from 46.4 to 87.2 with a mean score across studies of 71.0. Post-RP scores had a range slightly shifted to lower values (31 to 73) with a lower mean score of 50.5.

Radiotherapy

Men with normal sexual function at pre-treatment baseline.

Eight studies comprising 11 study arms reported findings regarding the impact of RT on sexual function of men who had normal sexual function at pre-treatment baseline.[276-282] Seven study arms focused on brachytherapy; the remainder focused on external beam RT. Follow-up durations ranged from 24 to 96 months. Sexual function recovery rates (variously defined) ranged from 20 to 75%.

Men with varied levels of sexual function at baseline. Eighty-seven study arms reported findings regarding men with varied levels of sexual function before undergoing external beam radiotherapy or

brachytherapy with or without androgen deprivation therapy for prostate cancer treatment.[63, 75, 84, 94, 102, 166, 223-227, 230, 232, 234, 237, 238, 241, 244, 246, 249, 253, 257, 264-266, 269, 273, 275, 283-306]

Of the 87 study arms, 34 arms evaluated men who had EBRT only (18 arms) or brachytherapy only (16 arms). The remaining study arms included men (or subsets of men) who had ADT and/or who had EBRT in addition to BT. A subset of studies used sexual function questionnaires at baseline and during follow-up. Fifteen study arms reported baseline and post-RP UCLA PCI sexual function scores; baseline scores ranged from 31 to 64. Thirteen of these study arms reported decreased final scores.

Twenty study arms reported EPIC-50 sexual function scores ranging from 19 to 71.5 at baseline with 19 arms reporting decreased scores post-RP. Similar patterns were reported by studies using other measures. Twenty-five study arms reported the percentage of men who had normal sexual function (definitions varied) before and after RP. Before RP, these percentages ranged from 0 to 90.3%. Post-RP the range was 0 to 79.9% with all studies reporting decreased percentages.

GUIDELINE STATEMENT 5:

Patients and partners should be counseled that patients treated with radical prostatectomy have different trajectories of sexual function decline and potential recovery compared to patients treated with radiotherapy.

(Moderate Recommendation; Evidence Strength Grade C)

Discussion

Systematic reviews

Five systematic reviews compared prostatectomy to radiotherapy in terms of sexual function outcomes. Four reviews concluded that prostatectomy is associated with higher rates of long-term sexual dysfunction compared to radiotherapy. Lardas et al. (2017) evaluated outcomes among active surveillance, RP, EBRT and brachytherapy patients.[186] Given the heterogeneity among studies, a meta-analysis was not performed. Men treated with surgery were the most likely to have persistent sexual functioning problems. Avila et al. (2018) also reported a comparative systematic review.[181] These authors carried out a meta-analysis. The largest decrements in sexual function occurred in men who had varying types of RPs [approximately 1.35 standard deviation (SD) decrease at one year], moderate decrement occurred in men who had EBRT (0.46 SD decrease), and the smallest decrements occurred in men who had brachytherapy (0.12 SD decrease). These patterns were present up to five years of follow-up. Wolff et al. (2015) and Peinemann et al. (2011) compared EBRT, BT, and RP. Both reviews indicated that men who had BT reported better sexual function than did men who had RPs.[187, 190] Similarly, Whiting et al. (2016) also reported that rates of sexual function recovery at 12 to 24 months ranged from 42 to 86% among men who had brachytherapy, 26 to 36% among men who had EBRT, and 19 to 76% among men who had RP.[189]

Individual studies

Twenty-six studies compared RPs to various forms of RT.[63, 75, 94, 102, 223-227, 230, 232, 234, 237, 238, 241, 244, 246, 249, 253, 257, 264-266, 269, 273, 275] The most consistent finding, reported in 20 studies, was that men who were treated with RP had greater decrements in sexual function than did men treated with various forms of RT (Figure 4). The plot below presents the UCLA-PCI sexual function data from the comparative studies. Baseline sexual function scores are on the X axis and change from baseline scores are on the Y axis. The RP study arms cluster to the right on the plot because men in these groups generally came into studies with higher baseline function levels. They also cluster toward the top of the plot, indicating the largest decrements in sexual function score.

SECTION 5:

Guideline Statements With Supporting Evidence

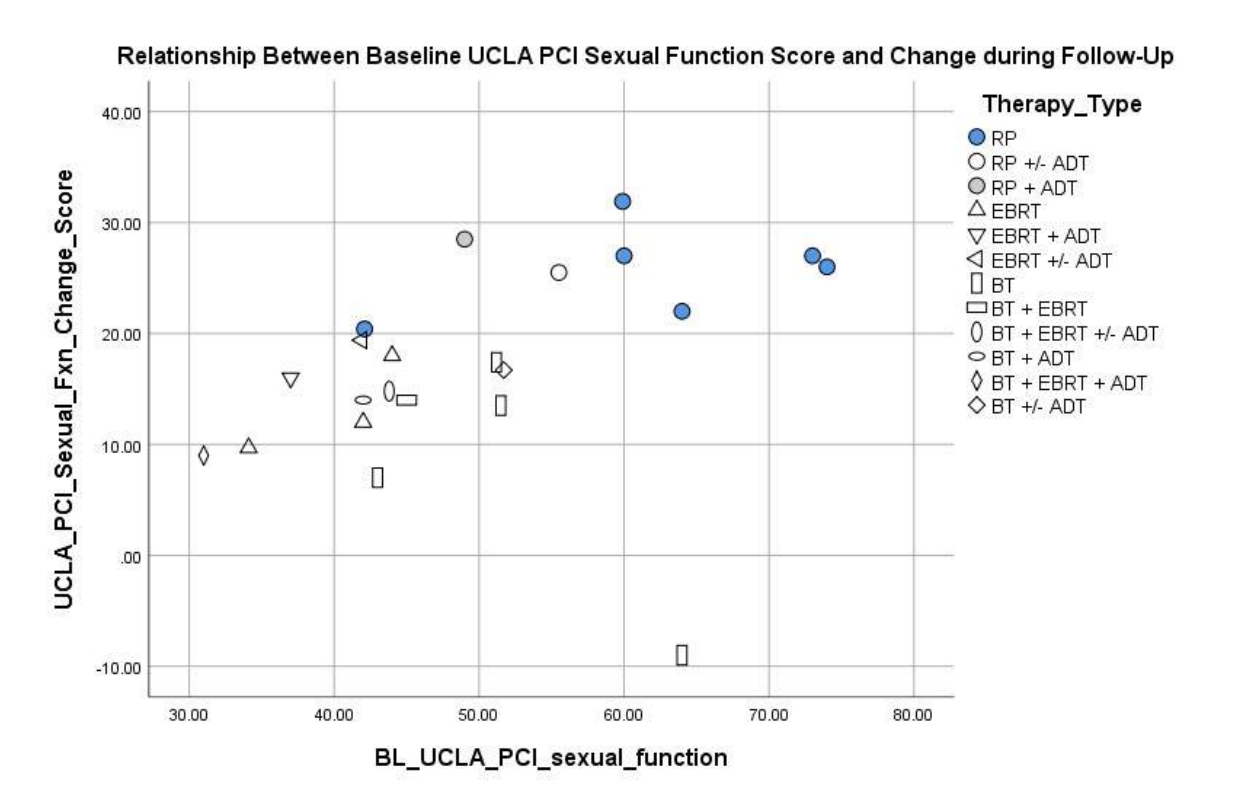


FIGURE 4. In studies that compared various types of therapy for prostate cancer, the figure depicts the relationship between UCLA PCI pre-treatment sexual function score and change in sexual function score during follow-up for men who underwent radical prostatectomy (RP) with or without androgen deprivation therapy (ADT), external beam radiation therapy (EBRT) with or without ADT, or brachytherapy (BT) with or without EBRT and/or ADT.

SECTION 5:

Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 6:

Patients and partners should be counseled that after prostate cancer therapies, most patients do not return to their pre-treatment erectile function levels.

(Strong Recommendation; Evidence Strength Grade B)

Discussion

See the detailed discussion under Guideline Statement 4; the same studies are referenced for this guideline statement. The variability in erectile function recovery after prostate cancer therapies (reviewed in detail below) is likely the result of many variables, including the specific surgical technique or radiation technique used, the surgeon's skill and experience if prostatectomy was performed, the patient's overall health, and how EF was measured before and after intervention. For detailed review of these issues, see Capogrosso et al. (2017).[307]

Men with normal erectile function before prostatectomy

A substantial proportion of men who undergo RPs, regardless of surgical technique or nerve-sparing category, do not return to pre-surgery sexual function levels as measured by validated questionnaires (the minority of studies) or as measured by varied definitions of sexual function recovery (the majority of studies). Sixty-three study arms reported findings for men who entered surgery with normal sexual function.[191-200, 202, 203, 205-221, 308-310] Forty-two of these study arms (approximately 67%) used nerve-sparing techniques (unilateral – 8 study arms; bilateral – 25 study arms; unilateral or bilateral – 9 study arms). There are insufficient data derived from validated questionnaires to determine whether nerve-sparing procedures consistently enhanced sexual function recovery post-RP or whether bilateral NS procedures were consistently more restorative than were unilateral procedures. However, all but one study reported percentages of men who had recovered sexual function (based on varying definitions) at the end of follow-up; those data allow exploration of aggregate effects.

Within individual studies that compared nerve-sparing (NS) and non-nerve-sparing techniques, higher rates of sexual function recovery were reported by men who had bilateral NS procedures compared to unilateral NS procedures and non-NS procedures. The only studies that reported sexual function recovery rates above 70% carried out bilateral NS procedures. Importantly, however, when data are aggregated across studies, the range of sexual function recovery rates for the three procedure types overlaps substantially at the middle and lower rates, indicating that a substantial proportion of NS procedures did not result in high rates of sexual function recovery in men who entered surgery with normal sexual function (see Appendix C for additional table and plot).

Men with varied levels of sexual function before prostatectomy

A substantial proportion of men with varied levels of baseline sexual function who undergo RPs, regardless of surgical technique or nerve-sparing category, do not return to pre-surgery sexual function levels as measured by validated questionnaires (the majority of studies) or as measured by varied definitions of sexual function recovery (the minority of studies).

Eight-five study arms reported findings for men who entered surgery with a range of baseline sexual function values (Figure 5). Fewer than 20% of these study arms used nerve-sparing techniques (unilateral – 6 study arms; bilateral – 4 study arms; unilateral or bilateral – 6 study arms), making it difficult to draw definitive conclusions for this group.

When UCLA PCI Sexual Function scores at baseline and final follow-up are plotted for all study arms with nerve-sparing category designated (men who entered surgery with normal sexual function as well as men with a range of sexual function), it is clear that nerve-sparing status is not a robust predictor of final score. Note that nerve-sparing has essentially no impact on final scores – the various types of nerve-sparing are scattered across the plot. Rather, final score is strongly correlated with pre-surgery baseline score (see discussion under Guideline Statement 15).

SECTION 5:

Guideline Statements With Supporting Evidence

Men with normal sexual function before radiotherapy

There are insufficient data to determine the precise impact of RT on sexual function recovery of men who had normal sexual function before RT. However, most studies report decreased sexual function during follow up regardless of RT type.

Men with varied levels of sexual function before radiotherapy

A substantial proportion of men who undergo RT, regardless of RT type, do not return to pre-RT sexual function levels as measured by validated questionnaires or as measured by meeting varied definitions of sexual function recovery.

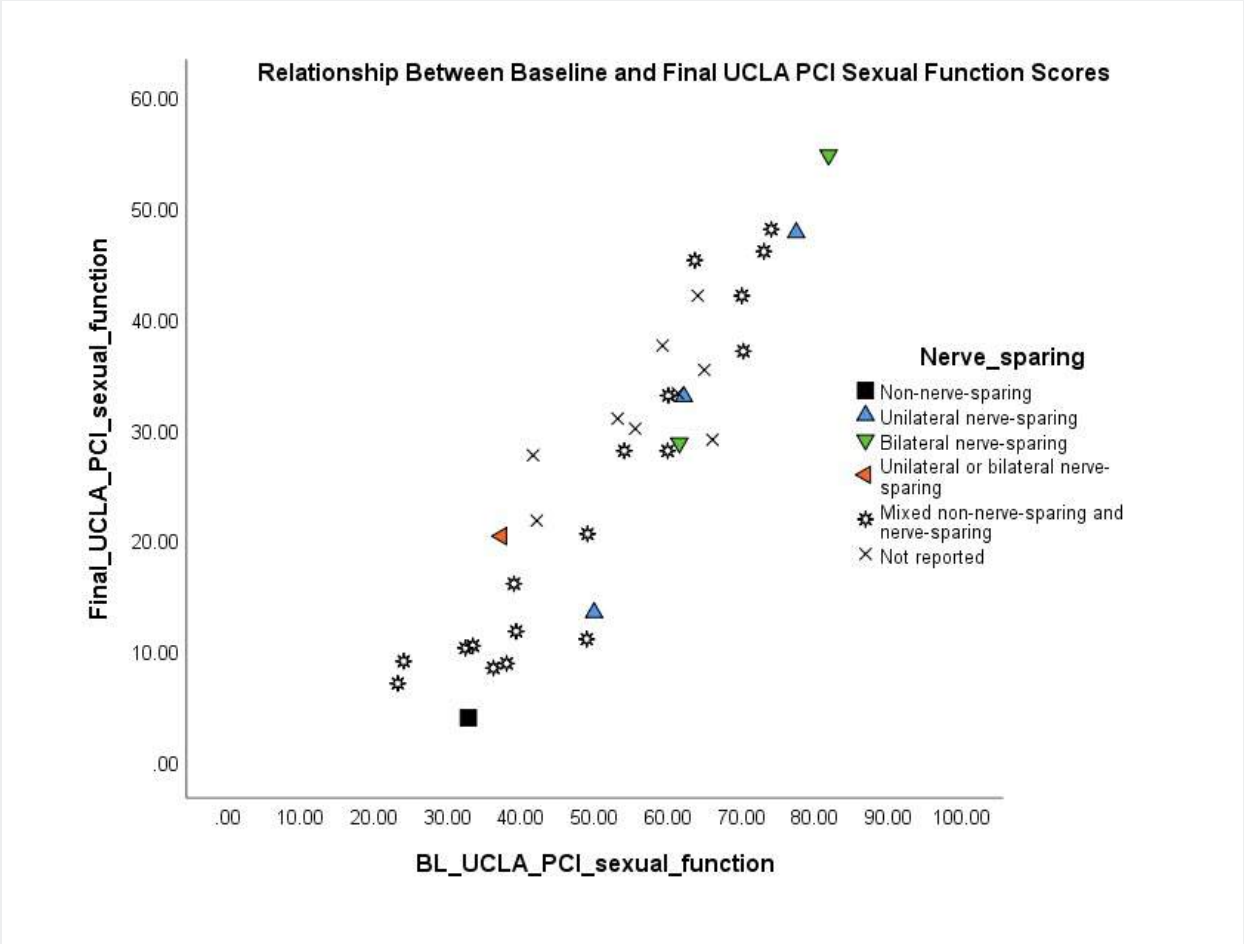


FIGURE 5. In studies of men who had a range of sexual function scores at pre-treatment baseline, the figure depicts the relationship between UCLA PCI pre-treatment baseline sexual function score and sexual function score at the end of follow-up for men who had prostatectomies that were non-nerve-sparing, unilateral nerve-sparing, or bilateral nerve-sparing; unilateral or bilateral nerve-sparing (for studies that did not differentiate outcomes between unilateral and bilateral groups); or non-nerve-sparing or nerve-sparing (for studies that did not differentiate outcomes between non-nerve-sparing and nerve-sparing groups).

SECTION 5:

Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 7:

Patients and partners should be advised that pre-existing erectile dysfunction is associated with a higher risk of post-treatment erectile dysfunction after radical prostatectomy, regardless of the surgical technique used, and after radiotherapy, regardless of the type of radiation employed.

(Strong Recommendation; Evidence Strength Grade B)

Discussion

There is a clear positive relationship between pre-surgery or pre-radiotherapy sexual function level and sexual function recovery at the end of follow-up such that men with better pre-intervention sexual function experience better sexual function recovery (Figure 6).

This relationship is present regardless of surgery or radiation type or technique and evident across different measures of sexual function. The relationship between baseline and final UCLA PCI sexual function scores is shown on the plot below with different forms of therapy designated (see Appendix C for plot of EPIC-50 baseline and final scores that demonstrate the same relationship).

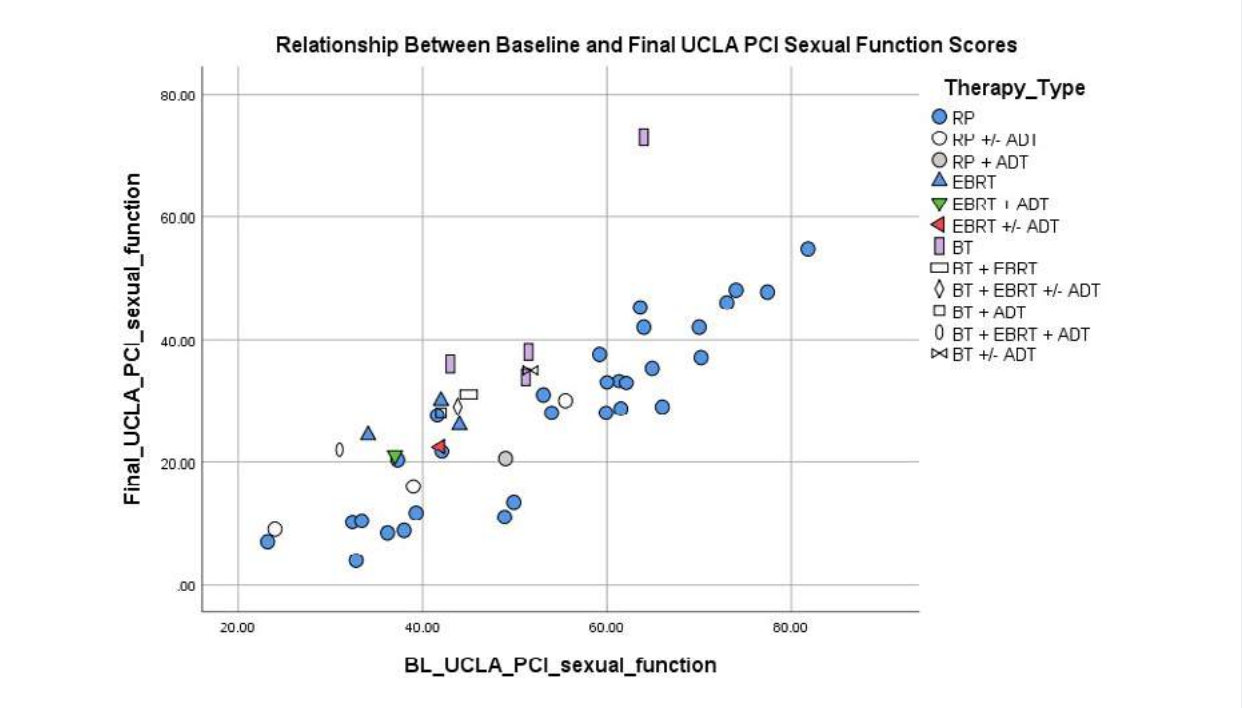


FIGURE 6. In studies that reported outcomes for various types of prostate cancer therapies (including studies that compared treatments as well as studies that reported on single treatments), the figure depicts the relationship between UCLA PCI pre-treatment sexual function score and sexual function score at the end of follow-up among men pre who underwent radical prostatectomy (RP) with or without androgen deprivation therapy (ADT), external beam radiation therapy (EBRT) with or without ADT, or brachytherapy (BT) with or without EBRT and/or ADT.

SECTION 5:

Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 8:

Patients and partners should be informed that there is no clear evidence supporting advantage of either robotic, laparoscopic, or open radical prostatectomy in terms of post-operative erectile function outcomes.

(Moderate Recommendation; Evidence Strength Grade C)

Discussion

There are insufficient data to determine whether higher sexual function recovery rates are reliably associated with specific surgical techniques (e.g., open RP vs. laparoscopic RP vs. robot-assisted laparoscopic RP). The strongest evidence is provided by a randomized clinical trial that compared open vs. robotic surgery and reported that there were no differences in rates of EF recovery, either short-term or long-term (24 months).[311, 312] Although uncontrolled individual studies suggest the superiority of one surgical technique over another (nerve sparing (NS) vs non nerve sparing), when data across studies are aggregated, pre-surgery sexual function level remains a critical variable that determines outcomes post-surgery. Four studies compared open to robot-assisted RPs. Fode et al. (2014) reported that men who had open RPs had lower rates of recovery (28.9%) compared to men who had a robot-assisted procedure (36.3%) at 12 months postop; these procedures were a mixture of non-NS and NS RPs.[201]

Haglind et al. (2015) reported that at 12 months post-surgery, 25% of men in the open group and 30% of the men in the robot-assisted group had recovered sexual function (also a mix of NS and non-NS procedures).[243] Kim et al. (2011) reported that men who had open NS RP had lower recovery rates (47.5%) compared to men who had robot-assisted NS procedures (83.8%) at 24 months postop, but more men in the robot-assisted group had bilateral procedures than in the open group. Moreover, the open group had a higher rate of ADT.[203] In contrast, Ludovico et al. (2013) reported that men who had open bilateral NS RPs had similar (and low) rates of sexual function recovery compared to men who had robot-assisted bilateral NS RPs (25 and 26.9%, respectively) at 12 months postop.[206]

Two systematic reviews compared laparoscopic vs. robot-assisted procedures and came to opposite conclusions. Huang et al. (2017) included 12 studies and evaluated sexual function recovery rates.[185] The meta-analysis indicated that recovery was more likely after robot-assisted RP compared to laparoscopic RP at 12 months follow-up (OR=2.20; 95% CI 1.41-3.43, $p<0.05$; $I^2 = 72\%$, $p<0.05$).

The authors did not address the significant heterogeneity in the analysis, and too few studies had a long enough follow up period, making the longer-term effects of RP type unclear. Ficarra et al. (2009) also compared laparoscopic vs. robot-assisted RP but did not carry out a meta-analysis, citing their concern with the lack of comparable valid measures across studies.[182] Six studies reported relevant findings; only one study documented higher rates of sexual function recovery among men who had the robot-assisted procedure compared to non-robot-assisted procedure. Note that many of the included studies in Huang et al. (2017) had not yet been published when this review was carried out.[185]

Three individual studies compared laparoscopic procedures to robot-assisted procedures. Asimakopoulos et al. (2011) compared bilateral NS robot-assisted RP to bilateral NS laparoscopic RP and reported that more men (77%) achieved sexual function recovery in the robot-assisted group compared to the non-robot group (32%) at 12 months postop.[191] Willis et al. (2011) also compared robot-assisted to laparoscopic RP; all men had bilateral NS procedures. At 12 months, more men in the robot-assisted group (87.5%) had recovered function compared to the laparoscopic only group (67%).[220] Berge et al. (2013) also compared robot-assisted to laparoscopic RP but used a mix of NS and non-NS procedures and reported at 12 months that similar percentages of men (Lap – 46.9%; Robot – 41.4%) had recovered function.[193] One study compared open to laparoscopic RP. Namiki et al. (2005) reported at 12 months that UCLA PCI sexual function scores were 11.7 (open procedure) and 8.4 (laparoscopic procedure) (baseline 39.3 and 36.2, respectively; mix of NS and non-NS procedures).[259]

Guideline Statements With Supporting Evidence

One study compared various forms of open procedures to laparoscopic procedures (mixed nerve-sparing categories). Namiki et al. (2006) compared open retropubic, open perineal, and laparoscopic RPs (mixed nerve-sparing categories).[313] At 12 months, UCLA PCI sexual function scores were 10.4 in the open retropubic group, 8.8 in the open perineal group, and 10.2 in the laparoscopic group (baseline scores 33.4, 38.0, and 32.4, respectively).

When UCLA PCI baseline and final follow-up scores are plotted for all prostatectomy studies, the robust relationship between baseline function level and post-surgery function level continues to be evident (Figure 7).

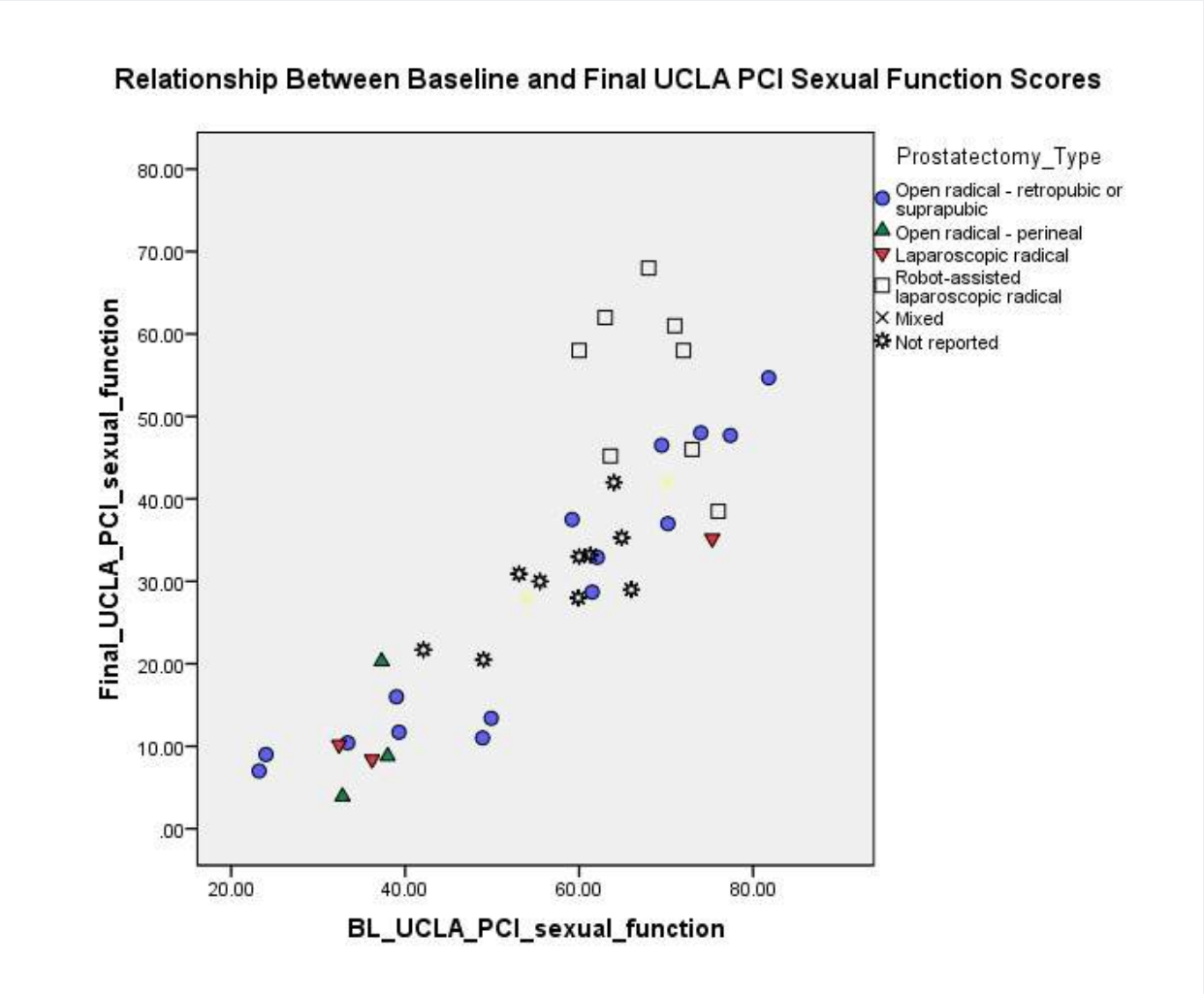


FIGURE 7. In studies that reported on men who had a range of sexual function scores at pre-treatment baseline, the figure depicts the relationship between UCLA PCI pre-treatment baseline sexual function score and sexual function score at the end of follow-up for men who had prostatectomies that were open radical with a retropubic or suprapubic approach, open radical with a perineal approach, laparoscopic radical, robot-assisted laparoscopic radical, mixed surgical approaches, or surgical approach not reported.

SECTION 5:
Guideline Statements With Supporting Evidence

ORGASMIC DYSFUNCTION

Orgasmic dysfunction has traditionally been neglected as a key outcome in the prostate cancer treatment literature. A majority of studies have looked at alterations in erectile dysfunction and sexual desire/libido changes with ADT. However, many men find orgasmic alterations after PCT very distressing. Moreover, men report that maintaining orgasmic function is very important for partner and marital satisfaction, relationship stability, and their own happiness.[314] Relationship satisfaction and happiness have been correlated with orgasm consistency, quality and satisfaction.[315]

GUIDELINE STATEMENT 9:

Patients and partners should be counseled that both prostatectomy and radiation therapy may be associated with orgasmic pain, decreased sexual desire, anodyspareunia during anal intercourse, and changes in ejaculatory function. Prostatectomy results in an immediate and complete loss of ejaculate volume, while radiation therapy is associated with a more gradual decline and variable reduction in ejaculate volume.

(Moderate Recommendation; Evidence Strength Grade C)

Discussion

The removal of the prostate results in a complete loss of ejaculate, an aspect of remaining orgasmic function that needs to be impressed on patients before surgery. One systematic review reported on the neglected side effects after radical prostatectomy.[183, 316]

Because of study heterogeneity, a meta-analysis was not performed. However, the authors concluded that alteration of orgasmic function occurred in up to 78% of men and orgasm-associated pain in up to 19% of men. A deterioration of sexual activity has also been associated with the severity of ejaculatory dysfunction, particularly with decreased volume or absence of semen.

After radiotherapy for prostate cancer ejaculatory ‘disturbances’ vary, from a reduction or absence of ejaculate volume (2%-56%), to discomfort during ejaculation (3-26%), and haemospermia (5-15%) (21, 25). Dissatisfaction with sex life has been reported in 25-60%, decreased libido in 8-53%, and decreased sexual desire in 12-58% of patients following PCT. A decreased intensity of orgasm, decreased frequency and rigidity of erections, and decreased importance of sex have also been reported.[317, 318]

In contrast to these negative consequences, there also have been reports of increased orgasm intensity, multiple orgasms, and improved ability to continue sexual activity.[183, 319] After prostatectomy, impaired sexual desire has been reported in 40.9% of men at six months and 34.1% of men at 24 months post-RP.[320]

SECTION 5:

Guideline Statements With Supporting Evidence



SEXUAL INCONTINENCE

Sexual incontinence includes two contexts in which urine is involuntarily lost: during arousal (sexual arousal incontinence) and during orgasm (climacturia). The mechanisms underlying both types of incontinence are unclear. In particular, the mechanism of orgasm-associated incontinence or climacturia following RP has yet to be elucidated. Koeman et al. hypothesized that urine loss at the time of orgasm was related to removal of the internal urethral sphincter during RP in conjunction with external sphincter relaxation.[321]

Others have associated climacturia to intrinsic sphincter deficiency, following the injury of the external urethral sphincter and its supporting structures during surgery.[322, 323] It is believed that the external urethral sphincter is the dominant provider of continence following RP. Therefore, at the moment of orgasm-related climax, it is conceivable that urine leakage would occur after RP. However, if this was entirely true, all men following RP would complain of climacturia. Moreover, most of the current literature has not found an association between climacturia and daytime urinary incontinence.[322, 324, 325] O'Neil and colleagues did demonstrate an association between climacturia and post-operative urinary incontinence.[326] Although it may be convenient to assume that climacturia is simply an extension of post-prostatectomy urinary incontinence, there is evidence that suggests otherwise. In the same trial, roughly 30% of patients with climacturia did not report urinary incontinence, and the rate was similar for the inverse. Additionally, the Nilsson et al study demonstrated that 86% of the 268 patients reporting climacturia were otherwise continent. After calculating the proportions of men reporting climacturia within different potentially associated variables, they found that previous transurethral resection of the prostate (TURP) increased the risk of experiencing climacturia (RR 1.4, 95% CI 1.0-2.0).[325] This suggests that not preserving the bladder neck, as it often happens during TURP procedures, might be related to orgasm-associated urinary incontinence. These data seem to suggest a potentially related yet distinct pathophysiology between climacturia and urinary incontinence.

Another potential mechanism involves loss of prostatic urethral length, possibly related to loss of penile length. Choi and colleagues demonstrated that loss of penile length post-operatively was an independent predictor of climacturia (OR 2.58, $p < .01$).[322] This finding was supported by a case-control study by Manassero et al in 2012. The authors investigated the incidence and video-urodynamic aspects of climacturia in patients who were otherwise continent after RP. Twenty-four of a pool of 84 men reported climacturia (28.6%). The series showed significantly shorter functional urethral length in the climacteric group when compared to controls ($p=0.02$), suggesting that urethral length may play a role in orgasm-associated incontinence.[327] Regardless, more studies will be necessary to fully characterize the condition.

SECTION 5:

Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 10:

Patients and partners should be counseled that sexual arousal incontinence and climacturia may occur after radical prostatectomy with the potential to recover with the recovery of urinary control.

(Strong Recommendation, Evidence Strength Grade C)

Discussion

Sexual incontinence may occur during arousal and/or as climacturia. Sexual incontinence is a condition as yet to be completely characterized. Available data suggest a prevalence of climacturia around 30%, ranging from 20% to 93%.[183, 322, 324-326, 328-330]

One systematic review reported on neglected side effects after radical prostatectomy. The authors concluded that urinary incontinence during sexual activity post-RP occurred in 25 to 93% of men.[183] The impact of climacturia on overall sexual satisfaction is not yet fully understood. We know that patients can experience significant humiliation that leads to avoidance of sexual relations and a decrease in quality of life.[321] A study reported "significant bother" in up to 47% of those men experiencing climacturia.[324]

The initial description of climacturia comes from a small series published by Koeman and colleagues in 1996.[321] Nine of 14 patients who had undergone prior prostatectomy and were able to achieve orgasm reported involuntary loss of urine at the time of orgasm. A larger study by Barnas and colleagues in 2004 reported an overall incidence of 93% (N=222/239) 39.5 months after RP.[328] However, the majority of these patients (n=184) reported symptoms occuring either occasionally or rarely, with only 16% reporting urine loss with every orgasm. When compared to the entire body of research, this estimation seems quite high. In 2006, Lee et al demonstrated an overall prevalence of 45.2% (n=16) in a series of 42 patients with a mean follow-up 23.6 months after open RP. Among these patients only 32% (n=6) reported symptoms more often than occasionally.[324] Several more recent studies have shown an incidence of sexual incontinence between twenty and forty percent. In 2007, Choi and colleagues demonstrated a prevalence of 20% in a cohort of 475 patients who presented for post-operative sexual dysfunction seven months following RP.[322] In 2011, Nilsson et al demonstrated a prevalence of 39% in a cohort of 691 men that remained sexually active after a median 2.2 years following open or robot-assisted laparoscopic RP.[325] The majority of these patients reported climacturia occurring in less than half of orgasms. A smaller study by Messaoudi et al that same year showed a prevalence of 25.4% in a 63 patient series after a median follow up of 26.8 months.[329] O'Neil and colleagues published a study in 2014 that demonstrated a prevalence of 28.3% in sexually active patients after receiving either open or robot assisted laparoscopic RP 20.3 months prior.[326] Later on, Frey et al demonstrated a prevalence of 27% in a cohort of 256 sexually active men 17 months after RP.[183] The largest and most recent study comes from Capogrosso et al in 2016 who followed patients for 84 months and reported climacturia in 29.5% of patients.[330]

Various covariates and independent predictors of climacturia have been described in the above studies. Choi et al identified shorter time since surgery to be an independent predictor of climacturia following RP.[322] This finding was supported by Capogrosso and colleagues who attempted to assess the recovery rate and predictors of climacturia by prospectively collecting data from 749 consecutive patients who underwent RP, both open and robotic-assisted. Twenty-nine percent of patients reported postoperative climacturia, with similar proportions between patients undergoing open and robotic surgery.[330] They studied the rates of recovery from climacturia over time and demonstrated a clear trend towards recovery of climacturia over time with 24% (n=53) of patients recovering at 84 months versus 2.3% and 5.5% at 12 and 24 months, respectively. After adjusting for age at surgery, nerve-sparing status, erectile function and urinary incontinence recovery, multivariable Cox regression analysis demonstrated robot-assisted laparoscopic surgery to be an independent predictor of a faster recovery of continence with orgasm. These findings suggest that climacturia following RP tends to improve throughout the post-operative period, although it may take a period of years.

SECTION 5:

Guideline Statements With Supporting Evidence

PENILE LENGTH LOSS AFTER RADICAL PROSTATECTOMY

GUIDELINE STATEMENT 11:

Patients and partners should be counseled that penile length and girth/volume loss may occur after radical prostatectomy.

(Moderate Recommendation, Evidence Strength Grade C)

Discussion

While subjective penile shortening is a common patient complaint post-RP, there are few data in the literature evaluating this consequence of RP. Frey et al. (2014) conducted a systematic review of neglected side effects after radical prostatectomy, including sexual dysfunctions. Because of study heterogeneity, a meta-analysis was not performed. The authors concluded that penile shortening occurs in up to 45% of men. Frey et al surveyed 316 men post-RP, 47% of whom reported a length loss of >1cm (with 33% reporting 1-3cm loss, 11% noted 3-5cm loss and 4% reported > 5cm penile length loss). Predictors of penile shortening included increasing BMI (OR 1.11, 95% CI 1.02-1.20, p=0.01) and ED (OR 1.81, 95% CI 1.07-3.10, p=0.03). Conversely, NSS (defined as bilateral or unilateral nerve-sparing) was protective against penile shortening (OR 0.32, 95% CI 0.16-0.95, p<0.001).[183] Similarly, Capogrosso et al noted high rates of subjective penile shortening post-op. Of 134 men evaluated at ≥ 24 months post-RP, 56% of men complained of penile shortening compared to pre-op.[330]

Objective penile shortening post-RP has also been evaluated. Montorsi et al performed an RCT to evaluate penile rehabilitation (REACTT) which compared tadalafil 5mg daily versus tadalafil 20mg on demand versus placebo. 423 men were randomized and the study duration was 9 months.

All men had bilateral NSS, although they specify that non-perfect NS was included. Penile length was measured pre-op and at 9 months post-op.

All groups experienced length loss (2.6 mm in the tadalafil 5mg daily group, 8.9 mm in the tadalafil 20mg on demand group, 6.6 mm in the placebo group), with the smallest loss among men who used daily tadalafil and the largest loss among men who used on-demand tadalafil.[331]

SECTION 5:

Guideline Statements With Supporting Evidence

PENILE CURVATURE (PEYRONIE'S DISEASE) AFTER RADICAL PROSTATECTOMY

GUIDELINE STATEMENT 12:

Patients and partners should be informed that radical prostatectomy may be associated with an increased risk of the development of penile curvature (Peyronie's disease; PD

(Conditional Recommendation, Evidence Strength Grade C)

Discussion

Ciancio and Kim evaluated 110 men post-RP who were seen for ED; 41% complained of subjective PD with 93% noting curvature and 24% reporting hourglass deformity (some men had both curvature and hourglass deformity). Approximately 69% of men had palpable plaque oan exam—a substantial percentage of men with PD post-RP. Interestingly, there were no significant predictors of PD (the use or timing of vacuum erectile device (VED) or an intracavernosal injection (ICI), NSS or pathologic variables).[332] More recently, Capogrosso et al also noted significant rates of penile deformity post-RP.

They evaluated 67 men post robotic-assisted laparoscopic prostatectomy (RALP) and 67 men post open radical prostatectomy (oRP). At ≥ 24 months post-RP, 21.6% of all men in the study noted a penile deformity (exclusive of penile shortening).[333] Post RP Frey et al surveyed 312 men with a mean age of 64 years at the time of RP. With a median follow-up of 17 months post-op, 30 men (9.6%) reported a new penile curvature post-op. Of the men with penile curvature, eight (26.7%) reported significant bother.[183]

Clinical experience suggests that penile deformities may also develop after radiotherapy for prostate cancer, although the frequency with which this occurs is not well investigated or reported in the current literature.

SECTION 5:

Guideline Statements With Supporting Evidence

ANDROGEN DEPRIVATION THERAPY (ADT)

GUIDELINE STATEMENT 13:

Patients and partners should be counseled regarding the diverse impacts of androgen deprivation therapy (ADT) (as a primary or as an adjuvant ADT) on sexual desire, erectile function, penile girth and length, ejaculatory function, orgasmic function and couples' intimacy.

(Strong Recommendation; Evidence Strength Grade C)

Discussion

Sexual desire Although studies suggest that all prostate cancer treatments may result in some degree of decreased sexual desire, androgen deprivation therapy (ADT) is consistently associated with the largest negative impact. To date, no high-level studies have directly compared the impact of various prostate cancer treatments on sexual desire/libido. Among men treated with ADT (orchiectomy or luteinizing hormone-releasing hormone), the rate of sexual inactivity increases by approximately 35%.[334] Although sexual inactivity may be related to erectile dysfunction or sexual desire/libido, when men were specifically asked about sexual interest, those reporting no interest rose by 26-39% post ADT. Additional analyses showed that 51% of men who had sexual interest before treatment changed to no interest after ADT, and 73% stopped all sexual activity. Among men requiring long-term ADT, sexual side effects, including reduced desire, may be mitigated by the use of intermittent treatment protocols where possible. Because ADT is frequently combined with radiation therapy protocols for varying amounts of time, any analysis of the sexual side effects of RT should specifically investigate the effects of ADT may be having.

While most men report diminution or total lack of sex drive on ADT, it is not universal. In addition, studies have shown that sexual activity is not solely driven by sexual desire/libido and that sexual desire/libido can be maintained while on ADT.[335] However, fatigue, loss of initiative, and sleep difficulty, possibly associated with hot flashes, are common and add to decreased sexual desire and challenges initiating sexual activity.[336] In addition, the duration of ADT side effects may last longer among older men and/or among men who started therapy with low testosterone levels.[337]

Shortening of the penis and shrinkage of the testicles ADT may exacerbate penile shortening already present as a result of surgery or radiation, and shrinkage of the testicles due to ADT is common.[338, 339] It is extremely important to forewarn patients of these potential changes. These effects may or may not be reversible, depending on patient specific factors such as age, prior therapies, etc.

Additional side effects can affect men's sexual body image and self-confidence Within one year of starting ADT, up to 70% of men experience weight gain of an average of 10 lbs.[340] The weight gain is typically due to an increase in body fat in the waist, hips, and thighs, resulting in a feminizing effect that men may report as distressing.

Gynecomastia Enlargement and tenderness of breast tissue can occur in a significant proportion of men on ADT and does not regress if ADT is stopped. It is more common in men receiving estrogen. It may occur during recovery from ADT when there is an imbalance of testosterone and estrogen in the breast tissue.[341] Radiation therapy with electron beam may lessen breast enlargement but may not prevent it completely.[342]

Loss of male body hair Loss of body hair is a common side effect of ADT and can be especially distressing if the patient does not expect it. It is usually reversible if ADT can be stopped.

Depression, anxiety, and emotional lability These symptoms are associated with ADT and may exacerbate pre-existing depressive symptoms. Irritability also can interfere with couple relationships.[343]

Orchiectomy The Panel notes that in some areas of the world orchiectomy is used instead of ADT.[344] Removal of the testicles, a visible and permanent change to a man's body, poses additional challenges for patient self-image and therapeutic efforts to optimize sexual function. Providing patients with clear and accurate information about the potential consequences of orchiectomy is an important component of patient counseling.

SECTION 5:
Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 14:

Patients and partners should be counseled that patients treated with combined ADT and radiotherapy are at risk for the cumulative sexual side effects associated with both ADT and radiotherapy.

(Strong Recommendation; Evidence Strength Grade C)

Discussion

The duration of these side effects typically exceeds the duration of radiotherapy, and may extend 3-6 months beyond the completion of ADT, depending on the dose and formulation used.

FERTILITY AND FAMILY PLANNING

Background

Prostate cancer therapies can affect patient fertility. Couples who may want to bear children should be thoroughly counseled regarding the potential effects of prostate cancer treatments on family planning decisions. Couples who are interested in fertility preservation are encouraged to seek consultation with a reproductive specialist and consider sperm banking prior to prostate cancer treatments if appropriate.

GUIDELINE STATEMENT 15:

Prior to undergoing prostate cancer therapies, clinicians should routinely ask prostate cancer patients (regardless of age) and their partners if future fertility is desired.

(Moderate Recommendation, Evidence Strength Grade C)

Discussion

It is incorrect to assume that men with prostate cancer, who tend to be older, do not wish to become biological fathers. The trend for fatherhood in general among older men has been growing, possibly influenced by the spread of assisted reproductive techniques (ART): between 1980 and 2006, the fertility rate for men aged >= 40 years of age increased nearly 30%.[345] Even older men undergoing prostate cancer treatments express interest in fertility; in a group of 510 men undergoing pre-operative evaluation for radical prostatectomy that were offered fertility counselling, 20% of the cohort expressed interest in cryopreservation despite a mean age of 64.[346]

In addition, since the diagnosis of prostate cancer for men under 55 years of age has increased nine-fold since 1977, today more younger men desiring fertility may also need to undergo prostate cancer treatments.[347] Furthermore, in older men considering biological fatherhood, the chance of a high rate of senescent sperm should always be taken into account.[348]

SECTION 5:
Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 16:

Patients interested in future fertility should be counseled that prostate cancer therapies may negatively affect their fertility potential. These patients could consider pre-treatment sperm banking and referral to a reproductive specialist as availability of assisted reproductive techniques and financial and cultural considerations allow.

(Moderate Recommendation, Evidence Strength Grade C)

Discussion

All therapies for prostate cancer have the potential to impact future fertility. This may be from anatomical causes, including fibrotic obstruction of the ejaculatory ducts following radiation therapies[349], and obstructive azoospermia from radical prostatectomy resulting in dry orgasm. Daniell et al demonstrated that hormonal levels were also significantly altered after external beam radiation, with lower levels of T, free T, and DHT, and higher levels of LH and FSH noted in men followed radiation therapy compared to men following prostatectomy, but this may be temporary.[350]

There is scarce literature on the effect of radiation therapy for men with prostate cancer on spermatogenesis. Not all countries routinely shield the testes in external radiation therapy, and the possibility of scatter, while likely minimal if at all, has not been studied in the prostate cancer population. One small study[351] (n=4) of men undergoing brachytherapy found it did not significantly alter sperm parameters, speculating the total dose of radiation calculated (18.88 cGy) was considered to be too low to have any significant effect on testicular tissues. However, they did recommend However, they did recommend that men 1) delay conception for 12 months after treatment and 2) sperm bank BEFORE treatment. In patients undergoing genital radiation for cancers other than prostate, it is known that radiation therapy can cause direct damage to the testicular germ cells, as well as Sertoli cells and Leydig cells. Specifically, radiation to the testes can induce azoospermia through Leydig cell dysfunction, at doses of >20 Gy, with single direct doses of just 4–6 Gy potentially producing azoospermia lasting ≥5 years.[349, 352] Spermatogonia are the most radiosensitive cells in the spermatogenesis pathway.[353] In men being treated for seminoma, scattered doses of radiation have been calculated for the remaining testis, and two-thirds developed oligo- or azoospermia after doses of 0.2–1.3 Gy.[354] Trottmann performed a review of the literature and deduced a threshold of direct irradiation of 15 cGy to the testicles was necessary to produce any reduction in sperm count: oligospermia was caused by 15 – 35 cGY, whereas 35 – 50 cGY caused azoospermia, suggesting a much lower threshold for tolerance.[355] Exposure of the testis to radiation may also affect sperm DNA quality, possibly affecting pregnancy outcomes and the health of the progeny. However, overall it is felt the radiation from brachytherapy or shielded testes from external beam therapy will have minimal to no effects on spermatogenesis, but no specific long-term studies have been conducted to confirm this to date.

Between 15 – 30% of men remain permanently infertile after chemotherapy, and chemotherapy such as docetaxel is used for castrate-resistant prostate cancer.[356] The fertility effect of chemotherapies has not yet been studied in men with prostate cancer, but in men of reproductive age with solid tumors receiving taxane-based chemotherapy, there were significant decreases in serum inhibin B and an increase of serum FSH with bilateral reduction in testicular size. Follow up was too short to know whether the gonadotoxicity is permanent or temporary.[357] It is recommended that fatherhood be delayed for a year after cytotoxic therapy.[358]

It is recommended that patients and partners delay family building following treatment with all forms of radiotherapy. After low-dose brachytherapy, due to the half-life of I125, it is recommended that the patients wait at least 3–4 months before trying to conceive, even though the direct effects of radiation on testicular tissues are minimal (<20 cGy).[351, 356] There is no data available on the effect of high-dose brachytherapy on testicular tissues or unshielded testes in men with prostate cancer who may receive doses high enough doses to cause reversible azoospermia.

SECTION 5:

Guideline Statements With Supporting Evidence

Given the risks to sperm, it is reasonable to consider sperm banking prior to prostate cancer therapies in couples interested in fertility. Access to sperm banking depends on the availability of assisted reproductive technique (ART) resources and other personal factors. While sperm cryopreservation is most often used for higher technology, such as in vitro fertilization (IVF), multiple banked specimens can be used for lower cost trials of intrauterine insemination prior to IVF. Sperm can also be surgically retrieved after prostate cancer treatments if higher ART is available.



SECTION 5:
Guideline Statements With Supporting Evidence

III. Assessment of sexual function and sexual distress

Introduction

A biopsychosocial sexual health assessment is critical in prostate cancer survivorship. Patients experience significant sexual difficulties from the beginning of treatment well into long-term survivorship, with a negative impact on their quality of life.[12, 84, 359] Patients and partners report difficulties finding information and coping.[20, 54, 360]

It is therefore incumbent on clinicians to regularly inquire about sexual concerns, beginning prior to treatment, soon thereafter, and during more widely spaced follow-up visits.

The intention behind conducting a sexual health assessment will dictate the depth and breadth of the assessment. Oncology clinicians can screen for concerns, then specialists trained in sexual health can provide a full biopsychosocial sexual health assessment and counsel patients and partners regarding treatment choices (Appendix C). Providers should use validated measures to carry out the assessment whenever possible.

It is important to note that while there are validated measures that assess relationship quality, couple coping, and sexual communication, a validated measure to assess sexual relationships is yet to be developed.[361-363]

GUIDELINE STATEMENT 17:

Clinicians should offer screening and assessment prior to prostate cancer therapy and regularly throughout follow-up, tailored to cultural context, sexual orientation, and gender identity.

(Clinical Principle)

Discussion

Screening provides an opportunity to identify immediate patient and partner concerns and refer individuals and couples to a sexual medicine and/or a sexual health expert for in-depth evaluation and treatment that addresses changes in the patient's sexual function, the patient's and partner's response to it, and its impact on the relationship. If sexual recovery is important to the patient and the couple, sexual function should be routinely assessed before and after prostate cancer therapy. Follow-up questions should also be routinely asked to ascertain the patient's satisfaction with his sexual function and his sexual relationship in order to plan supportive intervention. Without discussion, avoidance of sexual activity or complete cessation may result, even if patients and partners do not desire it. As one of the known barriers is discussing sex with a healthcare provider, in order to normalize this aspect of care, it is important for the healthcare provider to initiate the assessment and ask the questions.[86]

Culture and ethnicity affect the experience of prostate cancer diagnosis and treatment and shape perceptions and interpretations of resulting sexual dysfunction. Lingering mistrust of the medical system and poor relationships between patients and providers can hinder prostate cancer management in Black-American men.[364, 365] In addition, health literacy may affect the understanding of cancer therapies and treatments to ameliorate treatment-related sexual dysfunction. Poor prostate cancer knowledge was found in surveys of economically-disadvantaged men diagnosed with prostate cancer and should therefore be assessed. In these samples, which included a high-proportion of Black-American men, this finding was associated with decisional conflict, anxiety, and stress.[366-368] Along with health literacy, spirituality may be particularly important in certain cultural groups because it accords meaning to the experience of cancer and treatment consequences. In one study spirituality was found to be stronger in Black-American and Hispanic prostate cancer survivors than in Caucasian prostate cancer survivors.[369] Overall, these studies suggest the importance of considering culture-specific beliefs and values when assessing the impact of prostate cancer and its therapies on sexuality. Currently, there is still insufficient understanding of the impacts of

cultural values, societal norms, and health disparities on sexuality in prostate cancer patients. As a result, while currently available validated measures may be able to help with the assessment of sexual function, they are unable to assess the impact on the individual in the context of the relationship and community. Gay and bisexual men have reported that providers treat them routinely as if they were heterosexual.[17, 370] This misalignment makes it difficult for some patients to come out to their providers for fear that they will not be accepted. Historically, gay and bisexual men have suffered discrimination, and their fear of rejection is justified.[96, 371] It is therefore important for providers to inquire about the gender of the partner when assessing sexual health in prostate cancer survivorship. A male partner should be invited to participate in discussions of the sexual outcomes of prostate cancer treatment because his sex life will be affected by the patient's sexual outcomes. The provider can assess the need for any further support for both the patient and the gay or bisexual partner and provide referral to sexual medicine and or sexual health provider as necessary. In such cases however, most validated measures will have limited relevance to sexual practices of men who have sex with men, as they were developed with heterosexual samples. Further research is needed in this area.

Assessment of sexual function in transgender women is typically best conducted as an interview. While there are some similarities among trans women in the process of transition, every patient is different. The patient's preference about the use of pronouns, the extent of transition desired and transition completed, sex and gender of partners, sexual practices, timing of medical or surgical interventions, psychological and relationship status all individually and together vary from person to person. All these factors, described by Sterling and Garcia in their paper on proposed guidelines for prostate cancer screening for transgender women, affect sexual function, sexual pleasure, and sexual goals (Appendix B).[372] Without validated measures, assessment of sexual function in gender non-conforming individuals requires an individualized approach at this time. Research into how validated measures might be designed and tested for transgender women and gender non-conforming individuals is needed.

Body of Evidence Strength: Evidence is strength Grade C. The available studies are encouraging in their findings but generally are observational in design with small sample sizes.

SECTION 5:

Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 18:

In both pre and post prostate cancer therapy assessments, clinicians should pay attention to the presence of erectile dysfunction, low sexual satisfaction, low desire, orgasmic dysfunction [including altered orgasmic sensation, lack of orgasm (anorgasmia), painful orgasm (dysorgasmia) and orgasm-associated urinary incontinence (climacturia)], sexual arousal incontinence, changes in penile shape, girth, length or size, anodyspareunia, curvature, couples' sexual concerns and avoidance or cessation of sexual activity, and couples' sexual concerns.

(Strong Recommendation, Evidence Strength C)

Discussion

A comprehensive sexual health assessment must go beyond erectile dysfunction and address side-effects that are often neglected, such as orgasmic dysfunction, climacturia, and penile curvature.[373]

These additional issues may cause distress because they are generally not discussed. Patients who experience these side-effects, unmentioned by clinicians, may be unaware of the potential for their mitigation. As a result, working towards their resolution may require a collaboration between a urologist with sexual medicine training and a mental health provider with sexual health training. Together, they can provide a biopsychosocial approach to addressing the patient's concerns. Evaluating distress about these additional side-effects becomes an important aspect of an overall evaluation.[374]

Body of Evidence Strength: Evidence is strength Grade C. The available studies are encouraging in their findings but generally are observational in design with small sample sizes.



GUIDELINE STATEMENT 19:

Patients and partners should be counseled that an assessment of the partner's sexual function can help plan treatment designed to support couples' recovery of sexual intimacy.

(Clinical Principle)

Discussion

Changes in quality of life after prostate cancer therapies, as represented by functional status, including sexual function, are strongly linked with the degree of outcome satisfaction among patients as well as their partners.[63] All prostate cancer therapies are associated with distinct changes in quality-of-life domains related to sexual, and other functions which in turn influence patient and partner satisfaction. The focus of concern of patients for their sexual function is often not shared to an equal degree by their partners.[375] It is important to note that partners think and respond differently from patients to intimacy challenges that occur as a result of prostate cancer diagnosis and treatment.

It has become increasingly clear that partners play an important role in men's sexual recovery after prostate cancer. However, sexual health problems of female partners are often overlooked and/or unaddressed. Given the average age of 65 in prostate cancer patients, most female partners are menopausal or post-menopausal and have their own sexual function challenges. Previous studies assessing sexual function in both prostate cancer patients and their female partners indicate that a majority of female partners report significant symptoms of female sexual dysfunction, such as vaginal dryness and low desire which, given the age of this cohort of patients, may be related to menopause.[138, 376, 377] In addition, female partners may need specific types of support/intervention for their own sexual concerns.[50, 376] Studies have shown that partners tend to respond positively to interventions and may even change attitudes, for example appraise the illness more positively or decide that men can have a satisfying sex life despite erectile dysfunction.[378, 379] Patients and partners tend to perceive the partner's own sexual interest, not function, as critical to the couple's sexual recovery.[50] The recovery of sexual intimacy can be helped by the couples' engagement in intentional sex, patients' acceptance of erectile aids, and partners' interest in sex.[21] Partner involvement is also known to increase adherence to ED rehabilitation and treatment, improved sexual function, and better relationship satisfaction for both the patient and the partner.[380] Despite these findings, the assessment of partner sexual function remains often overlooked, with physician gender often influencing the frequency and depth at which this is assessed.[381] The timing of this pre-treatment assessment is important, as couples tend to stop communicating about their sex lives after the treatment decision has been made.[382]

SECTION 5:
Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 20:

Clinicians should use validated Patient Reported Outcome measures whenever appropriate and whenever possible to assess patients' sexual function and possibly partners' sexual function, as well as sexual distress, based on a clinical assessment of the patients' and partners' goal for sexual recovery.

(Clinical Principle)

Discussion

Patient Reported Outcomes (PROs) are self-report questionnaires which ask the patient to rate their symptoms or function. PROs are essential for high quality outcomes research in sexual medicine and can be valuable adjuncts to clinical practice. There are several advantages to PROs. In clinical care, patients' symptoms or functional limitations often go undetected, and even in structured clinical interactions, important symptoms may be missed up to half the time.[383] In research, PROs offer a more objective assessment compared to physician reporting. They also provide for a structured, multi-dimensional measurement of the symptom or outcome variable of interest. High quality PROs also allow for comparison of symptoms across studies, and help researchers evaluate the impact of different treatments or interventions. When using PROs, attention should be paid to patient sexual orientation as many commonly-used measures have not been normed on gay men and are not appropriate for gay men because they assume the patient is an insertive partner.

There are several steps to the development of a quality PRO. PROs should be systematically developed starting with qualitative studies with experts in the field and patients who have experienced difficulty with the symptom of interest. This qualitative work then leads to the delineation of specific themes and a draft PRO is developed with questions that assess these themes. Once the draft has been developed, "cognitive interviewing," a qualitative process, can be employed which asks patients about their understanding of specific words, phrases, and questions in the draft PRO. These qualitative processes allow for the PRO to be well grounded in the patient experience. The PRO is then tested to insure it meets specific psychometric properties. The most fundamental requirements for psychometric validity include reliability and validity. Reliability refers to the consistency or replicability of data, while validity reflects the degree to which an instrument or scale measures what it intends or claims to measure. Two essential indicators of validity for measures of sexual function are: sensitivity to diagnostic status (e.g., functional versus dysfunctional), and sensitivity to treatment change. Both are essential features of any scale which is designed to serve as a diagnostic and/or efficacy measure in either clinical or research settings. For a more detailed description of measurement development and validation procedures, please see the FDA Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims (2009).[384]

There are several key PROs of interest for the assessment of sexual function in prostate cancer patients and their partners described below (see Table 3 and Appendix D) for PROs samples). It must be noted that only one, the Patient Reported Outcomes Information System (PROMIS) measure, is able to measure sexual activity and sexual discomfort in gay and bisexual men and men who have sex with men.[385, 386] It is also important to acknowledge that these measures were normed in developed countries. Some have been used internationally and have been translated and validated as useful in other languages. However, PROs that are responsive to cultural, ethnic or racial sexual priorities have yet to be developed.

International Index of Erectile Function (IIEF)[387]

The IIEF is a widely used assessment of sexual function in men, and the Erectile Function Domain (EFD) is considered a gold standard for the assessment of erectile function. The IIEF is a 15-item self-report inventory which was developed by Rosen and colleagues to provide a brief, standardized measure of sexual function and capacity. The IIEF was established in conjunction with the clinical trial program for Sildenafil and has since served as a major endpoint for numerous clinical trials. The principal domains of the IIEF were identified through literature searches, review of existing instruments, and interviews with patients

suffering from erectile dysfunction. The IIEF represents quality of male sexual function in terms of five domain scores: erectile function, orgasmic function, sexual desire, sexual satisfaction, and overall satisfaction. The IIEF does not yield a total score. The scale has excellent psychometric properties, sensitivity for symptomatic change has been demonstrated, and it has been found to be highly robust in different ethnic and geographic populations. The IIEF has been validated in several languages other than English. While the IIEF is widely used, it does have limitations in men with prostate cancer. For example, the orgasmic function domain asks about ejaculation. Men who have had a radical prostatectomy will not ejaculate, and men who have had radiation treatment may have reduced ejaculate. As a result, the orgasmic function domain is not applicable to many men with prostate cancer.

Finally, the IIEF validation did not consider the difference in needed firmness for anal penetration. The term 'intercourse' refers to vaginal intercourse. A recent study has cast doubt about the value of using this measure with gay and bisexual men and men who have sex with men whose penetrative sexual behavior is different from that of heterosexual men.[388]

- *Erectile Function Domain (EFD) of the IIEF:* The most relevant domain of the IIEF for men with prostate cancer and male partners is the EFD. This is a six-question domain that assesses quality of erections and has been used as an outcome measure in many studies.
- *Sexual Health Inventory for Men (SHIM)[389]:* This scale contains five items of the EFD. The SHIM has been developed and validated, along with a diagnostic classification and an ED severity scale. This is a widely used screening tool for clinical use. It has also been used as an outcome measure for clinical studies. The difference between the SHIM and the EFD is one question (i.e., confidence in erections). A number of researchers have argued this is an important question and prefer the EFD as an outcome measure as compared to the SHIM.

Patient-Reported Outcomes Measure Information System (PROMIS)[386]

PROMIS is an NIH-funded initiative to develop and validate PROs for clinical research and practice. PROMIS PROs are patient-centered measures designed to assess physical, mental, and social health in adults and children. PROMIS measures are developed with excellent methodology following the qualitative and quantitative approach described above. PROMIS has developed SexFS, a system of sexual function measures for women and men. As such, these can be used to assess men with prostate cancer as well as female or male partners. The SexFS measures many sexual domains. The most applicable assessment scales for men with prostate cancer are in the domains of erectile function, interest in sexual activity, orgasm, anal discomfort, global satisfaction with sex life, specific sexual activities, and use of sexual aids.

The IIEF EFD and SHIM are widely used for measuring erectile function in men with prostate cancer and their male partners, however, adding PROMIS domains that measure interest in sexual activity, presence of anal sex, satisfaction with sex life, and anal discomfort, and the impact of urine during sex will create a more useful complement of measures for the sexual assessment of gay and bisexual men and men who have sex with men.

Erectile Dysfunction Inventory for Treatment and Satisfaction (EDITS)[390]

The EDITS scale was developed by Althof et al (1999). This PRO is a multi-dimensional scale to assess male treatment satisfaction following erectile dysfunction therapy. The EDITS explores the impact of patient and partner's satisfaction with treatment continuation. It measures concepts such as overall satisfaction with the treatment, the degree to which treatment met expectations, and likelihood of treatment continuation. The EDITS was developed by researchers and patients and has demonstrated excellent psychometric properties.

Self-Esteem and Relationship (SEAR) Questionnaire[391, 392]

The Self-Esteem and Relationship (SEAR) questionnaire was developed to assess the impact of erectile dysfunction on men's self-esteem and sexual relationship. This PRO was developed using focus groups, interviews with medical specialists, and literature review. The SEAR is a 14-item scale which assessed two domains: Sexual Relationship Satisfaction (8-items) and Confidence (6-items), the latter domain consisting of two sub-domains of Self-Esteem (4-items) and Overall Relationship Satisfaction (2-items). The SEAR has demonstrated excellent psychometric properties and been used in a number

of clinical trials. These trials have demonstrated its sensitivity to treatment effect, and have helped define a minimal clinically meaningful improvement (approx. 10 points across the domains/sub-domains).

Expanded Prostate Cancer Index Composite (EPIC)[393]

The EPIC is an expanded 50-item version of the UCLA-PCI 20-item questionnaire. The EPIC added items to the questionnaire to assess the broader issues of quality of life in men who had prostate cancer treatment. The EPIC includes subscales which assess urinary symptoms, bowel symptoms, hormone domain, and sexual function in men with prostate cancer. The UCLA-PCI was developed by experts and patients, and the EPIC was modified because of additional patient feedback. The sexual function scale is an 11-item scale which produces a sexual summary score as well as two subscales: sexual function and sexual bother.

The sexual function subscale assesses sexual desire, orgasm, and erectile function. The sexual bother scale assesses bother related to the areas assessed on the sexual function scale. The EPIC is widely used, including internationally, and has demonstrated good psychometric properties. Of the scales discussed, this is the only scale which was developed specifically for men with prostate cancer. An important criticism of the EPIC is that the sexual function and bother subscales combine desire, orgasm, and function. While these subscales will provide a sense of function and bother, they do not specifically separate and assess individually what are considered separate phases in the sexual response cycle for men.

Sexual Distress Scale in Men with Prostate Cancer (SDS)[394]

The SDS is available in long and short form. The scale is specifically validated with heterosexual and gay prostate cancer patients. Patients are asked questions about being 'unhappy in your sexual relationship, 'dissatisfied with your sex life', 'inferior because of sexual problems' and 'embarrassed about sexual problems.' The measure was validated for sexual distress in a general population of men and women with sexual dysfunction.

Peyronie's Disease Questionnaire (PDQ)[395]3

The PDQ is a PRO that was developed to measure the impact and severity of Peyronie's disease symptoms. The PDQ is a 15-item self-report questionnaire which has three domains: 1) psychological and physical symptoms, 2) penile pain, and 3) symptom bother. The PDQ was developed with sound PRO methodology which included input from experts in the field, development of a conceptual model, patient focus groups, cognitive interviews, and psychometric validation. The PDQ demonstrated good psychometric properties and confirmatory factor analysis verified the three theorized domains.

Female Sexual Function Index (FSFI)[396]

The FSFI is considered the gold standard to assess female sexual function, and a useful PRO to assess the sexual function of female partners of men with prostate cancer. The FSFI is a brief, self-report measure of female sexual function. It is a 19-item multiple-choice questionnaire assessing five domains of sexual function in women: 1) desire and subjective arousal, 2) lubrication, 3) orgasm, 4) satisfaction, and 5) pain/discomfort. The items were generated and tested for face validity by an expert panel. The scale has demonstrated excellent internal consistency, and discriminant validity for all subscales as well as the summary score. The FSFI has been used in numerous research studies and clinical trials, and it has been validated in several languages other than English. Users of FSFI should observe and respect cultural norms and priorities. Before implementing FSFI clinicians should gain acceptance from the couple and informed consent from the female partner to assess her sexual functioning. This may require additional education for the couple.

TABLE 3. Sexual Function and Distress Measures

SEXUAL FUNCTION	MEASURE ABBREVIATION
Erectile Function	EFD of the IIEF
Interest in Sexual Activity	PROMIS
Satisfaction with Sex Life	PROMIS
Bother Regarding Sexual Function	PROMIS
Orgasm	PROMIS
Sexual Self-Esteem	SEAR
Erectile Treatment Satisfaction	EDITS
Sexual Function and Bother	EPIC
Sexual Distress in Men with Prostate Cancer	SDS
Peyronie's Disease Questionnaire	PDQ
Female Sexual Function and Satisfaction	FSFI

SECTION 5:
Guideline Statements With Supporting Evidence

IV. Lifestyle modification

Introduction

The American Cancer Society Prostate Cancer Survivorship Care Guidelines recommend the following for health promotion: (1) Maintain a healthy weight; (2) Engage in at least 150 minutes/week of physical activity; (3) Eat a diet high in fruits, vegetables and whole grains; and (4) Avoid smoking.[43] Similarly, the American Urological Association guidelines on erectile dysfunction recommend that clinicians should counsel men with erectile dysfunction that lifestyle modifications, including changes in diet and increased physical activity, improve overall health and may improve erectile function.[397-398]

GUIDELINE STATEMENT 21:

Lifestyle modification should be recommended to patients to optimize their overall health and sexual health, including avoiding smoking, engaging in physical activity, weight loss, increasing consumption of healthful plant-based foods, and reducing consumption of red and processed meat.

(Clinical Principle)

In general, dietary patterns that are high in fruit, vegetables, whole grains, and fish are associated with a lower risk of erectile dysfunction; whereas, red and processed meat and refined grains are associated with more erectile dysfunction.[398, 399] In particular, plant-based foods can support erectile function through multiple mechanisms, including weight loss, increases in nitric oxide, less atherosclerosis, improved nerve function, and antioxidant properties.[400] Recent data suggests that men consuming more healthful plant-based diets are less likely to develop erectile dysfunction.[401] Similarly, physical activity is associated with a significantly lower risk of erectile dysfunction; whereas, obesity, smoking, and alcohol consumption have been associated with a higher prevalence of erectile dysfunction.[402] Interventional studies have shown that healthy lifestyle modification is associated with improvements in erectile function.[403]

Notably, erectile dysfunction due to prostate cancer treatments, such as radical prostatectomy or radiation therapy, are different than erectile dysfunction in general, so lifestyle approaches may not have the same impact in this population.[404] While studies have not demonstrated that lifestyle modifications improve sexual function after prostate cancer therapies, healthier lifestyles are associated with other positive effects in cancer survivors.

Obesity is a risk factor for prostate cancer specific mortality and biochemical recurrence. Some studies have reported that increased physical activity may decrease the risk of recurrence, improve survival, speed recovery from the effects of treatment, and prevent long-term treatment effects. In particular, exercise has been shown to maintain sexual activity among men undergoing hormonal therapy for prostate cancer and to prevent treatment toxicity.[405] Increasingly, interest has been focused on the importance of exercise to promote health in cancer in general, but also specifically to improve sexual health. Vear et al. reviewed the literature on the association between cardiac health and sexual health in prostate cancer[406] and, they propose this as an area worth pursuing in future research.

Diets that emphasize vegetables, fruits, and whole grains also may improve prostate cancer survival. Consumption of more healthful plant-based foods has been associated with weight loss, reduced risk of diabetes and other cardiovascular disease, as well as a lower risk of prostate cancer progression.[407-410] Stopping smoking and moderating alcohol consumption also help reduce the risk of cancer recurrence. There are several notable references in this domain.[411-414]

Overall, lifestyle modification, including avoiding smoking, physical activity, increasing consumption of healthful plant-based foods, and reducing meat consumption may reduce the risk of prostate cancer progression and preserve sexual quality of life. These same evidence-based recommendations for cardiovascular and overall health have been linked to sexual health as well.

SECTION 5:
Guideline Statements With Supporting Evidence

V. Psychosocial treatment

Introduction

The Panel uses a biopsychosocial framework to conceptualize treatment for sexual dysfunction that occurs as a result of prostate cancer therapies. This framework includes the man and his partner and addresses all the sexual consequences of prostate cancer therapies on functioning at the physiologic, psychological, relationship and socio-cultural levels.

Prostate cancer therapies affect all patients' sexual functioning to some extent. There is a clear need for psychosexual support. Men become distressed in response to the loss of sexual function. They worry about the impact on their partners and their relationships of their inability to perform sexually.[54, 415-417] Findings from descriptive and qualitative studies, as well as clinical experience over the past fifteen years, have informed the development of new interventions addressing multiple areas. As studies have shown the importance of including partners, many interventions now address patients as well as partners' concerns, with patient and partner consent. To be effective, patients and partners must agree about partner inclusion before couple-focused rehabilitation can proceed.

Studies evaluating psychosocial interventions have focused on individual or combined outcomes, such as acquisition of knowledge about the sexual side-effects of treatments and rehabilitation, use of erectile aids, attitudes towards erectile aids and erectile dysfunction, coping with loss and grief, coming to terms with altered sexuality and sex lives, and female partners' sexuality. Designs have included pre- and post-tests, randomized controlled trials (RCTs) and comparisons with historical cohorts. Evidence regarding the effectiveness of psychosocial interventions is strongest in the area of supportive counseling for the use of erectile aids.

GUIDELINE STATEMENT 22:

Clinicians should provide education and individualized sexual rehabilitation, and psychosexual support to patients and partners across the entire survivorship continuum, tailored to: prostate cancer therapy type, partnership status, cultural, ethnic, and racial context, sexual orientation, and gender identity.

(Strong Recommendation; Evidence Strength Grade C)

Discussion

Patients' and partners' needs may change over the course of care for prostate cancer. It is important to promote education about the side-effects of treatment and rehabilitation prior to cancer therapy. In later phases it is important to problem solve about erectile aids and discuss individual psychological and couple adjustment in the new sexual context. Research has shown that patients and partners may have overly optimistic expectations of sexual outcomes that can be mitigated through education.[140, 418, 419] Several studies have shown that counseling individual men and couples after prostate cancer therapy about pro-erectile aids increases their uptake.[420-422] Couples benefit when they are encouraged to communicate well and support each other during the recovery process.[423] Supporting the partner's needs and encouraging mutuality are critical aspects of a successful recovery of sexual intimacy.[18, 50]

Cultural, Ethnic and Racial Differences

Differences exist in sexual function outcomes between ethnic groups receiving prostate cancer care. Similarly, literature suggests that groups from different cultures are not equivalent in their perceptions of bother and impact on mental health and interpersonal relationships relating to sexual dysfunction following prostate cancer treatment.[76, 424, 425] Interpretation of sexual function outcomes is likely influenced by mental health, spirituality, social context, and medical

system conditions, adaptation to disparate access to care, and decisions about what care to choose – traditional vs western medicine. We don't know what role these mediating factors play in the relationship between prostate cancer treatment on sexual function outcomes. Research is still needed.

Too little research is available to make specific recommendations that address cultural, ethnic, and racial differences in sexual recovery. In this Guideline we highlight findings from available intervention studies that embrace a culturally sensitive approach: a telephone-delivered psychoeducation, telephone-based coping skills training and monitoring, cognitive behavioral stress management, and comprehensive integrative educational programs.[81, 426-429]

Pre-treatment Education

One of the most frequent complaints expressed by prostate cancer survivors and their partners is the lack of education and preparation for the sexual side-effects of prostate cancer treatment. Lack of preparation can result in unrealistic expectations of outcomes. Moreover, studies show that the lack of use of sexual aids by patients may reflect a lack of pre-treatment psychosexual support for the patient.[55, 140, 430] Several studies that used pilot RCT or pre-and post- designs used a psychoeducational approach either before or after prostate cancer therapy to alert couples to treatment-related sexual side-effects, realistic expectations of outcomes, options for rehabilitation, and the psychological impacts of sexual changes on the individual and the couple. Pre-treatment education for patients undergoing prostatectomy resulted in patients' and partners having increased knowledge and more realistic expectations of sexual and urinary outcomes.[419] Couples facing sexual changes resulting from the patient's androgen deprivation therapy were significantly more likely to remain sexually active if they were prepared at the beginning of treatment for the side-effects of treatment and rehabilitation strategies, than those who were not.[431]

Post-treatment Support

Post-treatment support helps couples maintain realistic expectations, bolsters confidence when it is flagging, and supports patients' and partners' belief that sexual pleasure and sexual expression is important and can be available despite sexual dysfunction after prostate cancer treatment. As men are coping with erectile dysfunction and other functional challenges, it is important to remind them and their partners that there are non-penetrative sexual activities, much like foreplay, that can lead to connection, pleasure, and orgasm. Manual stimulation, oral sex, and using sex toys such as vibrators stimulate pleasure by increasing blood flow to the stimulated area. These activities can become a part of an expanded sexual repertoire and be retained even if the patient experiences some erectile function recovery.

Findings from several studies show that psychoeducational interventions result in a reduction in patients' sexual bother, improved partners' sexual interest, increased patients' and partners knowledge and partners' acceptance of ED.[379, 431-433] Men who were given the opportunity to work through feelings about using erectile aids were more likely to use them.[420]



SECTION 5:
Guideline Statements With Supporting Evidence

Gay and Bisexual Men (GBM) and Men who have Sex with Men (MSM)

As GBM and MSM have historically experienced discrimination in healthcare, they may not feel comfortable disclosing their sexual orientation to clinicians. For these men relevant sexual health support after prostate cancer may be unavailable. Providing a clinical environment that reflects this patient population, such as including photos of male couples in clinic brochures or having inclusive art on clinic walls, will go a long way to make GBM and MSM comfortable opening up about their sexual concerns.

There are currently no evidence-based psychosexual support interventions specifically designed for GBM and MSM, although some interventions include specific content relevant to these men.[434] Providers should consider their unique needs when planning treatment, acknowledging that GBM and MSM have an expectation of an erection firm enough for anal penetration, may worry about when it is safe to resume anal penetration after treatment, and may grieve about the loss of ejaculate for the couple. Couples may have additional concerns relevant to the resumption of sexual activity when the usual sexual roles (top vs bottom) are no longer available.

Sexuality can be a core of GBM and MSM identity. Due to social discrimination, ignorance, and lack of acceptance by family and friends, gay and bisexual men can feel the need to keep their sexuality secret. Because of this and the "differentness" it causes, sexuality may play a more central role in their identity formation and social visibility. Sexual encounters as a component of social interaction can become a way of belonging to their minority group, and also something that distinguishes them from the majority. Being seen as physically strong and sexually potent is a core value in a large part of the gay community, as it is in the heterosexual community. While heterosexual men struggle with the impact of prostate cancer-related sexual problems on their sense of masculinity, gay and bisexual men may have an even harder time. Some gay and bisexual men may experience loss of libido as a loss of social energy. Sexual dysfunction may impair some men's sense of body image. As a result, gay men report that they feel sexually disqualified.[154]

Erectile dysfunction and penile shrinkage can have a significant effect on sexual role in GBM and MSM sexual activity. Erections for anal penetration require greater firmness than erections for vaginal intercourse. The loss of the ability to have a firm erection after surgical, radiation, or hormonal treatment can disrupt familiar sexual activity and upend typical roles that men take in an encounter. Being a "top" or a "bottom" may be a part of a gay man's sexual identity. If unable to attain a firm erection, some men and couples may be able to adapt to new roles. But not all couples will find adaptation acceptable. Providers must recognize these issues when counseling men regarding the use of pro-erectile aids and sexual adaptation.[17, 96, 435]

Gay and bisexual men value ejaculate beyond its reproductive role and its role in orgasmic sensation.[23] Ejaculate can be an aspect of erotic play and exchange. It is therefore extremely important that effects of prostate cancer therapies on ejaculate be discussed with patients when counseling them about treatment options for prostate cancer. Patients and partners should know for example, that they will likely experience a greater initial loss of semen with surgery than with radiation therapy for localized prostate cancer. However, over time they will still see diminished semen after treatment with radiation and hormonal therapy.[436, 437]

The prostate is a sexual organ and surgical removal of the prostate represents the full loss of a sexual organ. For many gay and bisexual men, this may represent an even bigger loss than it does for heterosexual men because of the increased role it often plays in erotic stimulation and sensation.[17] Radiation also leads to loss of prostate sensitivity.[396] Pre-treatment counseling can help men prepare for these losses.

The ability to engage in anal penetration is temporarily unavailable for GBM and MSM after prostate cancer surgery. Surgical intervention and repair are close to the anus and must heal before the tissues of the anus can be impacted by the stretching of the anal canal. Treatment with EBRT can result in more long-term difficulties, including narrowing as well as diminished tone and flexibility of the walls of the anus, potential fecal frequency or urgency, and bowel incontinence. Scarring of the tissues of the anus can lead to anal discomfort and pain. Patients

should understand these consequences as they make decisions about treatment options.

Helping gay and bisexual men prepare for change will promote their optimal recovery after prostate cancer treatment. Specific sexual practices should be discussed with emphasis on how different treatments will affect sexual practice, so that men can make informed treatment decisions. Allensworth-Davis et al. (Appendix B) present a model of care that incorporates the needs as well as the barriers to care for GBM, MSM, and transgender women throughout survivorship. In this model, effectively addressing patient's sexual concerns means acknowledging patient's reluctance to disclose sexual orientation and gender identity, and sensitivity to patients' fear of discrimination if sexual concerns are addressed.[438]

Men who are Single or Widowed

Supporting men who are single or widowed, and may or may not wish to have a relationship, is equally important. Single men will benefit from psychosocial support and guidance regarding sexual rehabilitation activities. Those who want to date may lack the confidence to have conversations with potential partners about their sexual challenges and about being able to satisfy a partner. Clinical experience has shown that men who are supported can work towards the goal of having a sexually intimate relationship successfully despite sexual dysfunction and the need to use erectile aids.

Trans Women and Non-gender Conforming Individuals

The needs of trans women and gender non-conforming individuals are not yet understood. It is estimated that, due to the protective role of hormonal treatment as a part of gender transition, they have a lower incidence of prostate cancer.[439] Discrimination makes screening for prostate cancer for this sexual minority population more difficult. However, trans women, and any individuals who still have a prostate, should be screened and diagnosed in an environment that is inclusive and welcoming. If diagnosed, they should be asked about their sexual concerns and needs for rehabilitation based on their anatomy and priorities. It is uncertain what kind of sexual distress trans women and gender non-conforming patients experience and what type of sexual losses will be meaningful. In order to plan a biopsychosocial approach to treatment for sexual dysfunction that is relevant, it is important that clinicians acknowledge the unique sexual concerns of these patients related to identity, history of hormonal and surgical treatment, and sexual goals throughout the continuum survivorship care. Sterling and Garcia suggest a conceptual model for prostate cancer screening for transgender women and gender non-conforming people that helps frame the issues to consider for this group. (Appendix B).[372]

Men not Interested in Pursuing Sexual Recovery

It is important to acknowledge that some men and some couples may not wish to pursue sexual recovery after prostate cancer treatment. While it is still important to ask about all patients' sexual goals, it is equally important to respect the choices of those who decline further sexual health support and to continue to provide opportunities to discuss sexual recovery in case this decision changes.

Clinical Environments

Clinical environments will make patients feel included and respected if they are decorated with images reflective of the diversity of cultures, ethnicities, races, sexual orientations, and gender identities. Handouts can be similarly composed. Intake forms that give an opportunity to specify one's gender, sexual orientation, culture, ethnicity, and racial identity can assure the patient of the likelihood that his individuality will be respected.

Body of Evidence Strength:
Body of evidence strength is Grade C. Evidence from randomized controlled trials and observational studies suggests that, without psychosexual support, patients do not achieve sexual recovery after prostate cancer treatment. The most robust evidence of effectiveness is available from seven RCTs with samples greater than 50 participants and pilot projects with pre and post design. The evidence is consistent across studies but lacks an adequate number of studies on specific topics.

SECTION 5:
Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 23:

Clinicians should normalize grief as a typical reaction to sexual losses and encourage patients and partners to whom sexual recovery is important to pursue sexual intimacy despite sexual losses.

(Strong Recommendation; Evidence Strength Grade C)

Discussion

Although many studies note that grief is a normal reaction to sexual losses, grief is not often addressed in psychosocial interventions. A couple's ability to successfully create a new and satisfying sexual relationship in the context of prostate cancer treatment and recovery requires addressing grief and other psychosocial issues.

Patients' sexual distress, loss of self-confidence, and loss of masculine self-esteem are important aspects of men's response to sexual losses. Men and couples can continue to be sexually active despite sexual dysfunction, if they come to terms with their sexual losses and use sexual aids. The Panel reviewed two studies that specifically addressed grief. One mixed methods study described the concept of grief as an important aspect of couples' sexual recovery after prostate cancer treatment.[21]

The other incorporated grief into the psychoeducational content of an intervention tested in an RCT.[434] A conceptual paper focusing on women with breast cancer highlighted grief about sexual losses as a disenfranchised aspect of the experience of cancer.[162] Walker et al., in their summary of the psychosocial challenges that patients and their partners face in their sexual recovery, included loss and grief as an important aspect of coping and re-establishing sexual viability after prostate cancer treatment.[160] This area of coping merits greater attention and testing in interventions.

Body of Evidence Strength:
Body of evidence strength is Grade C. Addressing grief as part of the process for dealing with post-treatment sexual dysfunction is a new and promising target for intervention. The available data, however, are limited. Future evidence may help refine how the concept of grief is used with patients and partners in clinical practice.

SECTION 5:
Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 24:

Clinicians should include the partner, if both the patient and partner agree, and provide support for couples coping with the sexual side-effects of prostate cancer therapy both directly and through referral for psychosexual treatment.

(Strong Recommendation, Evidence Strength Grade C)

Discussion

The emphasis on partner participation reflects the fact that most men with prostate cancer have sexual partners who will be affected by the man's sexual dysfunction. It also reflects the success of couple-based interventions. Many couples come to prostate cancer treatment in the context of strong, long-term relationships. The strength of those relationships can help them cope with the challenges of prostate cancer treatment and sexual recovery. The ability to communicate and develop strategies for maintaining sexual intimacy will help them navigate the new waters of a changed sexual relationship. Communication about sex is a skill not always present in these long-term relationships as sex can be non-verbal, yet satisfying.[25] Communication and sexual problem-solving become new skills that the couple must learn.

RCTs and pilot RCTs that have evaluated interventions addressing communication and sexual strategies have reported success in improving couples' relationship satisfaction, patients' uptake of sexual aids, partner sexual interest, and achievement of sexual goals.[252, 421, 431, 440] Receipt of spousal support was associated with greater relationship satisfaction.[252] Participation in a personalized, online intervention that coached sexual communication through a variety of interactive activities led to an increased likelihood of engaging in both penetrative and non-penetrative sexual activity within three months following definitive therapy for localized prostate cancer.[441]

Providing support for partners in interventions has led to improvement in partners' sexual interest and sexual function.[431] Studies suggest that partners benefit significantly from interventions by revising their appraisal of the illness and by increasing their ability to cope.[378] It is important that both healthcare providers and patients recognize that acknowledging and supporting partners' needs is a key component of couples' sexual recovery.

Body of Evidence Strength:
Body of evidence strength is Grade C. Interventions tested in randomized controlled trials and observational studies that involve the couple show greater promise toward improving a number of outcomes that enhance men's sexual and relationship quality of life.

SECTION 5:
Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 25:

Clinicians should support patients who are gay or bisexual, men who have sex with men, transgender women, and gender non-conforming patients and their partners with information relevant to their sexual experience and guide them towards meaningful support resources.

(Expert Opinion)

Discussion

Prostate cancer treatment-related sexual dysfunctions can both engage couples' strengths and create significant dilemmas for both the patient and the partner. On the positive side, men who have sex with men may have a greater ability to empathize with their affected partner's sorrow and frustration about his sexual problems after prostate cancer therapy than women in heterosexual couples. Men in committed relationships can also rely on the strength of affectional bonds built over time, and in some cases, the shared experiences and anxieties of prostate cancer diagnosis and treatment may even draw partners closer.

On the negative side, there is the dilemma of how to maintain sexual excitement when sex becomes less spontaneous, when there are changes in function as well as in appearance of genitals, and the likelihood of recovering the previously available excitement is low. Unlike heterosexual men who are partnered with post-menopausal women whose loss of estrogen leads to their own sexual challenges with arousal and vaginal lubrication, gay and bisexual men are likely to be partnered with or date men whose sexuality continues to be robust, fueled by normal testosterone levels. Men in long-term, committed relationships have reported a desire and ability to adjust to a new sexual paradigm either within their monogamous relationship or by opening up their relationship to other lovers to maximize eroticism and sexual satisfaction.[442, 443] In couples who engaged in penetrative sex, some have demonstrated flexibility to change roles in order to increase pleasure and satisfaction.

A recent survey study of sexual behavior among gay and bisexual men after prostate cancer treatment reported that two-thirds of men reported their sexual functioning as fair to poor with only 22% reporting erections adequate for insertive anal sex. For receptive anal sex, one-third of participants experienced anodyspareunia. Difficulty with erections was noted as a reason for not using condoms; three study participants HIV sero-converted after prostate cancer treatment.[92, 435] Anxiety about starting new relationships and having to disclose a sexual disability can be debilitating, resulting in avoidance, loneliness and depression.[17] A discussion of relationship challenges and referral to qualified sexual health experts is critical as an aspect of supporting gay and bisexual men with prostate cancer and their partners in survivorship.

Studies have emphasized that gay men sometimes have less social support than their heterosexual counterparts because more are single and some have lost family connections when they came out.[23, 444] Religion and spirituality are often considered positive, protective factors against psychological distress. Some studies have recognized that organized religion may have negative impacts on gay and bisexual men's relationships with their families of origin and also their mental health. As a result, these men often rely on friends and the gay community as their 'family'. Yet spirituality can be affirming for the individual and therefore a distinction between religion and spirituality should be made.[370, 445]

An increased value placed on sexuality in gay relationships may make it more difficult for gay men to seek support in their community when they lose confidence about their sexual function. General support groups are not a very useful resource. Online support channels, such as malecare.com, have been a valuable source of support. Healthcare providers should inquire on behalf of their patients about available sources of support, as they may be non-traditional or very limited. Men may need help finding the kind of support that would be most helpful to them after prostate cancer treatment. Although there is insufficient research on trans women and gender non-conforming patients' support needs, the same principles should be followed as those for gay and bisexual men and men who have sex with men because traditional resources may not be optimally suited for their needs.

SECTION 5:

Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 26:

Clinicians should refer patients, partners, and couples for whom education and support are insufficient for specialty psychosexual treatment.

(Clinical Principle)

Discussion

While the majority of patients and partners may benefit from education and support only, some will benefit from referral for sex therapy. These are typically patients and partners who have pre-existing sexual or relationship problems. Positive results of sex therapy have not been tested empirically, therefore are primarily reported by experienced clinicians. Patients and partners should be made aware that the work of sex therapy can be arduous and require commitment to change, as with any couples therapy.

Analyzing and treating barriers to emotional intimacy as a gateway to sexual intimacy is a core aspect of sex therapy work.

Using sensate focus exercises to reduce anxiety, as well as guidance towards expansion of sexual repertoire through adopting non-penetrative sexual activities (e.g., oral sex, manual stimulation, the use of vibrators to increase sexual pleasure), can result in a couple redefining their sexual relationship as sexually satisfying despite sexual dysfunction.



SECTION 5:
Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 27:

Clinicians should make patients and partners aware of group interventions and digital health/telemedicine methodologies that can increase access to sexual health support in prostate cancer survivorship.

(Moderate Recommendation, Evidence Strength Grade C)

Discussion

Sexual health support is generally not available for prostate cancer survivors in usual care. This is partially due to the lack of qualified providers in healthcare settings and to the lack of financial investment in survivorship care.[26] However, providers can help alleviate this gap in care by making patients aware of alternative ways of obtaining sexual health support. Some areas have local support groups. Additionally, online informational support resources can help patients and partners broaden their support system. Websites such as, malecare.org, have provided support for prostate cancer survivors successfully for two decades.[446]

Digital health/telemedicine is gaining ground as a methodology for overcoming barriers to care. Telemedicine reaches patients where they are. It reduces patients' costs, such as time off work and travel expenses. In one study an early online sexual health intervention was shown to be non-inferior to face-to-face support; other interventions, using telemedicine have followed suit.[377] Automatically generated emails with tailored self-management strategies, assessed through interactive voice response methodology, have shown a positive effect when men are able to choose symptoms they wished to manage.[433] An online, tailored, interactive intervention for couples increased the likelihood of early re-engagement in sexual activity after prostate cancer treatment.[441] A review by Kang et al. evaluated four randomized controlled trials of online sexual health interventions. Two focused on prostate cancer patients.[447] The studies demonstrated that an online program can reduce psychological distress and have a positive effect on physiologic sexual function, however this effect occurred in both patients and female partners who remained within the dysfunctional range. The online program also failed to improve relationship satisfaction. This review highlighted the fact that online interventions tend to have a high rate of attrition. They also demand technological agility that not all patients and partners can meet. Patients also must navigate online interventions without clinician support, and this can be emotionally challenging. Given the availability of the Internet, even in countries that have few clinical resources, digital health/telemedicine may become an important adjunct to prostate cancer oncology care. Further development, testing for usability, and evaluation for effectiveness of online interventions to support sexual health for those with prostate cancer, is needed.

Body of Evidence Strength:
Body of evidence strength is Grade C. Randomized controlled trials have shown that patients can benefit from various forms of digital interventions that support their sexual recovery after prostate cancer treatment. The available studies used a variety of interventions and do not provide a critical mass of evidence for a specific approach. This evidence is encouraging but still emerging.

SECTION 5:
Guideline Statements With Supporting Evidence

VI. Biomedical treatment

OPTIMIZING ERECTILE FUNCTION

Introduction

Erectile dysfunction (ED) is the most pervasive and widely-studied effect of prostate cancer treatments. The section focuses on the treatment of ED in the context of a full biopsychosocial treatment framework.

GUIDELINE STATEMENT 28:

Clinicians should consider nerve-sparing surgical treatment options, when available and oncologically safe, irrespective of baseline erectile function.

(Moderate Recommendation; Evidence Strength Grade C)

Discussion

The anatomic approach to nerve-sparing prostatectomy was pioneered by Dr. Patrick Walsh, with the ultimate goal of preserving erectile function following radical prostatectomy.[448, 449] Nerve-sparing techniques have ultimately evolved to include Veil of Aphrodite sparing adaptations designed to address the wide variation in nerve anatomy.[450] The use of pre-operative MRI to identify anatomic variants and tailor surgical nerve-sparing approaches has also been associated with improved post-surgical erectile function outcomes.[448] Studies that reported erectile function recovery rates among men who had various types of nerve-sparing procedures compared to non-nerve-sparing procedures generally reported higher EF recovery rates with NS techniques (see Discussion under Guideline Statement 6).

Meta-analytic evaluations of nerve-sparing vs. non-nerve-sparing techniques suggest that nerve-sparing techniques are associated with a higher probability of erectile function recovery, although there is considerable heterogeneity across studies in these rates.[451] Pooled data analysis of the limited number of studies (approximately 20% of the retrieved studies) that contained sufficient information for inclusion in the meta-analysis revealed a mean rate of EF recovery in patients receiving a bilateral NS surgery of 61.6% compared to 44.6% and 56.3% for patients treated with unilateral or non-NS RP, respectively.

Of note, there is large heterogeneity among studies reporting EF outcomes for bilateral-NS RP, with rate of EF recovery ranging from 20.4 to 90%, presumably due to differences in population characteristics and modality of EF assessment. Further, it is important to note that the majority of studies that reported data for NS vs non-NS techniques could not be included in our meta-analysis because of insufficient information about outcomes.

It is reasonable to consider that the same functional anatomic approach can also be applied to radiation treatment. Vessel-sparing radiation has been described as one technique designed to preserve sexual function while maintaining high levels of cure.[452] In a single-arm phase 2 trial of vessel-sparing radiotherapy, this approach effectively preserved erectile function, compared to historical series and model-predicted outcomes following nerve sparing RP or conventional radiotherapy, while maintaining tumor control.[282] Multicenter validation of this data is pending at the time of publication of this Guideline.

Body of Evidence Strength:
The body of evidence in support of this statement consists primarily of small observational studies; findings are promising but need replication in larger studies.

SECTION 5:
Guideline Statements With Supporting Evidence

PENILE REHABILITATION VS. ED TREATMENT

Introduction

In order to manage expectations, it is important for patients and partners to understand the difference between initiating a penile rehabilitation program proximal to prostate cancer therapy and treating erectile dysfunction that results from prostate cancer therapy.

The panel defined rehabilitation as the use of therapies before, during, or shortly after prostate cancer treatment to optimize erectile function (EF) recovery.

Rehabilitation studies typically are narrowly focused on restoration of physiological erectile function, with the goal of returning EF to pre-prostate cancer treatment baselines and/or optimizing responses to erectile dysfunction (ED) treatments. The rehabilitation approaches studied begin treatment soon after prostate cancer therapy. They administer medical treatments such as phosphodiesterase type 5 inhibitors (PDE5i), intracavernosal injections (ICI), or vacuum erectile devices (VED). Some approaches use pelvic floor exercise or physical exercise. They administer treatments on a regular schedule (e.g., daily, a certain number of times per week) to provide a consistent physiological stimulus to the erectile tissues.

The panel defined treatment as the use of methods to improve sexual function at any time after prostate cancer therapy to address sexual dysfunction, including erectile dysfunction. Treatment studies typically focus on treating ED that has occurred as a result of prostate cancer therapies, but without the goal of rehabilitation. When the treatment involves a psychotherapeutic approach, the focus may extend beyond EF *per se* to address other factors relevant to sexual dysfunction, such as the psychosocial functioning of the man, the partner, and the couple in the context of cancer survivorship. These studies focused on medical treatments beginning months to years after prostate cancer therapy, as well as studies that involve psychotherapeutic treatments, often beginning shortly after prostate cancer therapy to support the man and partner in effective coping and problem-solving strategies. The studies encompass the available treatments for ED and sexual dysfunction, including all treatments used for rehabilitation, additional surgical treatments (e.g., prostheses), as well as a wide range of psychotherapeutic approaches. Treatments include medical treatments of phosphodiesterase inhibitors, intracavernosal injections, intraurethral suppositories, and vacuum erection devices (PDE5i, ICI, IUS, VED).

PENILE REHABILITATION

GUIDELINE STATEMENT 29:

Clinicians should define the intent and goals of penile rehabilitation strategies on an individualized basis, including preservation of penile length, maintenance of corporal tissue quality, and early patient engagement in sexual recovery. Penile rehabilitation should not be equated with treatment for the recovery of unassisted erectile function.

(Clinical Principle)

Discussion

The goal of penile rehabilitation is distinct from that of treatment for erectile dysfunction. Penile rehabilitation following prostate cancer is intended to minimize the negative impact on male sexual function, and to engage patients in sexual recovery. Penile rehabilitation may include a combination of pharmacological and non-pharmacological strategies, aimed at preserving penile length and the quality of the corpora cavernosa. Penile rehabilitation is not synonymous with and does not ensure restoration of cavernous nerve activity.

SECTION 5:
Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 30:

Clinicians should counsel patients that use of phosphodiesterase type 5 inhibitors (PDE5i) for penile rehabilitation in the early post-prostatectomy period (up to 45 days post-surgery) does not improve rates of unassisted and PDE5i-assisted erectile function recovery at 12 months compared to placebo.

(Moderate Recommendation, Evidence Strength C)

Discussion

Randomized placebo-controlled trials.
Three RCTs addressed whether early administration of PDE5i vs. placebo post-RP improved unassisted erectile function (EF) and whether early administration of PDE5i vs. placebo improved responses to PDE5i.[331, 453, 454] Two of the trials also provided information about responses to PDE5i after the rehabilitation period.[331, 453] These trials provide the best evidence because they used the most rigorous study designs. In addition, two of the trials included placebo controls for mode of administration (on demand vs. nightly/daily).[331, 454] The inclusion criteria across trials were similar; men had BNSRP with normal preoperative erectile function.

Montorsi et al. (2008) administered placebo nightly and on demand (n=210), nightly vardenafil with on demand placebo (vardenafil 5 to 10 mg; n=210), or on demand vardenafil + nightly placebo (vardenafil 5 to 20 mg; n=208) for nine months beginning two weeks after BNSRP.[454] Patients then underwent a two-month drug washout period during which all patients received on demand placebo. Finally, patients were offered on demand vardenafil during a final two-month open-label phase.

During the double-blind phase, a significantly greater proportion of patients in the vardenafil on demand + nightly placebo group had IIEF-EF scores >/=22 (48.2%) compared to the placebo group (24.8%); the daily vardenafil + on demand placebo group was statistically indistinguishable from these two groups (32%). Note that this comparison only tests whether men post-RP are responsive to vardenafil vs. placebo; it does not assess whether rehabilitation was successful.

Rehabilitation success was tested in two ways. First, unassisted erectile function (EF) was measured at the end of the drug washout period. The proportions of patients who achieved an International Index of Erectile Function (IIEF) score on the EF subscale >=22 were statistically similar across groups: 28.9% for placebo, 24.1% for nightly vardenafil + on demand placebo, and 29.1% for on demand vardenafil + nightly placebo. The proportions of patients who answered “yes” to the Sexual Encounter Profile (SEP) question 3 (“Did your erection last long enough for you to have successful intercourse?”) also were statistically similar – 35% in the placebo group, 32% in the nightly vardenafil + on demand placebo group, and 40% in the on demand vardenafil + nightly placebo group. Second, EF was measured during the open-label phase during which all patients had access to on demand vardenafil. There were no differences across the three groups in the proportion of men who had IIEF-EF scores >/=22 (prior placebo – 47.8%; prior nightly vardenafil – 52.6%; prior on demand vardenafil – 54.2%).

Montorsi et al. administered placebo daily + on demand (n=141), daily tadalafil 5 mg + on demand placebo (n=139) or on demand tadalafil 20 mg + daily placebo (N=143) for 9 months beginning 45 days post-BNSRP.[331] Patients then underwent a 6-week drug washout period and EF was measured. The primary outcome was the percent of men in each group who achieved an IIEF-EF score >=22. During the double-blind phase, the percentage of patients achieving IIEF-EF scores >/=22 was significantly higher in the daily tadalafil + on demand placebo group (25.2%) compared to the placebo group (14.2%) but not compared to the on demand tadalafil + daily placebo group (19.7%). The daily tadalafil group also lost less penile length compared to placebo.

When unassisted EF was measured at the end of the drug washout period, these percentages were 19.1% for placebo, 20.9% for daily tadalafil + on demand placebo, and 16.9% for tadalafil on demand + daily placebo (differences not statistically significant). IIEF-EF scores were 12.5 in the placebo group, 13.6 in the daily tadalafil group, and 13.0 in the on demand tadalafil group (differences not significant). SEP Question 2 "yes" responses ("Were you able to insert your penis in your partner's vagina?") were 36.3% in the placebo group, 40.8% in the daily tadalafil group, and 35% in the on demand tadalafil group. SEP 3 responses were 28.5% in the placebo group, 28.8% in the daily tadalafil group, and 23.0% in the on demand tadalafil group. None of these differences were significant. During the open-label extension phase, the percentages of men with IIEF-EF scores >/=22 were statistically similar across the three groups (prior daily tadalafil – 32.4%; prior on demand tadalafil – 33.1%; prior placebo – 27%).

Padma-Nathan et al. (2008) administered placebo (n=42), sildenafil 50 mg (n=40), or sildenafil 100 mg (n=41) nightly for 9 months post-BNSRP beginning 30 days post-op. Patients then underwent an 8-week drug washout period and had EF evaluated.[453] This is the only trial with positive findings. Yet, the study was stopped early because of a presumed lack of treatment effect; only 76 men completed the full protocol. A positive response was defined as a combined score of >= 8 on IIEF-EF questions 3 and 4 and a positive response to "Were erections good enough for satisfactory sexual activity?" Positive responses were achieved by 4% of the placebo group, by 26.1% of the sildenafil 50 mg group and 28.6% of the sildenafil 100 group. There were no differences between the two sildenafil dose groups. Mean IIEF-EF scores were 8.8 in the placebo group, 12.4 in the sildenafil 50 mg group, and 13.7 in the sildenafil 100 mg group (not reported whether this difference was statistically significant).

Meta-analytic findings. We conducted the meta-analyses on the success criteria from the three trials to examine aggregate findings. Using each trial's success criterion, the meta-analyses below were performed (Figure 8). The forest plot presents the findings for unassisted EF. The pooled OR = 1.03 (95% CI 0.74 to 1.45, p = 0.84), indicates there is no statistically significant difference in unassisted EF between the active medication groups and placebo groups after drug washout. The I^2 for this analysis is 57.0% (p = 0.10). Heterogeneity is contributed by Padma-Nathan et al. as is clear on the plot.[453] Because this study has a small sample size compared to the other two studies, its weight in the analysis is minimal and therefore it contributes only minimally to the overall effect.

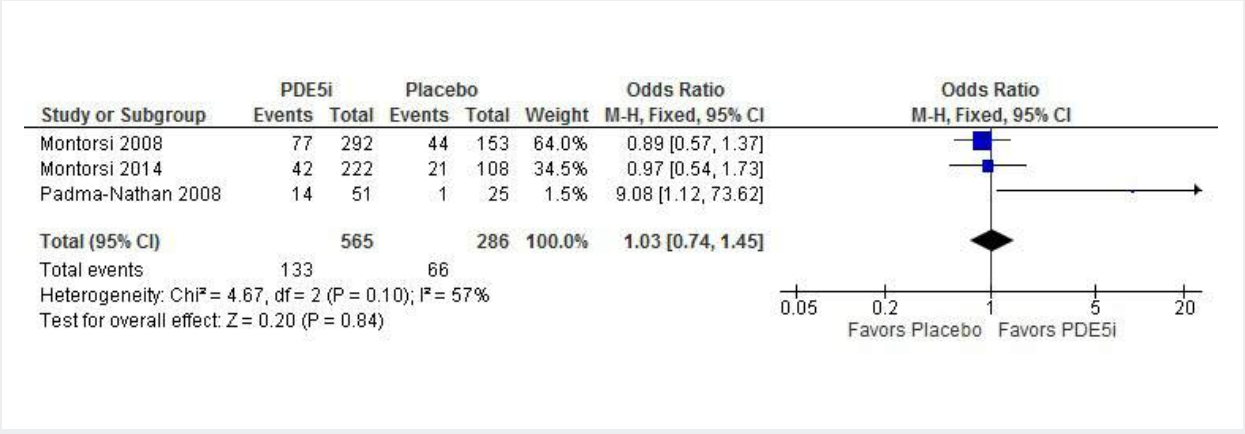


FIGURE 8. Meta-analytic findings for unassisted EF Forest plot of unassisted erectile function data from three placebo controlled randomized trials.

SECTION 5:
Guideline Statements With Supporting Evidence

The forest plot below presents the meta-analytic findings for EF in response to on demand PDE5i after drug washout and during additional open-label phases (Figure 9). The pooled OR = 1.29 (95% CI 0.94 to 1.76, p = 0.12), indicating that there is no statistically significant difference in success rates for men using PDE5i on demand who had prior exposure to placebo or PDE5i. The I^2 for this analysis is 0.0%, p = 0.8.

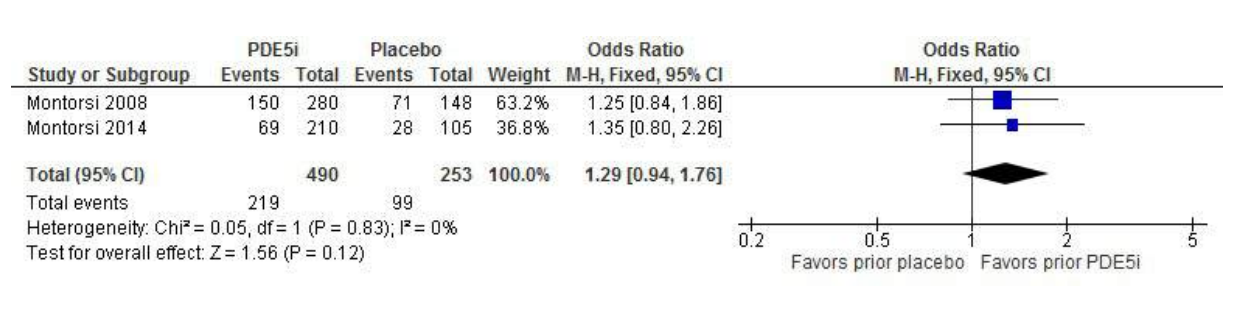


FIGURE 9. Forest plot of success rates in response to on demand PDE5i after drug washout from two placebo-controlled randomized trials.

Other randomized designs.
Eight randomized trials without placebo control groups provide additional information. These trials compared PDE5i at different doses, using different dosing regimens, to the no treatment groups and/or to groups receiving other types of ED treatments.[455-462] The inclusion criteria are relatively similar across these trials with most requiring a unilateral or bilateral nerve-sparing prostatectomy and normal or near-normal preoperative erectile function. However, because of substantial differences across trials in comparison groups and PDE5i regimens, the combined body of this research does not provide definitive evidence. In addition, several trials only test whether men post-RP who are taking PDE5i have better EF than men who are not taking PDE5i – a comparison which does not address the rehabilitation impact of early PDE5i initiation post-RP.

Discussion

Body of evidence strength Grade C for efficacy and for adverse events. The highest quality evidence is provided by three placebo-controlled randomized trials that provided conflicting findings. Strengths of this group of studies include the use of randomization and blinding to protect internal validity; all three trials had a low risk of bias. However, only two of the trials had adequate statistical power and additional placebo controls for dosing regimens (on demand vs. daily/nightly). An additional concern is that no trial lasted long enough to provide a definitive test of the rehabilitation strategy, given that it takes three to five years to recover erectile function following surgery. Further, if erectile recovery occurs over several years post-RP, then important questions about the duration of the rehabilitation phase remain unanswered (i.e., whether the rehabilitation protocol should continue for several years).

Additional information is provided by a group of randomized studies without placebo control groups; most of these studies have extremely small sample sizes. This group of studies ranges in methodological quality from poor (high risk of bias) to moderate (unclear risk of bias). The most frequent weakness is inadequate information about randomization and/or blinding. In addition, several studies rely on no treatment control groups; these groups are not optimal in studies of sexual function. As a group, these studies provide insufficient aggregate evidence for any particular approach because of variability in comparison groups and PDE5i regimens.

There are seven published systematic reviews with meta-analyses that address the use of PDE5i post RP.[463-468] The major conceptual flaw that is perpetuated in most of the meta-analytic findings is the failure to consider that the included trials had different purposes: rehabilitation vs. treatment. These reviews have limited utility.

SECTION 5:

Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 31:

Clinicians should advise patients that there is limited evidence to determine the benefit of non-PDE5i approaches for penile rehabilitation in order to promote recovery of erectile dysfunction.

(Moderate Recommendation, Evidence Strength Grade C)

Discussion

Non-PDE5i approaches for penile rehabilitation have been described, including intraurethral alprostadil, intracavernosal injections, psychotherapy, pelvic floor therapy, penile vibratory stimulation, aerobic exercise, and vacuum erection devices, either alone or in combination with PDE5i. However, there is insufficient evidence demonstrating the consistent benefit of any of these approaches in preserving erection potential and/or promoting recovery of erectile function.

Body of Evidence Strength:
Body of evidence strength is Grade C. Published studies are frequently observational, with variability in inclusion criteria, treatments and comparison groups, and measures. Additionally, small sample sizes raise the possibility of any positive findings being the result of idiosyncratic samples, and negative findings being the result of lack of adequate statistical power.



SECTION 5:

Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 32:

Patients and partners should be counseled that there is inefficient evidence to definitively support penile rehabilitation with PDE5i for the prevention of penile volume loss.

(Conditional Recommendation, Evidence Strength Grade C)

Discussion

In the REACTT trial by Montorsi et al, 423 men were randomized to tadalafil 5mg daily (n=139), tadalafil 20mg on demand (n=143) and placebo (n=141). Penile length was measured pre-RP and 9 months post-RP.[469] Compared to placebo, tadalafil 5mg daily was associated with reduced penile shortening (mean difference 4.1mm, p=0.032).

In contrast, Aydogdu et al failed to demonstrate a significant difference in penile volume post-RP in controls versus men on tadalafil.[460] Sixty-five men post-RP were randomized to a control group (no PDE5-I) or a treatment group that received 20mg of tadalafil a day for 3 days a week. All men had bilateral NSS. Penile girth and length were measure pre-op and at 3, 6, and 12 months post-op. Measurements were taken in the flaccid state and at 'maximum erection' which was induced with 30mg intracavernosal papaverine with self-stimulation. Results demonstrated that the control group had reduced length and girth at 3 months compared to their pre-op measurements in both the flaccid and erect states ($p<0.05$ for all).

While the tadalafil group experienced some volume loss at 3 months, this was not statistically significant. However, when comparing the controls versus treatment groups, there was no difference in length or girth changes between these groups ($p>0.05$). Thus, more data are needed to fully determine the role of penile rehabilitation with PDE5i to preserve penile volume post-RP.

There are limited data on a head to head comparison between PDE5i and intraurethral alprostadil with regard to preserved penile length post-RP. McCullough et al compared 97 men on intraurethral alprostadil (125 µg nightly) versus 59 men on sildenafil (50mg nightly).[470] These men were randomized to either treatment arm and the medications were initiated one month post-RP. Stretched penile length was evaluated pre-op and at 1, 3, 9, 10 and 11-months post-op. Both groups of men experienced nearly identical length loss. More data are needed to determine if either rehabilitation regimen is superior at preserving penile length.

Body of Evidence Strength:
Body of evidence strength is Grade C; there are limited data that have addressed this question.

SECTION 5:
Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 33:

Clinicians should counsel patients that there is insufficient evidence to fully determine the benefit of PDE5i use after radiation therapy as a strategy for penile rehabilitation.

(Conditional Recommendation, Evidence Strength C)

Discussion

Three randomized placebo-controlled trials have examined the use of PDE5i as a rehabilitation strategy after radiotherapy.[471-473] The trials differed in inclusion criteria: Ilic et al. focused primarily on men who had brachytherapy; Pisansky et al. evaluated men who had external RT or brachytherapy and excluded men on ADT; and, Zelefsky et al. focused on men who had external beam RT or brachytherapy or both with or without ADT. The Illic et al. and Zelefsky et al. trials followed men for two years. The Pisanksy et al. trial followed men for one year. The sample sizes in Ilic et al. were small (placebo – 13 men; sildenafil 14 men). Pisansky et al. evaluated 109 men who took placebo and 112 men who took tadalafil. Zelefsky et al. followed 67 men who took placebo and 135 men who took sildenafil. The medication phase in all three trials was six months and patients took daily medication or placebo.

Trial findings were contradictory with two trials reporting negative findings and one trial reporting selected positive findings. Ilic et al. and Pisansky et al. found no group differences in IIEF-Total scores, IIEF-EF scores at the end of the intervention, or IIEF-EF scores at final follow-up when some patients were using ED treatments. Pisansky et al. also reported no differences between groups in Locke Marital Adjustment scores for partners (94 and 95.4 in prior placebo and tadalafil groups, respectively) or in Sexual Adjustment Questionnaire scores for men (62.8 and 62.6, respectively).

Meanwhile, Zelefsky et al. reported similar findings but noted that overall satisfaction scores and sexual desire scores were higher at two years in men who had taken sildenafil compared to placebo. At the two-year point, 81.6% of men who had taken sildenafil for six months had functional erections with or without erectile medications compared to 56% of men who had taken placebo. It is worth noting that the Zelefsky trial used IIEF-EFD scores as an assessment of erectile function at a time point of 24 months post-treatment. In contrast, the Pisansky trial looked at EF outcomes less than one year post-RT and used the limited outcome of question 1 of the IIEF questionnaire, “How often were you able to get an erection during sexual activity?”.

An additional group of observational studies reported more positive findings, but the use of a no-treatment control group, or a single-group design make it difficult to contextualize findings.[474-476]

Body of Evidence Strength:
The available evidence is Grade C in strength given the contradictory findings of the randomized studies and the limited data from observational studies.

SECTION 5:

Guideline Statements With Supporting Evidence

ERECTILE DYSFUNCTION TREATMENT

Introduction

The Panel advocates the use of a biopsychosocial treatment framework to support men and partners in making treatment decisions, including full appreciation of sexual orientation and culture-specific priorities and concerns. For each treatment, the clinician's role is to ensure that the man and his partner have full understanding of the benefits and risks associated with that choice.

GUIDELINE STATEMENT 34:

Clinicians should provide support for patients' use of pro-erectile aids as well as non-penetrative sexual activity if they wish to continue to engage in sexual activity.

(Strong Recommendation; Evidence Strength Grade C)

Discussion

Studies have shown that patients do not use pro-erectile aids without psychosocial support, or at least not as effectively as they could.[55, 56, 417, 477] The use of a behavior therapy approach with men has shown promise in helping men with prostate cancer accept and use sexual aids.[420] The strongest evidence for the uptake of erectile aids comes from RCTs of interventions delivered to couples via in-person counseling with a therapist, or telephone counseling with nurses or peers.[478, 479]



The nurse or peer counseling intervention demonstrated sustained uptake outcomes at 5-year follow up.[480] Another study of an intervention that addressed stress for individual men in a group setting did not specifically include the use of erectile aids, however its positive effect on masculine self-confidence and sexual function suggests that addressing masculinity in the context of the loss of sexual function may improve men's openness to using erectile aids.[481] The discussion of and support for the use of pro-erectile aids should include education about both penetrative and non-penetrative sexual activity.

Body of Evidence Strength:
Body of evidence strength is Grade C.
A limited number of RCTs have shown that men are more likely to use pro-erectile aids if a partner is involved and psychosexual support is provided.

SECTION 5:

Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 35:

Clinicians should discuss all available erectile function treatment options with patients following all modalities of prostate cancer therapy, including PDE5i, intraurethral suppositories, intracavernosal injections (ICI), vacuum erection devices (VED), penile traction therapy, and penile implants. Clinicians should tailor recommendations based on patient preference, efficacy, and phase of sexual function recovery. This discussion should address benefits, risks, and contraindications associated with each option, as well as patient and partner goals.

(Clinical Principle)

Discussion

The purpose of therapy for erectile dysfunction is to support patients and partners in achieving their sexual function recovery goals. These goals may differ for many reasons, including age, culture, presence of other medical conditions, and priorities in the relationship. The Panel believes it is better to make all treatments available to patients and partners (rather than requiring a stepped care approach) because this will help individuals and couples achieve their sexual function recovery goals and enhanced quality of life.

PDE5 Inhibitors

Patient education is an important component of incorporating the use of PDE5i into sexual recovery. Specifically, men should be counselled that in order for PDE5i to support erections, there must be some cavernous nerve activity and men must be aroused. Education is also critical to support adherence.[482]

POST-RADICAL PROSTATECTOMY

(Evidence Strength Grade B)

Discussion

Five placebo-controlled randomized trials evaluated the use of PDE5i to treat ED post-prostatectomy (Brock et al. 2003, Montorsi et al. 2004, Cavallini et al. 2005, Nehra et al. 2005, Mulhall et al. 2013).[483-487] All trials included men with nerve-sparing RP, ED that emerged after the RP, and who administered PDE5i on demand for three to four months. The Cavallini trial evaluated sildenafil (100 mg) plus placebo compared to placebo only, or to sildenafil plus L-carnitine daily (propionyl-L-carnitine 2 grams/daily and acetyl-L-carnitine 2 grams/daily). Brock et al. and Nehra et al. trials evaluated vardenafil (10 or 20 mg) compared to placebo. Montorsi et al. trial evaluated tadalafil (20 mg) compared to placebo. All trials had moderate to large sample sizes except for Cavallini, in which had only 33 to 40 men were randomized to each group.

All five trials reported outcomes using subscales of the IIEF. Four trials reported that the active treatment groups had significantly higher IIEF-EF scores compared to the placebo groups (Brock et al. 2003, Montorsi et al. 2004, Cavallini et al. 2005, Mulhall et al. 2013).[483-485, 487] In addition, Cavallini et al. reported that men in the sildenafil plus L-carnitine group had higher IIEF-EF scores than did the sildenafil only group. There were no statistically significant dose response effects in trials that compared two drug doses (e.g., the higher dose did not produce significantly higher IIEF-EF scores compared to the lower dose).

Eleven studies evaluated PDE5i to treat ED post-RP using observational designs (Zippe et al. 1998, Lowentritt et al. 1999, Blander et al. 2000, Feng et al. 2000, Zagaja et al. 2000) Zippe et al. 2000, Raina et al. 2003, Ogura et al. 2004, Raina et al. 2004, Raina et al. 2004, Lee et al. 2008).[488-498] These studies had more diverse inclusion criteria, such as not requiring a nerve-sparing RP.

Sample sizes were relatively small with the exception of Lee et al. who reported on 846 men from the CAPSURE database, Raina et al. (2004) who followed 174 men, and Zagaja et al. who followed 170 men. There was a much greater range of follow-up durations

in this group of studies, ranging from one month to 24 months. Three studies did not report follow-up duration (Blander et al. 2000, Feng et al. 2000, Ogura et al. 2004). All studies focused on the use of on demand sildenafil except for Lee et al. in which men took sildenafil or tadalafil or vardenafil that was probably on demand (not explicitly stated).

Four studies reported findings using the IIEF. Lowentritt et al. reported that sildenafil 50-200 mg on demand at two months significantly improved IIEF-EF scores. Ogura et al. (2004), Raina et al. (2003), and Raina et al. (2004) all reported that sildenafil at varying doses improved pre- to post-treatment SHIM scores. Note that Raina et al. (2003) presents three-year follow-up data on patients originally assessed at one year in Zippe et al (2000).

Only one article was retrieved that addressed use of PDE5i among men post-RP from different cultures.[499] Namiki et al. reported that during the two years post-RP, 71.8% of U.S. men (total sample size 205) and 10.1% of Japanese men (total sample size 168) used PDE5i. Japanese men who used PDE5i reported better sexual function both before and after RP than did Japanese men who did not use PDE5i. In contrast, U.S. men who used PDE5i reported worse sexual function than did men who did not use PDE5i both before and after RP.

The PDE5i adverse event data from randomized and observational studies suggest that men post-RP report higher rates of AEs than do men who use PDE5i to address ED not associated with RP itself. These differences are most evident in AE rates reported in response to using sildenafil, the most well-studied PDE5i in these two groups [see table below; these data are also available from the American Urological Association's Erectile Dysfunction Guideline (https://www.auanet.org/guidelines/male-sexual-dysfunction-erectile-dysfunction-2018)]. Given that men with post-RP ED generally present with more severe ED than men with other ED causes, this phenomenon may be partly due to the need for higher medication doses.

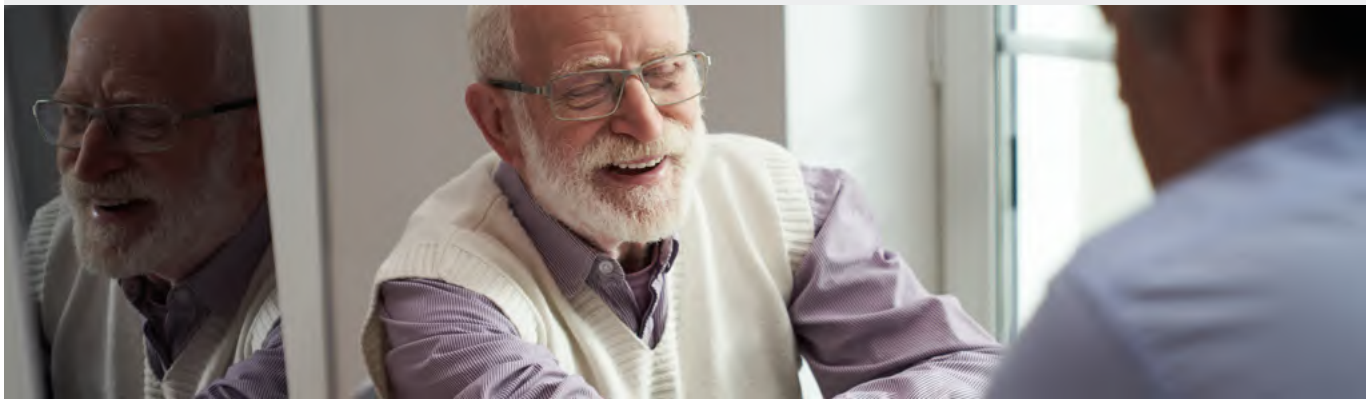
MEAN ADVERSE EVENT RATES IN STUDIES OF SILDENAFIL

SILDENAFIL	GENERAL POPULATION	POST-RP
Dyspepsia	4.81	10
Headache	11.15	16.55
Flushing	10.45	16.24
Nasal congestion	3.8	6.93
Visual disturbance	3.59	5.67
Myalgia	2.11	NR
Dizziness	2.68	8.63

TABLE 4. The table presents mean adverse event rates in studies that evaluated the use of sildenafil among men from the general ED population who had ED from various causes compared to men who used sildenafil to treat ED that occurred after radical prostatectomy.

SECTION 5:
Guideline Statements With Supporting Evidence

Body of Evidence Strength:
Body of evidence strength is Grade B. Five placebo-controlled randomized trials, ranging from low to unclear risk of bias, reported consistent findings. Strengths of this group of studies include adequate statistical power in most trials and the use of randomization, blinding, and placebo control groups to protect internal validity. Limitations include short follow-up durations (3-4 months) and, of note, all studies had one or more authors that were associated with the relevant pharmaceutical company and declared this relationship. As a group, the observational studies reported similar findings and provided some data at longer follow-up durations in more diverse samples.



POST-RADIOTHERAPY
(Evidence Strength Grade B)

Discussion

The highest quality evidence is provided by four placebo-controlled crossover trials (Incrocci et al. 2001, Incrocci et al. 2006, Harrington et al. 2010, Watkin-Bruner et al 2011).[500, 501] For Watkins-Bruner et al. (2011) additional findings are reported in Hanisch et al.; one other randomized design compared tadalafil 5 mg daily to tadalafil 20 mg on demand.[502-505] These trials were relatively short, with the active drug exposure phase in the crossovers lasting one to 1.5 months; Watkins-Bruner et al. and Ricardi et al. followed men for three months post-radiotherapy. Three trials evaluated sildenafil; two trials focused on tadalafil (see table). All trials used flexible on demand dosing except for Ricardi et al. Sample sizes ranged from 25-115 per treatment group. The men in Watkins-Bruner et al. had prior ADT exposure; the men in the other trials did not have ADT exposure.

All five trials reported findings using the IIEF and its subscales. In the placebo-controlled crossovers, scores were higher when men took an active treatment compared to when they took placebo. Generally, these differences were statistically significant. Of note is that men in Watkins-Bruner et al. generally had lower baseline scores and smaller increases in scores in both the placebo and active treatment conditions than in the other trials, suggesting a possible long-term impact of earlier ADT exposure.

In Ricardi et al., both dosing groups had higher scores compared to baseline without differences between groups, indicating that daily and on demand dosing were both effective. The authors note, however, that compliance was higher in the daily dosing group and adverse event rates were slightly lower. In 2006, Incrocci et al. reported additional findings in terms of the proportion of "yes" answers to the SEP 2 ("Were you able to insert your penis in your partner's vagina?") and SEP 3 ("Did your erection last long enough for you to have successful intercourse?") at the end of each phase as well as at the end of the study.[500] Percentages were significantly higher when men were in the active treatment group compared to the placebo group. Incrocci et al. (2001) and Harrington et al. reported the proportion of "yes" answers to various versions of a global efficacy

question with a similar pattern of findings (see table). Ricardi et al. also used a global efficacy question and reported no differences between men taking tadalafil daily vs. on demand. Hanisch et al. reported additional findings from RTOG 0215. These included Sexual Adjustment Questionnaire responses and Locke's Marital Adjustment scores for men and partners; no statistically significant differences were reported when the placebo and active drug phases were compared.

Data from an additional 1.5-month open label phase were provided by Incrocci et al. (2003) for Incrocci et al. (2001) and Incrocci et al. (2007) for Incrocci et al. (2006) (Incrocci, Hop et al. 2003, Incrocci, Slob et al. 2007).[317, 500, 506-508] IIEF (total and subscale) scores remained consistent with continued efficacy of PDE5i in men post-RT. Incrocci et al. (2003) queried men two years after the trial ended and reported that 60% no longer used sildenafil because of lack of efficacy, 16% had stopped use because of adverse events (dyspepsia, headache), and 24% were still using sildenafil.

Eleven observational studies evaluated the use of PDE5i post-RT (Kedia et al. 1999, Merrick et al. 1999, Weber et al. 1999, Zelefsky et al. 1999, Potters et al. 2001, Valicenti et al. 2001, Raina et al. 2003, Shemtov et al. 2004, Ohebshalom et al. 2005, Teloken et al. 2007, Lee et al. 2008).[280, 498, 509-517] In six studies, sample sizes were 50 or fewer men. In six studies men were followed for up to 1.5 months or follow-up duration was not reported. All studies administered sildenafil except for Lee et al. (2008) Lee analyzed the CAPSURE database and included men who took sildenafil, tadalafil, or vardenafil.

Generally, all studies reported some degree of efficacy with the use of PDE5i. The most useful information is provided by studies with the larger sample sizes and longer follow-up durations. While some studies reported information using the IIEF subscales, most studies reported other forms of outcomes. Lee et al. (2008) reported on 241 men in the CAPSURE database at 24 months of follow-up. Twenty seven percent of men had at least a 12-point increase in sexual function scores at two years; 33% of men reported at least a 16-point increase in sexual bother scores. At 36 months of follow up, Ohebshalom et al. (2005) compared 42 men who had brachytherapy to 68 men who had 3D-CRT. Similar proportions of men reported that sildenafil was effective at the measured time points up to three years, with a decline over time in these proportions. Potters et al. (2001) evaluated 84 men at 34 months after brachytherapy; 62% of men reported erections sufficient for intercourse using sildenafil. Teloken et al. (2007) compared 35 men who had RT with ADT to 117 men who had RT at 38 months follow-up. The proportion of men who reported erections sufficient for intercourse was lower (47%) in the ADT+RT group compared to the RT only group (61%).

The PDE5i adverse event data from randomized and observational studies suggest that men, post-RT, report higher rates of AEs than do men who use PDE5i to address erectile dysfunction post-RP. The same holds for men who have erectile dysfunction from non-RP or RT causes. These differences in AE rates are present in response to placebo conditions as well as in response to use of sildenafil (the most well-studied PDE5i; see AUA Erectile Dysfunction Guideline for detailed discussion of this issue; https://www.auanet.org/guidelines/guidelines/erectile-dysfunction-(ed)-guideline]

Body of Evidence Strength:
Four placebo-controlled crossover trials and one randomized design, that compared dosing regimens ranging from low to unclear risk of bias, reported consistent positive findings of PDE5i efficacy in this sample. The most common reason for the methodologist's rating of unclear risk of bias was inadequate information regarding randomization and/or blinding. Similar findings regarding efficacy were reported in two open-label clinical trial extensions, as well as in observational studies that provided information at longer follow-up durations.

SECTION 5:
Guideline Statements With Supporting Evidence

INTRACAVERNOSAL INJECTIONS
(Evidence Strength Grade C)

Discussion

Six observational studies evaluated the use of ICI to treat ED post-RP (Dennis & McDougal 1988, Claro et al. 2001, Raina et al. 2003, Mydlo et al. 2005, Albaugh & Ferrans 2010, Domes et al. 2012).[518-523] Single or combined ICI medications were used. Sample sizes ranged from extremely small, with three studies of 20, 14, and 34 participants respectively, to three more substantial studies with 168, 180, and 102 participants. Four studies reported IIEF-based outcomes.

In Raina et al (2003), 102 men underwent either bilateral nerve sparing (n = 40), unilateral nerve sparing (n = 19), or non-nerve sparing (n = 43). Pretreatment SHIM score 4.2 ± 3.5 and increased to 19.5 ± 8.8 post-injection. There were no statistically significant differences in the IIEF-5 responses or erectile hardness between the NS (n = 63) and non-NS (n = 39) groups. De Almeida Claro (2001) noted that 94.6% of 168 men using ICI post-RP reported that they were able to have sexual intercourse with a hard erection at home. Dennis & McDougal (1988) reported that 12 of 14 men using ICI had an erection sufficient for intercourse. Albaugh et al. evaluated the erectile improvement in 20 men who used ICI post-RP. Sexual Health Inventory for Men (SHIM), The Self Esteem and Relationship (SEAR) questionnaire, Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) questionnaire, and Quality of Life Index (QLI) were completed prior to initiation of ICI, one month after ICI commencement, and after 3 months. Erectile function scores improved significantly after treatment: mean SHIM score = 5.9 ± 5.4 at baseline vs 18.1 ± 4.8 at one month and 17.7 ± 7.2 at three months ($p < 0.001$). Sexual self-esteem and confidence in the sexual relationship also improved from 38.7 ± 23.5] at baseline to 61.7 ± 22.7 at one month and 64.2 ± 25.6 at three months ($p < 0.001$). Participants were satisfied with the treatment, with scores of 69.7 ± 22.4 at one month and 72.7 ± 23.1 at three months after ICI commencement. Domes et al (2012) reported on 117 men, all of whom had failed PDE5i[3]. Compared to baseline (pre-ICI) ICI was associated with significantly greater IIEF scores (20.8 ± 4.1 vs 16.0 ± 6.9, $P < 0.008$). Mydlo et al (2005) administered ICI to 32 post-RP patients, all of whom also had sub-optimal erections with PDE5i. These men reported an increase in SHIM scores while using ICI in conjunction with PDE5i and 68% of patents endorsed an increase in erectile function with PDE5i after starting ICI therapy.

The Domes (2012) study of 117 men post-RP who participated in a penile injection therapy program were unable to report more than minimal information regarding AEs r other the factors leading to attrition. ICI was most frequently discontinued because of patient-perceived ineffectiveness (48%), pain (21%), and prolonged erections (11%). Studies of men with ED from non-RP causes, who discontinued ICI, suggest that the most common reason for discontinuation is lack of efficacy (43.1%), followed by inconvenience (18.3%), change to another treatment (10.7%), loss of sexual desire/libido (6.7%), adverse events (5.5%), and return of spontaneous erections (2.8%).[524] AE rates may depend on the specific medication or combination of medications injected (see AUA ED guideline; Appendix B2; https://www.auanet.org/guidelines/erectile-dysfunction-(ed)-guideline#x8092). These data indicate the need for adequate education and monitoring when carrying out an intracavernosal injection program.

Body of Evidence Strength:
Body of evidence strength is Grade C. The available evidence is derived from observational studies with varied inclusion criteria. Half of the available studies had extremely small sample sizes. Limited data are available regarding AEs in men post-RP who use ICI.



INTRAURETHRAL SUPPOSITORY (MUSE)
(Evidence Strength Grade C)

Discussion

Raina administered intraurethral alprostadil in combination with sildenafil 100 mg to 23 men who had failed sildenafil only treatment.[525] They reported significant increases in SHIM scores with IU alprostadil alone and in combination with sildenafil. 70% of men were able to achieve penetration with combined therapy. McCullough et al. evaluated men who underwent RP and initiated either intraurethral alprostadil 125- 250 ug (n = 139) or sildenafil 50 mg (n = 73) nightly for 9 months.[462] After a washout phase, patients then used on-demand sildenafil 100 mg.

IIEF erectile function domain scores were similar between groups, suggesting that nightly intraurethral alprostadil and sildenafil similarly support EF post-RP. Costabile et al. reported on 270 men with ED post-RP.[526] These men were randomized to intraurethral alprostadil or placebo. At three months, 57% of men were able to have intercourse at least once with home use. Moreover, 70% of intraurethral alprostadil administrations resulted in successful intercourse. In another study by Raina et al., men were administered IU alprostadil 125-250 ug three times a week for 6 months (n = 56) compared to a control group (n=35).[527] The alprostadil group experienced significantly increased SHIM scores and higher rates of successful intercourse both with and without treatment. Only one study addressed AEs; Costabile et al. (1998) noted that approximately 39% of men reported penile pain.

The Panel notes that intraurethral alprostadil should not be prescribed until adequate instruction in the application of the medication is completed, an in-office administration of the medication has been performed, and a thorough explanation of the risks, benefits, and potential adverse events has occurred. In particular, an office administration of the first-dose and discussion of risks/benefits is important because higher doses of the medication (500, 1000 mg) can be associated with penile pain. Moreover, rare occurrences of hypotension occur in men who are status post RP.

Body of Evidence Strength:
Body of evidence strength is Grade C. The available evidence consists of three observational studies; only one study reported AEs (Costabile et al. 1998).

SECTION 5:
Guideline Statements With Supporting Evidence

VACUUM ERECTILE DEVICE
(Evidence Strength Grade C)

Discussion

Two randomized designs (Raina, et al 2006, Kohler et al. 2007) and one observational design reported on the use of VED as a rehabilitation strategy (Nason et al. 2016).[528-530] The studies varied in terms of comparison groups. Kohler et al. (2007) compared 17 men who began using VED one month post-RP to 11 men who began using VED 6 months post-RP. Raina et al. (2006) compared a no treatment control group of 35 men to 77 men who used the VED. Nason et al. (2016) studied a single group of 45 men. All three studies evaluated daily use without the constriction ring and use of the ring when attempting intercourse. The two randomized trials examined 9.5 or 9 months of treatment, respectively (follow up duration not reported in Nason et al. 2016). All three studies reported improved SHIM scores as a result of early VED use, while using the device or using other treatments (PDE5i). They reported other "improvements" variously defined. Kohler et al. (2007) reported that a smaller percentage of men (12%) experienced 2 cm or more penile shortening in the early use group compared to the later use group (45.5%). No men in either group, however, were able to have unassisted intercourse. Raina et al. (2006) reported that similar but small proportions of men were able to have unassisted intercourse by the end of the intervention (13.5% in the VED group; 11.4% in the no treatment group).

Studies using data from vacuum erection devices only report outcomes while the device is in use, not longitudinally. They thus do not include results after a washout period.[529] Preliminary data from a single RCT evaluating 2nd generation penile traction therapy suggest possible benefits in preserving erectile function and penile length when used in the early post-operative period following prostatectomy. However, external validation is warranted.[531]

Body of Evidence Strength:
Body of evidence strength is Grade C. The available studies suggest possible benefits to early VED use but appropriately powered randomized designs are needed to definitively quantify those benefits.

GUIDELINE STATEMENT 36:

Clinicians should inform patients with persistent erectile dysfunction after completion of prostate cancer therapies about the potential benefits and risks of penile implant surgery.

(Moderate Recommendation, Evidence Strength Grade C)

PENILE IMPLANT SURGERY
(Evidence Strength Grade C)

Discussion

Penile prostheses offer men the ability to generate an erection sufficient for penetrative sexual activity on demand, for as long and as frequently as desired. The risks of prosthesis implantation include the surgical risks (e.g., infection), possible changes in penile appearance, and the possibility of device malfunction. Men and their partners should be educated regarding the differences between prosthesis models (malleable, two- or three-piece inflatable) so they can make appropriate decisions, have realistic post-operative expectations, and realize high rates of satisfaction. In addition, men and partners should be advised that, although prostheses can be removed, the penis probably will not be responsive to other ED therapies after explant. The decision to undergo implant surgery should be considered irreversible.

Six observational studies reported findings for men who had implant surgery to treat ED post-RP (Schwartz et al. 2000, Ramsawh et al. 2005, Menard et al. 2011, Bozkurt et al. 2014, Antonini et al. 2016, Pillay et al. 2017).[532-537] In two of these studies (Schwartz et al. 2000, Ramsawh et al. 2005), men had implants placed simultaneous with the prostatectomy; the remaining studies implanted devices at various durations post-RP, either once ED had manifested and was not responsive to other therapies, or once other therapies resulted in unacceptable adverse events. EDITS and the IIEF were used to report patient and partner satisfaction. Sample sizes were greater than 50 in all studies, and follow up durations ranged from 1-5 years.

SECTION 5:
Guideline Statements With Supporting Evidence

Schwartz et al compared sexual satisfaction after immediate vs. delayed implant placement in post-RP men and found that men who underwent simultaneous penile impact during RP reported increased frequency of sexual activity per month. Ramsawh et al. compared men who had immediate implant placement to post-RP men who were using other ED treatments. They reported patient EDITS scores of 81 in the prosthesis group, compared to 55 in the group, without immediate implant placement. Patients with simultaneous placement of an implant also reported greater overall QOL and more frequent sexual contact than a comparison group of men who underwent RP alone. However, simultaneous placement of an implant at the time of RP has not been widely adopted, partly due to the concerns of increased risks, since adverse events were not clearly reported in these studies.

Menard et al. reported outcomes for penile implant surgery in patients a mean of 31.5 months post-RP. They reported significantly increased IIEF-EF scores after the penile implant (from 6 pre-op to 28 post-op). Among the patients with ED post-RP, 86% of men answered "Yes" to "Does your prosthesis enable you to achieve satisfactory sexual intercourse?". Bozkurt et al. evaluated patient and partner satisfaction. They reported EDITS score of 58 for patients with a history of RP and EDITS Partner Survey scores of 46. Only 3.4% of patients received 3-piece inflatable penile prosthesis in this study, which may have negatively affected patient/partner overall satisfaction. Antonini et al. reported significantly increased IIEF-5 scores with penile implant surgery for patients after laparoscopic RP with refractory ED to oral, ICI, and VED treatments (from 6.8 pre-implant to 20.4 post-implant). The patients' EDITS mean score reached 71, defined as very satisfied with the treatment. When EDITS or EDITS Partner Version were used as a measure of satisfaction with treatment, Pillay et al. reported patient scores of 91 and partner scores of 90. About 54% would recommend penile implants to others without reservations and 44% of patients would do so with some reservations.

Some studies suggest that men post-RP may have lower satisfaction rates after implant surgery compared to men with ED from other causes. Menard et al. compared men with ED post-RP to men with vasculogenic ED (not defined, but patients with Peyronie's disease, diabetes mellitus, revision surgery, history of priapism, spinal cord injury, neurological disorders, other pelvic surgery, and ED from multiple causes were excluded). The mean preimplantation IIEF total score was significantly lower in RP patients than in patients with vasculogenic ED (14.7 vs. 22.6). After penile implant surgery in RP patients, the scores for all IIEF domains improved, but the total score remained significantly lower in men post-RP compared to men with vasculogenic ED (63.1 vs. 68.5). Overall satisfaction rates, however, were not significantly different (86% in men post-RP; 91% in men with vasculogenic ED). Bozkurt et al. also compared men with ED post-RP to men with vasculogenic ED (not defined). Mean EDITS scores for post-RP men (58) and their partners (46) were significantly lower for men with vasculogenic ED (71) and their partners (65), respectively. In contrast, Antonini et al. reported no statistically significant differences for IIEF-5 (20.4 vs. 21.0) and EDITS scores (71 vs. 74) post-implant between men with ED post-RP and men with diabetes or metabolic syndrome. Based on EDITS scores, approximately 26.7% of men were moderately satisfied, and 67% of men were very or completely satisfied, after penile implants regardless of the etiology for ED.

There is a large literature that reported outcomes for men undergoing penile implant surgery for reasons other than prostate cancer therapy. In general, this literature reports high patient satisfaction rates, with mean rates >85% for inflatable prostheses and >75% for malleable models (see AUA ED Guideline for detailed discussion of these studies).

Studies that focused exclusively on men post-RP did not address AEs. Comparative studies did report AEs, however. Menard et al. reported the surgical complications after penile implantation for patients with ED post RP compared to patients with vasculogenic ED; complication rates were similar. However, blind entry into the retropubic space can carry a unique risk for patients with ED post-RP. A case of epigastric vein injury was encountered that required a lower quadrant incision for hemostasis. The overall rates of infection, mechanical failure, auto inflation, and other surgical complications requiring revision surgery were 1.1%, 3.3%, 1.1% and 4.4%, respectively, for post-RP implants. Findings were similar for patients with vasculogenic ED. Bozkurt et al. also reported

similar complication rates between men with ED post-RP and men with vasculogenic ED. The interoperative complications (crossover, crural perforation, urethral injury) and postoperative complications (infection, erosion and mechanical failure) were 6.6% and 8.3% for patients with ED post-RP vs. 3.6% and 9.7% for patients with vasculogenic ED, respectively. Comparison of complications after penile implantation surgery between patients with ED post-RP and patients with diabetes and metabolic syndrome was reported by Antonini et al. Again, there were no increased risks for infection, urethral erosion, prosthesis extrusion, and scrotal hematoma formation for men with a history of RP, compared to men with DM and metabolic syndrome. Based on available data, penile implant surgery for men with ED post-RP does not carry increased risks for common penile implant related complications compared to men with other ED etiologies. However, carefully entering into the retropubic space or using an alternative location for reservoir placement are advisable for men with a history of RP.

The broader literature on AEs after prosthesis surgery in men with varied ED etiologies also is informative; short- and long-term AEs are reviewed in detail in the AUA ED Guideline (see https://www.auanet.org/guidelines/guidelines/erectile-dysfunction-(ed)-guideline). The most serious AE is infection which usually requires removal of the prosthesis. In general, studies that assessed patient information forms indicated that prosthesis models that have infection-inhibiting coatings have lower infection rates compared to non-coated models. For example, Serefoglu et al (2012) compared the Titan Coloplast model with the hydrophilic coating (n=29,360) to the same model without the hydrophilic coating (n=7,031).[538] The infection rate was significantly lower (1.4%) for the model with the hydrophilic coating compared to no coating (4.6%). Carson et al. (2011) analyzed revision surgery for infection in antibiotic-impregnated inflatable devices compared to non-inflatable devices at up to 7.7 years of follow up.[539] Revision rates for antibiotic-impregnated devices were significantly lower at 1.1% (n = 35,737) than those for non-impregnated devices at 2.5% (n = 3,268).

The need for revision surgery because of device malfunction also is documented in the broader literature. Recent studies that evaluated prostheses with refinements to design and materials indicate that 90-95% of men will have a functioning prosthesis ten years post-implant.[540, 541]

Body of Evidence Strength:
Body of evidence strength for outcomes and adverse events for prostheses studies in men post-RP is Grade C. The available data were contributed by observational designs. Limited information was reported regarding patient characteristics such as the severity of ED or the presence of comorbidities. Adverse event reporting was limited to comparative studies.

SECTION 5:
Guideline Statements With Supporting Evidence

ADDITIONAL SEXUAL DYSFUNCTIONS

GUIDELINE STATEMENT 37:

If identified, altered orgasmic sensation, difficulty reaching orgasm or anorgasmia can be managed using a biopsychosocial approach.

(Expert Opinion)

Discussion

Orgasm can be deemed to be a cortical event, experienced phenomenologically, cognitively, and emotionally, and associated with striated muscle contraction, smooth muscle contraction of accessory glands, and sensory neuronal stimulation in the pelvic region. Prostate cancer therapies which remove or radiate the prostate and surrounding bladder neck, seminal vesicles, and vas deferens may result in altered orgasmic sensation or orgasmic threshold.[183, 542] Psychological variants such as depression and altered erectile function can further add to libido and motivational issues. The use of androgen deprivation therapy (ADT) may further reduce the chance of reaching orgasm physiologically, but also psychologically, due to reduced libido.

One study demonstrated that orgasm is a rare experience in men on ADT for prostate cancer (4%). Men who reached orgasm reported reduced ease of attainment and reduced intensity. Predictors of achieving orgasm were having a sexual partner and preservation of sexual desire.[543] The use of sex therapy techniques, pelvic floor therapy, and resumption of normal testosterone levels may help improve dysfunctions. Pelvic floor therapy has been described as helpful for chronic pelvic pain (CPP) management and for post radical prostatectomy incontinence training [544, 545]. Treatments for dysorgasmia may include pelvic floor therapy for general pelvic floor hypertonus, but no direct literature exists.

GUIDELINE STATEMENT 38:

Persistent, bothersome dysorgasmia may be treated using alpha-adrenergic blockers.

(Conditional Recommendation, Evidence Strength Grade C)

Discussion

Painful orgasm is distressing and can result in sexual avoidance, decreased sexual quality of life, and impaired relationships. In a review of the literature, between 3.2-18% of men were found to have dysorgasmia after RP.[546] Orgasmic pain may decrease with time (up to 2 years postop). Pain is variously described as pain in the penis (the majority of men), testes, or other areas (such as the rectum) (Barnas et al 2004) with the duration of pain in the majority of men being less than one minute, but with others, lasting hours.[328] Matsushita et al. found that 12% of patients complained of dysorgasmia within 6 months after RP, and Tewari (2012) found a prevalence of 3.2 % in patients younger than 60 after bilateral nerve sparing robot-assisted RP.[547, 548] Further studies are needed to define if robot-assisted approaches are associated with lower dysorgasmia potential. Only bilateral seminal vesicle sparing has been found to be a predictive factor of developing dysorgasmia.[549] Phamacologic treatment has met with some success. Clinicians used Tamsulosin 0.4 mg (an alpha-blocker that relaxes the smooth muscle of the bladder neck) for patients experiencing pain after RP. They based their treatment on the hypothesis that after RP the bladder neck closes during orgasm and may lead to painful spasm of the post–surgical vesicourethral anastomosis and/or pelvic floor musculature dystonia. In a follow-up to treatment, 77% reporting a significant decrease in pain, with 12% having complete resolution of their pain.[550]

Body of Evidence Strength:
Body of evidence strength is Grade C. The available literature consists of observational designs and is extremely limited.

GUIDELINE STATEMENT 39:

Patients and partners should be counseled regarding management strategies for bothersome sexual incontinence (including sexual arousal incontinence and climacturia), including psychological reframing.

(Clinical Principle)

Discussion

Management of sexual arousal incontinence and orgasm-associated incontinence consists of providing couples with strategies to manage the conditions so that sexual activity, if desired, can be undertaken. It is relevant to mention that no differences in the rate of climacturia have been found based on age, preoperative erectile function, nerve-sparing status, or daytime incontinence. Depending on the amount of climacturia, researchers have reported that patients have employed different coping strategies. These include emptying the bladder prior to sexual intercourse and the use of condoms.[324] Additional strategies include reducing fluid intake prior to sexual activity and adjusting the environment to allow for easy clean-up of urine. Anecdotally, daily use of tricyclic antidepressant imipramine or anti-muscarinic medications has also been suggested, although no formal outcome analyses have been performed.[542] Rather than avoid intimacy, patients also can be advised to use lubricants that disguise urine and to have towels on hand to wipe away any urine. It should be emphasized that urine is a non-harmful body fluid.

There are a limited number of studies examining the efficacy of surgical intervention for climacturia. In a series of 46 men with climacturia and stress urinary incontinence following radical prostatectomy, 100% had resolution of their climacturia after transobdurator sling placement, while 84% had resolution of stress urinary incontinence.[551, 552] Improvement in climacturia and SUI have also been described in small series of men undergoing mini-Jupette graft after radical prostatectomy, with >90% of patients noting significant or complete resolution of climacturia.[553, 554]

GUIDELINE STATEMENT 40:

Patients should be counseled that there are insufficient data regarding the efficacy of pelvic-floor rehabilitation, penile tension loop, a male sling operation or placement of an artificial urinary sphincter for the management of sexual incontinence (including sexual arousal incontinence and climacturia).

(Conditional Recommendation, Evidence Strength Grade C)

Discussion

The available studies focused on management of climacturia. Sighinolfi et al. evaluated the use of pelvic-floor rehabilitation strategies, including active pelvic-floor muscle exercises, electromyography biofeedback for strength and endurance, and electrical stimulation in a case series of 3 male patients with ED, as well as urinary incontinence and climacturia after RP.[555] All three patients showed a subjectively reduced rate of climacturia after 4 months of treatment. Mehta and colleagues studied the impact of a penile variable tension loop on climacturia and the level of distress on 124 patients and their partners.[556] They reported the degree of climacturia was small, moderate, and large in 16%, 72%, and 12% of patients, respectively, and 28%, 26% and 0%, respectively after treatment, all statistically significant findings ($p<0.01$). Distress levels were reported as 14% and 61% of patients and partners at baseline, respectively, and 2% and 11% at follow up ($p<0.01$). Although the study lacked a control group and multivariable analysis to adjust for potential confounders, the authors were able to provide a non-surgical alternative for the management of climacturia. Jain et al. assessed surgical placement of artificial urethral sphincter or male urethral sling in a small cohort of 11 patients with urinary incontinence and climacturia at a mean 33.5 months after RP. All patients reported improvement of climacturia after surgery.[557] Given that these procedures were performed in patients who also suffered from urinary incontinence, these results cannot be extrapolated to all patients suffering from climacturia. Moreover, if patients with climacturia are likely to experience resolution with time, some may consider placement of artificial sphincters or slings unnecessary in the long term.[556]

Body of Evidence Strength:
Evidence strength is Grade C. The relevant literature is extremely limited.

SECTION 5:
Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 41:

Clinicians may discuss the risk and benefits of testosterone therapy to improve low sexual desire in hypogonadal men following prostate cancer treatment.

(Moderate Recommendation, Evidence Strength Grade C)

Discussion

Although the specific etiologies and incidence rates for developing low sexual desire in men with prostate cancer have not been well defined, low testosterone is one of the most highly studied and commonly cited contributing factors. Similarly, testosterone therapy is one of the most common treatments used to improve low sexual desire in men. Several meta-analyses, including one performed by the American Urological Association Testosterone Guideline panel have reported that testosterone therapy results in statistically significant, although modest, improvements in sexual desire among men with low testosterone.[558, 559]

Body of Evidence Strength:
Body of evidence strength is Grade C; the evidence for use of testosterone among men following prostate cancer treatment is limited.

GUIDELINE STATEMENT 42:

Clinicians should counsel patients that there are inadequate data to quantify the risks versus benefits regarding testosterone therapy to treat low sexual desire in men with treated, or active, non-metastatic prostate cancer.

(Moderate Recommendation, Evidence Strength Grade C)

Discussion

The specific role for testosterone therapy in men with treated, active, and metastatic prostate cancer is unclear. Several small series have been reported of men with treated or non-metastatic prostate cancer who received testosterone for symptomatic hypogonadism and have shown minimal or no increased risk for prostate cancer progression.[560-568]

However, all studies evaluating the safety of testosterone in these settings have been non-randomized and include small cohorts with relatively short follow-up. These limitations are further highlighted by a meta-analysis which reported that an estimated 85,862 men would need to be randomized for one year to identify a 20% increased risk of developing prostate cancer.[569] As such, it is not possible at the present time to make any claims as to whether or not testosterone therapy is safe in cohorts of men with treated or untreated prostate cancer. There are also currently no studies which have evaluated the efficacy of other hormonal therapies on improving sexual desire in men with prostate cancer.

Body of Evidence Strength:
Evidence strength is Grade C; the relevant literature is extremely limited.

SECTION 5:

Guideline Statements With Supporting Evidence

VII. LIFESTYLE MODIFICATION STRATEGIES

GUIDELINE STATEMENT 43:

Clinicians should inform patients and partners about the importance and benefits of exercise for sexual health as a component of medical management related to ADT.

(Moderate Recommendation; Evidence Strength Grade C)

Discussion

Only about 12% of men with prostate cancer actually engage in regular physical activity levels that benefit overall health. Randomized clinical trials have shown the benefit of exercise on many aspects of wellbeing that support sexual health, such as body composition, fatigue/energy level, quality of life, physical function, social functioning, psychological distress, urinary problems, and cognitive decline.[570]

Body of Evidence Strength:
Evidence strength is Grade C; there is limited evidence in the ADT population.

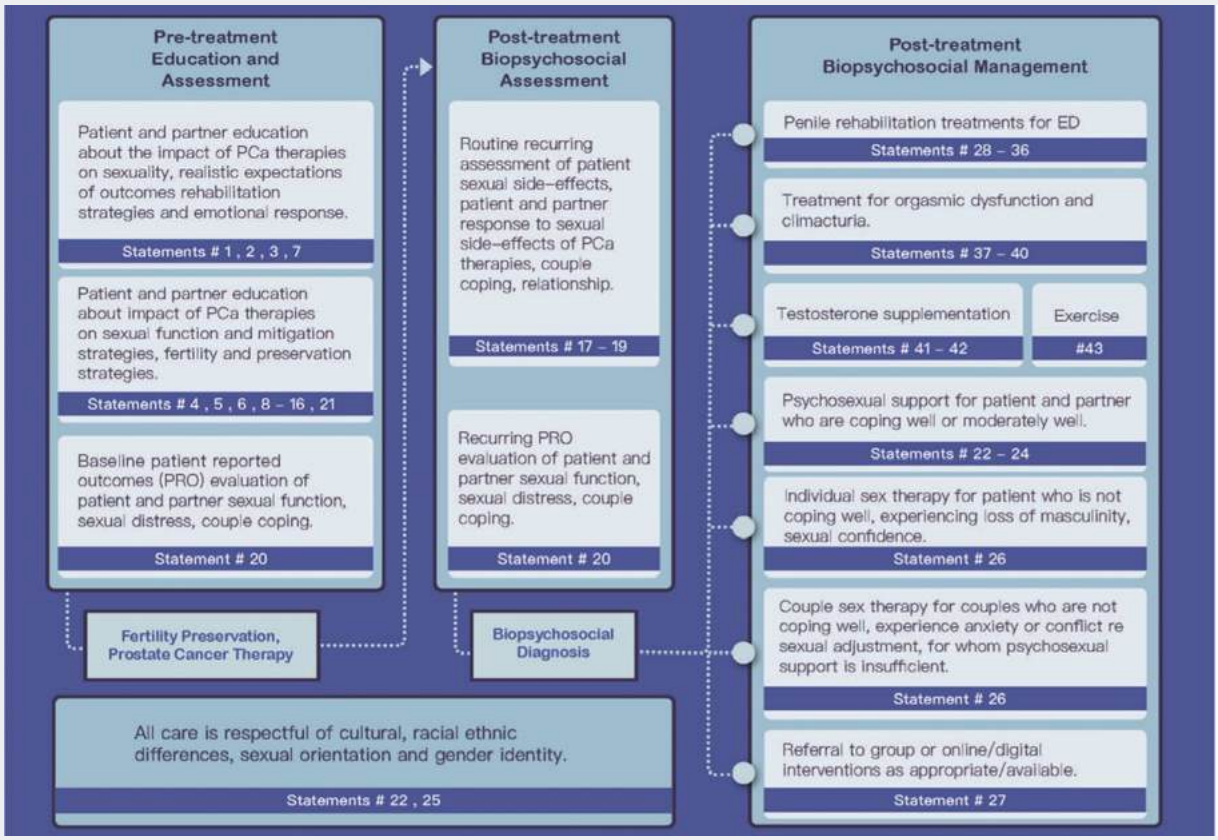


FIGURE 3 Guideline summary for clinician use. An at-a-glace summary of the guidelines. Guidelines statements are organized to suggest a pathway for a systematic approach to providing sexual health care to patients with prostate cancer and their partners.

SECTION 5:
Guideline Statements With Supporting Evidence

VIII. CLINICIAN EDUCATION AND TRAINING

Introduction

Despite the fact that sexual health concerns are paramount to many patients, the provision of adequate support services is lacking.[571] There are many reasons for this problem, including discomfort of the healthcare professionals in discussing sex or issues related to sexual health and lack of knowledge or resources, including access to sexual health providers. Some believe that cancer patients are more concerned about survival than about sexuality. These barriers are compounded for the LGBTI or adolescent/young adult community of patients, where there is even less expertise.

Limited access to sexual health education for clinicians has been reported by practitioners. Educational programs have typically either not been evaluated, shown limited efficacy, or were not necessarily perceived as beneficial.[572] An observational study confirmed that patient resources about the sexual side-effects of prostate cancer are often inadequate, with more than 50% of the materials reviewed written above a high school reading level, and a significant percentage lacking cultural sensitivity.[573]

GUIDELINE STATEMENT 44:

Clinicians should undergo sexual health education in interprofessional groups using case-based/reflective learning approaches, adopting a biopsychosocial lens and incorporating attention to ethnic and racial diversity and to sexual minorities.

(Strong Recommendation; Evidence Strength Grade C)

Discussion

In one study of a hospital-based intervention for clinicians, Jonsdottir and colleagues (2016) found the most common barriers identified by the participant clinicians to discussing sexuality were "lack of training" (38%) and "difficult issue to discuss" (27%).[574] Other studies also documented barriers to sexual health care as well as supportive care generally.[572, 575, 576] These authors argue for more development of multifaceted interventions, including education, that target the complex interplay of individual, organizational, and cultural factors.

Sexual health is not a standard component of medical or health professional education. This is troubling, given that men and partners often report inadequate support.[577-579] A number of studies have documented gaps in health care professional education either in sexual health care generally or in the context of prostate cancer.[577, 580-584] Two studies (Flynn, 2012; Traa, 2014), found that cancer patients had a high need for sexual health information that was rarely adequately addressed, though prostate cancer patients had the highest access to sexual health information.[577, 579] One study (Julien, 2010) and one review of 18 studies (Kotronoulas, 2009) examined nurses' behavior and beliefs with regard to sexual health care. These studies documented significant gaps in education and confidence, and revealed the belief among nurses that sexual health was not primarily their responsibility.[581, 582] Studies conducted with interprofessional groups document similar issues (e.g. Traa, 2014; Ussher, 2013).[579, 583] O'Brien et al. conducted semi-structured interviews with a purposive sample of 35 prostate cancer patients, with partners included in 18 interviews.[584] Men reported rarely being invited to discuss their sexual health concerns. Moreover, elderly participants specifically reported being embarrassed to raise the topic of sexual health with professionals due to their age.

There are limited studies available reporting on the outcomes of sexual health education programming in the context of cancer generally.[572, 574, 585] These studies used pre/post surveys to evaluate educational workshops. The Jonsdottir study also included a broad range of organizational strategies to support

practice change. One program, the Sexual Health & Rehabilitation e-Training program (SHARE-T) seems to be showing good outcomes specific to sexual health training in prostate cancer using a web-based design.[586, 587] The data from this project were not yet published at the time of writing this guideline, although one abstract is available.[586]

We identified several systematic integrative reviews and papers describing effective pedagogies in continuing health care education generally. One paper described strategies specific to sexual health care, but none were specific to sexual health or prostate cancer.[572, 588-594] These focus on what works in continuing education for health professionals; the role of interprofessional education; feasibility of web-based education; and reflective practice. In general, however, multifaceted, interprofessional education is recommended. In addition, web-based educational program design has been demonstrated to be feasible.[593] Overall, this body of research is not sufficiently robust to say definitively what works for whom.

The American Society for Clinical Oncology (ASCO) recently published a position paper and call for more education and competency training for providers to work effectively and meaningfully with sexual and gender minorities. We agree that this should be integrated into any sexual health education.[595] Competency in assessing sexual problems after PCTs should be a requirement of professional organizations administering accreditation for clinicians caring for patients with prostate cancer.



Body of Evidence Strength:
Body of evidence strength is Grade C. The retrieved literature is generally encouraging regarding the approaches described above, however, the volume of literature is limited and much of it constitutes indirect evidence.

SECTION 5:
Guideline Statements With Supporting Evidence

IX. HEALTHCARE PROGRAMS AND SYSTEMS

GLOBAL PERSPECTIVE ON HEALTHCARE SYSTEMS, COSTS, AND ACCESS TO CARE

Introduction

Prostate cancer is prevalent in all habited continents of the world, although incidence and mortality vary significantly. In 2018, nearly 1.3 million men were diagnosed with prostate cancer, most commonly in Oceania, North America, and Europe.[5] While incidence in sub-Saharan Africa and the Caribbean is more moderate, these regions have the highest mortality rate.

Prostate cancer therapy options are standardized, including local therapies such as surgery or radiation for early-stage disease and androgen deprivation for advanced disease. However, the impact of prostate cancer therapies on sexual function and sexual health can vary significantly by type of therapy and by the cultural importance of sexual matters. For example, a study comparing Japanese and American men noted differences in QOL questionnaires across races and levels of concern. When compared by race, Japanese prostate cancer patients overall noted worse sexual function but also reported less concern about sexual function than their American counterparts.[596]

The availability of educational materials and access to resources to support sexual recovery can vary widely by area. Notably, a lack of experts results in lack of education and resources to support sexual recovery.

We recommend the following guidelines as regards access to sexual recovery resources across healthcare systems both locally and globally.

GUIDELINE STATEMENT 45:

Providers and healthcare systems should develop culturally appropriate materials for counseling regarding the impact of prostate cancer treatment on sexual health.

(Moderate Recommendation; Evidence Strength Grade C)

Discussion

The definition of sexuality varies with cultural, ethnic, and racial conceptualizations. The value attached to aspects of sexuality can vary; cultural, racial, and ethnic awareness needs to be in place to adequately define the needs of the population being cared for and to use language and norms that are culturally acceptable. While more study is needed, it is clear that there are significant differences in the goals of men from different ethnic backgrounds. In a study evaluating Black African/Black Caribbean men, it was noted that support systems for these men differ from support systems reported by their White counterparts. In addition, "cultural definitions of masculinity influenced the meanings men gave to their post-treatment experiences".[597]

A study of Latino men found that cultural taboos about discussing sex and masculinity limited learning and hindered early detection. "Hopeful intentions came up against cultural taboos around sex, reproductive health, and intimacy that limited discussions between fathers and sons. Fathers were a valued source of information but play various roles, which affect sons' screening intentions".[598] Unpacking the way in which cultural expectations may serve as barriers to the recovery of sexual intimacy after prostate cancer therapies can inform interventions that support men while respecting the cultural context.

Communication about the side effects of treatment is complex: it has been documented that patients can have unrealistic expectations and experience regret after prostate cancer treatment as related to

side effects, including sexual side-effects.[140, 599] This unintentional miscommunication can be amplified if there are unrecognized cultural differences.

Cultural sensitivity is often lacking in prostate cancer educational materials. Choi et al. scored health education materials for prostate cancer survivors found in clinical offices. Sixteen percent of materials had unacceptable cultural sensitivity scores for their visual messaging, and materials were generally written above a high-school reading level.[573] Authors note that "prostate cancer-related materials available in health-care practices may not meet patient needs regarding content, cultural sensitivity, and readability." Overall, when developing educational materials for patients, it is a good idea to have patients, partners, and other stakeholders review them.

Body of Evidence Strength:
Evidence strength is Grade C. The available literature that has addressed these issues is extremely limited.



GUIDELINE STATEMENT 46:

Patient education programs about sexual recovery after prostate cancer therapies should be tailored to reflect local cultural influences, based on resources available in that region, conceptualization of sexual recovery, and of the priorities in that region.

(Expert Opinion)

Discussion

Cultural conceptions of sexual health are subject to regional differences and, as such, they often determine the support provided to men and their partners. These conceptions consequently impact how guidelines and standards are implemented by local institutions.[600]

It is important to realize that these conceptions can both facilitate and hinder the provision of adequate support for patients and their partners. Research is needed to develop greater understanding of these facilitators and barriers. Healthcare provider training can then be designed to reflect the concerns and needs of patients in a particular region. The goal is for patients to see providers who convey information that is locally relevant, respectful, and free of bias. As a result, they will be more likely to decide to receive psychosexual care. Understanding local, regional, and national conceptions of sexual health is a prerequisite to the successful development of sexual recovery programs.

SECTION 5:
Guideline Statements With Supporting Evidence

GUIDELINE STATEMENT 47:

All insurance providers should cover the treatment of sexual dysfunctions secondary to prostate cancer therapies in order to validate this clinically important aspect of prostate cancer care and to reduce disparities in access to care.

(Clinical Principle)

Discussion

The cost of medications and devices for the treatment of male erectile dysfunction can be considerable. There is paucity of data on the availability of these treatments globally, but it is safe to assume that they are out of reach of most men. Even in wealthy countries, sexual rehabilitation after prostate cancer treatment is not a part of usual health care. Insurance coverage for erectile aids for the management of prostate cancer treatment-related ED or for psychosexual therapy services is non-existent in most countries and only available by private insurance in the developed world. In the US, the largest national insurer of individuals over 65 years old, Medicare parts A and B, stopped coverage for medication in 2005 and vacuum erectile devices in 2015.[86] Regional Medicare coverage for inflatable penile prostheses varies from 0-100% depending on the insurance carrier.[601] Out of pocket cost for PDE-5 inhibitors can vary between pharmacies by as much as 38000%.[602]

The National Health Service of England has included coverage for treatment-related ED in their recommended coverage of branded PDE-5 inhibitors for men with prostate cancer. However, restrictions remain with respect to frequency and access (Cambridgeshire & Peterborough Joint Prescribing Group July 2016 updated July 2018). The US Veterans Health Administration, a predominantly male national integrated delivery system for US Veterans, similarly provides PDE5i doses for ED regardless of etiology, as well as ICI and intraurethral suppositories, with some restrictions on frequency and access, all at minimal cost. Penile implants are also available across sites, mitigating some access to care disparities. More broadly however, high cost and lack of coverage disproportionately limits access to medications and devices that can help men retain their ability to engage in penetrative sex.

Other healthcare systems create different barriers for sexual recovery amongst prostate cancer survivors. An example is The United Kingdom's National Health Service which restricts patients to the use of one tablet per week of PDE5i for on-demand dosing. Two published meta-analyses have shown superiority of daily tadalafil compared with on-demand treatment, as evidence by a 2-point improvement in IIEF scores, and significantly improved results in Sexual Encounter Profile, with 72% of patients expressing preference for the daily regime.[603, 604] In our experience, partner preference for freedom from "orchestrated sex" is even greater. Daily PDE5i use not only addresses the underlying pathology, but also removes some of the anxiety and apprehension that can result from on-demand treatment. Of note, on-demand use of PDE5i in the majority of studies equates with use 2-3 times per week, which is much lower than what is covered by the NHS. Most importantly these meta-analyses suggest increased efficacy for daily dosing in prostate cancer post-surgery.[331, 603, 604] These are some of the most challenging patients to treat, and both patients and urologists are demoralized when successfully treated patients are "de-prescribed" by GPs on instruction from NHS England.

SECTION 5:
Guideline Statements With Supporting Evidence

Salvage of non-responders to on-demand therapy

The British Society for Sexual Medicine (BSSM) and European Society for Sexual Medicine (ESSM) guidelines, the teaching syllabus of the European Academy of Sexual Medicine, and several expert reviews outline evidence based strategies for salvaging patients who are referred when on-demand treatment for ED has been ineffective.[605-608] It is well accepted that in a few cases re-counselling or a trial of a different medication might help, but usually this strategy just repeats the cycle of failure. Rigorous studies have shown that daily dosing can salvage 50% of these on-demand failures, and in extreme cases the combination of daily dosing with a short acting PDE5i can salvage even more.[609, 610]

Instead, the current NHS ban results in such patients being diverted to secondary care for costlier and more invasive second and third-line treatments, such as intra-cavernosal injection therapy or penile prosthesis surgery.[606] Furthermore, these second- and third-line treatments do not treat the underlying pathological process or co-morbidities. Meanwhile, clinicians are actually prevented from following guidance to support on-demand treatment failures with adjuvant sex-therapy, as this has been largely decommissioned across the country.[331, 605]

Unintended Consequences of the NHS England ban

When tadalafil became generic in October 2017, the manufacturers lowered production of 5mg tablets, anticipating that the NHS black-listing meant that it would not be prescribed. Yet the high volume of private prescriptions led to a national shortage. In response, companies increased the private prescription cost for a 5mg dose from £6 to £34, leaving patients to travel around the country seeking pharmacies still providing medication at the original price.

This situation has also affected patients who receive NHS prescriptions. As many NHS pharmacies have only been able to source Cialis, their costs have exploded from £6 to £34, or even £55 per dose. Meanwhile, with generic tadalafil 20mg tablets only £2.50 for four, many patients are taking higher doses than required purely to reduce costs.



06 FUTURE DIRECTIONS

SECTION 6:
Future Directions

There is a growing body of evidence to validate the concept that sexual health support is critical to the wellbeing of patients with prostate cancer and their partners. Additional investigation is necessary to broaden our current understanding—particularly regarding cultural factors that include race and ethnicity.



Cultural, Ethnic and Racial Diversity

Most of the extant research has been conducted in Europe and in English-speaking countries where research resources are more available. In these countries, attitudes to prostate cancer and sexuality are relatively similar. While there may be differences in screening and approaches to oncologic therapies, there is a common acceptance of the need to surveil or treat prostate cancer when it is detected. There is a recognition of sexual side-effects of treatment that are bothersome and an agreement that rehabilitation can be valuable.

Cancer stigma is present in some cultures and ethnic groups which leads to delay in cancer therapy. Similarly, social stigma about sexual side-effects is also a persistent factor in various cultures. Men lose stature in their families and communities when they experience sexual dysfunction. Furthermore, negative attitudes, religious prohibitions and laws that threaten specific sexual expressions (same sex relationships, transgender sexual identity) exist in some countries.

As a result, men may avoid cancer therapy in order to preserve sexual function and this can lead to late diagnosis and likely early death. We need to know how varying cultural mores and legal systems play a role in prostate cancer care, how men manage the stigma of cancer and sexual dysfunction, and how societal attitude and structural barriers affect care-seeking. The current lack of empirical research limits the development of culturally appropriate support for men and their partners, yet there are limited research resources in developing countries to pursue work in this domain.

Treatment for Sexual Dysfunctions

The most significant gap in the treatment of physiologic sexual dysfunction is the lack of evidence demonstrating convincingly that penile rehabilitation protocols improve the recovery of erectile function. Animal models have not translated well into human recovery and more research is needed to advance this area of survivorship care. At this time, the value of penile rehabilitation is largely psychological because it engages men and their partners in sexual recovery early, supports the development of proficiency in the use of erectile aids, and fosters the evolution of the couple's sex life to a successful paradigm despite erectile dysfunction.

Substantial evidence has demonstrated that treatment for erectile dysfunction following prostate cancer treatment leads to positive patient centered outcomes. Given the stigma associated with sexual dysfunction, however there is a major gap in care due to uncertainty about the acceptability of erectile dysfunction treatments in cultural and ethnic groups. Locally based research can answer questions about the acceptability of sexual aids. It is possible that education about the effectiveness of pro-erectile aids can reassure men and partners that a sexual life is possible after prostate cancer treatment and, in some cases, even make a positive contribution to acceptance of cancer treatment itself.

The value of psychosocial support for the use of pro-erectile treatments is now evidence based but is not implemented in the majority of prostate cancer treatment settings. Other aspects of psychosocial support, such as attentiveness to partners' needs and interventions for couples, are just emerging. Interventions tailored to sexual orientation and gender identity remain

undeveloped. More research into the needs and preferences of these populations is needed so that relevant interventions can be developed and tested.

Clinician Education

One of the ongoing barriers to appropriate sexual health support in prostate cancer is the lack of clinician expertise and competence. Education to address patients' and partners' sexual health concerns and rehabilitation must become an integrated part of multidisciplinary professional training for clinicians of all professions who care for prostate cancer patients. Competency based program development and pilot testing is needed to ensure relevance, quality, and patient outcomes.

Integration of Sexual Health Care in Prostate Cancer Survivorship

Cost is usually cited as the primary barrier to embedding a specialist in psychosexual care in an oncological treatment program. The lack of a specialist sends a message to patients and partners that sexual health and quality of life are not essential components of prostate cancer care or recovery. In contrast, embedded psychosexual care not only reduces the stigma of sexual dysfunction and help-seeking, it can also facilitate more efficient engagement with sexual rehabilitation strategies. Culturally appropriate methods for providing integrated sexual health care should be investigated.

RECOMMENDATIONS:

1. Funding sources should be identified to promote research on cultural, ethnic, and racial groups' attitudes towards sexuality, sexual practices, and preferences for support. Similarly, funding sources should be identified to promote research on sexual and gender minorities, such as men who have sex with men, trans women, and gender non-conforming patients.
2. Information resources about the sexual consequences of prostate cancer therapies and available treatments for sexual dysfunction should be developed, based on the understanding of what is acceptable and effective for different cultural, ethnic, and racial groups, as well as sexual and gender minorities. Various models of patient education communication should be tested.
3. Studies, including cohort quality of life studies, instrument evaluations, and intervention trials, should actively recruit diverse participants, including people of diverse cultural, ethnic, and racial identities, and sexual and gender minorities.
4. Continued research is needed to discover mechanisms underlying the physiologic potential for the recovery of erectile function following the various modalities of prostate cancer therapy.
5. Psychosocial treatments, tailored to cultural, ethnic, racial, sexual, and gender minority preferences, should continue to be developed and tested.
6. Clinical assessment tools for sexual health, tailored to patient sexual orientation and gender identity, should be developed and tested, as well as management pathways tailored to patient sexual orientation and gender identity.
7. Clinician education about prostate cancer should include information about the sexual side-effects of prostate cancer therapies, strategies for providing patients and partners with support, as well as information about access to treatment for sexual dysfunction.
8. International sexual medicine societies and multidisciplinary professional societies that have influence in professional education should develop advocacy for sexual health support in oncologic care.
9. Appropriate sources of funding should be identified so that healthcare systems can provide physical resources and expert clinicians to make biopsychosocial sexual health interventions accessible to patients and partners in prostate cancer survivorship.

APPENDIX A:
Search Words

Ovid MEDLINE Search Documentation

Database: Ovid MEDLINE		
Research Question	Search #	Strategy
Base Search Strategy	1	(((prostate or prostatic) adj3 (cancer or cancers or cancerous or neoplasm or neoplasms or tumor or tumors or tumorous)).ti,ab. or (prostatectomy or prostatectomies or Provenge or Sipuleucel or "androgen deprivation" or ADT or antiandrogen or apalutamide).ti,ab. or exp Prostatic Neoplasms/ or exp Prostatectomy/ or (exp Neoplasms/ and exp Prostate/)) and (((sexual or sex) adj3 (health or functional or function or functioning or dysfunction or dysfunctions or dysfunctional or physiological or physiologic or physiology or activity or activities or attitude or attitudes or behavior or behaviors or behaviour or behaviours or instinct or instincts)).ti,ab. or (sexuality or intimacy or intimate or intercourse or coitus or libido).ti,ab. or exp Sexual Behavior/or Sexuality/ or exp Sexual Health/ or exp Sexual Dysfunctions, Psychological/ or Libido/)
I. Impact of Diagnosis and Treatment	2	((functional or function or functioning or dysfunction or dysfunctions or dysfunctional or physiological or physiologic or physiology or activity or activities or physical or psychosocial or distress or distressing or distressed or bother or bothering or bothered or depression or depressive or depressing or depressed or anxiety or anxious or “quality of life” or QOL or “life quality” or HRQOL) adj10 (consequence or consequences or impact or impacts or impacted or impacting or effect or effects or effecting or effected or influence or influenced or influencing or influences)).ti,ab. and (Clinical Protocols/ or Practice Patterns, Physicians’/ or Algorithms/ or “Outcome and Process Assessment (Health Care)”/ or exp Consensus Development Conference/ or Guideline/ or Practice Guideline/ or Randomized Controlled Trial/ or Controlled Clinical Trial/ or Multicenter Study/ or Meta-analysis/ or Clinical Trial, Phase IV/ or Clinical Trial/ or exp Cohort Studies/) or *”Quality of Life”/ or *Depression/ or *”Depressive Disorder”/ or exp *Anxiety/ or exp Religion/ or Resilience, Psychological/ or (resilience or resiliency or (life adj2 meaning) or ((life or feeling or belief or beliefs) adj2 purpose) or religious or religion or religions or spiritual or spirituality or spiritualism or theology or church or churches or synagogue or synagogues or mosque or mosques or Christianity or Christian or Christians or Islam or Muslim or Muslims or Hindu or Hinduism or Buddhism or Buddhist or Jew or Jews or Jewish or Sikh or Sikhism or Catholic or Catholics or Catholicism).ti,ab. or exp Fertility/ or Fertility Preservation/ or (fertility or fecundity or fecundability or infertile or infertility or (family adj2 (planning or plan or plans))).ti,ab. or ((Social Support/ or Psychosocial Support Systems/) and (lack or need or limited or gap or needs or gaps or unmet).ti,ab.) or ((lack or need or limited or gap or needs or gaps or unmet) adj3 (support or supportive)).ti,ab.
	3	1 and 2
II. Assessment	4	Medical History Taking/ or Health Communication/ or ("biopsychosocial sexual assessment" or ((interview or interviewing or interviews or history or histories) adj2 (medical or family or taking or care))).ti,ab. or Pelvimetry/ or Physical Examination/ or Gynecological Examination/ or (((physical or gynecological) adj2 (assessment or assessments or assess or assesses or assessing or assessed or exam or exams or examination or examinations or examining or examined or examines)) or "pelvic floor" or "occupational therapy" or "physical therapy" or ((sexual or sex) adj2 (positioning or position or positions or positioned or pose))).ti,ab.
	5	1 and 4

APPENDIX A:
Search Words

Ovid MEDLINE Search Documentation

Database: Ovid MEDLINE		
Research Question	Search #	Strategy
III. Validated Measures	6	("Patient-Reported Outcomes Measurement Information System" or PROMIS).ti,ab. or ("Expanded Prostate Index Composite" or "Expanded Prostate Cancer Index Composite" or "Female Sexual Function Index" or "International Index of Erectile Function" or "International Index of Erectile Dysfunction" or ((((sexual or erectile or prostate) adj2 (function or functioning)) or "sexual orientation" or homosexual or homosexuals or heterosexual or heterosexuals or bisexual or bisexuals or bisexuality or transgender or transgendered or transsexual or transsexuals or transsexuality or gay or gays or lesbian or lesbians or queer or culture or cultural or culturally or norms) and (measures or measure or scale or scales or subscale or subscales or index)) or ("quality of life" adj4 (measures or measure or scale or scales or subscale or subscales or index)) or "Short Form Health Survey-12" or SF-12 or "Functional Assessment of Cancer Therapy-General" or FACT-G).ti,ab and (exp validation studies/ or (validation or validate or validating or validated).ti,ab.) or ("Distress Thermometer" or (distress adj2 (measures or measure or scale or scales or subscale or subscales or index))).ti,ab. or ("Patient Health Questionnaire" or PHQ-9 or "Hospital Anxiety and Depression Scale" or (("mental health" or anxiety or depression) adj2 (measures or measure or scale or scales or subscale or subscales or index))).ti,ab. or (((Masculinity or identity or masculine) and (measures or measure or scale or scales or subscale or subscales or index)) or "Masculinity in Chronic Disease Inventory").ti,ab. or ("Self-Esteem and Relationship Questionnaire" or "Dyadic Coping Inventory" or "6-item Sexual Communication Questionnaire" or ((self-esteem or relationship or relationships or "dyadic coping" or communication) adj4 (measures or measure or scale or scales or subscale or subscales or index))).ti,ab.
	7	1 and 6
IV. Interventions - Physiological	8	((exp Phosphodiesterase 5 Inhibitors/ or ((penile adj rehabilitation) or "phosphodiesterase type 5 inhibitors" or PDE5i or "phosphodiesterase 5 inhibitors" or "intracavernosal injections" or "intracavernosal injection" or ICI or "vacuum erection device" or "vacuum erection devices" or VED or "pelvic floor" or "testosterone replacement" or TRT or "combination treatment" or ((comorbidity or comorbid) adj (manage or manages or managing or managed or management))).ti,ab.) or ((suppositories or suppository or prostheses or prosthesis or prosthetic or ((lifestyle or life-style or diet or diets or nutrition or exercise or exercises or "physical activity") adj (modification or modifications or modify or modifying or modified or change or changes or changed or changing or choice or choices)) or non-medical or non-pharmacological or non-pharmacologic or non-pharmaceutical or nonmedical or nonpharmacological or nonpharmacologic or nonpharmaceutical or "complementary medicine" or "alternative medicine" or ((penile or penis) adj (shortening or shorten)) or orgasm or ejaculate or "Peyronie's Disease" or curvature or continence or incontinence).ti,ab.) or ("topical vaginal estrogen" or Estrance or Premarin or Vagifem or "vaginal moisturizers" or "vaginal moisturizer" or "vaginal lubricant" or "vaginal lubricants" or vibrator or vibrators or "clitoral pumps" or "clitoral pump" or dilator or dilators or ((partner or female or females or woman or women) adj3 "pelvic floor") or Flibanserin or "bladder prolapse" or "uterine prolapse").ti,ab.)and (Therapy.fs. or exp Therapeutics/ or (treatment or treatments or therapy or therapies or therapeutics or therapeutic).ti,ab.) and (Clinical Protocols/ or Practice Patterns, Physicians'/ or Algorithms/ or "Outcome and Process Assessment (Health Care)"/ or exp Consensus Development Conference/ or Guideline/ or Practice Guideline/ or Randomized Controlled Trial/ or Controlled Clinical Trial/ or Multicenter Study/ or Meta-analysis/ or Clinical Trial, Phase IV/ or Clinical Trial/ or exp Cohort Studies/)
	9	1 and 8

APPENDIX A:
Search Words

Ovid MEDLINE Search Documentation

Database: Ovid MEDLINE		
Research Question	Search #	Strategy
V. Interventions - Psychosocial	10	(psychosocial or relationship or relationships or intimacy or social).ti,ab. and ((education or educate or educating).ti,ab. or Patient Education as Topic/) or (psychosocial or relationship or relationships or intimacy or social).ti,ab. and ((peer adj3 (counseling or counselling or counselor or counselors)) or "peer support").ti,ab. or (psychosocial or relationship or relationships or intimacy or social).ti,ab. and ((group or couple or couples) adj3 (therapy or therapies or intervention or interventions)).ti,ab. or ((psychosocial or relationship or relationships or intimacy or social) adj3 (therapy or therapies or intervention or interventions)).ti,ab. not ((psychosocial or relationship or relationships or intimacy or social).ti,ab. and ((group or couple or couples) adj3 (therapy or therapies or intervention or interventions)).ti,ab.) or ((psychosocial or relationship or relationships or intimacy or social) and (web-based or internet-based)).ti,ab. or ((psychosocial or relationship or relationships or intimacy or social) and ((normalization adj2 grief) or "positive coping" or ((conceptualization or conceptual or conceptualize or reconceptualization or reconceptualize or belief or beliefs or thought or thoughts or attitudes) adj5 (sexuality or intimacy or erectile or erection or orgasm)) or anxiety or depression or "online support" or self-efficacy or self-management or self-care or "dyadic communication")).ti,ab.
	11	1 and 10
VI. Evidence gaps	12	("active surveillance" or "watchful waiting").ti. or (homosexual or homosexuality or homosexuals or bisexual or bisexuals or bisexuality or gay or gays or transgender or transgendered or transsexual or transsexuals or transsexuality or "single men" or (single adj4 (relationship or status)) or "marital status" or widower or widowered or unmarried or divorce or divorced).ti,ab. or exp Single Person/ or (("androgen deprivation" or ADT or antiandrogen or apalutamide) and ((sexually or sexual) adj2 (active or activity) or sexuality)).ti,ab. or exp Costs and Cost Analysis/ or (cost or costs or economic or economics or financial or financing or financed or finance or price or pricing).ti,ab.
	13	1 and 12

APPENDIX A:
Search Words

Ovid MEDLINE Search Documentation

Database: Ovid MEDLINE		
Research Question	Search #	Strategy
VII. Approaches	14	(multidisciplinary or transdisciplinary or interdisciplinary or interprofessional or ((team or teams) adj10 (composition or member or members or urologist or urologists or urological or "sexual medicine" or "sexual health" or psychologist or psychologists or psychiatrist or psychiatrists or "physical therapist" or "physical therapists" or nurse or nurses or survivorship or gynecologist or gynecologists))).ti,ab. or (PLISSIT or "Permission, Limited Information, Specific Suggestions, Intensive Therapy" or "Permission Limited Information Specific Suggestions Intensive Therapy").ti,ab. or ((national or federal or government) and (program or programs or resources or resource or strategy or strategies)).ti,ab.
	15	1 and 14
VIII. Challenges	16	((culture or cultural or culturally or norms or norm or value or values or ethnicity or ethnic or ethnicities) and (masculinity or masculine or relationship or relationships or sexuality or (partner adj (role or roles)))).ti,ab. or (access or accessibility).ti,ab. or ((provider or providers or professional or professionals or clinician or clinicians or physician or physicians or resident or residents or nurse or nurses or urologist or urologists or therapist or therapists or gynecologist or gynecologists or psychologist or psychologists or psychiatrist or psychiatrists) adj5 (training or train or trained or education or educate or educating or educated)).ti,ab. or (disparity or disparities or socioeconomic or ethnicity or "economic resources").ti,ab. or Healthcare Disparities/ or Health Status Disparities/) or ((guideline or guidelines or guidance or algorithm or algorithms or consensus or information or evidence) adj5 (dose or dosing or delivery or follow-up or long-term or lack or need or limited or gap)).ti,ab.
	17	1 and 16

The Ovid MEDLINE search strategy was translated to the search syntax and controlled vocabulary available in 5 additional databases:

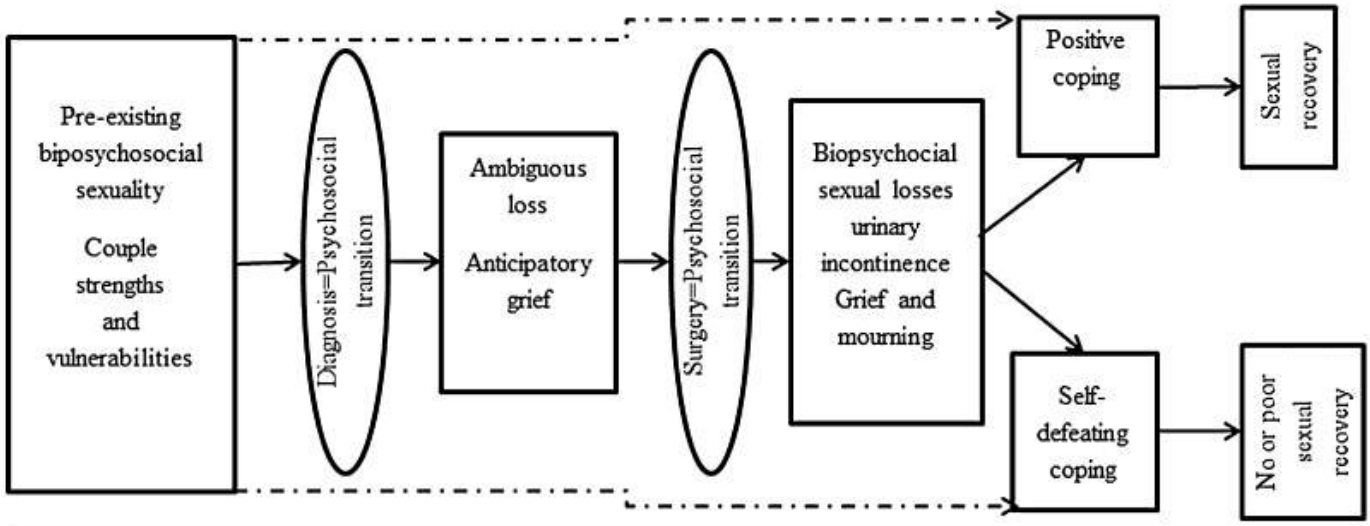
Scopus	**CINAHL**	**PsycINFO**	**LGBT Life**	**Embase**

APPENDIX B:
Models

Conceptual Model of Sexual Recovery after Prostate Cancer Treatment
From Wittmann et al., What Couples Say About their Sexual Recovery after Prostate Cancer Treatment, J Sex Med, 2015

Conceptual Model of the Sexual Challenges for Gay and Bisexual Men with Prostate Cancer

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Pre-existing developmental sexual losses: erectile dysfunction, post-menopausal symptoms
Pre-existing strengths: long term relationships, success coping with challenges
Pre-existing vulnerabilities: relationship problems, stressors, dislike of unspontaneous sex
Post diagnosis coping: anticipatory grief, faith in surgeon skill and couple strengths, willingness to work hard on recovery, minimization of nerve damage, belief that using sexual aids will be unnecessary
Biopsychosocial sexual losses: functional, confidence, familiar relationship
Post-surgery positive coping: normal grief and mourning, ongoing sexual activity, acceptance of sexual losses, use of sexual aids, partner's positive interest in sex regardless of menopause
Post-surgery self-defeating coping: inability to grieve sexual losses, no or infrequent sexual activity, relationship problems, stressors, inflexible sexuality, partner's low or no interest sex regardless of menopause

Figure 1 Revised model of couples' sexual recovery after prostate cancer treatment.

APPENDIX B:
Models

From Simon Rosser, B. R., et al. (Sexual and Relationship Therapy, 2016) The effects of radical prostatectomy on gay and bisexual men's sexual functioning and behavior: qualitative results from the restore study

Conceptual Model for Cancer Screening for Trans Women

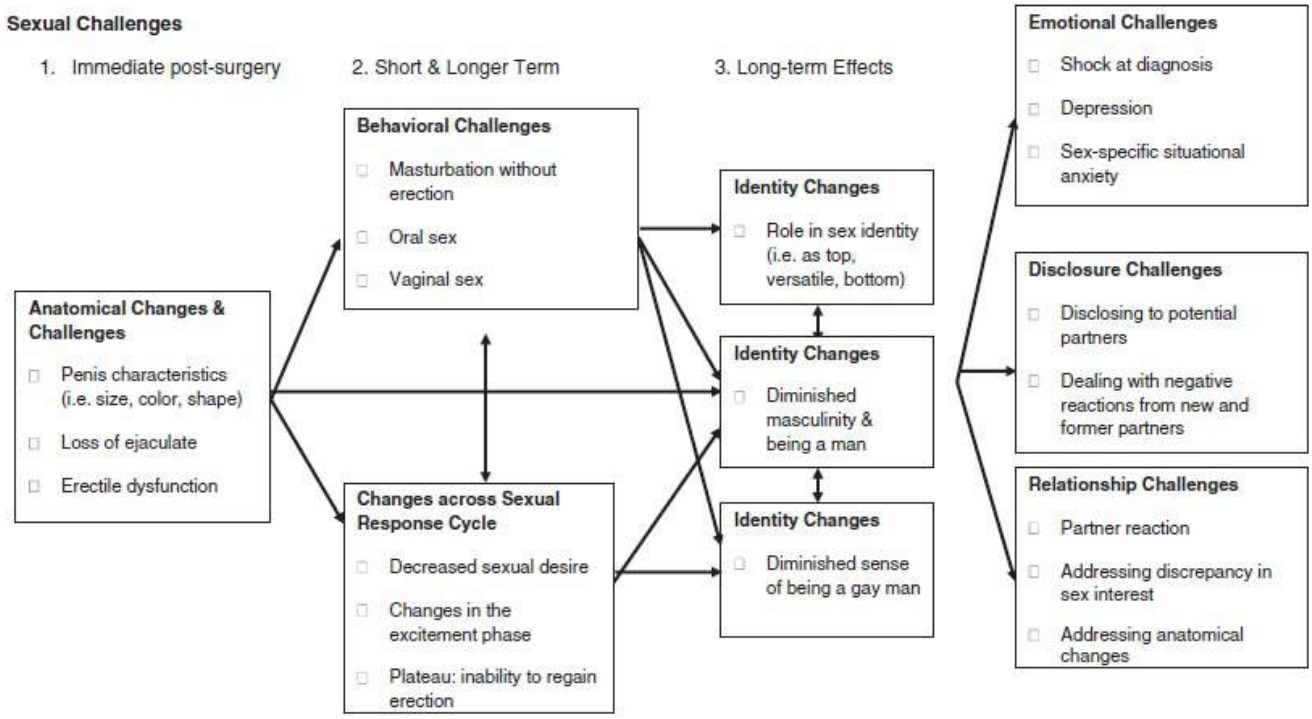


Figure 1. Visual schematic of the psychosexual effects of radical prostatectomy on gay and bisexual men ($N = 19$ in-depth qualitative interviews).

APPENDIX B:
Models

In Sterling & Garcia, Cancer screening in the transgender population: a review of current guidelines, best practices, and a proposed care model. Translational Andrology and Urology, 2020

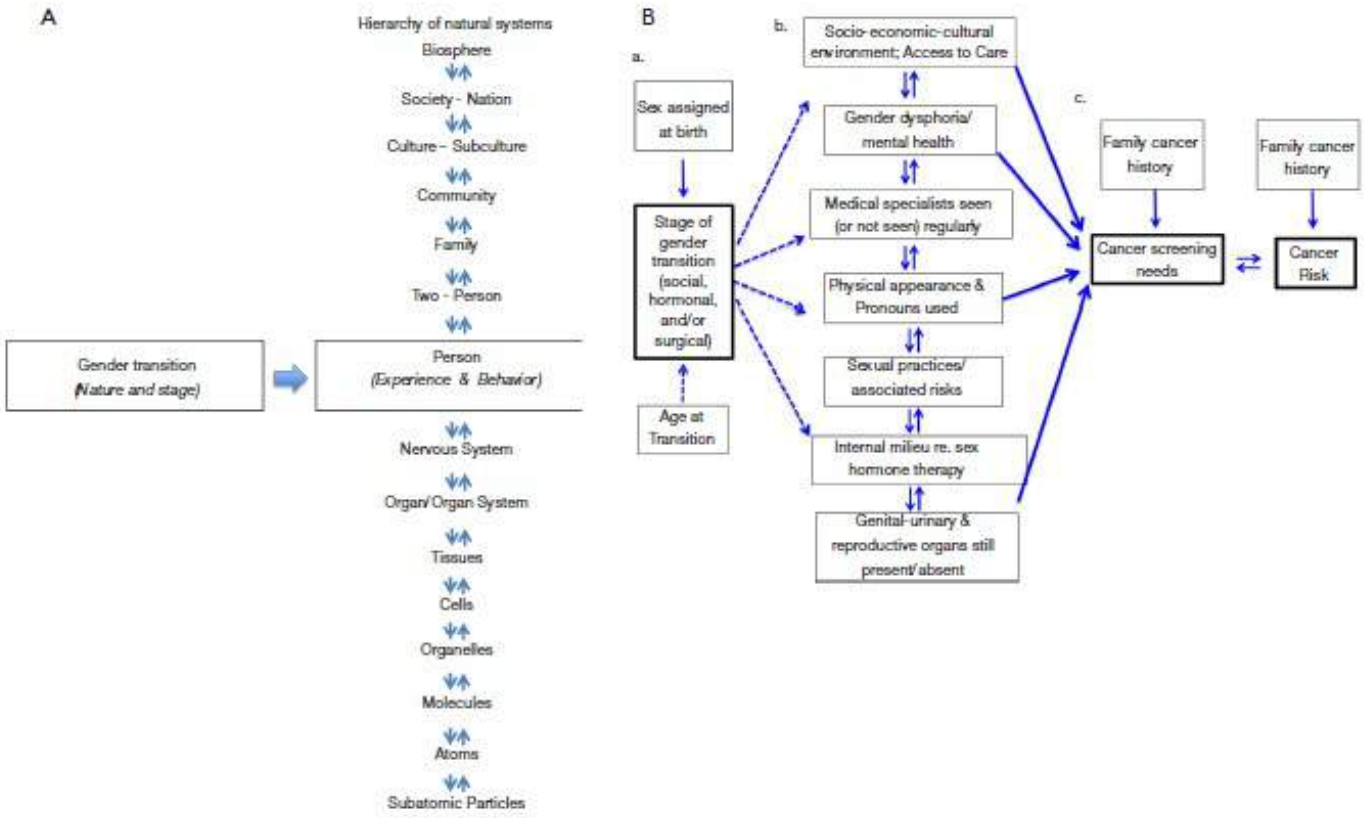
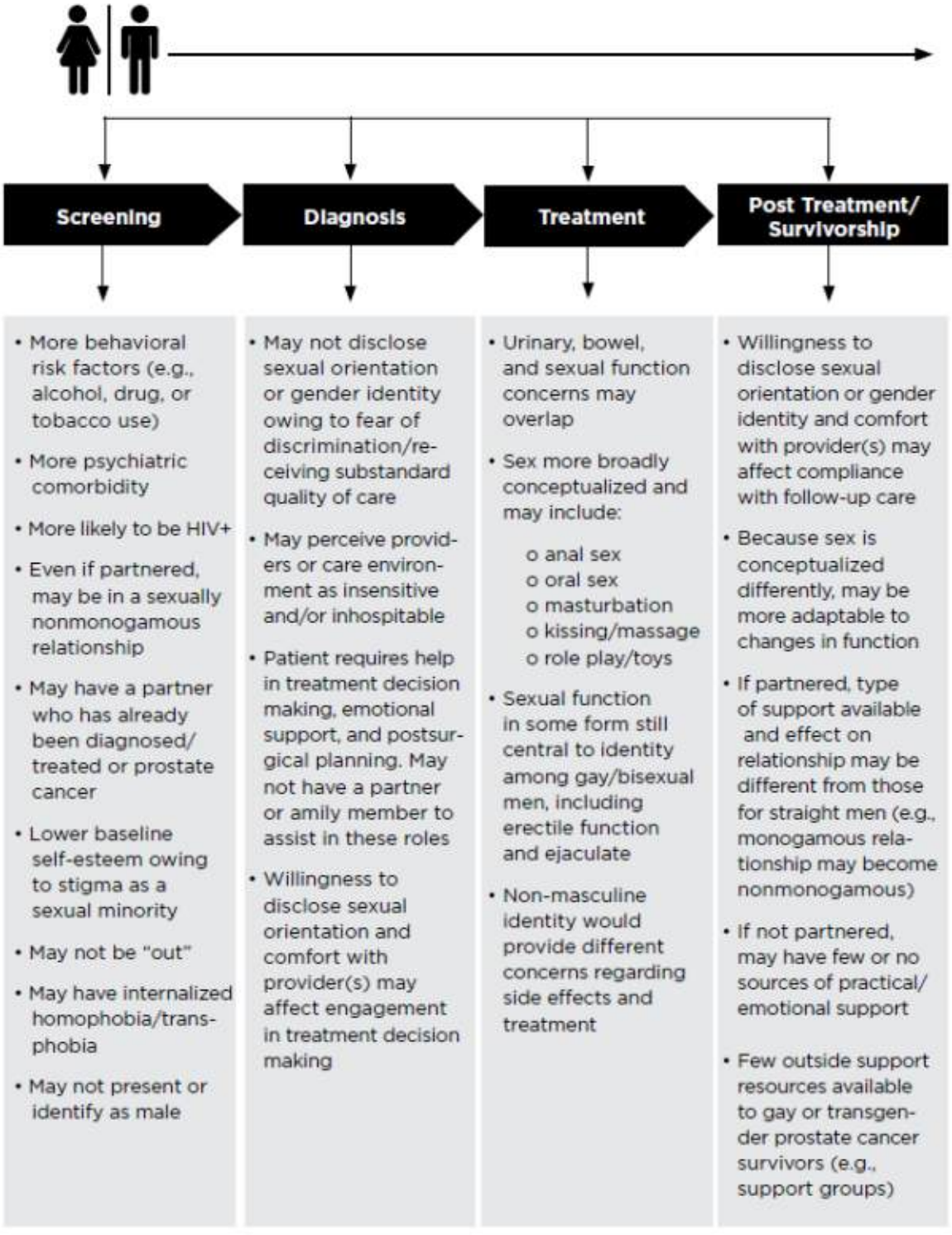


Figure 2 Gender transition and the biopsychosocial model. (A) Model for healthcare of the transgender and gender non-conforming individual that accounts for the complex interplay between the individual's gender transition, biological and social systems; (B) cancer risk at any given time is influenced by the multiple levels of organization that Engel describes in the biopsychosocial model.

APPENDIX B:
Models

Allensworth-Davies D, Blank TO, de Vries B and Lombardi E. Toward a more comprehensive model of prostate cancer care inclusive of gay and bisexual men and transgender women. In Ussher J, Perz J and Rosser BRS: Gay and Bisexual Men Living with Prostate Cancer, Harrington Park Press, New York, NY, 2018

FIGURE 14.1 Conceptual model of prostate cancer care for gay/bisexual men and transgender women



APPENDIX C:
Measures

International Index of Erectile Function (IIEF)

INTERNATIONAL INDEX OF ERECTILE FUNCTION (IIEF)

HOSPITAL NUMBER (IF KNOWN) ☐☐☐☐☐☐☐

NAME .....

DATE OF BIRTH ☐☐/☐☐/☐☐ AGE ☐☐

ADDRESS .....
.....
.....

Patient Questionnaire

TELEPHONE .....

These questions ask about the effects that your erection problems have had on your sex life over the last four weeks. Please try to answer the questions as honestly and as clearly as you are able. Your answers will help your doctor to choose the most effective treatment suited to your condition. In answering the questions, the following definitions apply:

- **sexual activity** includes intercourse, caressing, foreplay & masturbation
- **sexual intercourse** is defined as sexual penetration of your partner
- **sexual stimulation** includes situation such as foreplay, erotic pictures etc.
- **ejaculation** is the ejection of semen from the penis (or the feeling of this)
- **orgasm** is the fulfilment or climax following sexual stimulation or intercourse

APPENDIX C:
Measures

International Index of Erectile Function (IIEF)

	Over the past 4 weeks:	*Please check **one** box only*
☐ Q1	**How often were you able to get an erection during sexual activity?**	0 No sexual activity 1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always
☐ Q2	**When you had erections with sexual stimulation, how often were your erections hard enough for penetration?**	0 No sexual activity 1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always
☐ Q3	**When you attempted intercourse, how often were you able to penetrate (enter) your partner?**	0 Did not attempt intercourse 1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always
☐ Q4	**During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?**	0 Did not attempt intercourse 1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always
☐ Q5	**During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?**	0 Did not attempt intercourse 1 Extremely difficult 2 Very difficult 3 Difficult 4 Slightly difficult 5 Not difficult
☐ Q6	**How many times have you attempted sexual intercourse?**	0 No attempts 1 One to two attempts 2 Three to four attempts 3 Five to six attempts 4 Seven to ten attempts 5 Eleven or more attempts
☐ Q7	**When you attempted sexual intercourse, how often was it satisfactory for you?**	0 Did not attempt intercourse 1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always

APPENDIX C:
Measures

International Index of Erectile Function (IIEF)

☐ Q8	How much have you enjoyed sexual intercourse?	0 No intercourse 1 No enjoyment at all 2 Not very enjoyable 3 Fairly enjoyable 4 Highly enjoyable 5 Very highly enjoyable
☐ Q9	When you had sexual stimulation or intercourse, how often did you ejaculate?	0 No sexual stimulation or intercourse 1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always
☐ Q10	When you had sexual stimulation or intercourse, how often did you have the feeling of orgasm or climax?	1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always
☐ Q11	How often have you felt sexual desire?	1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always
☐ Q12	How would you rate your level of sexual desire?	1 Very low or none at all 2 Low 3 Moderate 4 High 5 Very high
☐ Q13	How satisfied have you been with your overall sex life?	1 Very dissatisfied 2 Moderately dissatisfied 3 Equally satisfied & dissatisfied 4 Moderately satisfied 5 Very satisfied
☐ Q14	How satisfied have you been with your sexual relationship with your partner?	1 Very dissatisfied 2 Moderately dissatisfied 3 Equally satisfied & dissatisfied 4 Moderately satisfied 5 Very satisfied
☐ Q15	How do you rate your confidence that you could get and keep an erection?	1 Very low 2 Low 3 Moderate 4 High 5 Very high

APPENDIX C:
Measures

Sexual Health Inventory for Men (SHIM)

Site Number: ☐☐☐☐ **Patient Number: ☐☐☐☐**

Sexual Health Inventory for Men (SHIM) or IIEF-5 (International Index of Erectile Dysfunction-5 questions)

The IIEF-5 score is the sum of the ordinal responses to the five items; thus, the score can range from 5 to 25.

Over the past 6 months:

1. How do you rate your confidence that you could get and keep an erection?	Very Low	Low	Moderate	High	Very High
	1	2	3	4	5
2. When you had erections with sexual stimulation, how often were your erections hard enough for penetration?	Almost never/never	A few times (much less then half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always/always
	1	2	3	4	5
3. During sexual intercourse, how often were you able to maintain your erection after you penetrated (entered) your partner?	Almost never/never	A few times (much less then half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always/always
	1	2	3	4	5
4. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?	Extremely difficult	Very Difficult	Difficult	Slightly difficult	Not Difficult
	1	2	3	4	5
5. When you attempted sexual intercourse, how often was it satisfactory for you?	Almost never/never	A few times (much less then half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always/always
	1	2	3	4	5

APPENDIX C:
Measures

Patient-Reported Outcomes Measure Information System (PROMIS)

Interest in Sexual Activity		
Directions: In the next set of questions, we are interesting in learning more about how interested you have been in sexual activity in the past 30 days		
1. **SFINT101**	How interested have you been in sexual activity?	1=Not at all 2=A little bit 3=Somewhat 4=Quite a bit 5=Very
2. **SFINT102**	How often have you felt like you wanted to have sex?	1=Never 2=Rarely 3=Sometimes 4=Often 5=Always
3. **SFINT103**	How often have you had sexual thoughts or fantasies while you were awake?	1=Never 2=Rarely 3=Sometimes 4=Often 5=Always
4. **SFINT104**	How often were you interested enough to start a sexual activity?	1=Never 2=Rarely 3=Sometimes 4=Often 5=Always

APPENDIX C:
Measures

Patient-Reported Outcomes Measure Information System (PROMIS)

Global Satisfaction with Sex Life		
Directions: In the next set of question, we are interested in learning more about how satisfied you have been with your sex life in the past 30 days.		
1. **SFSAT101**	How satisfied have you been with your sex life?	1=Not at all 2=A little bit 3=Somewhat 4=Quite a bit 5=Very
2. **SFSAT102**	How much pleasure has your sex life given you?	1=None 2=A little bit 3=Somewhat 4=Quite a bit 5=A lot
3. **SFSAT103**	How often have you thought that your sex life is wonderful?	1=Never 2=Rarely 3=Sometimes 4=Often 5=Always
4. **SFSAT104**	How satisfied have you been with your sexual relationship with a partner?	0=Have not had a partner in the past 30 days 1=Not at all 2=A little bit 3=Somewhat 4=Quite a bit 5=Very
5. **SFSAT105**	When you have had sexual activity, how much have you enjoyed it?	0=Have not had sexual activity in the past 30 days 1=Not at all 2=A little bit 3=Somewhat 4=Quite a bit 5=Very much
6. **SFSAT106**	When you have had sexual activity, how satisfying has it been?	0=Have not had sexual activity in the past 30 days 1=Not at all 2=A little bit 3=Somewhat 4=Quite a bit 5=Very
During the past 7 days:		
7. **SFSAT001**	In the past week, I have been satisfied with my sex life.	1=Not at all 2=A little bit 3=Somewhat 4=Quite a bit 5=Very much

APPENDIX C:
Measures

Patient-Reported Outcomes Measure Information System (PROMIS)

Therapeutic Aids		
Some couples use therapeutic aids, such as lubricants, medication, injections, during sexual activity. In the past 30 days, please tell us if you have used any of the therapeutic aids mentioned below, and if so, how often.		
1. **SFAID101**	How often have you used personal lubricants (such as KY Jelly or Astroglide) for sexual activity?	0=Have not had any sexual activity in the past 30 days 1=Never 2=Rarely 3=Sometimes 4=Often 5=Always
2. **SFAID102**	How often have you used vaginal moisturizers (such as Replens)?	0=Have not had any sexual activity in the past 30 days 1=Never 2=Rarely 3=Sometimes 4=Often 5=Always
3. **SFAID103**	Have you used hormones (for example, estrogen, testosterone, or progesterone) for sexual activity either as a patch on your skin, or a cream, tablet, or ring inserted into your vagina?	1=No 2=Yes 0=I don't know
4. **SFAID104**	Have you used a vaginal dilator?	1=No 2=Yes 0=I am not sure what vaginal dilator is
5. **SFAID105**	How often have you taken a pill such as Viagra, Cialis, or Levitra for sexual activity?	1=Never 2=Rarely 3=Sometimes 4=Often 5=Always
6. **SFAID106**	Have you taken testosterone for sexual activity?	1=No 2=Yes 0=I don't know
7. **SFAID107**	How often have you used an injection into your penis to get an erection?	1=Never 2=Rarely 3=Sometimes 4=Often 5=Always

APPENDIX C:
Measures

Erectile Dysfunction Inventory for Treatment and Satisfaction (EDITS)

The questions in this inventory ask about a sensitive topic, your sexual life with your wife or partner as well as your attitude toward and expectations from the treatment method you are using to help with your erection problem. Please answer the questions as honestly and candidly as you can. If any questions or terms are unclear, please ask for clarification.

1.	Overall, how satisfied are you with this treatment?	a. Very satisfied b. Somewhat satisfied c. Neither satisfied nor dissatisfied d. Somewhat dissatisfied e. Very dissatisfied
2.	During the past four weeks, to what degree has the treatment met your expectations?	a. Completely b. Considerably c. Half way d. A little e. Not at all
3.	How likely are you to continue using this treatment?	a. Very likely b. Moderately likely c. Neither likely nor unlikely d. Moderately unlikely e. Very unlikely
4.	During the past four weeks, how easy was it for you to use this treatment?	a. Very easy b. Moderately easy c. Neither easy nor difficult d. Moderately difficult e. Very difficult
5.	During the past four weeks, how satisfied have you been with how quickly the treatment works?	a. Very satisfied b. Somewhat satisfied c. Neither satisfied nor dissatisfied d. Somewhat dissatisfied e. Very dissatisfied
6.	During the past four weeks, how satisfied have you been with how long the treatment lasts?	a. Very satisfied b. Somewhat satisfied c. Neither satisfied nor dissatisfied d. Somewhat dissatisfied e. Very dissatisfied
7.	How confident has this treatment made you feel about your ability to engage in sexual activity?	a. Very confident b. Somewhat confident c. It has had no impact d. Somewhat less confident e. Very much less confident

APPENDIX C:
Measures

Erectile Dysfunction Inventory for Treatment and Satisfaction (EDITS)

8.	Overall, how satisfied do you believe your partner is with the effects of this treatment?	a. Very satisfied b. Somewhat satisfied c. Neither satisfied nor dissatisfied d. Somewhat dissatisfied e. Very dissatisfied
9.	How does your partner feel about your continuing to use this treatment?	a. My partner absolutely wants me to continue b. My partner generally prefers me to continue c. My partner has no opinion d. My partner generally prefers me to stop e. My partner absolutely wants me to stop
10.	How natural did the process of achieving an erection feel when you used this treatment over the past four weeks?	a. Very natural b. Somewhat natural c. Neither natural nor unnatural d. Somewhat unnatural e. Very unnatural
11.	Compared to before you had an erection problem how would you rate the naturalness of your erection when you used this treatment over the past four weeks in terms of hardness?	a. A lot harder than before I had an erection problem b. Somewhat harder than before I had an erection problem c. The same hardness as before I had an erection problem d. Somewhat less hard than before I had an erection problem e. A lot less hard than before I had an erection problem
Thank you for having completed the questionnaire.		

APPENDIX C:
Measures

APPENDIX II. The EDITS: Erectile Dysfunction Inventory Of Treatment Satisfaction, Partner Version

What treatment method is your husband or partner currently using for his erection problem?

The questions in this inventory ask about a sensitive topic, your sexual life with your husband or partner as well as your attitudes and experiences regarding treatment for his erection problem. Please answer the questions as honestly and candidly as you can. If any questions or terms are unclear, please ask for clarification.

1.	Overall, how satisfied are you with this treatment for your husband's or partner's erection problem?	a. Very satisfied b. Somewhat satisfied c. Neutral; neither satisfied nor dissatisfied d. Somewhat dissatisfied e. Very dissatisfied
2.	During the past four weeks, to what degree has the treatment met your expectations?	a. Completely b. Considerably c. Half way d. Somewhat e. Not at all
3.	Over the past four weeks, how has this treatment affected your sense of being sexually desirable?	a. It has made me feel much more sexually desirable b. It has made me feel somewhat more sexually desirable c. It has had no impact on my sense of being sexually desirable d. It has made me feel somewhat less sexually desirable e. It has made me feel less sexually desirable
4.	Over the past four weeks, how satisfied have you been with how long this treatment enhances your husband's or partner's ability to achieve an erection?	a. Very satisfied b. Somewhat satisfied c. Neutral, neither satisfied nor dissatisfied d. Somewhat dissatisfied e. Very dissatisfied
5.	How do you think your husband or partner feels about continuing this treatment?	a. I think that he very much wants to continue using this treatment b. I think that he somewhat wants to continue using this treatment c. I think my partner feels neutral about continuing to use this treatment d. I think that he somewhat wants to discontinue using this treatment e. I think that he very much wants to discontinue using this treatment

APPENDIX C:
Measures

Self-Esteem and Relationship (SEAR) Questionnaire

During the past 4 weeks...	
1.	I felt relaxed about initiating sex with my partner.
2.	I felt confident that during sex my erection would last long enough.
3.	I was satisfied with my sexual performance.
4.	I felt that sex could be spontaneous.
5.	I was likely to initiate sex.
6.	I felt confident about performing sexually.
7.	I was satisfied with our sex life.
8.	My partner was unhappy with the quality of our sexual relations.
9.	I had good self-esteem.
10.	I felt like a whole man.
11.	I was inclined to feel that I am a failure.
12.	I felt confident.
13.	My partner was satisfied with our relationship in general.
14.	I was satisfied with our relationship in general.
Response options	Almost always/always. Most times (much more than half the time). Sometimes (about half the time). A few times (much less than half the time). Almost never/never.

International Journal of Impotence Research (2004) 16, 30–38. doi:10.1038/sj.ijir.3901095

APPENDIX C:
Measures

Expanded Prostate Cancer Index Composite (EPIC)

EPIC-26 The Expanded Prostate Cancer Index Composite Short Form
This questionnaire is designed to measure Quality of Life issues in patients with Prostate cancer. To help us get the most accurate measurement, it is important that you answer all questions honestly and completely. Remember, as with all medical records, information contained within this survey will remain strictly confidential.

1. Over the **past 4 weeks**, how often have you leaked urine?

   More than once a day..... 1
   About once a day..... 2
   More than once a week..... 3 (Circle one number)
   About once a week..... 4
   Rarely or never..... 5

2. Which of the following best describes your urinary control **during the last 4 weeks**?

   No urinary control whatsoever 1
   Frequent dribbling..... 2 (Circle one number)
   Occasional dribbling..... 3
   Total control 4

3. How many pads or adult diapers per day did you usually use to control leakage **during the last 4 weeks**?

   None 0
   1 pad per day..... 1
   2 pads per day..... 2 (Circle one number)
   3 or more pads per day..... 3

4. How big a problem, if any, has each of the following been for you **during the last 4 weeks**?

   (Circle one number on each line)

	No Problem	Very Small Problem	Small Problem	Moderate Problem	Big Problem
a. Dripping or leaking urine	0	1	2	3	4
b. Pain or burning on urination.....	0	1	2	3	4
c. Bleeding with urination.....	0	1	2	3	4
d. Weak urine stream or incomplete emptying.....	0	1	2	3	4
e. Need to urinate frequently during the day	0	1	2	3	4

APPENDIX C:
Measures

Expanded Prostate Cancer Index Composite (EPIC)

5. Overall, how big a problem has your urinary function been for you **during the last 4 weeks**?

No problem	1	
Very small problem	2	
Small problem	3	(Circle one number)
Moderate problem	4	
Big problem	5	

6. How big a problem, if any, has each of the following been for you? (Circle one number on each line)

	No Problem	Very Small Problem	Small Problem	Moderate Problem	Big Problem
a. Urgency to have a bowel movement	0	1	2	3	4
b. Increased frequency of bowel movements	0	1	2	3	4
c. Losing control of your stools	0	1	2	3	4
d. Bloody stools	0	1	2	3	4
e. Abdominal/ Pelvic/Rectal pain	0	1	2	3	4

7. Overall, how big a problem have your bowel habits been for you **during the last 4 weeks**?

No problem	1	
Very small problem	2	
Small problem	3	(Circle one number)
Moderate problem	4	
Big problem	5	

8. How would you rate each of the following **during the last 4 weeks**? (Circle one number on each line)

	Very Poor to None	Poor	Fair	Good	Very Good
a. Your ability to have an erection?	1	2	3	4	5
b. Your ability to reach orgasm (climax)?	1	2	3	4	5

9. How would you describe the usual QUALITY of your erections **during the last 4 weeks**?

None at all	1	
Not firm enough for any sexual activity	2	
Firm enough for masturbation and foreplay only	3	(Circle one number)
Firm enough for intercourse	4	

APPENDIX C:
Measures

Expanded Prostate Cancer Index Composite (EPIC)

10. How would you describe the FREQUENCY of your erections **during the last 4 weeks**?

I NEVER had an erection when I wanted one	1	
I had an erection LESS THAN HALF the time I wanted one	2	
I had an erection ABOUT HALF the time I wanted one	3	(Circle one number)
I had an erection MORE THAN HALF the time I wanted one	4	
I had an erection WHENEVER I wanted one	5	

11. Overall, how would you rate your ability to function sexually **during the last 4 weeks**?

Very poor	1	
Poor	2	
Fair	3	(Circle one number)
Good	4	
Very good	5	

12. Overall, how big a problem has your sexual function or lack of sexual function been for you **during the last 4 weeks**?

No problem	1	
Very small problem	2	
Small problem	3	(Circle one number)
Moderate problem	4	
Big problem	5	

13. How big a problem **during the last 4 weeks**, if any, has each of the following been for you? (Circle one number on each line)

	No Problem	Very Small Problem	Small Problem	Moderate Problem	Big Problem
a. Hot flashes	0	1	2	3	4
b. Breast tenderness/enlargement	0	1	2	3	4
c. Feeling depressed	0	1	2	3	4
d. Lack of energy	0	1	2	3	4
e. Change in body weight	0	1	2	3	4

APPENDIX C:
Measures

Sexual Distress Scale in Men with Prostate Cancer (SDS)

Sexual Distress SDS - SF

Below is a list of feelings and problems that people sometimes have concerning their sexuality. Please read each item carefully, and circle the number that best describes how often that problem has bothered you or caused you distress in the past month including today.

Circle only one number for each item.

	Never	Rarely	Occasionally	Frequently	Always
1. Distressed about your sex life	0	1	2	3	4
2. Frustrated by your sexual problems	0	1	2	3	4
3. Stressed about sex	0	1	2	3	4
4. Worried about sex	0	1	2	3	4
5. Sexually inadequate	0	1	2	3	4

APPENDIX C:
Measures

Female Sexual Function Index (FSFI)©

Subject Identifier _____ Date _____

INSTRUCTIONS: These questions ask about your sexual feelings and responses during the past 4 weeks. Please answer the following questions as honestly and clearly as possible. Your responses will be kept completely confidential. In answering these questions the following definitions apply:

Sexual activity can include caressing, foreplay, masturbation and vaginal intercourse.

Sexual intercourse is defined as penile penetration (entry) of the vagina.

Sexual stimulation includes situations like foreplay with a partner, self-stimulation (masturbation), or sexual fantasy.

CHECK ONLY ONE BOX PER QUESTION.

Sexual desire or interest is a feeling that includes wanting to have a sexual experience, feeling receptive to a partner's sexual initiation, and thinking or fantasizing about having sex.

1. Over the past 4 weeks, how **often** did you feel sexual desire or interest?

   ☐ Almost always or always
   ☐ Most times (more than half the time)
   ☐ Sometimes (about half the time)
   ☐ A few times (less than half the time)
   ☐ Almost never or never

2. Over the past 4 weeks, how would you rate your **level** (degree) of sexual desire or interest?

   ☐ Very high
   ☐ High
   ☐ Moderate
   ☐ Low
   ☐ Very low or none at all

APPENDIX C:
Measures

Female Sexual Function Index (FSFI)©

Sexual arousal is a feeling that includes both physical and mental aspects of sexual excitement. It may include feelings of warmth or tingling in the genitals, lubrication (wetness), or muscle contractions.

3. Over the past 4 weeks, how **often** did you feel sexually aroused ("turned on") during sexual activity or intercourse?

   - ☐ No sexual activity
   - ☐ Almost always or always
   - ☐ Most times (more than half the time)
   - ☐ Sometimes (about half the time)
   - ☐ A few times (less than half the time)
   - ☐ Almost never or never

4. Over the past 4 weeks, how would you rate your **level** of sexual arousal ("turn on") during sexual activity or intercourse?

   - ☐ No sexual activity
   - ☐ Very high
   - ☐ High
   - ☐ Moderate
   - ☐ Low
   - ☐ Very low or none at all

5. Over the past 4 weeks, how **confident** were you about becoming sexually aroused during sexual activity or intercourse?

   - ☐ No sexual activity
   - ☐ Very high confidence
   - ☐ High confidence
   - ☐ Moderate confidence
   - ☐ Low confidence
   - ☐ Very low or no confidence

6. Over the past 4 weeks, how **often** have you been satisfied with your arousal (excitement) during sexual activity or intercourse?

   - ☐ No sexual activity
   - ☐ Almost always or always
   - ☐ Most times (more than half the time)
   - ☐ Sometimes (about half the time)
   - ☐ A few times (less than half the time)
   - ☐ Almost never or never

APPENDIX C:
Measures

Female Sexual Function Index (FSFI)©

7. Over the past 4 weeks, how **often** did you become lubricated ("wet") during sexual activity or intercourse?

   - ☐ No sexual activity
   - ☐ Almost always or always
   - ☐ Most times (more than half the time)
   - ☐ Sometimes (about half the time)
   - ☐ A few times (less than half the time)
   - ☐ Almost never or never

8. Over the past 4 weeks, how **difficult** was it to become lubricated ("wet") during sexual activity or intercourse?

   - ☐ No sexual activity
   - ☐ Extremely difficult or impossible
   - ☐ Very difficult
   - ☐ Difficult
   - ☐ Slightly difficult
   - ☐ Not difficult

9. Over the past 4 weeks, how often did you **maintain** your lubrication ("wetness") until completion of sexual activity or intercourse?

   - ☐ No sexual activity
   - ☐ Almost always or always
   - ☐ Most times (more than half the time)
   - ☐ Sometimes (about half the time)
   - ☐ A few times (less than half the time)
   - ☐ Almost never or never

10. Over the past 4 weeks, how **difficult** was it to maintain your lubrication ("wetness") until completion of sexual activity or intercourse?

    - ☐ No sexual activity
    - ☐ Extremely difficult or impossible
    - ☐ Very difficult
    - ☐ Difficult
    - ☐ Slightly difficult
    - ☐ Not difficult

APPENDIX C:
Measures

Female Sexual Function Index (FSFI)©

11. Over the past 4 weeks, when you had sexual stimulation or intercourse, how **often** did you reach orgasm (climax)?

- ☐ No sexual activity
- ☐ Almost always or always
- ☐ Most times (more than half the time)
- ☐ Sometimes (about half the time)
- ☐ A few times (less than half the time)
- ☐ Almost never or never

12. Over the past 4 weeks, when you had sexual stimulation or intercourse, how **difficult** was it for you to reach orgasm (climax)?

- ☐ No sexual activity
- ☐ Extremely difficult or impossible
- ☐ Very difficult
- ☐ Difficult
- ☐ Slightly difficult
- ☐ Not difficult

13. Over the past 4 weeks, how **satisfied** were you with your ability to reach orgasm (climax) during sexual activity or intercourse?

- ☐ No sexual activity
- ☐ Very satisfied
- ☐ Moderately satisfied
- ☐ About equally satisfied and dissatisfied
- ☐ Moderately dissatisfied
- ☐ Very dissatisfied

14. Over the past 4 weeks, how **satisfied** have you been with the amount of emotional closeness during sexual activity between you and your partner?

- ☐ No sexual activity
- ☐ Very satisfied
- ☐ Moderately satisfied
- ☐ About equally satisfied and dissatisfied
- ☐ Moderately dissatisfied
- ☐ Very dissatisfied

15. Over the past 4 weeks, how **satisfied** have you been with your sexual relationship with your partner?

- ☐ Very satisfied
- ☐ Moderately satisfied
- ☐ About equally satisfied and dissatisfied
- ☐ Moderately dissatisfied
- ☐ Very dissatisfied

APPENDIX C:
Measures

Female Sexual Function Index (FSFI)©

16. Over the past 4 weeks, how **satisfied** have you been with your overall sexual life?

- ☐ Very satisfied
- ☐ Moderately satisfied
- ☐ About equally satisfied and dissatisfied
- ☐ Moderately dissatisfied
- ☐ Very dissatisfied

17. Over the past 4 weeks, how **often** did you experience discomfort or pain during vaginal penetration?

- ☐ Did not attempt intercourse
- ☐ Almost always or always
- ☐ Most times (more than half the time)
- ☐ Sometimes (about half the time)
- ☐ A few times (less than half the time)
- ☐ Almost never or never

18. Over the past 4 weeks, how **often** did you experience discomfort or pain following vaginal penetration?

- ☐ Did not attempt intercourse
- ☐ Almost always or always
- ☐ Most times (more than half the time)
- ☐ Sometimes (about half the time)
- ☐ A few times (less than half the time)
- ☐ Almost never or never

19. Over the past 4 weeks, how would you rate your **level** (degree) of discomfort or pain during or following vaginal penetration?

- ☐ Did not attempt intercourse
- ☐ Very high
- ☐ High
- ☐ Moderate
- ☐ Low
- ☐ Very low or none at all

Thank you for completing this questionnaire

APPENDIX D:
Biopsychosocial Sexual Health Assessment

Presenting Problem:

What is the problem?

History and description of problem, including all aspects of the medical illness (prostate cancer) and the patient's understanding of the impact on sexual function and relationship.

Pre-treatment and current sexual function (both individual and in relationship) – erectile function, orgasmic function, climacturia, penile curvature (Peyronie's)

Solutions attempted to date, their success/failure, including use of medical and non-medical aids to sexual functioning (awareness and attitude to those)

Emotional response to the problem, altered sexual function/relationship, need for assistive devices/ medications, grief or lack thereof

History of sexual function from adolescence, including how sexual function was explained (if it was)

Current sexual relationship, including partner sexual function

History of current sexual relationship, including couple's sexual repertoire, mutuality, satisfaction

Current general quality of relationship, including communication, emotional intimacy, division of instrumental roles, parenting, etc., unresolved or chronic problems. Is there partner alignment regarding distress related to sexual problems?

History of medical problems/comorbidities and treatments

Include all current and past medical conditions, treatments including current medication, their success, resulting physical limitations, potential effect on sexual function/relationship, patient's understanding and feelings about it

History of mental health problems and treatments

Include psychotherapy, medical treatment, the patient's perception of their success (these may be a clue to transference in your relationship), effect on sexual function/relationship, patient's feelings about it

History of substance use/abuse

Include how recent, if and how treated, how successful, patient's feelings about it, effect on relationship

History of physical or sexual trauma

Include how recent, if and how treated, how successful, patient's sense of the extent to which this has been worked through, how it may affect him now and in the relationship

Additional current stressors

Developmental history (recommended only for mental health providers)

Quality of early primary relationships, including personalities of parents, significant sibling relationships, economic and cultural influences

Early personality of the patient, social relationships, enjoyment and success in school

Early sexual experiences, thoughts

Cognitive development – academic success, ambition, interests

Adolescent emotional, sexual cognitive development

Losses, trauma/sexual trauma, grief response, presence of supportive figures

Achievement of adult separation from family of origin: trace establishment of adult life via education, work, relationships, etc.

APPENDIX D:
Biopsychosocial Sexual Health Assessment

Ego functions (recommended only for mental health providers)

Cognitive function (intellect, memory, abstract reasoning)

Capacity for reflection/introspection

Observing ego (self-awareness)

Object relations (quality of relatedness)

Affect modulation (reactivity, temper, tendency toward depression, anxiety, etc.)

Psychological defenses (eg. intellectualization, denial, projection, compartmentalization, internalization, reaction formation, displacement)

Biopsychosocial formulation

Bio: congenital endowment, chronic illness(s) and physical limitations, particularly as they affect sexual function and sexual relationship

Psycho: patient's reaction to physical problems and their consequences for sexual function and sexual relationship, including grief, resistance, a sense of optimism/pessimism, use of defenses to cope. Also refers to on-going experience with anxiety/depression/PTSD or other types of psychological distress that may interfere with sexual function.

Social: how has the patient negotiated sexual relationship, helpful or unhelpful strategies used; include contextual issues, eg. lack of privacy, external stressors which may take away focus from the sexual relationship. Socio-cultural factors, such as cultural or religious beliefs, discrimination or stigma that may impact behavior/attitudes should be included.

PATIENTS SHOULD BE GIVEN FEEDBACK, USING THE BIOPSYCHOSOCIAL FORMULATION AND AN OUTLINE OF HOW SEXUAL CONCERNS IN EACH AREA CAN BE ADDRESSED

THE EVALUATION IS A WORKING HYPOTHESIS TO BE EVALUATED AND MODIFIED IN THE COURSE OF TREATMENT

APPENDIX E:
Tables and Figures

Supplementary Discussion for Guideline Statement 6:

The table and plot below present sexual function recovery data (variously defined across papers) for studies based on type of nerve-sparing procedure (non-NS, bilateral NS, unilateral NS, unilateral or bilateral NS, mixed NS and non-NS procedures, or not reported) graphed by follow-up duration. Note that most studies cluster in the 12 to 24 months range of follow-up. If nerve-sparing procedures consistently yielded better recovery rates regardless of surgical technique (e.g., open, laparoscopic, robot-assisted), then it would be expected that the nerve-sparing symbols cluster at the top of the plot regardless of follow-up duration. The bilateral NS symbols are the only symbols present at rates above 70% but both bilateral and unilateral procedures yielded a wide range of recovery percentages. At 12 months postop, for example, bilateral NS procedures yielded recovery rates ranging from about 20% to slightly over 90%. Studies that reported a mix of NS and non-NS procedures appear in the bottom two-thirds of this cluster. For the cluster of studies that reported findings at 24 to 30 months of follow-up, a large range is still present (from about 25% to 85%).

It is possible that the lower recovery percentages are the result of more stringent study definitions of recovery. Sixteen study arms reported values below 40%. Eleven of these 16 study arms required the achievement of a specific IIEF-5, IIEF-EF, or EPIC score with or without PDE5i. The lowest recovery rate of 7.6% required an IIEF-5 score of at least 22 (presumably without erectile aids although this is not stated.[199] This study is one of four study arms in which a subset of men had ADT and/or RT as adjunctive therapies. The second lowest value of 14.2% was reported by Augustin et al. (2002), in which a subset of men also had ADT; this definition required an erection sufficient for intercourse without erectile aids.[192]

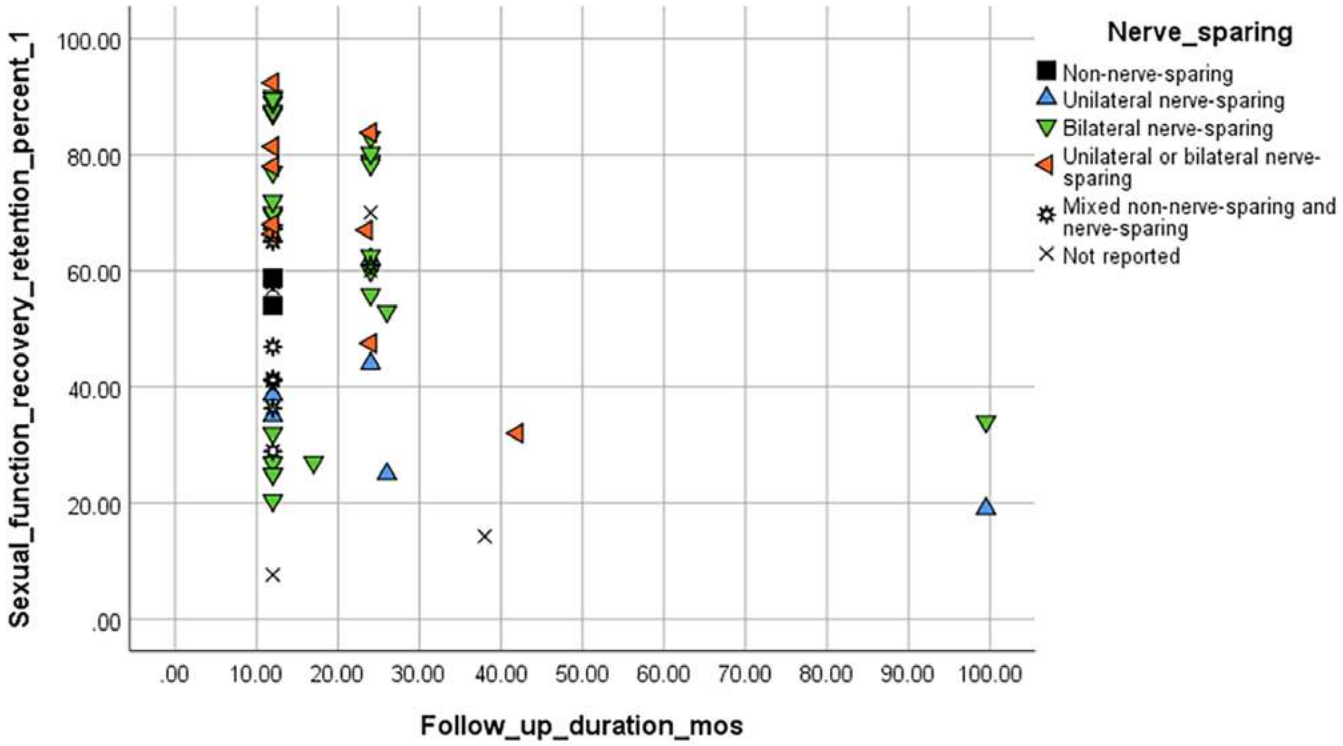
Percentage of Men With Normal Sexual Function Pre-Prostatectomy Who Achieved Sexual Function Recovery Post-Prostatectomy

Therapy_Type	Nerve_sparing	# study arms	Minimum	Maximum	Mean
RP	Non-nerve-sparing	2	54.00	58.70	56.35
	Unilateral nerve-sparing	8	19.00	68.00	44.69
	Bilateral nerve-sparing	25	20.40	90.00	61.64
	Unilateral or bilateral nerve-sparing	7	32.00	92.40	69.30
	Mixed non-nerve-sparing and nerve-sparing	8	28.90	65.00	47.30
	Not reported	5	40.00	70.00	57.00
RP +/- ADT	Unilateral or bilateral nerve-sparing	2	47.50	83.80	65.65
	Not reported	1	14.20	14.20	14.20
RP +/- ADT +/- RT	Not reported	1	7.60	7.60	7.60

APPENDIX E:
Tables and Figures

The plot below depicts the sexual recovery rates based on follow-up duration and nerve-sparing status. Neither follow-up duration nor nerve-sparing status are robust predictors of erectile function recovery post-RP. Note the large range of values plotted for various NS procedures and the absence of consistent patterns over time.

Percent of Men Achieving Sexual Recovery: Nerve-Sparing Status and Follow-Up Duration (months)

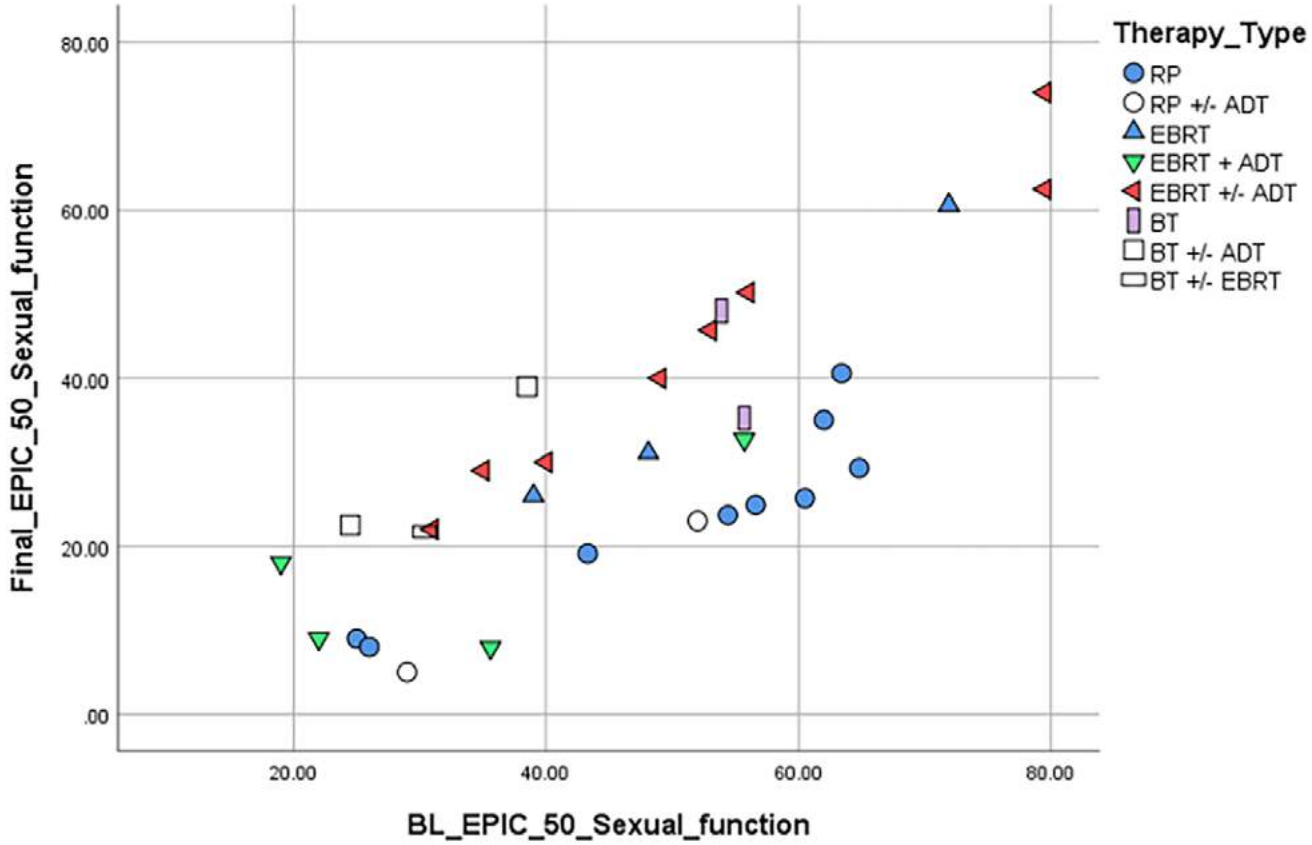


APPENDIX E:
Tables and Figures

Supplementary Discussion for Guideline Statement 7:

The relationship between baseline and final EPIC-50 sexual function scores is shown on the plot below with different forms of therapy designated. Note that there is a strong positive relationship between baseline sexual function score and post-treatment score such that the influence of therapy type is relatively limited.

Relationship Between Baseline and Final EPIC-50 Sexual Function Scores



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