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Guideline 19-6 REQUIRES UPDATING

A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Interventions to Address Sexual Problems in People with Cancer

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Report Date: April 28, 2016

Guideline 19-6 was reviewed in March 2023 and determined to REQUIRE UPDATING.
(See Section 6: Document Assessment and Review for details).

This guidance document requires updating to ensure the language and structure adheres to Equity, Diversity and Inclusion (EDI) principles and incorporates trauma sensitive care.

The existing recommendations remain relevant and it is still appropriate for this document to be available while this updating process unfolds. The PEBC has a formal and standardized process to ensure the currency of each document (PEBC Assessment & Review Protocol)

Guideline 19-6 is comprised of 6 sections. You can access the summary and full report here:
https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/531

Section 1:	**Recommendations**
Section 2:	**Guideline – Recommendations and Key Evidence**
Section 3:	**Guideline Methods Overview**
Section 4:	**Systematic Review**
Section 5:	**Internal and External Review**

Section 6: Document Assessment and Review

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PUBLICATIONS RELATED TO THIS REPORT

1. Barbera L, Zwaal C, Elterman D, McPherson K, Wolfman W, Katz A, Matthew A, and the Interventions to Address Sexual Problems in People with Cancer Guideline Development Group. Interventions to address sexual problems in people with cancer Curr Oncol. 2017 June; 24(3):192-200

2. Carter J, Lacchetti C, Andersen B, Barton D, Bolte S, Damast S et al., Interventions to Address Sexual Problems in People With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Adaptation of Cancer Care Ontario Guideline. Journal of Clinical Oncology - published online before print December 11, 2017

Guideline Report History

GUIDELINE VERSION	SYSTEMATIC REVIEW		PUBLICATIONS	NOTES AND KEY CHANGES
	Search Dates	Data		
Original version April 2016	2003 to 2015	Full Report	Web publication Journal publication	NA
Current Version April 2016	2015 to 2022	New data found in Section 6: Document Summary and Review Tool	Updated Web publication	2016 recommendations **REQUIRE UPDATING**

Table of Contents

Interventions to Address Sexual Problems in People with Cancer

Section 1: Recommendations

This section is a quick reference guide and provides the guideline recommendations only. For key evidence associated with each recommendation, see Section 2.

GUIDELINE OBJECTIVES

To examine effective strategies/interventions to manage sexual function side effects as a result of cancer diagnosis and/or treatment with the aim of decreasing distress, and improving quality of life for cancer survivors and their partners.

TARGET POPULATION

This guideline is applicable to adult men and women (and partners) of all sexual orientations living with cancer of any type. For the purposes of this guideline, men and women who were previously treated for a childhood cancer were not included.

INTENDED USERS

Healthcare practitioners such as oncologists, radiation therapists, urologists, gynaecologists, primary care providers, surgeons, nurses, physiotherapists, social workers, counsellors, psychologists and psychiatrists.

PREAMBLE

When first approaching this guideline, the Working Group chose to focus the guideline on sexual disorders that are known to arise in people with cancer. Sexual problems commonly include decreased desire, arousal disorders, pain (in women), and erectile dysfunction (in men). Sexual function is impacted in a multifactorial way by one's overall health (the patient and his/her partner), partner relationships, previous sexual history, medications, fatigue and stress, mood, body image, incontinence, and hormonal changes. Cancer can independently affect sexual function via changes in health, cancer treatment, body image, and changes in relationships.

The Working Group further chose to organize the guideline by conditions commonly seen in the clinic. The Working Group believed that criteria such as those listed in the *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* were not a good fit for this patient population and instead chose an *a priori* list of conditions, which we believed aligned well with common problems. It is hoped that this pragmatic approach will make the guideline easier to use for practitioners. The conditions include: sexual response, body image, intimacy and relationships, altered sexual function and satisfaction, vasomotor symptoms (women), and genital symptoms (women). Sexual response includes decreased desire, arousal, and alternate sensation in orgasm or anorgasmia for both sexes, and in men also includes erectile dysfunction and the absence of ejaculate. Body image conditions include those associated with urinary or fecal incontinence, ostomy, alopecia, mastectomy and lumpectomy, and changes in penile and testicular size and shape. Intimacy and relationship issues include the degree of comfort or closeness, and degree of sharing and communication with a partner. Sexual function and satisfaction encompasses the overall function of how the body reacts to sexual response and the satisfaction a person feels as a result of an intimate or sexual experience. Vasomotor symptoms are usually described as night sweats, hot flashes, and flushes. Genital symptoms in women include pelvic pain, vaginal dryness, and vaginal stenosis.

Interventions are organized by type, namely pharmacological, psychosocial counselling, or a device. Psychosocial counselling interventions are a group of nonpharmacological therapeutic interventions, which can address the psychological, sexual, social, personal, educational, or relational needs of a patient. However, these interventions may be provided in many different ways using various methods and techniques. In this guideline, all psychosocial or educational interventions are considered together. Further research is required to determine the key features of a psychosocial intervention that provide the most effective strategies in reducing sexual dysfunction.

It is important to acknowledge that men and women may have pre-existing difficulties with sexual response, sexual function, body image, intimacy, and relationships. This may complicate assessment and management.

Finally, while this guideline focuses on interventions, the most important thing a provider can do is to ask their patients if they are having any sexual health problems, if they would like to discuss these problems further, and if they would like information or a referral for help.

Note on the generalizability of disease site-specific evidence: The evidence to support the recommendations in women is primarily from studies including women with breast cancer and a small number of women with gynecological cancer. Similarly for men, the data are primarily from studies including men with prostate cancer and a few studies of men with colorectal cancer. The Expert Panel believe the results of these studies are generalizable and have merit for patients with all cancer types.

Note on implementation: The authors of this guideline encourage the users to read the Discussion section as it has a significant amount of clinical information regarding references and additional resources for clinics and physicians.

RECOMMENDATIONS

For all people with cancer

Recommendation 1
It is recommended that there be a discussion with the patient, initiated by a member of the healthcare team, regarding sexual health and dysfunction resulting from the cancer or its treatment. Ideally, the conversation would include the patient's partner, if partnered. This issue should be raised at the time of diagnosis and continue to be re-assessed periodically throughout follow-up. The Expert Panel believe that this is a vital recommendation. The recommendations that follow cannot be used unless someone has taken the initiative to ask. It is recommended that there be access to resources or referral information for the patient (and partner).

Women:

Condition: Sexual Response

Recommendation 1
The Expert Panel believe that psychosocial counselling should be offered to women with cancer, aiming to improve elements of sexual response such as desire, arousal, or orgasm. Current evidence does not support one type of psychosocial counselling to be superior to another. No recommendation can be made for pharmacological interventions.
Qualifying Statements
It is the opinion of the Expert Panel that any kind of regular stimulation (including masturbation) would likely be of benefit for improving sexual response, regardless of the stimulation used.

Condition: Body Image

Recommendation 2
It is recommended that psychosocial counselling be offered to women with cancer and body image issues. If a woman is partnered, evidence indicates that couples-based interventions are effective when compared with usual care. No recommendation can be made for or against group therapy (with or without exercise) for women with body image issues.

Condition: Intimacy/Relationships

Recommendation 3
It is recommended that psychosocial counselling be offered to women with cancer aiming to improve intimacy and relationship issues. If a woman is partnered, evidence indicates that couples-based interventions are effective when compared with usual care.

Condition: Overall Sexual Functioning and Satisfaction

Recommendation 4
The Expert Panel believe that psychosocial counselling directed at the individual or couple, or delivered in a group be offered to women with cancer who have problems with overall sexual functioning. Physical exercise or pelvic floor physiotherapy, in addition to psychosocial counselling, may also be of benefit.

Current evidence does not support a specific psychosocial counselling intervention to improve sexual functioning and satisfaction.

Condition: Vasomotor Symptoms

Recommendation 5

For women with vasomotor symptoms, hormone therapy is the most effective intervention. For women unwilling or unable to use hormonal therapy, alternatives exist; for example, paroxetine, venlafaxine, gabapentin, or clonidine.

Having a hormone-sensitive breast cancer is a contraindication to using systemic hormone therapy.

Psychosocial counselling (cognitive behavioural therapy) may provide a benefit and reduce vasomotor symptoms and should be offered.

Qualifying Statement

The Expert Panel emphasizes that women with non-hormone-sensitive cancers who develop vasomotor symptoms from their cancer treatment should be counselled to consider hormone therapy until the average age of menopause, approximately 51 years, at which point they should be re-evaluated. Risks typically cited for hormone therapy are derived from studies of post-menopausal women. Beyond the age of 51 years, hormone therapy is an individual therapy with few risks for symptomatic patients in their 50's. It should be intermittently evaluated for long-term use.

When not contraindicated, estrogen therapy alone (oral, transdermal, or vaginal) is recommended for women who have had a hysterectomy, as it has a more beneficial risk/benefit profile.

Paroxetine and fluoxetine should not be offered to women with breast cancer taking tamoxifen. Adverse events of clonidine include hypotension, light-headedness, headache, dry mouth, dizziness, sedation, and constipation. Sudden cessation can lead to significant elevations in blood pressure.

Condition: Genital Symptoms

Recommendation 6

Women with symptoms of vaginal atrophy, such as vaginal dryness, should be managed in the same way as women without cancer. Vaginal moisturizers for daily comfort and/or lubricants with sexual activity may be tried. For those who do not respond or whose symptoms are more severe at presentation, vaginal estrogen can be safely used.

Vaginal dilators may be of benefit in the management of vaginismus and/or vaginal stenosis.

Cognitive behavioural therapy and exercise may be useful to decrease lower urinary tract symptoms.

The Expert Panel believe that pelvic floor physiotherapy should also be offered to women with pain or other pelvic floor issues.

Qualifying statement

For women with hormone-positive breast cancer who are symptomatic and not responding to conservative measures, vaginal estrogen can be considered after a discussion.

Men:

Sexual Response

Recommendation 1

It is recommended that phosphodiesterase type 5 inhibitor (PDE5i) medications be used to help men with erectile dysfunction.

Men who do not respond to PDE5i medications should consider alternate interventions such as a vacuum erectile device (VED), medicated urethral system for erection, or intracavernosal injection.

There may be some benefit to initiating the use of any of the above interventions earlier after cancer treatment rather than later.

Qualifying Statement

The Expert Panel believe that men are best served by being offered a combination of psychosocial counselling with the aim of greater adaptation toward long-term use and PDE5i medication adherence together with PDE5i treatment. For men who are partnered, psychosocial counselling should be directed at the couple.

Men should be aware that it might take a long time for medications to work.

It is the opinion of the Expert Panel that any kind of regular stimulation (including masturbation) would likely be of benefit for improving sexual response, regardless of the stimulation used.

Contraindications include the use of nitrates in any form. Common acute side effects of PDE5i medications include headaches, flushing, dizziness, upset stomach, nasal congestion and dyspepsia.

Genital Changes

Recommendation 2

It is recommended that a VED be used daily to prevent penis length loss. There may be some benefit to initiating the use of VEDs earlier after cancer treatment rather than later. Early treatment with PDE5i medications may also be beneficial for this outcome.

Intimacy/relationships

Recommendation 3
The Expert Panel believe that individual or couples counselling should be offered for those wishing to improve relationship or intimacy issues. Current evidence does not support a particular intervention to improve intimacy or relationships.

Overall Sexual Functioning and Satisfaction

Recommendation 4
It is recommended that psychosocial counselling be offered to men with cancer (and partners) to potentially improve sexual functioning and satisfaction. It is also recommended that the use of pro-erectile agents and devices be considered, recognizing that most of the benefit is specifically for erectile dysfunction.
Qualifying Statement
Psychosocial counselling could be used to help couples integrate interventions into their usual sexual activities.

Condition: Vasomotor Symptoms

Recommendation 5
Men with vasomotor symptoms should be offered medication for symptomatic improvements. Options would include venlafaxine, medroxyprogesterone acetate, cyproterone acetate, and gabapentin. Acupuncture may be a suitable alternative.

Interventions to Address Sexual Problems in People with Cancer

Section 2: Guideline – Recommendations and Key Evidence

GUIDELINE OBJECTIVES

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TARGET POPULATION

This guideline is applicable to adult men and women (and partners) of all sexual orientations living with cancer of any type. For the purposes of this guideline, men and women who were previously treated for a childhood cancer were not included.

INTENDED USERS

Healthcare practitioners such as oncologists, radiation therapists, urologists, gynaecologists, primary care providers, surgeons, nurses, physiotherapists, social workers, counsellors, psychologists, and psychiatrists.

PREAMBLE

When first approaching this guideline, the Working Group chose to focus the guideline on sexual disorders that are known to arise in people with cancer. Sexual problems commonly include decreased desire, arousal disorders, pain (in women), and erectile dysfunction (in men). Sexual function is impacted in a multifactorial way by one's overall health (the patient and his/her partner), partner relationships, previous sexual history, medications, fatigue and stress, mood, body image, incontinence, and hormonal changes. Cancer can independently affect sexual function via changes in health, cancer treatment, body image, and changes in relationships.

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educational, or relational needs of a patient. However, these interventions may be provided in many different ways using various methods and techniques. In this guideline, all psychosocial or educational interventions are considered together. Further research is required to determine the key features of a psychosocial intervention that provide the most effective strategies in reducing sexual dysfunction.

It is important to acknowledge that men and women may have pre-existing difficulties with sexual response, sexual function, body image, intimacy, and relationships. This may complicate assessment and management.

Finally, while this guideline focuses on interventions, the most important thing a provider can do is to ask their patients if they are having any sexual health problems, if they would like to discuss these problems further, and if they would like information or a referral for help.

Note on the generalizability of disease site-specific evidence: The evidence to support the recommendations in women is primarily from studies including women with breast cancer and a small number of women with gynecologic cancer. Similarly for men, the data are primarily from studies including men with prostate cancer and a few studies of men with colorectal cancer. The Expert Panel believe the results of these studies are generalizable and have merit for patients with all cancer types.

Note on implementation: The authors of this guideline encourage the users to read the Discussion section as it has a significant amount of clinical information regarding references and additional resources for clinics and physicians.

Recommendation 1
It is recommended that there be a discussion with the patient, initiated by a member of the healthcare team, regarding sexual health and dysfunction resulting from the cancer or its treatment. Ideally, the conversation would include the patient's partner, if partnered. This issue should be raised at the time of diagnosis and continue to be re-assessed periodically throughout follow-up. The Expert Panel believe that this is a vital recommendation. The recommendations that follow cannot be used unless someone has taken the initiative to ask. It is recommended that there be access to resources or referral information for the patient (and partner).

Women:
Condition: Sexual Response

Recommendation 1
The Expert Panel believe that psychosocial counselling should be offered to women with cancer, aiming to improve elements of sexual response such as desire, arousal, or orgasm. Current evidence does not support one type of psychosocial counselling to be superior to another.

No recommendation can be made for pharmacological interventions.

Qualifying Statements

It is the opinion of the Expert Panel that any kind of regular stimulation (including masturbation) would likely be of benefit for improving sexual response, regardless of the stimulation used.

Key Evidence

Six studies (2 randomized controlled trials [RCTs], 1 case/control, and 3 pre/post intervention studies) used sexual response as an outcome [1-6]. The main recommendation is based on two studies [2,4]. One study randomized 40 women with breast cancer and mastectomy and their partners to either a combined brief psychosexual intervention or usual care [2]. Those in the intervention group experienced increased orgasm frequency and initiation of sex. The other study used a pre/post design combined with a wait list control [4]. Thirty-one women with either endometrial or cervical cancer were exposed to the mindfulness-based cognitive behavioural therapy (CBT) intervention. The intervention improved all domains of the Female Sexual Function Index.

Interpretation of Evidence

The Expert Panel believe that existing studies plus expert opinion support the recommendation for psychosocial counselling targeted at couples or individuals to improve sexual response. The data did not support a recommendation for group level interventions or for medications. There is no indication that any harm arises from any type of counselling.

One study has demonstrated improved sexual response with a clitoral stimulation device, but the evidence is limited and subject to bias [5]. The device that was studied received United States Food and Drug Administration approval for this indication.

Topical testosterone is also often considered when addressing low desire in women. The drug is not approved for women in the United States or Canada and, thus, not a focus of this review.

Condition: Body Image

Recommendation 2

It is recommended that psychosocial counselling be offered to women with cancer and body image issues.

If a woman is partnered, evidence indicates that couples-based interventions are effective when compared with usual care.

No recommendation can be made for or against group therapy (with or without exercise) for women with body image issues.

Key Evidence

One systematic review and two RCTs reported an improvement in body image outcomes [2,7,8]. The two positive RCTs included six sessions of couples-based counselling [2,8]. Two other RCTs evaluated a group intervention and had conflicting results [3,9].

Interpretation of Evidence

Overall, most studies found an improvement in body image after some type of counselling and found no undesirable effects. One systematic review concluded that individual and peer-group studies produced no or few significant benefits for body image [10]. For the two exercise/counselling studies that did not find a significant difference for body image, the focus of the studies was quality of life, which may have an effect on this outcome.

The overall quality of the evidence is moderate, although some studies are of higher quality. There is great heterogeneity in the studies. There are different interventions (peer-led, couples-based, group–based, CBT, relationship enhancement therapy, and combined brief psychosocial counselling). There is variation in the number of sessions (3 to 6) and some studies included exercise. There are also a variety of measures of body image. This heterogeneity makes it difficult to develop a recommendation for a specific type of counselling. However, the Expert Panel believe it would be reasonable to offer some type of counselling for women with any cancer diagnoses who are experiencing body image issues.

The Expert Panel noted that the counselling with a measurable impact included at least six sessions of counselling and that these studies provided couples-based counselling in the intervention, compared with usual care. Although the interventions were directed at the couple in the literature, the Expert Panel believe that individual psychosocial counselling would still be helpful for a woman with body image issues.

Condition: Intimacy/Relationships

Recommendation 3

It is recommended that psychosocial counselling be offered to women with cancer aiming to improve intimacy and relationship issues.

If a woman is partnered, evidence indicates that couples-based interventions are effective when compared with usual care.

Key Evidence

Three studies found a significant increase in intimacy and/or relationship scores using couples- or group-based interventions [2,8,11]. Two other RCTs evaluated group interventions and had nonsignificant results [3,12].

Interpretation of Evidence

The overall quality of the evidence was low to moderate; however, there was one larger higher-level quality study with individuals and two smaller higher-level studies with partners. There is great heterogeneity in the studies. There are different interventions (individual-based, couples-based, group–based, CBT, and other types of counselling therapy). There is variation in the number of sessions (3 to 12) as well as variation in the follow-up and outcome measures.

The three studies supporting this recommendation included partners in the intervention [2,8,13]; two higher-quality partner studies used a six-session intervention and found a significant difference in relationship scores [2,8]. The one high-quality individual study was an RCT with 210 patients, which evaluated group counselling. This study reported a significant improvement in relationship scores (Revised Dyadic Adjustment Scale) and communication with a six-session intervention [11].

No studies found any harms for patients associated with psychosocial counselling. The studies with small number of participants may have missed a statistical benefit.

Condition: Overall Sexual Functioning and Satisfaction

Recommendation 4

The Expert Panel believe that psychosocial counselling directed at the individual, couple, or delivered in a group be offered to women with cancer who have problems with overall sexual functioning. Physical exercise or pelvic floor physiotherapy, in addition to psychosocial counselling, may also be of benefit.

Current evidence does not support a specific psychosocial counselling intervention to improve sexual functioning and satisfaction.

Key Evidence

Four systematic reviews were identified [7,14-16]. Two specifically searched for psychosocial interventions and both concluded couples-based interventions were effective [7,14]. One concluded that interventions aimed at individuals were also beneficial [7]. The other identified that none of the studies aimed at groups were effective [14]. Two additional systematic reviews evaluated the use of vaginal dilators in women who received pelvic radiotherapy and concluded that dilator use did not improve overall sexual function [15,16].

Eight of 11 studies found that psychosocial counselling improved overall sexual functioning scores for women with cancer [3,6,8,9,11,13,17,18]. Three studies that included exercise in the intervention also found a positive effect on sexual functioning scores [19-21]. Two of the studies that included exercise targeted the pelvic floor muscles [20,21]; the third used a general exercise program [19].

Interpretation of Evidence

The studies were of moderate to low quality because there was heterogeneity among study designs, psychosocial counselling interventions, exercise interventions, and outcome measures. However, the higher-quality studies found that psychosocial counselling improved overall sexual functioning and no undesirable effects were reported. Also, the psychosocial counselling plus exercise studies were of high quality and found a significant improvement [19,20], and one exercise plus lubricant study of lower quality also found a significant improvement in sexual function scores [21].

Condition: Vasomotor Symptoms

Recommendation 5

For women with vasomotor symptoms, hormone therapy is the most effective intervention. For women unwilling or unable to use hormonal therapy, alternatives exist; for example, paroxetine, venlafaxine, gabapentin, or clonidine.

Having a hormone-sensitive breast cancer is a contraindication to using systemic hormone therapy.

Psychosocial counselling (CBT) may provide a benefit and reduce vasomotor symptoms and should be offered.

Qualifying Statement

The Expert Panel emphasizes that women with non-hormone-sensitive cancers who develop vasomotor symptoms from their cancer treatment should be counselled to consider hormone therapy until the average age of menopause, approximately 51 years, at which point they should be re-evaluated. Risks typically cited for hormone therapy are derived from studies of post-menopausal women. Beyond the age of 51 years, hormone therapy is an individual therapy with few risks for symptomatic patients in their 50's. It should be intermittently evaluated for long-term use.

When not contraindicated, estrogen therapy alone (oral, transdermal, or vaginal) is recommended for women who have had a hysterectomy, because it has a more beneficial risk/benefit profile.

Paroxetine and fluoxetine should not be offered to women with breast cancer taking tamoxifen. Adverse events of clonidine include hypotension, light-headedness, headache, dry mouth, dizziness, sedation, and constipation. Sudden cessation can lead to significant elevations in blood pressure.

Key Evidence

The majority of the evidence for this recommendation is from high-quality guidelines drafted for the general population. The Society of Obstetrics and Gynaecology Canada (SOGC) guideline [22] and the North American Menopausal Society (NAMS) guidelines [23,24] included studies with patients with cancer in their literature review.

One well-conducted RCT examined vasomotor symptoms as an outcome and found that CBT alone or in combination with an exercise program improved hot flashes and night sweats in breast cancer patients [19].

Paroxetine and fluoxetine inhibit CYP2D6 activity, which metabolizes tamoxifen into its active metabolites. Taking both drugs together may inhibit the effect of tamoxifen.

Interpretation of Evidence

New guidelines on this topic were developed from studies conducted both in people with cancer and the general population. There have been many studies conducted in the general population with regard to the management of this symptom. The Expert Panel believe that the management of vasomotor symptoms would be the same in all women and that high-quality guidelines on this issue should be used for women with non-hormone-sensitive cancers. Estrogen therapy (oral, transdermal, or vaginal) is recommended in those without contraindication, because it has a more beneficial risk-benefit profile than combined estrogen/progesterone therapy.

Condition: Genital Symptoms

Recommendation 6

Women with symptoms of vaginal atrophy, such as vaginal dryness, should be managed in the same way as women without cancer. Vaginal moisturizers for daily comfort and/or lubricants with sexual activity may be tried. For those who do not respond or whose symptoms are more severe at presentation, vaginal estrogen can be safely used.

Vaginal dilators may be of benefit in the management of vaginismus and/or vaginal stenosis.

CBT and exercise may be useful to decrease lower urinary tract symptoms.

The Expert Panel believe that pelvic floor physiotherapy should also be offered to women with pain or other pelvic floor issues.

Qualifying statement

For women with hormone-positive breast cancer who are symptomatic and not responding to conservative measures, vaginal estrogen can be considered after a discussion.

Key Evidence

Recommendations for vaginal moisturizers, lubricants, and estrogen were drawn from guidelines in the non-cancer population [22]. One study specifically in breast cancer patients did evaluate a specific lubricant and found it to improve dryness and dyspareunia [25].

Two systematic reviews did not find any evidence that vaginal dilation had an effect, positive or negative, on vaginal stenosis [15,16]. However, a recent prospective study found that the use of a vaginal dilator helped to prevent stenosis [26].

One large RCT of CBT ± physical exercise found both intervention arms improved lower urinary tract symptoms [19]. Two smaller studies found that pelvic floor rehabilitation improved either vaginal function or dyspareunia [20,21].

Interpretation of Evidence

The Expert Panel believe it is important to emphasize the role of physical examination to evaluate women with pain or other genitourinary complaints. Women need to be examined to determine the nature and cause of their pain to determine the best management approach.

Vaginal atrophy and vaginal dryness have the best interventions and evidence as described in other guidelines.

The Expert Panel believe there is a role for vaginal dilators for the prevention or treatment of vaginal stenosis. This is supported by the more recent trial [26]. Poor compliance and measurement issues may limit earlier studies of vaginal dilation.

The Expert Panel believe that women with cervical cancer treated with radiotherapy should use vaginal dilators to prevent stenosis. The Panel believe it important to emphasize to patients that preventing stenosis is important for physical examination and follow-up, and not solely as a measure to improve sexual function.

Pelvic floor physiotherapy may also be of benefit to women experiencing pain or other pelvic floor issues.

There are very little data for women on aromatase inhibitors and the use of vaginal estrogen in this group is controversial. Individual decisions need to be made to balancing risks and quality of life issues.

Men:
Sexual Response

Recommendation 1

It is recommended that phosphodiesterase type 5 inhibitor (PDE5i) medications be used to help men with erectile dysfunction.

Men who do not respond to PDE5i medications should consider alternate interventions such as a vacuum erectile device (VED), medicated urethral system for erection (MUSE), or intracavernosal injection (ICI).

There may be some benefit to initiating the use of any of the above interventions earlier after cancer treatment rather than later.

Qualifying Statement

The Expert Panel believe that men are best served by being offered a combination of psychosocial counselling together with PDE5i treatment. The aim of the psychosocial counselling is greater adaptation toward long-term use and PDE5i medication adherence For men who are partnered, psychosocial counselling should be directed at the couple.

Men should be aware that it might take a long time for medications to work.

It is the opinion of the Expert Panel that any kind of regular stimulation (including masturbation) would likely be of benefit for improving sexual response, regardless of the stimulation used.

Contraindications include the use of nitrates in any form. Common acute side effects of PDE5i medications include headaches, flushing, dizziness, upset stomach, nasal congestion and dyspepsia.

Key Evidence

Two systematic reviews, 12 RCTs and seven non-RCTs found a significant improvement in International Index of Erectile Function (IIEF) scores for patients taking PDE5i medications at least in the short term [27-48].

Five studies (4 RCTs and 1 non-RCT) compared medication given on a daily basis with an on-demand medication routine [41,49-51]. One found a significant difference in favour of daily use over on-demand at nine months using tadalafil, which went away after a six-week wash-out period [41], and another found a significant difference for on-demand over daily use using vardenafil, which went away after a two-month wash-out period [52].

Three moderate- to low-quality studies found a significant improvement in IIEF scores for the groups who started the PDE5i treatment early when compared with the delayed group [39,47,48].

Two systematic reviews [53,54], four good-quality studies (2 RCTs [55,56], 1 pre/post intervention [57], and 1 case/control study [6]) examined psychosocial interventions and found that psychosocial counselling improved IIEF, or other overall sexual functioning scores, and encouraged long-term use of erectile dysfunction treatment.

Interpretation of Evidence

Although the quality of the evidence is low when taking into account the heterogeneity of the types of studies, interventions, selective reporting, and types of treatments, most studies found a positive result when PDE5i medications was used to treat erectile dysfunction.

The heterogeneity of the studies suggest that the use of PDE5i can be used with cancer patients experiencing erectile dysfunction no matter the type of treatment used (i.e.,

radiation therapy, uni- or bilateral nerve-sparing radical prostatectomies, or mesorectal excision).

Although whether the effectiveness of PDE5i medication on sexual response is different when taken daily versus on-demand may depend on the type of PDE5i medication, it seems compliance and side effects may be better using a daily treatment protocol.

Three moderate- to low-quality studies found that earlier intervention with PDE5i post-treatment for prostate cancer may improve recovery of erectile function compared with later treatment.

Even though PDE5i medications may be most effective in men who underwent nerve-sparing surgery, it is recommended that they should be used as a first-line approach, regardless of the type of surgery.

The use of PDE5i is the least invasive method but, for those that prefer a non-drug approach, or do not respond to medication, alternatives exist. These include VEDs, MUSE, ICI, or the placement of a penile prosthesis.

Psychosocial counselling should be considered to help couples integrate interventions into their usual sexual activities. Psychosocial counselling may not directly overcome erectile dysfunction but it may help the couple have realistic expectations, adapt to ongoing use, and compliance and satisfaction with PDE5i medications, in addition to setting appropriate expectations. In the trials reviewed, a variety of formats seemed promising, including in-person, telephone, or Internet based.

Side effects of PDE5i medications include headaches, flushing, dizziness, upset stomach, nasal congestion and dyspepsia but, when used properly, these side effects are relatively mild and most disappear after a few hours. Side effects were generally not found to be a reason for participants to stop taking medications.

Genital Changes

Recommendation 2

It is recommended that a VED be used daily to prevent penis length loss. There may be some benefit to initiating the use of VEDs earlier after cancer treatment rather than later.

Early treatment with PDE5i medications may also be beneficial for this outcome.

Key Evidence

One RCT found that daily use of a VED significantly reduced the loss of penis length when compared with a control group [58]. One single-arm prospective study reported no loss in penis length when a VED was used daily, especially in those men who were compliant [59]. Both studies initiated the intervention soon after cancer surgery. All the data are from surgical patients.

One RCT using PDE5i also found that the use of PDE5i reduced penile length loss in the treatment group [41].

Interpretation of Evidence

There were few studies examining loss of penis length in men with prostate cancer. The three studies identified were of moderate quality overall.

Intimacy/Relationships

Recommendation 3

The Expert Panel believes that individual or couples counselling should be offered for those wishing to improve relationship or intimacy issues. Current evidence does not support a particular intervention to improve intimacy or relationships.

Key Evidence

One systematic review did not find conclusive evidence for improvements to relationship functioning in those studies that measured dyadic adjustment or marital distress [54].

Four RCTs found no difference in the counselling groups compared with the control groups using intimacy scales or the Dyadic Adjustment Scale [55,56,60-62]. One of the RCTs evaluating partner-assisted emotional disclosure did have a positive outcome for the Quality of Marriage Index [60,61].

Two nonrandomized studies also found no differences in relationships after counselling [63,64], but one pre-post study found a difference in Sexuality Supportive Needs Scale results over time [63].

Interpretation of Evidence

There were no studies that showed a significant improvement owing to any interventions. It may be that relationships that have endured a cancer experience may already be highly functioning and it may be difficult to measure improvements. The Expert Panel believe that psychosocial counselling will help overall, in assisting couples to adapt to sexual dysfunction, and adherence to and expectations for the use of medications and devices. It may also enhance couples' communication in general and communication related to sexual activities.

Overall Sexual Functioning and Satisfaction

Recommendation 4

It is recommended that psychosocial counselling be offered to men with cancer (and partners) to potentially improve sexual functioning and satisfaction. It is also recommended that the use of pro-erectile agents and devices be considered, recognizing that most of the benefit is specifically for erectile dysfunction.

Qualifying Statement

Counselling could be used to help couples integrate interventions into their usual sexual activities.

Key Evidence

Two systematic reviews found the psychosocial/educational interventions improved overall sexual functioning in men with prostate cancer [53,54].

Three studies (2 RCTs [65,66] and 1 case/control [6]) examining psychosocial counselling all found a significant improvement in sexual functioning, satisfaction, or confidence.

Three RCTs found a significant improvement in either sexual functioning or satisfaction or both when patients used PDE5i [31,41,67].

Interpretation of Evidence

Psychosocial counselling was found to improve overall sexual functioning or satisfaction using one-on-one or couples counselling with no undesirable effects being reported.

Although the quality of the evidence is low when taking into account the heterogeneity of the types of studies, multiple interventions, selective reporting, and types of treatments, most studies found improved overall sexual functioning and satisfaction when PDE5i medications was used to treat erectile dysfunction. The effect seemed to occur more in the short or medium term than longer term.

The heterogeneity of the studies suggest that the use of PDE5i can be used with cancer patients experiencing sexual dysfunction no matter the type of treatment used (i.e., radiation therapy, uni- or bilateral nerve-sparing prostatectomy, or mesorectal excision).

Condition: Vasomotor Symptoms

Recommendation 5

Men with vasomotor symptoms should be offered medication for symptomatic improvements. Options would include venlafaxine, medroxyprogesterone acetate, cyproterone acetate, or gabapentin. Acupuncture may be a suitable alternative.

Key Evidence

One RCT compared venlafaxine, medroxyprogesterone acetate, and cyproterone acetate and found all significantly improved Hot Flush Scores with medroxyprogesterone acetate and cyproterone acetate having a significantly better performance [68]. Another RCT found venlafaxine improved hot flush counts and severity at 12 weeks [69].

One RCT compared a placebo with three difference dosages of gabapentin with a placebo and found a larger dose (900 mg) was more effective in reducing the number of and severity of hot flashes compared with a placebo and a 300 mg dose [70]. In an open-

label continuation of this RCT, patients tended medicate themselves at a higher dose of 600 mg/day when allowed to modify the gabapentin regimen [71].

Four smaller studies examined the effect of acupuncture on hot flashes via traditional [72-74], electrostimulation [74], and auricular methods [75]. All four studies found significant decreases in the number and intensity of hot flashes after acupuncture, regardless of the method used.

Interpretation of Evidence

Only one RCT included a placebo arm and found a significant effect. The other RCTs compared various medications with each other and found a pre/post effect. The other studies were small and had a high risk of bias.

There seems to an effect of acupuncture but the data to support it are weaker and there is a risk of bias.

IMPLEMENTATION CONSIDERATIONS

For any intervention to be of use, standard evaluation of sexual health problems needs to be routine. Healthcare practitioners need to engage their patients in a conversation concerning sexual health issues. There may be a lack of awareness of the significant impact sexual issues on the quality of life of the patient and partner. There may be a lack of training and confidence among healthcare practitioners to have that initial conversation. As well, patients and the healthcare practitioner may feel embarrassed, preventing either from starting a conversation about sexual issues.

The Expert Panel believe some other barriers include a lack of resources such as a lack of knowledgeable people to provide support and counselling. Different regions may have different resources and different access to resources.

Costs to the patients include counselling, medication, and devices, which may or may not be paid for through the health system or insurance.

A resource manual for healthcare providers would help them to cover the basics of sexual health concerns including a list of educational and supportive care resources as well as a list of specialists for those patients that need more support.

Please read the Discussion section as it has a significant amount of clinical information regarding references and additional resources for clinics and physicians.

RELATED GUIDELINES

- Matthew A, Souter LH, Breau RH, Canil C, Haider M, Jamnicky R, et al. Follow-up care and psychosocial needs of survivors of prostate cancer. Toronto (ON): Cancer Care Ontario; 2015 June 16. Program in Evidence-based Care Guideline No.: 26-4.

Interventions to Address Sexual Problems in People with Cancer

Section 3: Guideline Methods Overview

This section summarizes the methods used to create the guideline. For the systematic review, see Section 4.

THE PROGRAM IN EVIDENCE-BASED CARE

The Program in Evidence-Based Care (PEBC) is an initiative of the Ontario provincial cancer system, Cancer Care Ontario (CCO). The PEBC mandate is to improve the lives of Ontarians affected by cancer through the development, dissemination, and evaluation of evidence-based products designed to facilitate clinical, planning, and policy decisions about cancer control.

The PEBC supports the work of Guideline Development Groups (GDGs) in the development of various PEBC products. The GDGs are composed of clinicians, other healthcare providers and decision makers, methodologists, and community representatives from across the province.

The PEBC is a provincial initiative of CCO supported by the Ontario Ministry of Health and Long-Term Care (OMHLTC). All work produced by the PEBC and any associated Programs is editorially independent from the OMHLTC.

BACKGROUND FOR GUIDELINE

The treatment of cancer can result in changes to sexual response, functioning, and sexuality. Radical prostatectomy or radiation treatment for prostate cancer has been associated with significant erectile dysfunction, while menopausal symptoms (e.g., hot flashes, vaginal dryness, and urinary incontinence) are very common in breast cancer survivors, depending on treatment modality.

Unlike some other physiological side effects of cancer treatment, sexual problems do not tend to resolve within the first few years post-treatment; rather, they may remain constant or even increase. To date, there has been little done to address sexual health functioning post cancer treatment. The lack of an intervention for people with sexual functioning issues can result in lower medical service utilization and a lower ability to cope with decreased health outcomes.

GUIDELINE DEVELOPERS

This guideline was developed by the Interventions to Address Sexual Problems in People with Cancer GDG (Appendix 1), which was convened at the request of the Psychosocial Oncology Program.

The project was led by a small Working Group of the Interventions to Address Sexual Problems in People with Cancer GDG, which was responsible for reviewing the evidence base, drafting the guideline recommendations, and responding to comments received during the document review process. The Working Group had expertise in radiation oncology, surgical oncology, psychology, sexual counselling, and health research methodology. Other members of the Interventions to Address Sexual Problems in People with Cancer GDG served as the Expert Panel and were responsible for the review and approval of the draft document produced by the Working Group. Conflict of interest declarations for all GDG members are summarized in Appendix 1, and were managed in accordance with the *PEBC Conflict of Interest Policy*.

GUIDELINE DEVELOPMENT METHODS

The PEBC produces evidence-based and evidence-informed guidance documents using the methods of the Practice Guidelines Development Cycle [76]. This process includes a systematic review, interpretation of the evidence by the Working Group and draft recommendations, internal review by content and methodology experts, and external review by Ontario clinicians and other stakeholders.

The PEBC uses the AGREE II framework [77] as a methodological strategy for guideline development. AGREE II is a 23-item validated tool that is designed to assess the methodological rigour and transparency of guideline development.

The currency of each document is ensured through periodic review and evaluation of the scientific literature and, where appropriate, the addition of newer literature to the original evidence base. This is described in the *PEBC Document Assessment and Review Protocol*. PEBC guideline recommendations are based on clinical evidence, and not on feasibility of implementation; however, a list of implementation considerations such as costs, human resources, and unique requirements for special or disadvantaged populations is provided along with the recommendations for information purposes. PEBC guideline development methods are described in more detail in the *PEBC Handbook* and the *PEBC Methods Handbook*.

Search for Existing Guidelines

A search for existing guidelines is generally undertaken prior to searching for existing systematic reviews or primary literature. This is done with the goal of identifying existing guidelines for adaptation, using the ADAPTE framework [78], or endorsement in order to avoid the duplication of guideline development efforts across jurisdictions. For this project, the following sources were searched in September 2014 for existing guidelines that addressed the research questions:

- Practice guideline databases: the Standards and Guidelines Evidence Directory of Cancer Guidelines (SAGE), Agency for Healthcare Research and Quality (AHRQ) National Guideline Clearinghouse, and the Canadian Medical Association Infobase.
- Guideline developer websites: National Institute for Health and Care Excellence (NICE), Scottish Intercollegiate Guidelines Network (SIGN), American Society of Clinical Oncology (ASCO), and National Health and Medical Research Council - Australia.

Only guidelines published after 2005 were considered. Guidelines that were considered relevant to the objectives and the research questions were then evaluated for quality using the AGREE II instrument [77]. A search for existing guidelines for adaptation or endorsement did not yield an appropriate source document. A search of the primary literature was required (see Section 4: **Evidence Review**).

As well, a second search for guidelines was conducted because the systematic review used for the primary literature evidence base did not include evidence regarding menopausal symptoms due to premature ovarian failure, which can be the result or side effect of cancer treatment. The second search was for guidelines relevant to menopausal symptoms for the general population and was conducted using the same databases listed above with only guidelines published after 2010 considered.

Six guidelines relevant to the menopausal symptoms were found and three were chosen to be included in the guideline because of their currency and relevance to the symptoms. (See Appendix 2 for AGREE II scores and Section 4 Evidence Review for a summary of recommendations.)

GUIDELINE REVIEW AND APPROVAL

Internal Review

For the guideline document to be approved, 75% of the content experts who comprise the GDG Expert Panel must cast a vote indicating whether they approve the document, or abstain from voting for a specified reason, and of those that vote, 75% must approve the document. In addition, the PEBC Report Approval Panel (RAP), a three-person panel with methodology expertise, must unanimously approve the document. The Expert Panel and RAP members may specify that approval is conditional, and that changes to the document are required. If substantial changes are subsequently made to the recommendations during external review, then the revised draft must be resubmitted for approval by RAP and the GDG Expert Panel.

External Review

Feedback on the approved draft guideline is obtained from content experts and the target users through two processes. Through the Targeted Peer Review, several individuals with content expertise are identified by the GDG and asked to review and provide feedback on the guideline document. Through Professional Consultation, relevant care providers and other potential users of the guideline are contacted and asked to provide feedback on the guideline recommendations through a brief online survey. This consultation is intended to facilitate the dissemination of the final guidance report to Ontario practitioners.

ACKNOWLEDGEMENTS

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- Sara Miller for copyediting.

Interventions to Address Sexual Problems in People with Cancer

Section 4: Systematic Review

INTRODUCTION

Sexual dysfunction in cancer patients is a significant problem. It was first documented 65 years ago [79]. Over the past decade or so, the literature has grown with numerous original articles and reviews documenting the prevalence of sexual dysfunction in cancer survivors. For example, in women with cervical cancer treated with radiotherapy, 85% reported persistent decreased interest and 35% to 55% reported vaginal symptoms [80]. Up to 70% of women with breast cancer report sexual function difficulties [81]. In men with prostate cancer receiving androgen deprivation therapy, loss of libido is reported by 58% to 90% of patients, erectile dysfunction by 73% to 95% of patients, and shortened penile length by up to 93% of patients [82]. Approximately 40% to 60% of men and 30% to 45% of women with rectal cancer report sexual difficulties of some type [83]. Erectile dysfunction and ejaculation difficulties are reported by up to 80% of men treated with total mesorectal excisions [84].

Physician assessment of sexual dysfunction is likely to underestimate the problem. Therefore, clinical assessment of sexual dysfunction may be aided by a patient-reported outcome measure. For both sexes, numerous patient-reported outcome measures exist. For men, the IIEF-5 [85] is commonly used for assessing erectile dysfunction. In women, the Female Sexual Function Index (FSFI) [86] is used most commonly amid a large number of other measures [87]. The wide range of measures available is reflected in the literature regarding prevalence of sexual dysfunction and evaluation of interventions to improve sexual dysfunction. Regardless, a comprehensive assessment is required prior to considering treatment.

More recently, investigators have begun to earnestly evaluate interventions to improve sexual dysfunction in cancer survivors. Systematic reviews are available but tend to be restricted to certain cancers or treatments.

The purpose of this guideline is to provide recommendations regarding interventions to improve sexual function in individuals with cancer. The guideline includes all interventions (pharmacological, psychosocial counselling, device, or a combination) and all cancer types. The guideline is organized by specific conditions with which a provider might be faced (Table 4-1). This guideline assumes that a comprehensive assessment has been completed in order to establish that a condition is present. Assessment of sexual function is not included in this document.

The Working Group of the Interventions to Address Sexual Problems in People with Cancer Guideline Development Group developed this evidentiary base to inform recommendations as part of a clinical practice guideline. Based on the objectives of this guideline (Section 2), the Working Group derived the research question outlined below.

RESEARCH QUESTION

What is the effectiveness of pharmacological interventions, psychosocial counselling, or devices to manage sexual problems after cancer treatment? More specifically, we examined issues in men and in women separately.

Table 4-1 Sexual Dysfunction Symptoms or Conditions

Women	Men
Sexual response • Decreased desire • Decreased arousal • Orgasm (alternate sensation and anorgasmia)	**Sexual response** • Decreased desire • Erectile dysfunction • Orgasm (alternate sensation and anorgasmia) • Absence of ejaculate
Body image • Urinary/fecal incontinence • Ostomies • Alopecia (loss of body hair) • Mastectomy and lumpectomy	**Body Image and Penile Changes** • Urinary/fecal incontinence • Ostomies • Alopecia (loss of body hair) • Penile/testicular changes in size and shape
Intimacy/relationships	**Intimacy /relationships**
Overall sexual function and satisfaction	**Overall sexual function and satisfaction**
Vasomotor symptoms	**Vasomotor symptoms**
Genital symptoms • Dryness • Vaginal stenosis • Pelvic pain • Graft-versus-host disease	**Other** • Fatigue • Dry mouth
Other • Fatigue • Dry mouth	

METHODS

This evidence review was conducted in two planned stages, including a search for systematic reviews followed by a search for primary literature. These stages are described in subsequent sections.

Search for Existing Systematic Reviews

A systematic search for primary literature was completed by CCO's Evidence Search and Review Service (ESRS) for the purpose of this project. The review used structured searches of Ovid MEDLINE, EMBASE, CINAHL, PsycINFO, and Cochrane Database conducted on March 6, 2013. However, due to the lack of intervention studies identified including hematological cancer patients, the ESRS conducted additional searches on May 1, 2014 in the same databases.

Key words and free-text terms were identified through a panel of experts and a review of similar studies. Search terms covered three main areas: cancer, sexual dysfunction, and interventions. Articles were limited to English-language publications and the past 10 years (2003-current). Search strategies excluded commentaries, editorials, letters and abstracts.

In addition to database searches, reviewers conducted hand searches of *The Journal of Sexual Medicine*, *Journal of Sex & Marital Therapy*, *Psycho-Oncology*, *The Journal of Psychosocial Oncology*, and *Supportive Care in Cancer* as well as web-searches through Google, NHS Evidence, the Commonwealth Fund, the Canadian Partnership against Cancer, and the National Cancer Institute.

In addition to this ESRS search, a further search for systematic reviews was conducted by the PEBC to update the literature search. MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews were searched from 2003 to September 2015 using Ovid to identify existing

systematic reviews that addressed one or more of the preceding sexual dysfunction symptoms. Medical Subject Heading terms related to sexual dysfunction, interventions, and cancer were combined with relevant text words and a search filter to identify systematic review citation (see Appendix 3 for the complete search strategy). Inclusion criteria included adult cancer patients, effects of a sexual health intervention, outcomes of sexual response, body image, intimacy or relationships, overall sexual function or satisfaction, and vasomotor or genital symptoms. The search was limited to the English language due to unavailability of translation services.

Identified systematic reviews were evaluated based on their clinical content and relevance. Relevant systematic reviews were assessed using the 11-item Assessment of Multiple Systematic Reviews (AMSTAR) [88] tool to determine whether existing systematic reviews met a minimum threshold for methodological quality and could be considered for inclusion in the evidence base (See Appendix 4 for AMSTAR results).

Search for Primary Literature

The ESRS systematic review identified all evidence until June 2013, so an update of that search was conducted by the PEBC using the ESRS search strategy on September 1, 2015.

Literature Search Strategy

The ESRS conducted structured searches of Ovid MEDLINE, EMBASE, CINAHL, PsycINFO, and Cochrane Database on March 6, 2013. Owing to the lack of intervention studies identified including hematological cancer patients, separate searches were also run by the ESRS on May 1, 2014 in the same databases.

The search strategies used a combination of key words and free-text terms related to cancer and sexuality. Database-specific search strategies were developed using the Ovid MEDLINE search as a template. Key words and free-text terms were identified through a panel of experts and a review of similar studies. Search terms covered three main areas: cancer, sexual dysfunction, and types of interventions. Search strategies excluded commentaries, editorials, letters, and abstracts.

Study Selection Criteria and Process

All hits from the Ovid literature search were input into reference management software (EndNote X6), where duplicate citations were removed. A review of the titles and abstracts that resulted from the search was conducted by one reviewer (CZ). For those items that warranted full-text review, one reviewer (CZ) reviewed each item and consulted the rest of the Working Group whenever there was uncertainty.

Studies were included if they met the following criteria:

- Evaluated an intervention for improving sexual function in cancer patients and/or survivors
- Adult cancer patients/survivors made up at least 50% of the sample. Interventions were included if they incorporated some component that explicitly targeted sexual functioning
- English language because of unavailability of translation services
- Published in 2003 or later
- No restrictions were placed on the type of outcome measures used
- There were no restriction on study design

Data Extraction and Assessment of Study Quality and Potential for Bias

Since the original ESRS review had no restrictions on outcomes used, the Working Group believe that in order to make practical recommendations, the outcomes should be organized

into functional outcomes: sexual response, body image, penile changes, intimacy or relationships, overall sexual function or satisfaction, and vasomotor or genital symptoms. As well, another exclusion criterion was added: case series with less than 20 people. Data extraction was conducted by one author (CZ) and was reviewed by a second independent individual using a data audit procedure. Disagreements were resolved by consensus. The following data were extracted from each relevant article: author, publication year, study population, number of participants, initial treatment, sexual condition, intervention characteristics, outcome measures and scores, attrition, and adverse events.

Synthesizing the Evidence

Owing to the expected clinical heterogeneity among studies (e.g., disease types, treatment, types of studies), the nature of the interventions, and the outcomes assessed, meta-analysis was not planned.

RESULTS

Search for Existing Systematic Reviews

The search for existing systematic reviews beyond the ESRS review (5 reviews) identified 12 reviews, eight of which were retrieved for full-text review. Thirteen reviews were evaluated for quality using the AMSTAR [88] (see Appendix 4 for scores).

Search for Primary Literature

The search for primary literature was updated and some studies from the original search were subsequently excluded because they had to do with compliance, which was not in the scope of the objectives or did not meet the post hoc selection criteria (at least 20 participant case series).

Literature Search Results

One hundred and three studies were identified that met the inclusion criteria (see Appendix 5). Table 4-2 summarizes the number and types of studies included per sexual dysfunction condition. Systematic reviews were found for most conditions but did not meet all of aspects to the conditions so primary literature was also searched.

Table 4-2. Studies selected for inclusion.

Conditions/Symptoms	Number of sources that were included
Women -Overall	5 systematic reviews [7,10,14-16] 12 RCTs [2,3,8,9,11,12,17,19,20,25,89,90] 8 other [1,4-6,13,21,26,91]
Sexual Response	0 systematic reviews 2 RCTs [2,3] 3 other [1,4,5]
Body Image	2 systematic reviews [7,10] 6 RCTs [2,3,8,9,19,20] 1 other [13]
Intimacy/relationships	0 systematic reviews 5 RCTs [2,3,8, 9,12] 3 other [4,5,13]
Overall Sexual Function and Satisfaction	4 systematic reviews [7,14-16] 11 RCTs [3,8,9,11,12,17-20,89,90]

	5 other [4-6,13,21]
Vasomotor symptoms	3 guidelines [22-24] 0 systematic reviews 4 RCTs [19,20,89,90]
Genital Symptoms	2 guidelines [22,92] 2 systematic reviews [15,16] 5 RCTs [11,19,20,25,89] 3 other [21,26,91]
Men -Overall	4 systematic reviews [27,28,53,54] 27 RCTs [30-41,49,50,52,55,56,58,60-62,65-67,93-95]
Sexual Response	2 systematic reviews [27,28] 20 RCTs [29-37,39-41,49,50,52,55,56,58,67,93-96] [30-38,40-42,50-52,56,57,59,68,93-95,106] 19 other [6,42-48,51,57,97-105]
Body Image	0 systematic reviews 2 RCTs [41,58] 1 other [59]
Intimacy/relationships	1 systematic review [54] [55] 5 RCTs [38,55,56,60,61] 3 other [63,64,106]
Overall Sexual Function and Satisfaction	2 systematic reviews [53,54] 6 RCTs [31,38,41,65-67] 3 other [6,106,107]
Vasomotor Symptoms	4 RCTs [68-70,74] 7 other [71-73,75,108-110]

Abbreviations: RCTs, randomized controlled trials

Study Design and Quality

The guidelines were evaluated for reporting quality using the AGREE II [78]. As well, the relevance of the guidelines was evaluated for context and their utility in Ontario recommendations.

The systematic reviews were assessed using the AMSTAR criteria [88]. Using these criteria, the scores of the reviews varied, but most scored well. Common limitations were a lack of a list of excluded studies and a lack of assessment of publication bias. The systematic reviews focussed on different interventions, populations, and outcomes, and provided valuable information to inform the objective of the guideline.

The primary studies included all levels of evidence, RCTs, prospective and retrospective cohort studies, case/control studies and case series of more than 20 participants. There were many methodological issues with the evidence. The most common limitations overall were low response rates, high attrition rates, no testing of sexual dysfunction before the intervention, lack of power calculations, selective reporting, lack of blinding of participants and assessors, and lack of randomization (see Appendix 6 for quality assessment tables and Appendix 7 for GRADE tables).

Outcomes

Women

There were five systematic reviews relevant to the objectives of the guideline [7,10,14-16]. There were 20 studies that examined interventions for female sexual dysfunction issues [1-6,8,9,11-13,17,19-21,25,26,89-91]. Many examined different outcomes using various scales and measures.The results of the studies were broken down into symptoms deemed important to patients and caregivers (see Appendix 8 for data tables).

Sexual Response (desire, arousal, orgasm)

Six studies examined sexual response as an outcome [1-6]. Two were RCTs [2,3] and three were pre/post intervention studies [1,4,5]. The studies were of moderate and lower quality. One study used a pharmacological intervention [1], three used a psychosocial intervention [2-4], and one used a therapeutic device [5]. Mathias et al. [1] gave patients bupropion in a small pre-post treatment study and found a significant increase in the Arizona Sexual Experience Scale. Brotto et al. [4] conducted a non-randomized pre-post study with a wait list control evaluating mindfulness-based (CBT) using the FSFI as a measure. They found a significant difference in arousal, lubrication, and orgasm domains when comparing pre-post scores after three 90-minute sessions. Kalaitzi et al. [2] found that six sessions of a Combined Brief Psychosexual Intervention (CBPI) with partners significantly improved sex initiation and orgasm frequency. Jun et al. [3] found no significant difference in sexual interest after a group-counselling program called Sexual Life Reframing Program. Ayaz et al. [6] used the PLISSIT model with colorectal patients with a stoma and found a significant improvement in the anorgasmia domain of the Golombok–Rust Inventory of Sexual Satisfaction (GRISS) Scale. Schroder et al. [5] studied a clitoral stimulation device in 13 women with cervical cancer and found significant differences pre-post treatment in the sexual desire, arousal, lubrication, and orgasm domains of the FSFI.

Body Image

Two systematic reviews examined the impact of psychosocial interventions on body image [7,10]. Hersch et al. [7], after analyzing seven studies, concluded that cognitive behavioural interventions may have a positive effect on body image. Scott et al. [10] identified 12 studies and concluded that individual and peer-group studies produced no or few significant benefits for body image.

Seven studies were identified examining body image [2,3,8,9,13,19,20]. Five studies used psychosocial counselling [2,3,8,9,13] [2,3,7,8,12] and two used a combination of counselling and exercise [19,20]. The quality of the studies for this outcome is moderate overall. Three of the psychosocial intervention studies included partners in the counselling sessions [2,8,13]. All had different counselling methods. Decker et al. [13], using systems theory-based counselling, found no difference within or between groups using the Body Image Scale. Kalaitzi et al. [2] found that six sessions of CBPI significantly improved the participants' body image satisfaction when naked or dressed. Baucom et al. [8], using the Self-image Scale, found a very large effect size for self-acceptance and partners' acceptance when comparing relationship enhancement therapy with the control group. Two of the psychosocial intervention studies had group-based interventions [3,9]. Sharif et al. [9] found a significant difference between the intervention and control arms using the European Organization for Research and Treatment of Cancer Quality of Life Breast Cancer (EORTC-QLQ-BR23) body image subscale with a peer-led group. The other study by Jun et al. [3] evaluated a sexual life reframing program using the Cancer Rehabilitation Evaluation System Questionnaire (CARES) Body Image subscale and did not find a significant difference between the control and intervention groups.

Two studies used a combination of counselling and physical exercise (PE) [19,20]. Duijts et al. [19] compared CBT with PE therapy and a combination of both. Using the EORTC-QLQ-BR23 body image subscale, no significant group differences were observed. This was a large

randomized study but body image was not the primary outcome. Yang et al. [20] compared a pelvic floor rehabilitation program plus counselling and one bio-feedback session with a usual care group and did not find a significant difference between groups using EORTC QLQ-CX24 body image subscale (Cervical Cancer Module) or using a bladder function score or bowel function score of the Australian Pelvic Floor Questionnaire.

Intimacy/Relationships

Seven studies examined the effect of a psychosocial intervention on intimacy and relationships [2-4,8,11-13]. The quality of the studies was moderate to low. Three studies included partners in the intervention. Decker et al. [13] found no statistical difference between the group receiving system theory-based counselling and the comparison group for the patients of their partners, using three different measures. Baucom et al. [8] found a large effect of Relationship Enhancement Therapy on both the patients and their partners using the Quality of Marriage Index. Kalaitzi et al. [2] found a significant difference in the Satisfaction with Relationship score in favour of the CBPI group. Of the four patient studies (3 group [3,11,12], 1 individual [4]), only Rowland et al. [11] found a significant difference between the psycho-educational group and the control group when questioned about partner communication, using the Revised Dyadic Adjustment Scale (DAS) questionnaire. Jun et al. [3], Brotto et al. [4], and Classen et al. [12] did not find any significant changes after counselling sessions using the Martial Intimacy Questionnaire, the Sexual Function Questionnaire Relationship Score, or the Illness Intrusiveness Ratings Scale.

An eighth study by Schroder et al. [5] evaluated the impact of a clitoral stimulation device and found no significant difference in the before and after DAS scores.

Overall Sexual Functioning and Satisfaction

Four systematic reviews examined studies using overall sexual functioning as an outcome [7,14-16]. Taylor et al. [14] found 17 studies covering psycho-educational interventions and concluded that none of the interventions delivered to groups of patients resulted in positive effects on overall sexual functioning since patients may not have felt comfortable openly discussing sexual issues in this environment. All the interventions delivered to couples reported some positive findings. Hersch et al. [7] searched for studies using psychosocial interventions. Six studies were found and it was concluded that counselling alone or with partners had some positive effects on sexual functioning. Miles and Johnson [15,16], in two systematic reviews, searched for studies examining the benefits and harms of vaginal dilation therapy for women receiving pelvic radiotherapy and found no evidence that vaginal dilation improves overall sexual function.

Sixteen studies examined interventions for overall sexual functioning and satisfaction }[3-6,8,9,11-13,17-21,89,90]. Ten studied psychosocial interventions, and were of moderate to lower quality [3,4,8,9,11-13,17,18,90]. In the two studies that used partners, Baucom et al. [8] found a medium effect size using the Derogatis Inventory of Sexual Functioning, and Decker et al. [13] did not find a significant difference between the intervention and usual care groups using the Watts Sexual Functioning scale. In the eight patient counselling studies (4 group [3,9,11,12], 4 individual [4,17,18,90]), various scales and questions were used to measure overall sexual function and satisfaction. Three studies used the FSFI to measure overall sexual function [4,18,90]. In one study, Schover et al. [90] (2011) found no difference between the in-person peer counselled (three sessions) versus telephone peer counselled (<30 minutes) groups or before or after the intervention when the groups were analyzed together. In another Schover et al. [18] study (2013), the self-help plus individual counselling group had significantly different FSFI scores than the web-based self-help group. Brotto et al. [4] used the FSFI and found a significant improvement in FSFI scores between the individual CBT group and the

waitlist group scores but no difference in the in the Female Sexual Distress Scale (FSDS) score for all study participants. Classen et al. [12] also used the FSDS and found a medium effect size in favour of the online support group. Rowland et al. [11] asked participants in psycho-educational counselling groups questions regarding sexuality and found no significant difference in terms of sexual satisfaction. Sharif et al. [9] used the EORTC-BR23 Sexual Function and Sexual Enjoyment subscales and found a significant difference in favour of the intervention for both. Jun et al. [3] used the CARES subscales for sexual interest and sexual dysfunction and found no significant difference between the Sexual Life Reframing Program counselling group and the usual care group. But they did find a significant difference for the sexual satisfaction using a Sexual Satisfaction Scale developed for Korean women. Marcus at el. [17] used a scale developed for their study on sexual dysfunction and found that a 16-session telephone counselling program significantly improved scores in the intervention group compared with the control group. Ayaz et al. [6], using the PLISSIT model, found a significant improvement in the case group compared with the control group in the overall GRISS scale score and the GRISS satisfaction subscale.

In the three combination physical/psychosocial studies, there were significant improvements in overall sexual function over time [19-21]. Duijts et al. [19] used a combination CBT and PE intervention and found a significant improvement in the Sexual Activity Questionnaire (SAQ) when comparing both the CBT-only group with the control group and the CBT/PE group with the control group. Yang et al. [20] found a significant difference between the pelvic floor exercise/counselling and usual care groups in the EORTC-QLQ CX24 Sexual Function subscale but not in the Sexual Worry, Sexual Activity and Sexual Enjoyment subscales. Juraskova et al. [21] conducted a Phase I/II study using pelvic floor relaxation with a vaginal moisturizer and olive oil and found a significant increase in the SAQ and the FSFI scores. Schroder et al. [5] found a significant increase in pre-post treatment in the FSFI and the Derogatis Interview for Sexual Functioning (DISF) scores for patients using the clitoral stimulation device. Sismondi et al. [89] in a large RCT found a significant improvement in the Women's Health Questionnaire (WHQ) Sexual Function Domain score in women taking tibolone compared with women on placebo. Tibolone is not approved for use in Canada.

Vasomotor Symptoms

Two societies recently released guidelines that provide recommendations for women with vasomotor symptoms; the SOGC and the NAMS. These guidelines were developed for women in general and included trials with women in cancer in the literature and are relevant for women with non-hormone-sensitive cancers. They form the main evidentiary basis for hormone prescribing in women with a history of cancer.

The SOGC developed a guideline for healthy women on the management of menopause with specific recommendations for women presenting with vasomotor or urogenital symptoms [22]. Their recommendations for vasomotor issues include:

- Healthcare providers should offer hormone therapy (HT), estrogen alone or combined with a progestin, as the most effective therapy for the medical management of menopausal symptoms.
- Progestins alone or low-dose oral contraceptives can be offered as alternatives for the relief of menopausal symptoms during the menopausal transition.
- Nonhormonal prescription therapies, including certain antidepressant agents, gabapentin, and clonidine, may afford some relief from hot flashes but have their own side effects. These alternatives can be considered when HT is contraindicated or not desired.
- There is limited evidence of benefit for most complementary and alternative approaches to the management of hot flashes. Without good evidence for effectiveness, and in the face of minimal data on safety, these approaches should not be recommended. Women should

be advised that, until January 2004, most natural health products were introduced into Canada as “food products” and did not fall under the regulatory requirements for pharmaceutical products. As such, most have not been rigorously tested for the treatment of moderate to severe hot flashes, and many lack evidence of efficacy and safety.

- Lifestyle modifications, including reducing core body temperature, regular exercise, weight management, smoking cessation, and avoidance of known triggers such as hot drinks and alcohol, may be recommended to reduce mild vasomotor symptoms.
- Healthcare providers should periodically review the risks and benefits of prescribing HT to a menopausal woman in light of the association between duration of use and breast cancer risk.
- Healthcare providers may prescribe HT for menopausal symptoms in women at increased risk of breast cancer with appropriate counselling and surveillance.
- Health care providers should clearly discuss the uncertainty of risks associated with systemic HT after a diagnosis of breast cancer in women seeking treatment for distressing symptoms (vasomotor symptoms or vulvovaginal atrophy).

The NAMS produced two positions statements [23,24] regarding vasomotor symptoms. One statement focuses on HT and the other focuses on non–HT for vasomotor symptoms. The 2012 HT guideline [24] recommends:

- Individualization is of key importance in the decision to use HT and should incorporate the woman’s health and quality of life priorities as well as her personal risk factors, such as risk of venous thrombosis, coronary heart disease, stroke, and breast cancer.
- The recommendation for duration of therapy differs for estrogen-progestogen therapy (EPT) and estrogen therapy (ET). For EPT, duration is limited by the increased risk of breast cancer and breast cancer mortality associated with three to five years of use; for ET, a more favourable benefit-risk profile was observed during a mean of seven years of use and four years of follow-up, a finding that allows more flexibility in duration of use.
- Women with premature or early menopause who are otherwise appropriate candidates for HT can use HT at least until the median age of natural menopause (age 51 years).
- Longer duration of treatment can be considered if needed for symptom management.
- Although ET did not increase breast cancer risk in the Women's Health Initiative, there is a lack of safety data supporting the use of ET in breast cancer survivors, and one RCT reported a higher increase in breast cancer recurrence rates.
- Both transdermal and low-dose oral estrogen have been associated with lower risks of venous thromboembolism and stroke than standard doses of oral estrogen, but RCT evidence is not yet available.

The NAMS 2015 statement on continuing use of systemic HT after age 65 years [111] states:

- Provided that the woman has been advised of the increase in risks associated with continuing HT beyond age 60 and has clinical supervision, extending HT use with the lowest effective dose is acceptable under some circumstances, such as for the woman who has persistent bothersome menopausal symptoms and for whom her clinician has determined that the benefits of menopause symptom relief outweigh the risks.
- Use of HT should be individualized and not discontinued solely based on a woman’s age. The decision to continue or discontinue HT should be made jointly by the woman and her healthcare provider.

The NAMS 2015 non-hormonal position statement [23] concludes:

- CBT and, to a lesser extent, clinical hypnosis have been shown to be effective in reducing vasomotor symptoms.

- Paroxetine salt is the only non-hormonal medication approved by the United States Food and Drug Administration for the management of vasomotor symptoms, although other selective serotonin reuptake/norepinephrine reuptake inhibitors, gabapentinoids, and clonidine show evidence of efficacy.
- Some therapies that may be beneficial for alleviating vasomotor symptoms are weight loss, mindfulness-based stress reduction, the S-equol derivatives of soy isoflavones, and stellate ganglion block, but additional studies of these therapies are warranted.
- There are negative, insufficient, or inconclusive data suggesting the following should not be recommended as proven therapies for managing vasomotor symptoms: cooling techniques, avoidance of triggers, exercise, yoga, paced respiration, relaxation, over-the-counter supplements and herbal therapies, acupuncture, calibration of neural oscillations, and chiropractic interventions. Incorporating the available evidence into clinical practice will help ensure that women receive evidence-based recommendations along with appropriate cautions for appropriate and timely management of vasomotor symptoms.

Four studies were found that assessed vasomotor symptoms and interventions in a cancer population [19,20,89,90]. Sismondi et al. [89] had participants take tibolone daily for two years and found a significant improvement in the WHQ Vasomotor Domain between the intervention and control groups at all measures of the study, i.e., 26, 52, 78 and 104 weeks. Schover et al. [56] found significant decreases in hot flashes for both the in-person and the telephone counselling groups. Duijts et al. [19], in a high-quality study, found a significant improvement in the Hot Flash Rating Scale scores for both the CBT plus exercise group and the CBT-only group compared with the control group. Yang et al. [20] did not find a significant difference between the pelvic floor rehabilitation group and the control group in the EORTC QLQ –CX24 Menopausal Symptoms Subscale.

Genital Symptoms

The SOGC and NAMS also have developed recommendations for women with genitourinary syndrome of menopause. These guidelines were developed for women without cancer, but are relevant for women with non-hormone-sensitive cancers. They form the main evidentiary basis for hormone prescribing in women with a history of cancer.

The SOGC guideline [22] recommends:

- Conjugated estrogen cream, an intravaginal sustained-release estradiol ring, and low-dose estradiol vaginal tablets are recommended as effective treatment for vaginal atrophy.
- Routine progestin co-therapy is not required for endometrial protection in women receiving vaginal ET in an appropriate dose.
- Vaginal lubricants may be recommended for subjective symptom improvement of dyspareunia.
- Because systemic absorption of vaginal estrogen is minimal, its use is not contraindicated in women with contraindications to systemic estrogen therapy, including recent stroke and thromboembolic disease. However, there are currently insufficient data to recommend its use in women with breast cancer who are receiving aromatase inhibitors (where the goal of adjuvant therapy is a complete absence of estrogen at the tissue level). Its use in this circumstance needs to be dictated by quality-of-life concerns after discussion of possible risks.
- Systemic ET should not be recommended for the treatment of postmenopausal urge or stress urinary incontinence given the lack of evidence of therapeutic benefit. Vaginal estrogen may, however, be recommended, particularly for the management of urinary urge incontinence.

- As part of the management of stress incontinence, women should be encouraged to try non-surgical options, including weight loss (in obese women). Pelvic floor physiotherapy, with or without biofeedback, weighted vaginal cones, functional electrical stimulation, and/or intravaginal pessaries can also be recommended.
- Behavioural modification, functional electrical stimulation, and antimuscarinic therapy are recommended for the treatment of urge urinary incontinence.
- Vaginal ET can be recommended for the prevention of recurrent urinary tract infections in postmenopausal women.

The NAMS management statement for symptomatic vulvovaginal atrophy [92] recommends:

- First-line therapies for women with symptomatic vulvovaginal atrophy include non-hormonal lubricants with intercourse and, if indicated, regular use of long-acting vaginal moisturizers.
- For symptomatic women with moderate to severe vulvovaginal atrophy and for those with milder vulvovaginal atrophy who do not respond to lubricants and moisturizers, ET either vaginally at low dose or systemically remains the therapeutic standard. Low-dose vaginal estrogen is preferred when vulvovaginal atrophy is the only menopausal symptom.
- For women with a history of breast or endometrial cancer, management depends on a woman's preference, need, understanding of potential risks, and consultation with her oncologist.
- ET carries a class effect risk of venous thromboembolism. Low-dose vaginal estrogen may carry a very low risk, but there has been no report of an increased risk in the vaginal estrogen clinical trials. Data in high-risk women are lacking.
- A progestogen is generally not indicated when low-dose vaginal estrogen is administered for symptomatic vulvovaginal atrophy. Endometrial safety data are not available for use longer than one year.
- Spotting or bleeding in a postmenopausal woman who has an intact uterus requires a thorough evaluation that may include transvaginal ultrasound and/or endometrial biopsy.
- For women treated for non-hormone-dependent cancer, management of vulvovaginal atrophy is similar to that for women without a cancer history.
- Vaginal ET, with appropriate clinical surveillance, can be continued as long as bothersome symptoms are present.
- Proactive education on vaginal health is recommended for postmenopausal women.

Two systematic reviews examined studies in women with cancer and vaginal dilation to prevent vaginal stenosis [15,16]. Miles et al. (2014) [15] found no RCTs comparing dilation versus no dilation in their systematic review for women receiving pelvic radiotherapy. Johnson et al. [16] found two trials showing that encouraging patients receiving pelvic radiotherapy to use dilation increased compliance of dilator use. Other studies were also found but were not of good methodological quality. Both systematic reviews concluded that there is no reliable evidence concerning routine vaginal dilation during or after pelvic radiotherapy and whether or not it decreases vaginal stenosis.

Eight studies examining genital symptom outcomes, such as vaginal dryness and dyspareunia, were of high or moderately high quality [11,19-21,25,26,89,91]. Three used pharmacological interventions [25,89,91]. Sismondi et al. [89] found that vaginal dryness significantly improved with tibolone in an RCT. Lee et al. [25] found that the use of vaginal pH-balanced gel significantly improved dryness and dyspareunia in the intervention group compared with the control group. In a Phase I/II study testing different topical testosterone doses, Witherby et al. [91] found a significant pre-post improvement for vaginal itching, dryness, and dyspareunia for all patients using an unvalidated measure, but no significant

difference between low or high doses. (Testosterone is not approved for women in Canada.) Rowland et al. [11] found no difference in dyspareunia scores with psycho-educational group counselling. Law et al. [26] found that of the patients who had a decrease in vaginal dilator size one month after radiation therapy, at six months 52% of patients returned to the pre-radiation therapy vaginal dilator size. The interpretation was that vaginal dilation was effective in minimizing stenosis.

Three studies used combination physical/psychosocial interventions [19-21]. Duijts at al. [19] found a significant improvement when comparing the CBT only, the exercise only and the CBT plus exercise groups with the control group using the Bristol Female Lower Urinary Tract Symptom Questionnaire in women with breast cancer. A clinically relevant improvement was found when comparing intervention and control groups for the sexual/vaginal function subscale of the EORTC QLQ-CX24 in the Yang et al. [20] study comparing pelvic floor rehabilitation and counselling versus usual care with patients with gynecological cancer. A significant improvement in visual analogue score pain assessment of dyspareunia for patients with breast cancer was found in the Juaskova et al. [21] study of pelvic floor muscle relaxation plus vaginal moisturizer use and olive oil use.

Men

There were 62 studies that examined interventions for male sexual dysfunction [6,30-52,55-75,93-110]. There were many different outcomes examined using various interventions, doses, scales, and measures. The studies were organized into symptom areas deemed important for patients and caregivers.

There were four systematic reviews that studied the effects of different interventions on sexual dysfunction for men with prostate cancer [27,28,53,54]. Both Miles et al. [27] and Montsori et al. [28] found that PDE5i are an effective treatment for erectile dysfunction in men after radical prostatectomy. Montorsi et al. [28] specifically studied sildenafil and concluded that the odds of responding improved 12-fold when there is preservation of at least one neurovascular bundle.

Lassen et al. [53] studied the effects of psycho-educational interventions following radical prostatectomy and found eight RCTs, six of which included partners. The authors concluded that psycho-educational interventions may improve urinary incontinence, bowel bother, sexual function and, to some extent, sexual bother. They suggested it would be sensible to implement post-prostatectomy psycho-educational interventions into nursing discharge planning. Chisholm et al. [54] found 16 RCTs that studied psychosocial interventions that addressed sexual or relationship functioning for men with prostate cancer and their partners. Five studies placed an emphasis on sexual functioning, and the majority (4 of 5) found a positive effect of the interventions on sexual function. The authors reported that interventions were more effective when using more complex strategies to target sexuality in men and in relationships. Those studies that had sexual functioning as a minor focus did not find an effect. The evidence was inconclusive regarding improvements in relationship functioning using dyadic adjustment or marital distress.

Sexual Response

Pharmacological Interventions

Thirty-nine different studies examined sexual response issues in men [6,30-37,39-52,55,56,58,67,93-95,97-105]. Two studies included colorectal cancer patients [29,42]. Park et al. [29] conducted an RCT using udenafil for 12 weeks and found that the treatment group had significant increase in their IIEF score after 12 and 24 weeks compared with the control group (not available in Canada). Nishizawa et al. [42] studied the use of different doses of PDE5i on men who had a total mesorectal excision and requested treatment for erectile dysfunction. In

this lower quality pre/post study, 11 of 16 men who had asked for treatment had a higher IIEF score after 12 months.

The remaining studies were conducted in men with prostate cancer. Four studies examined the use of PDE5i for men who had been treated with brachytherapy [30,43,44,103]. Three used the IIEF as a measure of sexual response [30,43,103] and all four together were of a lower quality [44]. Pahlajani et al. [43] conducted a non-RCT and found a significant difference between treatment and control groups at one year. A small RCT conducted by Illic et al. [30] found a difference between treatment and placebo groups at one and six months but not at one or two years. Raina et al. [103], using a prospective comparative cohort study, found that overall, the four-year natural erectile rate was 29% for those not using a PDE5i, but when patients who used a PDE5i are added, the overall potency rate increased to 70%. Pugh et al. [44] gave patients a low dose of tadalafil two weeks before starting brachytherapy and found that a significant increase in their Expanded Prostate Cancer Index Composite (EPIC) Questionnaire Sexual Function Score after 12 and 23 months, indicating improved sexual function and is sustained.

Six studies examined the effects of a pharmacological intervention on sexual response in men with prostate cancer who had received external beam radiotherapy [31-35,45,67]. One was an RCT [67], four used a randomized controlled cross-over design [31-35] and one was a pre/post-intervention study [45]. Taken together, the studies were of moderate to low quality because of a high risk of bias and selective reporting. Zelefsky et al. [67] found significant differences in the treatment and placebo groups at 12 months for the erectile function domain of the IIEF (IIEF-EF) but not for the total IIEF. However, when the scores were separated in androgen deprivation therapy (ADT)-treated (10%) and non-ADT-treated patients (90%), the non-ADT patients scores were significantly improved at all time periods for both scales. Bruner et al. [31], Incrocci et al. [32-34], and Harrington et al. [35] all had patients use the PDE5i in an on-demand dosage and all found a significant difference in IIEF scores in the groups using a PDE5i compared with the placebo controls. Fujioka et al. [45] also found a significant difference in the pre-post PDE5i use IIEF scores.

Eight studies assessed pharmacological interventions in men with prostate cancer who had undergone uni- or bilateral nerve-sparing surgery [36,37,40,41,46,51,52,100]. The studies were of a lower quality due to low numbers of participants, various dosing regimens, high attrition rates, and selective reporting. Five RCTs and one pre-test/post-test trial found a significant difference using the IIEF between the treatment and control groups [36,37,40,41,52,100]. One RCT examining penile rigidity found an increase in the proportion of men with penile rigidity in the treatment groups compared with the control group. Salonia et al. [51] did not find a significant difference between groups at 12 and 18 months but 73% of participants stopped using medications due to lower than expected treatment effects and a lack of interest in sex by themselves or partner. Natali et al. [100] in a retrospective study found at 24 months, the treatment groups (on demand versus a regimented rehabilitative program) were not significantly different from each other, but had significantly higher erectile rates then the no treatment group. In a small pre/post design study, Ogura et al. [46] found that patients had a significantly improved IIEF score after taking sildenafil.

Five studies of lower quality compared medication given on a daily basis versus an on-demand medication routine [41,49-52]. Four studies included patients treated with surgery [41,50-52] and one included patients treated with external beam radiation [49]. Ricardi et al. [49] evaluated the use of PDE5i on-demand versus daily in post-radiotherapy prostate cancer patients. At one month, both groups had a significant improvement in IIEF scores from baseline, but there was no significant difference between the on-demand or daily groups. Montorsi et al. [41] in 2013 compared the percentage of patients with IIEF scores over 21 when taking taladafil daily versus on-demand versus placebo. After nine months there was a significant difference

between the daily and placebo groups. After a six-week drug-free wash-out period, none of the groups were significantly different. In 2008, Montorsi et al. [52] conducted a double-blind placebo-controlled study on the use of nightly vardenafil versus vardenafil on demand. After the nine-month double-blind period, the proportion of patients with IIEF scores ≥22 (defined as mild erectile dysfunction) was significantly greater for the on-demand group. However, compliance was higher in the daily group, which also reported fewer side effects than the on-demand group. Pavlovich et al. [50] compared a nightly dosage of sildenafil plus an on-demand placebo, with a nightly dose of a placebo plus on-demand sildenafil and found no statistical difference between groups even after a one-month drug-free washout period. Salonia et al. [51], using three groups of patients in either a no treatment, daily' or on-demand treatment groups, found a significant difference at six months, but no significant difference among the three groups at 12 and 18 months. This study had a 73% attrition rate.

Three studies compared men with prostate cancer who initiated PDE5i treatment shortly after cancer treatment with those who initiated treatment at a later date [39,47,48]. Two studies included surgical patients [39,48] and one included brachytherapy patients. All of the studies were of lower quality because of poor designs or small number of participants. All three of the studies found a significant improvement in IIEF scores for the groups who started the PDE5i treatment early when compared with the delayed group [39,47,48].

In a retrospective study of a group of patients receiving a PDE5i, Ohebshalom et al. [101] reported that IIEF-EF domain scores were significantly higher in patients who received conformal radiation therapy compared with those who received brachytherapy. These observed differences may have been due to patient selection bias (e.g., age) in this retrospective study.

Three studies also looked at different pharmacological interventions [99,104,105]. Raina et al. [104] in a prospective series, compared MUSE with alprostadil to a non-MUSE group (patients may have tried other forms of therapy) and found that the MUSE group had significantly higher IIEF scores after nine months than the non-MUSE group. Mydio et al. [99] in a retrospective study found that 68% of the patients reported having a much better erection after starting ICI. Baltontin et al. [105] in a prospective case series found testosterone injections had a significant increase in IIEF scores at a median of 31 months after treatment started.

Psychosocial Interventions

Four good-quality studies examined psychosocial interventions using patients and partners [6,55-57]. Canada et al. [55] found that IIEF scores increased over time for all men with prostate cancer after counselling and that there were no differences among the patients in the couples counselling group compared with the individual counselling group. They also found that percentage of patients using erectile dysfunction treatment increased after initiation of psychosocial intervention (31% to 49% at six months). A study by Schover et al. [56] reported that there was a significant increase in IIEF scores for men treated for prostate cancer, for both the Internet-based counselling group and face-to-face counselling groups, over time with no difference between the groups. They also found that those who were using oral or invasive erectile dysfunction treatment had significantly higher IIEF scores than those who were not using erectile dysfunction treatment, but this factor was not controlled for in the analysis of the psychosocial intervention. Ayaz et al. [6] used the PLISSIT model with colorectal patients with a stoma and found a significant improvement in the premature ejaculation and impotence domains of the GRISS Scale. Reese et al. [57] found a moderate effect size in IIEF scores after telephone intimacy-enhancement counselling in men treated for colorectal cancer

Exercise therapy

Lin et al. [94] evaluated pelvic floor exercises in a high-quality RCT and reported a statistically significant difference in IIEF scores between intervention and control groups at six months and 12 months in men treated for prostate cancer. Although the results were statistically significant, it is unclear whether these results are clinically meaningful as average scores in both groups remained well within the range of moderate-severe erectile dysfunction. Almost 20% of patients reported using PDE5i, which was not controlled for in the final analysis. Cormie et al. [96] examined the effects of a 12-week exercise program including resistance and aerobic exercise in a high-quality RCT and found significant improvements in the sexual activity subscale of the EORTC-OL-PR25.

Therapeutic devices

Three studies of low quality evaluated the impact of vasculogenic erectile devices on erectile dysfunction in men with prostate cancer treated with surgery [58,97,98]. Megas et al. [97] prospectively compared tadalafil three times a week with penile prosthesis and found there was a significant difference in IIEF scores in favour of the prosthesis at 12 and 24 months after treatment. A retrospective study by Menard et al. [98] evaluated the IIEF scores of penile prosthesis implantation, comparing a group of prostate cancer patients who underwent radical prostatectomy to vasculogenic erectile dysfunction patients. IIEF scores improved significantly more in the radical prostatectomy group than vasculogenic group from pre-implantation to post-implantation. However, total IIEF scores were significantly lower in radical prostatectomy patients than in vasculogenic erectile dysfunction patients.

In Kohler et al., [58] patients were randomized to receive a VED either one month or six months after radical prostatectomy and were instructed to use the device for 10 minutes a day over a period of five months with no constriction ring. Authors reported significantly higher IIEF scores in the early treatment group than the late treatment group at three and six months after the operation.

Combination treatments

Three studies examined combination interventions in men with prostate cancer [93,95,102]. They were of moderate-low quality. Titta et al. [95], in a high-quality RCT, compared a group of patients receiving prostaglandin E1-ICI (PGE-ICI) to a group of patients receiving both PGE-ICI and sexual counselling. Although IIEF scores increased after PGE-ICI treatment in both groups, results were better in the combined intervention group than the PGE-ICI only group. Dropout reasons in the non-sexual counselling group were reported to be due to marital problems (n=3), drug cost (n=2), and to prolonged pain after injections (n=3). The counselling group yielded a significantly lower degree of medication discontinuance. Engel [93] conducted a study of tadalafil taken three times a week with or without the regular use of a VED and found a significant difference in IIEF-5 score in favour of the combination therapy. Raina et al. [102] observed improvement in penile rigidity, nocturnal erections and penetration rate when combining a PDE5i with a vacuum constriction device (VCD) in patients unsatisfied with the results of the VCD alone.

Body Image

Three studies evaluated body image (an outcome measured as penile length) in men with prostate cancer [41,58,59]. They were of moderate to low quality. Montorsi et al. [41], when comparing daily with on-demand use of tadalafil, found that the daily use group had significantly less loss of penis length than the on-demand group. Kohler et al. [58] randomized patients to the use of a VED every day either one month or six months after radical

prostatectomy and found that the proportion of patients with decreased penile length was significantly higher in the late treatment group than the early treatment group. In a prospective cohort of 39 patients, Dalkin et al. [59] found that in men who were at least 50% compliant with the VED use, 35 of 36 (97%) maintained their stretched penile length, compared with pre-surgery.

Intimacy/Relationships

Eight moderately high-quality studies used outcomes that measured intimacy or relationship issues [38,55,56,60-64,106]. Six were psychosocial couples-based interventions [55,56,60-64]; four were RCTs [38,55,56,60-62] and two were pre/post intervention studies [63,64]. Porter et al. [60,61] found a significant improvement over time in the Quality of Marriage Index scale for relationship quality in the psychosocial intervention group compared with the education-only group. Patients with high baseline levels of "holding back" showed greater improvements in relationship quality and intimacy, while patients with greater "expressiveness" showed improvements in relationship quality and intimacy immediately following the session but not in the longer term. None of the other studies found a significant difference between control and treatment groups or when comparing pre and post scores for intimacy/relationship measures [55,56,62-64]. Hanisch et al. [38] found no significant difference on Locke's Marital Adjustment Test in an RCT examining PDE5i use. Ramsawh et al. [106] authored a retrospective study of penile prosthesis use and did not find any significant changes in the DAS.

Overall Sexual Functioning and Satisfaction

Nine studies examined overall sexual function or satisfaction [6,31,38,41,65-67,106,107]. Three moderate quality studies used a psychosocial intervention [6,65,66]. Molton et al. [65] compared a 10-week CBT stress management intervention to a four-hour CBT management course and found that the 10-week course group scored better on the sexual function subscale of the UCLA Prostate Cancer Index. Siddons et al. [66] also used a CBT stress management group intervention and found a significant increase in sexual confidence using the Prostate Cancer-Related Quality of Life Scale. There were no differences on other domains for the DISF Self Report. Ayez et al. [6] found that using the PLISSIT model with patients with colorectal cancer and a stoma significantly increased the GRISS total score as well as the satisfaction domain when compared with the control group.

Four moderate-quality RCTs studies examined PDE5i versus placebo interventions using various doses, timings, and outcome measures [31,38,41,67]. Zelefsky et al. [67] found that patients using sildenafil daily had a significant improvement in overall satisfaction domain of the IIEF at 24 months. When score with separated into ADT and non-ADT groups, for non-ADT patients, overall satisfaction scores were significantly different between groups at six, 12, and 24 months. Montorsi et al. [41] found a significant difference in Sexual Encounter Question questions, five concerning satisfaction, and found a significant difference between the daily use and placebo groups at nine months, but not with any other comparisons. Bruner et al. [31] found a significant difference between the control and the intervention group using the SAQ but not a clinical meaningful difference. One small RCT by Hanisch et al. [38] did not report the PDE5i dose and did not find a significant difference on the SAQ between the treatment and placebo groups.

Lee et al. [107], in a retrospective study, compared radical prostatectomy and radiation therapy with both groups using PDE5i and found no difference between the two groups using the UCLA Prostate Cancer Index sexual functioning scale. Those with better pre-cancer sexual function were more likely better sexual function post-treatment. Pugh et al. used an early but

low dose of tadalafil in men with prostate cancer treated with brachytherapy and found a significant improvement in the EPIC sexual function domain in a pre-post comparison.

Ramsawh et al. [106] found the there was a significant different in the Erectile Dysfunction Inventory of Treatment Satisfaction score and the EORTC-QOL–Sexual Functioning Subscale between those that had received a penile prosthesis and those who did not. These differences were observed despite the use of alternative sexual aids (i.e., ICI, sildenafil, and/or VED) in 52.4% of the participants in the control group. However, this was a retrospective study with a significant risk of selection bias.

Vasomotor Symptoms

Eleven studies of lower quality examined hot flashes in men on ADT [68-75,108-110]. Seven used pharmacological interventions and assessed the effects of venlafaxine [68,69] [69,70], paroxetine [108,109], gabapentin [70,71], medroxyprogesterone acetate [68], cyproterone acetate [68], *Salvia officinalis* extract [110], or soy protein powder [69] on the number of and the severity of hot flashes. Four studies examined the ability of acupuncture to decrease hot flashes in men [72-75].

In an RCT, venlafaxine was not found to be better than the medications it was compared with and in fact was less effective than medroxyprogesterone acetate and cyproterone acetate [68]. Another RCT found venlafaxine improved hot flush counts and severity at 12 weeks [69]. Gabapentin was found to be effective in the larger dose (900 mg) compared with a placebo and a 300 mg dose in reducing the number and severity of hot flashes in an RCT comparing different gabapentin dosages [70]. In an open-label continuation of this RCT, patients tended to medicate themselves at a higher dose of 600 mg/day when allowed to modify the gabapentin regimen [71]. Two very small prospective studies found significant decreases in the number and severity of hot flashes in men taking paroxetine after four weeks [108,109]. One small prospective study found that *S. officinalis* extract decreased the Hot Flash Count and Hot Flash Severity Moyad score after 10 weeks [110].

Four smaller studies examined the effect of acupuncture on hot flashes via traditional [72-74], electrostimulation [74], and auricular methods [75]. All four studies found significant decreases in the number and intensity of hot flashes after acupuncture regardless of the method used.

Ongoing, Unpublished, or Incomplete Studies

Table 4-3. Ongoing trials.

Protocol ID	Title and details of trial
NCT00057759	Sildenafil in Treating Erectile Dysfunction in Patients With Prostate Cancer. Randomized clinical trial to study the effectiveness of sildenafil in treating erectile dysfunction in patients who have undergone radiation therapy and hormone therapy for prostate cancer in clinical trial RTOG-9910.
NCT01654458	A Randomized Controlled Trial of an Online Support Group for Sexual Distress Due to Gynecologic Cancer. The primary aim of this study is to determine whether a professionally facilitated, information-rich, online support group is beneficial for women who are sexually distressed due to gynecological cancer and the side effects of treatment.
NCT00931528	Tadalafil in Preventing Erectile Dysfunction in Patients With Prostate Cancer Treated With Radiation Therapy. This randomized Phase III trial is studying tadalafil to see how well it works compared with a placebo in preventing erectile dysfunction in patients with prostate cancer treated with radiation therapy.

NCT00483678	Couples Therapy to Enhance Intimacy Between Patients With Advanced or Recurrent Prostate Cancer and Their Partners. This randomized clinical trial is studying how well couples therapy enhances intimacy and reduces psychological distress in patients with advanced or recurrent prostate cancer and in their partners.
NCT02091765	KIS Study: A Study Evaluating the Effectiveness of an Internet-based Therapy Program for Sexuality and Intimacy Problems in Women Treated for Breast Cancer. The purpose of this study is to evaluate the efficacy and cost-effectiveness of an Internet-based cognitive behavioural therapy program in alleviating problems with intimacy and sexuality in women treated for breast cancer.
NCT00075855	Low-Dose Testosterone in Improving Libido in Postmenopausal Female Cancer Survivors. This randomized Phase III trial is studying how well low-dose testosterone works to improve libido in postmenopausal cancer survivors.
NCT02096783	Scripted Sexual Health Informational Intervention in Improving Sexual Function in Patients With Gynecologic Cancer. This randomized pilot clinical trial studies the feasibility of a pre-operative and/or post-operative scripted sexual health informational intervention and how well it works in improving sexual function in patients with gynecological cancer.
NCT01881022	An Internet-based Psychosexual Intervention for Couples Following Treatment for Breast Cancer (IPSIC). The purpose of this study is to develop and evaluate an online psychosexual program geared to the unique needs of couples experiencing sexual distress after breast cancer.
NCT00080808	Nerve-Sparing Radical Prostatectomy With or Without Nerve Grafting Followed by Standard Therapy for Erectile Dysfunction in Treating Patients With Localized Prostate Cancer. This randomized Phase II trial is studying nerve grafting and standard therapy to see how well they work compared with standard therapy alone in treating erectile dysfunction in patients undergoing nerve-sparing radical prostatectomy for localized prostate cancer.
NCT01603303	Preventing Sexual Dysfunction With Aromatase Inhibitors. The goal of this study is to learn if it is possible to prevent some aromatase inhibitor side effects, particularly problems with vaginal dryness and pain during sexual activity.
NCT01982058	Intimacy-Enhancing Couples' Intervention for Localized Prostate Cancer. This randomized clinical trial is studying how well therapy enhances communication and intimacy for men with early stage prostate cancer and for their partners.
NCT01697345	Breast Cancer, Aromatase Inhibitor Therapy, and Sexual Functioning: The Effects of Vaginal Testosterone Therapy. The purpose of this study is to evaluate the impact of using a daily compounded vaginal testosterone cream for four weeks (28 days) on breast cancer survivors' reported experience of vulvovaginal symptoms accompanying the use of aromatase inhibitors and their associated quality of life and sexual functioning.
NCT01159678	Online Psychoeducation for Sexual Dysfunction in Cancer Survivors (OPES). The purpose of this study is to test an online psychoeducational intervention for men and women with sexual difficulties after surgery for colorectal (men and women) or gynecological (women only) cancer.
NCT00343382	Pilocarpine in Treating Vaginal Dryness in Patients With Breast Cancer. This randomized Phase III trial is studying pilocarpine to see how well it works compared with a placebo in treating vaginal dryness in patients with breast cancer.

DISCUSSION

One of the most important recommendations that can be made in the context of this guideline is that providers must ask men and women who have been treated for cancer about their sexual function. A guideline regarding interventions is useless until a conversation has been started. Many practitioners still do not raise this issue [112,113]. Barriers such as lack of time [114], lack of training [115], and feeling uncomfortable [116,117] with the subject are often sited to explain why the question is not asked. Clinicians may even make assumptions

about who should be asked [118-120]. Similarly, patients may also feel uncomfortable [121], not want to make the provider uncomfortable [122], or be concerned that the medical team feels the issue is unimportant [121]. When the medical team leaves it to the patient to ask about sexual function issues, the conversation is unlikely to happen. Further, when practitioners fail to raise the issue it reinforces the patient's impression that their sexuality is not worthy of consideration. Clinicians need to approach patients regarding their sexual function, regardless of age, sexual orientation, or the presence of a partner, to see if they have issues or concerns and determine if the patient wishes to discuss further. For practices that routinely incorporate patient-reported outcome measures, an item regarding sexual function can be included [123]. Otherwise, simple approaches to open the door to a discussion have been described [124,125].

Counselling and education have a big role to play in addition to medications or devices. Psychosocial counselling can improve couple communication in general and specifically related to sexual activity [126-128]. It can also improve relationship adjustment [61,126]. Pre-existing difficulties may make assessment and treatment of post-cancer problems more difficult. It is important for patients to understand that they may have to define a "new normal" with respect to their sexual function. Society and media would have us believe that penetrative intercourse is the one acceptable definition of sex. But it can be fruitful for patients to consider developing new sexual "scripts".

Clinics or centres that are considering how to address the needs of patients may be guided by the nature of these recommendations. Discussions, such as those mentioned above, are potentially manageable by an interested primary oncologist. However, an individual who is able to provide education and short-term counselling is key. A doctor, nurse, social worker, or psychologist are all potential options. In addition, a medical provider who is able and comfortable providing discussion and prescriptions for therapeutics is very helpful. One such clinic, geared toward women, found the majority of patients had their needs met without need for referral to additional specialists or for longer-term therapy [129].

The evidentiary base for the guideline has numerous limitations that bear mentioning. For women, the majority of the studies were in breast cancer with some studies including gynecological patients. Similarly in men, the studies were almost exclusively prostate cancer with a few colorectal cancer studies. Absent were intervention studies including individuals with other malignancies, such as colorectal cancer (in women), hematological, or head and neck. Further research is needed to characterize the sexual impact of other cancer diagnoses and treatments, along with potential interventions.

The studies were extraordinarily heterogeneous with respect to experimental methods, nature of the interventions, and outcome measures used. With a few exceptions, the quality of the studies was poor or moderate at best: samples sizes were often small, *a priori* power calculations were not reported, high attrition rates were common (when attrition was reported), methods with a high risk of sample bias or reporting bias were common, follow-up times were short, and primary endpoints were unclear.

Some of the conditions we articulated prior to the literature search did not have any evidence at all, e.g., dry mouth, alopecia, or graft versus host disease. In men, the majority of the studies focused on erectile dysfunction and penetrative intercourse with much less effort directed toward other aspects of sexuality. In addition, the studies focused only on heterosexual individuals with no specific studies in the lesbian, gay, bisexual, or trans populations. Finally, there was a paucity of data to inform management of patients who are not in relationships but in whom sexual health issues should be considered.

Another outcome lacking evidence was the role of HT for younger women with premature ovarian failure and a history of cancer. Younger women may be reluctant to accept HT because of concerns regarding breast cancer and other negative impressions from the

Women's Health Initiative [130-132]. However, it is not appropriate to extrapolate results from the Women's' Health Initiative or other studies of post-menopausal women to women with premature ovarian failure. Women with premature ovarian failure are young and the long-term implications of using HT are not necessarily the same as those for older women, who likely have more co-morbid illness. The risk-benefit trade-off of HT in premature ovarian failure is not the same as in menopause. In women without cancer, premature ovarian failure increases the risk of adverse long-term outcomes. One study of women <45 years of age without cancer, who had an oophorectomy, indicates an increased mortality compared with age-matched controls [133]. Another observed a 41% increase in mortality among women who had an oophorectomy before age 50, without hormone replacement therapy [134]. Premature ovarian failure also increases the risk of skeletal, cardiovascular, neurological, and other conditions [135].

Vaginal estrogen use in women with breast cancer is an area of controversy. Some women, particularly those on tamoxifen or aromatase inhibitors, experience significant vaginal dryness and discomfort. A population-based nested case-controlled trial suggests no increased risk of cancer recurrence in women with breast cancer taking these drugs who also use vaginal estrogen [136]. A recent Committee Opinion from The American College of Obstetricians and Gynecologists reiterates the lack of data indicating harm [137]. Individualized decisions need to be made, with respect to the risk/benefit trade-off in such situations.

While there may be concern in using HT or vaginal estrogen for hormone-sensitive breast cancer, similar concerns do not exist for low-risk endometrial cancer. In a randomized study of 1236 women, there was no increased risk of recurrence with the use of estrogen replacement therapy [138]. The majority of women recruited to this study had grade 1 to 2 endometrioid adenocarcinoma with inner half myometrial invasion. Safety data are lacking for women with higher risk endometrial cancer (e.g. higher stage, higher grade). Progesterone alone may be an option for management of vasomotor symptoms for these women. Similarly, a multi-centre RCT of hormone therapy in 150 women with ovarian cancer and severe menopausal symptoms demonstrated no increased risk of recurrence. In fact, those in the HT arm had a better survival [139].

Genital graft-versus-host disease is a recognized complication for women with hematologic malignancies undergoing allogeneic stem cell transplants. Symptoms from genital graft-versus-host disease can be severe and are distinct from those typically seen from vulvo-vaginal atrophy. These patients require special care from a centre or clinic with particular expertise. A recent guideline describing management of these patients is available [140].

Topical testosterone is also often considered when addressing low desire in women. This has been evaluated in several studies [141-146]. While reports indicate an improvement in the number of satisfying sexual episodes, the drug is not approved for women in the United States or Canada and, thus, not a focus of this review. One trial specifically included women with cancer and was negative [145]. Long-term toxicity concerns, especially in women with cancer, remain. Women presenting with low desire need a detailed multifactorial assessment to determine contributing factors. Tibolone is another agent that has been evaluated in a large randomized trial in women with breast cancer and found to improve overall sexual function. This drug is not approved for use in Canada or the United States [89].

Erectile dysfunction following prostate cancer treatment remains a common side effect. Existing pro-erectile therapies (e.g., PDE5i, VED, MUSE, ICI) are very effective in helping men attain an erection sufficient for sexual activity following cancer treatment, when otherwise they would have had persistent erectile dysfunction. By contrast, the goal of "penile rehabilitation" is to intervene early with pro-erectile therapies to counteract the effects of the treatment damage, in the hopes of restoring baseline erectile function. Current research into the use of these agents for penile rehabilitation has not demonstrated their ability to restore

natural erectile function. While further research is required in the field, the use of pro-erectile agents does have benefits in terms of treating erectile dysfunction, improving psychological parameters such as self-esteem, and maintaining closeness and intimacy within couples. Other organizations have published similar recommendation guidelines in this area as well [147,148].

Testosterone therapy for men is another area of interest. In this review, only one study was identified where testosterone was a tested intervention with sexual response as an outcome [105]. This was a positive study but with only 20 participants in a pre/post design. Further research is required evaluating the efficacy of testosterone on sexual function outcomes.

It is clear from the literature that counselling has a big role to play in improving most of the outcomes studied. It is still not clear, however, what the ideal intervention might be or what the most important components are. Couples clearly seem to be a better target for certain conditions. The role of group interventions versus individual interventions is not clear. Numerous methods have been evaluated including in-person, telephone, and web based. All have positive findings in at least some studies. A minimum duration of therapy is also not clear.

CONCLUSIONS

Despite these limitations with the literature, it is possible to help patients with issues related to sexual function in the clinic. The first step is asking whether they have any sexual health problems, whether they would like to discuss these problems further, and whether they would like information or a referral for help. Medication or devices may be of help, but spending some time talking with them will be beneficial too. As treatments evolve, patients will live longer. It behooves the oncology community to develop the capacity to address the sexual harm caused by cancer diagnosis and treatment to this important aspect of being human.

Interventions to Address Sexual Problems in People with Cancer

Section 5: Internal and External Review

INTERNAL REVIEW

The guideline was evaluated by the Intervention to Address Sexual Problems in People with Cancer GDG Expert Panel and the PEBC Report Approval Panel (RAP) (Appendix 1). The results of these evaluations and the Working Group's responses are described below.

Expert Panel Review and Approval

Of the 14 members of the GDG Expert Panel, 12 members cast votes and two abstained, for a total of 86% response in January 2016. Of those that cast votes, 12 approved the document (100%). The main comments from the Expert Panel and the Working Group's responses are summarized in Table 5-1.

Table 5-1. Summary of the Working Group's responses to comments from the Expert Panel.

Comments	Responses
1. Change the title to better reflect all sexual issues, not just sexual function	We have modified the title of the guideline to be "Interventions to Address Sexual Problems in People with Cancer"
2. Change the issue "sexual function" to "overall sexual function"	We have modified all the places in the document that refer to "sexual function" as a condition to "overall sexual function" to be clearer.
3. Add an overarching recommendation regarding there being a discussion with the patient.	We have added an overarching recommendation.
4. For all recommendations, change the wording to start with what is recommended and then add information regarding evidence	We have modified all the recommendations to focus primarily on what is recommended and then state where there is a lack of evidence to make a recommendation.
5. Clarify that individual counselling may still be helpful on its own. No everyone has a partner but will still need counselling.	We have clarified the recommendations for partnered people and individuals.
6. The use of the drug tibolone is controversial because it is not available in Canada and there is only one study.	We have moved the discussion regarding tibolone to the discussion.
7. Clarify the qualifying statement for genital symptoms.	We added 'hormone-positive' to clarify the type of breast cancer and removed 'not taking aromatase inhibitors'. We also added a statement in the interpretation of evidence section to emphasize the need of individual decision-making.
8. Include more methods that may help sexual response in men.	We added another recommendation that if PDE5is did not work than alternate interventions such as a VED, MUSE or ICI may be considered.
9. Include a statement about how long medications etc may take to work for sexual response.	We added a qualifying statement that men should be aware that it might take a long time for medications to work.
10. Clarify that type of stimulation may help sexual response. Not just with a device.	We added for both women and men: The Expert Panel believes that any kind of regular stimulation (including masturbation) would likely be of benefit

	for improving sexual response, regardless of the stimulation used.
11. Clarify the difference between penile function and penile rehab.	We added information regarding the difference in the discussion section.
12. Change the term 'body image' in the male section to 'penile changes' since that was the evidence presented.	We modified the title of the condition/issue.
13. Add information regarding pro-erectile agents and devices into recommendation as in sexual response section.	We added: "It is also recommended that the use of pro-erectile agents and devices be considered, recognizing that most of the benefit is specifically for erectile dysfunction" to the recommendation.
14. Move statement regarding psychosocial counselling to the qualification section.	We added the qualifying statement: Psychosocial counselling could be used to help couples integrate interventions into their usual sexual activities.
15. Should there be something about vasomotor symptoms?	We conducted a specific search for vasomotor symptoms for men and added another recommendation section.
16. There are some United Kingdom guidelines available that should be added.	We found the guidelines and added them into the discussion section.
17. Add physiotherapists and surgeons into intended user section.	We added physiotherapists and surgeons into the intended user section.
18. You should add the paroxetine should not be used with women on tamoxifen.	We added "Paroxetine and fluoxetine should not be offered to women with breast cancer taking tamoxifen." to Recommendation 5 –Women.
19. There was no specific mention of head and neck cancers where facial disfigurement may have an effect on body image. You should state that head and neck cancers were not included in this review.	All cancers were searched for in the review but there was no evidence for interventions and head and neck cancers found specifically. The guideline was organized so that one could look at the symptom or condition and find a recommendation and the attempt was to not be cancer specific.
20. You should add some more explicit information about prostatectomy and PDE5i medications and length of time to use.	The Working Group believe that the information provided in the recommendations, qualifying statements and interpretation of evidence recognize that PDE5i medications are a first-line treatment for erectile dysfunction regardless of type of cancer or treatment and that there are alternate intervention if the person does not respond to the PDE5i medication. As well, the qualifying statements provide information regarding timing.
21. Recommendation 1: People with cancer. My only concern is that it's unclear where to send people – I think that psychosocial oncology should deal with this. My therapy waitlist is a year, and I can't start seeing everyone in the cancer clinic – a referral is not enough. It needs to be more specific.	The Implementation Considerations section deals with this as a resource manual would help any practitioner to be able to do something and only the more complicated ones would require higher level of expertise. Any one treating cancer should know the basics of the guideline and resources.

22. Recommendation 5: - Sexual Response – systemic estrogen is contraindicated, not just estrogen. In the qualifying statement, write that average age of menopause, which is 51.5 years. - Regarding estrogen alone for treatment of vasomotor symptoms. We usually only recommend systemic estrogen alone for women who have had a hysterectomy. I think the recommendation should be reworded. - Regarding use of hormone therapy after age 51. I think we should add that it is an individual therapy with few risks for symptomatic patients in their 50's and it should be intermittently re-evaluated for long-term use. (see the North American Menopausal Society's recent recommendations for long-term use).	We added the term "oral" to the recommendation before hormone therapy. The word "menopause" was added into the qualifying statement for Recommendation 5. We added, "for women who have had a hysterectomy" to the qualifying statement for Recommendation 5. We added "Beyond the age of 51.5 years, hormone therapy is an individual therapy with few risks for symptomatic patients in their 50's. It should be intermittently evaluated for long-term use." to the qualifying statements in Recommendation 5.
23. There needs to be mention of testosterone replacement therapy in men with erectile dysfunction, as it is in the new Canadian Testosterone Guidelines, published in the *Canadian Medical Association Journal*, and they recommend it as a potential treatment. The data from cancer are limited. We should add a paragraph in the discussion as to why we did not include testosterone supplementation for men.	There was only one study found that examined a testosterone intervention with a sexual function measureable outcome in men with cancer. We added a paragraph concerning testosterone supplementation for men in the discussion.
24. Regarding genito-urinary syndrome of menopause or vaginal and urinary atrophy and vaginal estrogen-this is not the same as systemic therapy in terms of dosage. We should not perpetuate the myths concerning any risk at all. In the National Institute for Health and Care Excellence guidelines recently released in Britain-they include possible usage to symptomatic breast cancer patients. There is a proposal that the United States Food and Drug Administration is considering to remove the black box label for these medications. They are currently available over the counter in Sweden. I think the language should be re-worded here.	We removed "of risks and quality of life issues" from the qualifying statement in Recommendation 6 –women.

RAP Review and Approval

Three RAP members, including the PEBC Director, reviewed this document in January 2016. The RAP approved the document January 18, 2016. The main comments from the RAP and the Working Group's responses are summarized in Table 5-2.

Table 5-2. Summary of the Working Group's responses to comments from RAP.

Comments	Responses
1. In Recommendation 1, remove key evidence heading and just leave as a recommendations since evidence was not really used.	We removed the Key Evidence heading and just left the wording in the recommendation.
2. Clarify the literature search details.	We have clarified the literature search detail and added more information regarding the Evidence Search and Review Service literature review.
3. Risks for and against hormone replacement therapy in women covered well. The erectile dysfunction agents – there was discussion about degree of benefit with late versus early start but there was not discussion on risks, i.e., hypertension, angina, death, etc. Not sure if these are rare and not seen if used appropriately. May want to comment if relevant.	The Working Group added: "Side effects of PDE5i medications in include headaches, flushing, upset stomach, nasal congestion and urinary tract infections but when used properly, these side effects are relatively mild and most disappear after a few hours." to the interpretation of evidence section in Recommendation 1 –men.
4. The inclusion criteria specified that the study populations in individual studies should include >50% of patients who are cancer survivors. While the authors commented that these guidelines included cancer patients, it would be nice to know that the majority of patients (>50% are indeed cancer patients) as is specified in the inclusion criteria of this guideline.	The NAMS and SOGC guidelines are likely not over 50% of cancer patients. The criteria for the guideline search are stated in Section 3 under guideline search methods.
5. I cannot find the name of the tool that is used to assess the quality of the individual studies.	The studies were evaluated for their quality and risk of bias; however, a particular tool was not used.
6. Female Recommendation 5: average age of 51.5 years. – where did this number come from	The average age of 51.5 years came from an Expert Panel member. The average age of menopause is 51 years according to the NAMS, but there are no research- or study-based references.
7. Sexual response qualifying statement: the Expert Panel believe that any kind of regular stimulation (including masturbation) would likely be of benefit for improving sexual response, regardless of the stimulation used – this seems very specific and does not really align with the evidence	This statement was found to be awkward but the fact that stimulation can help with sexual response is based on expert opinion –but the Expert Panel did not want to specify exactly what type of stimulation and not exclude self-stimulation. We modified the qualifying statement to start with: it is the opinion of the Expert Panel that any kind….
8. In the text on page 28, reference is made to two systematic reviews (references 6, 89). It seems like the negative studies are not mentioned and only the one support the recommendation is	We added those studies into the interpretation of evidence and added a statement regarding the primary focus of the studies.
9. The GRADE table corresponding to this recommendation divides the body image studies into psychosocial and combination physical/psychological, but the key evidence listed here is not described in this fashion	Studies were organized in a way to help organize the evidence but were also examined in a way to develop practical recommendations

10. Tibolone therapy. Should this study be omitted in the key evidence? It did include 2144 patients and was judged to be of high quality evidence in your GRADE table. Appreciate it is not licensed, but in my view, does not preclude it from being key evidence if there is no other reason to question its effectiveness as reported.	The Expert Panel discussed the study and found that it was controversial because it was only the one study and not approved and decided that it needed to be in the discussion and it is brought to attention there.
11. The recommendation for vacuum erectile devices (VEDs) specifies that the device be used daily. It seems to be that the early implementation is the more, if not at least as important factor (study compared implementation at one month versus six months). Perhaps that should be included in the recommendation? Should the recommendation specify this is for patients post prostatectomy?	We added "There may be some benefit to initiating the use of VEDs early after cancer treatment rather than later." to Recommendation 2 for men.
12. The recommendation states that the Expert Panel believes that … counseling should be offered. The key evidence states one systematic review DID NOT find conclusive evidence, four randomized controlled trials (RCTs) found NO difference, two non-randomized studies found NO difference…. Even though it is also stated that one RCT had a positive outcome and one pre-post study found a difference, the recommendation does not align with the evidence. The interpretation tries to explain why there is no difference, if stronger rationale on why the positive studies are better etc., it would align it better. At the moment, it just seems like it is significant based on opinion despite the evidence.	The Working Group believes that this recommendation is directed to those people wishing to improve the relationship or intimacy issues. It is not directed to all people.
13. Vaginal dilators: more specifics if possible would be helpful. The lack of harm with psychosocial intervention is stated in several areas. The side effects of the medications that are recommended, devices perhaps can be have a little more description.	The Working Group believes that more specific use of vaginal dilators is not possible since their use varies and there is little evidence to guide this. Information regarding side effects was added In the interpretation of evidence section of Recommendation 1 –women.
14. Psychosocial intervention is recommended for multiple indications. Some specifics on what they should look like would facilitate implementation. The division of indications into sexual response, intimacy/relationship/ overall sexual function, and satisfaction appear to have overlap. Psychosocial intervention is recommended for several of these. A paragraph tying them together, and how the psychosocial intervention may look like could be helpful toward implementation. There is emphasis on the need to enquire about sexual symptomatology. Some recommendations of key questions in the discussion may be quite enabling toward implementation. Some	This is examined and discussed in the discussion section. As well, papers are referenced that describe how to have these discussions with patients.

components of the sexual symptoms are in the realm of sexual therapist/gynecologists, urologists. Suggestions on when to refer to whom may also be helpful in implementation.	
15. Body image issues – this seems very generic, is this meant to apply to any body image issues or body image issues that are specific to cancer treatments?	It is stated in the preamble that people may have pre-existing difficulties that may complicate assessment and management. The recommendations apply to people that have to deal with issues caused by the cancer or cancer treatments.
16. Psychosocial counselling – this is recommended in multiple recommendations. I wonder if it would be helpful for the reader if there is a statement as to when psychosocial counselling is recommended	The Working Group believes it may be difficult to specify an exact time other than when there is a need for counselling. A discussion with the patient as stated in Recommendation 1 –overall would help guide the need.
17. Table 4: It is not intuitive why graft versus host disease is listed under genital symptoms. Similarly why fatigue and dry mouth is listed under sexual dysfunction symptoms	These issues are listed in Table 4-1 because these were the initial conditions believed to affect sexual function in people.

EXTERNAL REVIEW
External Review by Ontario Clinicians and Other Experts

Targeted Peer Review

Six targeted peer reviewers from Ontario who are considered to be clinical and/or methodological experts on the topic were identified by Intervention to Address Sexual Problems in People with Cancer GDG. Three agreed to be the reviewers (Appendix 1). Two responses were received. Results of the feedback survey are summarized in Table 5-3. The comments from targeted peer reviewers and the Working Group's responses are summarized in Table 5-4.

Table 5-3. Responses to nine items on the targeted peer reviewer questionnaire.

	Reviewer Ratings (N=2)				
Question	Lowest Quality (1)	(2)	(3)	(4)	Highest Quality (5)
1. Rate the guideline development methods.	0	0	0	1	1
2. Rate the guideline presentation.	0	0	0	1	1
3. Rate the guideline recommendations.	0	0	0	2	0
4. Rate the completeness of reporting.	0	0	0	1	1
5. Does this document provide sufficient information to inform your decisions? If not, what areas are missing?	0	0	1	0	1
6. Rate the overall quality of the guideline report.	0	0	0	0	0
	Strongly Disagree	(2)	Neutral (3)	(4)	Strongly Agree

	(1)				(5)
7. I would make use of this guideline in my professional decisions.	0	0	0	0	2
8. I would recommend this guideline for use in practice.	0	0	0	0	2
9. What are the barriers or enablers to the implementation of this guideline report?	• There are significant limitations in psychosocial resources in the community and the cancer system and this will be an impact for the recommendations on counselling. • Ensuring widespread dissemination. Also would be good to list specific books, both for the provider and the survivor, that are excellent guides (like all of Anne Katz's books).				

Table 5-4. Responses to comments from targeted peer reviewers.

Comments	Responses
1. The group "counsellors" should be added to the intended audience list.	The Working Group added counsellors to the target audience list.
2. I was surprised that no guidelines focused on sexual minority individuals and trans* individuals was included, apart from the following statement: " In addition, the studies focused only on heterosexual individuals with no specific studies in the lesbian, gay, bisexual, or trans populations." I believe that some attention to these groups should be made.	The original search strategy neither included nor excluded group of any sexual orientation. A subsequent search was conducted for interventions for sexual minority groups and none were identified. The Working Group comments on this limitation in the discussion.
3. The one area that is missing is related to the challenges that patients with head and neck cancer face with intimacy. On Table 4-1 under Body Image that there is no mention of outcomes related to structural changes in the mouth, other than dry mouth under 'other'. Individuals post-treatment for head and neck cancers have huge body image issues. I noted that this issue was raised in the external review and the answer was lack of evidence. While I appreciate this, I think the body image that head and neck patients have expressed to clinicians needs to be addressed in the guideline.	There are many subtypes of cancer patients for which there are no data and the Working Group did not want to make arbitrary decisions. That limitation of the subtype literature and is addressed in the discussion and the preamble. The Working Group added another comment in the preamble to emphasize this issue in the preamble.
4. It is not clear why a structured recommendation grade was not used?	Structured recommendation grades are not a part of the PEBC recommendation development process.
5. Recommendation 1 for women (that no recommendation regarding medications) was surprising in light of evidence that transdermal testosterone in cancer survivors with low desire did not significantly improve their sexual desire (Barton 2007 JNCI).	Since testosterone is not approved for women in Canada, it was not a focus of this guideline. The topic is however, addressed in the discussion. To clarify, the Working Group modified the recommendation to: No recommendation can be made for pharmacological interventions. As well, a sentence regarding the drug not being approved for women in the United States or

	Canada in the interpretation section of the recommendations.
6. Recommendation 6: consider using the term "vaginal insert" instead of "dilators" as these instruments do not actually "dilate" the vagina, and there seems to be a preference among pelvic floor physiotherapists to use the term insert.	The Working Group believes that most people still use the term “dilator”.
7. They recommend the use of clonidine for vasomotor symptoms, but no evidence is presented, and the possible harmful effects are not discussed. I would like to see evidence of this recommendation if it is to be included.	It is stated in the key evidence section that Recommendation 5 was based on the SOGC and NAMS guidelines. In the NAMS guideline it is stated that clonidine is used infrequently because of adverse events, including hypotension, light-headedness, headache, dry mouth, dizziness, sedation, and constipation. Sudden cessation can lead to significant elevations in blood pressure. (Level II evidence) The Working Group added this information to Recommendation 5 qualifying statement.
8. I would have liked to see some consideration of which member of the oncologic team may be ideally suited to address sexual function with survivors. Some anecdotal evidence suggests that nurses may be ideally suited for this.	The Working Group believes that it is not clear which member of team might be best for this function. The team member will depend on local or clinic resources.
9. There have been a few recent studies examining sexual function associated with graft-versus-host disease in bone marrow transplant survivors, and yet, graft-versus-host disease is only briefly noted in Table 4-1 with no mention of it in the text. There is an optimal opportunity for hematology oncologists to address genital pain and sexual function given the very high rates of genital graft-versus-host disease in bone marrow transplant survivors. The importance of vaginal insert use within the first two years following transplant should also be discussed.	In the original search by the ESRS, a separate search was conducted in October 2014 specifically for intervention studies with hematological cancer patients and none of the articles met the inclusion criteria. However, the Working Group realizes this is an important subpopulation and using a recent 2015 graft-versus-host disease guideline found in a scoping search, made comments regarding its’ recommendations in the discussion.

Professional Consultation

Feedback was obtained through a brief online survey of healthcare professionals and other stakeholders who are the intended users of the guideline. All medical and radiation oncologists, psychology/psychiatrists, nurses, and family physicians in the PEBC database were contacted by email to inform them of the survey. Three hundred and thirty-three professionals were contacted, all from Ontario. Thirty-nine (12%) responses were received. Twenty-nine stated that they did not have interest in this area or were unavailable to review this guideline at the time. The results of the feedback survey from 39 people are summarized in Table 5-5. The main comments from the consultation and the Working Group’s responses are summarized in Table 5-6.

Table 5-5. Responses to four items on the professional consultation survey.

	Number (%)				
General Questions: Overall Guideline Assessment	Lowest Quality (1)	(2)	(3)	(4)	Highest Quality (5)
1. Rate the overall quality of the guideline report.	1	0	2	28	8
	Strongly Disagree (1)	(2)	(3)	(4)	Strongly Agree (5)
2. I would make use of this guideline in my professional decisions.	0	3	5	22	9
3. I would recommend this guideline for use in practice.	1	1	4	22	11
4. What are the barriers or enablers to the implementation of this guideline report?	• Barriers listed in the professional consultation feedback include: lack of time, funding for counselling, resources, lack of knowledge and training, lack of sexual therapy experts, inter-professional politics and competition, access to appropriate psychosocial counselling, lack of a resource manual, people are uncomfortable talking about sexual problems, especially when cancer may appear to be the main priority, waitlists, language, willingness of patients and partners to undertake counselling, the document is too long and not user friendly, and more useful for physician with a large practice. • Enablers include having a summary of evidence, most of the recommendations are common sense, create a short 'clinical summary'.				

Table 5-6. Modifications/Actions taken/Responses regarding main written comments from professional consultants.

Comments	Responses
1. Need to add to the list of who can use this, specifically Nurse Practitioners. We are not just Nurses and should be added unless you say primary care providers, rather than just primary care physicians	The Working Group changed the intended user list from "primary care physicians" to "primary care providers" to be more inclusive to potential guideline users.
2. The research question states ..."manage sexual problems AFTER CANCER" and then on page 42 "...with a HISTORY OF cancer" , page 41 says ...."TREATED FOR cancer" then title says Interventions to Address Sexual Problems in People WITH Cancer" Each statement is different: the title implies that the patient still has cancer which is false - most of the discussion is due to the treatment of cancer leaving the patient in survivorship after curative approach. Consistency should be addressed and moreover, a title representing 1. ongoing effects after cancer and its treatment and 2.	The Working Group believes the title is inclusive and decided to keep it as it is.

the fact that the partner is a factor in evaluating sexual success. Perhaps the TITLE should read...."People affected by cancer" to involve the partners too (quote pg 28) or ....."People treated for cancer".	
3. You talked about hormones being somewhat contraindicated in breast but you do not mention that this applies also to endometrium.	The Working Group believes that this issue remains a judgement call and discussion for the physician and patient. HT for endometrial cancer and ovarian cancer has been added to the discussion.
4. There are a lot of individual questions that all have the answer "psychosocial counselling". Would it be better to group the issues where psychosocial counselling is the preferred intervention then perhaps include a bit more detail about the types of psychosocial counselling that could be considered? Not very clear about the psychosocial counselling (who to perform and any particular type) in the recommendation sections as is beyond the scope of practice of an oncologist or to possibly just state to refer the patient for the counselling.	More detail regarding types, timing of or length of counselling sessions cannot be provided because there is not enough evidence in the literature to specify the exact amount or types of counselling.
5. There are some internal inconsistencies within the document, such as estrogen alone has better evidence than estrogen and progesterone combinations, and later on the combination is recommended.	The recommendation regarding estrogen therapy alone is for women with a hysterectomy when not contraindicated (Recommendation 5, qualifying statement). Otherwise, combination therapy is recommended.
6. Not sure about the use of topical estrogen in women with hormone-sensitive tumours.	The Working Group wrote the recommendations so that options would be available if someone is uncomfortable with a therapy and recommend discussions with the patient.
7. The lack of specific interventions around psychosocial and pelvic floor exercise reduce utility for making specific recommendations.	There is no evidence for more information concerning specific programs.
8. I would be curious to know if there are any 'validated' questions that can be asked that are 'sensitive' in context of being acceptable to patients, and also 'sensitive and specific' as far as detecting sexual problems that could be provided for providers so as to meet recommendation 1.	This issue is raised in the discussion and there are some references provided in that section and below. • Dizon DS, Suzin D, McIlvenna S. Sexual health as a survivorship issue for female cancer survivors. Oncologist. 2014;19(2):202-10. • Bober SL, Reese JB, Barbera L, Bradford A, Carpenter KM, Goldfarb S, et al. How to ask and what to do: a guide for clinical inquiry and intervention regarding female sexual health after cancer. Curr Opin Support Palliat Care. 2015. • Flynn KE, Lindau ST, Lin L, Reese JB, Jeffery DD, Carter J et al. Development and validation of a single-item screener for self-

	reporting sexual problems in U.S. adults. J Gen Int Med. 2015;30(10) 1468-75.
9. Another comment is the production of a Primary Care Resource Manual to educate primary care physicians in the survivorship well follow-up as well as an Edmonton Symptom Assessment System/routine symptom management question.	The Psychosocial Oncology Program at Cancer Care Ontario is implementing the guideline and a Resource Manual is in the works.

CONCLUSION

The final guideline recommendations contained in Section 2 and summarized in Section 1 reflect the integration of feedback obtained through the external review processes with the document as drafted by the GDG Working Group and approved by the GDG Expert Panel and the PEBC RAP.

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Appendix 1: Expert Panel Members

Table 1.1 Members of the Interventions to Address Sexual Problems in People with Cancer Guideline Development Group and their Conflict of Interest declaration. (See the PEBC Conflict of Interest Policy).

Name	Affiliation	Declarations of interest
*Lisa Barbera Working Group Chair Radiation Oncologist Provincial Lead, Patient-Reported Outcomes	Cancercare Ontario, Sunnybrook Health Sciences Centre, Toronto, ON	Member of writing group for scientific network on female sexual health and cancer. CCO, Clinical lead, patient reported outcomes
*Andrew Matthew Senior Psychologist, Co-Lead, GU Survivorship Program	Princess Margaret Cancer Centre, Toronto, ON	None declared
*Dean Elterman Urologic Surgeon/Assistant Professor	Toronto Western Hospital Toronto, ON	Speaker, Advisory board for Lilly, Pfizer. Consultant to AMS, Pfizer, Lilly, Astellas. Received research support from Prostate Cancer Canada, AMS
*Anne Katz Clinical Nurse Specialist & Sexuality Counselor	CancerCare Manitoba Winnipeg, Manitoba	Employed as sexual counsellor at CancerCare Manitoba
*Wendy L. Wolfman Director, Mount Sinai Menopause Clinic	Mount Sinai Hospital, Toronto, ON	Received support from Pfizer for fellow and database Author of sexuality guideline for the Society of Obstetricians and Gynaecologists of Canada
*Kathy McPherson Natural Heritage Education Coordinator Patient Representative	Ontario Parks, Peterborough, ON	None declared
*Caroline Zwaal Health Research Methodologist	Program in Evidence-Based Care, McMaster University Hamilton, Ontario	None declared
Janet Ellis Psychiatrist	Sunnybrook Health Sciences Centre, Toronto ON	None declared
Dustin Costescu Obstetrician/Gynaecologist	McMaster University Hamilton, Ontario	Provides sexual therapy Pharmaceutical consultancy and Speakers bureau: Allergan, Bayer, Merck Medicolegal work: dyspareunia and vulvar pain
Angela Turner CSRT Supportive Care and Sexual Health.	Odette Cancer Centre, Toronto ON	None declared
Jennifer Blake CEO	The Society of Obstetricians and Gynaecologists of Canada (SOGC), Ottawa, ON	Provides public education in human sexuality as CEO of SOGC
Karen Syrjala	Fred Hutchinson Cancer,	None declared

Professor and Director, Biobehavioral Sciences Co-Director, Survivorship Program	Seattle, WA USA	
Sharon Bober Director, Sexual Health Program Assistant Professor, Dept of Psychiatry, Harvard Medical School	Dana-Farber Cancer Institute Boston, MA USA	None declared
Don Dizon Co-Founder and Director, The Oncology Sexual Health Clinic Clinical Co-Director, Gynecologic Oncology, Associate Professor of Medicine, Harvard Medical School	Massachusetts General Hospital Cancer Center, Boston, MA USA	None declared

* Working Group Member

Table 1.2 Report Approval Panel Members and their Conflict of Interest declaration. (See the PEBC Conflict of Interest Policy).

Name	Affiliation	Declarations of interest
Melissa Brouwers	Director Program in Evidence-based Care	None declared
Laurie Elit	Surgeon Juravinski Cancer Centre	None declared
Rebecca Wong	Professor/Radiation Oncologist Princess Margaret Hospital	None declared

Table 1.3 Targeted Peer Review Members their Conflict of Interest declaration. (See the PEBC Conflict of Interest Policy).

Name	Affiliation	Declarations of interest
Lori Brotto	Psychologist University of British Columbia	None declared
Esther Green	Director Canadian Partnership Against Cancer	None declared

Appendix 2: AGREE II Scores for Vasomotor and Genital Symptoms Guideline

Domain	SOGC: Managing Menopause 2014 [22]	NAMS: Non-hormonal Management of Menopause-Associated Vasomotor Symptoms - 2015 Position Statement [23]	NAMS: Management of Symptomatic Vulvovaginal Atrophy: 2013 Position Statement [92]	NAMS: The 2012 Hormone Therapy Position Statement [24,111]	ACOG: Management of Menopausal Symptoms 2014 [149]	Climacteric Journal: Global Consensus Statement on Menopausal Hormone Therapy [150]
Scope and Purpose	**97**	**81**	**69**	**72**	**86**	**19**
Stakeholder Involvement	**47**	**50**	**42**	**53**	**28**	**22**
Rigour of Domain	**55**	**68**	**32**	**29**	**40**	**11**
Clarity and Presentation	**86**	**97**	**81**	**83**	**64**	**81**
Applicability	**40**	**44**	**27**	**25**	**33**	**8**
Editorial Independence	**50**	**92**	**88**	**83**	**8**	**21**

Abbreviations: ACOG: American College of Obstetricians and Gynecologists; NAMS: North American Menopause Society; SOGC: Society of Obstetrics and Gynaecology Canada

Appendix 3: Literature Search Strategy

Table 3.1 Ovid MEDLINE and EMBASE Search Strategy from the Evidence Search and Review Service

No.	Search Term	Hits
1	exp Neoplasms/	2393526
2	exp Neoplasms, Hormone-Dependent/	5310
3	exp Gastrointestinal Neoplasms/	264143
4	exp Endometrial Neoplasms/	13736
5	exp Prostatic Neoplasms/	83967
6	exp Pelvic Neoplasms/	5788
7	exp Uterine Neoplasms/	97838
8	exp Uterine Cervical Neoplasms/	55380
9	exp Ovarian Neoplasms/	59372
10	exp Vulvar Neoplasms/	6694
11	exp Genital Neoplasms, Female/	168003
12	exp Breast Neoplasms/	199900
13	prostat* cancer$.tw.	62702
14	breast cancer$.tw.	147298
15	gastrointestinal cancer$.tw.	3667
16	genitourinary cancer$.tw.	295
17	gynecologic* cancer$.tw	2992
18	*Survivors/px (Psychology)	3443
19	or/1-18	2410375
20	exp Hormone Replacement Therapy/	19778
21	ovariectomy.tw.	7539
22	prostatectomy.tw.	17505
23	hysterectomy.tw.	22006
24	or/20-23	65756
25	cancer$.tw.	911064
26	24 and 25	17947
27	19 OR 26	2411084
28	exp Erectile Dysfunction/di, pp, px (Diagnosis, Physiopathology, Psychology)	4848
29	exp Libido/	3872
30	exp Sexual Dysfunction, Physiological	22122
31	exp Sexual Dysfunctions, Psychological/	25841
32	exp Sexual Behavior/di, pp, px, re (Diagnosis, Physiopathology, Psychology, Radiation Effects)	13475
33	exp Sexual Partners/px (Psychology)	2187
34	exp Sexuality/de, ph, px, re (Drug Effects, Physiology, Psychology, Radiation Effects)	6293
35	exp Phosphodiesterase 5 Inhibitors/	1045
36	**(sildenafil or tadalafil or vardenafil or alprostadil).tw.**	5003
37	MUSE.tw.	155
38	exp "Vaginal Creams, Foams, and Jellies"/	897
39	**((intracavernosal or vacuum) adj3 therap*).tw.**	544
40	(erect* adj2 (aid$ or device$)).tw.	138
41	("vacuum erectile device" or VED).tw	167

42	exp Dyspareunia/	1305
43	(sex* adj (function* or d#sfunct* or behav*)).tw.	27524
44	or/28-43	69258
45	Comment.pt	487780
46	Editorial.pt	309212
47	Letter.pt	761011
48	English Abstract/	1645992
49	Clinical conference.pt	6244
50	Or/45-49	2806694
51	(27 AND 44) NOT 50	4551
52	Limit 51 to English language	4388
53	Limit 52 to humans	4320
54	Limit 53 to “all adult (19 plus years)”	3047
55	Limit 54 to yr=”2003-Current”	1833

No.	Search Term	Hits
1	exp Neoplasms/	2381572
2	exp Neoplasms, Hormone-Dependent/	5282
3	exp Gastrointestinal Neoplasms/	262702
4	exp Endometrial Neoplasms/	13591
5	exp Prostatic Neoplasms/	83300
6	exp Pelvic Neoplasms/	5778
7	exp Uterine Neoplasms/	97259
8	exp Uterine Cervical Neoplasms/	55025
9	exp Ovarian Neoplasms/	59023
10	exp Vulvar Neoplasms/	6670
11	exp Genital Neoplasms, Female/	167068
12	exp Breast Neoplasms/	198572
13	prostat* cancer$.tw.	62058
14	breast cancer$.tw.	146015
15	gastrointestinal cancer$.tw.	3637
16	genitourinary cancer$.tw.	294
17	gynecologic* cancer$.tw	2955
18	*Survivors/px (Psychology)	3394
19	or/1-18	2398230
20	exp Hormone Replacement Therapy/	19678
21	ovariectomy.tw.	7507
22	prostatectomy.tw.	17367
23	hysterectomy.tw.	21885
24	or/20-23	65371
25	cancer$.tw.	903231
26	24 and 25	17788
27	19 OR 26	2398937
28	exp Erectile Dysfunction/di, pp, px (Diagnosis, Physiopathology, Psychology)	4829
29	exp Libido/	2859
30	exp Sexual Dysfunction, Physiological	21990
31	exp Sexual Dysfunctions, Psychological/	25703
32	exp Sexual Behavior/di, pp, px, re (Diagnosis, Physiopathology, Psychology, Radiation Effects)	13322

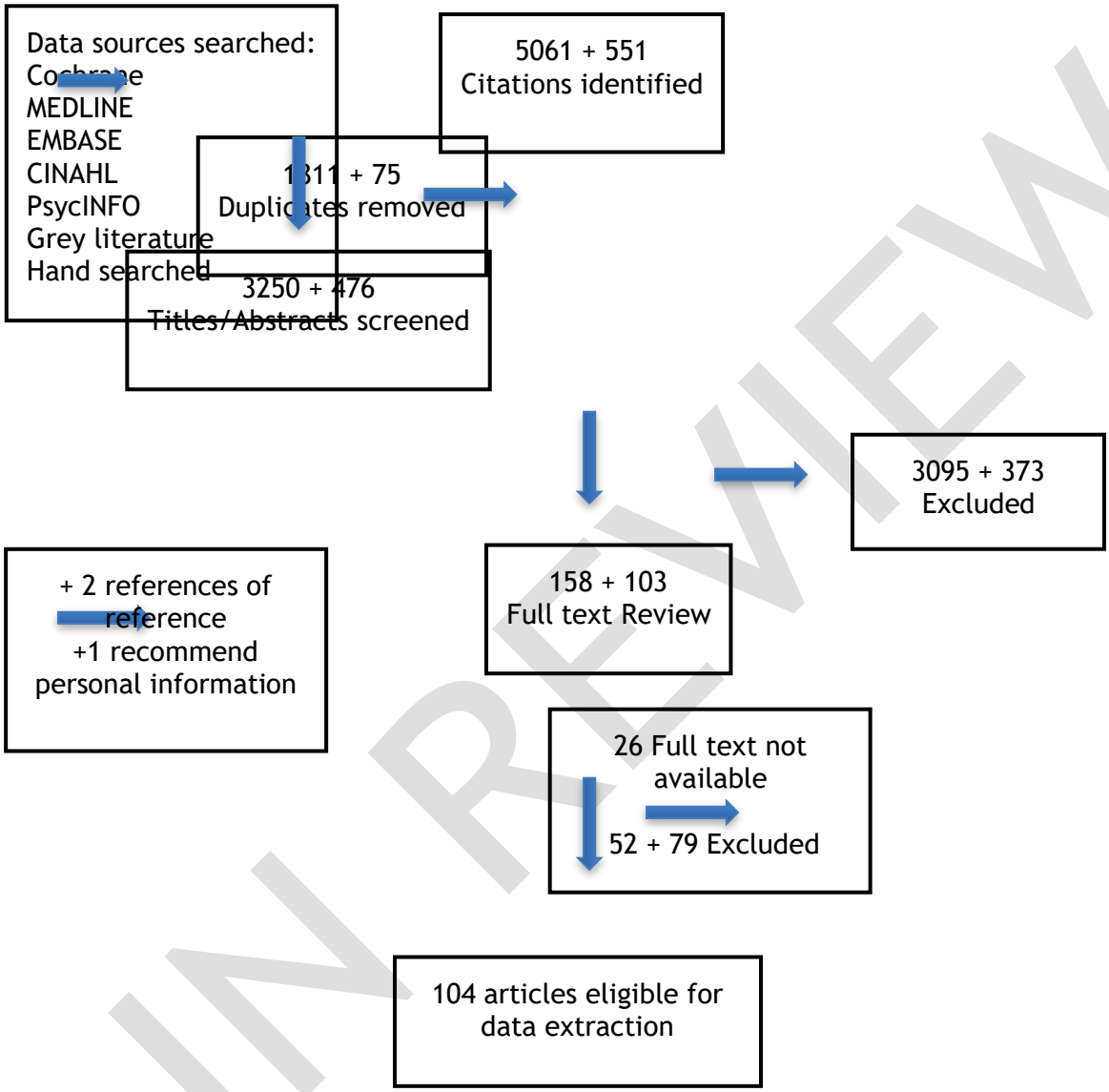
33	exp Sexual Partners/px (Psychology)	2150
34	exp Sexuality/de, ph, px, re (Drug Effects, Physiology, Psychology, Radiation Effects)	6220
35	exp Phosphodiesterase 5 Inhibitors/	1000
36	(sildenafil or tadalafil or varenafil).tw.	4331
37	MUSE.tw.	155
38	exp "Vaginal Creams, Foams, and Jellies"/	888
39	((intracavernosal or vacuum) adj3 therap*).tw.	441
40	(erect* adj2 (aid$ or device$)).tw.	136
41	("vacuum erectile device" or VED).tw	165
42	exp Dyspareunia/	1293
43	(sex* adj (function* or d#sfunct* or behav*)).tw.	27292
44	or/28-43	68468
45	Comment.pt	484706
46	Editorial.pt	307072
47	Letter.pt	758034
48	English Abstract/	1641701
49	“conference abstract”.mp	60
50	Or/45-49	2790472
51	27 AND 44 NOT 50	4512
52	Limit 52 to English language	4350
53	Limit 53 to humans	4282
54	Limit 54 to “all adult (19 plus years)”	3021
55	Limit 55 to yr=”2003-Current”	1807

Appendix 4. AMSTAR results for included systematic reviews

AMSTAR question	Systematic Reviews												
	Hersch [7] (2009)	Scott [10] (2009)	Taylor [14] (2011)	Miles [15] (2010)	Miles [15] (2014)	Johnson [16] (2010)	Flynn [151] (2009)	Denton [152] (2003)	Miles [27] (2007)	Brotto [153] (2010)	Montsori [28] (2005)	Lassen [53] (2013)	Chisholm [54] (2012)
1. Was an *a priori* design provided?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Was there duplicate study selection and data extraction?	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No
3. Was a comprehensive literature search performed?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes
5. Was a list of studies (included and excluded) provided?	No	No	No	Yes	Yes	Unclear	Yes	Yes	Yes	No	No	No	No
6. Were the characteristics of the included studies provided?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Was the scientific quality of the included studies assessed and documented?	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Unclear
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	Yes	Yes	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes
9. Were the methods used to combine the findings of studies appropriate?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10. Was the likelihood of publication bias assessed?	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes	No
11. Was the conflict of interest included?	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Appendix 5: PRISMA Flow Diagram

Figure 5.1. Primary Literature Search Results from the Evidence Search and Review Service plus update



Appendix 6: Quality Assessment Tables

Table 6.1 Study Quality Table for Female Evidence

Author	Level of evidence	Power Determination	Recruitment rate	Randomization	Allocation concealment	Blinding	Appropriate outcome assessment	Attrition	Screening for sexual dysfunction	Selective reporting
Baucom [8] (2009)	RCT	NR	NR	Yes	NR	Yes	Yes	7%	No	None
Brotto [4] (2012)	Non RCT	NR	29%	Not really	NR	No	Yes	0%	Yes	Low
Classen [12] (2013)	RCT	NR	37%	Yes	NR	No	Yes	NR	Yes	Low
Decker [13] (2012)	Non RCT	NR	42%	No	No	No	Yes	2%	No	High
Duijts [19] (2012)	RCT	90%	70%	Yes	NR	Yes	Yes	19%	No	None
Jun [3] (2011)	RCT	0.80	NR	Yes	NR	Yes	Some	25%	No	None
Juraskova [21] (2013)	Non RCT	NR	35%	No	No	No	Yes	35%	Yes	None
Kalatzi [2] (2007)	RCT	NR	NR	Yes	NR	No	Yes	NR	No	None
Law [26] (2015)	Non RCT	NR	94%	No	No	No	Yes	24%	N/A	None
Lee [25] (2011)	RCT	Yes	78%	Yes	NR	NR	Yes	12%	No	None
Marcus [17] (2010)	RCT	NR	86%	Yes	Yes	No	Yes	22%	No	None
Mathias [1] (2006)	Non RCT	NR	NR	No	No	No	OK	NR	Yes	None
Rowland [11] (2009)	RCT	NR	29%	Yes	NR	No	Some	13%	No	Low
Schover [90] (2011)	Non RCT	NR	NR	Kind of	NR	No	Yes	28% (38% after 1 year)	No	Low
Schover [18] (2013)	RCT	NR	60%	Yes	NR	No	Yes	22% (34% at 6 month)	Yes	None
Schroder [5] (2005)	Non RCT	NR	NR	No	No	No	Yes	13%	No	Low

Sharif [9] (2010)	RCT	Yes	NR	Yes	NR	Yes (assessor)	Yes	1%	No	None
Sismondi [89] (2011)	RCT	NR	88%	Yes	No	Yes	Yes	1%	Yes	None
Witherby [91] (2011)	Non RCT	89%	NR	No	No	Yes (analyst blinded)	No (adapted)	15%	Yes	None
Yang [20] (2012)	RCT	NR	76%	Yes	NR	Yes	Yes	29%	Yes	Low

Abbreviations: N/A: not applicable; NR: not reported; RCT: randomized controlled trial

Table 6.2 Study Quality Table for Male Evidence

Author	Level of evidence	Power Determination	Recruitment rate	Randomization	Allocation concealment	Blinding	Appropriate outcome assessment	Attrition	Screening for sexual dysfunction	Selective reporting
Ashmalia [72]	Non RCT	NR	42%	No	No	No	Yes	18%	Yes	None
Ayaz (2008)	Non RCT	NR	NR	No	No	No	Yes	0%	No	None
Balbontin [105]	Non RCT	NR	NR	No	No	No	Yes	10%	Yes	Moderate
Bannowsky [37] (2008)	RCT	NR	NR	Yes	No	No	Yes	NR	Yes	None
Beer [73]	Non RCT	NR	88%	No	No	No	Yes	0%	Yes	None
Bruner [31] (2011)	RCT	90%	NR	Yes	NR	Yes	Yes	45%	Yes	None
Canada [55] (2008)	RCT	NR	NR	Yes	NR	Yes	Yes	65%	Yes	Moderate
Chambers [63] (2011)	Non RCT	NR	NR	No	No	No	NR	15%	No	None
Collins [64] (2011)	Non RCT	NR	NR	No	No	No	Yes	17%	No	High
Cormie [96]	RCT	NR	58%	Yes	Yes	No	Yes	4%	Yes	Low
Dalkin [59] (2007)	Non RCT	NR	NR	No	No	No	Yes	O%	Yes	None
Engel [93] (2011)	RCT	NR	NR	Yes	No	No	Yes	13%	Yes	None
Frisk [74]	RCT	NR	NR	Yes	NR	Yes	Yes	6%	Yes	Low
Fujoka [45] (2004)	Non RCT	NR	76%	No	No	No	Yes	0%	No	None
Hanisch [38] (2012)	RCT	NR	33%	Yes	NR	Yes	Yes	NR	Yes	Low
Harding [75]	Non RCT	NR	NR	No	No	No	Yes	0%	Yes	None
Harrington [35] (2010)	RCT	80%	24%	Yes	NR	Yes	Yes	33%	Yes	Moderate

Ilic [30] (2013)	RCT	80%	73%	Yes	NR	Yes	Yes	N/A	Yes	None
Incroci [32] (2003)	RCT	NR	NR	Yes	NR	Yes	Yes	17%	Yes	None
Incroci [33,34] (2006, 2007)	RCT	N=50	17%	Yes	NR	Yes	Yes	15%	No	None
Irani [68]	RCT	N=92	NR	Yes	Yes	Yes	Yes	14%	Yes	None
Kohler [58] (2007)	RCT	NR	NR	Yes	NR	Yes	Yes	29%	Yes	Low
Lee [107] (2008)	Non RCT	NR	8%	No	No	No	Yes	NR	No	Low
Lin [94] (2012)	RCT	80%	86%	Yes	NR	Yes	Yes	1.5%	Yes	None
Loprinzi [70]	RCT	80%	NR	Yes	Yes	Yes	Yes	18%	Yes	None
Loprinzi [108]	Non RCT	80%	NR	No	No	No	Yes	28%	Yes	Low
Mccullogh [40] (2008)	RCT	NR	NR	Yes	NR	Yes	Yes	NR	Yes	None
Megas [97] (2012)	Non RCT	NR	78%	No	No	No	Yes	NR	Yes	Low
Menard [98] (2011)	Non RCT	NR	51%	No	NR	No	Yes	11%	N/A	None
Molton [65] (2008)	RCT	NR	NR	Yes	NR	Yes	Yes	16.5%	No	High
Montorsi [52] (2008)	RCT	NR	63%	Yes	NR	Yes	Yes	33%	Yes	Low
Montorsi [41] (2013)	RCT	NR	NR	Yes	NR	Yes	Yes	26%	Yes	Low
Moraska [71]	Non RCT	NR	67%	No	No	No	Yes	20%	Yes	Low
Mosbah [39] (2011)	RCT	NR	40%	Yes	NR	Yes	Yes	0%	Yes	None
Mulhall [48] (2005)	Case/ control	NR	NR	No	No	No	Yes	NR	N/A	Low
Mydio [99] (2005)	Non RCT	NR	69%	No	No	No	Yes	6%	Yes	Moderate
Natali [100] (2014)	Non RCT	NR	NR	No	No	No	Yes	31%	Yes	Low
Nishizawa [42] (2011)	Non RCT	NR	NR	No	No	No	Yes	NR	No –it was requested	Yes
Naoe [109]	Non RCT	NR	NR	No	No	No	Yes	0%	Yes	Low
Ogura [46] (2004)	Non RCT	NR	NR	No	No	No	Yes	37%	No	None
Ohebshalom [101] (2005)	Non RCT	NR	NR	No	No	No	Yes	10%	Yes	Low
Pace [36] (2010)	RCT	NR	NR	Yes	No	No	Yes	NR	Yes	Low
Pahlajani [43] (2010)	Non RCT	NR	NR	No	No	No	Yes	0%	No (adapted)	High
Park [29] (2015)	RCT	Yes	NR	Yes	Yes	Yes	Yes	8%	Yes	Low
Pavlovich [50] (2013)	RCT	NR	NR	Yes	NR	Yes	Yes	36%	Yes	None

Porter [60,61] (2009, 2012)	RCT	NR	25%	Yes	NR	No	Yes	28%	No	Low
Pugh [44] (2015)	Non RCT	NR	NR	No	No	No	Yes	NR	Yes	Low
Raina [103] (2003)	Non RCT	NR	44%	No	No	No	Yes	11%	Yes	Low
Raina [102] (2005)	Non RCT	NR	32%	Yes	No	No	Yes	22%	No	High
Raina [104] (2007)	Non RCT	NR	45%	No	No	No	Yes	20%	NR	Moderate
Ramsawh [106] (2005)	Non RCT	NR	NR	No	No	No	Yes	23%	N/A	None
Reese [57] (2012)	Non RCT	NR	40%	No	No	No	Yes	19%	Yes	None
Ricardi [49] (2010)	RCT	80%	60%	Yes	NR	Yes	Yes	15%	Yes	Low
Salonia [51] (2008)	Non RCT	NR	N/A	No	No	No	Yes	NR	Yes	Low
Schiff [47] (2006)	Non RCT	NR	8%	No	No	No	Yes	NR	Yes	Low
Schover [56] (2012)	RCT	NR	NR	Yes	NR	Yes	Yes	33%	Yes	Moderate
Siddons [66] (2013)	RCT	NR	6%	Yes	NR	No	Yes	0%	No	Low
Titta [95] (2006)	RCT	NR	NR	Yes	NR	No	Yes	14%	No	None
Vandecasteele [110]	Non RCT	NR	NR	No	No	No	Yes	10%	Yes	None
Vitolins [69]	RCT	80%	NR	Yes	NR	Yes	Yes	29%	Yes	None
Walker [62] (2013)	RCT	NR	16%	Yes	NR	Yes	Yes	0%	No	None
Zelefsky [67] (2014)	RCT	NR	NR	Yes	NR	Yes	Yes	NR	No	Low

Abbreviations: N/A: not applicable; NR: not reported; RCT: randomized controlled trial

Appendix 7: Grade Summary Tables

Table 7.1 Female Sexual Intervention Grade Summary Table

Female –sexual interventions										
Patients or population: women with cancer Setting: after cancer treatment Intervention: psychological or physical or pharmaceutical or a combination Comparison: usual care or waitlist control or control										
Outcomes	**Intervention**	**Comparison**	**Number of Partici-pants (studies)**	**Main findings**	**Quality of evidence (Risk of Bias)**	**Consistency**	**Directness**	**Precision**	**Publi-cation bias**	**Quality of Evidence (GRADE)**
Sexual Response (6 studies)	Pharmacologic al (Bupropion) (1 study)	None [17]	20 (Non-RCT)	Signif diff –pre-post scores	High risk of bias	N/A	N/A	N/A	N/A	Very low
	Psychosocial (4 studies)	Control [2]	40 dyads (RCT)	Signif diff /no signif diff	Moderate risk	0	0	0	N/A	Moderate - Low
		Control [3]	60 (RCT)	No signif diff						
		Waitlist [4]	31 (Non-RCT)	Signif diff pre-post scores						
		Case-control [6]	60 (Non-RCT)	Significant difference (pre-post)						
	Therapeutic Device (1 study)	None [5]	13 (Non-RCT)	Signif –pre-post scores	Low	N/A	N/A	N/A	N/A	Low –but not useful
Body Image (7 studies)	Psychosocial (5 studies)	Usual care [13]	65 dyads (Non-RCT)	No signif diff but pattern	Moderate	-1	0 -only breast cancer patients -some couple (3) -some individual in group (2)	-0.5	N/A	Moderate
		Control [2]	40 dyads (RCT)	Signif diff						
		Control [8]	14 Dyads (RCT)	Large effect size						
		Control [9]	99 (RCT)	Signif diff for time and group						
		Control [3]	60 (RCT)	No signif diff						

	Combination physical/psychological (2 studies)	Physical exercise or Control [19]	422 (RCT)	No signif diff	Low	0	0	0	N/A	High
		Control [20]	34 (RCT)	No signif dif						
Intimacy/ Relationships (8 studies)	Psychosocial (7 studies)	Usual Care [13]	65 dyads (Non-RCT)	Not signif	-1	-1	0 -some couple (3) -some individual in group (3) -individual (1)	-1	N/A	Low Dyads makes a difference
		Control [2]	40 Dyads (RCT)	Signif diff						
		Control [8]	14 Dyads (RCT)	Medium to large effect						
		Control [11]	210 (RCT)	Signif diff						
		Control [3]	60 (RCT)	Not signif						
		Waitlist [4]	31 (Non-RCT)	Not signif						
		Waitlist [12]	27 (RCT)	Not signif, but medium effect intimacy –adequate dose						
	Therapeutic Device (1 study)	None [5]	13 (Non-RCT)	Increase in DAS but not signif	0	N/A	N/A	N/A	N/A	Low –but not useful
Overall Sexual Functioning/ Satisfaction (17 studies)	Pharmacological (tibolone) (1 study)	Control [89]	2144 (RCT)	Signif diff	0	0	0	-0.5	N/A	High
	Psychosocial (11 studies)	Control [8]	14 dyads (RCT)	Medium effect size Partner large effect size	-1.5	-0.5	0 -some couple (2) -some individual in group (4) -individual (4)	-0.5	N/A	Low -mod Dyads makes a difference
		Usual care [13]	65 dyads (Non-RCT)	No signif diff						
		Control [11]	210 (RCT)	3 questions 2 Signif diff 1 not signif						
		Control [9]	99 (RCT)	Signif diff						
		Control [18]	58 (RCT)	Signif diff						

		Workbook vs. telephone [90]	300 (RCT)	Not signif						
		Control [17] [152]	304 (RCT)	Signif diff						
		Control [3]	60 (RCT)	Signif diff pre-post sex sat No signif for others						
		None [4]	31 (Non-RCT)	Signif diff pre-post						
		Waitlist [12]	27 (Non-RCT)	Not signif						
		Case-control [6]	60 (Non-RCT)	Significant difference (pre-post)						
	Combination physical/psychological (3 studies)	Control [19]	422 (RCT)	CBT/PE signif diff, med-large effect	0	0	0	0	N/A	High
		Control [20]	34 (RCT)	Signif diff Improvements over time						
	Combination physical/lubricant (1 study)	None [21]	25 (Non-RCT)	Signif improvements over time	0	N/A	N/A	N/A	N/A	Low
	Therapeutic Device (1 study)	None [5]	13 (Non-RCT)	Signif improvements	0	N/A	N/A	N/A	N/A	Low –but not useful
Vasomotor Symptoms (4 studies)	Pharmacological (tibolone) (1 study)	Control [89]	3133 (RCT)	Signif diff	0	0	0	-0.5	N/A	High
	Psychosocial (1 study)	Workbook vs. telephone [90]	300 (RCT)	Signif diff, no signif diff between groups	-1.0	N/A	N/A	N/A	N/A	Moderate
	Combination physical/psychological (2 studies)	Control or physical exercise [19]	422 (RCT)	Medium effect	0	-0.5	0	-0.5	N/A	High
		Control [20]	34 (RCT)	No signif diff Improvements over time						
Genital Symptoms	Pharmacological	Control [89]	3133 (RCT)	Signif diff	0	0	0	-0.5	N/A	High

(8 studies)	(tibolone, vaginal gel, moisturizer, testosterone) (3 studies)	Control [25]	96 (RCT)	Signif diff						
		Doses [91]	20 (Non-RCT)	Signif diff for overall						
	Psychosocial (1 study)	Control [11]	210 (RCT)	Not Signif	-1	0	0	0	N/A	Mod
	Therapeutic Device (1 study)	None [26]	109 (Non-RCT)	Not signif	-1.5	N/A	N/A	N/A	N/A	High
	Combination physical/psychological (2 studies)	Control or physical exercise [19]	422 (RCT)	Signif diff Medium effect	0	0	0	0	N/A	High
		Control [20]	34 (RCT)	Clinically relevant						
	Combination physical/lubricant (1 study)	None [21]	25 (Non-RCT)	Signif improvement over time	0	N/A	N/A	N/A	N/A	Low
Other-fatigue (1 study)	Psychological (1 study)	Control [8]	14 Dyads (RCT)	Large effect	0	N/A	0	0	N/A	High

Abbreviations: CBT: cognitive behavioural therapy; DAS: Dyadic Adjustment Scale; N/A: not applicable; PE: physical exercise; RCT: randomized controlled trial; Signif diff: significant difference

Table 7.2 Male Sexual Intervention Grade Summary Table

Male –sexual interventions -49 studies (studies may be listed twice under different outcomes)										
Patients or population: men with cancer Setting: after cancer treatment Intervention: psychological or physical or pharmaceutical or a combination Comparison: usual care or waitlist control or control										
Outcomes	Intervention	Comparison	Number of Participants (studies)	Main findings	Quality of evidence (Risk of Bias)	Consistency	Directness	Precision	Publication bias	Quality of Evidence (GRADE)
Sexual Response (42 studies)	Pharmacological (2 studies) -colorectal	Control [29]	80 (RCT)	Significant difference (12, 24 weeks)	Moderate-high	No serious inconsistency	No serious indirectness	Some imprecision	N/A	Moderate

		None [42]	16 (Non-RCT)	11 of 16 improved						
	Pharmacological - brachytherapy (4 studies)	Control [43]	69 (Non- RCT)	Significant difference (12mos)	Moderate	No serious inconsistency	Moderate	Some imprecision	N/A	Low Improved IIEF scores
		Control [30]	27 (RCT)	Significant (4, 24 wks) Not significant (12 wks, 1, 2 years)						
		50 or 100 mg before vs control [103]	86 (Non-RCT)	Significant difference but not reported (4yr)						
		None [44]	237 (Non-RCT)	Significant difference (12, 24 mo)						
	Pharmacological -external beam radiation (6 studies)	Control [67]	202 (RCT)	Significant for non-ADT Not signif for total	Moderate-High Not enough power Selective reporting	Some inconsistency -levels of intervention -length of follow-up	Some indirectness -different treatments	Serious imprecision -large ranges -no p values -range of scores	N/A	Moderate - Low May improve erection in medium to short term Short term in length For signif studies Longer showed no signif
		Control [31]	61 (RCT crossover)	Significant difference (12 wks)						
		Control [32]	60 (RCT crossover)	Significant difference (6 wks)						
		Control [33,34]	60 (RCT crossover)	Significant difference (6, 12 wks)						
		Control [35]	43 (RCT)	Significant difference (4wks)						
		None [45]	10 (Non-RCT)	Significant difference (12 mos)						
	Pharmacological -surgery (8 studies)	Control [41]	423 (RCT crossover)	Significant difference (9, 13 mos)	High Not enough power	Serious inconsistency -use of outcome measures -levels of intervention	Some indirectness -different treatments	Serious imprecision -large ranges -no p values	N/A	Low May improve erection in medium to short term Short term in length
		Control [52]	628 (RCT crossover)	Significant difference btwn daily/placebo (9 mos) Not signif at 13 mos						
		Control [40]	54 (RCT)	Significant difference (p=NR) (48 wks)						

						-levels of follow-up -levels of intervention				For significant studies Longer showed no significance
		Control [36]	40 (RCT)	Significant difference (24 wks)						
		Control [37]	41 (RCT)	Significant difference (1 yr)						
		On demand vs. daily vs. no treatment [51]	100 (Non-RCT)	No significant difference (18 mos)						
		On demand vs. rehab vs. no treatment [100]	147 (Non-RCT)	Significant difference between none and treatment groups						
		None [46]	43 (Non-RCT)	Significant difference (NR)						
	Pharmacological PDE5i "on-demand" vs. Daily PDE5i (5 studies)	Control [41]	423 (RCT)	Significant difference (9 mos) Not 10.5, 13.5 mos	Low	No serious inconsistency	Some indirectness -different treatments -different interventions	No serious imprecision	N/A	Moderate, low -one study not good – self-selected into groups
		Control [49]	52 (RCT)	Significant difference over time for both groups (1, 3 mos) Not significant between (1, 3 mos)						
		Control [52]	628 (RCT crossover)	Significant difference (9 mos) Not 13 mos						
		Control [50]	100 (RCT)	Not signif (when adjusted for NNS) (12, 13 mos)						
		Control [51]	100 (non RCT)	Not signif (18 mos)						
	Pharmacological Early PDE5i vs. Late PDE5i (3 studies)	Early vs. late [47]	210 (Non-RCT)	Significant difference (18, 24, 30, 36 mos)	High	No serious inconsistency -similar results	Serious indirectness -different treatments -some different intervention	Serious imprecision -no data given -large SD	N/A	Moderate, low
		Early vs. late [48]	84 (Non-RCT)	Significant difference (2 yr)						
		Early vs. late [39]	18 (RCT)	Significant difference (36 mos)						

	Pharamcological PDE5i after either Brachytherapy vs. CRT (1 study)	Dose -NR [101]	110 (Non-RCT)	Significant difference (<12 mos, between 13-24 mos, between 25-36 mos)	High	-	-	-	N/A	Low -no dose reported
	Pharmacological—Other (3 studies)	Dose –variable [104]	73 (Non-RCT)	Significant difference (9 mos)	High	Serious inconsistency -different treatments -different interventions	Serious indirectness -different treatments -different intervention levels -different outcome measures	Serious imprecision -no SD -small sample size large SD when given	N/A	Very low -some drugs not usually used
		Dose –variable [99]	32 (Non-RCT)	Not reported						
		None [105]	20 (Non-RCT)	Significant difference (12, 24 wks)						
	Psychosocial (4 studies)	Control	84 dyads (RCT)	Significant difference (post, surgery, 3 mos)	Moderate	No serious inconsistency	No serious indirectness	Moderate imprecision -large SD	N/A	Moderate Good studies 1 way too small
		Web-based vs. face to face [56]	186 dyads (RCT)	Significant difference for all groups over time, not between (12 mos)						
		Case-control [6]	60 (Non-RCT)	Significant difference (pre-post)						
		None [57]	9 dyads (Non-RCT)	No significant difference (1 mo)						
	Physical/ Exercise Therapy (2 studies)	Control [94]	62 (RCT)	Significant difference (overall)	Low	No serious inconsistency	No serious indirectness	No serious imprecision	N/A	High PDE5i used but not controlled for in analysis
		Control [96]	57 (RCT)	Significant difference (12, 24 wks)						
	Therapeutic Devices (3 studies)	Early vs. late VED [58]	23 (RCT)	Significant difference (3, 6 mos)	Moderate-high	No serious inconsistency	Some serious	Moderate imprecision	N/A	Moderate, low

		PP vs. PDE5i [97]	54 (Non-RCT)	Significant difference (12, 14 mos)			indirectness -different interventions	-large SD		
		PP on RP vs vaso ED [98]	90 (Non-RCT)	Significant difference (follow-up)						
	Combination Treatments (3 studies)	PGE-ICI + counselling vs. Control [95]	57 (RCT)	Significant difference (18 mos)	Moderate - high	No serious inconsistency	Serious indirectness -different intervention	Moderate imprecision -large SD or not given	N/A	Moderate
		PDE5i vs, PDE5i + VED [93]	23 (RCT)	Significant difference (12 mos)						
		VED vs. VED+ PDE5i [102]	109 (Non-RCT)	No significant difference (9 mos)						
Body Image /Penile Changes (3 studies)	Pharmacological (1 study)	Daily vs. on-demand vs. placebo [41]	423 (RCT)	Significant difference (9 mos) Daily	Low	-	-	-	N/A	High
	Therapeutic Devices (2 studies)	Waitlist Control [58]	23 (RCT)	Significant difference (3, 6 mos)	High	No serious inconsistency	No serious indirectness	Moderate imprecision -large SD	N/A	Low
		None [59]	39 (Non-RCT)	Significant difference (9 mos)						
Intimacy/ Relationship (8 studies)	Psychosocial (6 studies)	Control [60,61]	130 dyads (RCT)	Significant difference -QMI(8 wks) No significant difference –MSIS (8 wks)	Moderate-high	No serious inconsistency	Serious indirectness -different treatments -different intervention -different populations	No serious imprecision	N/A	Moderate
		Usual [62]	27 couples (RCT)	Medium effect size –PAIR, DAS (6 mos)						
		None [63]	20 couples (Non-RCT)	Significant difference (6 mos)						
		Control [55]	84 dyads (RCT)	No significant difference (3,6 mos)						
		Control [56]	186 couples (RCT)	No significant differences (1 yr)						
		None [64]	10 couples (Non-RCT)	No significant difference (2 mos)						

	Pharmacological PDE3i vs. Placebo (1 study)	Control [38]	24 dyads (RCT - Crossover study)	No significant difference (24 wks)	High	-	-	-	N/A	Low
	Therapeutic Devices (1 study)	Control [106]	92 (non-RCT)	No significant difference (yrs)	Moderate	-	-	-	N/A	Moderate
Overall Sexual Functioning/ Satisfaction (9 studies)	Psychosocial (3 studies)	Control [65]	101 (RCT)	Significant difference (13 wks)	Moderate	Some serious inconsistency	No serious indirectness	Some serious imprecision	N/A	Moderate
		Control [66]	60 (RCT)	Significant difference and non significant						
		Case-control [6]	60 (non RCT)	Significant difference (pre/post)						
	Pharmacological PDE5i vs. Placebo (4 studies)	Control [67]	202 (RCT)	Significant difference (24 mos) and non-ADT	Moderate	No serious inconsistency	Serious indirectness -different treatments -different outcome measures	No serious imprecision	N/A	Moderate
		Daily vs. on-demand vs. placebo [41]	423 (RCT)	Significant difference (9 mos) Daily vs. placebo						
		Control [31]	61 (RCT-crossover)	Significant difference (25 wks)						
		Control [38]	24 dyads (RCT)	No significant difference (24 wks)						
	Pharmacological—Other (1 study)	RP vs RT [107]	1087 (Non-RCT)	No significant difference (1 yr)	High	-	-	-	N/A	Low
	Therapeutic Devices (1 study)	Control [106]	92 (Non-RCT)	Significant difference (yrs)	High	-	-	-	N/A	Low
Vasomotor Symptoms (11 studies)	Pharmacological (7 studies)	Placebo + milk powder vs. venlafaxine +milk powder vs. placebo +	120 (RCT)	Significant difference	High	No serious inconsistency	No serious indirectness	No serious imprecision	N/A	Moderate/ Low

		soy powder vs. venlafaxine + soy powder [69]								
		venlafaxine vs. medroxyprogesterone acetate vs. cyproterone acetate [68]	919 (RCT)	Significant difference						
		Gabapentin doses [70]	214 (RCT)	Some significant differences						
		None [71]	147 (Non-RCT)	Decreases						
		None [108]	18 (Non-RCT)	Decreases						
		None [109]	10 (Non-RCT	Significant difference						
		None [110]	10 (Non-RCT)	Significant difference						
	Acupuncture (4 studies)	With or without electro-stimulation [74]	31 (RCT)	No significant difference btwn groups but for both over time	High	No serious inconsistency	No serious indirectness	No serious imprecision	N/A	Low
		None [72]	14 (Non-RCT)	Significant difference						
		None [73]	22 (Non-RCT)	Significant difference						
		None [75]	60 (Non-RCT)	Significant difference						

Abbreviations: ADT: androgen deprivation therapy; DAS: Dyadic Adjustment Scale; IIEF: International Index of Erectile Function; MSIS: Miller Social Intimacy Scale; N/A: not applicable; NR: not reported; PAIR: Personal Assessment of Intimacy in Relationships; PDE5i: phosphodiesterase type 5 inhibitor; PP: penile prosthesis; QMI: Quality of Marriage index; RCT: randomized controlled trial; RP: radical prostatectomy; RT: radiation therapy; VED: vasculogenic erectile dysfunction

Appendix 8: Data tables

Female data -21 studies

Table 8.1 Sexual Response -6 studies

Condition	Intervention	Author, study type	Population, diagnosis	Comparison/ Follow-up	Main findings	Comments
Pharmacological Interventions -1 study						
Decreased desire (Libido)	Bupropion (antidepressant) therapy 150 mg	Mathias [1] (2006) Non-controlled prospective study	20 breast cancer patients; post treatment, on hormonal therapy.	Before bupropion vs. after Assessments at baseline, 4 weeks and 8 weeks	Arizona Sexual Experience Scale (ASEX) scores at baseline, 4 weeks and 8 weeks p values compared to baseline. Total Score: 23.45 (SD=3.81); 18.45 (SD=3.96) p< 0.05; 18.95 (SD=5.02) p<0.05.	Also: Altered Sexual Functioning /Satisfaction No major side effects were found requiring interruption of therapy; one case of insomnia and one case of dry mouth No control Small sample size Attrition NR
Psychosocial Interventions -4 studies						
Desire, orgasm	Combined Brief Psychosexual Intervention (CBPI) with a sex therapist (six sessions)	Kalaitzi [2] (2007) Randomized Controlled Trial	40 breast cancer patients with mastectomy and partners (20 couples intervention and 20 couples control)	CBPI vs. control (before-after) Assessments at 2 days before mastectomy and 3 months after mastectomy	Statistically different in p-values between CBPI and control in the following: Orgasm frequency (p=0.027); Initiative for sex (p=0.001) No difference in: Sexual desire (p=0.725); Intercourse frequency (p=0.140), Masturbation frequency (p=0.32).	Also: Body Image and Intimacy/Relationship Lots of individual measures Attrition NR
Sexual Interest	Sexual Life Reframing Program (Group counselling) (Six weekly, two hour sessions)	Jun [3] (2011) Randomized Controlled Trial	60 patients (22 intervention; 23 control)	Sexual Life Reframing Program vs. usual care	Cancer Rehabilitation Evaluation System questionnaire (CARES) subscales Sexual interest: Counselling: Pre: 1.61 (SD=0.93) Post: 1.37 (SD=0.87) Control: Pre: 1.59 (SD=0.78); Post: 1.53 (SD=0.73)	Also: Body image, Intimacy/ Relationships and Altered Sexual Function/Satisfaction 25% attrition rate

					No significant difference (t=-0.76, p=0.45)	
Arousal, desire, satisfaction	Mindfulness-based CBT (Three 90-minute individual sessions; 1 per month)	Brotto [4] (2012) Pre/post intervention study	31 endometrial or cervical cancer patients Nine in waitlist group, 22 in immediate treatment group	Before mindfulness-based CBT vs. after Assessments at pre-treatment, post-treatment and at a six month follow-up	Female Sexual Function Index (FSFI) Treatment Group Mean Domain Scores: Pre-treatment; Post-treatment; Desire: Pre: 1.82 (SD=0.92); Post: 2.94 (SD=1.41) p=0.00011 Arousal: Pre: 3.00 (SD=1.10) Post: 4.47 (SD=1.35) p=0.00009; Lubrication: Pre: 2.70 (SD=1.64); Post: 4.42 (SD=1.16) p=0.000026; Orgasm: Pre: 3.38 (SD=1.65); Post: 4.40 (SD=1.45) p=0.00016; There were no significant changes in scores from the post-treatment to 6-month follow-up. Changes in sexual arousal to erotic film: Subjective sexual arousal score: No significant increase pre-post intervention, p>0.05. Perception of genital arousal: Significant increase pre-post intervention: p=0.027 Physiological changes: as measured by Vaginal Pulse Amplitude; pre/post intervention: no significant difference, p=0.05.	Also: Altered Sexual Functioning /Satisfaction and Intimacy/ Relationship 28.7% response rate For waitlist control, there was no significant effect from baseline to pre-treatment on any measures all p>0.0045 Confusing with waitlist being added to scores Women receiving hormone therapy had significantly higher baseline lubrication scores on the FSFI (mean 5.0, SD 1.25) compared to women not receiving hormones (mean 2.4, SD 1.55). The two groups did not differ on any other measure.
Anorgasmia	PLISSIT model 8 counselling sessions at 2 week internals	Ayaz [6] (2008) Case-Control Study	60 colorectal cancer patients (30 cases, 30 controls)	Before intervention and post intervention	Golombok–Rust Inventory of Sexual Satisfaction (GRISS) Anorgasmia domain: Treatment: 5.89 (SD=3.5); 7.11 (SD=4.2)	Colorectal cancer Also: Sexual Function/Satisfaction

			For males (21) and female (9) and partners		Control: 5.80 (SD=4.1); 12.10 (SD=2.8) p<0.05	
Therapeutic Devices – 1 study						
Sexual Response	Clitoral therapy device (CTD) 4 times weekly for 3 months during foreplay and self-stimulation	Schroder [5] (2005) Comparative Pilot study Pre-post intervention	13 irradiated cervical cancer patients	Before CTD therapy vs. after Assessments at baseline and at 3 months	Female Sexual Function Index (FSFI) Statistically significant improvements were noted in all six domains at the 3-month evaluation. sexual desire (p=0.004), arousal (p=0.004), lubrication (p=0.004), orgasm (p=0.004), sexual satisfaction (p=0.004), pain (p=0.004).	Also: Altered Sexual Functioning /Satisfaction and Intimacy/ Relationships 13% attrition rate

Table 8.2 Body Image -7 studies

Condition	Intervention	Author, study type	Population, diagnosis	Comparison/ Follow-up	Main findings	Comments
Psychosocial Interventions -5 studies						
Body image -Dyads	Counselling based on systems theory (Three 60-minute sessions)	Decker [13] (2012) Non-randomized Experimental Trial	65 breast cancer patients and their partners. (26 dyads face-to-face; 14 telephone only; 25 usual care)	Intervention vs. usual care Assessments at pre-treatment, post-treatment and 6 months post-treatment	Body Image Scale Intervention Group: Pre-treatment: 40.5; Post-treatment: 42; 6-month follow-up: 42.5. Comparison Group: Pre-treatment: 40; Post-treatment: 40.25; 6-month follow-up: 41.	Also: Altered Sexual Functioning /Satisfaction and Intimacy/ Relationships The consent rate for participation was 60% once telephone group added 2% attrition rate
Body Image -Dyads	Combined Brief Psychosexual Intervention (CBPI) with a sex therapist (Six sessions)	Kalaitzi [2] (2007) Randomized controlled trial	40 breast cancer patients with mastectomy and partners (20 couples intervention	CBPI vs. control (before-after) Assessments at 2 days before mastectomy	Statistically different in p-values between CBPI and control in the following: Satisfaction with body image when naked (p=0.001); Satisfaction with body image when dressed (p=0.035);	Also: Sexual Response and Intimacy/ Relationships Attrition NR

			and 20 couples control)	and 3 months after mastectomy	Feeling attractive (p<0.001)	
Self-image -Dyads	Relationship enhancement therapy (CBT) with therapist (Six, 75-minute, bi-weekly sessions with a therapist)	Baucom [8] (2009) Randomized Controlled Trial	14 breast cancer patients and partners (8 intervention and 6 control)	Relationship enhancement (CBT) vs. usual care Assessments at pre-treatment, post-treatment and 12 months post-treatment	Self-Image Scale (SIS) for self-acceptance and perception of partners' acceptance. Effect size for self-acceptance: Pre to post-treatment: d=0.85, Pre-treatment to 1 year follow-up: d=1.02. Effect size for perception of partners' acceptance: Pre-treatment to post-treatment: d=0.21, Pre-treatment to1 year follow-up: d=0.80.	Also: Altered Sexual Functioning /Satisfaction, Intimacy/ Relationships and Other (fatigue) 7% attrition rate
Body Image	Peer –led education. 4 -1 hour sessions on a weekly basis for one month (Group counselling)	Sharif [9] (2009) Randomized Controlled Trial	99 breast cancer patients (49 intervention and 50 control)	Peer-led session vs. usual care	EORTC –BR23 Functioning Score for Body Image (EORTC -QLQ-BR23) Intervention: Pre: 68.19 (SD=25.21) Post: 82.14 (SD=14.29) 2 month post: 93.87 (SD=6.31) Control: Pre: 73.33 (SD=24.51) Post: 72.33 (SD=23.35) 2 month post: 71.00 (SD=23.21) Time/Group difference p=0.001	Also: Altered Sexual Functioning /Satisfaction Attrition: 1%
Body image	Sexual Life Reframing Program (Group counselling) (Six weekly, two hour sessions)	Jun [3] (2011) Randomized Controlled Trial	60 breast cancer patients (22 intervention; 23 control)	Sexual Life Reframing Program vs. usual care	Cancer Rehabilitation Evaluation System questionnaire (CARES) subscale Pre-treatment; Post-treatment scores Counselling: 1.95 (1.12); 1.88 (1.21) Control: 2.29 (1.26); 1.75 (1.18) No Significant difference (t=1.60, p=0.12)	Also: Sexual Response, Altered Sexual Functioning /Satisfaction and Intimacy/ Relationships 25% attrition rate
Combination Therapies -2 studies						

Body Image	CBT or Physical Exercise therapy (or both) (CBT –six weekly 90 minutes group sessions; PE -12 week, individually tailored, home-based exercise program 2.5 -3 hours per week)	Duijts [19] (2012) Randomized Controlled Trial	422 breast cancer patients (109 CBT; 104 PE; 106 CBT/PE; 103 control)	CBT vs. Physical Exercise (PE) vs. CBT+PE vs. wait-list control 3, 6 months	European Organization for Research and Treatment of Cancer Quality of Life Breast Cancer questionnaire (EORTC -QLQ-BR23) body image subscale. No significant overall group differences over time were observed.	Also: Altered Sexual Function/Satisfaction Vasomotor Symptoms and Genital Symptoms 19% attrition rate
Body Image/ Bladder Function/ Bowel Function	Pelvic floor rehabilitation program One 45-minute exercise session (biofeedback and core exercise) and 30 minute counselling session per week over 4 weeks	Yang [20] (2012) Randomized Controlled Trial	34 gynecological cancer patients (17 intervention and 17 control)	Pelvic floor rehabilitation program vs. usual care	The European Organization for Research and Treatment of Cancer Quality-of-Life questionnaire cervical cancer module (EORTC QLQ-CX24) Mean Score. Body image subscale: Intervention Group: Pre-treatment: 43.2 (SD=19.0) Post-treatment: 37.0 (SD=18.6) Comparison Group: Pre-treatment: 38.2 (SD=16.5) Post-treatment: 35.3 (SD=10.7) No significant difference. Australian Pelvic Floor Questionnaire Between group differences: Bladder function score*: Regression β =0.15 (95% CI=−0.57 to −1.23) t-value =0.771, df=17, p=0.452 Bowel function score*: Regression β =-0.15 (95% CI=−0.66 to −1.31) t-value =0.69, df=17, p=0.497	Also: Altered Sexual Functioning /Satisfaction and Vasomotor Symptoms *A higher symptom score represents a higher perception of the symptom. Lower scores reflect positive effect of intervention. Differences in health-related quality of life scores between groups were considered clinically relevant at ≥10 points. 29% attrition

Table 8.3 Intimacy/relationships -8 studies

Condition	Intervention	Author, study type	Population, diagnosis	Comparison/ Follow-up	Main findings	Comments
Psychosocial Interventions -7 studies						
Relationship Intimacy and Adjustment	Counselling based on systems theory (Three, 60-minute sessions)	Decker [13] (2012) Non-randomized Experimental Trial	65 breast cancer patients and their partners. (26 dyads face-to-face; 14 telephone only; 25 usual care)	Intervention vs. usual care Assessments at pre-treatment, post-treatment and 6 months post-treatment	Heatherington Intimate Relationship Scale Score Intervention Group; Comparison Group Pre-treatment: 72; 71 Post-treatment: 73; 67.5 6-month follow-up: 72.5; 68 Partners, Intervention Group; Comparison Group Pre-treatment: 64; 65.5 Post-treatment: 64.5; 62.5 6-month follow-up: 64; 62 Dyadic Adjustment Scale (DAS) Intervention Group; Comparison Group: Pre-treatment: 118; 115.5 Post-treatment: 118; 111 6-month follow-up: 118.5; 110 No statistical differences.	Also: Altered Sexual Functioning /Satisfaction and Body Image Higher scores indicate greater levels of intimacy 2% attrition
Satisfaction with relationship	Combined Brief Psychosexual Intervention (CBPI) with a sex therapist (six sessions)	Kalaitzi [2] (2007) Randomized Controlled Trial	40 breast cancer patients with mastectomy and partners (20 couples intervention and 20 couples control)	CBPI vs. control (before-after) Assessments at 2 days before mastectomy and 3 months after mastectomy	Satisfaction with Relationship score CBPI group: Pre-treatment: 3.75 (95% CI=±0.48) Post-treatment: 4.45 (95% CI=±0.28) Control group: Pre-treatment: 3.3 (95% CI=±0.40) Post-treatment: 3.65 (95% CI=±0.46) Difference between groups: p=0.012 Statistically different in p-values between CBPI and control in the following: Orgasm frequency (p=0.027); Initiative for sex (p=0.001); Satisfaction with relationship (p=0.012)	Also: Sexual Response and Body Image Lots of individual measures Attrition NR

					No difference in: Sexual desire (p=0.725); Intercourse frequency (p=0.140), Masturbation frequency (p=0.32).	
Relationship satisfaction	Relationship enhancement therapy (CBT) with therapist (Six, 75-minute, bi-weekly sessions with a therapist)	Baucom [8] (2009) Randomized Controlled Trial	14 breast cancer patients and partners (8 dyads intervention and 6 control)	Relationship enhancement (CBT) vs. usual care Assessments at pre-treatment, post-treatment and 12 months post-treatment	Quality of Marriage Index (QMI) Effect size: Pre-treatment to post-treatment: d=0.48, Pre-treatment to1 year follow-up: d=0.77 Partners: Effect size: Pre-treatment to post-treatment: d=0.64, Pre-treatment to1 year follow-up: d=0.34 Derogatis Inventory of Sexual Functioning (DISF) Effect size for drive and relationship: Pre-treatment to post-treatment d=0.34, Pre-treatment to 1-year follow-up d=0.42 Partners: Effect size for drive and relationship: Pre-treatment to post-treatment d=0.38, Pre-treatment to 1-year follow-up d=1.04	Also: Body Image and Other (fatigue) 7% attrition
Relationship Adjustment	Pscyho-educational group counselling Six, 2-hour weekly group meetings	Rowland [11] (2009) Randomized Controlled Trial	210 breast cancer patients (83 intervention; 127 control)	Pscyho-educational group intervention vs. print materials only	Revised Dyadic Adjustment Scale (RDAS) Per-protocol analysis: Intervention vs. control, p=0.017 Improved communication w/partner: Per-protocol analysis: Intervention vs. control, p=0.012	Also: Altered Sexual Functioning /Satisfaction and Genital Symptoms Very odd statistics and randomization 13% attrition

Marital Intimacy	Sexual Life Reframing Program (group counselling) (Six weekly, two hour sessions)	Jun [3] (2011) Randomized Controlled Trial	60 breast cancer patients (22 intervention; 23 control)	Sexual Life Reframing Program vs. usual care	Marital Intimacy Questionnaire Pre-treatment; Post-treatment Scores Counselling: Pre: 22.79 (SD=5.49) Post: 24.74 (SD=3.63) Control: 20.91 (SD=4.80); 21.52 (SD=4.59) No significant difference (t=1.10, p=0.29)	Also: Sexual Response, Altered Sexual Functioning /Satisfaction and Body Image 25% attrition rate
Relationship	Mindfulness-based CBT (Three 90- minute individual sessions; 1 per month)	Brotto [4] (2012) Pre/post intervention study	31 endometrial or cervical cancer patients Nine in waitlist group, 22 in immediate treatment group	Before mindfulness-based CBT vs. after Assessments at pre-treatment, post-treatment and at a six month follow-up	Sexual Function Questionnaire (SFQ) Relationship Score Pre-and post-treatment and follow-up. Pre: 2.56 (SD=1.27); Post: 3.68 (SD=3.35); Follow-up: 2.99 (SD=1.33)	Also: Altered Sexual Functioning /Satisfaction and Sexual Response 28.7% response rate Confusing with waitlist being added to scores
Intimacy and Relationship	GyneGals (Online counselling) 12 week web-based support group	Classen [12] (2013) Wait-listed Randomized Controlled Trial	27 gynecological patients, 13 in immediate group, 14 in waitlist	Web-support group (GyneGals) vs. wait list control Pre-post treatment and 4, 8 month follow-up	Illness Intrusiveness Ratings Scale (IIRS) Pre/post Mean Difference Scores; Effect Size d. Subscale Intimacy: Intention to treat: Treatment (N=18) 0.19 (SD=1.33); Waitlist (N=12) -0.17 (SD=1.21). d=0.28, p=0.46. Adequate dose (12 posts on website). Treatment (N=10) 0.75 (SD=1.01); Waitlist (N=12) -0.17 (SD=1.21). d=0.82, p=0.07. Subscale Relationship: Intention to treat: Treatment (N=19) -0.04 (SD=0.68); Waitlist (N=12) -0.01 (SD=0.82). d=0.03, p=0.94. Adequate dose (12 posts on website).	Also: Altered Sexual Functioning /Satisfaction 37% recruitment rate Low participation and differential participation in the two groups. Group 2 had personal communication with moderator before the start.

					Treatment (N=11) -0.15 (SD=0.50); Waitlist (N=12) -0.01 (SD=0.82). d=-0.21, p=0.64.	
Therapeutic Devices – 1 study						
Intimacy and Relationship	Clitoral therapy device (CTD) 4 times weekly for 3 months during foreplay and self-stimulation	Schroder [5] (2005) Comparative Pilot study Pre-post intervention	13 irradiated cervical cancer patients	Before CTD Therapy vs. after Assessments at baseline and at 3 months	Dyadic Adjustment Scale (DAS) Pre-score: 104 Post score: 111; p=0.13	Also: Sexual Response and Altered Sexual Functioning /Satisfaction

Table 8.4 Overall Sexual Functioning and Satisfaction -16 studies

Condition	Intervention	Author, study type	Population, diagnosis	Comparison/ Follow-up	Main findings	Comments
Pharmacological Interventions (1 study)						
Sexual Function Tibolone and Livial are both 'not active ' in Health Canada database	2.5 mg tibolone daily for 2 years	Sismondi [89] (2011) Randomized Controlled Trial	3133 breast cancer patients (1575 intervention and 1558 on placebo)	Tibolone daily vs. placebo	Women's Health Questionnaire (WHQ) Sexual Function Domain score changes Baseline; mean change score at: 26, 52, 78, 104 weeks Intervention: 0.503; -0.160; -0.183; -0.177; -0.196 Placebo: 0.549; -0.062; -0.055; -0.023; -0.055 Significant difference ($p<0.05$) between score in intervention and placebo groups at weeks 26, 52,78,104	Also: Vasomotor Symptoms and Genital Symptoms Women using Tamoxifen showed less improvement in climacteric symptoms with tibolone, than women only receiving tibolone without any adjuvant therapy. Low attrition but % NR
Psychosocial Interventions -11 studies						
Sexual Functioning	Relationship enhancement therapy (CBT) with therapist	Baucom, [8] (2009) Randomized controlled trial	14 breast cancer patients and partners	Relationship enhancement (CBT) vs. usual care	Derogatis Inventory of Sexual Functioning (DISF) Effect size for drive and relationship: Pretest-posttest d=0.34, Pretest-1 year follow-up d=0.42	Also: Intimacy/ Relationships, Body Image and Other (Fatigue)

	(Six 75-minute, bi-weekly sessions with a therapist)		(8 intervention and 6 control)	Assessments at pre-treatment, post-treatment and 12 months post-treatment	Partners: Effect size for drive and relationship: Pretest-posttest d=0.38, Pretest-1 year follow-up d=1.04	
Sexual Functioning	Counselling based on systems theory (Three, 60-minute sessions)	Decker [13] (2012) Non-randomized Experimental Trial	65 breast cancer patients and their partners. (26 dyads face-to-face; 14 telephone only; 25 usual care)	Intervention vs. usual care Assessments at pre-treatment, post-treatment and 6 months post-treatment	Watts Sexual Functioning Scale Score Intervention Group: Pre-treatment: 55.5; Post-treatment: 56; 6-month follow-up: 55.5. p=NR Comparison Group: Pre-treatment: 53.5; Post-treatment: 51.5; 6-month follow-up: 53.5. p=NR	Also: Intimacy/ Relationships and Body Image 2% Attrition
Satisfaction with Sex	Pscyho-educational group counselling Six, 2-hour weekly group meetings	Rowland [11] (2009) Randomized Controlled Trial	210 breast cancer patients (83 intervention; 127 control)	Pscyho-educational group intervention vs. print materials only	Satisfaction with variety of sex: Per-protocol intervention vs. control, p=0.226 Satisfaction with sexual relationship: Per-protocol intervention vs. control, p=0.017 Improved comfort with sexuality: Per-protocol intervention vs. control, p=0.025	Also: Intimacy/ Relationship and Genital Symptoms Very odd statistics and randomization 13% attrition
Sexual Function and Sexual Enjoyment	Peer –led education. 4 -1 hour sessions on a weekly basis for one month (Group counselling)	Sharif [9] (2009) Randomized Controlled Trial	99 breast cancer patients (49 intervention and 50 control)	Peer-led session vs. usual care	EORTC –BR23 Functioning Score for Sexual Function Intervention: Pre: 27.13 (SD=16.27) Post: 43.02 (SD=15.09) 2 month post: 64.34 (SD=13.88) Control: Pre: 24.63 (SD=19.48) Post: 23.91(SD=18.80) 2 month post: 19.35 (SD=22.82) Time/Group difference p=0.001 EORTC –BR23 Functioning Score for Sexual Enjoyment Intervention: Pre: 26.82 (SD=18.58)	Also: Body Image Very wide confidence intervals Attrition: 1%

					Post: 46.34 (SD=19.54) 2 month post: 76.42 (SD=18.62) Control: Pre: 22.48 (SD=22.67) Post: 21.70 (SD=22.86) 2 month post: 20.15 (SD=23.16) Time/Group difference p=0.001	
Sexual Functioning	On-line web-based self-help web site plus three supplemental individual counselling sessions	Schover [18] (2013) Randomized Controlled Trial	58 breast or gynaecological cancer patients (27 intervention and 31 control)	Self-help web site vs. self-help website plus counselling	Female Sexual Function Index (FSFI) Within group pre-post treatment: Counselled group: effect size = 3.41, p<0.001 Self-help group: 0.054 Between-group difference, p=0.024 Menopausal Sexual Interest Questionnaire (MSIQ) Within group pre-post treatment: Counselled group: p<0.001 Self-help group: p=0.082 Between-group difference, p=0.011	Dropout rates was 22% during treatment and 34% at 6 month follow-up Although gains remained significant at 6-month follow-up, most women did not attain the 26.6 score considered to mark "normal sexual function"
Sexual desire, satisfaction	SPIRIT workbook plus peer counselling (three in-person sessions or<30 minutes of telephone counselling	Schover [90] (2011) Randomized study without controls	300 African – American breast cancer patients (151 peer counselled, 146 telephone)	Before counselling vs. after (and telephone vs. in-person) Assessments at baseline, post intervention (6 weeks), 6 and 12 months follow-up	Female Sexual Function Index (FSFI) Total Score for Entire Sample: Baseline: 18.2 (SD=10.7) Post intervention: 18.1 (SD=10.7) 6 months: 18.5 (SD=10.8) 12 months: 17.3 (SD=10.7) No significant differences pre/post or between groups.	Large attrition rate 41% of peer counselling and 35% of phone counselling completed last questionnaire. For FSFI, a score below 26.55 indicates sexual dysfunction. Mean scores at all points remained in dysfunctional range. Large SD
Sexual Dysfunction	Telephone counselling program 16 sessions of 45 minutes each, every two weeks (9) , then one month intervals	Marcus [17] (2010) Randomized Controlled Trial	304 breast cancer patients 152 intervention 152 control	Baseline, 3, 6, 12, 18 months	Sexual Dysfunction Scale (developed for study) p-value changes from baseline; 12 months; 18 months intervention: 0.0001; 0.0002 control: 0.29; 0.36 Significant differences: p=0.03; p=0.04	22% Attrition rate
Sexual Function	Sexual Life Reframing Program (Group counselling)	Jun [3] (2011)	60 patients (22 intervention; 23 control)	Sexual Life Reframing Program vs. usual care	Sexual dysfunction: Counselling: Pre: 1.47 (SD=1.31); Post: 1.39 (SD=1.07)	Also: Body image and Intimacy/ Relationships 25% attrition rate

	(Six weekly, two hour sessions)	Randomized Controlled Trial			Control: Pre: 1.40 (SD=1.07); Post: 1.53 (SD=1.09) No significant difference (t=-0.63, p=0.53) Sexual satisfaction questionnaire for Korean women: Counselling: Pre: 41.89 (SD=13.63); Post: 47.16 (SD=9.49) Control: Pre: 42.35 (SD=10.37); Post: 38.96 (SD=10.02) Significant difference (t=3.77, p<0.001	
Sexual Function and Sexual Distress	Mindfulness-based CBT (Three 90- minute individual sessions; 1 per month)	Brotto [4] (2012) Pseudo-randomized study /pre-post intervention study	31 endometrial or cervical cancer patients Nine in waitlist group, 22 in immediate treatment group	Before mindfulness-based CBT vs. after Assessments at pre-treatment, post-treatment and at a six month follow-up	Female Sexual Function Index (FSFI) Treatment group scores: Pre- and post-treatment; follow-up. Total score: Pre: 18.36 (SD=6.57) Post: 26.13 (SD=5.01) p=0.000304; Follow-up: 24.18 (SD=5.66) There were no significant changes in scores from the post-treatment to follow-up. Female Sexual Distress Scale (FSDS) Score Pre-and post-treatment and follow-up for whole group. Pre: 23.19 (SD=10.42); Post: 14.71 (SD=10.74); Follow-up: 17.13 (SD=11.68) No significant difference.	Also: Intimacy/ Relationship and Sexual Response 28.7% response rate Confusing with waitlist being added to scores 0% Attrition rate
Sexual Distress	GyneGals (Online counselling) 12 week web-based support group	Classen [12] (2013) Waitlisted Randomized Controlled Trial	27 gynecological patients, 13 in immediate group, 14 in waitlist	Web-support group (GyneGals) vs. wait list control	Female Sexual Distress Scale (FSDS-R) Pre/post Mean Difference Scores; Effect Size d. Intention to treat: Treatment (N=21) 2.54 (SD=9.59);	Also: Intimacy/ Relationship 37% recruitment rate

				Pre-post treatment and 4, 8 month follow-up	Waitlist (N=14) 0.26 (SD=3.19). d=0.31, p=0.40. Adequate dose (12 posts on website). Treatment (N=11) 3.82 (SD=9.43); Waitlist (N=14) 0.26 (SD=3.19). d=0.51, p=0.20.	Low participation and differential participation in the two groups. Group 2 had personal communication with moderator before the start. Attrition NR
Sexual Satisfaction	PLISSIT model 8 counselling sessions at 2 week internals	Ayaz [6] (2008) Case-Control Study	60 colorectal cancer patients (30 cases, 30 controls) For males (21) and female (9) and partners	Before intervention and post intervention	Golombok–Rust Inventory of Sexual Satisfaction (GRISS) Total score: pre-post intervention Treatment: 33.44 (SD=12.0); 36.78 (SD=17.3) Control: 36.70 (SD=13.4), 63.80 (SD=11.5); p<0.05 Satisfaction domain: Treatment: 3.22 (SD=2.7); 3.22 (SD=2.8) Control: 3.4 (SD=2.2); 8.0 (SD=2.5) p<0.05	Colorectal cancer Also: Sexual Response
Combination Therapies -3 studies						
Sexual Functioning	CBT or Physical Exercise therapy (or both) (CBT –six weekly 90-minutes group sessions; PE -12 week, individually tailored, home-based exercise program 2.5-3 hours per week)	Duijts [19] (2012) Randomized Controlled Trial	422 breast cancer patients (109 CBT; 104 PE; 106 CBT/PE; 103 control)	CBT vs. Physical Exercise (PE) vs. CBT+PE vs. wait-list control 3, 6 months	Sexual Activity Questionnaire (SAQ) between group difference, p value and effect size. Baseline -3 months CBT-control: p=0.134, d=0.31 PE –control; p=0.969, d=0.01 CBT/PE –control: p=0.443, d=0.15 Baseline -6 months CBT-control: p=0.042, d=0.42 PE –control: 0.488, d=0.15 CBT/PE –control: p=0.002, d=0.65	Also: Body Image and Vasomotor Symptoms and Genital Symptoms 19% attrition rate
Sexual Function	Pelvic floor rehabilitation program	Yang [20] (2012)	34 gynecological	Pelvic floor rehabilitation program vs.	The European Organization for Research and Treatment of Cancer (EORTC) Quality-of-Life questionnaire	Also: Body Image, Genital Symptoms and Vasomotor Symptoms

	One 45-minute exercise session (biofeedback and core exercise) and 30 minute counselling session per week over 4 weeks	Randomized Controlled Trial	cancer patients (17 intervention and 17 control)	usual care	cervical cancer module (EORTC QLQ-CX24) Mean Score. Sexual function score*: Between group differences. p=0.048 Regression B =−0.55 (95% CI=−0.86 to −0.01) t value =−2.292, df=9, p=0.048 Sexual Worry subscale*: Intervention Group: Pre-treatment: 40.7 (SD=22.7) Post-treatment: 25.6 (SD=18.5) Control Group: Pre-treatment: 38.8 (SD=17.5) Post-treatment: 35.6 (SD=14.3) Sexual Activity subscale*: Intervention Group: Pre-treatment: 23.7 (SD=21.2) Post-treatment: 33.7 (SD=20.8) Control Group: Pre-treatment: 18.8 (SD=15.4) Post-treatment: 15.3 (SD=14.3) Sexual Enjoyment subscale*: Intervention Group: Pre-treatment: 23.3 (SD=17.9) Post-treatment: 27.3 (SD=16.5) Control Group: Pre-treatment: 20.8 (SD=14.9) Post-treatment: 24.6 (SD=16.3)	-Lower scores reflect positive effect of intervention. *A higher symptom score represents a higher perception of the symptom. Differences in health-related quality of life scores between groups were considered clinically relevant at ≥10 points. Lower score reflects a positive effect of intervention. 29% attrition
Sexual Functioning/Sexual Satisfaction	Pelvic floor muscle relaxation (PFM) 2x/day; apply a polycarbophil-based vaginal moisturizer (Replens) three times/week to alleviate vaginal dryness, use olive oil as a lubricant during intercourse for 26 weeks	Juraskova [21] (2013) Phase I/II study	25 breast cancer patients	PFM relaxation exercise; vaginal moisturizer and olive oil Assessment at baseline, 4, 12 and 26 weeks	Sexual Activity Questionnaire (SAQ) (range 0–24) Baseline: 7.2 (SE=3.19) Week 4: 12.3 (SE=4.28) Week 12: 12.5 (SE=4.73) Week 26: 11.6 (SE=4.26) Significant improvement over time (estimate =0.63, SE=0.124, p<0.001) Female Sexual Function Index (FSFI) Sexual satisfaction scores: (range 0.8-6) Baseline: 2.4 (SE=1.37) Week 4: 3.3 (SE=1.78)	Also: Genital Symptoms Average compliance with twice/day PFM exercises was 80%, and the average compliance with using Replens® three times/week was 88%, over the 26 weeks.

					Week 12: 3.7 (SE=1.44) Week 26: 3.5 (SE=1.4) Significant improvement over time (estimate, 0.15; SE, 0.043; p<0.001)	
Therapeutic Devices – 1 study						
Sexual Function and sexual satisfaction	Clitoral therapy device (CTD) 4 times weekly for 3 months during foreplay and self-stimulation	Schroder [5] (2005) Comparative Pilot study Pre-post intervention	13 irradiated cervical cancer patients	Before CTD Therapy vs. after Assessments at baseline and at 3 months	Female Sexual Function Index (FSFI) (Max possible score 36) The median total FSFI score increased from 17 (baseline) to 29.4 (3 month) (range, 2–36; p=0.003). Derogatis Interview for Sexual Functioning (DISF) Overall median total raw score increased from 46 to 95; p=0.003 (maximal score 118). All domain scores had significant improvements.	Also: Sexual Response and Intimacy/ Relationships 13% attrition rate

Table 8.5 Vasomotor symptoms -4 studies

Condition	Intervention	Author, study type	Population, diagnosis	Comparison/ Follow-up	Main findings	Comments
Pharmacological Intervention -1 study						
Vaginal dryness Tibolone and Livial are both 'not active' in Health Canada database	2.5 mg tibolone daily for 2 years	Sismondi [89] (2011) Randomized Controlled Trial	2144 breast cancer patients (1078 intervention and 1066 on placebo)	Tibolone daily vs. placebo	Women's Health Questionnaire (WHQ) Vasomotor Domain score changes Baseline; mean change score at: 26, 52, 78, 104 weeks Intervention: 0.928; -0.331; -0.334; -0.359; -0.403 Placebo: 0.950; -0.167; -0.187; -0.208; -0.206 Significant difference (p<0.05) between score in intervention and placebo groups at weeks 26, 52,78,104	Also: Altered Sexual Function/ Satisfaction and Genital Symptoms Women using Tamoxifen showed less improvement in climacteric symptoms with tibolone, than women only receiving tibolone without any adjuvant therapy. Low attrition but % NR
Psychosocial Interventions -1 study						

Hot flashes	SPIRIT workbook plus peer counselling (three in-person sessions or<30 minutes of telephone counselling	Schover [90] (2011) Pseudo-randomized study without controls	300 African – American breast cancer patients (151 peer counselled, 146 telephone)	Before counselling vs. after (and telephone vs. in-person) Assessments at baseline, post intervention (6 weeks), 6 and 12 months follow-up	Menopausal Symptom Scale Total Score for Entire Sample: Baseline: 1.8 (SD=1.4) Post intervention: 1.7 (SD=1.4) 6 months: 1.6 (SD=1.4) 12 months: 1.7 (SD=1.3) p=0.0063 No significant differences between groups.	Large attrition rate 41% of peer counselling and 35% of phone counselling completed last questionnaire. For FSFI, a score below 26.55 indicates sexual dysfunction. Large SD
Combination Therapies -2 studies						
Hot Flashes and Night Sweats	CBT or Physical Exercise therapy (or both) (CBT –six weekly 90 minutes group sessions; PE -12 week, individually tailored, home-based exercise program 2.5-3 hours per week)	Duijts [19] (2012) Randomized Controlled Trial	422 breast cancer patients (109 CBT; 104 PE; 106 CBT/PE; 103 control)	CBT vs. Physical Exercise (PE) vs. CBT+PE vs. wait-list control 3, 6 months	Hot Flash Rating Scale –problem rating between group difference, p value and effect size Baseline -3 months CBT-control: p<0.001, d=0.49 PE –control: p=0.130, d=0.17 CBT/PE –control: p<0.001, d=0.56 Baseline -6 months CBT-control: p=0.001, d=0.40 PE –control: p=0.952, d=0.01 CBT/PE –control: p=0.001, d=0.39	Also: Altered Sexual Functioning /Satisfaction, Body Image and Genital Symptoms 19% attrition rate
Menopausal Symptoms	Pelvic floor rehabilitation program One 45-minute exercise session (biofeedback and core exercise) and 30 minute counselling session per week over 4 weeks	Yang [20] (2012) Randomized Controlled Trial	34 gynecological cancer patients (17 intervention and 17 control)	Pelvic floor rehabilitation program vs. usual care	The European Organization for Research and Treatment of Cancer (EORTC) Quality-of-Life questionnaire cervical cancer module (EORTC QLQ-CX24) Mean Score. Menopausal symptoms*: Intervention Group: Pre-treatment: 32.6 (SD=12.1) Post-treatment: 29.6 (SD=15.4) Control Group: Pre-treatment: 34.2 (SD=20.8) Post-treatment: 33.9 (SD=18.4)	Also: Body Image, Altered Sexual Function/Satisfaction and Genital Symptoms Lower scores reflect positive effect of intervention. *A higher symptom score represents a higher perception of the symptom. Differences in health-related quality of life scores between groups were considered clinically relevant at ≥10 points.

						29% attrition

Table 8.6 Genital symptoms -8 studies

Condition	Intervention	Author, study type	Population, diagnosis	Comparison/ Follow-up	Main findings	Comments
Pharmacological Interventions -3 studies						
Vaginal dryness Tibolone and Livial are both 'not active ' in Health Canada database	2.5 mg tibolone daily for 2 years	Sismondi [89] (2011) Randomized Controlled Trial	2144 breast cancer patients (1078 intervention and 1066 on placebo)	Tibolone daily vs. placebo	Dryness scores from 1-5 (none to severe) Baseline score; mean change score and percent at week 104 Intervention group: 1.79; −0.46 (SD=1.06), −25.7% Placebo group: 1.85; −0.29 (SD=1.00), -15.7% Effect size: −0.18. p<0.0001	Also: Altered Sexual Function/ Satisfaction and Vasomotor Symptoms Women using Tamoxifen showed less improvement in climacteric symptoms with tibolone, than women only receiving tibolone without any adjuvant therapy. Low attrition but % NR
Dyspareunia, dryness with pain	Vaginal pH balanced gel (pH 4.0)	Lee [25] (2011) Randomized Controlled Trial	96 breast cancer patients (44 intervention; 42 control)	Vaginal topical pH-balanced gel vs. placebo Assessment at 12 weeks	Visual Analogue scale Dryness with pain: At Baseline: Intervention: 8.2 (SD=0.826) Placebo: 7.92 (SD=0.895) p=0.104 At endpoint: Intervention: 4.23 (SD=1.396) Placebo: 6.51 (SD=1.506) p<0.001 Dyspareunia: At Baseline: Intervention: 8.23 (SD=0.991) Placebo: 8.11 (SD=0.955) p=0.426 At endpoint: Intervention: 5.48 (SD=1.095) Placebo: 6.11 SD=1.421) p=0.040	Adverse effects were reported in 19 participants (38.8%) treated with vaginal pH-balanced gel compared with 16 participants (32.7%) in the placebo group. Vulvovaginal irritation/burning sense (p=0.299) and itching (p=0.116) were the most common symptoms. Attrition=12%

Vaginal itching/dryness or dyspareunia -add note –not Health Canada approved	Topical testosterone therapy (300 µg or 150µg) for four weeks	Witherby [91] (2011) Phase I/II pilot study Non-randomized experimental study	20 breast cancer patients; 10 at 300 µg 10 at 150 µg	Before vaginal testosterone vs. after Assessments at baseline, 4 weeks and 8 weeks	Total symptom score (n=20): (1-mild; 2-moderate; 3-severe) Baseline: 5.9 (SD=1.9); 4 wks: 2.1 (SD 1.77); p<0.001; 8 wks: 1; p=0.003 Dyspareunia score (n=14) Baseline: 3; 4 wks: 1; p=0.001; 8 wks: 2; p=0.003 Vaginal dryness score (n=20) Baseline: 2; 4 wks: 0; p<0.001; 8 wks: 1.5; p=0.017 Vaginal itching score (n=20); Baseline: 1; 4 wks: 1; p=0.049; 8 wks: 0; p=0.14 Difference in high vs. low dose testosterone symptom scores: Total symptom score: High dose:-1.3; Low dose:-0.8; p=0.37 Dyspareunia: High dose: 2.0; Low dose: 1.5; p=0.13 Vaginal dryness: High dose: 2; Low dose: 1.5; p=0.9 Vaginal itching: High dose:0; Low dose: 0; p=0.33	Symptom scores were assessed using a questionnaire developed for this study. The total symptom score was based on the individual scores added together. The difference in improvement of clinical symptoms between high- and low-dose testosterone was not significant for the mean total symptom score so the total scores were combined for analysis. Not validated measures Attrition=15%
Psychosocial Interventions -1 study						
Dyspareunia	Pscyho-educational group counselling Six, 2-hour weekly group meetings	Rowland [11] (2009) Randomized Controlled Trial	210 breast cancer patients (83 intervention; 127 control)	Pscyho-educational group intervention vs. print materials only	Pain with sex question Per-protocol intervention vs. control, p=0.090 Pain interfering with pleasure question Per-protocol intervention vs. control, p=0.286	Also: Altered Sexual Function/ Satisfaction and Intimacy/ Relationship Very odd statistics and randomization 13% attrition
Therapeutic Device -1 study						
Vaginal stenosis	Vaginal dilator use 1x or 3x per week	Law [26] (2015) Prospective Study	109 gastro-intestinal and gynecological cancer patients after pelvic RT	Before pelvic RT vs after	Maintenance or returning to pre-RT vaginal dilator (VD) size (% of patients). At 1 month Post RT, 51/105 (49%) decreased VD size Of those: at six months:	Adherence rates: For 3x/week group: 4 weeks: 45% (49/108) 35 weeks: 20% (21/106) 52 weeks: 5% (5/104) For 1x/week group:

					24/46 (52%) returned to baseline size at twelve months: 29/41 (71%) returned to baseline size Mean percent adherence was higher in patients who maintained or returned to pre-RT VD size compared to those did not return to pre-RT VD size 6 months (68% vs. 45%, p=0.03) 12 months (57% vs. 39%, p=0.05)	4 weeks: 69% (74/108) 48 weeks: 34% (35/104) 52 weeks: 12% (12/104) Reported a 42% mean adherence rate across all groups over the 1-year period. 24% attrition rate
Combination Therapies -3 studies						
Lower urinary tract symptoms	CBT or Physical Exercise therapy (or both) (CBT –six weekly 90-minute group sessions; PE -12 week, individually tailored, home-based exercise program 2.5-3 hours per week)	Duijts [19] (2012) Randomized Controlled Trial	422 breast cancer patients (109 CBT; 104 PE; 106 CBT/PE; 103 control)	CBT vs. Physical Exercise (PE) vs. CBT+PE vs. wait-list control 3, 6 months	Bristol Female Lower Urinary Tract Symptoms Questionnaire (BFLUTS) between group difference, p value and effect size Baseline -3 months CBT-control: p<0.001, d=0.33 PE –control: p<0.001, d=0.33 CBT/PE –control: p=0.001, d=0.29 Baseline -6 months CBT-control: p=0.007, d=0.32 PE –control: p=0.021, d=0.28 CBT/PE –control: p=0.036, d=0.25	Also: Altered Sexual Function/Satisfaction, Body Image and Vasomotor Symptoms 19% attrition rate
Sexual/vaginal Function	Pelvic floor rehabilitation program One 45-minute exercise session (biofeedback and core exercise) and 30-minute counselling session per week over 4 weeks	Yang [20] (2012) Randomized Controlled Trial	34 gynecological cancer patients (17 intervention and 17 control)	Pelvic floor rehabilitation program vs. usual care	The European Organization for Research and Treatment of Cancer (EORTC) Quality-of-Life questionnaire cervical cancer module (EORTC QLQ-CX24) Mean Score. Sexual/vaginal function subscale: Intervention Group: Pre-treatment: 12.5 (SD=10.7) Post-treatment: 27.3 (SD=11.7) Comparison Group: Pre-treatment: 20.7 (SD=16.5) Post-treatment: 17.0 (SD=12.1)	Also: Altered Sexual Function/ Satisfaction, Body Image and Vasosmotor Differences in health-related quality of life scores between groups were considered clinically relevant at ≥10 points. 29% attrition

Dyspareunia	Pelvic floor muscle relaxation (PFM) 2x/day; apply a polycarbophil-based vaginal moisturizer (Replens) three times/week to alleviate vaginal dryness, use olive oil as a lubricant during intercourse for 26 weeks	Juraskova [21] (2013) Phase I/II study	25 breast cancer patients	PFM relaxation exercise; vaginal moisturizer and olive oil Assessment at baseline, 4, 12 and 26 weeks	Visual analogue score pain assessment of dyspareunia (VAS-DYS) (range 0–10) Baseline: 7.0 (SE=2.40) Week 4: 4.4 (SE=2.35) Week 12: 2.5 (SE=1.67) Week 26: 2.7 (SE=2.31) Significant improvement over time (-0.55; SE=0.059; p<0.001)	Also: Altered Sexual Functioning /Satisfaction Average compliance with twice/day PFM exercises was 80%, and the average compliance with using Replens® three times/week was 88%, over the 26 weeks.

Table 8.7 Other -1 study

Condition	Intervention	Author, study type	Population, diagnosis	Comparison/ Follow-up	Main findings	Comments
Psychological Interventions						
Fatigue	Relationship enhancement therapy (CBT) with therapist (Six, 75-minute, bi-weekly sessions with a therapist)	Baucom [8] (2009) Randomized controlled trial	14 breast cancer patients and partners (8 intervention and 6 control)	Relationship enhancement (CBT) vs. usual care Assessments at pre-treatment, post-treatment and 12 months post-treatment	Brief Fatigue Inventory (BFI) Effect size: Pre-treatment to post-treatment d=1.67, Pre-treatment to 1 year follow-up d=0.90	Also: Intimacy and Relationships, Self-image and Sexual Functioning 7% attrition rate

Male data – 62 studies

Table 8.8 Sexual Response -44 studies (includes studies listed twice under different headings)

Condition	Intervention	Author, study type	Population, diagnosis	Comparison/ Follow-up	Main findings	Comments
Pharmacological Interventions 2 studies -colorectal cancer						
Erectile Dysfunction	Udenafil (50mg) daily for 12 weeks	Park [116] (2015) Randomized Controlled Trial	80 colorectal cancer patients (40 treatment; 40 control)	Udenafil vs. placebo 12, 24 weeks	International Index of Erectile Function (IIEF-5) At baseline, 12 and 24 weeks: Treatment Group: 9.4, 14.3, 15.3 Control: 8.8, 10.8, 13.2 Significant difference at 12, 24 weeks: p<0.001 Sexual Encounter Profile (SEP) (change from baseline) Q2 (Were you able to insert your penis into your partner's vagina?) At 12 and 24 weeks: Treatment Group: 18, 19 Control: 10, 13 Significant difference at 12, 24 weeks: p<0.05 Q3 (Did your erections last long enough for you to have successful intercourse?) At 12 and 24 weeks: Treatment Group: 8, 8 Control: 1, 6 Significant difference at 12 weeks: p<0.05	Total mesorectal excision Attrition -9%
Erectile Dysfunction	25mg of Sildenafil and 5mg of Vardenafil, or 50mg of Sildenafil and 10mg Vardenafil	Nishizawa [42] (2011) Pre-post-intervention study	16 colorectal cancer patients that requested to receive treatment	Before vs. after treatment 3, 12 months	International Index of Erectile Function (IIEF) At 12 months: 11 of 16 cases had an improvement of sexual function based on an IIEF	Total mesorectal excision Attrition -NR
Radiation –brachytherapy -pharmacological Intervention -4 studies						

Erectile dysfunction	Sildenafil (25-50 mg), daily for 12 months	Pahlajani [43] (2010) Non-Randomized Controlled Trial	69 prostate cancer patients (31 treatment; 38 control)	Sildenafil (early treatment) vs. no treatment (before vs. after) 6, 12 months	International Index of Erectile Function (IIEF-6) At 12 months: Treatment Group: 17.9 Control: 9.3 Significant difference: p<0.01	Brachytherapy Attrition -0%
Erectile Dysfunction	Sildenafil (50 mg for first month then 100 mg for 5 months), daily	Ilic [30] (2013) Randomized Controlled Trial	27 prostate cancer patients (14 treatment; 13 placebo)	Sildenafil vs. placebo 4, 8, 12, 24 weeks, 1, 2 years	International Index of Erectile Function (IIEF-5) Mean score At Baseline: Treatment group: 24.0 (20–25) Control group: 24.0 (13–25); p=0.70 At 4 weeks: Treatment group: 24.0 (2–25) Control group: 21.0 (1–25); p=0.02 At 12 weeks: Treatment group: 23.5 (4–25) Control group: 20.0 (1–25) p=0.08 At 24 weeks: Treatment group: 24.5 (3–25) Control group: 21.0 (1–25) p=0.02 At 1 year: Treatment group: 15.5 (2–25) Control group: 18.0 (1–25) p=0.66 At 2 years: Treatment group: 19.0 (1–25) Control group: 20.0 (1–24) p=0.48	Treated with I-125 seed implant (mainly seed brachytherapy) No difference in side effects between groups Attrition -0%
Erectile Dysfunction	Sildenafil (50 mg or 100 mg), before sexual encounter	Raina [103] (2003) Prospective comparative cohort study	86 prostate cancer patients (43 treatment; 43 control)	Sildenafil treatment vs. no treatment (self-selected) (before vs. after) 8, 16, 24, 32, 40, 48 months	International Index of Erectile Function (IIEF-5) Mean score Before brachytherapy, after ^{125}I seed implantation, after sildenafil use (4 years): Treatment group: (43 patients) 20.17 (SD=1.26); 9.82 (SD=0.43); 18.30 (SD=1.23) Group that did initiate therapy: (36 patients) 19.13 (SD=1.26); 12.17 (SD=1.76); 15.76 (SD=1.13) (potent group only 23/36 patients) Significant difference: not reported	Undergoing ^{125}I seed radiotherapy Also: Altered Sexual Function/ Satisfaction Attrition -37% The overall 4-year natural potency rate was 29%, when including patients who used sildenafil citrate, the overall

						potency rate increased to 70%.
Erectile Dysfunction	Tadalafil (10 mg 2x weekly) starting 2 weeks before brachytherapy and encouraged for at least 6 months after brachytherapy	Pugh [44] (2015) Pre-post study	237 prostate cancer patients	Tadalafil treatment Baseline, 12, 24 months	Expanded Prostate Cancer Index Composite (EPIC) Questionnaire Sexual Function Score, at Baseline, 50.9 (SD=27.9) Mean change score at 12, 24 months -7.5 ($p<0.001$); -8.7 ($p<0.001$) Are your erections firm enough for sexual activity? Percent yes. At Baseline, 12, 24 months 74%, 70%, 72% Are your erections firm enough for intercourse? Percent yes. At Baseline, 12, 24 months 62%, 48%, 56%	Low-dose-rate prostate Brachytherapy Attrition -NR
Radiation -external beam –pharmacological Intervention -6 studies						
Erectile Dysfunction	Sildenafil (50 mg daily) for 6 months (Different start times for patients on ADT or not)	Zelefsky [67] (2014) Randomized Controlled Trial	202 prostate cancer patients (125 treatment, 77 placebo)	Sildenafil vs. placebo 6, 12, 24 months	International Index of Erectile Function (IIEF) Total and EF domain scores Total IIEF: at 12 and 24 months Treatment group: (quartile 1-3) 58.00 (41.50-66.75); 58.00 (39.00-65.00) Placebo group: 51.00 (34.50-63.50); 54.50 (29.75-64.75) p=0.070; p=0.186 EF Domain score: at 12 and 24 months Treatment group: 25.00 (18.50-29.00); 24.50 (14.00-29.00) Placebo group: 20.70 (13.25-27.75); 24.00 (8.75-29.00) p=0.024; p=0.262	External Beam Radiotherapy (EBRT), brachytherapy or brachytherapy combined with EBRT Also: Altered Sexual Function/ Satisfaction Broke scores into ADT (10% of patients) and non-ADT (90%) For non-ADT patients; EF and IIEF scores were significantly different between groups at 6 (p=0.021/p=0.030) and 12 months (p=0.018/p=0.043) Attrition -NR

Erectile Dysfunction	Sildenafil (50 or 100 mg) before sexual encounter for 12 weeks	Bruner [31] (2011) Randomized Controlled Cross-over Trial	61 prostate cancer patients	Sildenafil vs. placebo (crossover trial) 12 weeks, 25 weeks (12 weeks after crossover)	International Index of Erectile Function (IIEF) Individual scores (range of means from items) at 12 weeks: Treatment group; 2.0-3.1 Control group: 1.4-2.9 Statistical difference p=0.009 For those with clinically meaningful change, IIEF erectile function domain score (8% placebo only vs. 25% sildenafil only, p=0.03)	External Beam Radiotherapy and Short-Term Androgen Deprivation Therapy <120 days Also: Altered Sexual Function/ Satisfaction Mild AEs caused by sildenafil were reported by 4% of all patients Attrition -16%
Erectile Dysfunction	Sildenafil (50 mg) before sexual encounter (100 mg at 2 weeks if needed) for 12 weeks	Incrocci [32] (2003) Randomized Controlled Cross-over Trial	60 prostate cancer patients (46 in open label phase)	Sildenafil vs. placebo (crossover study) 2, 6, 8, 12, 14, 20 weeks, 2 years	International Index of Erectile Function (IIEF) range score Individual scores (range of means from items) at 6 weeks: Treatment group; 2.6-3.2 Control group: 1.5-2.8 Statistical difference p<0.04 After 6 week open label score range: 2.4-3.5 Global efficacy assessment questions (GEQ) At 6 weeks: Has the treatment you have been taking improved your erections? Treatment group: 45% Placebo: 8% p<0.001 Has the treatment you have been taking led to successful intercourse? Treatment group: 55% Placebo: 18% p<0.001	Three-dimensional conformal external beam radiotherapy Also: Altered Sexual Function/ Satisfaction Attrition -17%
Erectile Dysfunction	Tadalafil (20 mg) (or placebo) on demand for 6	Incrocci [33,34] (2006, 2007)	60 prostate cancer patients (51	Tadalafil vs. placebo	International Index of Erectile Function (IIEF) Range score	Three-dimensional conformal external beam radiotherapy

	weeks; then crossed over to alternate medication; 6 week open-label extension phase	Randomized Controlled Cross-over Trial	patients in open label phase)	(crossover trial) 6, 12, 18 weeks	Individual scores (range of means from items) at 6 weeks: Treatment group; 2.3-4.4 Control group: 1.4-4.0 Statistical difference p<0.0001 After 6 week open label range: 3.0-4.2 p<0.001 compared to baseline (except for questions 10, 11, 12) Global Efficacy Questions (2-GEQ) At 6 weeks: Has the treatment you have been taking improved your erections? Treatment group: 67% Placebo: 20% p<0.001 After open-label treatment: 84% Has the treatment you have been taking led to successful intercourse? Treatment group: 48% Placebo: 9% p<0.001 After open label: 69% Sexual Encounter Profile Diary: 767 attempts for sexual intercourse (400 with Tadalafil and 367 with placebo); both medians were 6.0 per patient.	Also: Altered Sexual Function/ Satisfaction Side effects: no difference p=0.9 Attrition -0%
Erectile Dysfunction	Sildenafil (50 or 100 mg), taken prior to 4 sexual encounters	Harrington [35] (2010) Randomized Controlled Cross-over Trial	43 prostate cancer patients	Sildenafil vs. placebo (crossover trial) 4 weeks	International Index of Erectile Function (IIEF-5) Mean score Data not provided: significant difference; p<0.001	External beam radiation treatment Sildenafil was associated with mild flushing, nasal stuffiness or indigestion in 8–10% patients and moderate flushing in 10% Attrition -33%

Erectile Dysfunction	Sildenafil (50 mg)	Fujioka [45] (2004) Pre-post intervention study	10 prostate cancer patients	Before Sildenafil vs. after 3, 12 months	International Index of Erectile Function (IIEF-5) Mean score At baseline: 6.2 At 12 months: 13.6 p<0.001	High-dose rate brachytherapy with external beam radiation therapy Attrition -0%
Pharmacological Interventions – 8 -Surgery						
Erectile Dysfunction	Tadalafil (20 mg on demand or 5 mg daily)	Montorsi [41] (2013) Randomized Controlled Trial	423 prostate cancer patients (139 on demand; 143 once a day; 141 placebo)	Tadalafil (on demand) vs. Tadalafil (once a day) vs placebo at 9 mos, after 6 wk drug free washout (DFW)	International Index of Erectile Function (IIEF-EFD) percentage of patients with score ≥ 22 At 9 months Daily: 25.2% On demand: 19.7% Placebo: 14.2% Daily vs. placebo: OR: 2.2 (95% CI, 1.2–4.0), p=0.016; On demand vs. placebo: OR: 1.5 (95% CI, 0.8–2.9), p=0.210 At 10.5 months (after 6 wk DFW) Daily: 20.9 % On demand: 16.9% Placebo: 19.1% Daily vs. placebo: OR: 1.1 (95% CI, 0.6–2.1), p=0.675; On demand vs. placebo: OR: 0.9 (95% CI, 0.5–1.7), p=0.704 Sexual Encounter Question (SEP) Q3 Did your erection last long enough for you to have successful intercourse? At month 9, 10.5, 13.5 Daily: 33.7%, 28.8%, 52.4% On demand: 24.1%, 23%, 45.8% Placebo: 21.6%, 28.5%, 40.8% Daily vs. placebo: significant difference, p<0.05 at 9 months	Bilateral Nerve-Sparing Radical Prostatectomy Also: Altered Sexual Function/ Satisfaction and Body Image Attrition=26%
Erectile Dysfunction	Vardenafil (10 mg) titrated between 5-20	Montorsi [52] (2008)	628 prostate cancer patients (210	Vardenafil nightly vs. Vardenafil	International Index of Erectile Function (IIEF-EFD) % with a score ≥ 22	Bilateral Nerve-Sparing Radical Prostatectomy

		Randomized Controlled Cross-over Trial	placebo; 210 Vardenafil nightly; 208 Vardenafil on demand)	Vardenafil on demand vs. placebo 9, 11, 13 months 2 month wash out period and 2 month open label	At 9, 13 months Treatment group: Nightly: 32.0%, 52.6% On demand: 48.2%, 54.2% Placebo group: 24.8%, 47.8% Statistical difference at 9 months: On demand vs. placebo: p=0.0001; Nightly vs. on demand: p=0.0065 At 13 months: no significant difference between groups. Sexual Encounter Profile (SEP) Q3 (Did your erections last long enough for you to have successful intercourse?) Success rate At 9, 13 months: Treatment group: Nightly: 34.5%, 59.8% On demand: 45.9%, 62.6% Placebo group: 25%, 57.1% Statistical difference: nightly vs. placebo: p=0.0344; on demand vs. placebo: p=0.0001 No statistical differences between groups after open label period.	Also: Altered Sexual Function/ Satisfaction Attrition -33%
Erectile Dysfunction	Sildenafil (50 or 100mg) daily for 36 weeks	McCullough [40] (2008) Randomized Controlled Trial	54 prostate cancer patients (17 treatment (50mg); 18 treatment (100mg); 19 placebo)	100mg Sildenafil vs. 50mg Sildenafil vs. placebo 36 weeks	Nocturnal Penile Tumescence and Rigidity (NPTR) Rigiscan (measures radial rigidity) time with R≥55% for a minimum of 10 minutes At 48 weeks post surgery: R≥55% was decreased profoundly 4 weeks after surgery. No treatment group regained baseline values during the trial, but R≥55% in the sildenafil groups increased several-fold from the nadir compared with little change in the placebo group. 100 mg treatment group 36% (base) and 65% (tip) of baseline values by the end of the trial	Bilateral Nerve-sparing Radical Prostatectomy Attrition –NR

					Over the past 4 weeks, have your erections been good enough for satisfactory sexual activity? At 48 weeks: 100 mg: 6/18 (33%) 50 mg: 4/17 (24%) Placebo: 1/19 (5%); p=NR	
Erectile dysfunction	Sildenafil (50 or 100 mg), daily for 8 weeks	Pace [36] (2010) Randomized Controlled Trial	40 prostate cancer patients (20 treatment; 20 control)	Sildenafil vs. no treatment 3, 6, 12, 24 weeks	International Index of Erectile Function (IIEF-EFD) Mean score At 24 weeks: Treatment group: 25.2 Control: 17.4 Significant difference: p<0.05	Bilateral nerve sparing radical prostatectomy. Started Sildenafil 2 weeks after surgery. Grouped two levels of treatment together. Attrition -NR
Erectile dysfunction	Sildenafil (25 mg), daily	Bannowsky [37] (2008) Randomized Controlled Trial	41 prostate cancer patients (23 treatment; 18 control)	Sildenafil vs. no treatment 6, 12, 24, 36, 52 weeks	International Index of Erectile Function (IIEF-5) Mean score At 52 weeks: Treatment group: 14.1 Control group: 9.3 Significant difference: p<0.001	Unilateral or bi lateral nerve sparing prostatectomy Attrition -NR
Erectile dysfunction	Sildenafil (50mg), Vardenafil (10mg), or Tadalafil (10mg), daily +titration	Salonia [51] (2008) Non randomized experimental trial (participants chose the treatment they preferred)	100 prostate cancer patients (36 “on-demand”; 15 “daily use”; 49 control)	PDE5i on demand vs. PDE5i daily vs. no treatment (before vs. after) 6, 12, 18 months	International Index of Erectile Function (IIEF-EFD) Mean score At 6, 12, 18 months: Treatment Group (on demand): 17.3 (SD=9.8); 22.5 (SD=8.4); 22.5 (SD=7.8) Treatment Group (daily): 19.0 (SD=8.6); 21.5 (SD=6.1); 23.5 (SD=2.1) Control group: 8.9 (SD=5.2); 17.5 (SD=9.9); 19.4 (SD=9.6) Significant difference: p <0.001; p=0.12; p=0.42	Bilateral nerve-sparing radical retropubic prostatectomy (BNSRRP) Overall discontinuation rate of 72.5% (37 of 51 patients -28 due to the effect being lower than expectations)
Erectile Dysfunction	On Demand: Sildenafil (100mg) + 20mg tadalafil (20mg) and vardenafil or	Natali [100] (2014) Retrospective Study	147 prostate cancer patients (36 no treatment; 23	Group A: No treatment vs. Group B: On demand vs. Group C:	International Index of Erectile Function (IIEF-5) number with a score ≥ 22 At 24 months: No Treatment group: 22 (61%)	Bilateral or unilateral nerve sparing prostatectomy Attrition rate: 31%

	RRehab: Sildenafil (100 mg) or vardenafil (20mg) 3x/week or tadalafil (20 mg) 2x/week		on demand; 88 rehab)	Regimented rehabilitative program	Overall treatment group: 79 (71%) On demand group: 63 (72%) Rehab group: 16 (70%) Significant difference between no treatment and treatment groups combined p<0.02 No significant difference between treatment groups.	
Erectile Dysfunction	Sildenafil (25mg, if ineffective then 50mg)	Ogura [46] (2004) Pre-post intervention study	43 prostate cancer patients	Before Sildenafil vs. after	International Index of Erectile Function (IIEF-5) Mean score At baseline: 4.3 At end of study: 11.4; p<0.0001 Men who underwent non-NS procedures had no response to sildenafil.	Radical retropubic prostatectomy Some adverse events but no patients discontinued taking sildenafil because of adverse effects. Attrition -37%
Pharmacological Interventions – PDE5i "on-demand" vs. Daily PDE5i -5 studies						
Erectile Dysfunction	Tadalafil (20 mg on demand or 5 mg daily)	Montorsi [41] (2013) Randomized Controlled Trial	423 prostate cancer patients (139 on demand; 143 once a day; 141 placebo)	Tadalafil (on demand) vs. Tadalafil (once a day) vs placebo at 9 mos, 10.5 after 6 wk drug free washout (DFW), 13.5 months	International Index of Erectile Function (IIEF-EFD) percentage of patients with score ≥ 22 At 9, 10.5, 13.5 months Daily: 25.2%, 20.9%, 32.4 On demand: 19.7%, 16.9%, 33.1% Placebo: 14.2%, 19.1%, 27.0% At 9 months: Daily vs. placebo: OR: 2.2 (95% CI, 1.2–4.0), p=0.016; On demand vs. placebo: OR: 1.5 (95% CI, 0.8–2.9), p=0.210 At 10.5 months: Daily vs. placebo: OR: 1.1 (95% CI, 0.6–2.1), p=0.675; On demand vs. placebo: OR: 0.9 (95% CI, 0.5–1.7), p=0.704 At 13.5 months: Daily vs. placebo: OR: 1.3 (95% CI, 0.8–2.3), p=0.273 On demand vs. placebo: OR: 1.4 (95% CI, 0.8–2.3), p=0.259).	Bilateral Nerve-Sparing Radical Prostatectomy Also: Altered Sexual Function/ Satisfaction and Body Image Attrition=26%

					Sexual Encounter Question (SEP) Q3 Did your erection last long enough for you to have successful intercourse? At month 9, 10.5, 13.5 Daily: 33.7%, 28.8%, 52.4% On demand: 24.1%, 23.0%, 45.8% Placebo: 21.6%, 28.5%, 40.8% Daily vs. placebo: significant difference, p<0.05 at 9 months	
Erectile Dysfunction	Tadalafil (20 mg on demand or 5 mg daily)	Ricardi [49] (2010) Randomized Controlled Trial	52 prostate cancer patients (27 on demand; 25 once a day)	Tadalafil (on demand) vs. Tadalafil (once a day) (before vs. after) 4, 12 weeks	International Index of Erectile Function (IIEF-EFD) Mean score (SD) Baseline, 1 month: On Demand: 6 (SD=2.9); 22.05 (SD=7.67); p<0.0001 Daily: 6.26 (SD=3.84); 27.09 (SD=2.35); p<0.01 Daily vs. on-demand: No difference between groups at one month or 3 months; p=0.22; p=0.19 Were you able to insert your penis into your partner's vagina? For both arms over time Baseline: not reported One month: 95.7%; p<0.0001 Daily vs. on-demand: No difference between groups at one month or 3 months; p=0.34; p=0.19 Sexual Encounter Profile (SEP) Q3 Did your erection last long enough for you to have successful intercourse? For both arms over time: Baseline: 6.2% One month: 71.5%; p<0.0001 No difference between groups at one month or 3 months; p=0.39; p=0.27	Three-dimensional conformal radiation therapy Also: Altered Sexual Function/ Satisfaction No statistically significant difference was shown between two arms for side effects. Attrition -15%

Erectile Dysfunction	Vardenafil (10 mg) titrated between 5-20 mg	Montorsi [52] (2008) Randomized Controlled Cross-over Trial	628 prostate cancer patients (210 placebo; 210 vardenafil nightly; 206 Vardenafil on demand)	Vardenafil nightly vs. vardenafil on demand vs. placebo 9, 11, 13 months 2 month wash out period and 2 month open label	International Index of Erectile Function (IIEF-EFD) % with a score ≥ 22 At 9, 13 months Treatment group: Nightly: 32.0%, 52.6% On demand: 48.2%, 54.2% Placebo group: 24.8%, 47.8% Statistical difference at 9 months: On demand vs. placebo: p=0.0001; Nightly vs. on demand: p=0.0065 At 13 months: no significant difference between groups. Sexual Encounter Profile (SEP) Q3 (Did your erections last long enough for you to have successful intercourse?) Success rate At 9, 13 months: Treatment group: Nightly: 34.5%, 59.8% On demand: 45.9%, 62.6% Placebo group: 25%, 57.1% Statistical difference: nightly vs. placebo: p=0.0344; on demand vs. placebo: p=0.0001 At 13 months: No statistical differences between groups after open label period.	Bilateral Nerve-Sparing Radical Prostatectomy Also: Altered Sexual Function/ Satisfaction Attrition -33%
Erectile Dysfunction	Sildenafil (50 mg) on demand with nightly placebo or nightly Sildenafil (50 mg) with on demand placebo	Pavlovich [50] (2013) Randomized Controlled Trial	100 prostate cancer patients (50 Sildenafil on demand; 50 Sildenafil nightly)	Sildenafil) on demand with nightly placebo vs. nightly Sildenafil with on demand placebo 12 months and then at 13 months after 1 month drug	International Index of Erectile Function (IIEF-EF) score At 12, 13 months: Nightly: 16.7; 13.8 On demand; 18.5, 19.2 p=0.456; p=0.022 But this difference at 13 months was not significant when adjusted for nerve sparing score (NSS) (p=0.071).	Bilateral Nerve-Sparing Radical Prostatectomy Attrition -33% Mean NSS was slightly higher in the on-demand cohort (7.1 vs. 6.5, p=0.033).

				free washout period		
Erectile dysfunction	Sildenafil (50mg), Vardenafil (10mg), or Tadalafil (10mg), daily +titration	Salonia [51] (2008) Non randomized experimental trial Participants self –selected into groups	100 prostate cancer patients self-selected to groups (36 "on-demand"; 15 "daily use"; 49 control)	PDE5i on demand vs. PDE5i daily vs. no treatment (before vs. after) 6, 12, 18 months	International Index of Erectile Function (IIEF-EFD) Mean score At 6, 12, 18 months: Treatment Group (on demand): 17.3 (SD=9.8); 22.5 (SD=8.4); 22.5 (SD=7.8) Treatment Group (daily): 19.0 (SD=8.6); 21.5 (SD=6.1); 23.5 (SD=2.1) Control group: 8.9 (SD=5.2); 17.5 (SD=9.9); 19.4 (SD=9.6) Significant difference treatment groups and control: p <0.001; p=0.12; p=0.42	Bilateral nerve-sparing radical retropubic prostatectomy (BNSRRP) Overall discontinuation rate of 72.6 % (37 patients)
Pharmacological Interventions – Early PDE5i vs. Late PDE5i -3 studies						
Erectile Dysfunction	Sildenafil (50 or 100mg) as needed or Vardenafil (10 or 20mg) 2xweek	Schiff [47] (2006) Retrospective cohort study	210 prostate cancer patients (85 early; 125 late)	Early (<1yr post-BT) vs. late (≥1yr post-BT) Sildenafil or Vardenafil 6, 18, 24, 30, 36 months	International Index of Erectile Function (IIEF-EFD) Mean score Early group vs. late: At Baseline: not significantly different At 18, 24, 30 and 36 months: P=0.04; p=0.03; p=0.04; p=0.03	Brachytherapy Attrition –NR
Erectile Dysfunction	Sildenafil (100mg) or 'trimix' (papaverine 30 mg/mL, phentolamine 1 mg/mL and prostaglandin-E1 (PGE1) 10µg/mL) or 'bimix' (papaverine 30 mg/mL, phentolamine 1 mg/mL) 3/week for 1 year	Mulhall [48] (2010) Case-control study	84 prostate cancer patients (48 early; 36 delayed)	Early Sildenafil± ICI (<6mo post-RP) vs. late Sildenafil± ICI (≥6mo post-RP) 4, 8, 12, 18 months	International Index of Erectile Function (IIEF-EFD) Mean score Two years after surgery: Early treatment group: 22 Delayed treatment group: 16 P<0.001	Bilateral nerve-sparing RP Attrition –NR

Erectile Dysfunction	Sildenafil (50 or 100 mg) 2/week for 6 months or ICI (PGE1)	Mosbah [39] (2011) Randomized Controlled Trial	18 prostate cancer patients (9 early started treatment at 2nd month after surgery; 9 late; started treatment at 6 months after surgery)	Early (2mo post-RP) vs. late (6mo post-RP) Sildenafil 6 months	International Index of Erectile Function (IIEF-EFD) Mean score At 36 months: Early treatment group: 21.7 (SD=6.5) Late treatment group: 13.1 (SD=7.7) Statistical difference: p=0.02 Comparison between pre- and postoperative (2nd month) IIEF questionnaire domains in both groups (p<0.05)	Nerve-Sparing Radical Cystoprostatectomy Also: Body Image Attrition -0%
Radiation therapy Intervention –2 different Radiation Therapy -1 study						
Erectile Dysfunction	Sildenafil (dose NR)	Ohebshalom [101] (2005) Retrospective Study	110 prostate cancer patients (68 CRT; 42 BT)	Brachytherapy vs. CRT (also 1 year vs. 2 year vs. 3 year follow up) 1, 2, 3 years	International Index of Erectile Function (IIEF-5) Mean score Less than 12 months: BT: 26 (SD=5) CRT: 23 (SD=4) p =0.02 13 to 24 months: BT: 22(SD=6) CRT: 19 (SD=4) p<0.01 25 to 36 months: BT: 17 (SD=9) CRT: 15 (SD=8) p=0.03	3-dimensional conformal external beam irradiation vs brachytherapy Attrition -0%
Pharmacological Interventions – Other -3 studies						
Erectile Dysfunction	Testosterone 1000 mg to start and then adjusted to reach free testosterone concentration of > 11.7 ng/dL Every 3 months for 1st year, then every 6 months	Balbontin [105] (2014) Prospective Case Series	20 prostate cancer patients	Before vs. after treatment	International Index of Erectile Function (IIEF-5) At baseline; 31 month median: 17.8, 22.1, p=0.002	Brachytherapy No cases of prostate cancer progression or recurrence
Erectile Dysfunction	Medicated Urethral system for Erection (MUSE)	Raina [104] (2007) Prospective study	73 prostate cancer patients	MUSE 3x/week vs. no treatment or treatment as necessary	International Index of Erectile Function (SHIM) Mean score Before RP: after RP; at 9 months (number of men)	Nerve sparing radical prostatectomy Attrition -32%

	Alprostadil (125 or 250 ug) 3/week for 9 months or ICIs, or sildenafil, or VCD		(38 treatment; 35 observation)	(ICIs, sildenafil, or VCD as per preference) 1, 3, 6, 9 months	Treatment group (21): 21.46 (SD=3.22); 6.78 (SD=2.72); 18.92 (SD=2.27) p<0.05 within group, over time No treatment group (13): 15.8 p=significant but not reported The control patients who recovered penile function, 71% were dissatisfied with the quality of their erections and sought adjuvant therapy.	Reasons stated for discontinuing included lack of efficacy or insufficient erections in nine, reduced sexual interest in five and urethral pain and/or burning in four.
Erectile Dysfunction	Sildenafil (100mg) or Vardenafil (20mg) and then added ICI therapy with Alprostadil (15 or 20 ug)	Mydlo [99] (2005) Retrospective Study	32 prostate cancer patients	Before (Sildenafil or Vardenafil only) vs. after (Sildenafil or Vardenafil + ICI-Alprostadil) 7 months	International Index of Erectile Function (SHIM) Mean score 22 of 32 men (68%) reported having a much better erection after starting ICI therapy. Before ICI: After ICI Sildenafil (12): 14.3; 23.4 Vardenafil (10): 14.9; 24.1 p=NR	Nerve-sparing radical retropubic prostatectomy Attrition -6%
Psychosocial Interventions -4 studies						
Erectile Dysfunction	Counseling (couples or individual) 4 sessions about 1 hour each	Canada [55] (2005) Randomized Controlled Trial	84 dyads (38 couple; 46 individual Prostate cancer patients and survivors	Couples counselling vs. individual counselling (and before versus after) 3, 6, months	International Index of Erectile Function (IIEF) Mean score Baseline, post treatment, 3, 6 month follow-up 24.8 (SD=18.7); 36.3* (SD=17.3); 38.9* (SD=21.0); 31.1 (SD=20.1) p<0.0001 for model across time *p<0001 compared with baseline Individual vs. Couple: There were no significant differences between these groups in terms of sexual function scores (FSFI or IIEF), marital satisfaction scores (R-DAS), or psychological distress scores (BSI). Percentage of patients using erectile dysfunction treatment increased after	Radical prostatectomy or radiation therapy Also: Intimacy/ Relationships and Altered Sexual Function / Satisfaction 61% attended all sessions Attrition -39%

					initiation of psychosocial intervention (31% to 49% at 6 months).	
Erectile Dysfunction	Internet-based counseling or face-to-face counseling for 3-sessions	Schover [56] (2012) Randomized Controlled Trial Pre/post post hoc analysis	186 couples (48 waitlist; 60 FF, 55 WEB1, 71 WEB2) Prostate cancer patients and survivors	Internet-based counselling vs. face-to-face counselling vs. wait list control (before vs. after) 3, 6, 12 months	International Index of Erectile Function (IIEF-5) Mean score At baseline and 12 months: 29.7 (SD=17.9); 36.2 (SD=22.4); p<0.001 over time Scores did not differ between groups and were analyzed altogether	Localized prostate cancer (T1-3N0M0) with either definitive surgery or radiotherapy Also: Intimacy/ Relationship Attrition -34%
Erectile Dysfunction	PLISSIT model 8 counselling sessions at 2 week internals	Ayaz [6] (2008) Case-Control Study	60 colorectal cancer patients (30 cases, 30 controls) For males (21) and female (9) and partners	Before intervention and post intervention	Golombok–Rust Inventory of Sexual Satisfaction (GRISS) Premature ejaculation domain: Treatment: 6.71 (SD=2.3); 5.67 (SD=2.1) Control: 6.50 (SD=2.3); 7.75 (SD=3.2) p<0.05 Impotence domain: Treatment: 2.62 (SD=2.2); 3.10 (SD=2.3) Control: 2.50 (SD=2.1); 5.75 (SD=4.1); p<0.05	Colorectal cancer Also: Sexual Function/Satisfaction
Erectile Dysfunction	Telephone intimacy enhancement counseling 4x 50 minute sessions	Reese [57] (2012) Pre-post intervention Study	9 dyads Colorectal cancer patients For male (5) and female (4)	Before telephone intimacy enhancement vs. after 1 month	International Index of Erectile Function (IIEF-5) Mean score Baseline: post treatment 26.0 (SD=16.2); 29.6 (SD=16.8) Effect size =0.22	Also: Intimacy/ Relationships and Altered Sexual Function/ Satisfaction 78% of patients reported they liked the telephone-based nature of the program Attrition -19%

Physical/Exercise Therapy Interventions -2 studies						
Erectile Dysfunction	Pelvic Floor Muscles Exercises Daily for 3 months	Lin [94] (2012) Randomized Controlled Trial	62 patients (35 intervention; 27 control)	Pelvic floor-muscle exercises vs. wait list control Baseline, 3, 6, 9, 12 months	International Index of Erectile Function (IIEF-5) Mean score At baseline, 3, 6, 9, 12 months Intervention group: 5.06 (SD=0.24); 5.80 (SD=2.26); 6.34 (SD=3.46); 6.63 (SD=3.65); 8.14 (SD=4.86) Control group: 5.00 (SD=0.00); 5.04 (SD=0.19); 5.00 (SD=0.00); 5.44 (SD=0.85); 5.96 (SD=0.98) p=0.16; 0.055; 0.028; 0.071; 0.014 Overall group effect in favour of the intervention group: (F=8.61, p<0.05)	Radical Prostatectomy PDE5i used but not controlled for in analysis Attrition -1.5%
Erectile Dysfunction	Resistance exercise (2x/week) and aerobic exercise (150 min/week) program for 12 weeks	Cormie [96] (2013) Randomized Controlled Trial	57 prostate cancer patients (29 intervention, 28 control)	Exercise vs. usual care 12 weeks	European Organization for Research and Treatment of Cancer prostate cancer-specific module (EORTC QLQPR25) sexual activity subscale (libido and activity) At baseline: Treatment group: 21.3 (SD=28.1) Control group: 19.8 (SD=28.1); At 12 weeks: Treatment group: 23 (SD=25.) Control group: 9.3 (SD=12.5), p=0.045 At 24 weeks: Treatment group: 24.5 (3–25) Control group: 21.0 (1–25) p=0.02	Androgen Deprivation Therapy Attrition=1%
Therapeutic Devices -3 studies						
Erectile Dysfunction	Vacuum Erectile Device 10 min/ day	Kohler [58] (2007) Randomized Controlled Trial	28 prostate cancer patients (17 early; 11 late)	Early vacuum erectile device (VED) (1mo after prostatectomy) vs. late (6mo) 1, 3, 6, 9, 12 months	International Index of Erectile Function (IIEF-5) Mean score At 3 and 6 months: Early treatment group: 11.5 (SD=9.4); 12.4 (SD=8.7) Late treatment group: 1.8 (SD=1.4)) 3.0 (SD=1.9) p=0.008; p=0.012	Radical retropubic prostatectomy Also: Body Image PDE-5I use allowed 6 months after RP Attrition -18%

Erectile Dysfunction	Penile Prosthesis or Tadalafil (20 mg) 3 times per week	Megas [97] (2012) Prospective Study	54 prostate cancer patients (25 prosthesis, 29 Tadalafil)	Penile prosthesis vs. Tadalafil Pre operative, post operative, 12, 24 months	International Index of Erectile Function (IIEF-5) Mean score Pre- post-surgery, 12, 24 months Penile Prosthesis: 23.8 (SD=1.6); 6.3 (SD=0.7); 26.4 (SD=1.3); 26.7 (SD=1.3) Tadalafil: 24 (SD=1.7); 6.2 (SD=0.7); 14 (SD=2.4); 14.3 (SD=2.5) p=0.725; p=0.573; p<0.001; p<0.001	Nerve Sparing Retropubic Radical Prostatectomy
Erectile Dysfunction	Penile prosthesis	Menard [98] (2011) Retrospective Study	90 prostate cancer patients, 131 ED patients (non-cancer)	Penile prosthesis in RP patients vs. penile prosthesis in vasculogenic ED patients 3 months	International Index of Erectile Function (IIEF-EFD) Mean score Preimplantation to follow up: RP patients: 6.1 (SD=3.3); 28.1 (SD=3.5) Vasculogenic patients: 9.2 (SD=4.5); 28.8 (SD=2.6); p=0.02 International Index of Erectile Function (IIEF-5) Mean score Preimplantation to follow up: RP patients: 14.7 (SD=5.9); 63.1 (SD=7.0) Vasculogenic patients: 22.6 (SD=10.8); 68.5 (SD=6.9); p=0.005	Radical Prostatectomy Mean follow-up of RP patients was 37.6 (SD= 26.8) months. Mean interval between RP and PP implantation was 31.5 (SD=28.7) months. Attrition -11%
Combination Treatments -3 studies						
Erectile Dysfunction	Prostaglandin E1 – intracavernosal injection therapy (PGE-ICI) (10 ug, twice per week) Psychodynamic-oriented short-term sexual therapy at each follow-up visit at	Titta [95] (2006) Randomized Controlled Trial	57 prostate cancer patients (29 sexual counseling + PGE1ICI; 28 ICI only)	PGE-ICI alone vs. PGE-ICI plus sexual counselling before vs. after surgery, 3, 18 months	International Index of Erectile Function (IIEF-5) Mean score Post surgery, 3, 18 months PGE-ICI plus counselling: 8.4; 23.4; 26.5 Control group: 8.4; 21.7; 24.3 Significant difference at 18 months: p<0.05	Non-Nerve-Sparing Radical Retropubic Prostatectomy or Cystectomy The counselling group yielded a significantly lower degree of discontinuance (P < 0.05

	3, 6, 9, 12, 18 months					Attrition -14%
Erectile Dysfunction	Tadalafil 20 mg per day 3x week With or without Vacuum erection device (VED) 5 days per week 10 minutes per day.	Engel [93] (2011) Randomized Controlled Trial	23 prostate cancer patients (13 Tadalafil plus VED 10 Tadalafil only)	Tadalafil alone vs. Tadalafil + VED Average 9 months	International Index of Erectile Function (IIEF-5) Mean score Baseline, Post surgery, 12 months Baseline for both groups: 24.7 Post surgery, 12 months Treatment group: 1.2, 18.9 Control group: 1.8, 11.1 p=NS, p<0.05 Were you able to achieve vaginal penetration? Percent yes Baseline, Post surgery, 12 months Baseline for both groups: 100% Post surgery for both group: 0% 9, 12 months: Treatment group: 92%, 92% Control group: 43%, 57%, p<0.05, p=NS Were you able to have intercourse to orgasm? Baseline for both groups: 100% Post surgery for both group: 0% 9, 12 months: Treatment group: 69%, 92% Control group: 14%, 29% p=NS, p>0.05	Bilateral Nerve-Sparing Radical Prostatectomy Attrition -22% VED use had an 100% compliance rate. Tadalfil use had a 40% (Tadalafil only) and 38% (Tadalafil + VED) adherence rate.
Erectile Dysfunction	Vacuum constriction device (VCD) and sildenafil (100mg), before sexual encounter. Non-responders included addition of Sildenafil to treatment protocol.	Raina [102] (2005) Observational Study	109 prostate cancer patients Minimal data provided on 74 patients only (treatment group only), with follow-up data provided on a subset of	VCD alone vs. VCD + Sildenafil Average 9 months	International Index of Erectile Function (IIEF-5) Mean score Post surgery, 9 months Post surgery for both groups: 4.8 (SD=1.61) Treatment group: 18.5 (SD=8.20) Control group: 14.5 (SD=5.63) No significant difference p=NR Return of nocturnal erections at 8 months post surgery:	Radical prostatectomy Attrition -22% VCD had an 80% compliance rate Reasons for discontinuance included discomfort (55%), unable to get

			31 patients only (treatment group were non-responders who received additional treatment)		Treatment group: 29% Control group: 0% The penile rigidity improvement after adding sildenafil (76% versus 55%) resulted in a greater penetration rate (70% versus 52%)	an airtight seal (8%), social inconvenience (17%), and penile bruising (20%)

Table 8.9 Body Image /Penile Changes -3 studies

Condition	Intervention	Author, study type	Population, diagnosis	Comparison/ Follow-up	Main findings	Comments
Pharmacological -1 study						
Change in penile length	Tadalafil (20 mg) on demand or 5 mg daily)	Montorsi [41] (2013) Randomized Controlled Trial	423 prostate cancer patients (143 on demand; 139 once daily; 141 placebo)	Tadalafil (on demand) vs. Tadalafil (once a day) vs placebo at 9 mos	Change in Stretched Penis Length Daily: -2.2 mm On demand: -7.9 mm Placebo: -6.3 Significant difference between daily and placebo, p=0.032 and daily and on demand, p=0.003 No significant difference between on demand and placebo,	Bilateral Nerve-Sparing Radical Prostatectomy Also: Sexual Response and Altered Sexual Function/ Satisfaction Attrition=26%
Therapeutic Devices -2 studies						
Penile changes in shape and size	Vacuum Erectile Device (VED) use daily	Kohler [58] (2007) Randomized Controlled Trial	28 prostate cancer patients (17 early; 11 late)	Early vacuum erectile device (1mo after prostatectomy) vs. late (6mo) 1, 3, 6, 9, 12 months	Stretched Penis Length (cm) At 3 and 6 months Group 1: −0.24 (−1.04 to 1.05; p=0.7); 0.6 (−2.53 to 1.29); p=0.5 No significant loss Group 2: -1.87 (−3.26 to 0.48; p=0.013); -1.82 (−3.2 to 0.47; p=0.013). Significant loss Number of patients with at least a 2 cm for penile shortening at the last follow-up number of patients: Group 1: 2/17 (12%) Group 2: 5/11 (45%)	Radical retropubic prostatectomy Also: Sexual Response PDE-5I use allowed 6 months after RP Attrition -29%

					p=0.044 No significant differences in penile girth, flaccid penile length, or suprapubic fat pad dimensions.	
Change in penile length	Vacuum Erectile Device use daily starting day after catheter removed	Dalkin (2007) [59] Prospective Cohort Study	39 prostate cancer patients	Before radical prostatectomy vs. after daily vacuum erectile device (VED) for 9 months	Stretched penile length mean (cm) Pre: 12.7 cm 90 days postoperative: 12.3 cm p>0.05 In men who were at least 50% compliant with the VED use, 35/36 (97%) maintained their stretched penile length.	Radical prostatectomy

Table 8.10 Intimacy/Relationships -8 studies

Condition	Intervention	Author, study type	Population, diagnosis	Comparison/ Follow-up	Main findings	Comments
Psychosocial Interventions -6 studies						
Intimacy/ Relationship	Partner-assisted emotional disclosure or education/ support only 4 face-to-face 75-minute sessions	Porter [60,61] (2009,2012) Randomized Controlled Trial	130 dyads (65 intervention; 65 control) Patients with gastrointestinal cancer and partners	Partner - assisted emotional disclosure vs. couples education/ support 3, 8 weeks	Quality of Marriage Index (QMI) Significant improvement in relationship quality over time for the intervention group compared to the education-only group (B=-0.07. SE=0.03, p=0.02). Miller Social Intimacy Scale (MSIS) No significant time by treatment effect for intimacy.	Gastrointestinal Cancer Attrition -28% Patients with high baseline levels of "holding back" showed greater improvements in relationship quality (p<0.0001) and intimacy (p<0.05) that were maintained for 8 weeks; while, patients with greater "expressiveness" showed improvements in relationship quality (p<0.05) and intimacy (p<0.05) immediately following the session but not in the longer term
Intimacy/ Relationship	Information booklet +	Walker [62] (2013)	27 couples	Information booklet +	Personal Assessment of Intimacy in Relationships (PAIR)	Androgen Deprivation Therapy

	educational session (1 hour private session)	Randomized Controlled Trial	Prostate cancer patients (allocation not described)	educational session vs. usual care 6 Months	(Groups not significantly different at baseline) 6 month change scores Treatment group: 4.75 (SD=8.57) Control: -3.17 (SD=17.40) Effect size=0.58; p=0.205 Dyadic Adjustment Scale (DAS) 6 month change scores Treatment group: 1.02 (SD=4.53) Control: -4.60 (SD=6.31) Effect size=1.02; p=0.191	Attrition –NR but mentions significant attrition in control group at one site
Intimacy/ Relationship	Peer-support counseling 8 intervention sessions over the phone: 2 before surgery, then at 2, 4, 6, 10, 16 and 22 weeks post surgery	Chambers [63] (2011) Pre-post intervention study	20 couples: Prostate cancer patients and partners	Before peer-support counseling vs. after 3, 6 months	Sexuality Care Needs: sexuality needs subscale Pre-surgery; 3 and 6 months post surgery Patient: 10.0 (SD=12.7); 24.4 (SD=23.5); 25.0 (SD=26.5) Partner: 3.2 (SD=8); 28.8 (SD=30.4); 25.6 (SD=29.2) Time effects: p<0.01 Sexuality supportive care needs increased between baseline and 3 months post-surgery (p = 0.002).	Radical prostatectomy Attrition -NR Also –main purpose is testing the peer support
Intimacy/ Relationship	Counseling (couples or individual) 4 sessions about 1 hour each	Canada [55] (2005) Randomized Controlled Trial	84 dyads (38 couple; 46 individual Prostate cancer patients and survivors	Couples counseling vs. individual counseling (and before versus after) 3, 6, months	Abbreviated Dyadic Adjustment Scale (R-DAS) Baseline, post treatment, 3, 6 month follow-up Males: 25.3 (SD=4.8); 25.3 (SD=4.7); 25.7 (SD=5.0); 24.8 (SD=4.9); p=0.64 across time Females: 24.5 (SD=5.6); 24.5 (SD=5.0); 25.1 (SD=5.2); 24.0 (SD=5.9) p=0.715 across time Individual vs. Couple:	Radical prostatectomy or radiation therapy Also: Sexual Response and Altered Sexual Function/ Satisfaction 61% attended all sessions Attrition -39%

					There were no significant differences between these groups in marital satisfaction scores (R-DAS).	
Intimacy/ Relationship	Internet-based counseling or face-to-face counseling for 3-sessions	Schover [56] (2012) Randomized Controlled Trial	186 couples (60 FF, 55 WEB1, 71 WEB2) (48 were wait listed) Prostate cancer patients and survivors	Internet-based counseling vs. face-to-face counseling vs. wait list control (before vs. after) 3, 6, 12 months	Abbreviated Dyadic Adjustment Scale (A-DAS) Mean Score No significant differences between any groups At baseline; 1 year follow-up Patients: 24.4 (SD=4.7); 24.6 (SD=4.5) Partners: 24.7 (SD=5.0); 24.7 (SD=5.2) No significant difference across time	Localized prostate cancer (T1-3N0M0) with either definitive surgery or radiotherapy Also: Sexual Response Attrition -34%
Intimacy/ Relationship	Cognitive existential couples therapy 6 weekly 90 minute couple sessions	Collins [64] (2011) Pre-post intervention Study	10 couples Prostate cancer patient and partner	Before Cognitive Existential Couples Therapy vs. after 2 months	Family Relationship Index (FRI) Cancer Support Inventory (CSI) No significant differences were found.	Recent diagnosis of PC localized to the prostate gland (T1–T3, NO, MO) Pilot Study Nine out of 10 participating couples who agreed to be interviewed about their experience of CECT revealed that it had been of value. Attrition -17%
Pharmacological Interventions – PDE5i vs. Placebo -1 study						
Intimacy/ Relationship	Sildenafil (dose NR)	Hanisch [38] (2012) Randomized Controlled Trial	24 dyads Prostate cancer patients and partners	Sildenafil vs. placebo (crossover study) 12-25 weeks	Locke's Marital Adjustment Test (LMAT) Mean Score Patients: Treatment: 1.5 (SD=12.4) Placebo: -0.78 (SD=12.5) p=0.37 Partners: Treatment: -0.50 (8.9) Placebo: -2.5 (9.9) p=0.35	Radiotherapy and some ADT (40% of patients) Also: Altered Sexual Function/ Satisfaction Attrition -NR

Therapeutic Devices -1 study						
Intimacy/ Relationship	Penile prosthesis	Ramsawh [106] (2005) Retrospective Study	92 prostate cancer patients (50 intervention; 42 control)	Penile prosthesis vs. no treatment NR	Dyadic Adjustment Scale (DAS) Treatment group: 113.74 (SD=14.00) Control group: 108.43 (SD=16.71) p=0.110	Simultaneous placement of a penile prosthesis at radical retropubic prostatectomy Also: Altered Sexual Function /Satisfaction Attrition -23%

Table 8.11 Overall Sexual Functioning and Satisfaction -9 studies

Condition	Intervention	Author, study type	Population, diagnosis	Comparison/ Follow-up	Main findings	Comments
Psychosocial Interventions -3 studies						
Sexual Function	CBT Stress Management 10 weeks of 2 hour group sessions	Molton [65] (2008) Randomized Controlled Trial	101 prostate cancer patients (60 intervention; 41 control)	10-week CBT-Stress Management vs. 4-hour CBT-Stress Management (control) Week 12-13 of study	UCLA-Prostate Cancer Index (sexual function subscale) CBSM treatment group assignment was a significant predictor of post intervention sexual functioning (ß=0.14, p<0.05) Men with higher interpersonal sensitivity, those assigned to the CBSM intervention showed larger pre-post change in sexual functioning versus controls (ß=0.19, p<0.05).	Radical prostatectomy Conducted a sub-group analysis on men with interpersonal sensitivity. Attrition -17%
Sexual Function Sexual Satisfaction	CBT Stress Management 8 group sessions	Siddons [66] (2013) Randomized Controlled Trial	60 prostate cancer patients (34 intervention; 26 control)	8 session CBT vs. waitlist Pre –post intervention	Derogatis Interview for Sexual Functioning—Self-Report (DISF-SR) Domain Scores Sexual Cognition Intervention: 20.073 Waitlist: 20.441; p=0.864 Sexual Behaviour:	Radical prostatectomy Response rate -24%

					Intervention: 9.173 Waitlist: 10.959; p=0.223 Satisfaction with Orgasm: Intervention: 4.742 Waitlist:5.885; p=0.301 Prostate Cancer-Related Quality of Life Scale (PCa-QoL) Domain score Sexual Confidence; Intervention: 6.147 Waitlist: 8.956; p=0.004	
Sexual Satisfaction	PLISSIT model 8 counselling sessions at 2-week intervals	Ayaz [6] (2008) Case-Control Study	60 colorectal cancer patients (30 cases, 30 controls) For males (21) and female (9) and partners	Before intervention and post intervention	Golombok–Rust Inventory of Sexual Satisfaction (GRISS) Total score: pre-post intervention Treatment: 26.38 (SD=8.5); 27.24 (SD=8.7) Control: 29.35 (SD=10.5), 41.10 (SD=13.5); p<0.05 Satisfaction domain: Treatment: 3.67 (SD=2.7); 4.62 (SD-3.6) Control: 4.15 (SD=3.2); 7.0 (SD=3.4) p<0.05	Colorectal cancer Also: Sexual Response
Pharmacological Interventions –PDE5i vs. Placebo -4 studies						
Sexual Satisfaction	Sildenafil (50 daily) for 6 months (Different start times for patients on ADT or not)	Zelefsky [67] (2014) Randomized Controlled Trial	202 prostate cancer patients (125 treatment, 77 placebo)	Sildenafil vs. placebo 6, 12, 24 months	International Index of Erectile Function (IIEF) Overall satisfaction (OS) domain scores OS Domain score: at 12 and 24 months (quartile 1-3) Treatment group: 8.00 (4.00-9.00); 8.00 (5.00-9.00) Placebo group: 6.00 (4.00-8.00); 6.00 (4.00-8.00); p=0.069; p=0.048 Scores were broken into ADT (10% of patients and non-ADT 90%) For non-ADT patients; OS scores were significantly different between groups	External Beam Radiotherapy, brachytherapy or brachytherapy combined with EBRT Also: Altered Sexual Function/ Satisfaction Attrition -NR

					at 6 (p=0.003), 12 months (p=0.027) and 24 months (p=0.033)	
Sexual Satisfaction	Tadalafil (20 mg) on demand or 5 mg daily)	Montorsi [41] (2013) Randomized Controlled Trial	423 prostate cancer patients (139 on demand; 143 once a day; 141 placebo)	Tadalafil (on demand) vs. Tadalafil (once a day) vs placebo at 9 mos, 10.5 mos (after 6 weeks drug free washout) and 13.5 mos (after 2 mos open label period)	Sexual Encounter Question (SEP) Q5 Were you satisfied overall with this sexual experience? At month 9, 10.5, 13.5 Daily: 25.4%, 16.3%, 40.8% On demand: 17.7%, 10.5%, 35.0% Placebo: 14.0%, 19.1%, 29.4% Daily vs. placebo: significant difference, p<0.05 at 9 months, no other comparisons were statistically significant.	Bilateral Nerve-Sparing Radical Prostatectomy Also: Sexual Response and Altered Sexual Function/ Satisfaction Attrition= 26%
Sexual Function	Sildenafil (50 or 100 mg) before sexual encounter for 12 weeks	Bruner [31] (2011) Randomized Controlled Cross-over Trial	61 prostate cancer patients	Sildenafil vs. placebo (crossover trial) 12 weeks, 25 weeks (12 weeks after crossover)	Sexual Adjustment Questionnaire (SAQ) The mean improvement was 2.58 (p=0.02) Based on the proportion of patients achieving a clinically meaningful change, there was no sildenafil effect (18% placebo only vs. 23% sildenafil only, p=0.53).	External Beam Radiotherapy and Short-Term Androgen Deprivation Therapy <120 days Also; Sexual Response Mild AEs caused by sildenafil were reported by 4% of all patients Attrition -16%
Sexual Function	Sildenafil (dose NR)	Hanisch [38] (2012) Randomized Controlled Trial	24 dyads Prostate cancer patients and partners	Sildenafil vs. placebo (crossover study) 12-25 weeks	Sexual Adjustment Questionnaire (SAQ) Mean score Patients: Treatment: 5.5 (SD=11) Placebo: 3.2 (SD=12) p=0.25 Partners: Treatment: 7.6 (6.8) Placebo: 3.8 (8.6) p=0.07	Radiotherapy and some ADT (40% of patients) Also: Intimacy/ Relationships Attrition -NR
Pharmacological Interventions – PDE5i vs. after Radical Prostatectomy vs. PDE5i after Radiation Therapy -1 study						

Sexual Function	PDE5i (dose NR)	Lee [107] (2008) Retrospective cohort	1087 patients (846 RP; 241 RT)	Radical prostatectomy (+PDE5i) vs. radiation therapy (+PDE5i) 6 months, 1, 2 years	UCLA PCI: Sexual Functioning response rate (%): (higher=better) At baseline: not reported 1 year or less: RP: 35, RT: 35 Greater than 1 year: RP: 28, RT: 25 Mean change scores: RP: 6.4, RT: 5.1 No difference response rates between the groups	Either prostatectomy or radiation therapy Baseline difference between groups Found that baseline sexual function score (before cancer treatment and before PDE5i treatment) were associated with change in sexual function score, and that a better baseline sexual function score was associated with a higher likelihood of response to PDE5i. Attrition -NR
Therapeutic Devices -1 study						
Sexual Satisfaction	Penile prosthesis	Ramsawh [106] (2005) Retrospective Study	92 prostate cancer patients (50 intervention; 42 control)	Penile prosthesis vs. no treatment Patients had procedure between 1993-2000	Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS): Treatment Group: 81.03 (SD=18.68) Control: 54.86 (SD=28.78) p<0.001 European Organization for the Research and Treatment of Cancer Quality of Life (EORTC QOL –Sexual Functioning Subscale) Treatment group: 2.2 (SD=2.32) Control: 5.22 (SD=3.12); p<0.001	Simultaneous placement of a penile prosthesis at radical retropubic prostatectomy Also: Intimacy/ Relationship These differences were observed despite the use of alternative sexual aids (i.e. ICI, Sildenafil, and/or VED) in 52.4% of the participants in the control group Attrition -23%

Table 8.12 Vasomotor Symptoms -11 studies

Condition	Intervention	Author, study type	Population, diagnosis	Comparison/ Follow-up	Main findings	Comments
Pharmacological -7 studies						
Hot Flashes	Milk protein powder (20 mg/d), venlafaxine (75 mg/d), soy protein powder (20 mg/d + 160 mg isoflavones)	Vitolins [69] (2013) Randomized Controlled Trial	120 prostate cancer patients	Placebo + milk powder vs. venlafaxine +milk powder vs. placebo + soy powder vs. venlafaxine + soy powder 12 weeks	Hot Flash Count and Hot Flash Severity decreased significantly in all arms (p<0.001) at 12 weeks Hot Flash Symptom Severity Score decreased significantly in each arm (p<0.001) at 12 weeks No significant differences between arms.	Androgen Deprivation Therapy There was a benefit at 2 weeks for venlafaxine that disappeared at 12 weeks.
Hot Flashes	Venlafaxine (75 mg) daily; medroxyprogesterone acetate (20 mg) daily; or cyproterone acetate (100 mg) daily	Irani [68] (2010) Randomized Controlled Trial	919 prostate cancer patients	venlafaxine (75 mg) daily vs. medroxyprogesterone acetate (20 mg) daily vs. or cyproterone acetate (100 mg) daily	Hot Flush Score median daily change from baseline for each condition, p compared to baseline at 4, 8 weeks venlafaxine group: -47.2% (IQR =-74.3--2·5); -56·7% (IQR=-80.9 to -21.7), p<0.0001 cyproterone group: -94·5% (IQR= -100·0--74·5); -100·0% (IQR=-100.0 to -83.5), p<0.0001 medroxyprogesterone group: -83.7% (IQR=-98.9- -64.3); -100·0% (IQR=-100.0 to -83.5), p<0.0001 Decreases in hot-flush score were significantly larger in the cyproterone and medroxyprogesterone groups than venlafaxine group p<0.0001 No difference between cyproterone and medroxyprogesterone groups, p>0.2.	Androgen Deprivation Therapy (Six months treatment with leuprorelin)
Hot Flashes	Gabapentin (300 mg) daily/ 28 days; gabapentin (300 mg) daily for 7 days and	Loprinzi [70] (2009) Randomized Controlled Trial	214 prostate cancer patients	1. Gabapentin (300 mg) daily for 28 days vs. 2. gabapentin (300 mg) daily	Hot Flash Score median % change for each condition: p vs. placebo 1. 22.8 (95% CI=12.1-33.0), p=0.80 2. 31.8 (95% CI=16.5-40.5). p=0.72 3. 45.5 (95% CI=31.1-50.6), p=0.10	Androgen Deprivation Therapy Attrition=23%

	then 2x daily for 21 days; gabapentin (300 mg) daily for 7 days then 2x daily for 7 days and then 3x daily for 14 days			for 7 days and then twice daily for 21 days, vs. 3. gabapentin (300 mg) daily for 7 days then twice daily for 7 days and then thrice daily for 14 days, vs. 4. placebo × 28 days.	4. 21.5 (95% CI=11.3-30.0) Hot Flash Frequency: median % change for each condition: 1. 29.7 (95% CI=13.1-36.9), p=0.75 2. 33.8 (95% CI=22.2-47.1), p=0.60 3. 45.5 (95% CI=35.2-56.3), p=0.02 4. 27.0 (95% CI=12.1-36.1)	Other significant difference were: 300 mg/day vs. 900 mg/day; Hot flash score, p=0.05; Hot Flash Frequency, p=0.03
Hot Flashes	Continuation of above study: Open label gabapentin	Moraska [71] (2010) Prospective Study	147 prostate cancer patients from Lorpinzi (2009) study	Gabapentin (600 mg) daily by end of study. (8 weeks) Before vs. after	Hot Flash Score median % decrease change at 12 weeks for each original condition with 4th week as a baseline: 1. 57%, 2. 39%, 3. 19%, 4. 4%	Androgen Deprivation Therapy Patients tended to end up at higher doses than 300 mg/d when allowed to modify their gabapentin regimen, changing daily dosing to achieve maximal efficacy.
Hot Flashes	Paroxetine (12.5mg/d week 1; 25 mg/d for week 2; 37.5 mg/d for week 3; any of the above for week 4)	Loprinzi [108] (2004) Prospective Study	18 prostate cancer patients	Before vs. after treatment 4 weeks	Number of Hot Flashes during a day; Baseline; 4 wks 6.2; 2.5, p=NR 50% decrease (CI=34-92%) Severity of hot flashes (1:not at all; 5: intermediate, 10; extremely severe) Baseline, 4 wks: 10.6; 3.0, p=NR 59% decrease (95% CI=31-87%)	Androgen Deprivation Therapy
Hot Flashes	Paroxetine (10 mg) daily for 4 weeks	Naoe [109] (2006)	10 prostate cancer	Before vs. after treatment	Number of Hot Flashes during a day; Baseline; 4 wks 3.5 (SD=2.6); 2.0 (SD=2.7), p=0.009	Androgen Deprivation Therapy

		Prospective Study	patients on ADT	4 wks	Severity of hot flashes (1:not at all; 5: intermediate, 10; extremely severe) Baseline, 4 wks: 4.6 (SD=3.1); 2.0 (SD=2.7), p=0.033	
Hot Flashes	*Salvia officinalis* extract (150 mg) 3x/d	Vandecasteele [110] (2012) Prospective Study	10 prostate cancer patients	Before vs. after treatment 10 weeks	Hot Flash Count and Hot Flash Severity Moyad score Baseline: 112 (SD=71) 10 weeks: 59 (SD=54) p =0.002	Androgen Deprivation Therapy There was a significant benefit shown at 1 week, p=0.024
Acupuncture -4 studies						
Hot Flashes	Acupuncture (12 bilateral points) 30 min, 2x weekly for the first 2 weeks and once weekly for 10 weeks with or without electro-stimulation	Frisk [74] (2009) Randomized Controlled Trial	31 prostate cancer patients	Acupuncture with (EA) or without (TA) electro-stimulation	Median number of Hot Flushes daily Baseline; 4 wk; 8 wk; 12 wk; 6 mo; 12 mo. Electro-stimulation 7.4 (IQR=5.5-12.0); 7.6 (IQR=4.9-8.7); 6.3 (IQR=3.6-7.5); 4.1 (IQR=2.0-6.5); 5.5 (IQR=2.6-7.4); 6.2 (IQR=4.2-6.5) Traditional 6.4 (IQR=5.2-9.4); 4.8 (IQR=3.0-6.6); 3.7 (IQR=2.0-6.9); 3.4 (IQR=1.8-6.3); 4.0 (IQR=1.7-7.2); 4.1 (IQR=2.7-5.2) No significant difference between groups overtime, p=0.25	Androgen Deprivation Therapy At 12 weeks, 57% (EA) and 47% (TA) of men had a median decrease in hot flushes of over 50%
Hot Flashes	Acupuncture (10 bilateral points) 2x/week for 4 weeks with electro-stimulation	Ashamalia [72] (2010) Prospective Study	14 prostate cancer patients	Before vs. after treatment 2, 6, weeks and 8 month	Hot Flash Score (hot flash frequency x severity) Baseline: 28.3 (SD=29.3) 2 weeks: 10.3 (SD=16.8), p=0.0001 6 weeks: 7.5 (SD=10.9), p=0.0001 8 months: 7.0 (SD=8.4), p=0.001 86% of patients experienced >50% improvement in HFS by the 2nd week. 100% experienced >50% improvement by the 6th week.	Androgen Deprivation Therapy Attrition=1%

					91% maintained a >50% improvement at 8 mos	
Hot Flashes	Acupuncture 2x/week for 4 weeks, then weekly for 6 weeks with electro-stimulation	Beer [73] (2010) Prospective Study	22 prostate cancer patients	Before vs. after treatment 4, 8 weeks	Percentage of men with 50% reduction in Hot Flash Score (hot flash frequency x severity) Baseline: 100% 4 weeks: 60% 8 weeks: 52% At 4 weeks, 41% (95% CI=21-64) had an > 50 % reduction in hot flashes. At 7 weeks, 55% (95% CI=32-76) had an > 50 % reduction in hot flashes.	Androgen Deprivation Therapy Attrition=NR
Hot Flashes	Auricular acupuncture (5 bilateral points) 40 min, 1x weekly for 10 weeks	Harding [75] (2008) Prospective Study	60 prostate cancer patients	Before vs. after treatment	Number of Hot Flushes during a day; Baseline; 4 wks; 10 wks 7.2 (SD=4.9); 3.8 (SD=3); 2.2 (SD=21.) p<0.05 Reduction in number of hot flushes: daytime=69%; night-time=50% Intensity of hot flushes (Out of 6) Baseline; 4 wks; 10 wks 3.2 (SD=0.8); 2.7 (SD=1.5); 1.6 (SD=1.4), p<0.05 Reduction in intensity of hot flushes: daytime=70%; night-time=63%	Androgen Deprivation Therapy (luteinizing-hormone releasing hormone)

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Guideline 19-6: Section 6

Interventions to Address Sexual Problems in People with Cancer

Document Review Summary

A. Matthew, D. Sivajohanathan and Members of the Interventions to Address Sexual Problems in People with Cancer Guideline Development Group

March 7, 2023

Guideline 19-6 was reviewed in 2023 and was determined to REQUIRE UPDATING.

This means that the guidance document needs updating to ensure that the recommendations reflect current evidence and practice. The existing recommendations remain relevant and it is still appropriate for this document to be available while the updating process unfolds.

OVERVIEW

The original version of this guidance document was released by Ontario Health (Cancer Care Ontario)'s Program in Evidence-based Care in 2016. The original guideline included searches completed by Cancer Care Ontario's Evidence Search and Review Service, as well as an updated search using a PEBC search strategy.

In December 2019, this document was assessed in accordance with the PEBC Document Assessment and Review Protocol and was determined to require a review. As part of the review, a PEBC methodologist (DS) conducted an updated search of the literature. One clinical expert (MA) reviewed and interpreted the new eligible evidence and proposed the existing recommendations should be updated.

DOCUMENT ASSESSMENT AND REVIEW RESULTS

Questions Considered

1. What is the effectiveness of pharmacological interventions, psychosocial counselling, or devices to manage sexual problems after cancer treatment? More specifically, we examined issues in men and in women separately.

Literature Search and New Evidence
The new search (January 2015 to June 2022) was conducted using the PEBC search strategy. A total of 60 studies met the inclusion criteria; 30 studies for men and 30 studies for women. An additional search for ongoing studies on clinicaltrials.gov yielded 16 relevant ongoing RCTs. Brief results of these searches are shown in the Document Review Tool.

Impact on the Guideline and Its Recommendations
While the new data support existing recommendations, the current recommendations do not take into consideration Equity, Diversity, Inclusion (EDI) principles. The guideline also fails to examine research specific to EDI populations. There's a strong connection between sexual health and gender diversity, orientation, racial, cultural, and ethnic factors which this guideline does not address. Hence, it is recommended that this guideline be UPDATED.

Document Review Tool

Number and Title of Document under Review	Guideline 19-6: Interventions to Address Sexual Problems in People with Cancer
Original Report Date	April 28, 2016
Date Assessed (by DSG or Clinical Program Chairs)	December 6, 2019
Health Research Methodologist	Duvaraga Sivajohanathan
Clinical Expert	Dr. Andrew Matthew
Approval Date and Review Outcome (once completed)	March 10 2023

Original Question(s):

2. What is the effectiveness of pharmacological interventions, psychosocial counselling, or devices to manage sexual problems after cancer treatment? More specifically, issues were examined in men and in women, separately.

Target Population:

This guideline is applicable to adult men and women (and partners) of all sexual orientations living with cancer of any type. For the purposes of this guideline, men and women who were previously treated for a childhood cancer were not included.

Study Selection Criteria:

As per the original study selection criteria, studies were included if they met the following criteria:

- Evaluated an intervention for improving sexual function in cancer patients and/or survivors
- Adult cancer patients/survivors made up at least 50% of the sample. Interventions were included if they incorporated some component that explicitly targeted sexual functioning
- English language because of unavailability of translation services
- No restrictions were placed on the type of outcome measures used
- There were no restrictions on study design

Due to the volume of studies found in this review, studies were restricted to RCTs.

Search Details:

- January 2015 to June 17, 2022 (MEDLINE, PsycINFO) using the Program in Evidence-Based Care (PEBC)'s search strategy. The search strategy is highlighted below.
- January 2015 to July 2022 (clinicaltrials.gov using the search terms "cancer AND sexual", "erectile dysfunction AND cancer" and "body image AND cancer")

Summary of new evidence:
There was a total of 685 hits (after deduplication) of guidelines and systematic reviews from MEDLINE and PsycInfo. There were no guidelines or systematic reviews published that examined the scope the current guideline and as a result, it was decided to focus on the primary literature.

There was a total of 2700 hits for primary literature after deduplication from MEDLINE and PsychInfo. Of these, 58 studies met the inclusion criteria; 30 studies for men and 28 studies for women. The search for ongoing studies on clinicaltrials.gov yielded 16 relevant ongoing RCTs.

Details from the included trials are summarized in the tables below. Tables 1 to 5 summarize the studies for men by outcome. Tables 6 to 10 summarize the studies for women by outcome. Table 11 summarizes ongoing RCTs.

Clinical Expert Interest Declaration:
AM declared no conflict of interest.

1. Does any of the newly identified evidence contradict the current recommendations? (i.e., the current recommendations may cause harm or lead to unnecessary or improper treatment if followed)	No.
2. Does the newly identified evidence support the existing recommendations?	Yes.
3. Do the current recommendations cover all relevant subjects addressed by the evidence? (i.e., no new recommendations are necessary)	Yes, but the current recommendations do not take into consideration Equity, Diversity, Inclusion (EDI) principles. It also fails to examine research specific to EDI populations. There's a strong connection between sexual health and gender diversity, orientation, racial, cultural, and ethnic factors which this guideline does not address.
Review Outcome as recommended by the Clinical Expert	UPDATE
If outcome is UPDATE, are you aware of trials now underway (not yet published) that could affect the recommendations?	No
DSG/Expert Panel Commentary	NA

Table 1. Main findings of studies for assessing erectile dysfunction/function by intervention in male patients.

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
Pharmacological interventions					
Canat et al (2015) [1]	129 patients with prostate cancer who underwent retropubic bilateral nerve-sparing RP with or without lymph node dissection	Erectile dysfunction	6 weeks & 12 months after surgery	Treatment 1: Patients using tadalafil 20 mg three times per week Treatment 2: Patients using tadalafil 20 mg on demand Control: Patients not using PDE5is.	IIEF-6 • At 6 weeks, there were no significant differences among the three groups with respect to the IIEF-6 scores. • At 12 months, the IIEF-6 score was significantly higher in patients receiving Treatment 1. There were no significant differences between Treatment 2 and Control groups.
Park et al (2015) [2]	80 male patients who underwent total mesorectal excision for rectal cancer	Erectile dysfunction	At the end of treatment and 12 weeks after treatment completion	Treatment: Udenefil 50 mg for 12 weeks Control: Placebo 50 mg for 12 weeks	IIEF-5 • At the end of treatment, the change in IIEF-5 scores from the baseline was significantly higher in the udenafil group compared with the placebo group ($p<0.05$). SEP Q2 and Q3, GAQ • Responses to SEP Q2, SEP Q3, and GAQ were significantly higher in the udenafil group compared with the placebo group ($p<0.001$).
REACTT study Patel et al (2015) [3] Mulhall et al (2016) [4]	423 patients who underwent nerve-sparing RP for organ-confined, non-metastatic prostate cancer	Erectile dysfunction	9 and 13.5 months	9-month treatment with Treatment 1: Tadalafil 5 mg once daily Treatment 2: Tadalafil 20 mg on demand Control: Placebo Followed by 6-week drug-free washout and	IIEF-EF • 22.3% of patients receiving tadalafil once daily had achieved “back-to-baseline” IIEF-EF, compared with 11.3% receiving tadalafil on demand and 7.8% receiving placebo. • The treatment group difference at the end of double-blind treatment was not maintained after the drug-free washout.

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
				3-month open-label tadalafil once daily	
Naccarato et al (2016) [5]	56 patients who opted for RP with preservation and without preservation of neurovascular bundles as the treatment of prostate cancer	Erectile dysfunction	At diagnosis and at the end of the 12 weekly sessions of psychotherapy	Treatment 1: Group psychotherapy Treatment 2: lodenafil 80 mg/week Treatment 3: Group psychotherapy + lodenafil 80 mg/week Control: Placebo	IIEF-5 • When comparing groups at baseline and at the end of protocol, only the treatment group receiving both group psychotherapy and lodenafil showed no significant worsening of the IIEF-5 (p=0.25).
Jo et al (2018) [6]	120 patients with prostate cancer who presented for RALP	Erectile dysfunction	3, 6, 9 and 12 months	Treatment 1: Sildenafil 100 mg twice/week for 3 months immediately after catheter removal Treatment 2: Sildenafil 100 mg twice/week 3 months after RALP	IIEF-5 • Full recovery was significantly higher during the 12 months in the early group than in the delayed group (p<0.001). • There was no significant difference in total IIEF scores between the 2 groups at 12 months (p=0.074). SEP Q2 and Q3 • There was no significant difference in SEP Q2 between the 2 groups at 12 months (p=0.271). • For SEP Q3, the early group showed a statistically higher rate at 12 months after surgery (p=0.014)
Mulhall et al (2018) [7]	131 men undergoing bilateral nerve-sparing open RP for the treatment of prostate cancer	Erectile dysfunction	18 and 24 months	Treatment: Tacrolimus 2 mg/day for 7 days prior to surgery and within 24-36 hrs after the surgery, and 3 mg/day upon discharge for 6 months Control: Placebo	IIEF-EF • At 18 months, there was no difference between the two groups' mean EF domain scores (p=0.09) time to achieve response to PDE5i.

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
Siltari et al (2019) [8]	118 men with prostate cancer	Erectile dysfunction	3, 6, 9, and 12 months after surgery	Treatment: Atorvastatin 80mg/day from study inclusion to day of surgery Control: Placebo	IIEF-5 • Preoperative atorvastatin treatment had no statistically significant effect on erectile function after prostatectomy as compared with placebo
Patel et al (2021) [9]	63 men with prostate cancer	Erectile dysfunction	3, 6, 9, and 12 months after surgery	Treatment: Erythropoietin Control: Placebo	IIEF-EF • There was no statistically significant difference in IIEF-EF scores at 6 months comparing erythropoietin to placebo (p=0.50) or at other time points (p=0.45). Quality of Erection Questionnaire • No difference between arms (p=0.48)
Pencina et al (2021) [10]	114 men who had undergone RP for low-grade, organ-localized prostate cancer, undetectable PSA for ≥2 years after RP and have testosterone deficiency	Erectile dysfunction	12 weeks	Treatment 1: 1 mg OPK-88004 daily for 12 weeks (later discontinued) Treatment 2: 5 mg OPK-88004 daily for 12 weeks Treatment 3: 15 mg OPK-88004 daily for 12 weeks (added later) Control: Placebo	IIEF, MSHQ There were no significant differences in the change from baseline in erectile function domain scores among the intervention arms either using the IIEF (p=0.15) or the MSHQ erection domain score (p=0.08)
Zhang et al (2021) [11]	100 patients with localized prostate cancer	Erectile dysfunction	After 6 months and 12 months of treatments	Treatment 1: 5 mg oral tadalafil daily Treatment 2: VED treatment for 15 min twice daily Treatment 3: 5 mg oral tadalafil daily + VED	IIEF-5 • IIEF-5 scores were higher in patients who received tadalafil and VED compared to the control after both 6 months (p<0.0001) and 12 months (p<0.0001). • No significant differences in return to the target EF using the IIEF-5 were noted between the groups (p=0.090)

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
				treatment for 15 min twice daily Control: Control group	SEP Q2 and Q3 • Successful penetration in those who had VED combined with tadalafil daily was significantly higher than in the control group (p=0.015).
Pelvic floor muscle therapy					
Geraerts et al (2015) [12]	33 patients with persistent erectile dysfunction, minimum 1 year after RP	Erectile dysfunction	3 months after end of PFMT	Treatment: Started PFMT immediately after surgery Control: Started PFMT at 15 months after surgery	IIEF • The treatment group had a significantly better erectile function than the control group at 15 months after surgery (p= 0.025).
de Lira et al (2019) [13]	31 patients undergoing open retropubic RP for localized prostate cancer	Erectile dysfunction	3 months after RP	Treatment: Two preoperative PFMT sessions including exercises. Patients performed exercises during the preoperative period and resumed them after removal of the urethral catheter. Patients exercised 3 times/day at progressively higher intensities. Control: Usual post-RP care	IIEF-5 • IIEF-5 scores were similar in the treatment and control groups (p>0.05)
Exercise					
Galvao et al (2022) [14]	57 patients with prostate cancer with established bone metastases	Erectile dysfunction	3 months after exercise	Treatment: 12-week exercise program comprising resistance, aerobic and flexibility training Control: Usual care	IIEF • After adjusting for baseline values, there were no significant differences for any measure of sexual function and activity following exercise

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
Shockwave therapy					
Zewin et al (2018) [15]	152 sexually active men with muscle invasive bladder cancer	Erectile dysfunction	1, 3, 6, and 9months postoperatively	Treatment 1: Shock wave lithotripsy group without any erectogenic agents Treatment 2: PDE5i group who received oral sildenafil 50 mg daily for 6 months only. Control: No therapy	IIEF-5 • There was no significant difference in all domains of IIEF score among the 3 groups during all follow-up periods EHS • There was no significant difference in EHS during the follow-up periods among the 3 groups
Baccaglini et al (2022) [16]	92 men who underwent RP	Erectile dysfunction	16 weeks	Treatment: Tadalafil 5 mg/day + low-intensity extracorporeal shockwave therapy Control: Tadalafil at a dose of 5 mg/day	IIEF-5 • A difference between groups was detected when accessing the final median IIEF-5 score (p=0.006); however, this was not sufficient to meet primary clinical outcome
Counselling					
Karlsen et al (2021) [17]	Patients with prostate cancer who underwent RP and had a female partner	Erectile dysfunction	Baseline, 8 and 12 months	Treatment: ProCan treatment (up to six 1-hr couple counselling sessions + up to three 1-hr individual sessions in PMFT) plus usual treatment Control: Usual treatment	IIEF-5 • No significant effect of the intervention was found on erectile function at 8 months or 12 months
Yoga					
Ben-Josef et al (2017) [18]	68 men with prostate cancer	Erectile dysfunction	Baseline, end of course (6-9 weeks)	Treatment: Yoga twice weekly Control: No yoga	IIEF • The yoga group remained unchanged over time, but the control group showed a decrease in function during the same period. The differences between treatment groups were significant at 4

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
					weeks (p=0.047) but not at final reading (p=0.314)
Hyperbaric oxygen therapy					
Chiles et al (2018) [19]	102 men with prostate cancer who underwent robot-assisted bilateral nerve-sparing RP	Erectile dysfunction	18 months	Treatment: Hyperbaric oxygenation therapy Control: Air	IIEF • No statistically significant differences were observed in median IIEF scores between the two groups (p=0.676). EPIC-26 • No difference was observed between the groups at baseline or at 18 months

Abbreviations: EF, Erectile function; EDITS, Erectile Dysfunction Inventory of Treatment Satisfaction; EHS, Erection Hardness Score; EPIC-26, Expanded Prostate Cancer Index Composite; GAQ; Global Assessment Question; IIEF, International Index of Erectile Function; MSHQ, Male Sexual Health Questionnaire; PDE5i, Phosphodiesterase type 5 inhibitor; PFMT, Pelvic floor muscle therapy; PSA, Prostate-specific antigen; Q, Question; RALP, Robot-assisted laparoscopic radical prostatectomy; RP, Radical prostatectomy; SEP, Sexual encounter profile; VED, Vacuum erectile device

Table 2. Main findings of studies for assessing urinary incontinence by intervention in male patients.

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
Pharmacological interventions					
Canat et al (2015) [1]	129 patients with prostate cancer who underwent retropubic bilateral nerve-sparing RP with or without lymph node dissection	Urinary continence	6 weeks & 12 months after surgery	Treatment 1: Patients using tadalafil 20 mg three times per week Treatment 2: Patients using tadalafil 20 mg on demand Treatment 3: Patients not using PDE5is.	IPSS, ICIQ-SF • There was no significant difference between the treated groups and the control group with respect to the continence status at 12 months after the surgery.
REACTT study Patel et al (2015) [3] Mulhall et al (2016) [4]	423 patients who underwent nerve-sparing RP for organ-confined, non-metastatic prostate cancer	Urinary incontinence	9 and 13.5 months	9-month treatment with Treatment 1: Tadalafil 5 mg once daily Treatment 2: Tadalafil 20 mg on demand Treatment 3: Placebo followed by 6-week drug-free washout and 3-month open-label tadalafil once daily	EPIC • EPIC urinary domain scores improved in all 3 treatment groups during double-blind treatment and continued to improve during open-label tadalafil • In older patients (aged 61-68 years) urinary incontinence domain-scores improved significantly with tadalafil once a day versus placebo (p=0.04)
Patel et al (2021) [9]	63 men with prostate cancer	Urinary Function	3, 6, 9, and 12 months after surgery	Treatment: Erythropoietin Control: Placebo	EPIC There was no difference in EPIC urinary domain scores between the two arms at 12 months
Exercise					
Galvao et al (2022) [14]	57 patients with prostate cancer with established bone metastases	Urinary incontinence	3 months after exercise	Treatment: 12-week exercise program comprising resistance, aerobic and flexibility training Control: Usual care	EORTC-PR25 • No significant differences for any measures of urinary and bowel function.

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
Shockwave therapy					
Baccaglini et al (2022) [16]	92 men who underwent RP	Urinary incontinence	16 weeks	Treatment: Tadalafil 5 mg/day + low-intensity extracorporeal shockwave therapy Control: Tadalafil at a dose of 5 mg/day	Continence was measured by pads/day. • There was no significant difference between the groups for continence (p=0.962).
Counselling					
Karlsen et al (2021) [17]	Patients with prostate cancer who underwent RP and had a female partner	Urinary incontinence	Baseline, 8 and 12 months	Treatment: ProCan treatment (up to six 1 hr couple counselling sessions + up to three 1 hr individual sessions in PMFT) plus usual treatment Control: Usual treatment	EPIC-26 • No significant effects were found on urinary incontinence, although improvements were seen at 8 months and 12 months.
Pelvic floor muscle therapy					
de Lira et al (2019) [13]	31 patients undergoing open retropubic RP for localized prostate cancer	Urinary incontinence	Three months after RP	Treatment: Two preoperative PFMT sessions including exercises. Patients were instructed to perform the exercises throughout the preoperative period and to resume them immediately after removal of the urethral catheter. Patients exercised three times a day at progressively higher intensities. Control: Usual post-RP care	ICIQ-SF • Pre-RP protocol of two physical therapist-assisted sessions of PFMT plus instructions did not significantly improve urinary continence at three months after RP
Strojek et al (2021) [20]	76 men with prostate cancer who received RP	Urinary incontinence	12 weeks after PMFT	Treatment: 24 individual sessions of physiotherapist-guided PFMT (twice a week	EPIC-26 • There is a statistically significant and large reduction of the

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
				over 3 months) two weeks following the surgery Control: No intervention	parameter values after the treatment for the overall urinary difficulties and incontinence.
Yoga					
Ben-Josef et al (2017) [18]	68 men with prostate cancer undergoing external beam radiation therapy	Urinary incontinence	Baseline, end of course (6-9 weeks)	Treatment: Yoga twice weekly Control: No yoga	IPSS • Although urinary symptom scores increased for both groups in the beginning half of the radiation therapy course, the yoga group's scores returned toward baseline during the latter half of the treatment period. This improvement in urinary incontinence can be partly explained by the effect of the yoga poses on pelvic floor muscle strength as the patients became increasingly proficient in their yoga practice. • There was a statistically significant effect of time ($p<0.0001$) but no significant effect of treatment ($P=0.1022$).
Hyperbaric oxygen therapy					
Chiles et al (2018) [19]	102 men with prostate cancer who underwent robot-assisted bilateral nerve-sparing RP	Urinary incontinence	18 months	Treatment: Hyperbaric oxygenation therapy Control: Air	EPIC-26 • No statistically significant differences were observed between the 2 groups on any outcome measure

Abbreviations: EORTC-QLQ-PR25, European Organization for Research and Treatment of Cancer - Quality of Life Questionnaire - Prostate Cancer Module; EPIC, Expanded Prostate Cancer Index Composite; hr, hour; ICIQ-SF, Incontinence Questionnaire - Short Form; IPSS, International Prostate Symptom Score; PDE5i, Phosphodiesterase type 5 inhibitor; PFMT, Pelvic floor muscle therapy; RP, Radical prostatectomy

Table 3. Main findings of studies for assessing sexual functioning and satisfaction by intervention in male patients.

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
Pharmacological interventions					

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
REACTT study Patel et al (2015) [3] Mulhall et al (2016) [4]	423 patients who underwent nerve-sparing RP for organ-confined, non-metastatic prostate cancer	Erectile dysfunction	9 and 13.5 months	9-month treatment with Treatment 1: Tadalafil 5 mg once daily Treatment 2: Tadalafil 20 mg on demand Control: Placebo followed by 6-week drug-free washout and 3-month open-label tadalafil once daily	EPIC-26 • Patients' EPIC sexual domain-scores improved significantly with tadalafil once a day versus placebo (p=0.004).
Naccarato et al (2016) [5]	56 patients who opted for RP with preservation and without preservation of neurovascular bundles as the treatment of prostate cancer	Sexual satisfaction	At diagnosis and at the end of the 12 weekly sessions of psychotherapy	Treatment 1: Group psychotherapy Treatment 2: Lodenafil 80 mg/week Treatment 3: Group psychotherapy + lodenafil 80 mg/week Control: Placebo	IIEF-5 • In satisfaction with their sex life, only those receiving group psychotherapy and lodenafil showed a significant improvement in sexual satisfaction (p=0.013) while those receiving only group psychotherapy showed a significant worsening (p=0.0003).
Pencina et al (2021) [10]	114 men who had undergone RP for low-grade, organ-localized prostate cancer	Sexual function	12 weeks	Treatment 1: 1 mg OPK-88004 daily for 12 weeks Treatment 2: 5 mg OPK-88004 daily for 12 weeks Treatment 3: 15 mg OPK-88004 daily for 12 weeks Control: Placebo	MSHQ, DISFM • There were no significant differences in changes in other domains of sexual function (e.g., arousal, ejaculation, orgasm) assessed using either the DISFM or the MSHQ
Exercise					
Mardani et al (2021) [21]	80 prostate cancer survivors	Sexual function	6 weeks & 12 weeks after exercise procedure	Treatment: 12-week exercise program consisting of one session of group exercise per week and three sessions of	EORTC QLQ-C30

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
				individual exercise per week managed by the participants Control: Routine healthcare for the treatment of prostate cancer and instructions to maintain their customary physical activities and dietary patterns	• In the intervention group, statistically significant improvements in sexual functions (p=0.0001) were reported.
Schumacher et al (2021) [22]	Pooled data from 2 RCTs that investigated the role of exercise in 115 patients with prostate cancer receiving ADT	Sexual function	6 months after exercise	Treatment: Exercise Control: Usual care	EORTC-QLQ-C30 and -PR25 • No significant between-group change was observed in sexual functioning between the exercise and control group.
Galvao et al (2022) [14]	57 patients with prostate cancer with established bone metastases	Sexual function Sexual satisfaction	3 months after exercise	Treatment: 12-week exercise program comprising resistance, aerobic and flexibility training Control: Usual care	EORTC-QLQ-PR25, IIEF, EPIC • After adjusting for baseline values, there were no significant differences for any measure of sexual function and activity following exercise
Shockwave therapy					
Zewin et al (2018) [15]	152 sexually active men with muscle invasive bladder cancer	Sexual satisfaction	1, 3, 6, and 9 months postoperatively	Treatment 1: Shock wave lithotripsy group without any erectogenic agents Treatment 2: PDE5i group who received oral sildenafil of 50 mg daily for 6 months only. Control: No therapy	IIEF-5 • There was no significant difference in all domains of IIEF score between the three groups during all follow-up periods • In the three groups, there was a significant increase in intercourse satisfaction and overall satisfaction domain scores.
Counselling					
Chambers et al (2015)	189 heterosexual couples where the man had been	Sexual Function	Baseline, 3, 6, and 12 months	Treatment 1: Phone support/counselling was	IIEF • There were no significant group differences for men's self-reported

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
(2019) [23,24]	diagnosed with prostate cancer and treated surgically			telephone-delivered by nurse counsellors Treatment 2: Phone support/counselling was telephone-delivered by peer support volunteers Control: Usual care	sexual function and satisfaction at the each of the time points post-surgery and at 2-5 years follow-up.
Wootten et al (2017) [25]	142 men diagnosed with localized prostate cancer and had received, or were currently receiving, treatment with curative intent	Sexual satisfaction	3 & 6 months	Treatment 1: Participants received access to online psychological intervention, My Road Ahead (MRA) Treatment 2: Participants received access to MRA plus the moderated forum Control: Participants received access to the moderated forum only.	IIEF • A significant improvement in total sexual satisfaction was observed only for participants who were allocated to MRA + forum with a large effect size (p=0.004)
Nelson et al (2019) [26]	53 men who had undergone a RP	Sexual function	4 and 8 months	Treatment: Standard care penile rehabilitation program plus the Acceptance and Commitment Therapy (ACT) intervention Control: Standard care penile rehabilitation plus an Enhanced Monitoring intervention	IIEF, EDITS, PHR-QOL, • At both time points, the ACT intervention, compared to the Enhanced Monitoring control group, reported no difference in sexual self-esteem, sexual confidence, and sexual bother.
Penedo et al (2020) [27]	192 men diagnosed with stage III or IV prostate cancer, and had undergone ADT and experienced an	Sexual function	1 year	Treatment: 10-week tablet-delivered cognitive-behavioral stress management (CBSM) Control: Health promotion	EPIC • Sexual functioning scores decreased over time in both the treatment and control arms

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
	ADT-related symptom				
Karlsen et al (2021) [17]	Patients with prostate cancer who underwent radical prostatectomy and had a female partner	Sexual functioning	Baseline, 8 and 12 months	Treatment: ProCan treatment (up to six 1 hr couple counselling sessions + up to three 1hr individual sessions in PMFT) plus usual treatment Control: Usual treatment	IIEF-5 • No significant effect of the intervention was found on sexual function at 8 months or 12 months.
Wittman et al (2022) [28]	142 couples where the male had been diagnosed with localized prostate cancer	Sexual function	3 and 6 months after treatment	Treatment: TrueNTH Sexual Recovery Intervention, a tailored, interactive, web-based tool, on patients' and their partners' recovery of sexual intimacy after prostate cancer treatment Control: Standard informational sources	PROMIS-GSSL • At the 6-month follow-up. GSSL scores were not significantly different between the intervention and control arms for patients (p=0.4) or their partners (p=0.5). • Three months after treatment, intervention patients and partners reported more engagement in penetrative and nonpenetrative sexual activities than controls.

Abbreviations: ADT, Androgen deprivation therapy; DISFM, DeRogatis Inventory of Sexual Function for Men; EDITS, Erectile Dysfunction Inventory of Treatment Satisfaction; EORTC-QLQ-C30, European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire - Core; EORTC-QLQ-PR25, European Organization for Research and Treatment of Cancer - Quality of Life Questionnaire – Prostate Cancer Module; EPIC, Expanded Prostate Cancer Index Composite; IIEF, International Index of Erectile Function; MSHQ, Male Sexual Health Questionnaire; PHR-QOL, Prostate-Health Related Quality of Life; PROMIS-GSSL, Patient-Reported Outcomes Measurement Information System - Global Satisfaction With Sex Life; RCT, Randomized controlled trial; RP, Radical prostatectomy

Table 4. Main findings of studies for assessing relationship and intimacy by intervention in male patients.

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
Pharmacological treatment					
Naccarato et al (2016) [5]	56 patients who opted for RP with preservation and without preservation of neurovascular bundles as the treatment of prostate cancer	Relationship and intimacy	At diagnosis and at the end of the 12 weekly sessions of psychotherapy	Treatment 1: Group psychotherapy Treatment 2: lodenafil 80 mg/week Treatment 3: Group psychotherapy + lodenafil 80 mg/week Control: Placebo	IIEF-5 • When asked about satisfaction in intimacy with a partner, only those who received group psychotherapy and lodenafil showed significant improvement at the end of the protocol (p=0.045) and those who received lodenafil only showed a significant worsening (p=0.014).
Counselling					
Chambers et al (2015) (2019) [23,24]	189 heterosexual couples where the man had been diagnosed with prostate cancer and treated surgically	Relationship and intimacy	Baseline, 3, 6, and 12 months	Treatment 1: Phone support/counselling was telephone-delivered by nurse counsellors Treatment 2: Phone support/counselling was telephone-delivered by peer support volunteers Control: Usual care	Revised Dyadic Adjustment Scale • At 4 years post-surgery, women in usual care had greater marital satisfaction than women in the peer group (p=0.005) and women in the nurse group also had greater marital satisfaction than women in the peer group (p=0.006). • Women in usual care had greater feelings of intimacy at 2 years (p=0.035) and 4 years post-surgery (p=0.013) than women in the peer group. Further, women in usual care had greater feelings of intimacy at 2 and 5 years post-surgery compared with women in the nurse group.
Couper et al (2015) [29]	62 patients with prostate cancer and their partner	Relationship and intimacy	10 weeks and 9 months	Treatment: Cognitive existential couple therapy Control: Usual care	FRI • Relationship cohesion (p=0.03) and relationship function (p=0.01) improved for younger patients.

Abbreviations: FRI, Family Relationship Index; IIEF, International Index of Erectile Function; RP, Radical prostatectomy

Table 5. Main findings of studies for assessing penile length by intervention in male patients.

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
Pharmacological treatment					
Zhang et al (2021) [11]	100 patients with localized prostate cancer	Change in penile length	After 6 months and 12 months of treatments	Treatment 1: 5 mg oral tadalafil daily Treatment 2: VED treatment for 15 min twice daily Treatment 3: 5 mg oral tadalafil daily + VED treatment for 15 min twice daily Control: Control group	• After 6 months and 12 months of treatment, the PLNES of the patients in the VED and VED + tadalafil groups was much longer than in the control group. In addition, the PLNES of the patients in the VED and VED + tadalafil groups were much longer than that in the tadalafil only group after 12 months of treatment.
Pelvic floor muscle therapy					
Geraerts et al (2016) [12]	33 patients with persistent erectile dysfunction, minimum 1 year after RP	Change in penile length	3 months after end of PFMT	Treatment: Started PFMT immediately after surgery Control: Started PFMT at 15 months after surgery	VAS scale • At 15 months, the treatment group scored significantly better than the control group regarding the change in hardness, length, tumescence, and elevation.

Abbreviations: PFMT, Pelvic floor muscle therapy; PLNES, Penile length in the non-erectile state; RP, Radical prostatectomy; VAS, Visual analogue scale; VED, Vacuum erectile device

Table 6. Main findings of studies for assessing sexual function and satisfaction by intervention in female patients

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
Pharmacological intervention					
Barton et al (2022) [30]	230 postmenopausal women diagnosed with breast or gynecologic cancer	Sexual function	Baseline, weeks 5 and 9	Treatment 1: Extended-release bupropion 150 mg once daily Treatment 2: Extended-release bupropion 300 mg once daily Control: Placebo one daily	FSFI • At 9 weeks, there were no statistically significant differences in change of the desire subscale or total scores of the FSFI between groups.
Vaginal gel					
Goetsch et al (2015) [31]	46 breast cancer survivors with dyspareunia	Sexual function	Baseline, 1 and 2 months	Treatment: 4% aqueous lidocaine Control: Saline After one month of blinded trials, all patients received lidocaine in an open-label trial	Sexual Function Questionnaire, FSDS-Revised • Users of lidocaine reported less pain during intercourse in the blinded phase (p=0.007) • Sexual distress decreased (p<0.001), and sexual function improved in all but one domain after use of lidocaine
Hickey et al (2016) [32]	38 postmenopausal breast cancer patients	Sexual discomfort	Baseline, 1, 2 and 3 months	Randomized crossover design Treatment: Silicone-based lubricant Control: Water-based lubricant	SAQ-D • Water- and silicone-based lubricants did not differ statistically in efficacy based on total sexual discomfort (p=0.06) • Pain/discomfort during penetration improved more during silicone-based lubricant use than during water-based lubricant use (p=0.02)
Advani et al (2017) [33]	57 postmenopausal women with early-stage breast cancer starting aromatase inhibitors	Sexual function	Baseline, 6 and 12 months	Treatment 1: 6-month supply of a hyaluronic acid-based vaginal moisturizer and a vaginal lubricant and dilator, plus access to an educational website and phone coaching Treatment 2: 6-month supply of a prebiotic vaginal moisturizer and a vaginal lubricant and dilator, plus access to an	FSFI • The combined active treatment group had less sexual distress (p= 0.02) at 6 months than the Usual Care group. • At 6 months, the hyaluronic acid-based vaginal moisturizer group improved significantly more than the prebiotic vaginal moisturizer group on FSFI total score (p=0.04).

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
				educational website and phone coaching Control: Usual care	
Hirschberg et al (2017) [34]	61 women with hormone receptor-positive early breast cancer receiving NSAI	Sexual function	Baseline, weeks 3 and 12	Treatment: 0.005% estriol vaginal gel Control: Placebo	FSFI • Active treatment significantly improved vaginal dryness and global scores of symptoms and signs. • Active treatment also increased the total FSFI score and all the FSFI domains, except for pain.
Kim et al (2017) [35]	136 premenopausal breast cancer survivors	Sexual function	Baseline and 8 weeks	Treatment: a pH-balanced gel was administered three times per week at bedtime as well as during sexual intercourse for 8 weeks Control: Placebo	FSFI • Overall FSFI score and the frequency of sexual dysfunction also did not differ between the two groups although both groups showed a significant improvement at follow-up.
Counselling					
Esplen et al (2018) [36]	194 breast cancer survivors	Sexual function	Baseline, 8 weeks, 6 and 12 months	Treatment: Restoring Body Image After Cancer (ReBIC), an 8-week group intervention using guided imagery within a group-therapy approach + reference book Control: Reference book	FSFI • There was no statistically significant difference between the groups in sexual functioning.
Fatehi et al (2019) [37]	118 breast cancer survivors	Sexual function Sexual satisfaction	Baseline, 3 months	Treatment: Six weekly psychosexual counselling sessions that lasted from 90 to 120 min Control: Usual care	FSFI, ISS, SQOL-F • Sexual function (FSFI) scores and sexual quality of life (SQOL-F), had statistically significant differences between the two groups at 3 months ($p<0.001$) • There was no significant difference in the total Larson ISS score between the two groups at 3 months ($p=0.073$)

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
Khoei et al (2020) [38]	75 women with a breast cancer diagnosis	Sexual function	Weeks 6 and 12	Treatment 1: In-person, individual counselling using the PLISSIT model Treatment 2: Grouped Sexuality Education (GSE) Control: Routine care	13-item sexual distress questionnaire • GSE and PLISSIT were both effective in improving sexual behaviors ($p<0.0001$) with a positive change in sexual capacity, motivation, and performance after 6 and 12 weeks post-intervention follow-ups. • GSE model showed a greater efficacy than the PLISSIT model.
Schofield et al (2020) [39]	319 women with gynecological cancer scheduled to receive radiotherapy with curative intent	Sexual satisfaction	Baseline, before first radiotherapy, 2-4 weeks, 3, 6 and 12 months	Treatment: 4 nurse-led consultations plus 4 peer-led telephone sessions Control: Usual care	SVQ • Average Global Sexual Satisfaction scores did not differ significantly between groups at baseline or at follow-up. The group by time interaction was not significant ($p=0.11$)
Shi et al (2020) [40]	91 patients who had undergone radical hysterectomy for early-stage cervical cancer	Sexual function	Baseline, 3 and 6 months	Treatment: Nurse-led 4-week PERMA model-based psychology intervention Control: Usual care	FSFI • Participants in the intervention group showed significant improvements in sexual function compared with participants in the control group at 3 and 6 months post-intervention ($p=0.005$ and $p=0.001$, respectively)
Couple-based intervention					
Reese et al (2019) [41]	29 breast cancer survivors	Sexual function Sexual satisfaction	Baseline & 4 weeks	Treatment: 4- session couple-based Intimacy Enhancement intervention delivered via telephone Control: Educational session	FSFI • There was no difference in sexual functioning between the treatment and control group
Cognitive behaviour therapy					
Hummel et al (2017) [42]	169 breast cancer survivors	Sexual function Sexual satisfaction	Baseline, 10 weeks after start of therapy and at 24	Treatment: 24 weeks of therapist-guided internet-based cognitive behavioural therapy	FSFI, SAQ, FSDS-R, • Compared with the control group, the intervention group showed a significant improvement over time in overall sexual functioning (0.031), which was reflected

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
			weeks (end of therapy)	Control: An information booklet addressing sexuality issues after breast cancer treatment was provided with a follow-up to answer any questions	in an increase in sexual desire (p<0.001), sexual arousal (p= 0.008), and vaginal lubrication (p=0.013). • No significant effects were observed for orgasmic function, sexual satisfaction, intercourse frequency, relationship intimacy, marital functioning, psychological distress, or health-related quality of life.
Atema et al (2019) [43]	254 breast cancer survivors	Sexual function	Baseline, 10 weeks, 24 weeks	Treatment 1: A therapist-guided 6-week iCBT group Treatment 2: A self-guided 6-week iCBT group Control: Usual care	SAQ No significant overall group-by-time interactions were observed for any of the scales that assessed sexual functioning
Education					
DuHamel et al (2016) [44]	70 female rectal and anal cancer survivors	Sexual dysfunction	Baseline, 4 months, 8 months	Treatment: 4-session Cancer Survivorship Intervention-Sexual Health Control: Assessment only	FSFI • Sexual functioning scores did not differ between the study arms at both the 4- and 8-month follow-up
Li et al (2016) [45]	226 cervical cancer patients	Sexual function	Baseline, 6 months	Treatment: Patients in the intervention group received an individual home-based, nurse-led health program + conventional nursing education Control: Conventional nursing education	FSFI • Significant differences in change scores between the groups were found for sexual function (p=0.000) with a significant increase in scores in the treatment group and a decrease in scores in the control group
Lubotzky et al (2019) [46]	82 women scheduled for pelvic radiation therapy to treat gynecological or anorectal cancer	Sexual Function Sexual satisfaction	Baseline, 3, 6 and 12 months	Treatment: A study-developed psychosexual rehabilitation booklet Control: Standard information materials	SAQ, Sexual Vaginal Changes Questionnaire • No significant differences between the two groups were found on sexual measures.

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
Abedini et al (2020) [47]	80 women diagnosed with breast cancer	Sexual satisfaction	Baseline, 1, 2, and 3 months	Treatment: 3 sessions of a psychological individual intervention which included psychoeducation regarding their diagnosis and personalized intervention strategies that lasted 60-90 min Control: Usual care	ISS • The intervention group showed a positive increasing trend in the sexual satisfaction scores over time while the control group participants had a negative trend ($p<0.05$). • There were also statistical differences in the sexual satisfaction scores at each follow-up month ($p<0.05$) showing longer term effects with a significant increase in sexual satisfaction over time.
Chow et al (2020) [48]	202 women with newly diagnosed gynecological cancer	Sexual function Sexual satisfaction	Baseline, 12 weeks	Treatment: A 4-session, 12-week-long, culturally appropriate psychoeducational intervention program Control: Attention from the research nurse on four occasions within the same time interval in which the program was applied to the intervention group	C-SVQ • No significant between-group differences were observed in the subscale scores of sexual interest, global sexual satisfaction, vaginal changes, and sexual functioning.
Kang et al (2022) [49]	109 women with newly diagnosed stage I-III breast cancer	Sexual functioning	Baseline, 1 and 6 months	Treatment: A structured education program (BODY) for 4 weeks Control: No educational program	EORTC QLQ-BR23 • The intervention group reported higher levels of sexual functioning compared to the control group at follow-up
Wellness program					
Anderson et al (2015) [50]	55 women aged 45 to 60 years with one moderate to severe menopausal symptom and a	Sexual function	Baseline, 12 weeks	Treatment: A lifestyle intervention (The Pink Women's Wellness Program) that included clinical consultations and a tailored health education program	GCS, FACT- Breast and -General • Women in the intervention group reported clinically significant reductions in many menopausal symptoms, and sexual dysfunction at 12 weeks compared with the control group.

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
	history of breast cancer			Control: A booklet on breast cancer and early menopause and continued usual care	
Hypnosis					
Barton et al (2019) [51]	87 women who have or have had breast or gynecologic cancer	Sexual satisfaction	Baseline, 6 weeks	Treatment: Hypnosis (three sessions, one every 2 weeks) Control: Progressive muscle relaxation (three sessions, one every 2 weeks)	PROMIS • There was significant difference in sexual satisfaction scores between the two groups.

Abbreviations: C-SVQ, Chinese-version Sexual Function-Vaginal Changes Questionnaire; EORTC QLQ-BR23 European Organization for Research and Treatment of Cancer - Quality of Life Questionnaire - Breast Cancer Module; FACT, Functional Assessment of Cancer Therapy; FSFI, Female Sexual Function Index; FSDS, Female Sexual Distress Scale; FSDS-R, Female Sexual Distress Scale Revised; GCS, Greene Climacteric Scale; iCBT, Internet-based cognitive behavioural therapy; ISS, Index of Sexual Satisfaction; NSAI, nonsteroidal aromatase inhibitors; SAQ, Sexual Activity Questionnaire; SAQ-D, Sexual Activity Questionnaire Discomfort subscale; SQOL-F, Sexual quality of life

Table 7: Main findings of studies for assessing body image by intervention in female patients.

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
Exercise					
Paulo et al (2019) [52]	36 older breast cancer survivors	Body image	Baseline, 6 and 9 months	Treatment: Resistance + aerobic exercise program Control: Stretching	EORTC QLQ-BR23 • Body image presented a significant time x group interaction (p=0.01) • The post hoc test revealed that the exercise group demonstrated improved body image after 3 months of combined training compared to baseline (p<0.001) and after 6 months in relation to 3 months of training
Counselling					
Esplen et al (2018) [36]	194 breast cancer survivors	Body image	Baseline, 8 weeks, 6 and 12 months	Treatment: Restoring Body Image After Cancer (ReBIC), an 8-week group intervention using guided imagery within a group-therapy approach + reference book Control: Reference book	BIS, BIBCQ • Women in the intervention group reported significantly less concern/distress about body appearance (p<0.01), decreased body stigma (p<0.01) compared with women in the control group.
Farnam et al (2021) [53]	100 breast cancer survivors	Body image	2 and 3 months	Treatment: Good Enough Sex model-based sexual counselling - 4 sessions of 120-190-minute sexual counselling (partners were present for 2 sessions) Control: Educational content in the form of 4 one-hour voice files in the Telegram group chat	BIS • There was a statistically significant difference in the mean scores for body image between the intervention and control group (p<0.001)
Hamidi et al (2022) [54]	60 women with breast cancer	Body image	Baseline, 1 month	Treatment: Social network-based support program was held in eight sessions (two 45min sessions per week) on WhatsApp messenger	BIS • There was no significant difference in BIS scores between the treatment and control arm (p=0.700).

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
				Control: Eight sessions (two 45min per week) were held on WhatsApp messenger where they received audio and video files whose content was not related to sexual self-concept	
Couple-based intervention					
Reese et al (2019) [41]	29 breast cancer survivors	Body Image	Baseline & 4 weeks	Treatment: 4- session couple-based Intimacy Enhancement intervention delivered via telephone Control: Educational session	BIS • A small effect was found for a reduction in body image distress in the treatment group
Cognitive behaviour therapy					
Hummel et al (2017) [42]	169 breast cancer survivors	Body image	Baseline, 10 weeks after start of therapy and at 24 weeks (end of therapy)	Treatment: 24 weeks of therapist-guided internet-based cognitive behavioral therapy Control: An information booklet addressing sexuality issues after breast cancer treatment was provided with a follow-up to answer any questions	EORTC-QLQ-BR23 • The intervention group reported greater improvement in body image (p=0.009)
Sherman et al (2018) [55]	304 breast cancer survivors (disease-free stage I-III) who had experienced at least one negative event related to bodily changes after breast cancer	Body image	1 week, 1 and 3 months	Treatment: My Changed Body, a Web-based psychological intervention to alleviate body image-related stress Control: Expressive writing	BIS, BAS, SCSSF Participants who received My Changed Body reported significantly less body image-related distress (p=0.035) and greater body appreciation (p=0.004) and self-compassion (p<0.001) than expressive writing participants
Hypnosis					
Barton et al (2019) [51]	87 women who have or have had breast or gynecologic cancer	Body image	Baseline, 6 weeks	Treatment: Hypnosis (three sessions, one every 2 weeks)	Impact of Treatment Scale • Both groups reported significant improvements on body image over

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
				Control: Progressive muscle relaxation (three sessions, one every 2 weeks)	time with no significant difference between groups (p = 0.15).
Education					
Bandani et al (2021) [56]	38 women with breast cancer	Body image	Baseline, 7 weeks	Treatment: A mobile health educational intervention where text messages were sent to the intervention group via WhatsApp messenger for 7 weeks on a daily schedule Control group: No messages One month after completing the post-test, educational text messages were sent to the control group for 2 weeks.	BICI There was a significant difference in the mean score of body image concern inventory in the intervention group (p=0.002) after the intervention compared with the control group
Kang et al (2022) [49]	109 women with newly diagnosed stage I-III breast cancer	Body image	Baseline, 1 and 6 months	Treatment: A structured education program (BODY) for 4 weeks Control: No educational program	EORTC-QLQ-BR23 • The intervention group reported significantly better body image compared to the control group (p<0.01)

Abbreviations: BAS, Body Appreciation Scale; BIBCQ, Body Image After Breast Cancer Questionnaire; BICI, Body Image Concern Inventory; BIS, Body Image Scale; EORTC-QLQ-BR23, European Organization for Research and Treatment of Cancer - Quality of Life - Breast Cancer Questionnaire; SCSSF, Self-Compassion Scale–Short Form

Table 8. Main findings of studies for assessing genital symptoms by intervention in female patients.

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
Vaginal gel					
Goetsch et al (2015) [31]	46 breast cancer survivors with dyspareunia	Dyspareunia	Baseline, 1 and 2 months	Treatment: 4% aqueous lidocaine Control: Saline After one month of blinded trials, all patients received lidocaine in an open-label trial	FSFI, Numerical Rating Score • Users of lidocaine reported less pain during intercourse in the blinded phase (p=0.007). • After open-label lidocaine use, 37 (90%) of 41 reported comfortable penetration.
Kim et al (2017) [35]	136 premenopausal breast cancer survivors	Dyspareunia	Baseline and 8 weeks	Treatment: a pH-balanced gel was administered three times per week at bedtime as well as during sexual intercourse for 8 weeks Control: Placebo	FSFI • There was no difference between the two groups, both experienced a significant improvement of dyspareunia • Vaginal pH and vaginal maturation index were slightly but significantly improved only in the pH-balanced group.
Advani et al (2017) [33]	57 post-menopausal women with early-stage breast cancer starting aromatase inhibitors	Dyspareunia	Baseline, 6 and 12 months	Treatment 1: 6-month supply of a hyaluronic acid-based vaginal moisturizer and a vaginal lubricant and dilator + access to an educational website and phone coaching Treatment 2: 6-month supply of a prebiotic vaginal moisturizer and a vaginal lubricant and dilator + access to an educational website and phone coaching Control: Usual care	FSFI • The combined active treatment group had less dyspareunia (p= 0.07) at 6 months than the Usual Care group. • At 6 months, the hyaluronic acid-based vaginal moisturizer group improved significantly more than the prebiotic vaginal moisturizer group on FSFI total score (p= 0.04).

Abbreviations: FSFI, Female Sexual Function Index

Table 9. Main findings of studies for assessing relationship and intimacy by intervention in female patients.

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
Couple-based intervention					
Reese et al (2019) [41]	29 breast cancer survivors	Intimacy	Baseline & 4 weeks	Treatment: 4 session couple-based Intimacy Enhancement intervention delivered via telephone Control: Educational session	DSCS, PAIR • For the relationship outcomes, there was a medium to large effect seen for an increase in sexual communication, no effect for emotional intimacy, and a small to medium effect seen for reduction in relationship quality.
Price-Blackshear et al (2020) [57]	77 young women diagnosed with breast cancer and their romantic partners	Relationship	Baseline and 8 weeks	Treatment 1: Couples Mindfulness-Based Intervention (C-MBI) Control: Online MBI (I-MBI)	DAS, QMI • In the C-MBI condition, patients reported lower levels of dyadic adjustment after the intervention and their partners showed relatively no change, whereas both patients and partners in the I-MBI condition reported somewhat higher levels of dyadic adjustment after the intervention • Relationship quality was largely unchanged for patients and their partners in the I-MBI, but, in the C-MBI, both patients and their partners reported lower relationship quality after the intervention
Zhang et al (2022) [58]	104 couples coping with gynecological cancer	Relationship	2 and 3 months	Treatment: Nurse-led couples intervention developed based on the Preliminary Live with Love Conceptual Framework plus routine nursing care Control: Routine nursing care	Olson Marital Quality Questionnaire (ENRICH) • No significant difference in the sexual life scores for both patient-reported and husband-reported between the intervention and control groups
Cognitive behaviour therapy					
Hummel et al (2017) [42]	169 breast cancer survivors	Relationship & intimacy	Baseline, 10 weeks after start of therapy and at 24	Treatment: 24 weeks of therapist-guided internet-based cognitive behavioral therapy	PAIR • No significant effects were observed between the treatment and control groups for relationship intimacy

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
			weeks (end of therapy)	Control: An information booklet addressing sexuality issues after breast cancer treatment was provided with a follow-up to answer any questions	
Education					
Chow et al (2020) [48]	202 women with newly diagnosed gynecological cancer	Relationship & intimacy	Baseline, 12 weeks	Treatment: A 4-session, 12-week-long, culturally appropriate psychoeducational intervention program Control: attention from the research nurse on four occasions within the same time interval in which the program was applied to the intervention group	C-SVQ • The intervention group had a significantly higher intimacy score, compared with the control group (p=0.001)

Abbreviations: DSCS, Dyadic Sexual Communication Scale; C-SVQ, Chinese-version Sexual Function-Vaginal Changes Questionnaire; PAIR, Personal Assessment of Intimacy in Relationships; DAS, Dyadic Adjustment Scale; QMI, Quality of Marriage Index

Table 10. Main findings of studies for assessing vasomotor symptoms by intervention in female patients.

Author, study type	Population, diagnosis	Condition	Follow-up	Comparison	Main findings
Wellness Program					
Anderson et al (2015) [50]	55 women aged 45 to 60 years with one moderate to severe menopausal symptom and a history of breast cancer	Vasomotor symptoms	Baseline, 12 weeks	Treatment: A lifestyle intervention (The Pink Women's Wellness Program) that included clinical consultations and a tailored health education program Control: A booklet on breast cancer and early menopause and continued usual care	GCS, FACT- Breast and -General • Women in the intervention group reported clinically significant reductions in somatic symptoms, vasomotor symptoms, and overall menopausal symptoms at 12 weeks compared with the control group.
Cognitive behaviour therapy					
Atema et al (2019) [43]	254 breast cancer survivors	Vasomotor symptoms	Baseline, 10 weeks, 24 weeks	Treatment 1: A therapist guided 6-week iCBT group Treatment 2: A self-guided 6 week iCBT group Control: Usual care	FACT-Endocrine symptoms • The guided and self-managed iCBT groups reported a significant decrease in the perceived impact of hot flushes and night sweaters ($p<0.001$) and improvement in sleep quality ($p<0.001$)

Abbreviations: FACT-ES, Functional Assessment of Cancer Therapy - Endocrine Symptoms; GCS, Greene Climacteric Scale; iCBT, Internet-based cognitive behaviour therapy

Table 11. Ongoing trials in male and female patients from ClinicalTrials.gov.

Protocol ID	Title	Recruitment Status	Estimated Completion Date
NCT05242770	Feasibility of Pelvic Physical Therapy for Sexual Dysfunction in Gynecologic Oncology Survivors Summary: To investigate the use of pelvic physical therapy for gynecologic cancer survivors who report sexual dysfunction	Recruiting	June 2023
NCT03801031	Sexual Dysfunction in Gynecologic Oncology Patients Summary: To compare the use of lidocaine with placebo that is applied vaginally immediately prior to any sexual encounters for approximately 6 months while maintaining a journal of sexual encounters and pain	Recruiting	June 2021
NCT04472104	Mindfulness-based Treatment for Sexual Difficulties Following Breast Cancer Summary: To compare 8 weekly sessions of group Mindfulness-Based Cognitive Therapy for sexuality with 8 weekly sessions of a sex education treatment for breast cancer survivors	Active, not recruiting	December 2023
NCT05461534	The Effect of Mindfulness Yoga on Sexual Functioning for Breast Cancer Survivors Summary: To evaluate the effects of mindfulness yoga on sexual function, female breast cancer survivors with sexual dysfunction were divided into a mindfulness yoga intervention group and a control group	Not yet recruiting	August 2024
NCT03343093	Restore: Improving Sexual Outcomes of Gay and Bisexual Prostate Cancer Survivors Summary: To identify whether a structured rehabilitation program is effective in addressing the major sexual and urinary problems caused by Prostate cancer treatment.	Active, not recruiting	August 2023
NCT04713917	Prospective Evaluation of Innovative Therapeutic Approaches of Vaginal and Sexual Dysfunction After Breast Cancer Treatment: a Randomized Multicenter Controlled Trial Summary: To assess the one-year superiority of bio physical inductor (C02 laser compared with the standard treatment (hyaluronic acid gel) and compared with chemical bio inductor (injection of hyaluronic acid) in breast cancer survivors with vulvovaginal atrophy	Not yet recruiting	February 2024
NCT05222282	Sexual Health in Patients with Hematologic Malignancies - Symptom Assessment and Management Summary: To compare nurse-led sexual consultations with screening questionnaire prior to consultation and genital examination with doctor with usual care	Recruiting	January 2026
NCT04619485	Sexual and Vaginal Health in Breast Cancer Women Receiving Aromatase Inhibitors Before and After CO2 Laser Therapy: A Randomized, Double-blind, Sham-controlled Trial - LIGHT Study Summary: To evaluate sexual and vaginal health in breast cancer survivors receiving aromatase inhibitors with genitourinary syndrome of menopause, before and after CO2 laser therapy compared to a sham-controlled group.	Active, not recruiting	August 2022
NCT03420547	Renewing Intimacy and Sexuality (RISE): A Pilot Program to Support Marital Intimacy and Sexual Health of Female Cancer Patients in Singapore Summary: To compare participants receiving the RISE intervention with those receiving in first 6 weeks	Recruiting	July 2022

NCT03803696	Randomized Trial of a Multimodal Sexual Dysfunction Intervention for Hematopoietic Stem Cell Transplant Survivors Summary: To evaluate the impact of Enhanced Standard Care vs Multimodal Intervention to Address Sexual Dysfunction to improve sexual function in stem cell transplant survivors on participants' sexual function, quality of life, and mood	Recruiting	December 2024
NCT03930797	Addressing Sexual Concerns in Breast Cancer Survivors: Randomized Controlled Trial of a Novel Couple-Based Intervention Summary: To evaluate an intimacy enhancement intervention in early breast cancer survivors	Active, not recruiting	May 2023
NCT03967379	Multimodal Mobile Intervention Application to Address Sexual Dysfunction in Hematopoietic Stem Cell Transplant Survivors Summary: To evaluate whether the use of a mobile app can help transplant survivors experiencing sexual health problems.	Recruiting	July 2023
NCT05129332	The Impact of Vaginal Dilator Therapy on Pain Scores and Sexual Function Among Women with Gynecologic and Breast Cancers Experiencing Dyspareunia: a Randomized Controlled Trial Summary: To assess the difference in mean patient-reported pain scores and sexual function between women with gynecologic or breast cancers experiencing dyspareunia who are assigned to vaginal dilator use with vaginal moisturizer compared with vaginal moisturizer alone over 16 weeks.	Not yet recruiting	February 2023
NCT03257670	Prospective Randomized Trial Comparing Treatment of Dyspareunia with Fractional CO2 Laser Therapy Versus 4% Topical Lidocaine Gel in the Setting of Breast Cancer Survivors Summary: to determine if therapy with a CO2 laser to the vagina is more effective than lidocaine to the opening of the vagina before intercourse to reduce painful intercourse in women who are breast cancer survivors	Recruiting	June 2022
NCT03862599	Low Intensity Extracorporeal Shock-wave Therapy in Penile Rehabilitation After Radical Prostatectomy Summary: To evaluate the efficacy and safety of low-intensity shockwave therapy in men with ED following prostatectomy surgery	Recruiting	August 2023
NCT05558007	Phase 2 Clinical Trial to Evaluate Safety and Efficacy of BZ371A In A Gel Applied in Patients That Performed Radical Prostatectomy Summary: To determine efficacy, safety and tolerability of topically applied BZ371A in patients that experienced radical prostatectomy, in combination with daily tadalafil compared to placebo	Not yet recruiting	October 2022

Database: Ovid MEDLINE(R) <1996 to June 16, 2022>
Search Strategy:
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1 sexual.mp. or Sexual Dysfunction, Physiological/ or Sexual Behavior/ or Sexual Dysfunctions, Psychological/ (198010)
2 cancer.mp. or Neoplasms/ (1573539)
3 1 and 2 (10787)
4 limit 3 to (english language and humans and yr="2010 -Current") (6689)
5 (comment or letter or editorial or note or erratum or short survey or news or newspaper article or patient education handout or case report or historical article).pt. (1841548)
6 4 not 5 (6526)
7 Intervention Studies/ or intervention.mp. (589712)
8 6 and 7 (572)

Database: APA PsycInfo <1987 to June Week 2 2022>
Search Strategy:
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1 sexual.mp. or exp Inhibited Sexual Desire/ or exp Female Sexual Dysfunction/ or exp Sexual Satisfaction/ or exp Sexual Function Disturbances/ (173033)
2 cancer.mp. or exp Neoplasms/ (75686)
3 1 and 2 (3223)
4 exp Screening Tests/ or screening.mp. or exp Screening/ (95180)
5 3 not 4 (2740)
6 intervention.mp. or exp Intervention/ (306604)
7 5 and 6 (349)

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DEFINITIONS OF REVIEW OUTCOMES

1. **ARCHIVE** – ARCHIVE means that a Clinical Expert and/or Expert Panel has reviewed new evidence pertaining to the guideline topic and determined that the guideline is out of date or has become less relevant. The document will no longer be tracked or updated but may still be useful for academic or other informational purposes. The document is moved to a separate section of our website and each page is watermarked with the words "ARCHIVE."

2. **ENDORSE** – ENDORSE means that a Clinical Expert and/or Expert Panel has reviewed new evidence pertaining to the guideline topic and determined that the guideline is still useful as guidance for clinical decision making. A document may be endorsed because the Expert Panel feels the current recommendations and evidence are sufficient, or it may be endorsed after a literature search uncovers no evidence that would alter the recommendations in any important way.

3. **UPDATE** – UPDATE means the Clinical Expert and/or Expert Panel recognizes that the new evidence pertaining to the guideline topic makes changes to the existing recommendations in the guideline necessary but these changes are more involved and significant than can be accomplished through the Document Assessment and Review process. The Expert Panel advises that an update of the document be initiated. Until that time, the document will still be available as its existing recommendations are still of some use in clinical decision making, unless the recommendations are considered harmful.