Ontario
Cancer Care Ontario
Action Cancer Ontario

Guideline 19-6

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

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PEBC Report Citation (Vancouver Style): Barbera L, Zwaal C, Elterman D, McPherson K, Wolfman W, Katz A, Matthew A et al. Interventions to Address Sexual Problems in People with Cancer. Toronto (ON): Cancer Care Ontario; *2016 April 28*. Program in Evidence-Based Care Guideline No.: 19-6.

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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

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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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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.

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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

The Interventions to Address Sexual Problems in People with Cancer GDG would like to thank the following individuals for their assistance in developing this report:

- Melissa Brouwers, Sheila McNair, Hans Messersmith, Roxanne Crosby, Duvaraga Slvajohanathan, Laurie Elit, Rebecca Wong, Lori Brotto and Esther Green for providing feedback on draft versions.
- Umangjot Bharaj and Crystal Su for conducting a data audit.
- Sara Miller for copyediting.

Interventions to Address Sexual Problems in People with Cancer

Section 4: Systematic Review

A systematic review manuscript based on this Guideline has been submitted to a peer-reviewed journal. The full Guideline will be posted here once the publication process is completed.

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 (1)	(2)	Neutral (3)	(4)	Strongly Agree (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	The Working Group believes the title is inclusive and decided to keep it as it is.

and its treatment and 2. 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	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 Professor and Director, Biobehavioral Sciences	Fred Hutchinson Cancer, Seattle, WA USA	None declared

Co-Director, Survivorship Program		
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

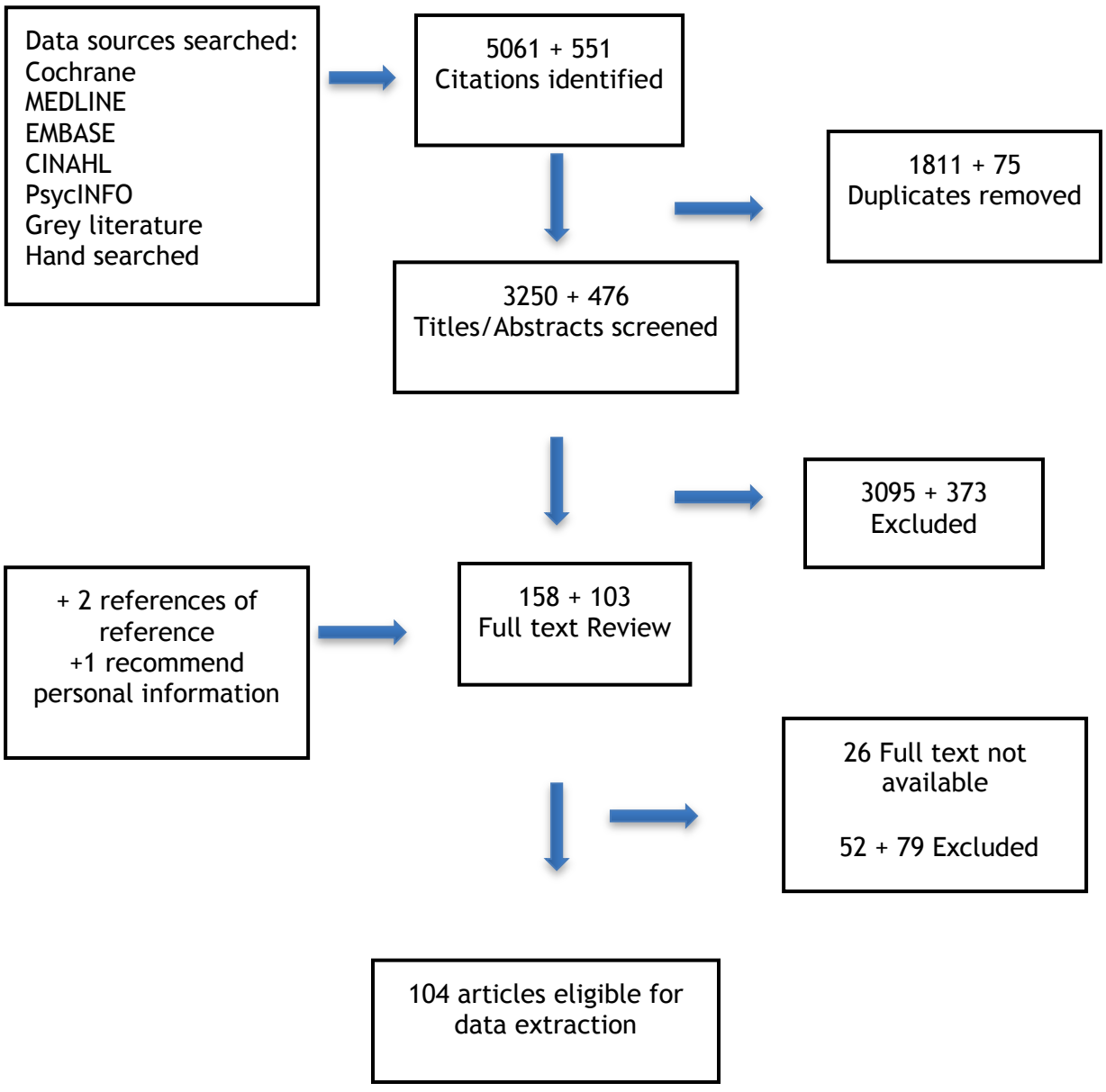
33	exp Sexual Partners/px (Psychology)	2150
34	exp Sexuality/de, ph, px, re (Drug Effects, Physiology, Psychology, Radiation Effects)	6220
35	exp Phosphodiesterase 5 Inhibitors/	1000
36	(sildenafil or tadalafil or varenafil).tw.	4331
37	MUSE.tw.	155
38	exp "Vaginal Creams, Foams, and Jellies"/	888
39	((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	300	Not signif						

		vs. telephone [90]	(RCT)							
		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 (8 studies)	Pharmacological (tibolone,	Control [89]	3133 (RCT)	Signif diff	0	0	0	-0.5	N/A	High
		Control [25]	96	Signif diff						

	vaginal gel, moisturizer, testosterone) (3 studies)		(RCT)							
		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	11 of 16 improved						

			(Non-RCT)							
	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 -levels of follow-up	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 For significant
		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)						

		Control [36]	40 (RCT)	Significant difference (24 wks)		-levels of intervention				studies Longer showed no significanc e
		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)						
	Pharmacologic al 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 intervention s	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)						
	Pharmacologic al 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 indirectness	Moderate imprecision -large SD	N/A	Moderate, low
		PP vs. PDE5i	54	Significant						

		[97]	(Non-RCT)	difference (12, 14 mos)			-different interventions			
		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	Control [38]	24 dyads (RCT -	No significant difference (24 wks)	High	-	-	-	N/A	Low

	PDE3i vs. Placebo (1 study)		Crossover study)							
	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 + soy powder vs. venlafaxine +	120 (RCT)	Significant difference	High	No serious inconsistency	No serious indirectness	No serious imprecision	N/A	Moderate/ Low

		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) No significant difference (t=-0.76,	Also: Body image, Intimacy/ Relationships and Altered Sexual Function/Satisfaction 25% attrition rate

					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) For males (21) and female (9)	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) Control: 5.80 (SD=4.1); 12.10 (SD=2.8) p<0.05	Colorectal cancer Also: Sexual Function/Satisfaction

			and partners			
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 and 20 couples control)	CBPI vs. control (before-after) Assessments at 2 days before mastectomy and 3 months after	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); Feeling attractive (p<0.001)	Also: Sexual Response and Intimacy/ Relationships Attrition NR

				mastectomy		
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 ß =0.15 (95% CI=−0.57 to −1.23) t-value =0.771, df=17, p=0.452 Bowel function score*: Regression ß =-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 (Six 75-minute, bi-weekly sessions	Baucom, [8] (2009) Randomized controlled trial	14 breast cancer patients and partners (8 intervention	Relationship enhancement (CBT) vs. usual care Assessments at	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)

	with a therapist)		and 6 control)	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) Randomized Controlled	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)	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 Pre-post	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); Waitlist (N=14) 0.26 (SD=3.19).	Also: Intimacy/ Relationship 37% recruitment rate Low participation and differential participation

				treatment and 4, 8 month follow-up	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.	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 One 45-minute exercise session	Yang [20] (2012) Randomized Controlled	34 gynecological cancer patients (17	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.	Also: Body Image, Genital Symptoms and Vasomotor Symptoms

	(biofeedback and core exercise) and 30 minute counselling session per week over 4 weeks	Trial	intervention and 17 control)		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) Week 12: 3.7 (SE=1.44) Week 26: 3.5 (SE=1.4)	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.

					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: 24/46 (52%) returned to baseline	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:

					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	Pahlajani [43] (2010)	69 prostate cancer	Sildenafil (early	International Index of Erectile Function (IIEF-6)	Brachytherapy

	months	Non-Randomized Controlled Trial	patients (31 treatment; 38 control)	treatment) vs. no treatment (before vs. after) 6, 12 months	At 12 months: Treatment Group: 17.9 Control: 9.3 Significant difference: p<0.01	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	Bruner [31] (2011)	61 prostate cancer	Sildenafil vs. placebo	International Index of Erectile Function (IIEF)	External Beam Radiotherapy and

	sexual encounter for 12 weeks	Randomized Controlled Cross-over Trial	patients	(crossover trial) 12 weeks, 25 weeks (12 weeks after crossover)	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)	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 weeks; then crossed over to	Incrocci [33,34] (2006, 2007) Randomized	60 prostate cancer patients (51 patients in open label	Tadalafil vs. placebo (crossover trial) 6, 12, 18	International Index of Erectile Function (IIEF) Range score Individual scores (range of means from items) at 6 weeks:	Three-dimensional conformal external beam radiotherapy Also: Altered Sexual

	alternate medication; 6 week open-label extension phase	Controlled Cross-over Trial	phase)	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.	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)	10 prostate cancer patients	Before Sildenafil vs. after	International Index of Erectile Function (IIEF-5) Mean score	High-dose rate brachytherapy with external beam

		Pre-post intervention study		3, 12 months	At baseline: 6.2 At 12 months: 13.6 p<0.001	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) Randomized Controlled Cross-over	628 prostate cancer patients (210 placebo; 210 Vardenafil nightly; 208	Vardenafil nightly vs. Vardenafil Vardenafil on demand vs. placebo	International Index of Erectile Function (IIEF-EFD) % with a score ≥ 22 At 9, 13 months Treatment group: Nightly: 32.0%, 52.6%	Bilateral Nerve-Sparing Radical Prostatectomy Also: Altered Sexual Function/

		Trial	Vardenafil on demand)	9, 11, 13 months 2 month wash out period and 2 month open label	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.	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 Over the past 4 weeks, have your erections been good enough for satisfactory sexual activity?	Bilateral Nerve-sparing Radical Prostatectomy Attrition –NR

					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 RRehab: Sildenafil (100 mg) or vardenafil (20mg)	Natali [100] (2014) Retrospective Study	147 prostate cancer patients (36 no treatment; 23 on demand; 88 rehab)	Group A: No treatment vs. Group B: On demand vs. Group C: Regimented rehabilitative program	International Index of Erectile Function (IIEF-5) number with a score ≥ 22 At 24 months: No Treatment group: 22 (61%) Overall treatment group: 79 (71%) On demand group: 63 (72%) Rehab group: 16 (70%)	Bilateral or unilateral nerve sparing prostatectomy Attrition rate: 31%

	3x/week or tadalafil (20 mg) 2x/week				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). Sexual Encounter Question (SEP) Q3 Did your erection last long enough for	Bilateral Nerve-Sparing Radical Prostatectomy Also: Altered Sexual Function/ Satisfaction and Body Image Attrition=26%

					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	628 prostate cancer patients (210 placebo; 210 vardenafil nightly; 206	Vardenafil nightly vs. vardenafil on demand vs. placebo 9, 11, 13	International Index of Erectile Function (IIEF-EFD) % with a score ≥ 22 At 9, 13 months Treatment group: Nightly: 32.0%, 52.6%	Bilateral Nerve-Sparing Radical Prostatectomy Also: Altered Sexual

		Trial	Vardenafil on demand)	months 2 month wash out period and 2 month open label	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.	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 free washout period	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).
Erectile dysfunction	Sildenafil (50mg), Vardenafil (10mg), or Tadalafil (10mg), daily +titration	Salonia [51] (2008) Non randomized	100 prostate cancer patients self-selected to groups (36	PDE5i on demand vs. PDE5i daily vs. no treatment (before vs.	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)	Bilateral nerve-sparing radical retropubic prostatectomy (BNSRRP)

		experimental trial Participants self –selected into groups	"on-demand"; 15 "daily use"; 49 control)	after) 6, 12, 18 months	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	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) Alprostadil (125 or 250 ug) 3/week for 9 months or ICIs, or sildenafil, or VCD	Raina [104] (2007) Prospective study	73 prostate cancer patients (38 treatment; 35 observation)	MUSE 3x/week vs. no treatment or treatment as necessary (ICIs, sildenafil, or VCD as per preference) 1, 3, 6, 9 months	International Index of Erectile Function (SHIM) Mean score Before RP: after RP; at 9 months (number of men) 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.	Nerve sparing radical prostatectomy Attrition -32% 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 Prostate cancer patients and survivors	84 dyads (38 couple; 46 individual	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 initiation of psychosocial intervention (31% to 49% at 6 months).	Radical prostatectomy or radiation therapy Also: Intimacy/ Relationships and Altered Sexual Function / Satisfaction 61% attended all sessions Attrition -39%
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	Radical Prostatectomy PDE5i used but not controlled for in analysis Attrition -1.5%

					(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)	
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 3, 6, 9, 12, 18 months	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 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	Bilateral Nerve-Sparing Radical Prostatectomy Attrition -22% VED use had an 100% compliance rate. Tadalfil use had a 40% (Tadalafil only)

					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	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 31 patients only (treatment group were non-responders who received additional treatment)	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: 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%)	Radical prostatectomy Attrition -22% VCD had an 80% compliance rate Reasons for discontinuance included discomfort (55%), unable to get 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%) p=0.044 No significant differences in penile girth, flaccid penile length, or suprapubic fat pad dimensions.	Radical retropubic prostatectomy Also: Sexual Response PDE-5I use allowed 6 months after RP Attrition -29%
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 + educational session (1 hour private session)	Walker [62] (2013) Randomized Controlled Trial	27 couples Prostate cancer patients (allocation not described)	Information booklet + educational session vs. usual care 6 Months	Personal Assessment of Intimacy in Relationships (PAIR) (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	Androgen Deprivation Therapy Attrition –NR but mentions significant attrition in control group at one site
Intimacy/ Relationship	Peer-support counseling	Chambers [63] (2011)	20 couples: Prostate cancer	Before peer-support	Sexuality Care Needs: sexuality needs subscale	Radical prostatectomy

	8 intervention sessions over the phone: 2 before surgery, then at 2, 4, 6, 10, 16 and 22 weeks post surgery	Pre-post intervention study	patients and partners	counseling vs. after 3, 6 months	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).	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: There were no significant differences between these groups in marital satisfaction scores (R-DAS).	Radical prostatectomy or radiation therapy Also: Sexual Response and Altered Sexual Function/ Satisfaction 61% attended all sessions Attrition -39%
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	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)	Localized prostate cancer (T1-3N0M0) with either definitive surgery or radiotherapy Also: Sexual Response Attrition -34%

				months	No significant difference across time	
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	Population,	Comparison/	Main findings	Comments

		type	diagnosis	Follow-up		
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: 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	Radical prostatectomy Response rate -24%
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:	Colorectal cancer Also: Sexual Response

					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	
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 at 6 (p=0.003), 12 months (p=0.027) and 24 months (p=0.033)	External Beam Radiotherapy, brachytherapy or brachytherapy combined with EBRT Also: Altered Sexual Function/ Satisfaction Attrition -NR
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	61 prostate cancer patients	Sildenafil vs. placebo (crossover trial) 12 weeks, 25	Sexual Adjustment Questionnaire (SAQ) The mean improvement was 2.58 (p=0.02)	External Beam Radiotherapy and Short-Term Androgen Deprivation Therapy <120 days

		Cross-over Trial		weeks (12 weeks after crossover)	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).	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;	Irani [68] (2010) Randomized Controlled	919 prostate cancer patients	venlafaxine (75 mg) daily vs. medroxyprogesterone acetate (20 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-	Androgen Deprivation Therapy (Six months treatment with leuprorelin)

	or cyproterone acetate (100 mg) daily	Trial		vs. or cyproterone acetate (100 mg) daily	-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.	
Hot Flashes	Gabapentin (300 mg) daily/ 28 days; gabapentin (300 mg) daily for 7 days and 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	Loprinzi [70] (2009) Randomized Controlled Trial	214 prostate cancer patients	1. Gabapentin (300 mg) daily for 28 days vs. 2. gabapentin (300 mg) daily 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.	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 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)	Androgen Deprivation Therapy Attrition=23% 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)	Hot Flash Score median % decrease change at 12 weeks for each original condition with 4th week as a baseline: 1. 57%,	Androgen Deprivation Therapy Patients tended to end up at higher

				Before vs. after	2. 39%, 3. 19%, 4. 4%	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) Prospective Study	10 prostate cancer patients on ADT	Before vs. after treatment 4 wks	Number of Hot Flashes during a day; Baseline; 4 wks 3.5 (SD=2.6); 2.0 (SD=2.7), p=0.009 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	Androgen Deprivation Therapy
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	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);	Androgen Deprivation Therapy At 12 weeks, 57% (EA) and 47% (TA) of men had a median

	once weekly for 10 weeks with or without electro-stimulation				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	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. 91% maintained a >50% improvement at 8 mos	Androgen Deprivation Therapy Attrition=1%
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	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%	Androgen Deprivation Therapy (luteinizing-hormone releasing hormone)

	weeks				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%	