

# Interventions for sexual dysfunction following treatments for cancer in women (Review)

Candy B, Jones L, Vickerstaff V, Tookman A, King M



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[Intervention Review]

# Interventions for sexual dysfunction following treatments for cancer in women

Bridget Candy<sup>1</sup>, Louise Jones<sup>1</sup>, Victoria Vickerstaff<sup>1</sup>, Adrian Tookman<sup>2</sup>, Michael King<sup>3</sup>

<sup>1</sup>Marie Curie Palliative Care Research Department, UCL Division of Psychiatry, London, UK. <sup>2</sup>Marie Curie Hospice, London, UK.

<sup>3</sup>UCL Mental Health Sciences, University College Medical School, London, UK

Contact address: Bridget Candy, Marie Curie Palliative Care Research Department, UCL Division of Psychiatry, 6th Floor, Maple House, 149 Tottenham Court Road, London, W1T 7NF, UK. [b.candy@ucl.ac.uk](mailto:b.candy@ucl.ac.uk). [bridget@metaclarity.com](mailto:bridget@metaclarity.com).

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## ABSTRACT

### Background

The proportion of people living with and surviving cancer is growing. This has led to increased awareness of the importance of quality of life, including sexual function, in those affected by cancer. Sexual dysfunction is a potential long-term complication of many cancer treatments. This includes treatments that have a direct impact on the pelvic area and genitals, and also treatments that have a more generalised (systemic) impact on sexual function.

This is an update of the original Cochrane review published in Issue 4, 2007, on interventions for treating sexual dysfunction following treatments for cancer for men and women. Since publication in 2007, there has been an increase in the number of trials for both men and women and this current review critiques only those for women. A review in press will present those for men.

### Objectives

To evaluate the effectiveness of interventions for treating sexual dysfunction in women following treatments for cancer. To assess adverse events associated with interventions.

### Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL 2015, Issue 9), MEDLINE, EMBASE, PsycINFO, AMED, CINAHL, Dissertation Abstracts and the NHS Research Register. The searches were originally run in January 2007 and we updated these to September 2015.

### Selection criteria

We included randomised controlled trials (RCTs) that assessed the effectiveness of a treatment for sexual dysfunction. The trial participants were women who had developed sexual dysfunction as a consequence of a cancer treatment. We sought evaluations of interventions that were pharmaceutical, mechanical, psychotherapeutic, complementary or that involved physical exercise.

### Data collection and analysis

Two review authors independently extracted the data and assessed trial quality. We considered meta-analysis for trials with comparable key characteristics.

## **Main results**

Since the original version of this review we have identified 11 new studies in women. The one study identified in the earlier version of this review was excluded in this update as it did not meet our narrower inclusion criteria to include only interventions for the treatment, not prevention, of sexual dysfunction.

In total 1509 female participants were randomised across 11 trials. All trials explored interventions following treatment either for gynaecological or breast cancer. Eight trials evaluated a psychotherapeutic or psycho-educational intervention. Two trials evaluated a pharmaceutical intervention and one pelvic floor exercises. All involved heterosexual women. Eight studies were at a high risk of bias as they involved a sample of fewer than 50 participants per trial arm. The trials varied not only in intervention content but in outcome measurements, thereby restricting combined analysis. In the trials evaluating a psychotherapeutic intervention the effect on sexual dysfunction was mixed; in three trials benefit was found for some measures of sexual function and in five trials no benefit was found. Evidence from the other three trials, two on different pharmaceutical applications and one on exercise, differed and was limited by small sample sizes. Only the trial of a pH-balanced vaginal gel found significant improvements in sexual function. The trials of pharmaceutical interventions measured harm: neither reported any. Only one psychological intervention trial reported that no harm occurred because of the intervention; the other trials of psychological support did not measure harm.

## **Authors' conclusions**

Since the last version of this review, the new studies do not provide clear information on the impact of interventions for sexual dysfunction following treatments for cancer in women. The sexual dysfunction interventions in this review are not representative of the range that is available for women, or of the wider range of cancers in which treatments are known to increase the risk of sexual problems. Further evaluations are needed.

## **PLAIN LANGUAGE SUMMARY**

### **Interventions for sexual dysfunction following treatments for cancer**

#### **Background**

In women sexual dysfunction is a potential complication of many types of cancer treatments.

This review evaluated the effectiveness of treatments (interventions) of any kind, for example drugs or exercise, for treating sexual dysfunction in women following cancer treatment.

The review is an update of one published in 2007 that assessed the effectiveness of interventions for men and women. We decided to present this revised review separately for women because of the increase in the number of trials. Another review for men is underway.

#### **Study characteristics**

We identified 11 new trials on interventions for women in September 2015. We excluded one trial that was included in the earlier version of this review because it assessed treatment for preventing sexual dysfunction and was no longer relevant to this review. Interventions differed in their content and how the researchers measured benefit. Eight of the interventions involved psychological support such as counselling on sexual matters, or peer support. One of the others was of a testosterone cream, another tested a vaginal pH-balanced gel and the other was of pelvic floor exercise. The findings from six of the trials are weak because they involved small numbers of women.

#### **Key results**

Across the trials the impact on sexual function was different. This makes it difficult to derive clear conclusions. For instance, in those that evaluated a psychological support treatment, four studies found that it improved some measures of sexual function but not others, but five found that it did not improve sexual function according to any of the measures used. For the other interventions tested, only the trial of the vaginal gel found improvements in sexual function and no side effects were reported. Only one of the psychological interventions reported that no harm occurred because of the intervention. The other trials of psychological support did not assess harm. This is an important gap as some women may find it distressing to discuss personal sexual problems as part of their treatment.

Further evaluations are needed for all interventions. Current studies have only explored effectiveness in women with gynaecological and breast cancers, but there is a risk of sexual problems after treatments for other cancers. New evaluations need to involve larger numbers of participants.

## BACKGROUND

This review is an update of a previously published review in the Cochrane Database of Systematic Reviews (Issue 4, 2007) on 'Interventions for sexual dysfunction following treatments for cancer' (Miles 2007). This review presents the findings on the effectiveness and safety of interventions for sexual dysfunction in women following treatments for cancer. In its earlier version the review involved interventions for both men and women following treatments for cancer, and preventative treatments for sexual dysfunction. A separate review, in press, will report on interventions for men. Interventions for the prevention of sexual dysfunction are not included in either of these reviews.

### Description of the condition

Sexual dysfunctions are characterised by a disturbance in sexual desire and in the psychological and physiological changes that characterise the sexual response (Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) (DSM-5 2013)).

The DSM-5 recognises three sexual dysfunctions in women:

- sexual interest/arousal disorder;
- genitopelvic pain/penetration disorder;
- female orgasmic disorder.

Sexual dysfunction poses challenges to one's social, mental, emotional and physical wellbeing. In cancer, it is an important indicator of quality of life both in people undergoing treatments and in those surviving the disease (Ozyilkkan 1995). It may occur as a result of the nature of a cancer, such as a cancer that affects the mechanics or hormonal pathways in sexual function, as a result of the treatment for cancer such as surgery, chemotherapy or radiotherapy that may have local or systemic and hormonal effects, and it may occur from the emotional trauma of receiving a diagnosis or indeed living with cancer for the patient as well as their sexual partner. The causes of sexual dysfunction following cancer treatments may be multi-factorial but it may often result from the direct effects of the treatment. A hysterectomy, for example, may disrupt the pelvic anatomy and the local nerve supplying the pelvic floor, which are part of the trunk stability mechanism involved in sexual arousal, and this may be accompanied by loss of vaginal lubrication and sensation (Jackson 2006). Other cancer treatments may affect sexual function, for example chemotherapy may induce the symptoms of menopause, in particular vaginal dryness. Sexual dysfunction following a cancer treatment may also relate to lowered physical fitness, symptoms of depression or anxiety, and changes to self esteem and feelings of sexuality (Greenwald 2008; Pignata 2001; Stead 2007; Tabano 2002; Wiggins 2008). Although some treatment-related sexual dysfunction effects are short-term, sexual dysfunction is one of the more prevalent long-term complications following many types of life-saving cancer treatment (Ananth 2003; Ganz 1998; Syrjala 1998).

Sexual dysfunction following cancer treatments is becoming an increasingly important issue to tackle. With an aging global population, improved diagnosis and better cancer treatments, more people are living with and surviving cancer. For example, the US Centers for Disease Control and Prevention estimated that the number of cancer survivors in the US increased from 3 million in 1971 to 11.6 million in 2007, and of those in 2007 the largest group of survivors in women was those with breast cancer (CDC 2011). Sexual dysfunction is a known problem for people receiving various cancer treatments, including those for cancer of the bladder (Bhatt 2006; Zippe 2004), head and neck (Low 2009; Singer 2008), and rectum (Hendren 2005; Ho 2011). However, much of the research to date on the prevalence and treatments for sexual dysfunction following cancer treatments has focused on cancer treatments that have a direct impact on the genitals or other areas of the body involved in sexual functioning. It has been estimated that 50% of women who undergo gynaecological cancer treatments suffer long-term sexual dysfunction as a result (National Cancer Institute 2012). There is also evidence for a high prevalence of sexual dysfunction following treatments for breast cancer, where in one survey it was found in 45% women (Kedde 2013), and in another survey 76% had sexual dysfunction (Goldfarb 2009). A review found that the incidence of sexual dysfunction in women following radical rectal cancer resection varied from 19% to 62% (Cowan 2013).

Despite recognition of the problem, sexual morbidity remains under-treated in this patient group (Hill 2011). This is, in part, because of the embarrassment associated with sexual dysfunction not only from the patient's point-of-view but from that of clinicians (Denning 2013). In addition, sexual interest/arousal disorders in general may be under-recognised (Montgomery 2008).

### Description of the intervention

There are various types of interventions available for the treatment of sexual dysfunction in women, these include:

- complementary and alternative medicine interventions such as the herbal therapies ginkgo and ginseng;
  - exercises to strengthen the pelvic floor;
  - mechanical interventions such as lubricating gels and clitoral therapy devices;
  - pharmacological interventions including hormonal therapies such as testosterone or oestrogen (these may be applied topically or taken orally);
  - psychotherapeutic and psycho-educational interventions such as counselling or psychotherapy, which aim to reduce the sexual dysfunction as well as improve the patient's communication skills with their sexual partner.
- Psychotherapeutic interventions may be combined with education to facilitate an understanding of treatment and its effects.

The range of interventions is in part explained by the range of causes of sexual dysfunction, but also because it is known that the appropriateness, effectiveness and suitability of each intervention vary between individual patients.

### How the intervention might work

The various types of interventions work in different as well as complex ways, with some mechanisms of action poorly understood. We briefly consider the mechanisms of action according to the following groupings.

#### Complementary and alternative medicine

There are various complementary and alternative medicines that are used to try to enhance sexual function. Their mechanisms of action are often unknown. Maca is an Andean plant belonging to the mustard family and it has been used for centuries to enhance fertility (Shin 2010). Maca is also reported to improve sexual function in healthy human populations (Gonzales 2003). *Ginkgo biloba* has been evaluated for depression-induced sexual dysfunction (Cohen 1998).

#### Exercises to strengthen the pelvic floor

Pelvic floor muscles give structural support to the pelvic organs (urethra, vagina and rectum). Pelvic floor dysfunction may be a direct outcome of gynaecological cancers and various cancer treatments. For example, radical hysterectomy and radiotherapy of the pelvic area may disrupt the anatomy and the local nerve supply to the pelvic floor muscles (Jackson 2006). This disruption may lead to urinary continence and a lack of sexual arousal. Pelvic floor exercises may reduce these problems by increasing muscle tone.

#### Mechanical

There are various mechanical devices for sexual dysfunction. In women a clitoral therapy device such as a hand-held battery powered vacuum creates a gentle suction to engorge the clitoris blood flow and thereby increase sensation (Schroder 2005).

#### Pharmacological

The relationship between endogenous testosterone levels and sexual function in women has not been clearly established. However, testosterone therapy has been found to improve the signs and symptoms of hypoactive sexual desire (Hubayter 2008). Exogenous oestrogen will increase vaginal blood flow and lubrication, and oestrogen therapy has been shown to improve clitoral sensitivity and the ability to reach orgasm (Berman 1999).

#### Psychotherapeutic and psycho-educational

Although evidence for the effectiveness of psychotherapeutic interventions is limited, the role of psychological processes in sexual function is acknowledged (Kazdin 2009). Normal sexual function is a biopsychosocial process that relies on the co-ordination of not only endocrine, vascular and neurological factors but also psychological factors (Allahdadi 2009). Treatment of sexual dysfunction in women with a psychotherapeutic intervention is a common approach in clinical practice (Berner 2012). There are a number of psychotherapy approaches including cognitive behaviour therapy, counselling and relationship therapy. Some interventions may include educational aspects, such as a discussion on the value of intimate communication with sexual partner and advice on vaginal lubrication.

#### Why it is important to do this review

Trials evaluating the effectiveness of treatments for sexual dysfunction often exclude patients with other major health problems, such as cancer. As cancer and its treatments disrupt physiological and anatomical integrity, it is not possible to simply extrapolate the results of these trials into the cancer field.

With the world's aging population, and improved diagnosis and better cancer treatments, more people are living with and surviving cancer. It is recognised that sexual morbidity is a major cause of poor quality of life. A growing number of treatments are being developed and evaluated; it is important to review their efficacy, safety and acceptability. This review is an update of an earlier Cochrane review on interventions for sexual dysfunction following treatments for cancer in men and women (Miles 2007). Since its publication many more trials have been undertaken. In light of this growth we have split this review. In this current update we evaluate only interventions for women. The update on interventions for men will be reported elsewhere in a new review.

## OBJECTIVES

- To evaluate the effectiveness of interventions for treating sexual dysfunction in women following treatments for cancer.
- To assess adverse events associated with interventions.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

We only included randomised controlled trials (RCTs). Published trials that were provided in full rather than in abstract only (such as a conference abstract) were eligible. There was no language restriction. In the case of cross-over trials, we only reported the first period results (if available) in this review in order to exclude any carry-over effect. Trials undertaken in any care setting, including hospital and community, were eligible.

### Types of participants

Trial participants were women (aged 16 years or over), receiving any active treatment for any cancer or who had previously received any treatment for cancer. Participants must have been functioning sexually with a partner prior to cancer treatment. Participants at the start of the trial needed to have experienced any type of sexual dysfunction (however identified) subsequent to cancer treatment. If participants were not required for trial inclusion to have sexual dysfunction subsequent to cancer treatment, we included the study if it reported:

- 50% or more having sexual dysfunction following treatment;
- subgroup analysis on those with documented sexual dysfunction subsequent to cancer treatment;
- mean/average score in both trial arms at early measurement post-treatment indicating a level of sexual dysfunction.

We did not use the DSM-5 criterion that the duration of the sexual dysfunction had to be at least six months. We felt that this may not be relevant in this patient group as a significant proportion may have advanced disease with a prognosis of less than six months.

### Types of interventions

We included evaluations of any type of intervention for treating sexual dysfunction following a treatment for cancer. These included pharmacological, mechanical, psychotherapeutic and psycho-educational, complementary medicine or exercise. The intervention for sexual dysfunction could be compared with a placebo, usual care or another active treatment.

We did not include trials of preventative strategies to refine the cancer treatment, such as peritoneal vaginoplasty in combination with a radical hysterectomy.

For this update, we only included studies of interventions for the treatment of sexual dysfunction in women, not the prevention of sexual dysfunction.

### Types of outcome measures

#### Primary outcomes

The primary outcomes of interest were efficacy in regards to improved sexual function, quality of life and safety. We evaluated efficacy using the following outcomes:

- the proportion of participants within each trial arm with improved sexual function;
- mean scores on standardised sexual function questionnaires; these included the Female Sexual Function Index (FSFI), which involves 19 items yielding an overall sexual function score in addition to subscale scores for sexual desire, arousal, lubrication, orgasm and satisfaction (Rosen 2000);
- mean scores on standardised quality of life measures including the Quality of Marriage Index, which involves six items of marital quality (Norton 1983).

We evaluated safety using the following outcomes:

- number and type of adverse effects;
- number of participants who dropped out due to adverse effects.

#### Secondary outcomes

The secondary outcomes of interest were efficacy in regards to psychological and physiological functioning, and symptoms of disease.

We reported measured outcomes on sexual dysfunction relating to the patient's sexual partner.

#### Exclusion criteria

We did not include data from observational cohort or cross-sectional studies, nor RCTs evaluating the effectiveness of preventative measures such as breast reconstruction, or avoidance of one particular therapy. We did not include studies comprising of healthy volunteers or patients who reported sexual dysfunction subsequent to non-cancer treatments.

### Search methods for identification of studies

#### Electronic searches

In the original review we searched for interventions for both men and women (Miles 2007). In this review we also planned to review interventions for both men and women. It was the high number of relevant studies found from these update searches which led us, to permit timely completion, to split the review into one on interventions for sexual dysfunction following treatments for cancer in women, and one on interventions for sexual dysfunction following treatments for cancer in men.

We searched the following electronic databases irrespective of language and publication status for the 2015 update:

- Cochrane Central Register of Controlled Trials (CENTRAL 2015, Issue 9);
- MEDLINE (1966 to August 2015);
- EMBASE (1980 to September 2015);
- PsycINFO (1966 to September 2015);

- AMED (1985 to August 2015);
- CINAHL (1966 to September 2015);
- National Health Service Research Register (containing the Medical Research Council Directory) (1990 to January 2007);
  - *meta*Register of controlled trials (*mRCT*) ([www.controlled-trials.com/mrct](http://www.controlled-trials.com/mrct)), ClinicalTrials.gov ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)) and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (<http://apps.who.int/trialsearch/>) to September 2015.

Please see [Appendix 1](#) for search strategies.

### Searching other resources

We checked for further relevant trials via the reference lists and undertook forward citation tracking for included trials. We also checked for further relevant trials via the reference lists of any related reviews.

### Data collection and analysis

Two authors (BC, LJ) screened the keywords and abstracts of electronic citations. Where they appeared to be relevant, we obtained the full texts.

### Selection of studies

Following screening, two review authors (BC, LJ) assessed the full text of potentially eligible citations for inclusion. If differences of opinion had arisen we planned to discuss this with the other review authors (VV, MK and AT) and if resolution had been difficult, we planned to attempt to contact the study authors for clarification. We documented studies excluded after full-text assessment, giving reasons for exclusion.

### Data extraction and management

We designed a data extraction form for this review. Where possible, we extracted the following information for each trial.

- Methods: trial design, duration, allocation method, masking and care setting.
  - Aim and inclusion criteria.
  - The number of patients eligible, the number randomised and reasons why any patients were not included in the trial.
  - The number of participants evaluated at follow-up(s), reasons for loss to follow-up and how the trials, if stated, handled deviations from randomised allocation and missing response.
  - Participant characteristics: their age, gender, cancer and treatment, and measure of sexual function at baseline.
  - Content of the intervention including who delivered it, duration and number of sessions and the mode of delivery (including whether it was conducted with individuals or in a

group setting). We also report whether the content of the intervention was standardised by the use of a manual.

- Comparison intervention including content, duration and mode of delivery.
  - Outcome data at the end of treatment and at the end of follow-up, including how it was measured. We extracted details on all outcomes on which authors collected measurements but only provide details in our results of those relevant to this review, specifically on sexual function, quality of life and safety, and of psychological and physiological functioning and symptoms of disease. We extracted, as appropriate, all outcome data on our outcomes of interest if they were reported in the trial papers. These included baseline scores, change scores and scores at follow-up between the trial arms.
    - We also planned to extract any qualitative evidence in the included studies, such as analysis of participants' views on the value of the intervention.

Where information was lacking, we attempted to contact the trial authors or trial sponsors.

Two review authors (BC/VV) independently extracted data. One author (BC) entered the extracted data into [Review Manager 2014](#) and a second author checked the data; specifically LJ checked entries on trial description and VV checked entries on trial findings. If there had been any discrepancies, the other review authors would have been consulted and discrepancy resolved by consensus.

### Assessment of risk of bias in included studies

Two authors independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions*, resolving any disagreements by discussion ([Higgins 2011](#)). We completed a 'Risk of bias' table for each included study. We assessed the following for each study.

- Random sequence generation (checking for possible selection bias). We assessed the method used to generate the allocation sequence as: low risk of bias (any truly random process: random number table; computer random number generator); and unclear risk of bias (method used to generate sequence not clearly stated). We excluded studies using a non-random process, which were therefore at high risk of bias (odd or even date of birth; hospital or clinic record number).
  - Allocation concealment (checking for possible selection bias). The method used to conceal allocation to interventions before assignment determines whether the intervention allocation could have been foreseen in advance of, or during, recruitment, or changed after assignment. We assessed the methods as: low risk of bias (telephone or central randomisation; consecutively numbered, sealed, opaque envelopes); and unclear risk of bias if the method was not clearly stated. We excluded studies that did not conceal allocation, which were therefore at high risk of bias (open list).

- Blinding of participants and personnel (performance bias). We assessed the methods used to blind study participants and outcome assessors from knowledge of which intervention a participant received. We assessed the methods as: low risk of bias if the study stated that it was blinded and described the method used to achieve blinding: identical tablets, matched in appearance and smell; and unclear risk of bias if the study stated that it was blinded but did not provide an adequate description of how blinding was achieved. We judged a study as high risk if there was no blinding or incomplete blinding, and the outcome was likely to have been influenced by lack of blinding. We also judged a study as high risk if blinding was attempted but it was likely that the blinding could have been broken and the outcome was likely to be influenced by lack of blinding.

- Incomplete outcome data (attrition bias). We assessed whether there was attrition bias due to the amount, nature or handling of incomplete outcome data. We judged the study as having low risk of attrition bias if there were no missing outcome data or the reasons for missing data were unlikely to be related to true outcome, or missing data and reasons for it were similar across trial arms, or the missing data had been imputed using appropriate methods. We judged the study as high risk if the reason for missing outcome data was likely to be related to the outcome, with either imbalance across trial arms in numbers of reasons for missing data and if an inappropriate application of simple imputation was potentially used. We judged the study as unclear risk if there was insufficient reporting of attrition to permit judgement of low or high risk.

- Sample size (checking for possible biases confounded by small size). Small studies have been shown to overestimate treatment effects, probably because the conduct of small studies is more likely to be less rigorous, allowing critical criteria to be compromised (Zhang 2013). We considered studies to be at low risk of bias if they had 200 participants or more, at unclear risk if they had 50 to 200 participants, and at high risk if they had fewer than 50 participants.

- Selective outcome reporting (checking if there was a selection of a subset of the original variables recorded on the basis of the results). We assessed selective outcome reporting, if a protocol was available, by comparing outcomes in the protocol and published report. If they were the same we assessed it as low risk in this domain, if they differed we considered it as high risk. If a protocol was not available, then we compared the outcomes listed in the methods section of an article with the outcomes for which results were reported. If they differed we considered the study as high risk. If a protocol was not available and even though the outcomes listed in the methods section and the results section were the same, we considered the study as having an unclear risk of bias in this domain.

We incorporated the results of the 'Risk of bias' assessment into the review through systematic narrative description and commentary about each item.

## Measures of treatment effect

Treatment effects were measured using dichotomous data or ordinal rating scales.

### Dichotomous data

Where dichotomous data were reported (if data were available) we planned to extract or generate odds ratios (ORs) and their 95% confidence intervals (CIs) where appropriate.

### Continuous data

We assessed effect measures for ordinal data as continuous data. Where continuous data were reported, we planned to extract or generate the mean difference (MD) from the means and standard deviations.

### Unit of analysis issues

For any identified cluster-randomised controlled trials we planned to check for errors in the unit of analysis and, if errors were found and sufficient data were available, to recalculate the results using the appropriate unit of analysis (Higgins 2011). For data arising from RCTs with a cross-over design, if available, we planned to use in any combined analysis only data from the first comparative phase prior to cross-over. This decision was based on the possibility of a 'carry-over' of treatment effect from the experimental or comparative treatment.

### Dealing with missing data

Missing studies can result from an inadequate search for data or from publication bias in that papers with negative findings are less likely to be published. How we dealt with this is detailed in [Search methods for identification of studies](#) and in [Assessment of reporting biases](#).

We anticipated finding a significant amount of loss to follow-up in this review. This was due either to the patient's declining health and the caregiver's need for more time with their loved one, or because of the death of the patient. We report attrition rates, per trial, in the 'Risk of bias' tables (see [Characteristics of included studies](#)). This included, if available, per trial arm reasons for attrition, and whether the trial analysis entailed any re-inclusions. We did not undertake any imputation for missing participant data.

A common item missing in outcome data is the standard deviation for continuous outcomes. Where data were not reported, but might be available, we attempted to contact the study authors. We attempted contact with them up to two times. If contact with the author was not possible, we planned to calculate or impute this using relevant data, only if a minority of the trials (to be combined in a meta-analysis) had a missing standard deviation (Higgins 2008). If we had undertaken such imputation we planned to perform sensitivity analyses to assess its impact on combined analysis.

We did not exclude trials on the basis of missing data. In the [Discussion](#) section we address the potential impact of missing data on the findings of the review.

### Assessment of heterogeneity

If meta-analysis had been possible, we would have assessed statistical heterogeneity between trials using the Chi<sup>2</sup> test and I<sup>2</sup> statistic (a Chi<sup>2</sup> P value of less than 0.05 or an I<sup>2</sup> value equal to or more than 50% is considered to indicate substantial heterogeneity). If substantial heterogeneity was identified, we planned to undertake subgroup analyses to investigate its possible sources.

### Assessment of reporting biases

If meta-analysis had been possible we would have sought to explore publication bias visually using funnel plots. In our interpretation of the plots we planned to use the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)).

### Data synthesis

For any combined analysis that had been possible, as the patient populations were quite variable in age and treatments (as were the interventions), we would have employed random-effects meta-analyses.

### Subgroup analysis and investigation of heterogeneity

Subgroup analysis explores whether the overall effect varies with different trial populations and with the nature and content of the interventions. In this update we planned the following subgroup analysis:

- trials of participants with severe sexual dysfunction;
- trials of participants with advanced cancer.

### Sensitivity analysis

We planned to perform sensitivity analyses in order to explore (by excluding trials) the influence of the following factors:

- unpublished trials;
- trials with high risk of bias.

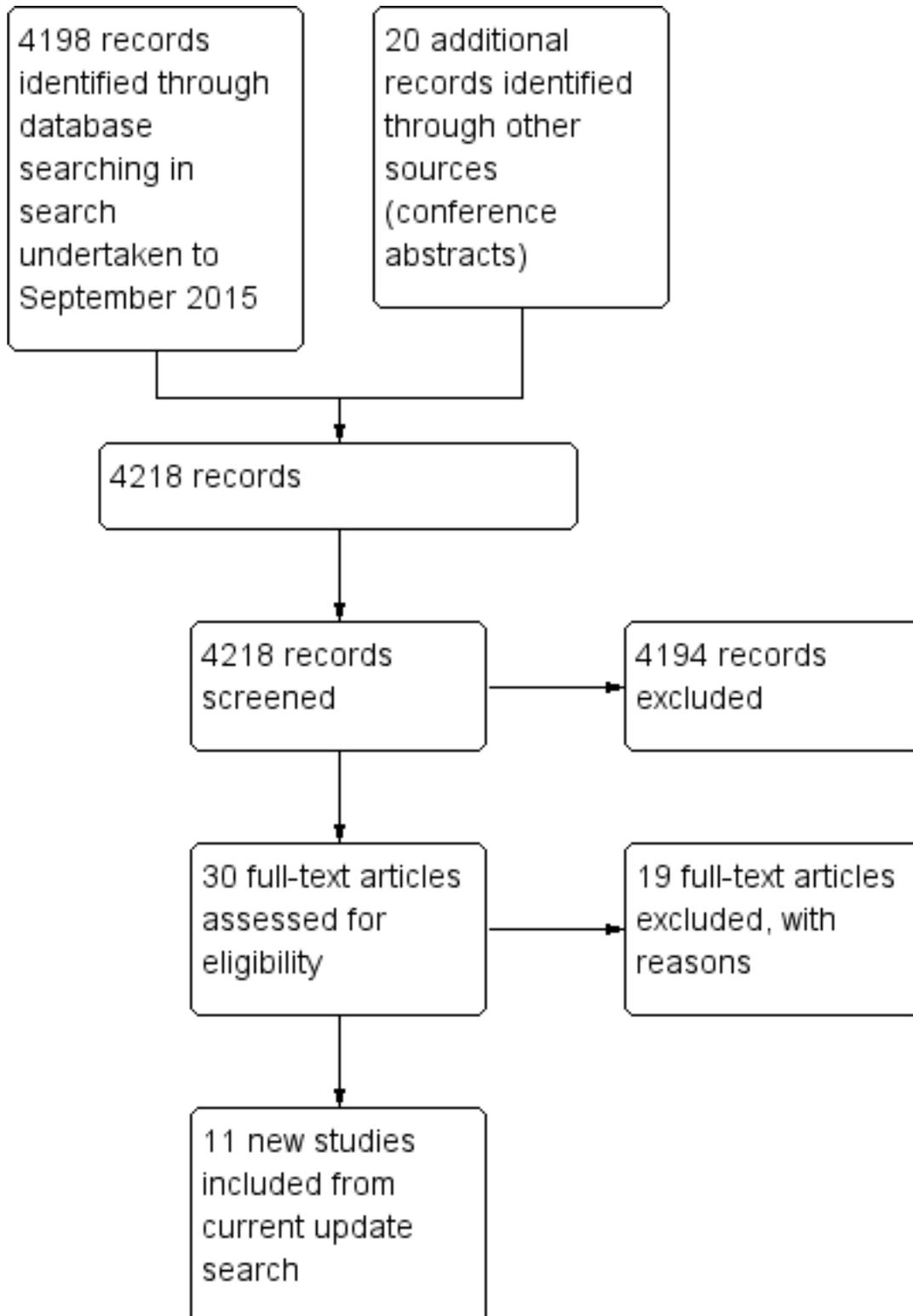
## RESULTS

### Description of studies

#### Results of the search

In this 2015 update we searched for both interventions for men and women; two review authors independently screened 85% of 4218 citations identified. Thirty studies evaluating interventions for women appeared to be relevant at citation assessment. At full-text assessment, 11 studies were eligible ([Aktas 2015](#); [Barton 2007](#); [Baucom 2009](#); [Classen 2013](#); [Lee 2011](#); [Marcus 2010](#); [Rowland 2009](#); [Schover 2011](#); [Schover 2013](#); [Svensk 2009](#); [Yang 2012](#)). We found two further articles at full-text assessment that related to studies in progress ([DuHamel 2013](#); [Schofield 2013](#)) (see [Characteristics of ongoing studies](#)) and we excluded seven further articles because they did not fulfil the inclusion criteria, as they did not report sexual outcomes or were not a RCT. Details of these studies and those excluded in the original review (and involving populations of women) are in the table [Characteristics of excluded studies](#). We found seven studies that are awaiting classification (see [Characteristics of studies awaiting classification](#)). The interventions for men identified in this updated search are reviewed in another Cochrane review, which is in progress. The search process is documented in [Figure 1](#).

Figure 1. Study flow diagram.



We excluded one RCT identified in the original review in this update as it no longer fitted our tighter inclusion criteria, as it is a preventative intervention (Pitkin 1971).

## Included studies

The 11 completed trials randomised 1509 female participants (Aktas 2015; Barton 2007; Baucom 2009; Classen 2013; Lee 2011; Marcus 2010; Rowland 2009; Schover 2011; Schover 2013; Svensk 2009; Yang 2012).

The trials were undertaken in populations from four countries. Most were undertaken in US populations (Aktas 2015; Barton 2007; Baucom 2009; Marcus 2010; Rowland 2009; Schover 2011; Schover 2013). Others were undertaken in Canada (Classen 2013), South Korea (Lee 2011; Yang 2012), and Sweden (Svensk 2009).

One of the trials was of cross-over design (Barton 2007); the remainder were of parallel design. Three of the studies were feasibility or pilot trials (Baucom 2009; Classen 2013; Yang 2012). Two studies compared different forms of delivery of an intervention (Schover 2011; Schover 2013), and two used wait-list controls (Classen 2013; Schover 2011). Four trials involved samples of fewer than 50 participants (Baucom 2009; Classen 2013; Svensk 2009; Yang 2012). Four had samples of over 100 participants (Barton 2007; Marcus 2010; Rowland 2009; Schover 2011). None of the trials reported drug, staff or project pharmaceutical funding or affiliation.

All trials involved participants that had breast or gynaecological cancer. Where reported, the mean age of participants ranged across trials from 44 to 57 years. The treatments the participants underwent for cancer were surgery, radiation, endocrine therapy and/or chemotherapy.

As per the inclusion criteria participants in the majority of trials had documented poor sexual functioning following a cancer treatment (Barton 2007; Baucom 2009; Classen 2013; Lee 2011; Marcus 2010; Rowland 2009; Schover 2011; Schover 2013; Svensk 2009; Yang 2012). We included another trial as the authors were explicit in assuming that for a high proportion of the participants the cancer treatment would result in sexual dysfunction (Aktas 2015). Across the studies how sexual dysfunction was measured varied. This included self report and scales specifically developed for the project. Validated tools used included the Changes of Sexual Functioning Questionnaire (Clayton 1997), Derogatis Inventory of Sexual Functioning (Derogatis 1979), the Female Sexual Distress Revised Scale (Derogatis 2008), Female Sexual Function Index (Rosen 2000), and the sexual function subscale of the Australian Pelvic Floor Questionnaire (Baessler 2009). Only one trial specifically set out to only include those with severe sexual dysfunction (Classen 2013), although in two other trials the scores obtained on the scales used for sexual dysfunction suggested

overall a significant problem (Lee 2011; Schover 2011). One trial evaluated sexual outcomes in both the women and their partners (Baucom 2009).

All involved participants were in a couple relationship, although only two of the trials documented that participants were sexually active prior to the cancer treatment (Aktas 2015; Classen 2013). In three trials the intervention was started during active treatment for cancer of surgery, radiography or chemotherapy (Aktas 2015; Baucom 2009; Svensk 2009); for one of these studies the treatment, radiology, was ongoing (Svensk 2009). In one other trial the intervention was started just after the treatment for cancer (Marcus 2010). In another the mean number of months since treatment for cancer ended was 24.3 in the intervention group and 31.3 in the control group (Classen 2013). In the remaining six trials time since cancer treatment was not reported (Barton 2007; Lee 2011; Rowland 2009; Schover 2011; Schover 2013; Yang 2012).

In three trials the effect of the intervention on sexual dysfunction was the primary focus (Aktas 2015; Barton 2007; Schover 2013). In five of the other trials there was no declared primary outcome; in four of these sexual dysfunction was one of several measures of wellbeing, including quality of life, mental health and distress, body image, spiritual wellbeing and personal growth (Baucom 2009; Marcus 2010; Schover 2011; Svensk 2009). In the fifth trial the other measures related to the impact of an exercise intervention on pelvic floor muscles (Yang 2012). In the other two included studies sexual dysfunction was a secondary outcome; in one the primary outcome was feasibility of the intervention (Classen 2013), and in the other mental health (Rowland 2009).

Further details on these trials are documented in the table [Characteristics of included studies](#).

## Trial interventions

The interventions evaluated were pharmacological, psychotherapeutic, psycho-educational or exercise. Most trials (8/11) evaluated an intervention involving psychotherapeutic techniques. Within these interventions there was heterogeneity in content.

### Pharmacological interventions

Two types of pharmacological interventions were tested:

- Topical testosterone cream;
- Vaginal pH-balanced gel.

### Psychotherapeutic/psycho-educational

The focus and delivery of the psychotherapeutic and psycho-educational interventions varied and included:

- Art therapy;

- Counselling one to one, in group or by telephone. This included professional counselling or peer support. Topics included discussion of sexual matters, relationship functioning, quality of life and information on treatment;
  - Relationship enhancement;
  - Web-based support and information.

**Exercise**

- Pelvic floor exercises with and without biofeedback.

Further descriptions of the included trials can be found in the [Characteristics of included studies](#) table.

**Outcomes evaluated**

There was variation across the trials in how the effect of the intervention on sexual function was measured, as well as for other types of outcomes, including quality of life and psychological functioning. Where there was overlap, the trials differed in how they presented their results.

**Excluded studies**

We excluded 49 studies in the previous version of this review and 19 at this update.

The main reasons for exclusion of studies were that the report was a discussion paper, not a RCT, the study did not include cancer patients or that the evaluation had no sexual function outcomes. Reasons for exclusion for all excluded studies are listed in the [Characteristics of excluded studies](#) table.

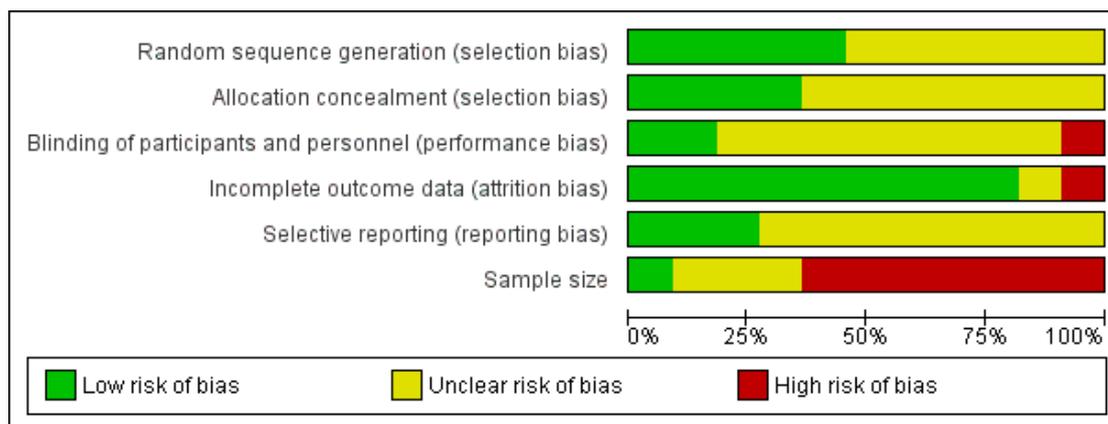
**Ongoing studies**

There are seven relevant trials in progress ([Davis 2015](#); [DuHamel 2013](#); [Gessler 2015](#); [Hummel 2015](#); [NCT00459134 2015](#); [NCT02091765 2015](#); [Schofield 2013](#)). The trials vary. For example, one of the studies in progress is testing a psychotherapeutic intervention in female survivors of anal or rectal cancer ([DuHamel 2013](#)); another is testing a psychotherapeutic intervention in women following treatments for gynaecological cancer ([Schofield 2013](#)). Further details on these trials are documented in the table [Characteristics of ongoing studies](#).

**Risk of bias in included studies**

All trials were vulnerable to a number of biases, most commonly selection bias. See [Figure 2](#) and [Figure 3](#).

**Figure 2. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.**



**Figure 3. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.**

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Sample size
Aktas 2015	?	?	?	+	?	-
Barton 2007	+	+	+	+	+	?
Baucom 2009	+	+	?	+	+	-
Classen 2013	?	?	?	+	?	-
Lee 2011	+	+	+	+	+	-
Marcus 2010	?	?	?	+	?	?
Rowland 2009	?	?	?	+	?	+
Schover 2011	?	?	?	-	?	?
Schover 2013	?	?	?	?	?	-
Svensk 2009	+	+	-	+	?	-
Yang 2012	+	?	?	+	?	-

## Allocation

Most trials (n = 8) did not report the method of randomisation sequence generation (Aktas 2015; Barton 2007; Baucom 2009; Classen 2013; Marcus 2010; Rowland 2009; Schover 2011; Schover 2013). The method concealment of allocation was described adequately in three of the trials (Barton 2007; Baucom 2009; Svensk 2009).

## Blinding

Two trials were at a low risk of performance bias (Barton 2007; Baucom 2009).

In the other trials the risk was either high, as the authors stated that the trial was single-blinded, or the risk was unclear as they provided no details.

## Incomplete outcome data

The risk of attrition bias was low in most trials (n = 6) (Barton 2007; Baucom 2009; Classen 2013; Marcus 2010; Svensk 2009; Yang 2012).

## Selective reporting

The risk of selective reporting was unclear in most studies (n = 8) as they did not reference a protocol or clearly state primary outcomes.

## Other potential sources of bias

Seven trials were at a high risk of bias as they involved fewer than 50 participants in each trial arm (Aktas 2015; Baucom 2009; Classen 2013; Lee 2011; Schover 2013; Svensk 2009; Yang 2012).

## Effects of interventions

The effects of the interventions are reported as fully as possible. Some trials did not report for all outcomes assessed the actual scores for or number of participants experiencing an outcome.

## Pharmaceutical interventions

Two trials evaluated a pharmaceutical intervention.

### Testosterone cream versus placebo

One cross-over trial of 150 women with cancer evaluated the effect of testosterone 2% in Vanicream versus plain Vanicream in the control group (Barton 2007). As per the inclusion criteria, at baseline all participants had a decrease in sexual desire. This was

defined as a score of less than 8 on a 0- to 10-point scale with 10 being highest interest (actual scores not provided). Participants were instructed to apply a spoonful of the cream (intervention treatment or control) onto a large area of their abdomen or thighs. The trial reported cross-over periods separately and so according to our protocol we only report the pre-cross-over results.

### Sexual function

Outcomes for sexual desire/interest and frequency of desire were captured using the Changes in Sexual Functioning Questionnaire (CSFQ) (Clayton 1997). The overall score for the scale runs from 0 to 100, with higher scores representing poorer outcome.

Using the CSFQ for the summed score of desire/interest and frequency of desire it was found that there was no significant difference in effect between the trial arms. The first cross-over mean score in the intervention group was 48.53 and in the control group it was 44.41. The mean difference (MD) in change from baseline was 1.08 (95% confidence interval (CI) -2.78 to 4.94). Neither was there a significant difference in the CSFQ subscale on feelings of sexual pleasure (MD 4.67, 95% CI -0.10 to 9.44) (see Table 1 for the actual scores).

### Quality of life

Quality of life was not measured.

### Adverse effects

The trial reported no significant difference between trial arms in adverse effects of acne, voice deepening, abnormal hair loss or growth, peripheral oedema or headache. The actual numbers of participants suffering these events were not reported.

### Secondary and other outcomes

The Profile of Mood States (POMS) was used to measure psychological function. They also reported the findings of a subscale on vitality. There was no significant difference between trial arms for both outcomes (MD -3.37, 95% CI -8.15 to 1.01; MD -2.20, 95% CI -6.84 to 2.44) (see Table 1 for the actual scores). Impact on physical symptoms of cancer were not reported.

### **pH-balanced vaginal gel versus placebo**

In one trial, 98 women with breast cancer were randomised to either apply three times a week a pH-balanced vaginal gel or a placebo gel (Lee 2011). The women had experienced menopause after chemotherapy or endocrine therapy. In both trial arms, participants at baseline reported a high degree of dyspareunia. On a scale of 0 to 10 with 10 being the highest score for dyspareunia, the baseline mean in the intervention group was 8.23 (standard deviation (SD) 0.99) and in the control group 8.20 (SD 0.95). Likewise the score (using the same scoring system) for vaginal dryness with pain was high: in the intervention group it was 8.20 (SD 0.83) and in the control group 7.92 (SD 0.89).

### **Sexual function**

Effectiveness of the gel was measured by whether it reduced dyspareunia and vaginal dryness. This was measured using a visual analogue scale of 0 to 10 with higher scores reflecting poorer function/more severe symptoms.

At 12 weeks of treatment there was a significant difference favouring those in the intervention group in reduced dyspareunia and other measures of vaginal health, including reduced vaginal dryness (mean dyspareunia 5.48 (SD 1.06) in the intervention group, mean dyspareunia 6.11 (SD 1.42) in the control group; MD -0.63, 95% CI -1.13 to -0.13); mean vaginal dryness 4.23 (SD 1.40) in the intervention group and 6.51 (SD 1.51) in the control group; MD -2.28, 95% CI -2.85 to -1.71).

### **Quality of life**

Quality of life was not measured.

### **Adverse effects**

The most common adverse effect was the sensation of vaginal burning or irritation; there was no significant difference between the trial arms in the proportions of women experiencing this (18/49 in the intervention group versus 13/49 in the control group; odds ratio (OR) 1.61, 95% CI 0.68 to 3.80). There were no reported severe adverse effects.

### **Secondary and other outcomes**

Impact on symptoms of cancer and psychological functioning were not reported.

### **Psychotherapeutic and psycho-educational**

Eight trials assessed the effectiveness of a psychotherapeutic intervention or psycho-educational intervention (Aktas 2015; Baucom 2009; Classen 2013; Marcus 2010; Rowland 2009; Schover 2011; Schover 2013; Svensk 2009). The content of four interventions was specific to sexual matters (Aktas 2015; Baucom 2009; Classen 2013; Schover 2013). Three were broader in topic, covering in addition to sexual matters other quality of life issues such as physical, psychological, social and spiritual wellbeing (Marcus 2010; Rowland 2009; Schover 2011). The intervention in the other trial was art therapy and it did not explore sexual matters (Svensk 2009). Instead it provided participants with a medium for expression and reflection. It was included as sexual functioning was a specific outcome. The interventions not only varied in content, but in how they were delivered and in their comparison. In brief:

- Specialist nurse counselling on sexual matters (Aktas 2015). The comparison group received usual post-cancer treatment care;
- Face-to-face counselling on relationship enhancement compared with an active control of provision of a list of support services (Baucom 2009);
  - Online support group to address the psychosexual impact of cancer compared with a wait-list control (Classen 2013);
  - Telephone counselling on living with physical change, sexuality, relationships and economic change compared with an active control of a list of support services (Marcus 2010);
  - Sexual relationship enhancement intervention compared to an active control of an educational leaflet (Rowland 2009);
  - Peer counselling aiming to improve knowledge and reduce symptoms relating to sexual dysfunction compared to participant-initiated call to receive brief telephone counselling on sexual dysfunction (Schover 2011);
  - Online intervention on sexual and fertility consequences of cancer and treatment (Schover 2013). Participants' use of the website was guided by a counsellor in one trial arm and not in the other arm;
  - Art therapy intervention compared with a control group who had usual care (Svensk 2009).

Detailed information regarding treatment arms and outcomes is provided in the [Characteristics of included studies](#).

This diversity and complexity of interventions precluded any taxonomy of simple labels that would accurately summarise efficacy per intervention type. It also precluded classification into general themes and groups. Moreover the trials varied in how they measured impact on sexual functioning, with five not reporting their findings in a way that was appropriate for combined analysis (Baucom 2009; Marcus 2010; Rowland 2009; Schover 2011; Schover 2013). Therefore for these reasons their results are presented individually.

## **Results**

Three studies found that a psychotherapeutic or psycho-educational intervention had a beneficial effect on some measures of sexual function (Aktas 2015; Baucom 2009; Marcus 2010). In others the benefit of the intervention was either unclear (Rowland 2009; Schover 2013), or no difference was found in sexual function in comparison with the control intervention (Classen 2013; Schover 2011; Svensk 2009). Two trials reported a significant improvement in quality of life in the intervention group compared to the control group (Baucom 2009; Svensk 2009), but in another no difference was found (Schover 2011). Only one study specifically set out to measure adverse events (Baucom 2009). Four studies evaluated psychological health, such as symptoms of depression or anxiety (Baucom 2009; Marcus 2010; Rowland 2009; Schover 2011), and four evaluated physical functioning, impact on symptoms of cancer or impact of treatment on menopausal symptoms (Baucom 2009; Schover 2011; Schover 2013; Svensk 2009).

#### Aktas 2014

Aktas 2015 tested whether a specialist nurse counselling service compared to usual care would improve sexual satisfaction in 70 women following a hysterectomy for gynaecological cancer. Sexual dysfunction was not measured at baseline, however the authors assumed that most of the women would develop sexual problems because of their cancer treatments. The nurses visited the women in the intervention group three times a week until hospital discharge, and subsequently at home at one and 12 weeks. The nurse discussed sexual problems with the women including body image, self confidence, the fear of being rejected, loss of desire, sexual intercourse, vaginal sensitivity, vaginismus, dyspareunia, inability to reach orgasm, shortening of the vagina and incomplete penis penetration.

#### Sexual function

Sexual outcomes were measured using the Golombok Rusk Inventory of Sexual Satisfaction (GRISS), which involves 28 items graded on a Likert scale (Rust 1985). It provides a total score on satisfaction with sexual function and scores for 12 subscales of which seven were assessed in this study. The lower the scores the greater the sexual function.

At 12 weeks, using the total score for the GRISS, there was a statistically significant difference favouring the intervention group (mean 7.15 in the intervention group and 9.46 in the control group (MD -1.40, 95% CI -2.27 to -0.53).

There were mixed outcomes on the GRISS subscales. There was significantly more improvement in the intervention group in:

- sexual non-communication (MD -1.63, 95% CI -2.52 to -0.74);
- anorgasmia (difficulty reaching orgasm) (MD -1.73, 95% CI -2.56 to -0.90);
- avoidance (MD -2.11, 95% CI -3.65 to -0.57);

- non-sensuality (MD -1.93, 95% CI -3.45 to -0.41).

There was no significant difference between the trial arms in:

- frequency of sexual contact (MD -0.11, 95% CI -1.01 to 0.79);
- vaginismus (MD -1.27, 95% CI -2.91 to 0.37);
- sexual dissatisfaction (MD 0.43, 95% CI -0.66 to 1.52).
- the proportion of women who had resumed sexual relations by 12 weeks (7/35 in the intervention group and 10/35 in the control group; OR 2.36, 95% CI 0.88 to 6.34).

Actual scores on the subscales are reported in Table 2.

#### Quality of life and adverse effects

Quality of life and adverse effects were not reported on.

#### Secondary and other outcomes

No other outcomes were reported.

#### Baucom 2009

Baucom 2009 conducted a pilot study of 14 couples, in which the wife had early-stage breast cancer. Mean baseline sexual functioning in both trial arms using the sexual drive and relationship subscale of the Derogatis Inventory of Sexual Functioning (DISF-SR) suggested a level of sexual dysfunction. Higher scores suggested greater sexual function, drive and satisfaction, and better relationship. For both trials arms the score was below mid-score (16) on this subscale, with a mean score of 11.50 in the intervention group and a mean score of 10.33 in the comparison group. All women had received cancer treatment and in most cases it involved surgery. Couples were randomised to either counselling for relationship enhancement or an active control of provision of a list of community support services. The intervention used a cognitive behavioural approach and consisted of six sessions in which the therapist discussed with the couple how to share feelings and thoughts and to reach decisions jointly. The focus was on cancer-related topics including fear, mortality, sexuality and body image. The small number of participants meant that inferential statistics were not used. Instead the researchers looked at between-group effect sizes, taking into account in their analysis the change scores for each participant. They reported that overall there was greater improvement in couples in the intervention group in all outcomes in relation to relationship and sexual functioning.

#### Sexual function

The outcomes were sexual functioning and drive using a four-item domain of the DISF-SR of which the mean in the intervention group 13.00 (SD 3.11) and in the control group 9.80 (SD 5.93);

### *Quality of life*

Relationship satisfaction was assessed using the Quality of Marriage Index (QMI), with higher scores indicating greater quality. QMI mean in the intervention group 39.71 (SD 3.45) and in the control group 40.20 (SD 5.07).

### *Adverse effects*

No adverse effects were reported.

### *Secondary and other outcomes*

They reported fewer overall physical symptoms secondary to cancer treatment, such as nausea and dizziness, in the intervention group compared to the control group. The study did not report any general measures of psychological functioning. See Table 3 for the actual scores for all outcomes reported.

### **Classen 2013**

Classen 2013, in a feasibility study, included 27 women who were sexually distressed following gynaecological cancer treatment. In this trial they sought to identify women whose distress was “above and beyond what might ordinarily occur for women with gynaecologic cancer”. This was defined as scoring at least 24 on the Female Sexual Distress Revised Scale. This is higher than the recommended cutoff of 11 for sexual distress. Actual baseline scores were not provided.

The women had received, on average two to three years earlier, surgery, chemotherapy or radiotherapy for gynaecological cancer and were randomised in the study to an online support group, GynecGals, or a wait-list control. The aim of the 12-week online support group was to address the psychosexual impact of cancer and its treatments. It involved a closed group discussion forum moderated daily by two psychologists, who posted weekly a message on the forum to introduce discussion topics such as coping with emotional challenges or exploring sexuality. A dedicated website provided psycho-educational material to support the discussion.

### *Sexual function*

Sexual function was measured using the Female Sexual Distress Scale (FSDS).

No significant difference was found on sexual distress using the FSDS between those who received psychosexual support compared to the wait-list control group in an intention-to-treat analysis or in an analysis of only those who actively used the forum (MD 2.28, 95% CI -2.15 to 6.71; MD 3.56, 95% CI -2.26 to 9.38, respectively). See Table 4 for the actual mean scores.

### *Quality of life and adverse effects*

Quality of life and adverse effects were not measured

### *Secondary and other outcomes*

The main outcome of this study was feasibility and they found that the majority of women found the website content to be appropriate (15/21) and felt comfortable about discussing their sexual concerns (14/21) in a forum. Using the Hospital Anxiety and Depression Scale (HADS) and the Illness Intrusion Rating Scale there was no significant difference in psychological functioning (for example, for HADS intention-to-treat analysis: MD 0.13, 95% CI -2.44 to 2.70). See Table 4. Physiological functioning and impact on physical symptoms of disease were not reported.

### **Marcus 2010**

Marcus 2010, in a multi-centre study, included 304 women who had just completed treatment for breast cancer, which in the majority of cases (74%) involved chemotherapy. Sexual function was measured by using a 25-item scale, which was composed of questions developed specifically for the project. Scores ranged from 0 to 100 with higher scores indicating greater sexual dysfunction. At baseline participants on average had a level of sexual dysfunction, as suggested by mean scores between 40 and 50 (actual scores not provided). The 152 participants randomised to the intervention received 16- to 45-minute telephone counselling sessions on topics regarding living with physical change, sexuality, relationships and economic change. Those randomised to the comparison group received a mailed booklet listing services in the community relevant to breast cancer.

Their findings were from a before and after comparison in each trial arm. They were not a direct comparison of effects between the trial arms.

Sexual function was measured at follow-up as it was for baseline. The Impact of Events Scale was used to measure cancer-specific distress and the Center for Epidemiologic Studies Depression Scale to measure depression.

### *Sexual function*

For sexual function they reported an overall significant improvement in the intervention group in mean changes scores from baseline at 12 and 18 months follow-up (at 18 months the effect size was 0.23, P value = 0.04), and likewise for “personal growth”, described as deriving benefit from the cancer experience at 12 and 18 months (at 18 months the effect size was 0.22, P value = 0.03). The comparison group showed no change from baseline. The actual scores on these scales per trial arm were not reported.

### *Quality of life and adverse effects*

Adverse effects were not reported and neither were outcomes for quality of life.

### *Secondary and other outcomes*

In both trial arms there was an improvement when comparing mean scores for cancer-specific distress and depression. Outcomes on symptoms of disease were not reported. The actual scores on these scales per trial arm were not reported.

### **Rowland 2009**

[Rowland 2009](#) studied 155 women treated for breast cancer who were randomised to either a psycho-educational programme or an active control involving an educational leaflet entitled 'Facing forward: a guide for cancer survivors'. All who were invited onto the trial had reported that they had problems with body image, sexuality and intimacy and/or communication with a partner. At baseline on a scale of 1 to 6, with higher scores indicating a better outcome, pain with sex was 4.1 in the intervention group and 4.3 in the control group. The intervention consisted of six two-hour weekly group meetings, which aimed to enhance participants' communication skills, reduce anxiety in intimate situations and provide information on sexual anatomy, menopause and sexual dysfunction.

### *Sexual function*

The study's secondary outcomes were sexual function, via Likert scale (scores range from 1 to 6) items on satisfaction, pain and comfort, and relationship functioning using the Revised Dyadic Adjustment Scale (scores range from 0 to 69). For both outcomes the higher the scores the better the function. Baseline relationship functioning was 50.4 in the intervention group and 50.8 in the control group.

No significant differences were found in mean change scores from baseline to four-month follow-up between the trial arms in sexual satisfaction in regards to variety of sex and sexual relationship outcomes (MD 0.13, 95% CI -0.24 to 0.50; MD 0.10, 95% CI -0.30 to 0.50, respectively). Neither were there significant differences for most other outcomes relating to sex and relationships:

- pain interfering with pleasure (MD 0.30, 95% CI -0.12 to 0.72);
- improved comfort with sexuality (MD 0.20, 95% CI 0.00 to 0.40);
- comfort about being touched (MD -0.20, 95% CI -0.23 to 0.63);
- comfort in undressing (MD 0.40, 95% CI -0.21 to 1.01);
- comfort in being nude (MD 0.40, 95% CI -0.06 to 0.86);
- impact of cancer on sex (MD -0.10, 95% CI -0.37 to 0.17).

However, in the case of pain during sexual activity, impact on relationship and communication there were significant differences favouring those in the intervention group (MD 0.80, 95% CI 0.20 to 1.40; MD 2.40, 95% CI 1.02 to 3.78, MD 0.30, 95% CI 0.07 to 0.53, respectively). See [Table 5](#) for the actual mean scores.

### *Quality of life and adverse effects*

Adverse events were not reported and neither were outcomes for quality of life.

### *Secondary and other outcomes*

The study's primary outcome was mental health using the Mental Health Index-32. The index provides a total score with higher scores indicating better mental health. There was no significant difference in mean change in score from baseline to follow-up in those in the intervention group compared to those in the control group (MD 3.10, 95% CI -0.18 to 6.38). See [Table 5](#) for the actual mean scores.

Outcomes on impact on symptoms of disease were not reported.

### **Schover 2011**

[Schover 2011](#) randomised 300 African American women who were breast cancer survivors to either receiving a workbook and regular peer counselling or a workbook and participant-initiated telephone counselling. Participants at baseline had sexual dysfunction as defined on the Female Sexual Function Index (FSFI), with a mean score across the sample of 18.2 (the recommended score for indicating sexual dysfunction is less than 26.5 ([Conaglen 2010](#))). The intervention workbook was designed specifically for African American women to improve knowledge and reduce symptoms relating to sexual dysfunction, menopause and distress about infertility. In the peer counsellor group participants met the counsellor individually three times a week for six weeks. Each session focused on a chapter of the workbook. The telephone counselling group were given the workbook and the counsellor's contact details and they were encouraged to call her.

The trial measured a range of outcomes at six and 12 months, which included spiritual wellbeing using the Functional Assessment of Cancer, relationship functioning using the Dyadic Adjustment Scale, emotional distress using the Brief Symptom Inventory (BSI), mental distress using the Global Severity Index and sexual function using the FSFI.

### *Sexual function*

Using mixed model analysis they found overall no significant change across time in either group in sexual function. The exact scores for this outcome are not provided by the authors.

### *Quality of life and adverse events*

Adverse effects were not reported and neither were outcomes for quality of life.

### *Secondary and other outcomes*

Using mixed model analysis they found overall no significant change across time in either group in relationship functioning, in total score for menopausal symptoms or childbearing distress. They found depression decreased after treatment in the peer-counselled group to less than 2.5 but increased in the telephone-counselled group to nearly 4, but by 12 months depressive symptoms in the two groups were very similar, around a score of 3. The exact scores for any of these outcomes are not provided by the authors. Outcomes on physiological functioning were not reported.

### **Schover 2013**

[Schover 2013](#) randomised 58 women with breast or gynaecological cancer to either receive counselling and use of a password-protected website or “self-help”, which entailed access to the website without counselling support. All participants had some indication at baseline of sexual dysfunction using the FSFI as indicated by a score of less than 15 (scores for this scale ranged from 2 to 36, with the lower the score the poorer the sexual function). Actual scores for the participants were not provided. The intervention website provided information on the sexual and fertility consequences of their cancer and treatment, on management of vaginal dryness and pain, sexual issues and pelvic floor exercises. Those in the counselling group were given three sessions to guide them through the website and to discuss behavioural homework. At three and six months post-treatment sexual outcomes were measured using the FSFI and Menopausal Sexual Interest Questionnaire (MSIQ). Emotional distress was measured using the BSI and quality of life using the Quality of Life in Adult Cancer Survivors scale. The treatment effect was explored by using linear mixed models regression.

### *Sexual function*

Based on the FSFI scale they found a significant treatment effect in improved sexual function in those who received counselling (mean change of 7.44 from baseline to post-treatment (no SD provided)). However, this was not apparent in a subgroup analysis of those who were sexually active; the authors did not provide actual data on this. Using the MSIQ scale there was also a significant effect in those in the counselling group (mean change score 13.22 from baseline to post-treatment, SD not provided), but this was only apparent to three months.

### *Quality of life*

Quality of life was found to improve significantly in the self help group only. Full data on this outcome was not provided by the authors.

### *Adverse effects*

Adverse effects were not reported.

### *Secondary and other outcomes*

Emotional distress using the BSI at follow-up was reduced in the self help group by 3.73, and in the counselled group by 2.63, but this was not significant. Full data on this outcome was not provided by the authors.

Outcomes on physiological functioning and symptoms of disease were not reported.

### **Svensk 2009**

[Svensk 2009](#), in a trial of 41 women with breast cancer, tested the effect of five weeks of individual art therapy sessions compared with a control group who did not receive art therapy. Participants had a reduced level of sexual function and enjoyment at the first assessment following breast cancer treatments. This was indicated by the lower baseline scores for the European Organization for Research and Treatment of Cancer Quality of Life module (EORTC QLQ-BR23) subscale on sexual functioning at baseline in both trial arms (mean 25.44 in the intervention group and 25.00 in the control group, compared to 38.60 in the intervention group and 30.16 in the control group at first follow-up). The therapy, based on phenomenological methods, aimed to provide time and space for expression and reflection, to give support in the process of restoring body image and to act as a supporting agency.

### *Sexual function*

The EORTC QLQ-BR23 instrument was used to measure sexual outcomes, and the impact of treatment and cancer on symptoms and body image. It is comprised of 23 items. A higher score for sexual functioning indicates a better level of functioning. After radiation treatment there was no significant difference between trial arms in sexual function at two months (MD 8.44, 95% CI -8.01 to 24.89) and at six months (MD 5.88, 95% CI -10.15 to 21.91). In the intervention group the baseline mean was 25.44 (SD 19.54) and at six months it was 43.21 (SD 24.52). In the control group the mean at baseline was 25.00 (SD 21.97) and at six months it was 28.33 (SD 26.55).

There was no significant difference in sexual enjoyment at two months (MD 2.40, 95% CI -16.61 to 21.41) or at six months (MD -3.17, 95% CI -23.43 to 17.09). See [Table 6](#).

### *Quality of life*

Quality of life was measured using the Swedish version of the World Health Organization (WHO) instrument WHOQOL-BREF. At two and six months there was a significant difference favouring the intervention in quality of life (MD 12.08, 95% CI 0.39 to 23.77; MD 17.50, 95% CI 7.14 to 27.86, respectively).

### *Adverse effects*

Adverse effects were not reported.

### *Secondary and other outcomes*

Using the European Organization for Research and Treatment of Cancer (EORTC) QLQ-BR23 there was no significant difference between the trial arms at two and six months follow-up in body image, cancer therapy side effects, 'breast symptoms', 'arm symptoms', being upset by hair loss, physiological health, psychological health and quality of social relationships. This is apart from being upset about hair loss at two months, where there was a significant difference favouring those in the intervention group. See [Table 6](#). Physiological functioning were not reported.

### **Exercise**

One trial of 28 women evaluated the effect of exercise on sexual function ([Yang 2012](#)). The women had pelvic floor dysfunction following a radical hysterectomy and pelvic lymph node dissection for gynaecological cancer. The trial compared four weeks of pelvic floor muscle training with a control group receiving no training. At the start of the intervention in both trial arms the overall mean for sexual function using the sexual function subscale of the Pelvic Floor Questionnaire indicated sexual dysfunction. Total scores on the scale ranged from 0 to 20. Eight items on the scale covered sufficient lubrication, vaginismus, coital incontinence, vaginal laxity, dyspareunia and 'sexual bother'. A zero score meant that there was no problem in any of the items. In the intervention group the mean score was 6.02 and in the control group 4.62.

### *Sexual function*

Sexual function was measured at four weeks via self report (yes or no), the Australian Pelvic Floor Questionnaire (APFQ) using a four-point scoring system (0 = no problem to 3 = severe problem) and the cervical cancer-specific EORTC QLQ CX24, which

assessed function using three items. Single-item measures on the EORTC QLQ CX24 were used in this study to assess sexual worry, activity and enjoyment. The trial had mixed outcomes for sexual function.

The trial reported no significant difference between trial arms in the number of participants at follow-up who were sexually functioning (8/12 in the intervention group compared with 5/12 in the control group; OR 2.80, 95% CI 0.53 to 14.74). In contrast, the mean score using the EORTC QLQ CX24 was significantly different between trial arms, favouring those who received the intervention (MD 10.30, 95% CI 1.48 to 19.12), as was the mean change score from baseline to follow-up for sexual function using APFQ (MD -3.20, 95% CI -5.55 to -0.85).

Using the EORTC QLQ CX24 the authors found no significant difference between trial arms in sexual worry or enjoyment but they found a difference in sexual activities favouring the intervention group (MD -10.00, 95% CI -22.25 to 2.25; MD 2.70, 95% CI -9.45 to 14.85; MD 18.40, 95% CI 5.18 to 31.62, respectively). Actual mean scores per trial arm were not reported.

### *Quality of life*

Quality of life outcomes were not reported.

### *Adverse effects*

The authors stated a physical therapist and a trained evaluator monitored adverse effects and any participants experiencing an aggravation of pelvic floor symptoms or difficulty in continuing the exercises was excluded from the final assessment. They did not provide the numbers of those excluded for these events.

### *Secondary and other outcomes*

Psychological and physiological functioning, and symptoms of disease were not reported.

## **DISCUSSION**

This is the first update of the 2007 Cochrane systematic review on interventions for sexual dysfunction following treatment for cancer in women ([Miles 2007](#)). The original publication included interventions for men and for women. It identified only one trial of an intervention for women. This trial was not included in this update as it no longer fitted the tighter inclusion criteria, which excluded trials on preventative treatments. Since the original review, as demonstrated in our identification of 11 new trials and two in progress, there has been much more research interest in

interventions for women. Three-quarters of the trials evaluated interventions that involved a psychotherapeutic element; the others evaluated a pharmaceutical gel, testosterone cream and a pelvic floor exercise. The trials involved women with gynaecological or breast cancer. Overall, the trials were mostly not of high quality as they under-reported design features. Three were pilot or feasibility studies involving small samples and in which the primary aim was not to test effectiveness. We did not identify any randomised controlled trials (RCTs) that evaluated a complementary or alternative medicine intervention.

## Summary of main results

The variation in interventions evaluated, including between those that involved a psychotherapeutic element, is the main reason why there is no combined analysis in this review. Psychotherapeutic interventions involved sexual counselling, art therapy, peer support or relationship therapy; overall they showed a mixed effect on sexual functioning. The evidence that testosterone cream, pH-balanced vaginal gel or pelvic floor exercise improves sexual function is weak. The evidence for each of these interventions is limited to one study and involved in three of the four studies fewer than 50 participants per arm. Evidence on potential harms was under-reported in all studies. This is apart from the trial on a topical cream and the one on a pH-balanced vaginal gel, which reported no significant increase in adverse effects in those in the intervention group compared to those allocated a placebo. Surprisingly few trials assessed quality of life, mental health or physiological functioning, therefore it is difficult to derive any conclusions on the effect of these interventions on these outcomes. The two trials of pharmaceutical interventions measured harm and neither reported any. Only one of the psychological intervention trials reported that no harm occurred because of the intervention; the other trials did not measure harm.

## Overall completeness and applicability of evidence

We searched widely for evidence using 11 citation databases and using search terms to help identify as wide a range of interventions as possible. We found some notable gaps in the evidence. We did not identify any RCTs evaluating a complementary therapy or alternative medicine, despite trials of these interventions, such as *Ginkgo biloba*, being tested in other populations. However, a limitation is that we did not search foreign language databases, therefore we may have missed some studies, for example Chinese herbal medicines and acupuncture. In any further update we recommend that these need to be considered.

We also identified no completed trials of interventions that were evaluated in populations with cancers other than breast or gynaecological cancer. However, one of the trials in progress is assessing

an intervention following treatment for rectal or anal cancer. This is an important omission as colorectal cancer is one of the most commonly diagnosed cancers and the treatment, such as surgery and radiation, is likely to affect sexual function (Donovan 2010). Moreover, it is known that head and neck cancer survivors struggle with disfigurement and changes in body image, and have increased social isolation, all of which may lead to sexual difficulties (Low 2009; Singer 2008). Another limitation is that all trials were undertaken in advanced western societies, with the majority being undertaken in US populations. Therefore our findings may not be applicable to other populations, in particular where cultural practices in regards to sexual matters may be different.

## Quality of the evidence

We could not adequately assess risk of bias in that we found all trials to have at least one methodological item under-reported, including blinding or randomisation sequence generation. The quality of the evidence is also weakened as eight of the trials had samples of fewer than 50 participants per trial arm. Some of these were also pilot studies, the focus of which was on feasibility rather than effectiveness.

## Potential biases in the review process

We undertook a comprehensive search of 11 databases; the last search was completed in September 2015. More recently published eligible studies will be captured at the next update. We identified seven potentially eligible studies in progress from trial registers and conference abstracts. In further updates of this review we recommend consideration of searching foreign language databases. At least two authors undertook all steps of this review. This limited the risk of errors in determining study eligibility, data extraction, 'Risk of bias' assessment and data synthesis.

## Agreements and disagreements with other studies or reviews

There are two recent relevant systematic reviews of psychotherapy in general populations. Both are non-Cochrane reviews evaluating psychotherapeutic interventions in both men and women (Berner 2012; Fruhauf 2013). The review by Berner 2012 included 20 trials but only two of these included women with sexual dysfunction. They found no benefit of the interventions for women. The review by Fruhauf 2013 included 34 trials that compared the psychosocial intervention with a comparison group. They found in combined analysis of five trials an improvement in sexual function in those who received sexual skills training. However, it is important to note that these reviews were undertaken in non-cancer populations and therefore their findings are not necessarily transferable to the populations considered in our review.

## AUTHORS' CONCLUSIONS

### Implications for practice

This update found insufficient evidence for the effectiveness of topical pharmacological treatments, psychotherapeutic interventions and pelvic floor exercises. Apart from the pharmacological treatment we found limited evaluations of any potential harms these interventions may incur.

### Implications for research

Improved diagnosis and treatments for cancer mean that more people will be living with and surviving cancer, and of these a significant proportion may have sexual dysfunction. Further evidence is needed on treatments for sexual dysfunction from high-quality trials with large samples that fully report key methodological characteristics and harms. It is difficult to suggest which interventions might be most useful for further evaluation, as the trials we evaluated were at risk of biased results. Across the trials there was also minimal overlap in how the intervention was evaluated. Future trials need to consider preparatory stages in intervention development, to increase appropriateness and need, such as in the case of psychotherapeutic interventions, for example those recommended in the Medical Research Council (MRC) guidelines on developing and evaluating complex interventions (Craig 2008). They also need to fully report details of the intervention. Consideration is also needed of the choice of outcome measures that are appropriate to the patient population and the nature of the intervention, such as measures of sexual function, quality of life and mental health.

The trials evaluated in this review varied in design; some included a comparative arm with no additional support for sexual dysfunction and others compared the intervention arm with an active control. Future research should consider the appropriateness of a control group that is given no support despite sexual dysfunction. Perhaps

at the very least trialists should consider using a comparative arm for which the provision of usual care for sexual dysfunction is provided.

Sexual dysfunction is difficult to treat in this population as it may result from multiple causes, not all of which are a direct outcome of the cancer treatment. These causes include the emotional stress of having the diagnosis and its impact on daily living, as well as natural aging. Thus it may be a particularly difficult disorder to treat.

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\* Indicates the major publication for the study

## CHARACTERISTICS OF STUDIES

### Characteristics of included studies *[ordered by study ID]*

#### Aktas 2015

Methods	Randomised, controlled, single-centre trial	
Participants	Entered trial: 70 US women with gynaecological (42% ovarian and 42% endometrial) cancer who underwent surgery, chemotherapy or radiotherapy for their cancer. Most (62%) had a hysterectomy and chemotherapy. Highest disease stage was 3, at baseline 45% had reached this stage. All were sexually active before treatment. SD was not measured early in the trial, however the authors assumed that most of the women would developed sexual problems because of the cancer treatment. 14% in both trial arms had a higher education. The average age was 49.3 years. They were required to abstain from sex for the first 8 weeks following surgery	
Interventions	<p>Nursing care service to discuss sexual issues  Aim: to investigate the effect of a nurse care service on the sexual satisfaction of patients with gynaecologic cancer  Interventionist: nurse  Intervention: nursing counselling service involving additional specialist nursing care and consultancy at hospital and at home. Nurse discussed sexual issues including loss of the body part, body image, fear of being rejected, loss of reproductive function, loss of desire, decrease in vaginal sensitivity, decrease in sexual intercourse, decrease in vaginal sensitivity, vaginismus, dyspareunia, inability to reach orgasm, shortening of the vagina and incomplete penis penetration  Comparison: usual care following hospital protocols  Time since cancer treatment: at the start of the intervention patients were undergoing cancer treatment  Intensity of intervention: nurse visits 3 times a week whilst in hospital and twice at home at 1 and 12 weeks  Time length of intervention: not clear</p>	
Outcomes	An Interview Questionnaire, Home Visit Monitoring Questionnaire and Golombok Rust Inventory of Sexual Satisfaction (GRISS), which contains 28 items and 7 subscales on vaginismus, anorgasmia, infrequency, non-communication, dissatisfaction, non-sensuality and avoidance	
Notes	-	
<b><i>Risk of bias</i></b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Unclear risk	No details provided
Allocation concealment (selection bias)	Unclear risk	No details provided

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	70 entered. 2 and 3 patients died in the intervention and control groups respectively during the whole course of the project implementation
Selective reporting (reporting bias)	Unclear risk	Protocol not published and does not state primary outcomes
Sample size	High risk	Fewer than 50 participants per trial arm

**Barton 2007**

Methods	Randomised, cross-over, controlled, single-centre trial (phase III)
Participants	Entered trial: 150 postmenopausal US female survivors of breast cancer. To be eligible all participants needed to report a decrease in sexual desire. This was defined as a score < 8 on a 0 to 10 scale with 10 being the highest interest. To derive this they used the combined desire/interest (3 questions) and desire/frequency (2 questions) subscales of the Changes of Sexual Functioning Questionnaire (CSFQ). Eligible patients had to have a sexual partner. 131 were analysed. Mean age was 52.3 years. 80% of participants had been treated with chemotherapy
Interventions	Pharmacological Topical cream intervention Aim: whether transdermal testosterone would increase sexual desire in female cancer survivors Interventionist: no details Intervention: daily 10.4 mg testosterone cream (Vanicream 2% testosterone) in 1/8 teaspoon Comparison: placebo Vanicream 1 dose maximum per day Intervention duration: 4 weeks Time since cancer treatment: No details Time length of intervention: 4 weeks of each of the trial arm treatments
Outcomes	1. The primary outcome was sexual desire, which was measured using combined subscales of desire/interest and desire/frequency of the CSFQ Other scales were: 2. Derogatis Interview for Sexual Functioning/Self-Report Scale 3. Profile of Mood States 4. SF-36 Analysis at 4 and 8 weeks
Notes	-

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Central office, computer-generated
Allocation concealment (selection bias)	Low risk	Done by the central office
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Patients and all personnel were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	18/150 patients lost to follow-up; reasons provided
Selective reporting (reporting bias)	Low risk	Clearly provides results for all primary outcomes
Sample size	Unclear risk	Sample of 150; 50 to 199 per treatment arm

**Baucom 2009**

Methods	Randomised, parallel, controlled pilot trial
Participants	Early-stage female breast cancer. Sample 14 US couples. An aim of the intervention was to improve sexual function. Baseline sexual functioning using the sexual drive and relationship subscale of Derogatis Inventory of Sexual Functioning was below mid-score (16), suggesting a level of SD. Cancer treatment involved surgery (n = 11), chemotherapy (n = 3) and radiation (n = 1). Median age was 50 years, age range 30 to 80 years
Interventions	<p>Psychotherapeutic</p> <p>Directed to patient and partner. The intervention is based on a cognitive behavioural approach that has demonstrated considerable efficacy in alleviating and preventing relationship distress</p> <p>Aim: to pilot a couple-based intervention programme for breast cancer that teaches couples how to minimise negative effects and maximise positive functioning during this difficult time</p> <p>Interventionist: clinical psychology therapists trained in couple therapy and in the effects of cancer on relationship functioning</p> <p>Intervention content: couple-based relationship enhancement</p> <p>6 sessions of 75 minutes each. The sessions included (1) approaching breast cancer as a couple, (2) medical education regarding breast cancer, (3) communication skills for decision-making and sharing thoughts regarding cancer issues, (4) promoting healthy sexual adaptation and body image, (5) maintaining positives in life and (5) findings benefits and meaning in life. The content of each session could vary but the format was similar; they began with an update of the women's treatment for breast cancer and then</p>

	<p>reviewed homework assignments. The material provided per session was individualised to the couple. The session closed with the therapist providing a summary of the session and assigning the next homework session</p> <p>Comparison: usual care. Couples received a list of community resources for additional support. They did not receive cancer education or any form of psychological intervention</p> <p>Duration of intervention: 6 weeks held bi-weekly</p> <p>Time since cancer treatment: cancer treatment ongoing</p>	
Outcomes	<p>No primary outcome declared</p> <ol style="list-style-type: none"> <li>1. Quality of Marriage Index (QMI)</li> <li>2. Derogatis Inventory of Sexual Functioning (DISF-SR)</li> <li>3. Brief Symptom Inventory (BSI-18)</li> <li>4. Post-traumatic Growth Inventory (PGI)</li> <li>5. Functional Assessment of Cancer Therapy (FACT-B)</li> <li>6. Self Image Scale (SIS)</li> <li>7. Brief Fatigue Inventory (BFI)</li> </ol> <p>1-year follow-up</p>	
Notes	-	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Low risk	Computer-based random number generator
Allocation concealment (selection bias)	Low risk	Couples and the assessor were blind to subsequent treatment assignment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	One couple in the intervention group dropped out because they felt the intervention did not meet their needs as the woman required additional treatments for cancer and one couple were lost in the control group as the woman died
Selective reporting (reporting bias)	Low risk	Results for all outcomes provided
Sample size	High risk	Fewer than 50 participants per trial arm

**Classen 2013**

Methods	Randomised, controlled, parallel, single-centre feasibility trial	
Participants	27 Canadian, sexually-distressed (as measured by scoring at least 24 on the Female Sexual Distress Revised Scale, which is higher than the recommended cutoff of 11 so as they identified women whose distress was “above and beyond what might ordinarily occur for women with gynaecologic cancer”) female gynaecologic cancer patients subsequent to cancer treatment entered the trial. The women had received surgical, medical and/or radiation treatment for gynaecological cancer. They were currently disease-free for a minimum of 3 months. Mean age in the intervention group was 39.9 years and in the wait-list control 44.6 years. Age range was 28 to 59 years. Over 70% were Caucasian	
Interventions	<p>Psychotherapeutic intervention</p> <p>Aim: feasibility study examining the participation rates and preliminary outcomes for an online support group designed specifically for women who are sexually distressed subsequent to gynaecologic cancer treatment</p> <p>Interventionist: psychologists co-ordinated the discussion forum</p> <p>Intervention 1: 'GyneGals', hosted on 2 websites with weekly discussion topics. One website hosted the discussion forum, which allowed women access to an online group. The support group was a closed group only accessible to members and the research team. The other website housed the psycho-educational material, which was only accessible by members and the research team. The 2 websites were linked. In week 10 of the intervention, a 90-minute text-based chat session was offered in which the participants could interact in real time with a gynaecologic oncologist and radiation oncologist as well as the moderators</p> <p>Comparison group: wait-list control, whenever the user wanted to (at least once a week)</p> <p>Duration of intervention: 12 weeks</p> <p>Time since cancer treatment: required to be disease-free for a minimum of 3 months and no more than 5 years post-diagnosis</p>	
Outcomes	<p>The primary outcome was feasibility of the trial and intervention</p> <p>The secondary outcomes were:</p> <ol style="list-style-type: none"> <li>1. Female Sexual Distress Scale - revised, 13-item</li> <li>2. HADS</li> <li>3. Illness Intrusiveness Ratings Scale</li> <li>4. GyneGals exit questionnaire to assess participant's satisfaction with intervention</li> </ol> <p>Follow-up at 4 and 8 months</p>	
Notes	-	
<b><i>Risk of bias</i></b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Unclear risk	No details provided
Allocation concealment (selection bias)	Unclear risk	No details provided

**Classen 2013** (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	23/27 completed the study
Selective reporting (reporting bias)	Unclear risk	No details provided
Sample size	High risk	Fewer than 50 participants per trial arm

**Lee 2011**

Methods	Randomised, controlled, parallel, single-centre trial	
Participants	<p>98 women entered the trial with a history of primary breast cancer managed by chemotherapy or hormonal therapy, experienced menopause for a period of at least 12 months before the study, and at baseline in both trial arms on average there was a high degree of vulvovaginal dryness with pain (with a score of 10 indicating the highest score; in the intervention group the score was over 8.20 and in the placebo group 7.92) and dyspareunia (with a score of 10 indicating the highest score; in both the intervention and placebo groups it was over 8). Excluded were natural menopause, medical disease or other complications, other malignancies, a hysterectomy or oophorectomy, use of medication for uro-gynaecologic problems, unexplained vaginal bleeding and previous use of systemic or local sex hormones</p> <p>Mean age in the intervention group was 45 years and in the control group 44. At baseline in both trial arms participants (or most) reported painful intercourse. Over half of the participants were treated with chemotherapy plus hormonal therapy; the others were treated either by chemotherapy only or hormonal therapy only</p>	
Interventions	<p>Intervention: pH-balanced gel; the gel contained lactic acid to maintain the vaginal pH at about 4</p> <p>Comparison: placebo gel (pH 7.2)</p> <p>Both gels were applied via a vaginal applicator 3 times per week at bedtime</p> <p>Time length of intervention: 12 weeks</p> <p>Time since cancer treatment: not reported</p>	
Outcomes	Vaginal dryness and dyspareunia measured by visual analogue scale, vaginal health index and vaginal pH	
Notes	-	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>

Random sequence generation (selection bias)	Low risk	Random assignment was made from a confidential list of permuted blocks of 4 by a third party before the study
Allocation concealment (selection bias)	Low risk	Random assignment was made from a confidential list of permuted blocks of 4 by a third party before the study
Blinding of participants and personnel (performance bias) All outcomes	Low risk	The same-sized vaginal gel tubes with or without lactic acid (pH 4.0 and pH 7.2, respectively) were packaged identically by the manufacturer and labelled with sequential numbers according to the randomisation code
Incomplete outcome data (attrition bias) All outcomes	Low risk	5/49 lost to follow-up in the intervention arm and 7/42 in the placebo arm
Selective reporting (reporting bias)	Low risk	Results for primary outcomes provided
Sample size	High risk	Fewer than 50 participants per trial arm

**Marcus 2010**

Methods	Multi-centred, randomised, parallel, controlled trial
Participants	304 US female breast cancer patients post-treatment, which included chemotherapy, radiation therapy, surgery and tamoxifen, entered the trial. The most common cancer treatment was chemotherapy (226/306). Most participants were aged between 41 and 60 years. At baseline there was a level of SD as documented in a figure (degree of SD not stated). It was assessed using a scale of 25 items of which some of the items were developed specifically for this project
Interventions	<p>Psycho-therapeutic</p> <p>Aim: to determine whether a telephone counselling programme can improve psychosocial outcomes among breast cancer patients post-treatment</p> <p>Interventionist: psychosocial oncology counsellor</p> <p>Intervention content: telephone counselling programme augmented with additional print materials. Patients were given the choice to prioritise counselling on 1 of 6 themes of the materials: these were living with uncertainty, living with physical change, living with self change, sexuality after breast cancer, living in relationships and living with economic change. The aim was to enhance adaptation by normalising feelings of uncertainty and preparing survivors for unanticipated disruption across quality of life domains (physical, emotional, social, sexual and economic). The intervention also included printed material (stress management guide), relaxation tapes, written activities (including self monitoring) and feedback on progress at session 10</p> <p>Comparison group: received a resource directory for breast cancer</p> <p>Duration of intervention: 16 sessions of 45 minutes each over 1 year, first 9 provided at</p>

**Marcus 2010** (Continued)

	2 weekly time points Time since cancer treatment: states “just” completed treatment for breast cancer
Outcomes	Primary outcome: none declared 1. Cancer-specific distress: Impact of Event Scale (IES) 2. Depression: Center for Epidemiologic Studies Depression Scale (CES-D) 3. Sexual Dysfunction using the Sexual Dysfunction Scale (not referenced) 4. Personal growth from cancer experience: questions derived for survey Assessment at 3, 6, 12 and 18 months
Notes	-

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details on randomisation
Allocation concealment (selection bias)	Unclear risk	No details provided
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	The response rates at each follow-up did not differ by trial arm. 243/304 completed; reasons not provided
Selective reporting (reporting bias)	Unclear risk	No details provided
Sample size	Unclear risk	50 to 199 per treatment arm

**Rowland 2009**

Methods	Randomised, parallel, controlled trial involving 3 arms; 1) Intervention, 2) Intervention participants randomised to intervention but declined intervention but follow-up, 3) Control group
Participants	411 US women with breast cancer who had completed all cancer therapy except Tamoxifen entered the trial. 294 completed the trial. Mean age 57 years in the intervention group and 56 in the control group (range 35 to 86). Participants had either lumpectomy, mastectomy only or mastectomy and reconstruction. Around half had also received chemotherapy. Mean years since diagnosis: 3 years in the control group, 2.8 in the intervention group. Majority (over 80%) Anglo-American. Majority (over 70%) married. Minority (third) were educated to postgraduate level. Around half of the participants were employed. All who were invited had reported in an earlier study that they had problems with body image, sexuality and intimacy and/or communication with a partner. Degree

	of sexual problems were not further detailed
Interventions	<p>Psychotherapeutic: the intervention was derived from the trialists' conceptual model of the development of SD in breast cancer survivors</p> <p>Directed at the patient</p> <p>Aim: hypothesis that women in the intervention arm would experience greater improvement in their emotional wellbeing as well as body image, comfort and satisfaction with sexual functioning and partner communication than women randomised to the control group</p> <p>Interventionist: medical social workers</p> <p>Intervention content: psychoeducational group programme derived from the trialists' conceptual model of the development of sexual dysfunction. The programme aimed to improve satisfaction with sexual functioning and intimate relationships by providing information, enhancing communication skills and reducing anxiety in intimate situations. To ensure quality control investigators review audiotapes of a subset of sessions</p> <p>Comparison group: received an educational pamphlet: 'Facing forward: a guide for cancer survivors'</p> <p>Duration of intervention: 6 weekly 2-hour meetings</p> <p>Time since cancer treatment: not stated</p>
Outcomes	<p>Primary outcome was the Mental Health Index from the Medical Outcomes Study</p> <p>Secondary outcomes included Likert scale items to measure sexual outcomes</p> <p>Outcomes assessed 4 months after treatment</p>
Notes	83/284 (29%) randomised to the intervention group did not agree to take part in the intervention. The primary reasons were inconvenience in time or location of the sessions, the participant's perception that she was not distressed and did not need the intervention and being too busy

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details provided
Allocation concealment (selection bias)	Unclear risk	No details provided
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	95/411 lost to follow-up; no reasons stated for loss
Selective reporting (reporting bias)	Unclear risk	No details provided
Sample size	Low risk	More than 200 participants per trial arm

**Schover 2011**

Methods	Randomised, parallel, controlled trial
Participants	300 African American women who were breast cancer survivors entered the trial. Participants at baseline had sexual dysfunction using the Female SFI: the mean score across the entire sample was 18.2 (the recommended score for indicating sexual dysfunction is less than 26.5). Treatments for cancer varied; most commonly it was surgery and/or chemotherapy or radiotherapy. Mean age 54 years. Time since cancer diagnosis 6.5 years
Interventions	<p>Psychotherapeutic Directed at the patient Aim: to assess the effectiveness of the peer counselling programme compared with brief telephone counselling and to examine the influence of socio-medical factors on reproductive problems and the outcome of the intervention</p> <p>Interventionist: trained counsellors who were African American breast cancer survivors Intervention 1: Sisters Peer Counseling involving a 77 page workbook plus 3 sessions with a trained peer counsellor. Each 60- to 90-minute session focused on a chapter of the workbook. Each chapter began with a list of topics (such as how to overcome vaginal dryness) and the survivor rated the importance of each topic before the counselling session; this helped to tailor the focus of the discussion Intervention 2: telephone counselling, which included being sent the workbook and being invited to call the counsellor using a prepaid telephone card for up to 30 minutes to discuss the workbook</p> <p>Duration of treatment: 3 sessions over 6 weeks Time since cancer treatment: not stated</p>
Outcomes	Emotional distress, sexual function, relationship satisfaction, spirituality, menopause symptoms and knowledge. Outcomes assessed up to 1 year after start of the intervention
Notes	-

***Risk of bias***

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Minimisation techniques - a form of adaptive randomisation. They do not provide details on sequence generation
Allocation concealment (selection bias)	Unclear risk	No details provided
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details provided
Incomplete outcome data (attrition bias) All outcomes	High risk	189/300
Selective reporting (reporting bias)	Unclear risk	No details provided

Schover 2011 (Continued)

Sample size	Unclear risk	50 to 199 per treatment arm
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Schover 2013

Methods	Randomised, parallel, controlled trial	
Participants	58 US survivors of localised breast or gynaecologic cancers entered the trial. The majority (71%) had received chemotherapy, 7% pelvic radiation and 19% were taking tamoxifen. Mean age 58 years. Over 59% had at least 4 years college education, the majority were white (79%) and married (81%). 81% had breast cancer, the others gynaecologic. 54% were at cancer stage I. Mean years since diagnosis 3.5. 48% had a comorbid condition including diabetes, depression and hypertension. All had some indication at baseline of sexual dysfunction using the Female Sexual Function Index (FSFI) as indicated by a score of less than 26.5. Scores for this scale range from 2 to 36, with the lower the score the poorer is sexual function	
Interventions	<p>Web-based intervention called Tendrils: sexual renewal for women after cancer                      Intervention directed at the patient                      Aim: the efficacy of a trial of an Internet-based intervention for cancer-related female sexual dysfunction with the support of 3 counselling sessions compared to when the website is used as a self help site                      Intervention: website with sections describing the sexual and fertility consequences of their cancer and treatment, an interactive vulva self portrait with pain and pleasure mapping, sex after menopause; management of vaginal dryness and pain; causes and treatment options for loss of desire or orgasm problems; resuming sex. It also involved videos of women cancer survivors and vignettes played by actors illustrating common problems and coping strategies. A therapist manual provided guidance and content checklists during 3 counselling sessions. These were provided by 2 masters level mental health professionals. The counsellors guided women through the website and discussed behavioural homework                      Comparison: self help, which involved access to the website but no provision of a counsellor                      Duration of intervention: 12 weeks                      Time since cancer treatment: unclear</p>	
Outcomes	<p>The primary outcome was the FSFI. Other outcomes were the Menopausal Sexual Internet Questionnaire, the Brief Symptom Inventory, Global Severity Index and the Quality of Life in Adult Cancer Survivors                      Outcomes were assessed at end of treatment and at 3- and 6-month follow-up</p>	
Notes	-	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Unclear risk	Randomisation stated, no details provided

**Schover 2013** (Continued)

Allocation concealment (selection bias)	Unclear risk	No details provided
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details provided
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No details provided
Selective reporting (reporting bias)	Unclear risk	No details provided
Sample size	High risk	Fewer than 50 participants per trial arm

**Svensk 2009**

Methods	Randomised, controlled, parallel trial
Participants	42 Swedish women with breast cancer who were undergoing radiotherapy entered the trial. Median age in the intervention group was 59.5 years and in the control group 55 years. Participants had a reduced level of sexual function and enjoyment at the first assessment following breast cancer treatments. This was indicated by the lower baseline scores for the EORTC QLQ-BR23 subscale on sexual functioning at baseline in both trial arms
Interventions	Intervention: art therapy involving 5 individual sessions for 1 hour a week. The aim was to offer time and space for expression and reflection, to give support in the process of restoring body image and to reduce stress. Sessions were based on a phenomenological method of art therapy Comparison: no details Intervention length: 5 weeks Time since cancer treatment: ongoing
Outcomes	Sexual functioning measured using the EORTC Quality of Life Questionnaire, version 1.0. It includes 23 items to assess as well as sexual functioning and enjoyment, disease symptoms, side effects, body image and future perspectives Quality of life using (1) the Swedish version of the WHO instrument WHOQOL-BREF. This involves 26 items in 4 domains: physical, psychological, social relationships and environment, and the (2) the European Organization for Research and Treatment of Cancer Instrument Outcomes measured before randomisation and start of radiotherapy, 2 months later and 6 months later
Notes	-

***Risk of bias***

Bias	Authors' judgement	Support for judgement
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**Svensk 2009** (Continued)

Random sequence generation (selection bias)	Low risk	“computer generated”. Stratification was done according to whether the patient had received adjuvant chemotherapy before radiotherapy treatment or not
Allocation concealment (selection bias)	Low risk	The randomisation was computer-generated at the Regional Centre of Oncology at Umeå University
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants could not be blinded because of the nature of the intervention; does not state that the analyst or other personnel were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	42/42 completed the study
Selective reporting (reporting bias)	Unclear risk	No protocol is available and study report does not state a primary outcome
Sample size	High risk	Fewer than 50 participants per trial arm

**Yang 2012**

Methods	Randomised, parallel, controlled pilot trial
Participants	34 South Korean women with gynaecological cancer who had radical hysterectomy entered and 24 completed trial. Study included because at the start of the intervention in both trial arms the overall mean on sexual function using the sexual function score of the Pelvic Floor Questionnaire indicated sexual dysfunction. Total scores in scale range from 0 to 20. 8 items on the scale cover sufficient lubrication, vaginismus, coital incontinence, vaginal laxity, dyspareunia and sexual bother. A zero score means no problem in any of the items. In the intervention group the mean score was 6.02 and in the intervention group 4.62. Mean age 52 years
Interventions	<p>Exercise intervention</p> <p>Intervention directed at patient</p> <p>Aim: to investigate the effectiveness of this pelvic floor rehabilitation programme on pelvic floor function and quality of life in gynaecological cancer survivors</p> <p>Interventionist: physiotherapist</p> <p>Intervention content: intensive pelvic floor muscle training incorporated with core exercise. The exercise is with biofeedback via a vaginal silicon pressure sensor. There was also per session a 30-minute counselling session, which involved life-style advice, evaluation and encouragement. In the first week patients learnt about the anatomy and function of the pelvic floor muscles</p> <p>Comparison group received usual health care</p> <p>Duration of intervention: weekly for 4 weeks of 45 exercises of 30 minutes duration</p> <p>Time since cancer treatment: does not specify but less than 5 years</p>

Outcomes	Primary outcome not stated (1) Pelvic floor dysfunction questionnaire (2) Pelvic floor muscle strength (3) Motor evoked potential (MEP) of the sacral nerve (4) Patient-reported health-related quality of life (HRQOL) measured using the European Organization for Research and Treatment of Cancer (EORTC) quality of life questionnaire QLQ-C30 (a 30-item multidimensional questionnaire on global health/quality of life) and the EORTC QLQ-CX-24 (a specific cervical cancer module of patients' experience, body image and sexuality) Outcomes were assessed at 4 weeks	
Notes	-	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Low risk	Computerised, stratified block randomisation
Allocation concealment (selection bias)	Unclear risk	No details provided
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding of participants not possible because of the nature of the intervention. To avoid knowledge of an individual's training progression and thereby potentially influencing the process of measurement the training sessions and strength measurements were administered by different people. Outcome evaluators were blinded to group allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Similar in both arms and reasons provided
Selective reporting (reporting bias)	Unclear risk	No details provided
Sample size	High risk	Fewer than 50 participants per trial arm

CSFQ: Changes of Sexual Functioning Questionnaire

EORTC: the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire

FSFI: Female Sexual Function Index

HADS: Hospital Anxiety and Depression Scale

SD: sexual dysfunction

WHOQOL-BREF: World Health Organization quality of life instrument

### Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Badger 2005	SD not mentioned
Barber 2002	Article includes sexual functioning, but cancer patients were not included
Barrett-Connor 1996	It is unlikely that these “healthy menopausal women” are cancer patients
Berman 2003	No cancer patients
Boesen 2011	No documented evidence that at the start of the intervention the participants had SD
Brotto 2012	Around half of the participants were not randomised and there was no separate analysis for those who were randomised
Burstein 1999	This is not a RCT and alternative medicine was not an intervention for SD
Chow 2014	Does not differentiate whether the SD was before or after the cancer treatment
Christensen 1983	No baseline of SD provided
Davis 2004	Exploratory study of psychosocial needs of women with breast cancer. Not an intervention for SD following treatments for cancer
Decruze 1999	Not a RCT
Dennerstein 1979	No cancer patients
Doorenbos 2006	No SD outcome
Floter 2002	No cancer patients
Ganz 2000	Subjects were peri or postmenopausal (they had to have been amenorrhoeic for at least 6 months). The cause of sexual dysfunction was not studied in this sample and some women may have had problems that preceded the cancer diagnosis or could have been attributed to treatment
Given 2004	No SD outcome
Goetsch 2014	No outcomes on sexual function
Hasenbring 1999	No SD outcome
Huang 2013	Patients with cancer were excluded
Izuo 1967	No sexual function outcomes
Jefferies 2006	No established baseline report of SD

(Continued)

Jones 2006	No sexual function outcomes
Jung Hoon 2006	No sexual function outcomes
Juraskova 2013	No comparative arm
Kylstra 1999	Not a treatment for SD
Lengacher 2009	No sexual function outcomes
Lepore 2015	No outcomes on sexual function
Loprinzi 2011	No sexual outcomes
Marsden 2001	Subjects are postmenopausal. The cause of sexual dysfunction was not studied in this sample and some women may have had problems that preceded the cancer diagnosis or could have been attributed to treatment
Moore 1999	No cancer patients
Morales 2004	Tamoxifen: not a treatment for SD
Mulhall 2006	Discussion paper
Munarriz 2002	No cancer patients
Munstedt 1998	Not evaluating treatment for SD
Narvaez 2008	Less than 50% reported sexual problems at baseline
Nho 2013	Not a RCT
Nieman 2003	No cancer patients
Nikander 2003	No sexual outcome measures
Northouse 2002	SD not specifically mentioned
Northouse 2013	Does not measure sexual function outcomes
Park 2015	Not a randomised trial
Pietrzak 2007	Not a treatment for SD
Pitkin 1971	Intervention was a preventative treatment
Ponzone 2005	Discussion article
Rawlins 1999	Discussion article

(Continued)

Reese 2014	6 relevant participants; it is not clear whether for any one the sexual concerns started after treatment or prior to treatment for cancer
Robinson 1999	No established baseline report of SD
Schover 2006	Does not provide outcomes per trial arm
Schroder 2005	Not a RCT
Scott 2004	Participants on average had poor sexual functioning prior to cancer treatment
Seidman 2000	No cancer patients
Serewel 1990	No cancer patients.
Shabani 2014	Does not measure sexual outcomes
Sherwin 1984	Not about treatments for SD following treatment for cancer
Sherwin 1985	No cancer patients
Shifren 2000a	No cancer patients
Suckling 2006	Discussion paper
Sweeney 2002	Not an intervention for SD
Theobald 2002	No SD outcomes
Thompson 2003	SD is under “ other symptoms” with other non-SD symptoms, therefore data are not evaluable
van der Meulen 2014	No sexual function outcomes
Vos 2006	No SD outcomes
Warkentin 2006	Not a RCT
Watts 1995	No cancer patients
Wei 2005	This is a poor quality report of a RCT of psychotherapy for 1 week before and 1 week after an (unspecified) operation for cervical cancer. The baseline level of “sexual functioning” amongst participants is not reported, either before or after the operation. It is unclear who the male participants were and who answered the questionnaire The sexual outcome “sexual satisfaction” is self reported using what appears to be a single question The figures given are not explained (so it is not clear whether they are means or medians, for example) The randomisation procedure is not well explained
Wenzel 1999	An assessment for SD and not a treatment

(Continued)

Wenzel 2015	Although SD measure d it is part of a global score (with no reported subscale) on gynaecological problems
Wu 2014	Does not measure sexual dysfunction

RCT: randomised controlled trial

SD: sexual dysfunction

### Characteristics of studies awaiting assessment *[ordered by study ID]*

#### Esplen 2014

Methods	RCT
Participants	Breast cancer survivors
Interventions	Group therapy and guided imagery
Outcomes	Sexual functioning
Notes	Conference abstract of a study that has been completed - probably fits eligibility criteria - await full published version

#### Goetsch 2015

Methods	RCT
Participants	Breast cancer survivors
Interventions	Analgesic liquid
Outcomes	Penetration pain and sexual distress
Notes	Conference abstract of study that has been completed - probably fits eligibility criteria - await full published version

#### Gremore 2014

Methods	RCT
Participants	Patients with head and neck cancer and their partners
Interventions	Couple-based psychosocial intervention
Outcomes	Not clear

**Gremore 2014** (Continued)

Notes	Study in progress - unclear if eligible
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**Hickey 2015**

Methods	RCT
Participants	Women with breast cancer
Interventions	Lubricant for vaginal dryness
Outcomes	Sexual discomfort
Notes	Publication only of a conference abstract with preliminary findings

**Jensen 2014**

Methods	RCT
Participants	Patient undoing a radical cystectomy
Interventions	Home-based exercises
Outcomes	Quality of life measures
Notes	Study in progress - unclear if eligible

**Paterson 2015**

Methods	RCT
Participants	Breast cancer survivors
Interventions	Mindfulness-based stress reduction programme
Outcomes	Sexual distress and body image disturbances
Notes	Conference abstract of a study that is in progress - unclear if fits eligibility criteria

**Willems 2015**

Methods	RCT
Participants	Cancer survivors
Interventions	Web-based tailored intervention on psychosocial and lifestyle support

**Willems 2015** (Continued)

Outcomes	Not stated
Notes	Conference abstract of a study that is in progress - unclear if fits eligibility criteria

RCT: randomised controlled trial

**Characteristics of ongoing studies** [ordered by study ID]**Davis 2015**

Trial name or title	-
Methods	RCT
Participants	Women with breast cancer being treated with an aromatase inhibitor
Interventions	300 µg intravaginal testosterone therapy
Outcomes	Sexual dysfunction
Starting date	-
Contact information	-
Notes	-

**DuHamel 2013**

Trial name or title	Cancer Survivorship Intervention-Sexual Health (CSI-SH)
Methods	Pilot RCT
Participants	Female rectal and anal cancer survivors
Interventions	4 intervention sessions focused on different topics including education about the impact of treatment and specific strategies for sexual health. The first 3 sessions were followed by booster telephone sessions to review the strategies
Outcomes	Assessments were at baseline and approximately 4 and 8 months post-baseline with measures of quality of life (EORTC-QLQ-C30), Sexual Functioning (FSFI) and psychological wellbeing (e.g. Impact of Events Scale-Revised: IES-R)
Starting date	Not reported
Contact information	duhamelk@mskcc.org

**DuHamel 2013** (Continued)

Notes	-
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**Gessler 2015**

Trial name or title	Developing a Stepped Approach to improving sexual Function aFteR treatment fOr gyNaecological cancer (SAFFRON)
Methods	RCT
Participants	Women treated for gynaecological cancer
Interventions	The stepped care intervention will be developed over the first 6 months of the project. It will involve psychological therapies
Outcomes	Sexual function
Starting date	January 2014
Contact information	s.gessler@ucl.ac.uk
Notes	-

**Hummel 2015**

Trial name or title	KIS Study: a study evaluating the effectiveness of an internet-based therapy program for sexuality and intimacy problems in women treated for breast cancer
Methods	RCT
Participants	Breast cancer survivors
Interventions	Behavioural: internet-based cognitive behavioural therapy
Outcomes	Sexuality problems
Starting date	December 2012
Contact information	l.hummel@nki.nl
Notes	ClinicalTrials.gov Identifier: NCT02091765

**NCT00459134 2015**

Trial name or title	L-Arginine supplements in treating women who are cancer survivors
Methods	RCT
Participants	Cancer survivors with sexual dysfunction
Interventions	L-Arginine supplements
Outcomes	Sexual function
Starting date	2007; study is reported to have been completed but no publication of results identified
Contact information	Not provided
Notes	-

**NCT02091765 2015**

Trial name or title	KIS Study: a study evaluating the effectiveness of an Internet-based therapy program for sexuality and intimacy problems in women treated for breast cancer. ID NCT02091765
Methods	RCT
Participants	Breast cancer survivors with intimacy problems
Interventions	Internet-based cognitive behavioural therapy
Outcomes	Sexuality problems
Starting date	2014
Contact information	Neil K Aaronson n.aaronson@nki.nl
Notes	-

**Schofield 2013**

Trial name or title	The PeNTAGOn study (peer and nurse support trial to assist women in gynaecological oncology)
Methods	RCT
Participants	Women in gynaecological oncology receiving curative radiotherapy
Interventions	A nurse- and peer-led support programme
Outcomes	Primary outcome: psychological distress. Secondary outcomes: patient quality of life, symptom distress, unmet supportive care needs, preparation for treatment, psychosexual functioning and vaginal stenosis

**Schofield 2013** (Continued)

Starting date	Not reported
Contact information	Penelope.schofield@petermac.org
Notes	-

RCT: randomised controlled trial

## DATA AND ANALYSES

This review has no analyses.

## ADDITIONAL TABLES

**Table 1. Barton 2007 scores for sexual functioning**

Measure	Arm	Mean score (95% CI) Week 4*	Mean score (95% CI) Week 8**
Changes in Sexual Functioning Questionnaire	Rx/placebo	5.69 (4.13 to 10.63)	6.87 (6.42 to 11.38)
	Placebo/Rx	3.40 (2.08 to 6.75)	8.17 (7.36 to 13.82)
Changes in Sexual Functioning Questionnaire, Pleasure subscale	Rx/placebo	9.38 (7.00 to 11.23)	9.33 (6.84 to 16.49)
	Placebo/Rx	4.71 (0.43 to 8.98)	11.04 (9.03 to 18.59)
Profile of Mood States	Rx/placebo	-0.55 (-3.77 to 2.67)	1.07 (-1.89 to 4.03)
	Placebo/Rx	3.02 (-0.27 to 6.31)	5.11 (2.16 to 8.07)
Profile of Mood States, Vitality subscale	Rx/placebo	0.56 (-2.58 to 3.71)	1.82 (-1.74 to 5.39)
	Placebo/Rx	2.76 (-0.52 to 6.04)	4.68 (2.01 to 7.34)

CI: confidence interval

Rx: intervention

\*Pre-cross-over; \*\*Post-cross-over

**Table 2. Aktas 2014 follow-up subscale scores for sexual function**

Measure*	Mean score at follow-up in intervention group	Mean score at follow-up in control group
Sexual non-communication	5.14 (SD 2.07)	6.94 (SD 1.28)
Anorgasmia	8.83 (SD 1.79)	11.26 (SD 1.42)
Avoidance	6.34 (SD 3.13)	9.60 (SD 2.94)
Non-sensuality	7.43 (SD 3.09)	10.20 (SD 2.90)
Infrequency of sexual contact	6.03 (SD 1.58)	6.43 (SD 1.77)
Sexual dissatisfaction	7.0 (SD 2.82)	9.63 (SD 2.45)
Vaginismus	9.26 (SD 3.01)	12.17 (SD 3.31)

SD: standard deviation

**Table 3. Baucom 2009 follow-up scores for sexual functioning**

Measure	Mean score (SD) at follow-up in intervention group	Mean score (SD) at follow-up in control group
Sexual drive and relationship	13.00 (3.11)	9.80 (5.93)
Relationship satisfaction	39.71 (3.45)	40.20 (5.07)
Brief Symptom Inventory	6.71 (5.77)	15.80 (20.91)
Post-traumatic Growth Inventory	62.00 (29.10)	66.20 (35.73)
Functional Well-being FACT-B	3.22 (0.34)	2.89 (0.91)
Self-image Scale - self acceptance	21.29 (4.75)	19.20 (9.09)
Self-image Scale - partner acceptance	21.96 (2.27)	21.50 (4.79)
Brief Fatigue Inventory	2.98 (0.96)	3.22 (2.25)
Usual pain	2.29 (1.50)	2.40 (1.67)
Rotterdam Symptom Inventory	18.71 (2.36)	23.80 (9.81)

SD: standard deviation

**Table 4. Classen 2013 follow-up subscale scores for sexual function**

Measure	Mean change from baseline score at follow-up in intervention group	Mean change from baseline score at follow-up in control group
Sexual function intention-to-treat*	2.54 (SD 9.59)	0.26 (SD 3.19)
Sexual function actively used*	3.82 (SD 9.43)	0.26 (SD 3.19)
Anxiety and depression** intention-to-treat	0.63 (SD 4.39)	0.50 (SD 2.91)
Anxiety and depression** actively used	1.73 (SD 3.93)	0.50 (SD 2.91)
Intimacy*** intention-to-treat	0.19 (SD 1.33)	-0.17 (SD 1.21)
Relationship*** intention-to-treat	-0.04 (SD 0.68)	-0.01 (SD 0.82)
Instrumental*** intention-to-treat	-0.22 (SD 0.85)	-0.10 (SD 1.26)
Intimacy***	0.75 (SD 1.01)	-0.17 (SD 1.21)

**Table 4. Classen 2013 follow-up subscale scores for sexual function** (Continued)

Relationship***	-0.15 (SD 0.50)	-0.01 (SD 0.82)
Instrumental**	*-0.21 (SD 0.71)	-0.10 (SD 1.26)

\* Measured using the Female Sexual Distress Scale.\*\* Measured using the Hospital Anxiety and Depression Scale. \*\*\*Measured using the Illness Intrusiveness Ratings Scale.

SD: standard deviation

**Table 5. Rowland 2009 follow-up subscale scores for sexual and psychological function**

Measure	Mean baseline (SD) and change score (SD) at follow-up in intervention group	Mean baseline (SD) and change score (SD) at follow-up in control group
Satisfaction with variety of sex	4.0 (1.1), 0.1 (1.2)	4.0 (1.0), -0.03 (1.0)
Satisfaction with sexual relationship	4.8 (1.1), 0.0 (1.5)	4.7 (1.4), -0.3 (1.3)*
Pain with sex	3.8 (2.0), 0.7 (1.9)	4.1 (1.9), -0.1 (1.7)
Pain interfering with pleasure	4.4 (1.7), 0.3 (1.4)	4.4 (1.7), 0.0 (1.1)
Improved comfort with sexuality*	3.3 (0.6)	3.1 (0.6)
Comfort about being touched	4.7 (1.6), 0.1 (1.4)	4.6 (1.6), -0.1 (1.2)
Comfort undressing	4.7 (1.7), 0.2 (1.9)	5.0 (1.4), -0.2 (1.8)
Comfort being nude	5.3 (1.4), 0.3 (1.3)	5.2 (1.4), -0.1 (1.6)
Impact of cancer on sex	2.6 (1.0), 0.1 (0.8)	2.4 (1.0), 0.2 (0.9)
Impact on relationship	50.9 (5.7), 1.1 (4.0)	51.0 (5.6), -1.3 (4.6)
Improved communication*	3.5 (0.7)	3.2 (0.7)
Mental health	80.8 (11.6), -0.7 (10.4)	82.6 (9.2), -3.8 (9.4)

\* Measured at follow-up only

SD: standard deviation

**Table 6. Svensk 2009 follow-up scores**

<b>Measure</b>	<b>Mean score (SD) at follow-up in intervention group</b>	<b>Mean score (SD) at follow-up in control group</b>
Sexual function at 2 months	38.60 (24.88)	30.16 (28.20)
Sexual function at 6 months	34.21 (24.52)	28.33 (26.55)
Sexual enjoyment at 2 months	56.25 (26.44)	53.85 (25.60)
Sexual enjoyment at 6 months	69.05 (24.34)	72.22 (27.83)
Overall quality of life at 2 months	78.75 (14.68)	66.67 (22.82)
Overall quality of life at 6 months	85.00 (12.57)	67.50 (20.03)
Physical health at 2 months	68.75 (13.51)	61.39 (19.71)
Physical health at 6 months	74.82 (13.33)	63.93 (19.80)
Psychological health at 2 months	70.83 (15.29)	63.69 (15.87)
Psychological health at 6 months	73.96 (10.28)	69.38 (13.13)
Social relationships at 2 months	74.58 (14.43)	69.44 (15.66)
Social relationships at 6 months	77.50 (12.99)	71.67 (16.31)
Body image at 2 months	81.67 (24.57)	80.95 (20.77)
Body image at 6 months	91.25 (12.82)	83.33 (27.64)
Adverse effects at 2 months	14.76 (11.13)	20.33 (12.23)
Adverse effects at 6 months	10.24 (7.61)	14.97 (12.71)
Breast symptoms at 2 months	20.42 (16.10)	21.03 (14.58)
Breast symptoms at 6 months	17.08 (11.30)	20.63 (17.80)
Arm symptoms at 2 months	16.11 (21.77)	26.46 (29.71)
Arm symptoms at 6 months	15.56 (20.52)	18.52 (17.33)
Upset by hair loss at 2 months	11.11 (19.25)	50.00 (23.57)
Upset by hair loss at 6 months	25.00 (16.67)	50.00 (70.71)

SD: standard deviation

## APPENDICES

### Appendix I. Search strategies

#### Electronic database search terms as used in 2015 update

The search terms used reflected the three components to our research question:

- interventions for SD;
- SD variants;
- treatments for cancer.

The search terms are for both men and women; this is because initially we planned to include interventions for both sexes in one review. The findings were only split when it became apparent that the number of trials would prevent timely completion of a review covering both interventions for men and for women.

#### CENTRAL (The Cochrane Library)

#1 MeSH descriptor: [Alprostadil] explode all trees

#2 MeSH descriptor: [Papaverine] explode all trees

#3 MeSH descriptor: [Phentolamine] explode all trees

#4 MeSH descriptor: [Yohimbine] explode all trees

#5 MeSH descriptor: [Apomorphine] explode all trees

#6 MeSH descriptor: [Potassium Channels] explode all trees

#7 (alprostadil or androgel or Apomorphine or britaject or aromatase inhibitors or agonist of melancortin receptor or Adcirca or alpha adrenoceptor agonist or alpha-2 adrenoceptor agonist or androgel or arginine or botox or botulinum toxin or bromocriptine or cialis or dopaminergic agents or caverject or clomipramine or cyproheptadine or clonidine or delquamine or edex or hormone therapy or Isoxsuprine or intracavernosal vasodilators or levitra or Lignocaine or l-arginine or lodenfil or Methitest or methyl testosterone or midodrin or mianserin or moclobemide or mirtazapine or mianserin or moclobemide or ortho-gynest or ovestin or papaverine or papaverine-phentolamine or phentolamine or parlodel or phentolamine or potassium channel openers or progestational agents or premarin or prempo or prostins or Prostaglandins or prostaglandin E1 or pentoxifylline or potassium channels or Phosphodiesterase Type 5 or PDE5i or penile suppository or reboxetine or sildenafil or tadalafil or tampovagan or topical or topical cream or vagifem or vaginal cream or vaginal lubricant or vaginal or viagra or vasomax or Viagel or vardenafil or vasodilator or virilon or vasoactive or staxyn or topical estrogen cream or trental or vasodilan or viridal or yohimbine or android or androgen therapy or testosterone or testosterone cream or testosterone gel or testred):ti,ab,kw (Word variations have been searched)

#8 MeSH descriptor: [Testosterone] explode all trees

#9 MeSH descriptor: [Penile Implantation] explode all trees

#10 MeSH descriptor: [Penile Prosthesis] explode all trees

#11 MeSH descriptor: [Prosthesis Implantation] explode all trees

#12 (testosterone replacement or testosterone or venous constriction rings or vacuum device\* or vacuum erect\* or penile implant\* or penile arterialisation or venous litigation or prosthesis implant\* or vacuum constriction device or vacuum therapy\* or vibrat\* or vibrostimulation or electroejaculation or prolong ring\*):ti,ab,kw (Word variations have been searched)

#13 MeSH descriptor: [Aromatase Inhibitors] explode all trees

#14 (vaginal dilator\* or arginine or android or methyl testosterone or testosterone cream or vaginal lubricant or vaginal estradiol ring or vaginal estradiol ring or vaginal estrogen ring or vaginal oestrogen ring or topical estrogen cream or vaginal cream or estrogen replacement of ERT or estrogen replacement or aromatase inhibitors):ti,ab,kw (Word variations have been searched)

- #15 MeSH descriptor: [Estriol] explode all trees
- #16 MeSH descriptor: [Estrogens, Conjugated (USP)] explode all trees
- #17 MeSH descriptor: [Vaginal Creams, Foams, and Jellies] explode all trees
- #18 MeSH descriptor: [Ginkgo biloba] explode all trees
- #19 MeSH descriptor: [Pausinystalia] explode all trees
- #20 MeSH descriptor: [Turnera] explode all trees
- #21 MeSH descriptor: [Panax] explode all trees
- #22 MeSH descriptor: [Hypericum] explode all trees
- #23 MeSH descriptor: [Patient Education as Topic] explode all trees
- #24 MeSH descriptor: [Psychological Techniques] explode all trees
- #25 MeSH descriptor: [Psychotherapy] explode all trees
- #26 MeSH descriptor: [Counseling] explode all trees
- #27 MeSH descriptor: [Sex Counseling] explode all trees
- #28 MeSH descriptor: [Cognitive Therapy] explode all trees
- #29 (psychological intervention\* or psycholog\* or behavior\* or behaviour\* or cognitive behav\* therapy or cognitive therap\* or psychotherap\* or counsel\* or sex therap\* or patient educat\* or behav\* therapy or CBT or couple therap\* or couple intervention or couple-based or intimacy enhancing or mindfulness or patient education or psychological techniques or psychosexual or psychotherapy or psycho-somatic or Rational emotive therap\* or restoring intimacy or relaxation or relaxation therap\* or relaxation training or psychosocial or Sensual, body image or sex-counsel\* or sexual communication or sexual rehabilitation or sexuality or self-esteem or self concept or stress or psycho-education or sexual life reframing or coping skills or motivational counselling or anxiety management training or marital therap\* or group therap\* or focal therap\* or psychodynamic therap\* or supportive therap\* or psychoanalyses or interpersonal therap\* or individual therap\* or problem solving or emotional support or hypnosis or bibliotherap\* or sexual skills therap\* or systematic desensitization or hypnotherapy\* or radical emotive therap\* or psychodynamic or psychoeducational):ti,ab,kw (Word variations have been searched)
- #30 MeSH descriptor: [Phosphodiesterase 5 Inhibitors] explode all trees
- #31 MeSH descriptor: [Vasodilator Agents] explode all trees
- #32 (Phosphodiesterase Type 5 or PDE5i or adcirca or cialis or levitra or Viagra or vardenafil or sildenafil or tadalafil):ti,ab,kw (Word variations have been searched)
- #33 MeSH descriptor: [Aromatase Inhibitors] explode all trees
- #34 MeSH descriptor: [Apomorphine] explode all trees
- #35 (estriol or femprox):ti,ab,kw (Word variations have been searched)
- #36 conjugated estrogens:ti,ab,kw (Word variations have been searched)
- #37 estrogen ring:ti,ab,kw (Word variations have been searched)
- #38 estrogen therapy:ti,ab,kw (Word variations have been searched)
- #39 estrogen replacement:ti,ab,kw (Word variations have been searched)
- #40 estradiol ring:ti,ab,kw (Word variations have been searched)
- #41 vaginal oestrogen ring:ti,ab,kw (Word variations have been searched)
- #42 estrogen cream:ti,ab,kw (Word variations have been searched)
- #43 topical oestrogens:ti,ab,kw (Word variations have been searched)
- #44 (oestrogen or epimestrol):ti,ab,kw (Word variations have been searched)
- #45 (estradiol or oestrogenic steroids):ti,ab,kw (Word variations have been searched)
- #46 (estrone or ethinyl estradiol or mestranol or quinestrol):ti,ab,kw (Word variations have been searched)
- #47 (oestradiol or Dienestrol or estriol or estetrol):ti,ab,kw (Word variations have been searched)
- #48 "selective oestrogen receptor modulator":ti,ab,kw (Word variations have been searched)
- #49 (clomiph or raloxifene or tamoxifen or toremife or clomid or clomifene or clomifert or serophene or raloxifene or keoxifene):ti,ab,kw (Word variations have been searched)
- #50 (evista or dimethylamine or novaldex or tomaxithen or soltamox or zitazonium or menerba):ti,ab,kw (Word variations have been searched)
- #51 (femarelle or toremifene or serm or bazedoxifene):ti,ab,kw (Word variations have been searched)
- #52 ly-139481:ti,ab,kw (Word variations have been searched)
- #53 ly-156758:ti,ab,kw (Word variations have been searched)
- #54 MF-101:ti,ab,kw (Word variations have been searched)
- #55 DT56a:ti,ab,kw (Word variations have been searched)

#56 LY-117018:ti,ab,kw (Word variations have been searched)

#57 (arginine or acupuncture or DHEA or dehydroepiandrosterone or damiana or ginkgo or ginkgo bilboa or Hypericum or Panax or pausinyntalia or Turnera or turner diffusa or yohimbine or l-arginine, or pycnogeno, or viacreme or viagel or sensual or ginseng or st john's wort or complimentary medicine\* or alternative medicine\* or alternative therap\* or alternative remed\* or complimentary therap\* or complimentary remed\*):ti,ab,kw (Word variations have been searched)

#58 (dilation or dilators or eros therap\* or eros clitoral vacuum device or vaginal dilators or vibrator or vibrostimulation or mechanical stretching of tissues or cock ring or electroejaculation or magnetic stimulation or penile implantation or penile prosthesis or penile implant or penile arterialisation or penile vibratory stimulation or prosthesis implant\* or prolong ring or muse or venous constriction ring\* or venous ligation or vacuum device\* or vacuum constriction device\* or vacuum therapy or vacuum pump or penile injection):ti,ab,kw (Word variations have been searched)

#59 (kegel exercise\* or lubricant\* or lubrication or pelvic floor biofeedback or yoga or cream\* or foam\* or jellies or muscle relaxation or vaginal exercise or physical exercise or olive oil or physiotherapy or weight lifting or physical training or pelvic floor muscle control or self touch or penile rehabilitation or erectile rehabilitation or physiotherap\* or cavernous nerve regeneration, or sonic hedgehog or glial growth factor 2 or GGF2 or magnetic stimulation or cavernous nerve stimulation or low-intensity extracorporeal shockwave therapy or nerve stimulation):ti,ab,kw (Word variations have been searched)

#60 (alpha adrenoceptor agonist\* or alpha adrenoceptor antagonist or midodrin or vasodilan or isoxsuprine or pentoxifylline or trental or delquamine or pseudoephedrine or desipramine or cyproheptadine or lignocaine):ti,ab,kw (Word variations have been searched)

#61 MeSH descriptor: [Complementary Therapies] explode all trees

#62 (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59 or #60 or #61)

#63 MeSH descriptor: [Sexual Dysfunctions, Psychological] explode all trees

#64 MeSH descriptor: [Sexual Dysfunction, Physiological] explode all trees

#65 MeSH descriptor: [Erectile Dysfunction] explode all trees

#66 MeSH descriptor: [Lubrication] explode all trees

#67 MeSH descriptor: [Coitus] explode all trees

#68 MeSH descriptor: [Copulation] explode all trees

#69 ((sex\* near/3 (dysfunct\* or satisf\* or problem\* or symptom\* or arousal\* or activit\*)) or orgasm or libido or lubricat\* or impotence or dyspareunia or hypoactive sexual desire disorder or sexual aversion or coitus or coition):ti,ab,kw (Word variations have been searched)

#70 (sexual intercourse or erectile dysfunction or erect\* or sexual attraction or copulation or intimacy or procreat\* or relations or sex or sex act or sexual congress or sexual relation or arousal or penile erection or vaginal dryness or sexual pain or (pain\* near/3 intercourse) or (sex\* near/3 pain\*) or vaginismus or (sexual\* near/2 wellbeing) or (sexual\* near/2 well being) or sexual function\* or (pain next (urogenital or vulval or vaginal or perineal or penile or testicular or ileostomy or colostomy or urostomy))):ti,ab,kw (Word variations have been searched)

#71 (ejaculation dysfunction or premature ejaculation or early ejaculation or delayed ejaculation or retarded ejaculation or anejaculation or painful ejaculation or retrograde ejaculation or anterograde ejaculation or inhibited ejaculation or erectile difficulty or erectile dysfunction or loss of libido or lack of libido):ti,ab,kw (Word variations have been searched)

#72 #63 or #64 or #65 or #66 or #67 or #68 or #69 or #70 or #71

#73 MeSH descriptor: [Neoplasms] explode all trees

#74 MeSH descriptor: [Brachytherapy] explode all trees

#75 MeSH descriptor: [Radiotherapy, Conformal] explode all trees

#76 MeSH descriptor: [Radiotherapy, Adjuvant] explode all trees

#77 MeSH descriptor: [Chemotherapy, Adjuvant] explode all trees

#78 MeSH descriptor: [Mastectomy] explode all trees

#79 MeSH descriptor: [Prostatectomy] explode all trees

#80 (irradiat\* or radiotherap\* or chemotherap\* or mastectom\* or breast conserv\* or prostatectom\* or brachytherp or radiation or prostectomy or oncology or excisional surgery or hysterectomy or radical surgery or vulvar surgery or cryotherpy or androgen suppression or androgen deprivation or abdominoerineal resection or AP resection or APR or anterior resection or extralevator abdominoperineal excision or ELAP or colostomy or mutilating surgery or vulval reconstruction or vaginal reconstruction or penile reconstruction or breast reconstruction or breast implants):ti,ab,kw (Word variations have been searched)

#81 (neoplasm\* or cancer\* or carcinoma\* or neoplasia\* or adenocarcinoma\* or tumor or malignan\* or tumour\*):ti,ab,kw (Word variations have been searched)

#82 (chemotherap\* or mastectomy or breast conserv\* or oophorectomy or hormone therapy or hormone treatment):ti,ab,kw (Word variations have been searched)

#83 #73 or #74 or #75 or #76 or #77 or #78 or #79 or #80 or #81 or #82

#84 #62 and #72 and #83

### **MEDLINE (OVID)**

1. exp Alprostadil/
2. exp Papaverine/
3. exp Phentolamine/
4. exp Yohimbine/
5. exp Apomorphine/
6. exp Potassium Channels/
7. (alprostadil or androgel or Apomorphine or britaject or aromatase inhibitors or agonist of melancortin receptor or Adcirca or alpha adrenoceptor agonist or alpha-2 adrenoceptor agonist or androgel or arginine or botox or botulinum toxin or bromocriptine or cialis or dopaminergic agents or caverject or clomipramine or cyproheptadine or clonidine or delquamine or edex or hormone therapy or Isoxsuprine or intracavernosal vasodilators or levitra or Lignocaine or l-arginine or lodenfil or Methitest or methyl testosterone or midodrin or mianserin or moclobemide or mirtazapine or mianserin or moclobemide or ortho-gynest or ovestin or papaverine or papaverine-phenolamine or phenolamine or parlodel or phentolamine or potassium channel openers or progestational agents or premarin or prempo or prostins or Prostaglandins or prostaglandin E1 or pentoxifylline or potassium channels or Phosphodiesterase Type 5 or PDE5i or penile suppository or reboxetine or sildenafil or tadalafil or tampovagan or topical or topical cream or vagifem or vaginal cream or vaginal lubricant or vaginal or viagra or vasomax or Viagel or vardenafil or vasodilator or virilon or vasoactive or staxyn or topical estrogen cream or trental or vasodilan or viridal or yohimbine or android or androgen therapy or testosterone or testosterone cream or testosterone gel or testred).tw.
8. exp Testosterone/
9. exp Penile Implantation/
10. exp Penile Prosthesis/
11. exp Prosthesis Implantation/
12. (testosterone replacement or testosterone or venous constriction rings or vacuum device\* or vacuum erect\* or penile implant\* or penile arterialisation or venous litigation or prosthesis implant\* or vacuum constriction device or vacuum therapy\* or vibrat\* or vibrostimulation or electroejaculation or prolong ring\*).tw.
13. exp Aromatase Inhibitors/
14. (vaginal dilator\* or arginine or android or methyl testosterone or testosterone cream or vaginal lubricant or vaginal estradiol ring or vaginal estradiol ring or vaginal estrogen ring or vaginal oestrogen ring or topical estrogen cream or vaginal cream or estrogen replacement of ERT or estrogen replacement or aromatase inhibitors).tw.
15. exp Estriol/
16. exp "Estrogens, Conjugated (USP)"/
17. exp "Vaginal Creams, Foams, and Jellies"/
18. exp Ginkgo biloba/
19. exp Pausinystalia/
20. exp Turnera/
21. exp Panax/
22. exp Hypericum/
23. exp Patient Education as Topic/
24. exp Psychological Techniques/
25. exp Psychotherapy/
26. exp Counseling/
27. exp Sex Counseling/
28. exp Cognitive Therapy/
29. (psychological intervention\* or psycholog\* or behavior\* or behaviour\* or cognitive behav\* therapy or cognitive therap\* or psychotherap\* or counsel\* or sex therap\* or patient educat\* or behav\* therapy or CBT or couple therap\* or couple intervention or couple-based or intimacy enhancing or mindfulness or patient education or psychological techniques or psychosexual or psychotherapy or psycho-somatic or Rational emotive therap\* or restoring intimacy or relaxation or relaxation therap\* or relaxation training or psycho-

social or Sensual, body image or sex-counsel\* or sexual communication or sexual rehabilitation or sexuality or self-esteem or self concept or stress or psycho-education or sexual life reframing or coping skills or motivational counselling or anxiety management training or marital therap\* or group therap\* or focal therap\* or psychodynamic therap\* or supportive therap\* or psychoanalyses or interpersonal therap\* or individual therap\* or problem solving or emotional support or hypnosis or bibliotherap\* or sexual skills therap\* or systematic desensitization or hypnotherapy\* or radical emotive therap\* or psychodynamic or psychoeducational).tw.

30. exp Phosphodiesterase 5 Inhibitors/

31. exp Vasodilator Agents/

32. (Phosphodiesterase Type 5 or PDE5i or adcirca or cialis or levitra or Viagra or vardenafil or sildenafil or tadalafil).tw.

33. exp Aromatase Inhibitors/

34. exp Apomorphine/

35. (estriol or femprox).tw.

36. conjugated estrogens.tw.

37. estrogen ring.tw.

38. estrogen therapy.tw.

39. estrogen replacement.tw.

40. estradiol ring.tw.

41. vaginal oestrogen ring.tw.

42. estrogen cream.tw.

43. topical oestrogens.tw.

44. (oestrogen or epimestrol).tw.

45. (estradiol or oestrogenic steroids).tw.

46. (estrone or ethinyl estradiol or mestranol or quinestrol).tw.

47. (oestradiol or Dienestrol or estriol or estetrol).tw.

48. selective oestrogen receptor modulators.tw.

49. (clomiph or raloxifene or tamoxifen or toremife or clomid or clomifene or clomifert or serophene or raloxifene or keoxifene).tw.

50. (evista or dimethylamine or novaldex or tomaxithen or soltamox or zitazonium or menerba).tw.

51. (femarelle or toremifene or serm or bazedoxifene).tw.

52. ly-139481.mp.

53. ly-156758.mp.

54. MF-101.mp.

55. DT56a.mp.

56. LY-117018.mp.

57. (arginine or acupuncture or DHEA or dehydroepiandrosterone or damiana or ginkgo or ginkgo bilboa or Hypericum or Panax or pausinyntalia or Turnera or turner diffusa or yohimbine or l-arginine, or pycnogeno, or viacreme or viagel or sensual or ginseng or st john's wort or complimentary medicine\* or alternative medicine\* or alternative therap\* or alternative remed\* or complimentary therap\* or complimentary remed\*).tw.

58. (dilation or dilators or eros therap\* or eros clitoral vacuum device or vaginal dilators or vibrator or vibrostimulation or mechanical stretching of tissues or cock ring or electroejaculation or magnetic stimulation or penile implantation or penile prosthesis or penile implant or penile arterialisation or penile vibratory stimulation or prosthesis implant\* or prolong ring or muse or venous constriction ring\* or venous ligation or vacuum device\* or vacuum constriction device\* or vacuum therapy or vacuum pump or penile injection).tw.

59. (kegel exercise\* or lubricant\* or lubrication or pelvic floor biofeedback or yoga or cream\* or foam\* or jellies or muscle relaxation or vaginal exercise or physical exercise or olive oil or physiotherapy or weight lifting or physical training or pelvic floor muscle control or self touch or penile rehabilitation or erectile rehabilitation or physiotherap\* or cavernous nerve regeneration, or sonic hedgehog or glial growth factor 2 or GGF2 or magnetic stimulation or cavernous nerve stimulation or low-intensity extracorporeal shockwave therapy or nerve stimulation).tw.

60. (alpha adrenoceptor agonist\* or alpha adrenoceptor antagonist or midodrin or vasodilan or isoxsuprine or pentoxifylline or trental or delquamine or pseudoephedrine or desipramine or cyproheptadine or lignocaine).tw.

61. exp Complementary Therapies/

62. or/1-61

63. exp Sexual Dysfunctions, Psychological/ or exp Sexual Dysfunction, Physiological/

64. exp Erectile Dysfunction/

65. exp Lubrication/

66. exp Coitus/

67. exp Copulation/  
 68. ((sex\* adj3 (dysfunct\* or satisf\* or problem\* or symptom\* or arousal\* or activit\*)) or orgasm or libido or lubricat\* or impotence or dyspareunia or hypoactive sexual desire disorder or sexual aversion or coitus or coition).tw.  
 69. (sexual intercourse or erectile dysfunction or erect\* or sexual attraction or copulation or intimacy or procreat\* or relations or sex or sex act or sexual congress or sexual relation or arousal or penile erection or vaginal dryness or sexual pain or (pain\* adj3 intercourse) or (sex\* adj3 pain\*) or vaginismus or (sexual\* adj2 wellbeing) or (sexual\* adj2 well being) or sexual function\* or (pain adj (urogenital or vulval or vaginal or perineal or penile or testicular or ileostomy or colostomy or urostomy))).tw.  
 70. (ejaculation dysfunction or premature ejaculation or early ejaculation or delayed ejaculation or retarded ejaculation or anejaculation or painful ejaculation or retrograde ejaculation or anterograde ejaculation or inhibited ejaculation or erectile difficulty or erectile dysfunction or loss of libido or lack of libido).tw.  
 71. or/63-70  
 72. exp Neoplasms/  
 73. exp Brachytherapy/  
 74. exp Radiotherapy, Conformal/  
 75. exp Radiotherapy, Adjuvant/  
 76. exp Chemotherapy, Adjuvant/  
 77. exp Mastectomy/  
 78. exp Prostatectomy/  
 79. (irradiat\* or radiotherap\* or chemotherap\* or mastectom\* or breast conserv\* or prostatectom\* or brachytherp or radiation or prostectomy or oncology or excisional surgery or hysterectomy or radical surgery or vulvar surgery or cryotherpy or androgen suppression or androgen deprivation or abdominoerineal resection or AP resection or APR or anterior resection or extralevator abdominoperineal excision or ELAP or colostomy or mutilating surgery or vulval reconstruction or vaginal reconstruction or penile reconstruction or breast reconstruction or breast implants).tw.  
 80. (neoplasm\* or cancer\* or carcinoma\* or neoplasia\* or adenocarcinoma\* or tumor or malignan\* or tumour\*).tw.  
 81. (chemotherap\* or mastectomy or breast conserv\* or oophorectomy or hormone therapy or hormone treatment).tw.  
 82. or/72-81  
 83. 62 and 71 and 82  
 84. randomized controlled trial.pt.  
 85. controlled clinical trial.pt.  
 86. randomized.ab.  
 87. placebo.ab.  
 88. drug therapy.fs.  
 89. randomly.ab.  
 90. trial.ab.  
 91. or/84-90  
 92. exp animals/ not humans.sh.  
 93. 91 not 92  
 94. 83 and 93

#### **EMBASE (OVID)**

1. exp Alprostadil/
2. exp Papaverine/
3. exp Phentolamine/
4. exp Yohimbine/
5. exp Apomorphine/
6. exp Potassium Channels/
7. (alprostadil or androgel or Apomorphine or britaject or aromatase inhibitors or agonist of melancortin receptor or Adcirca or alpha adrenoceptor agonist or alpha-2 adrenoceptor agonist or androgel or arginine or botox or botulinum toxin or bromocriptine or cialis or dopaminergic agents or caverject or clomipramine or cyproheptadine or clonidine or delquamine or edex or hormone therapy or Isoxsuprine or intracavernosal vasodilators or levitra or Lignocaine or l-arginine or lodenfil or Methitest or methyl testosterone or midodrin or mianserin or moclobemide or mirtazapine or mianserin or moclobemide or ortho-gynest or ovestin or papaverine or papaverine-phentolamine or phentolamine or parlodel or phentolamine or potassium channel openers or progestational agents or

premarin or prempo or prostins or Prostaglandins or prostaglandin E1 or pentoxifylline or potassium channels or Phosphodiesterase Type 5 or PDE5i or penile suppository or reboxetine or sildenafil or tadalafil or tamopvagan or topical or topical cream or vagifem or vaginal cream or vaginal lubricant or vaginal or viagra or vasomax or Viagel or vardenafil or vasodilator or virilon or vasoactive or staxyn or topical estrogen cream or trental or vasodilan or viridal or yohimbine or android or androgen therapy or testosterone or testosterone cream or testosterone gel or testred).tw.

8. exp Testosterone/

9. exp Penile Implantation/

10. exp Penile Prosthesis/

11. exp Prosthesis Implantation/

12. (testosterone replacement or testosterone or venous constriction rings or vacuum device\* or vacuum erect\* or penile implant\* or penile arterialisation or venous ligation or prosthesis implant\* or vacuum constriction device or vacuum therapy\* or vibrat\* or vibrostimulation or electroejaculation or prolong ring\*).tw.

13. exp Aromatase Inhibitors/

14. (vaginal dilator\* or arginine or android or methyl testosterone or testosterone cream or vaginal lubricant or vaginal estradiol ring or vaginal estradiol ring or vaginal estrogen ring or vaginal oestrogen ring or topical estrogen cream or vaginal cream or estrogen replacement of ERT or estrogen replacement or aromatase inhibitors).tw.

15. exp Estriol/

16. exp "Estrogens, Conjugated (USP)"/

17. exp "Vaginal Creams, Foams, and Jellies"/

18. exp Ginkgo biloba/

19. exp Pausinystalia/

20. exp Turnera/

21. exp Panax/

22. exp Hypericum/

23. exp Patient Education as Topic/

24. exp Psychological Techniques/

25. exp Psychotherapy/

26. exp Counseling/

27. exp Sex Counseling/

28. exp Cognitive Therapy/

29. (psychological intervention\* or psycholog\* or behavior\* or behaviour\* or cognitive behav\* therapy or cognitive therap\* or psychotherap\* or counsel\* or sex therap\* or patient educat\* or behav\* therapy or CBT or couple therap\* or couple intervention or couple-based or intimacy enhancing or mindfulness or patient education or psychological techniques or psychosexual or psychotherapy or psycho-somatic or Rational emotive therap\* or restoring intimacy or relaxation or relaxation therap\* or relaxation training or psycho-social or Sensual, body image or sex-counsel\* or sexual communication or sexual rehabilitation or sexuality or self-esteem or self concept or stress or psycho-education or sexual life reframing or coping skills or motivational counselling or anxiety management training or marital therap\* or group therap\* or focal therap\* or psychodynamic therap\* or supportive therap\* or psychoanalyses or interpersonal therap\* or individual therap\* or problem solving or emotional support or hypnosis or bibliotherap\* or sexual skills therap\* or systematic desensitization or hypnotherapy\* or radical emotive therap\* or psychodynamic or psychoeducational).tw.

30. exp Phosphodiesterase 5 Inhibitors/

31. exp Vasodilator Agents/

32. (Phosphodiesterase Type 5 or PDE5i or addcirca or cialis or levitra or Viagra or vardenafil or sildenafil or tadalafil).tw.

33. exp Aromatase Inhibitors/

34. exp Apomorphine/

35. (estriol or femprox).tw.

36. conjugated estrogens.tw.

37. estrogen ring.tw.

38. estrogen therapy.tw.

39. estrogen replacement.tw.

40. estradiol ring.tw.

41. vaginal oestrogen ring.tw.

42. estrogen cream.tw.

43. topical oestrogens.tw.

44. (oestrogen or epimestrol).tw.
45. (estradiol or oestrogenic steroids).tw.
46. (estrone or ethinyl estradiol or mestranol or quinestrol).tw.
47. (oestradiol or Dienestrol or estriol or estetrol).tw.
48. selective oestrogen receptor modulators.tw.
49. (clomiph or raloxifene or tamoxifen or toremife or clomid or clomifene or clomifert or serophene or raloxifene or keoxifene).tw.
50. (evista or dimethylamine or novaldex or tomoxithen or soltamox or zitazonium or menerba).tw.
51. (femarelle or toremifene or serm or bazedoxifene).tw.
52. ly-139481.mp.
53. ly-156758.mp.
54. MF-101.mp.
55. DT56a.mp.
56. LY-117018.mp.
57. (arginine or acupuncture or DHEA or dehydroepiandrosterone or damiana or ginkgo or ginkgo bilboa or Hypericum or Panax or pausinyustalia or Turnera or turner diffusa or yohimbine or l-arginine, or pycnogeno, or viacreme or viagel or sensual or ginseng or st john's wort or complimentary medicine\* or alternative medicine\* or alternative therap\* or alternative remed\* or complimentary therap\* or complimentary remed\*).tw.
58. (dilation or dilators or eros therap\* or eros clitoral vacuum device or vaginal dilators or vibrator or vibrostimulation or mechanical stretching of tissues or cock ring or electroejaculation or magnetic stimulation or penile implantation or penile prosthesis or penile implant or penile arterialisation or penile vibratory stimulation or prosthesis implant\* or prolong ring or muse or venous constriction ring\* or venous ligation or vacuum device\* or vacuum constriction device\* or vacuum therapy or vacuum pump or penile injection).tw.
59. (kegel exercise\* or lubricant\* or lubrication or pelvic floor biofeedback or yoga or cream\* or foam\* or jellies or muscle relaxation or vaginal exercise or physical exercise or olive oil or physiotherapy or weight lifting or physical training or pelvic floor muscle control or self touch or penile rehabilitation or erectile rehabilitation or physiotherap\* or cavernous nerve regeneration, or sonic hedgehog or glial growth factor 2 or GGF2 or magnetic stimulation or cavernous nerve stimulation or low-intensity extracorporeal shockwave therapy or nerve stimulation).tw.
60. (alpha adrenoceptor agonist\* or alpha adrenoceptor antagonist or midodrin or vasodilan or isoxsuprine or pentoxifylline or trental or delquamine or pseudoephedrine or desipramine or cyproheptadine or lignocaine).tw.
61. exp Complementary Therapies/
62. or/1-61
63. exp Sexual Dysfunctions, Psychological/ or exp Sexual Dysfunction, Physiological/
64. exp Erectile Dysfunction/
65. exp Lubrication/
66. exp Coitus/
67. exp Copulation/
68. ((sex\* adj3 (dysfunct\* or satisf\* or problem\* or symptom\* or arousal\* or activit\*)) or orgasm or libido or lubricat\* or impotence or dyspareunia or hypoactive sexual desire disorder or sexual aversion or coitus or coition).tw.
69. (sexual intercourse or erectile dysfunction or erect\* or sexual attraction or copulation or intimacy or procreat\* or relations or sex or sex act or sexual congress or sexual relation or arousal or penile erection or vaginal dryness or sexual pain or (pain\* adj3 intercourse) or (sex\* adj3 pain\*) or vaginismus or (sexual\* adj2 wellbeing) or (sexual\* adj2 well being) or sexual function\* or (pain adj (urogenital or vulval or vaginal or perineal or penile or testicular or ileostomy or colostomy or urostomy))).tw.
70. (ejaculation dysfunction or premature ejaculation or early ejaculation or delayed ejaculation or retarded ejaculation or anejaculation or painful ejaculation or retrograde ejaculation or anterograde ejaculation or inhibited ejaculation or erectile difficulty or erectile dysfunction or loss of libido or lack of libido).tw.
71. or/63-70
72. exp Neoplasms/
73. exp Brachytherapy/
74. exp Radiotherapy, Conformal/
75. exp Radiotherapy, Adjuvant/
76. exp Chemotherapy, Adjuvant/
77. exp Mastectomy/
78. exp Prostatectomy/

79. (irradiat\* or radiotherap\* or chemotherap\* or mastectom\* or breast conserv\* or prostatectom\* or brachytherp or radiation or prostectomy or oncology or excisional surgy or hysterectomy or radical surgery or vulvar surgery or cryotherpy or androgen suppression or androgen deprivation or abdominoerineal resection or AP resection or APR or anterior resection or extralevator abdominoperineal excision or ELAP or colostomy or mutilating surgery or vulval reconstruction or vaginal reconstruction or penile reconstruction or breast reconstruction or breast implants).tw.
80. (neoplasm\* or cancer\* or carcinoma\* or neoplasia\* or adenocarcinoma\* or tumor or malignan\* or tumour\*).tw.
81. (chemotherap\* or mastectomy or breast conserv\* or oophorectomy or hormone therapy or hormone treatment).tw.
82. or/72-81
83. 62 and 71 and 82
84. random\$.tw.
85. factorial\$.tw.
86. crossover\$.tw.
87. cross over\$.tw.
88. cross-over\$.tw.
89. placebo\$.tw.
90. (doubl\$ adj blind\$).tw.
91. (singl\$ adj blind\$).tw.
92. assign\$.tw.
93. allocat\$.tw.
94. volunteer\$.tw.
95. Crossover Procedure/
96. double-blind procedure.tw.
97. Randomized Controlled Trial/
98. Single Blind Procedure/
99. or/84-98
100. (animal/ or nonhuman/) not human/
101. 99 not 100
102. 83 and 101

### PsycINFO (OVID)

1. exp Papaverine/
2. exp Yohimbine/
3. exp Apomorphine/
4. (alprostadil or androgel or Apomorphine or britaject or aromatase inhibitors or agonist of melancortin receptor or Adcirca or alpha adrenoceptor agonist or alpha-2 adrenoceptor agonist or androgel or arginine or botox or botulinum toxin or bromocriptine or cialis or dopaminergic agents or caverject or clomipramine or cyproheptadine or clonidine or delquamine or edex or hormone therapy or Isoxsuprine or intracavernosal vasodilators or levitra or Lignocaine or l-arginine or lodenfil or Methitest or methyl testosterone or midodrin or mianserin or moclobemide or mirtazapine or mianserin or moclobemide or ortho-gynest or ovestin or papaverine or papaverine-phenolamine or phenolamine or parlodel or phentolamine or potassium channel openers or progestational agents or premarin or prempo or prostins or Prostaglandins or prostaglandin E1 or pentoxifylline or potassium channels or Phosphodiesterase Type 5 or PDE5i or penile suppository or reboxetine or sildenafil or tadalafil or tampovagan or topical or topical cream or vagifem or vaginal cream or vaginal lubricant or vaginal or viagra or vasomax or Viagel or vardenafil or vasodilator or virilon or vasoactive or staxyn or topical estrogen cream or trental or vasodilan or viridal or yohimbine or android or androgen therapy or testosterone or testosterone cream or testosterone gel or testred).tw.
5. exp Testosterone/
6. (testosterone replacement or testosterone or venous constriction rings or vacuum device\* or vacuum erect\* or penile implant\* or penile arterialisation or venous litigation or prosthesis implant\* or vacuum constriction device or vacuum therapy\* or vibrat\* or vibrostimulation or electroejaculation or prolong ring\*).tw.
7. (vaginal dilator\* or arginine or android or methyl testosterone or testosterone cream or vaginal lubricant or vaginal estradiol ring or vaginal estradiol ring or vaginal estrogen ring or vaginal oestrogen ring or topical estrogen cream or vaginal cream or estrogen replacement of ERT or estrogen replacement or aromatase inhibitors).tw.
8. exp Hypericum/

9. exp Psychotherapy/
10. exp Counseling/
11. exp Cognitive Therapy/
12. (psychological intervention\* or psycholog\* or behavior\* or behaviour\* or cognitive behav\* therapy or cognitive therap\* or psychotherap\* or counsel\* or sex therap\* or patient educat\* or behav\* therapy or CBT or couple therap\* or couple intervention or couple-based or intimacy enhancing or mindfulness or patient education or psychological techniques or psychosexual or psychotherapy or psycho-somatic or Rational emotive therap\* or restoring intimacy or relaxation or relaxation therap\* or relaxation training or psycho-social or Sensual, body image or sex-counsel\* or sexual communication or sexual rehabilitation or sexuality or self-esteem or self concept or stress or psycho-education or sexual life reframing or coping skills or motivational counselling or anxiety management training or marital therap\* or group therap\* or focal therap\* or psychodynamic therap\* or supportive therap\* or psychoanalyses or interpersonal therap\* or individual therap\* or problem solving or emotional support or hypnosis or bibliotherap\* or sexual skills therap\* or systematic desensitization or hypnotherapy\* or radical emotive therap\* or psychodynamic or psychoeducational).tw.
13. (Phosphodiesterase Type 5 or PDE5i or adcirca or cialis or levitra or Viagra or vardenafil or sildenafil or tadalafil).tw.
14. exp Aromatase Inhibitors/
15. exp Apomorphine/
16. (estriol or femprox).tw.
17. conjugated estrogens.tw.
18. estrogen ring.tw.
19. estrogen therapy.tw.
20. estrogen replacement.tw.
21. vaginal oestrogen ring.tw.
22. estrogen cream.tw.
23. topical oestrogens.tw.
24. (oestrogen or epimestrol).tw.
25. (estradiol or oestrogenic steroids).tw.
26. (estrone or ethinyl estradiol or mestranol or quinestrol).tw.
27. (oestradiol or Dienestrol or estriol or estetrol).tw.
28. selective oestrogen receptor modulators.tw.
29. (clomiph or raloxifene or tamoxifen or toremife or clomid or clomifene or clomifert or serophene or raloxifene or keoxifene).tw.
30. (evista or dimethylamine or novaldex or tomaxithen or soltamox or zitazonium or menerba).tw.
31. (femarelle or toremifene or serm or bazedoxifene).tw.
32. ly-139481.mp.
33. ly-156758.mp.
34. MF-101.mp.
35. DT56a.mp.
36. LY-117018.mp.
37. (arginine or acupuncture or DHEA or dehydroepiandrosterone or damiana or ginkgo or ginkgo bilboa or Hypericum or Panax or pausinyntalia or Turnera or turner diffusa or yohimbine or l-arginine, or pycnogeno, or viacreme or viagel or sensual or ginseng or st john's wort or complimentary medicine\* or alternative medicine\* or alternative therap\* or alternative remed\* or complimentary therap\* or complimentary remed\*).tw.
38. (dilation or dilators or eros therap\* or eros clitoral vacuum device or vaginal dilators or vibrator or vibrostimulation or mechanical stretching of tissues or cock ring or electroejaculation or magnetic stimulation or penile implantation or penile prosthesis or penile implant or penile arterialisation or penile vibratory stimulation or prosthesis implant\* or prolong ring or muse or venous constriction ring\* or venous ligation or vacuum device\* or vacuum constriction device\* or vacuum therapy or vacuum pump or penile injection).tw.
39. (kegel exercise\* or lubricant\* or lubrication or pelvic floor biofeedback or yoga or cream\* or foam\* or jellies or muscle relaxation or vaginal exercise or physical exercise or olive oil or physiotherapy or weight lifting or physical training or pelvic floor muscle control or self touch or penile rehabilitation or erectile rehabilitation orphysiotherap\* or cavernous nerve regeneration, or sonic hedgehog or glial growth factor 2 or GGF2 or magnetic stimulation or cavernous nerve stimulation or low-intensity extracorporeal shockwave therapy or nerve stimulation).tw.
40. (alpha adrenoceptor agonist\* or alpha adrenoceptor antagonist or midodrin or vasodilan or isoxsuprine or pentoxifylline or trental or delquamine or pseudoephedrine or desipramine or cyproheptadine or lignocaine).tw.
41. exp Alternative Medicine/
42. exp Sexual Function Disturbances/

43. exp Erectile Dysfunction/  
 44. exp Coitus/  
 45. exp Copulation/  
 46. ((sex\* adj3 (dysfunct\* or satisf\* or problem\* or symptom\* or arousal\* or activit\*)) or orgasm or libido or lubricat\* or impotence or dyspareunia or hypoactive sexual desire disorder or sexual aversion or coitus or coition).tw.  
 47. (sexual intercourse or erectile dysfunction or erect\* or sexual attraction or copulation or intimacy or procreat\* or relations or sex or sex act or sexual congress or sexual relation or arousal or penile erection or vaginal dryness or sexual pain or (pain\* adj3 intercourse) or (sex\* adj3 pain\*) or vaginismus or (sexual\* adj2 wellbeing) or (sexual\* adj2 well being) or sexual function\* or (pain adj (urogenital or vulvar or vaginal or perineal or penile or testicular or ileostomy or colostomy or urostomy))).tw.  
 48. (ejaculation dysfunction or premature ejaculation or early ejaculation or delayed ejaculation or retarded ejaculation or anejaculation or painful ejaculation or retrograde ejaculation or anterograde ejaculation or inhibited ejaculation or erectile difficulty or erectile dysfunction or loss of libido or lack of libido).tw.  
 49. exp Neoplasms/  
 50. exp Brachytherapy/  
 51. exp Radiation Therapy/  
 52. exp Chemotherapy/  
 53. exp Mastectomy/  
 54. (irradiat\* or radiotherap\* or chemotherap\* or mastectom\* or breast conserv\* or prostatectom\* or brachytherp or radiation or prostectomy or oncology or excisional surgery or hysterectomy or radical surgery or vulvar surgery or cryotherpy or androgen suppression or androgen deprivation or abdominoerineal resection or AP resection or APR or anterior resection or extralevator abdominoperineal excision or ELAP or colostomy or mutilating surgery or vulvar reconstruction or vaginal reconstruction or penile reconstruction or breast reconstruction or breast implants).tw.  
 55. (neoplasm\* or cancer\* or carcinoma\* or neoplasia\* or adenocarcinoma\* or tumor or malignan\* or tumour\*).tw.  
 56. (chemotherap\* or mastectomy or breast conserv\* or oophorectomy or hormone therapy or hormone treatment).tw.  
 57. clinical trials/  
 58. (randomis\* or randomiz\*).tw.  
 59. (random\$ adj3 (allocat\$ or assign\$)).tw.  
 60. ((clinic\$ or control\$) adj trial\$).tw.  
 61. ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj3 (blind\$ or mask\$)).tw.  
 62. (crossover\$ or "cross over\$").tw.  
 63. random sampling/  
 64. Experiment Controls/  
 65. Placebo/  
 66. placebo\$.tw.  
 67. exp program evaluation/  
 68. treatment effectiveness evaluation/  
 69. ((effectiveness or evaluat\$) adj3 (stud\$ or research\$)).tw.  
 70. or/57-69  
 71. or/1-41  
 72. or/42-48  
 73. or/49-56  
 74. 70 and 71 and 72 and 73

## AMED (OVID)

(No RCT filter added)

1. (alprostadil or androgel or Apomorphine or britaject or aromatase inhibitors or agonist of melancortin receptor or Adcirca or alpha adrenoceptor agonist or alpha-2 adrenoceptor agonist or androgel or arginine or botox or botulinum toxin or bromocriptine or cialis or dopaminergic agents or caverject or clomipramine or cyproheptadine or clonidine or delquamine or edex or hormone therapy or Isoxsuprine or intracavernosal vasodilators or levitra or Lignocaine or l-arginine or lodenfil or Methitest or methyl testosterone or midodrin or mianserin or moclobemide or mirtazapine or mianserin or moclobemide or ortho-gynest or ovestin or papaverine or papaverine-phentolamine or phentolamine or parlodel or phentolamine or potassium channel openers or progestational agents or premarin or prempo or prostins or Prostaglandins or prostaglandin E1 or pentoxifylline or potassium channels or Phosphodiesterase



or st john's wort or complimentary medicine\* or alternative medicine\* or alternative therap\* or alternative remed\* or complimentary therap\* or complimentary remed\*).tw.

38. (dilation or dilators or eros therap\* or eros clitoral vacuum device or vaginal dilators or vibrator or vibrostimulation or mechanical stretching of tissues or cock ring or electroejaculation or magnetic stimulation or penile implantation or penile prosthesis or penile implant or penile arterialisation or penile vibratory stimulation or prosthesis implant\* or prolong ring or muse or venous constriction ring\* or venous ligation or vacuum device\* or vacuum constriction device\* or vacuum therapy or vacuum pump or penile injection).tw.

39. (kegel exercise\* or lubricant\* or lubrication or pelvic floor biofeedback or yoga or cream\* or foam\* or jellies or muscle relaxation or vaginal exercise or physical exercise or olive oil or physiotherapy or weight lifting or physical training or pelvic floor muscle control or self touch or penile rehabilitation or erectile rehabilitation or physiotherap\* or cavernous nerve regeneration, or sonic hedgehog or glial growth factor 2 or GGF2 or magnetic stimulation or cavernous nerve stimulation or low-intensity extracorporeal shockwave therapy or nerve stimulation).tw.

40. (alpha adrenoceptor agonist\* or alpha adrenoceptor antagonist or midodrin or vasodilan or isoxsuprine or pentoxifylline or trental or delquamine or pseudoephedrine or desipramine or cyproheptadine or lignocaine).tw.

41. exp Complementary Therapies/

42. exp Sexual Dysfunctions, Psychological/ or exp Sexual Dysfunction, Physiological/

43. exp Erectile Dysfunction/

44. exp Lubrication/

45. exp Coitus/

46. exp Copulation/

47. ((sex\* adj3 (dysfunct\* or satisf\* or problem\* or symptom\* or arousal\* or activit\*)) or orgasm or libido or lubricat\* or impotence or dyspareunia or hypoactive sexual desire disorder or sexual aversion or coitus or coition).tw.

48. (sexual intercourse or erectile dysfunction or erect\* or sexual attraction or copulation or intimacy or procreat\* or relations or sex or sex act or sexual congress or sexual relation or arousal or penile erection or vaginal dryness or sexual pain or (pain\* adj3 intercourse) or (sex\* adj3 pain\*) or vaginismus or (sexual\* adj2 wellbeing) or (sexual\* adj2 well being) or sexual function\* or (pain adj (urogenital or vulval or vaginal or perineal or penile or testicular or ileostomy or colostomy or urostomy))).tw.

49. (ejaculation dysfunction or premature ejaculation or early ejaculation or delayed ejaculation or retarded ejaculation or anejaculation or painful ejaculation or retrograde ejaculation or anterograde ejaculation or inhibited ejaculation or erectile difficulty or erectile dysfunction or loss of libido or lack of libido).tw.

50. or/42-49

51. exp Neoplasms/

52. exp Brachytherapy/

53. exp Radiotherapy/

54. exp Mastectomy/

55. (irradiat\* or radiotherap\* or chemotherap\* or mastectom\* or breast conserv\* or prostatectom\* or brachytherp or radiation or proctectomy or oncology or excisional surgerj or hysterectomy or radical surgery or vulvar surgery or cryotherpy or androgen suppression or androgen deprivation or abdominoerineal resection or AP resection or APR or anterior resection or extralevator abdominoperineal excision or ELAP or colostomy or mutilating surgery or vulval reconstruction or vaginal reconstruction or penile reconstruction or breast reconstruction or breast implants).tw.

56. (neoplasm\* or cancer\* or carcinoma\* or neoplasia\* or adenocarcinoma\* or tumor or malignan\* or tumour\*).tw.

57. (chemotherap\* or mastectomy or breast conserv\* or oophorectomy or hormone therapy or hormone treatment).tw.

58. or/1-41

59. or/51-57

60. 50 and 58 and 59

## **CINAHL (EBSCO)**

S91 S81 AND S90

S90 S82 OR S83 OR S84 OR S85 OR S86 OR S87 OR S88 OR S89

S89 (allocat\* random\*)

S88 (MH "Quantitative Studies")

S87 (MH "Placebos")

S86 placebo\*

S85 (random\* allocat\*)

S84 (MH "Random Assignment")  
S83 (Randomized control\* trial\*)  
S82 (singl\* blind\* ) or (doubl\* blind\* ) or (tripl\* blind\* ) or (trebl\* blind\* ) or (trebl\* mask\* ) or (tripl\* mask\* ) or (doubl\* mask\* ) or (singl\* mask\* )  
S81 S60 AND S68 AND S79  
S80 S60 AND S68 AND S79  
S79 S69 OR S70 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 Search modes - Boolean/Phrase  
Interface - EBSCOhost Research  
Databases  
S78 (neoplas\* or cancer\* or carcinoma\* or neoplasia\* or adenocarcinoma\* or tumor or malignan\* or tumour\*)  
S77 (chemotherap\* or mastectomy or breast conserv\* or oophorectomy or hormone therapy or hormone treatment)  
S76 (irradiat\* or radiotherap\* or chemotherap\* or mastectom\* or breast conserv\* or prostatectom\* or brachytherp or radiation or prosectomy  
or oncology or excisional surgey or hysterectomy or radical surgery or vulvar surgery or cryotherpy or androgen suppression or androgen deprivation or abdominoerineal resection or AP resection or APR or anterior resection or extralevator abdominoperineal excision or ELAP or colostomy or mutilating surgery or vulval reconstruction or vaginal reconstruction or penile reconstruction or breast reconstruction or breast implants)  
S75 (MH "Prostatectomy+")  
S74 (MH "Mastectomy+")  
S73 (MH "Chemotherapy, Adjuvant")  
S72 (MH "Radiotherapy, Adjuvant")  
S71 (MH "Radiotherapy, Conformal")  
S70 (MH "Brachytherapy")  
S69 (MH "Neoplasms+")  
S68 S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67  
S67 (ejaculation dysfunction or premature ejaculation or early ejaculation or delayed ejaculation or retarded ejaculation or anejaculation or painful ejaculation or retrograde ejaculation or anterograde ejaculation or inhibited ejaculation or erectile difficulty or erectile dysfunction or loss of libido or lack of libido)  
S66 (pain N1 (urogenital or vulval or vaginal or perineal or penile or testicular or ileostomy or colostomy or urostomy))  
S65 ((pain\* N3 intercourse) or (sex\* N3 pain\*) or vaginismus or (sexual\* N2 wellbeing) or (sexual\* N2 well being) or( sexual function\*))  
S64 ((sex\* N3 (dysfunct\* or satisf\* or problem\* or symptom\* or arousal\* or activit\*)) or orgasm or libido or lubricat\* or impotence or dyspareunia or hypoactive sexual desire disorder or sexual aversion or coitus or coition)  
S63 (MH "Coitus")  
S62 (MH "Impotence")  
S61 (MH "Psychosexual Disorders+")  
S60 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 (MH "Alternative Therapies+")  
S58 (alpha adrenoceptor agonist\* or alpha adrenoceptor antagonist or midodrin or vasodilan or isoxsuprine or pentoxifylline or trental or delquamine or pseudoephedrine or desipramine or cyproheptadine or lignocaine)  
S57 (kegel exercise\* or lubricant\* or lubrication or pelvic floor biofeedback or yoga or cream\* or foam\* or jellies or muscle relaxation or vaginal exercise or physical exercise or olive oil or physiotherapy or weight lifting or physical training or pelvic floor muscle control or self

touch or penile rehabilitation or erectile rehabilitation or physiotherap\* or cavernous nerve regeneration, or sonic hedgehog or glial growth factor 2 or GGF2 or magnetic stimulation or cavernous nerve stimulation or low-intensity extracorporeal shockwave therapy or nerve stimulation)

S56 (dilation or dilators or eros therap\* or eros clitoral vacuum device or vaginal dilators or vibrator or vibrostimulation or mechanical stretching of tissues or cock ring or electroejaculation or magnetic stimulation or penile implantation or penile prosthesis or penile implant or penile arterialisation or penile vibratory stimulation or prosthesis implant\* or prolong ring or muse or venous constriction ring\* or venous litigation or vacuum device\* or vacuum constriction device\* or vacuum therapy or vacuum pump or penile injection)

S55 (arginine or acupuncture or DHEA or dehydroepiandrosterone or damiana or ginkgo or ginkgo bilboa or Hypericum or Panax or pausinystalia or Turnera or turner diffusa or yohimbine or l-arginine, or pycnogeno, or viacreme or viagel or sensual or ginseng or st john's wort or complimentary medicine\* or alternative medicine\* or alternative therap\* or alternative remed\* or complimentary therap\* or complimentary remed\*)

S54 "LY-117018"

S53 "DT56a"

S52 "MF-101"

S51 "ly-156758"

S50 "ly-139481"

S49 (femarelle or toremifene or serm or bazedoxifene)

S48 (evista or dimethylamine or novaldex or tomoxithen or soltamox or zitazonium or menerba)

S47 (clomiph or raloxifene or tamoxifen or toremife or clomid or clomifene or clomifert or serophene or raloxifene or keoxifene)

S46 "selective oestrogen receptor modulators"

S45 (oestradiol or Dienestrol or estriol or estetrol)

S44 (estrone or ethinyl estradiol or mestranol or quinestrol)

S43 (estradiol or oestrogenic steroids)

S42 (oestrogen or epimestrol)

S41 topical oestrogens

S40 estrogen cream

S39 vaginal oestrogen ring

S38 vaginal oestrogen ring

S37 estradiol ring

S36 estrogen replacement

S35 estrogen therapy

S34 estrogen ring

S33 conjugated estrogens

S32 (estriol or femprox)

S31 (MH "Apomorphine")

S30 (MH "Aromatase Inhibitors+")

S29 (Phosphodiesterase Type 5 or PDE5i or adcirca or cialis or levitra or Viagra or vardenafil or sildenafil or tadalafil)

S28 Vasodilator Agents

S27 (MH "Phosphodiesterase Inhibitors+")

S26 (psychological intervention\* or psycholog\* or behavior\* or behaviour\* or cognitive behav\* therapy or cognitive therap\* or psychotherap\* or counsel\* or sex therap\* or patient educat\* or behav\* therapy or CBT or couple therap\* or couple intervention or couple-based or intimacy enhancing or mindfulness or patient education or psychological techniques or psychosexual or psychotherapy or psycho-somatic or Rational emotive therap\* or restoring intimacy or relaxation or relaxation therap\* or relaxation training or psycho-social or Sensual, body image or sex-counsel\* or sexual communication or sexual rehabilitation or sexuality or self-esteem or self concept or stress or psycho-education or sexual life

reframing or coping skills or motivational counselling or anxiety management training or marital therap\* or group therap\* or focal therap\* or  
 psychodynamic therap\* or supportive therap\* or psychoanalyses or interpersonal therap\* or individual therap\* or problem solving or emotional  
 support or hypnosis or bibliotherap\* or sexual skills therap\* or systematic desensitization or hypnotherapy\* or radical emotive therap\*  
 or  
 psychodynamic or psychoeducational)  
 S25 (MH "Cognitive Therapy")  
 S24 (MH "Sexual Counseling")  
 S23 (MH "Counseling+")  
 S22 (MH "Psychotherapy+")  
 S21 (MH "Psychological Techniques+")  
 S20 (MH "Patient Education+")  
 S19 (MH "St. John's Wort")  
 S18 (MH "Ginseng")  
 S17 (MH "Ginkgo Biloba")  
 S16 (MH "Vaginal Creams, Foams and Jellies")  
 S15 (MH "Estrogens, Conjugated")  
 S14 (MH "Estriol")  
 S13 (vaginal dilator\* or arginine or android or methyl testosterone or testosterone cream or vaginal lubricant or vaginal estradiol ring  
 or  
 vaginal estradiol ring or vaginal estrogen ring or vaginal oestrogen ring or topical estrogen cream or vaginal cream or estrogen replacement  
 of  
 ERT or estrogen replacement or aromatase inhibitors)  
 S12 (MH "Aromatase Inhibitors+")  
 S11 (testosterone replacement or testosterone or venous constriction rings or vacuum device\* or vacuum erect\* or penile implant\* or  
 penile  
 arterialisation or venous ligation or prosthesis implant\* or vacuum constriction device or vacuum therapy\* or vibrat\* or vibrostimulation  
 or  
 electroejaculation or prolong ring\*)  
 S10 (MH "Prostheses and Implants+")  
 S9 (MH "Penile Prosthesis")  
 S8 (MH "Testosterone+")  
 S7 (alprostadil or androlog or Apomorphine or britaject or aromatase inhibitors or agonist of melancortin receptor or Adcirca or alpha  
 adrenoceptor agonist or alpha-2 adrenoceptor agonist or androlog or arginine or botox or botulinum toxin or bromocriptine or cialis  
 or  
 dopaminergic agents or caverject or clomipramine or cyproheptadine or clonidine or delquamine or edex or hormone therapy or  
 Isoxsuprine or  
 intracavernosal vasodilators or levitra or Lignocaine or l-arginine or lodenfil or Methitest or methyl testosterone or midodrin or mianserin  
 or  
 moclobemide or mirtazapine or mianserin or moclobemide or ortho-gynest or ovestin or papaverine or papaverine-phentolamine or  
 phentolamine or  
 parlodel or phentolamine or potassium channel openers or progestational agents or premarin or prempo or prostins or Prostaglandins  
 or  
 prostaglandin E1 or pentoxifylline or potassium channels or Phosphodiesterase Type 5 or PDE5i or penile suppository or reboxetine  
 or sildenafil  
 or tadalafil or tampovagan or topical or topical cream or vagifem or vaginal cream or vaginal lubricant or vaginal or viagra or vasomax  
 or Viagel  
 or vardenafil or vasodilator or virilon or vasoactive or staxyn or topical estrogen cream or trental or vasodilan or viridal or yohimbine or  
 android or androgen therapy or testosterone or testosterone cream or testosterone gel or tested)  
 S6 (MH "Apomorphine")  
 S5 (MH "Yohimbine")  
 S4 (MH "Yohimbine")

S3 (MH “Yohimbine”)  
S2 (MH “Phentolamine”)  
S1 (MH “Papaverine”)

## WHAT'S NEW

Last assessed as up-to-date: 8 September 2015.

Date	Event	Description
5 May 2015	New search has been performed	We have updated this review to include the results of a new search and added 'Risk of bias' tables
20 February 2015	New citation required and conclusions have changed	We have split the original review on interventions for sexual dysfunction following treatments for cancer into two reviews; the findings on interventions for sexual dysfunction for men following cancer treatments will now be reported in a separate review. We changed the inclusion criteria to only include interventions specifically developed to treat sexual dysfunction; this led to the exclusion of a study previously included because it was a preventative study. We have added 11 new trials and the conclusions have changed in the light of this new evidence

## HISTORY

Protocol first published: Issue 4, 2005

Review first published: Issue 4, 2007

Date	Event	Description
8 February 2011	Amended	Contact details updated.
24 September 2010	Amended	Contact details updated.
9 November 2009	Amended	Contact details updated.
13 May 2009	Amended	Contact details updated.
30 October 2008	Amended	Converted to new review format.

## CONTRIBUTIONS OF AUTHORS

In the 2015 update: BC carried out the searching and screening, reviewed documents, assessed quality and extracted data, analysed data and first drafted the review. LJ advised on methods, screened, checked data extraction and commented on the draft. Input was given to the protocol and final review. VV advised on statistics, checked the analysis and commented on the draft. AT contributed to the original idea, advised on methods and commented on the draft. MK contributed to the original idea, advised on methods and contributed to the draft. All authors read the final draft. BC is responsible for further updates.

## DECLARATIONS OF INTEREST

BC has no relevant conflicts of interest to declare. VV has no relevant conflicts of interest to declare. AT has no relevant conflicts of interest to declare. MK and LJ are grant holders on a ongoing funded NIHR pilot randomised trial of a stepped care intervention for women with sexual dysfunction after treatment for gynaecological cancer.

## SOURCES OF SUPPORT

### Internal sources

- Marie Curie Cancer Care supported the review authors BC, LJ and VV, UK.

### External sources

- No sources of support supplied

## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

This review is an update of an earlier review that included interventions for sexual dysfunction following treatments for cancer in both women and men ([Miles 2007](#)). This review only includes interventions for treating sexual dysfunction following treatments for cancer in women. All sections have been revised to reflect the patient group. The inclusion criteria for sexual dysfunction have been amended, to make it clear what is eligible. More detail is also provided on outcomes of interest.

## INDEX TERMS

### Medical Subject Headings (MeSH)

Administration, Intravaginal; Erectile Dysfunction [therapy]; Neoplasms [\*therapy]; Phosphodiesterase Inhibitors [therapeutic use]; Prostatic Neoplasms [therapy]; Psychotherapy; Randomized Controlled Trials as Topic; Sexual Dysfunction, Physiological [etiology; \*therapy]; Sexual Dysfunctions, Psychological [\*therapy]; Uterine Cervical Neoplasms [therapy]; Vacuum; Vaginal Creams, Foams, and Jellies [administration & dosage]

## **MeSH check words**

Adult; Female; Humans; Male