Effectiveness of physical exercise to decrease sexual dysfunction in adults with cardiovascular disease: a systematic review protocol

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Review question/objective

This systematic review aims to identify, appraise and synthesize the best available evidence on the effectiveness of physical exercise interventions on sexual function in adult patients with cardiovascular disease and sexual dysfunction. More specifically, the review question is:

1. What is the effectiveness of physical exercise intervention compared to usual care or a non-physical exercise intervention in reduction of sexual dysfunction in adult patients with cardiovascular disease and sexual dysfunction?

Background

Sexuality is an important part of people's physical and mental health.¹,² There is an increased prevalence of sexual dysfunction inpatients with cardiovascular disease³-⁵ due to physical and mental changes associated with cardiovascular disease, and also from side effects of medication.⁶,⁷ Sexual dysfunction has a negative impact on quality of life and well-being in persons with cardiovascular disease, and sexual dysfunction is associated with an increase in anxiety and depression.⁸-¹¹ There is some evidence to suggest that physical activity may potentially improve sexual function in individuals with chronic heart failure.¹²

Sexual dysfunction and its relation to cardiovascular disease

Male sexual dysfunction is often associated with erectile dysfunction, defined as the persistent inability to obtain or maintain an erection which enables satisfying sexual activity.¹³ Erectile dysfunction is associated
with age, but can also be triggered by both physical and psychogenic conditions and is often related to vascular disease such as diabetes, hypertension and heart disease. In addition, factors such as smoking and obesity are also associated with a higher incidence of erectile dysfunction. Sexual dysfunction in women is divided into physical and psychological causes including:

- lack of sexual interest or desire;
- inability to become physically or mentally aroused;
- inability to achieve orgasm;
- vaginismus which is a muscular reflex that prevents penetration; and
- dyspareunia, which is pain during intercourse.

The most common dysfunction in women is a lack of sexual interest or desire.

A number of medications which have favorable prognostic effect in patients with cardiovascular disease also increase the risk of developing sexual dysfunction in both men and women. Drugs used to treat erectile dysfunction may also adversely interact with drugs used to treat cardiovascular disease. As such, alternative treatments for sexual dysfunction are worth investigating.

**Instruments for measuring sexual dysfunction**

When investigating sexual dysfunction in clinical research, various instruments are used including self-reported questionnaires and interview-based questionnaires. Self-reported questionnaires are the most frequently used tool to measure sexual dysfunction in clinical research. A number of questionnaires for example the International Index of Erectile Function (IIEF) and the Brief Male Sexual Function Inventory for urology (BFSI) have been tested for validity and reliability which are considered to be fundamental characteristics of good measurement.

**Prevalence and incidence of sexual dysfunction**

Sexual dysfunction has been investigated in both men and women with established cardiovascular disease and found to be highly prevalent in this population. The prevalence of sexual dysfunction in both male and female patients with chronic heart failure has been studied in several populations and found to be between 75% and 89%.

The majority of research investigating sexual dysfunction, however, has been conducted on men and focuses on erectile dysfunction. In studies investigating males with ischemic heart disease, the prevalence of erectile dysfunction ranged from 39% to 74%. Data from the Massachusetts Male Aging Follow up Study (MMAS) including 1709 males showed that 35% of men aged 40 to 70 had moderate to complete erectile dysfunction and showed that age and cardiovascular disease were the most common variables associated with erectile dysfunction. Data from the Health Professionals Follow up Study (HPFS) including 31,742 males examining the impact of obesity, physical activity, alcohol use and smoking on the development of erectile dysfunction found that physical activity was significantly inversely associated with erectile function.
Men who expended physical activity equivalent to running nearly 1.5 hours per week or doing rigorous outdoor work for three hours per week had a 0.8 relative risk (95% CI 0.7–0.9) of erectile dysfunction compared to men performing limited physical activity.\(^5\)

Furthermore, emotional components such as depression and impaired quality of life, which are highly common in patients with cardiovascular disease, are also associated with sexual dysfunction,\(^27, 28\) and one study showed that men with untreated depression were nearly twice as likely to develop erectile dysfunction as those without depression.\(^29\)

**Current treatment strategies**

Despite the fact that several sets of international guidelines recommend health professionals address the topic of sexuality with cardiovascular patients,\(^30, 31\) this is rarely done in practice.\(^32, 33\) Health professionals express that it is difficult to talk about sexuality with patients and do not feel they have the required knowledge assume that patients are embarrassed or anxious.\(^33\)

In general there is no consensus or practice on how or where patients with cardiovascular disease and sexual dysfunction should be treated. Some patients are treated with phosphodiesterase-5 (PDE-5) inhibitors for example sildenafil and tadalafil, and a few are referred to sexological clinics. Treatment with PDE-5 inhibitors is effective for about 50% to 80% of those treated (36) but is directed primarily towards men and towards those with sexual dysfunction of a physical etiology. In cardiovascular patients that do not respond to the drug, where its use is contraindicated because of treatment with nitrates, and also in women, there is no consensus on what alternative treatment should be offered.

**Alternative treatment strategies**

There is evidence that suggests that physical activity may prevent and also improve erectile dysfunction in men who have not already developed cardiovascular disease.\(^5, 34\) Whether this is the case in patients with already established cardiovascular disease has yet to be determined, but it is plausible to believe and a number of studies pointing in that direction.\(^12, 35\) A trial studying the effect of four weeks of supervised physical training, including home exercise for patients, who have had a myocardial infarction, found that patients more often return to sexual activity if they have exercised.\(^35\) Another trial indicates that eight weeks of physical training show improvement in male heart failure patients' sexuality.\(^12\) This study measured three parameters: partner relationship, the quality of penile erection and personal wellness. There was a significant improvement in all parameters in relation to the control group. Conversely there is literature where physical interventions have shown no effect on heart patients' sexuality.\(^36\)

Physical exercise is generally perceived as health promotion and is a regular part of many rehabilitation programs for chronically ill patients. Whether a physical intervention targeting sexual dysfunction should be an alternative or adjunct to conventional treatment is an interesting thought. Due to these conflicting results there is a need for a detailed study of the literature in order to investigate the real effect of a physical intervention on sexual dysfunction in patients with cardiovascular disease.
An initial search in the databases CINAHL, JBI COnNECT+, PubMed and Cochrane Library shows that no systematic review on this topic exists, or is currently underway.

**Keywords**
Sexual dysfunction; Cardiovascular disease; Erectile dysfunction; Exercise

**Definitions**
For the purpose of this review, the following definitions will be used:

**Sexual dysfunction** in this study is defined as either reduced activity or reduced ability to perform sexual activity. Activity is defined as the frequency of sexual fulfillment. Ability is the person’s ability to achieve an erection or to achieve vaginal lubrication and reach an orgasm.\(^{13,15}\)

**Cardiovascular diseases** are defined as a group of disorders of the heart and blood vessels and include ischemic heart disease, heart failure, hypertension, congenital heart disease, rheumatic heart disease, deep vein thrombosis, pulmonary embolism, stroke or peripheral vascular disease.\(^{37}\)

**Inclusion criteria**

**Types of participants**
This review will consider studies that include male and female patients with cardiovascular disease over the age of 18 years, with sexual dysfunction measured by a validated and reliable instrument or by a decrease in the level of sexual activity.

**Types of intervention**
This review will consider studies that evaluate the effect of any physical exercise intervention. Physical interventions will include exercise training interventions such as, for example, aerobic exercise, bicycle exercise, running exercise or individually designed exercise interventions or a combination of these.

**Comparator**
It is anticipated that the effect of any physical exercise intervention will be compared with a control group that did not receive any physical exercise intervention, or received usual care.

**Types of outcomes**
The outcome measure will be change in sexual function measured by validated and reliable instruments such as self-reported questionnaires that cover male or female sexual dysfunction.

Additionally, outcome measures such as percentage improvement in sexual activity measured as number of activities before and after the intervention will be considered.

**Types of studies**
All randomized controlled trials (RCT) evaluating the efficacy of physical exercise intervention on sexual dysfunction in patients with cardiovascular disease will be considered. Other types of studies including non-randomized controlled trials, quasi-experimental and observational studies will be considered if RCTs are not located in the literature search. Due to authors’ nationality, studies published in English, Danish, Swedish
and Norwegian will be considered for inclusion in this review. Databases will be searched from their inception to the current date.

**Search strategy**

The search strategy aims to identify all relevant published and unpublished studies. A three step-search strategy will be conducted. An initial search of Medline, CINAHL and Embase will be undertaken followed by analysis of the text words contained in the title and abstract, and of index terms used to describe the article. The initial search terms were chosen in discussion with a research librarian in order to reach a maximum amount of articles.

A second search using all identified keywords and index terms will then be performed in all included databases. Thirdly, reference lists of all identified articles will be searched for additional studies and citation searches will be applied.

Databases to be included are: PubMed, CINAHL, Embase, Scopus, Swemed+, PsycINFO®. Health technology database, Cochrane Central Trials Register and Turning research into practice. The search for unpublished studies will include grey literature and unpublished material such as conference papers, research reports, and dissertations will be sourced wherever possible. The sources searched to locate unpublished studies include: ProQuest Dissertations and Theses, Index to Theses, Grey Literature Report and the websites of relevant associations such as the International Society for Sexual Medicine (ISSM), the European Society for Sexual Medicine (ESSM) and the Sexual Medicine Society of North America (SMSNA).

Initial keywords/ search terms to be used will be:

- Exercise or exercise test or exercise therapy or exercise/psychology or pelvic floor or training or physical activity

  and

- Cardiovascular disease or heart disease or hypertension or heart failure or congenital heart disease or rheumatic heart disease or deep vein thrombosis or pulmonary embolism or stroke or peripheral vascular disease

  and

- Sexual dysfunction/physiological or sexual dysfunction/psychological or erectile dysfunction or sexual function
Assessment of methodological quality

Quantitative papers selected for retrieval will be assessed by two independent reviewers for methodological validity prior to inclusion in the review using standardised critical appraisal instruments from the Joanna Briggs Institute Meta Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) (Appendix I). Any disagreements that arise between the reviewers will be resolved through discussion, or with a third reviewer.

Data extraction

Quantitative data will be extracted from papers included in the review using the standardised data extraction tool from JBI-MAStARI (Appendix II). The data extracted will include specific details about the interventions, populations, study methods and outcomes of significance to the review question and specific objectives.

Data synthesis

Quantitative data will, where possible, be pooled in statistical meta-analysis using JBI-MAStARI. All results will be subject to double data entry. Effect sizes expressed as weighted mean difference or odds ratio for continuous as well as categorical data and their 95% confidence intervals will be calculated for analysis. Heterogeneity will be assessed statistically using the standard Chi-square. Where statistical pooling is not possible, the findings will be presented in narrative form including tables and figures to aid in data presentation where appropriate.

Conflicts of interest

None identified.

Acknowledgements

None.
References


34. Derby CA, Mohr BA, Goldstein I, Feldman HA, Johannes CB, McKinlay JB. Modifiable risk factors and erectile dysfunction: can lifestyle changes modify risk?. *Urology* 2000; Aug 1;56(2):302-6.


Appendix I – JBI-MAStARI critical appraisal instrument

JBI Critical Appraisal Checklist for Randomised Control / Pseudo-randomised Trial

<table>
<thead>
<tr>
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<th>Yes</th>
<th>No</th>
<th>Unclear</th>
<th>Not Applicable</th>
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<tbody>
<tr>
<td>1. Was the assignment to treatment groups truly random?</td>
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<td>2. Were participants blinded to treatment allocation?</td>
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<td>3. Was allocation to treatment groups concealed from the allocator?</td>
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<td>4. Were the outcomes of people who withdrew described and included in the analysis?</td>
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<td>5. Were those assessing outcomes blind to the treatment allocation?</td>
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<td>6. Were the control and treatment groups comparable at entry?</td>
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<td>7. Were groups treated identically other than for the named interventions</td>
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<td>8. Were outcomes measured in the same way for all groups?</td>
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<td>9. Were outcomes measured in a reliable way?</td>
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<td>10. Was appropriate statistical analysis used?</td>
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Overall appraisal: Include □ Exclude □ Seek further info. □

Comments (including reason for exclusion)


Appendix II – JBI-MAStARI data extraction instruments
## JBI Data Extraction Form for Experimental / Observational Studies

### Reviewer ___________________________  Date ___________________________

### Author ___________________________  Year ___________________________

### Journal ___________________________  Record Number ___________________________

#### Study Method

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<th>Quasi-RCT</th>
<th>Longitudinal</th>
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<td>Observational</td>
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<td>Other</td>
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#### Participants

**Setting**

**Population**

#### Sample size

**Group A** __________  **Group B** __________

#### Interventions

**Intervention A**

**Intervention B**

### Authors Conclusions:

### Reviewers Conclusions:
Study results

### Dichotomous data

<table>
<thead>
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<th>Outcome</th>
<th>Intervention (X) number / total number</th>
<th>Intervention (Y) number / total number</th>
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### Continuous data

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<th>Outcome</th>
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<th>Intervention (Y) number / total number</th>
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