# SEXUAL MEDICINE

# Physical Activity to Improve Erectile Function: A Systematic Review of Intervention Studies

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## ABSTRACT

**Introduction:** The leading cause of erectile dysfunction (ED) is arterial dysfunction, with cardiovascular disease as the most common comorbidity. Therefore, ED is typically linked to a web of closely interrelated cardiovascular risk factors such as physical inactivity, obesity, hypertension, and metabolic syndrome. Physical activity (PA) has proved to be a protective factor against erectile problems, and it has been shown to improve erectile function for men affected by vascular ED. This systematic review estimated the levels of PA needed to decrease ED for men with physical inactivity, obesity, hypertension, metabolic syndrome, and/or manifest cardiovascular diseases.

Aim: To provide recommendations of levels of PA needed to decrease ED for men with physical inactivity, obesity, hypertension, metabolic syndrome, and/or cardiovascular diseases.

**Methods:** In accord with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, a systematic review was performed of research articles specifically investigating PA as a possible treatment of ED. The review included research on ED from physical inactivity, obesity, hypertension, metabolic syndrome, and/or cardiovascular diseases. All available studies from 2006 through 2016 were checked for the predetermined inclusion and exclusion criteria to analyze the levels of PA needed to decrease ED.

**Results:** 10 articles met the inclusion criteria, all suggesting various levels of PA needed to decrease ED for men with relevant risk factors for ED. The results of the review provided sufficient research evidence for conclusions regarding the levels of PA necessary to decrease ED.

**Conclusion:** Recommendations of PA to decrease ED should include supervised training consisting of 40 minutes of aerobic exercise of moderate to vigorous intensity 4 times per week. Overall, weekly exercise of 160 minutes for 6 months contributes to decreasing erectile problems in men with ED caused by physical inactivity, obesity, hypertension, metabolic syndrome, and/or cardiovascular diseases. **Gerbild H, Larsen CM, Graugaard C, Areskoug Josefsson K. Physical Activity to Improve Erectile Function: A Systematic Review of Intervention Studies. Sex Med 2018;X:XXX–XXX.** 

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#### INTRODUCTION

Sexuality is an important part of physical and mental health.<sup>1</sup> Erectile dysfunction (ED) is the most common sexual dysfunction in men,<sup>2–7</sup> and it is defined as the inability to attain or maintain a penile erection of sufficient quality to permit satisfactory sexual activity.<sup>3,5,7–12</sup> Whether aging, heterosexual couples continue to be sexually active seems, to a large extent, determined by the sexual function of the male partner.<sup>13</sup> ED has a negative impact on quality of life and well-being, and it is further associated with anxiety and depression.<sup>7,14</sup> In consequence, ED is increasingly recognized as a public health challenge,<sup>15</sup> although it is frequently neglected in clinical practice.<sup>12</sup>

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ED affects 1/3 of all men, and the prevalence of ED increases with age.<sup>2,5,6,16,17</sup> Epidemiologic studies have demonstrated that physical inactivity, obesity, hypertension (HTN), metabolic syndrome (MetS), atherosclerosis, and manifest cardiovascular diseases (CVDs) are risk factors for ED,<sup>2,4,6,7,14,15,17–22</sup> because the prevalence of ED is increased in these general population groups.<sup>4,17,23–26</sup> Furthermore, the prevalence of ED increases with the number of risk factors present.<sup>5</sup>

Penile erection is a hemodynamic process involving increased arterial inflow and restricted venous outflow<sup>3,6</sup>; therefore, ED can be an early warning sign of poor vascular function. Thus, ED has been coined "penile angina"<sup>24</sup> because it can be predictive of future CVD<sup>12</sup> and because CV risk factors and CVD frequently lead to ED.<sup>3,4,6,18,27–29</sup> Endothelial inflammation, which disrupts nitric oxide (NO) production, is a central determinant of vascular diseases including ED.<sup>4–6,29</sup> Neuronal and endothelial NO mediates the vascular component of sexual arousal by causing engorgement of the corpora cavernosa tissue and subsequent erection of the penis. It is well recognized that erectile blood flow is regulated by constriction or relaxation of the smooth muscle cells of penile arterial vessels.<sup>3,19,21,28</sup>

To diagnose and quantify the severity of ED, the International Index of Erectile Function (IIEF)<sup>9</sup> and the abridged 5-item version (IIEF-5)<sup>10</sup> are the most commonly used patientreported outcome measures.<sup>12</sup> The main therapeutic strategy in clinical health care is to compensate for ED by using phosphodiesterase type 5 inhibitor medications. However, phosphodiesterase type 5 inhibitors only temporarily restore erectile function, and they have been found to be ineffective in a significant proportion of men with ED.<sup>21</sup> Moreover, phosphodiesterase type 5 inhibitors do not appear to have any long-term impact on the underlying vascular dysfunction,<sup>21</sup> and they do not have any curative effect on endothelial or arterial dysfunctions or erectile problems.<sup>3,11,21,29-31</sup> Additional medical treatment possibilities are scarce, although the role of non-pharmacologic lifestyle interventions in lessening the burden of ED has increasingly been recognized.<sup>3,12,14,32,33</sup>

Physical activity (PA) can potentially decrease ED,<sup>7,21</sup> and PA has been identified as the lifestyle factor most strongly correlated with erectile function and the most important promoter of vascular health.<sup>19,28</sup> Thus, moderate- and vigorous-intensity PA is associated with normal erectile function and lower risk of ED.<sup>6,18–20,25,27,29,34,35</sup> The protective effect of PA also applies to men with obesity, HTN, and MetS.<sup>19,36–38</sup> PA causes improved endothelial function and NO production,<sup>6,24,28,29,39</sup> and PA has consistently been shown to advance erectile function.<sup>5,19,21,29,39</sup>

Hence, there is strong evidence that frequent PA significantly improves erectile function.<sup>3,11,12,31</sup> Previous reviews have assessed the association between PA and ED,<sup>3,5,12,14,33</sup> but the quality and quantity of PA needed (ie, modalities, duration, intensity, and frequency<sup>39</sup>) are insufficiently described,<sup>12,14</sup>

although knowledge of these is essential for clinical guidance of patients with ED. $^{4,12,19,28,40}$ 

To provide recommendations for PA-induced improvement of erectile function in men characterized by physical inactivity, obesity, HTN, MetS, and/or manifest CVD, we need in-depth knowledge of the specific modality, duration, intensity, and frequency of PA required to treat ED successfully. A systematic review of clinical intervention studies could provide this knowledge or indicate the need for future research in this field.

## AIM

The aim of the study was to provide recommendations of levels of PA needed to decrease ED for men with physical inactivity, obesity, HTN, MetS, and/or manifest CVDs.

#### **METHODS**

#### Search Strategy

A systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines based on PICO (patient, intervention, comparison, and outcome<sup>41</sup>) and the "Building Block Search Strategy."<sup>42</sup> The PubMed, Embase, and Cochrane databases were systematically searched to identify studies eligible for the review. The following search terms were used: *physical activity*, *physical endurance*, *physical conditioning*, *exercise*, *exercises*, *training*, *aerobic*, *fitness*, and *resistance training* in combination with *erectile dysfunction*, *erection dysfunction*, and *impotence*.

An initial screening of titles and abstracts was performed with Covidence<sup>43</sup> to identify potentially relevant studies, after which the full texts of the identified studies were examined. Reference lists of eligible articles were manually checked for additional relevant studies. The search strategy is provided in Appendix B. Only full-text studies written in English were included. The search was performed on January 25, 2017. The PRISMA checklist is provided in Appendix A.

#### Inclusion Criteria

The studies included in the review meet the following inclusion criteria:

- 1. Study design: randomized controlled trials (RCTs) or controlled trials (CTs)
- Study population: men at least 18 years old with arterial ED and men characterized by physical inactivity, obesity, HTN, MetS, and/or manifest CVD
- 3. Study intervention: any exercise protocol involving PA to decrease ED
- 4. Baseline and follow-up measurements: ED measured using the IIEF score (maximum = 30 points) or IIEF-5 score (maximum = 25 points)<sup>9,10,44</sup> and exercises measured by modality, duration, intensity, and frequency

# **Exclusion** Criteria

Exclusion criteria were studies including population groups with ED caused by neurologic disorders, hormone disorders, psychiatric disorders, cancers, diabetes mellitus, HIV, liver or kidney diseases, major surgery, radiotherapy, or side effects of medications.

# Data Collection and Analysis

2 researchers independently reviewed the full texts of all potentially relevant articles for eligibility and to ensure compliance with the inclusion criteria. Eventual disagreements were resolved through discussion to reach consensus.

Studies included in the analyses were registered with the name of the first author, year of publication, population group (physical inactivity, obesity, HTN, MetS, or CVD), country of origin, study design, age, sample size, numbers of participants in the intervention group, and numbers of participants in the control group.

In accord with the PRISMA guidelines, 2 researchers independently evaluated the risk of bias in the selected studies using the Risk of Bias Assessment Tool (ROBAT)<sup>45</sup> in Covidence.<sup>43</sup> Factors considered in the evaluation of bias included sequence generation (selection bias), allocation sequence concealment (selection bias), blinding (performance and detection bias), incomplete outcome data (attrition bias), and selective outcome reporting (reporting bias). The ROBAT was applied to RCTs and CTs with extra attention to selection bias for CTs as recommended by Higgins et al.<sup>45</sup> Any disagreements were discussed until an agreement was reached.

Studies reporting the IIEF or IIEF-5 score in the intervention and control groups at baseline and in follow-up were extracted as follows: (i) in relation to mean IIEF or IIEF-5 score at follow-up for the intervention and control groups; (ii) the score in relation to  $ED^{9,10}$ : "no ED," "mild ED," "mild to moderate ED," "moderate ED," or "severe ED"; and (iii) the improvement of erectile function analyzed by calculating the relative change. In illustrations of improvements of erectile function and of IIEF score at baseline and follow-up, all IIEF-5 measurements were scaled to the IIEF range ( $\times 30/25$ ) to compare the studies.

Data related to the intervention level and amount of the PA intervention were extracted for the following levels: (i) modality: aerobic, resistance training; (ii) intensity: mild, moderate, or vigorous; (iii) duration: length of each session; (iv) frequency: number of sessions per week; (v) weekly dose in minutes or hours; (vi) the period of the program in weeks, months, or years (follow-up duration); and (vii) delivery and location factors: supervised or unsupervised intervention and additional goals. In addition, dimensions of PA were explored in relation to the included risk groups.

# RESULTS

Initially, 1,950 records relevant to the research terms were found in the selected databases (Figure 1). Of these, 332 duplicates were removed, leaving 1,618 publications. After the 1st screening, 1,566 records were excluded because they did not meet the inclusion criteria. 52 potentially eligible studies were identified. After examining the full texts of these articles, 42 studies were excluded because the requested data were not reported, leading to the inclusion of 10 studies.<sup>46–55</sup>

#### Studies Included in Analysis

The eligible studies included 7 RCTs and 3 CTs. Studies were divided into 5 study groups: physical inactivity, obesity, HTN, MetS, and/or manifest CVD. For each study group, 1 to 4 studies were found (Table 1). Participants' ages ranged from 41 to 62 years (mean = 55 years). The studies were mostly performed in Europe.

#### Risk of Bias in Individual Studies

In general, the risk of bias for each study was estimated to be moderate (Table 2). The studies by Maio et al<sup>47</sup> and Khoo et al<sup>48</sup> had the lowest risk of bias. Nearly half (40%) the studies had a risk of selection bias, and blinding of investigators was unclear in most studies (90%). However, the most common risk of bias was lack of blinding of participants and staff (Figure 2).

#### Improvements in Erectile Function by PA

Erectile function was measured in 6 studies using the IIEF-5 and in 4 studies using the IIEF (Table 3).

In 4 of the 6 studies using the IIEF-5, mean erectile function was reported at baseline and follow-up for men in the intervention and control groups, respectively. In these 4 studies, the mean IIEF-5 score ranged from 11.0 to 18.1 at baseline for men in the intervention group and from 10.5 to 18.3 for men in the control group. At follow-up, the mean IIEF-5 score ranged from 14.4 to 20.7 for men in the intervention group and from 11.0 to 20.1 for men in the control group. 1 study did not report the IIEF-5 score for the control group but reported that the outcome IIEF-5 score did not differ from the baseline IIEF-5 score.53 Another study did not report the mean IIEF-5 score at followup for the intervention or control group.<sup>55</sup> However, the study reported that, at baseline, 34% and 36% of men in the intervention and control groups, respectively, had normal erectile function and that, at follow-up, 56% and 38% of men in the intervention and control groups, respectively, had normal erectile function.

In 3 of the 4 studies using the IIEF, mean erectile function score was reported at baseline and follow-up for the intervention and control groups (Table 3). At baseline, mean IIEF score ranged from 10.8 to 15.8 for men in the intervention group and from 8.1 to 15.5 for men in the control group. At follow-up, mean IIEF score ranged from 15.1 to 26.8 for men in the

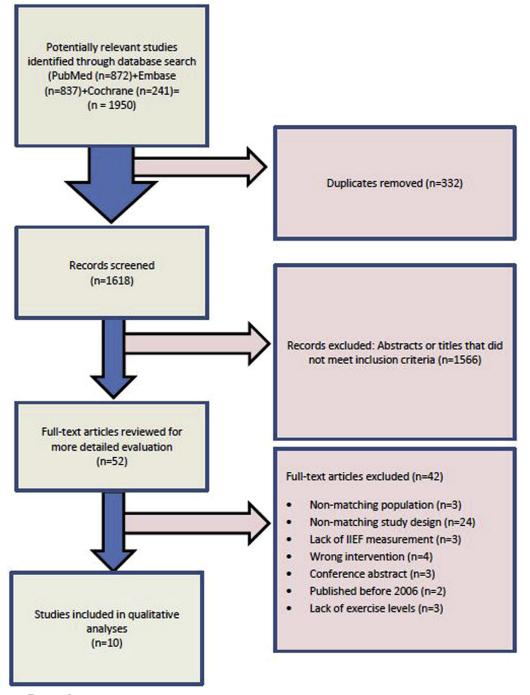


Figure 1. Flowchart of data collection process. IIEF = International Index of Erectile Function.

intervention group and from 8.9 to 24.7 for men in the control group. Begot et al<sup>54</sup> did not report the mean IIEF score at baseline or follow-up for the intervention or control group. However, they reported that, at baseline, 84% and 83% of men in the intervention and control groups, respectively, had ED. At follow-up, 12% and 93% of men in the intervention and control groups, respectively, had ED.

The ED score was "mild" at baseline for the intervention and control groups in 5 studies (Table 3). In contrast to the control

groups, the intervention groups in the 3 studies by Kalka et  $al^{51-53}$  achieved an improvement of erectile function, which remained in the category "mild." In Maio et  $al^{47}$  and Khoo et  $al^{48}$  the control groups also achieved an improvement in erectile function, but the improvement of the control groups was not as high as in the intervention groups.

In 3 studies, ED at baseline was "moderate" for the intervention and control groups (Table 3). Only in 1 study did the control group achieve an improvement in erectile function,

| Study               | Year | Population<br>group | Country of<br>origin | Study<br>design | Age (y), range<br>(mean ± SD) | Sample<br>size, N | Intervention<br>group, n | Control<br>group, n |
|---------------------|------|---------------------|----------------------|-----------------|-------------------------------|-------------------|--------------------------|---------------------|
| 1. Maio et al       | 2010 | PAI                 | Italy                | RCT             | 40–60 (50.2 ± 6.6)            | 60                | 30                       | 30                  |
| 2. La Vignera et al | 2011 | PAI                 | Italy                | СТ              | 48–62 (57.3 ± 0.5)            | 50                | 30                       | 20                  |
| 3. Esposito et al   | 2009 | Obesity             | USA                  | RCT             | 35–55 (45.5 ± 6.9)            | 209               | 104                      | 105                 |
| 4. Khoo et al       | 2013 | Obesity             | Singapore            | RCT             | 30–60 (41.7 ± 6.4)            | 90                | 36                       | 39                  |
| 5. Lamina et al     | 2009 | HTN                 | Ethiopia             | RCT             | 50–70 (62.1 ± 5.2)            | 43                | 22                       | 21                  |
| б. Maresca et al    | 2013 | MetS                | Italy                | RCT             | 40–70 (68.5 ± 3.2)            | 20                | 10                       | 10                  |
| 7. Kalka et al      | 2013 | CVD*                | Poland               | RCT             | (62.1 <u>+</u> 8.6)           | 138               | 103                      | 35                  |
| 8. Kalka et al      | 2015 | CVD*                | Poland               | СТ              | (62.1 ± 8.8)                  | 150               | 115                      | 35                  |
| 9. Kalka et al      | 2016 | CVD*                | Poland               | СТ              | (60.4 ± 9.3)                  | 124               | 89                       | 35                  |
| 10. Begot et al     | 2015 | CVD <sup>†</sup>    | Portugal             | RCT             | 40-70 (58 ± 10)               | 86                | 41                       | 45                  |
|                     |      |                     |                      |                 | Mean 55                       | Total<br>970      |                          |                     |

Table 1. Studies included in the analysis

CT = controlled trial; CVD = cardiovascular disease; HTN = hypertension; MetS = metabolic syndrome; PAI = physically inactive; RCT = randomized controlled trial.

\*Invasively treated for ischemic heart disease.

<sup>†</sup>Myocardial infarctions.

which was "mild to moderate" ED at follow-up. At follow-up, the intervention group in all 3 studies achieved an improvement in erectile function. In the study by La Vignera et al,<sup>46</sup> ED at follow-up was "mild to moderate," and in the studies by Lamina et al<sup>49</sup> and Maresca et al,<sup>50</sup> ED was "mild."

In all studies, the intervention group achieved an improvement in erectile function (Figure 3). According to the relative improvement of erectile function, the intervention groups achieved an improvement of 14% to 86%. In all studies, the intervention group achieved an improvement in erectile function (Figure 3), where all IIEF-5 measurements had been scaled to the IIEF range ( $\times$ 30/25).

According to the relative improvement in erectile function, the intervention groups achieved an improvement of 14% to 86% (Figure 4).

| The intervention group in the studies by Maresca et $al^{50}$ and        |
|--|
| Maio et al <sup>47</sup> achieved an improvement in erectile function of |
| 86% and 70%, respectively. For the control group, the change             |
| varied from a worsening of 5% to an improvement of 59%                   |
| relative to the applied IIEF and IIEF-5 scores (Table 3, Figure 4).      |

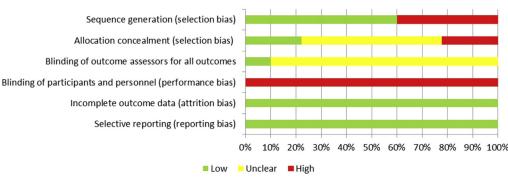
# Dimensions of PA in Relation to Included Risk Groups

Levels of PA in relation to the included risk groups (physical inactivity, obesity, HTN, MetS, and/or manifest CVD) are presented in Tables 3 and 4. In the 2 studies of physically inactive men without diagnoses other than ED,<sup>46,47</sup> the men received supervision in improving PA and exercised aerobically with moderate intensity for 150 and 180 minutes per week, respectively, over a period of 3 months. Men in the intervention

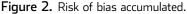
| Study                  | Study<br>design | Sequence<br>generation<br>(selection bias) | Allocation<br>concealment<br>(selection bias) | Blinding of<br>outcome<br>assessors<br>for all<br>outcomes | Blinding of<br>participants<br>and personnel<br>(performance<br>bias) | Incomplete<br>outcome<br>data<br>(attrition bias) | Selective<br>reporting<br>(reporting bias) |
|------------------------|-----------------|--|---|--|---|---|--|
| Khoo et al, 2013       | RCT             | Low  | Low   | Low  | High  | Low   | Low  |
| Maio et al, 2010       | RCT             | Low  | Low   | Unclear  | High  | Low   | Low  |
| Esposito et al, 2009   | RCT             | Low  | Unclear                                       | Unclear  | High  | Low   | Low  |
| Kalka et al, 2013      | RCT             | Low  | Unclear                                       | Unclear  | High  | Low   | Low  |
| Lamina et al, 2009     | RCT             | Low  | Unclear                                       | Unclear  | High  | Low   | Low  |
| Begot et al, 2015      | RCT             | Low  | Unclear                                       | Unclear  | High  | Low   | Low  |
| Maresca et al, 2013    | RCT             | High                                       | Unclear                                       | Unclear  | High  | Low   | Low  |
| Kalka et al, 2015      | CT              | High                                       | High  | Unclear  | High  | Low   | Low  |
| Kalka et al, 2016      | CT              | High                                       | High  | Unclear  | High  | Low   | Low  |
| La Vignera et al, 2011 | СТ              | High                                       | High  | Unclear  | High  | Low   | Low  |

CT = controlled trial; RCT = randomized controlled trial.

Table 2. Risk-of-bias summary



# **Risk of Bias**



groups achieved a relative improvement in erectile function of 70% and 50%, respectively.

In the 2 studies of sedentary obese men with ED, the PA was supervised and moderate, and the men exercised for 24 and 6 months, respectively. In the study by Esposito et al,<sup>55</sup> the amount of training for the intervention group was at least 150 minutes per week; in the study by Khoo et al,<sup>48</sup> the intervention and control groups trained for at least 90 to 150 and 200 to 300 minutes per week, respectively. In these 2 studies, weight loss was an additional goal. Because Esposito et al did not report the IIEF-5 score in the intervention and control groups at follow-up, the relative erectile improvement cannot be analyzed. In the study by Khoo et al, the intervention and control groups achieved relative improvements of erectile function of 14% and 10%, respectively.

The study by Lamina et al<sup>49</sup> was the only study of sedentary and hypertensive men with ED. The intervention group was involved in supervised, interval-based exercise of moderate to vigorous intensity. Over 8 weeks, the intervention group trained for 135 to 180 minutes per week, and a relative improvement in erectile function of 32% was achieved.

Men affected by ED and MetS participated in the study by Maresca et al.<sup>50</sup> The intervention group underwent a 2-month training program under the supervision of a cardiologist and a physiotherapist. The training program consisted of PA of moderate intensity for 120 minutes per week, and the intervention group achieved a relative improvement in erectile function of 86%.

The study by Begot et  $al^{54}$  and the 3 studies by Kalka et  $al^{51-53}$  represented studies of men with CVD and ED. In the study by Begot et al, the target group was treated for acute myocardial infarction, and in the studies by Kalka et al, the target groups were invasively treated for ischemic heart disease. In all 4 studies, the PA was aerobic. In the studies by Kalka et al, the intensity was moderate to vigorous, and only Begot et al reported an intensity of mild to moderate. In the study by Begot et al, the intervention group received supervision in improving PA and participants were physically active for 120 to 200 minutes per

week over a period of 1 month. Because Begot et al did not report the IIEF-5 score in the intervention and control groups at follow-up, the relative erectile improvement cannot be determined. In the studies conducted by Kalka et al, the training intervention groups performed aerobic PA for 135 minutes per week over a period of 6 months. In addition, a resistance training program was performed twice a week. In all 3 studies, the intervention group achieved a relative improvement in erectile function of 15%.

# Levels of PA for All Included Studies

Levels of the PA intervention programs in the included studies of men with physical inactivity, obesity, HTN, MetS, and/or manifest CVD in relation to IIEF score are presented in Table 3, and details of the levels of the PA programs are presented in Table 4. Levels of PA are described in more detail because of the variability of PA in the included studies.

#### Modalities of PA

In all 10 studies, the PA training modality for the intervention group was aerobic.

#### Intensity of PA

The intensity of the aerobic PA training program was moderate in all studies. In 5 of the studies, the moderate intensity was supplemented by intervals of vigorous intensity. Only 1 study had PA intensity of mild to moderate.<sup>52</sup> In 4 studies,<sup>51–53,55</sup> the moderate aerobic PA exercises were supplemented with resistance training programs.

#### Duration of Sessions of PA

In 9 of the studies, the duration of each PA session varied from 30 to 60 minutes. In 4 of these studies, the minimum duration was at least 40 minutes, which also was the mean duration of sessions for all 10 studies. Only 1 study accepted a minimum duration of 20 minutes for each PA session.<sup>47</sup>

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| Study (population<br>group)              | Intervention group   | Control group  | Study<br>follow-up | IIEF measure      | Mean IIEF* or IIEF-5 <sup>†</sup><br>score at baseline<br>(SD of range)                               | Mean IIEF* or IIEF-5 <sup>†</sup><br>score at follow-up<br>(SD of range)                                    | Relative<br>improvement<br>of mean IIEF |
|--|--|--|--------------------|-------------------|---|---|---|
| Maio et al, 2010 (PAI)                   | Aerobic, moderate<br>intensity, ≥3<br>h/wk + PDE5I;<br>mean PA = 3.4<br>h/wk   | PDE5I, mean<br>PA = 0.43 h/wk                                | 3 mo               | IIEF (max = 30)   | I = 15.8 (4.2), mild;<br>C = 15.5 (4.2), mild   | l = 26.8 (2.2), no;<br>C = 24.7 (2.6), mild   | I = 70%; C = 59%                        |
| La Vignera et al, 2011<br>(PAI)          | Aerobic, mild to<br>moderate intensity<br>(40–60% of<br>HR <sub>max</sub> ), 150 min/wk                                    | Mediterranean diet   | 3 mo               | IIEF-5 (max = 25) | I = 11.0 (1.0),<br>moderate; C = 10.5<br>(0.7), moderate  | I = 16.5 (1.0), mild to<br>moderate; C = 11.0<br>(0.7), moderate  | I = 50%; C = 5%                         |
| Esposito et al, 2009<br>(obesity)        | Aerobic, moderate<br>intensity, ≥5<br>sessions of 30<br>min/wk +<br>resistance training                                    | Guidance on<br>increasing level of<br>PA and healthy<br>food | 2γ                 | IIEF-5 (max = 25) | I = 17.6 (3.8), mild;<br>C = 17.8 (3.7), mild;<br>$I = 34\%^{\texttt{$}};$<br>$C = 36\%^{\texttt{$}}$ | I = mean IIEF-5 score<br>NR; C = mean<br>IIEF-5 score NR;<br>I = 56% <sup>¶</sup> ;<br>C = 38% <sup>¶</sup> | NA                                      |
| Khoo et al, 2013<br>(obesity)            | Aerobic, moderate<br>intensity (55–70%<br>HR <sub>max</sub> ), 5–7<br>sessions of 30–60<br>min, total = 200<br>–300 min/wk | Moderate-intensity<br>aerobic PA 90—150<br>min/wk + diet     | 24 wk              | IIEF-5 (max = 25) | I = 18.1 (0.9), mild;<br>C = 18.3 (0.9), mild   | l = 20.7 (0.7), mild;<br>C = 20.1 (0.8), mild   | I = 14%; C = 10%                        |
| Lamina et al, 2009<br>(HTN)              | Aerobic, moderate to<br>vigorous intensity<br>(60–79% HR <sub>max</sub> ),<br>3 sessions of<br>45–60 min/wk                | Advised not to<br>increase PA                                | 8 wk               | IIEF (max = 30)   | I = 11.5 (5.3),<br>moderate; C =: 8.1<br>(4.0), moderate  | l = 15.1 (4.9), mild; C =<br>8.9 (3.9), moderate  | I = 32%; C = 10%                        |
| Maresca et al, 2013<br>(MetS)            | Aerobic, moderate<br>intensity (65%<br>VO <sub>2</sub> ), 3 sessions of<br>40 min/wk +<br>tadalafil                        | Informed about<br>usefulness of PA +<br>tadalafil            | 2 mo               | IIEF (max = 30)   | I = 10.8 (2.0),<br>moderate; C = 11.2<br>(2.1), moderate  | I = 20.1 (2.3), mild;<br>C = 14.2 (2.2), mild<br>to moderate  | I = 86%; C = 27%                        |
| Kalka et al, 2013<br>(CVD <sup>‡</sup> ) | Aerobic, moderate to<br>vigorous intensity,<br>3 sessions of 45<br>min/wk +<br>resistance exercises                        | Received general<br>health advice +<br>health advice         | б то               | IIEF-5 (max = 25) | I = 12.5 (5.9), mild;<br>C = 12.3 (5.8), mild   | l = 14.4 (6.8), mild;<br>C = 12.4 (5.7), mild   | I = 15%; C = 1%                         |

(continued)

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| Study (population<br>group)               | Intervention group  | Control group   | Study<br>follow-up | IIEF measure      | Mean IIEF* or IIEF-5 <sup>†</sup><br>score at baseline<br>(SD of range)         | Mean IIEF* or IIEF-5 <sup>†</sup><br>score at follow-up<br>(SD of range)        | Relative<br>improvement<br>of mean IIEF |
|---|---|---|--------------------|-------------------|---|---|---|
| Kalka et al, 2015<br>(CVD <sup>†</sup> )  | Aerobic, moderate to<br>vigorous intensity,<br>3 sessions of 45<br>min/wk + peak +<br>resistance training | Individual<br>recommendation<br>about active<br>lifestyle | б то               | IIEF-5 (max = 25) | l = 12.5 (6.0), mild;<br>C = NA   | I = 14.4 (6.9), mild;<br>C = NA (does not<br>differ from C at<br>baseline)      | I = 15%; C = 0%                         |
| Kalka et al, 2016<br>(CVD <sup>§</sup> )  | Aerobic, moderate to<br>vigorous<br>intensity +<br>resistance training                                    | Recommendation<br>about active<br>lifestyle               | б то               | IIEF-5 (max = 25) | I = 13.2 (5.7), mild;<br>C = $13.2^{+}$ , mild                                  | l = 15.4 (6.5), mild;<br>C = 12.4 (5.7), mild                                   | I = 15%; C = -5%                        |
| Begot et al, 2015<br>(CVD <sup>II</sup> ) | Aerobic, mild to<br>moderate intensity,<br>4 sessions of<br>30–50 min/wk                                  | Usual care, guidance<br>on continuing PA                  | 1 то               | IIEF (max = 30)   | I = mean IIEF score<br>NR; C = mean IIEF<br>score NR; I = 84%<br>ED; C = 83% ED | I = mean IIEF score<br>NR; C = mean IIEF<br>score NR; I = 12%<br>ED; C = 93% ED | NA                                      |

C = control; CVD = cardiovascular disease; ED = erectile dysfunction; HTN = hypertension; HR<sub>max</sub> = maximum heart rate; I = intervention; IIEF = International Index of Erectile Function; IIEF-5 = 5-item International Index of Erectile Function; max = maximum score; MetS = metabolic syndrome; NA = not available; NR = not reported; PA = physical activity; PAI = physically inactive; PDE5I = phosphodiesterase type 5 inhibitor; VO<sub>2</sub> = oxygen consumption per unit time.

\*Score 26-30 = no ED; score 17-25 = mild ED; score 11-16 = moderate ED; score  $\le 10 =$  severe ED.

<sup>†</sup>Score 22-25 = no ED; score 17-21 = mild ED; score 12-16 = mild to moderate ED; score 8-11 = moderate ED; score 5-7 = severe ED.

<sup>‡</sup>Implicitly reported in the article.

<sup>s</sup>Invasively treated for ischemic heart disease.

<sup>II</sup>Myocardial infarctions.

<sup>¶</sup>Percentage with normal erectile function.

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# ARTICLE IN PRESS

#### Physical Activity to Improve Erectile Function

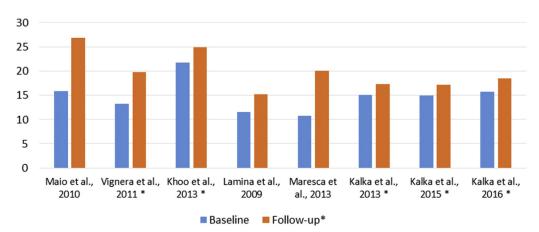




Figure 3. IIEF scores at baseline and follow-up for intervention. IIEF = International Index of Erectile Function.

#### Frequency of PA

The weekly frequency of the PA sessions varied from 3 to 7 (mean frequency = 4). In 5 studies, the standard frequency was 3 weekly PA sessions. Only 1 study had a PA frequency of up to 7 sessions per week.<sup>48</sup>

#### Weekly Dose of PA

Doses of PA varied from 120 to 300 minutes per week (mean weekly dose = 157 minutes, or  $\sim 2$  hours 30 minutes).

# Training Period of PA

The PA programs varied from 1 to 24 months (mean training period =  $\sim 6$  months). Thus, the study by Maio et al<sup>47</sup> had the longest follow-up duration of 2 years, and the study by Begot et al<sup>54</sup> had the shortest follow-up duration of 1 month.

# Delivery of PA and Additional Interventions and Goals of the Included Studies

In almost all programs, individual supervision of participants was included. In addition, the programs involving obesity

# focused on dietary counseling, aiming at lower energy intake and decreased body weight (Tables 3 and 4).

The control groups varied between not increasing their PA level and having a high level of PA.

# DISCUSSION

Several reviews have demonstrated that PA protects against arterial ED.<sup>7,18,19,28</sup> Previous research regarding the decrease of ED has focused mainly on the statistically significant effects of PA<sup>3,12</sup> and the underlying physiologic mechanisms,<sup>5</sup> concluding that PA is an effective, non-invasive, and non-pharmacologic intervention against ED in men. However, the levels of PA needed to treat ED remain uncertain.

The aim of this review was to enhance the understanding of the levels of PA (ie, modality, intensity, duration of sessions, frequency, weekly dose, and training period) needed to improve erectile function for men with physical inactivity, obesity, HTN, MetS, and/or manifest CVD. Among the included studies, there was a wide variation of the dose of PA and training periods,

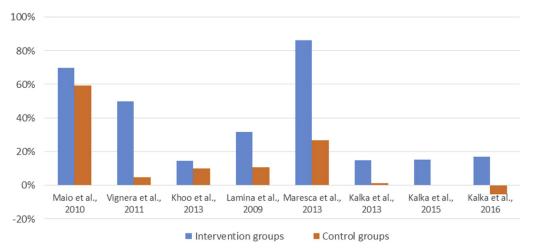


Figure 4. Relative improvements in International Index of Erectile Function scores.

| Table 4. Levels of physical activity for the intervention gro | up in relation to relative improvements of erectile function |
|---|--|
|---|--|

| Study (population<br>group)       | PA modality (aerobic,<br>anaerobic, weight-<br>resistance training)                      | Intensity (mild,<br>moderate, vigorous)                   | Duration/<br>session | Sessions/<br>wk | PA dose/wk  | Training<br>period | Delivery and location<br>factors   | Relative<br>improvement<br>of IIEF or<br>IIEF-5 score |
|-----------------------------------|--|---|----------------------|-----------------|-------------|--------------------|--|---|
| Maio et al, 2010 (PAI)            | Regular aerobic<br>PA (running,<br>cycling, jogging,<br>swimming); mean<br>PA = 3.4 h/wk | Moderate (55–64%<br>of HR <sub>max</sub> )                | 20—60 min            | 3–5             | ≥180 min    | 3 mo               | Individual supervised<br>training program;<br>education about PA<br>as treatment of<br>ED + PDE5I        | 70%   |
| La Vignera et al,<br>2009 (PAI)   | Aerobic  | Mild to moderate (40<br>—60% of HR <sub>max</sub> )       | 30 min               | 5               | 150 min     | 3 mo               | +Mediterranean diet  | 50%   |
| Esposito et al, 2009<br>(obesity) | Aerobic (jogging,<br>swimming, skiing)   | Moderate  | ≥30 min              | 5               | ≥150 min    | 2 у                | Individual guidance<br>on increasing PA;<br>decrease body<br>weight (≥5%);<br>improve quality<br>of diet | NA  |
|                                   | Progressive<br>circuit-type<br>resistance<br>training                                    | Moderate to vigorous                                      | NA                   |                 |             |                    |  |   |
| Khoo et al, 2013<br>(obesity)     | Aerobic<br>(brisk walking,<br>jogging, cycling,<br>swimming)                             | Moderate (55–70%<br>of HR <sub>max</sub> )                | 30—60 min            | 5–7             | 200—300 min | 24 wk              | Supervised exercises;<br>decrease daily<br>energy intake   | 14%   |
| Lamina et al, 2009<br>(HTN)       | Aerobic, on bicycle<br>ergometer   | Moderate to vigorous<br>(60–79% of<br>HR <sub>max</sub> ) | 45–60 min            | 3               | 135—180 min | 8 wk               | Supervised training +<br>stopped all forms<br>of medication  | 32%   |
| Maresca et al, 2013<br>(MetS)     | Aerobic, on bicycle<br>ergometer   | Moderate<br>(65% VO <sub>2peak</sub> )                    | 40 min               | 3               | 120 min     | 2 mo               | Supervised by<br>physiotherapist +<br>tadalafil  | 86%   |
| Kalka et al, 2013<br>(CVD*)       | Aerobic progressive<br>interval endurance<br>training on<br>ergometer bicycle            | Moderate to vigorous                                      | 45 min               | 3               | 135 min     | б то               | Supervised training  | 15%   |
|                                   | General fitness,<br>8—10 resistance<br>training exercises,<br>12—15 reps each            | Maximum level 13 of<br>15 (Borg scale)                    | NA                   |                 |             |                    |  |   |

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| Table 4. Continued                       |   |   |                      |                 |             |                    |                                       |   |
|--|---|---|----------------------|-----------------|-------------|--------------------|---------------------------------------|---|
| Study (population<br>group)              | PA modality (aerobic,<br>anaerobic, weight-<br>resistance training)           | Intensity (mild,<br>moderate, vigorous)                   | Duration/<br>session | Sessions/<br>wk | PA dose/wk  | Training<br>period | Delivery and location<br>factors      | Relative<br>improvement<br>of IIEF or<br>IIEF-5 score |
| Kalka et al, 2015<br>(CVD*)              | Aerobic progressive<br>interval endurance<br>training on<br>ergometer bicycle | Moderate to vigorous<br>(40–70% of<br>HR <sub>max</sub> ) | 45 min               | 3               | 135 min     | 6 то               | Supervised training                   | 15%   |
|  | Gym exercises, 8—10<br>resistance training<br>exercises, 12—15<br>reps each   | Maximum level 13 of<br>15 (Borg scale)                    | NA                   | 2               |             |                    |                                       |   |
| Kalka et al, 2016<br>(CVD*)              | Aerobic progressive<br>interval endurance<br>training on<br>ergometer bicycle | Moderate to vigorous<br>(40—70% of<br>HR <sub>max</sub> ) | NA                   | 3               | _           | 6 то               | Supervised training                   | 15%   |
|  | Gym exercises, 8—10<br>resistance training<br>exercises, 12—15<br>reps each   | Maxima level 13 of 15<br>(Borg scale)                     | NA                   | 2               |             |                    |                                       |   |
| Begot et al, 2015<br>(CVD <sup>†</sup> ) | Progressive aerobic<br>walking program  | Mild to moderate  | 30—50 min            | 4               | 120—200 min | 1 mo               | Telephone supervised<br>outdoor, home | NA  |

based

Physical Activity to Improve Erectile Function

 $CVD = cardiovascular disease; HR_{max} = maximum heart rate; HTN = hypertension; IIEF = International Index of Erectile Function; IIEF-5 = 5-item International Index of Erectile Function; NA = not available; PA = physical activity; PAI, physically inactive; PDE5I = phosphodiesterase type 5 inhibitor; reps = repetitions; VO<sub>2peak</sub> =peak oxygen consumption.$ 

\*Invasively treated for ischemic heart disease.

<sup>†</sup>Myocardial infarctions.

ranging from 1 month to 2 years. This variability could have affected the results in this review.

Our results indicate that continuous and interval-based aerobic training improve erectile function for men with arterial ED. PA with moderate intensity and intervals of vigorous intensity seems to be one of the key elements in determining the efficiency of the applied physical exercise, which is in concordance with findings in the systematic review and meta-analysis of Silva et al<sup>12</sup> and Lamina et al.<sup>3</sup> Our review also showed that resistance training can complement aerobic exercises.

Regarding the weekly dose of aerobic PA required to treat ED successfully, our study indicated a volume of 4 sessions of moderate- to high-intensity training lasting 40 minutes per session, corresponding to a weekly dose of 160 minutes. This result is in line with the review by Hehemann and Kashanian,<sup>14</sup> which recommended the same dose based on guidelines for decreasing HTN. However, Khoo et al<sup>48</sup> indicated that weekly exercise of 200 to 300 minutes of moderate-intensity training results in a much greater improvement of IIEF score in obese men than 90 to 150 minutes of weekly training. However, because the study group included obese men, the findings might not be applicable to normal-weight men with arterial ED. According to the World Health Organization (WHO),<sup>56</sup> healthy adults should exercise for at least 150 minutes of moderate-intensity aerobic PA or 75 minutes of vigorous-intensity PA per week. This constitutes slightly lower levels of PA than needed to decrease ED according to the results of this review. The recommendations by the WHO to gain additional health effects are to increase the intensity and number of weekly minutes. Thus, by following the general advice regarding PA, ED should be decreased.

Other important non-pharmacologic interventions such as diet, weight loss, pelvic floor muscle training, and smoking cessation also improve erectile function for men with arterial ED.<sup>6,20,22,29,32</sup> Further research is needed regarding combined lifestyle interventions including PA.

The results of this review point to a need for further research regarding the effect of PA on arterial ED for men with physical inactivity, obesity, HTN, MetS, and/or manifest CVDs and research regarding the effect of PA with longer periods of followup, resistance training in addition to aerobic training, and the effects of the WHO recommendations on ED. Further, a review of improvements of specific physiologic markers of physical fitness correlated to the decrease of ED is warranted, because this could increase our understanding of the positive effect of PA on ED.

#### **Recommendations and Clinical Implications**

This review suggests that PA is an effective intervention to treat arterial ED. PA is rarely used in clinical practice to improve erectile function,<sup>12</sup> which represents a paradox and is far from optimal considering the effect of PA on arterial ED. The results of this review support supervised, aerobic PA with moderate to vigorous intensity as a rational recommendation for men with

ED, indicating a potential key role for physiotherapists in the treatment of arterial ED. Physiotherapists are specialized in guiding and supervising PA as a tool of health promotion, aiming to improve the patient's level of PA within the scope of the individual patient's preferences and possibilities.<sup>57</sup> To treat men with ED optimally, physiotherapists need basic qualifications regarding sexual dysfunctions, sexual health, and sexual rehabilitation<sup>58</sup> and knowledge and competence in using PA as an intervention to treat ED. Therefore, this review emphasizes the need for evidence-based guidelines for clinical practice that support PA-centered improvement of erectile function. By better understanding the complex web of factors influencing erectile function and overall vascular health, physiotherapists and other health care providers can help their patients prevent vascular diseases and thereby improve their sexual health. This offers an immediate motivation for men to change their lifestyle habits to improve their CV health.

This review indicates that 40 minutes of supervised, aerobic PA of moderate intensity 4 times weekly for 6 months improves erectile function for men with arterial ED caused by physical inactivity, obesity, HTN, MetS, and/or manifest CVD. PA at moderate intensity can be successfully supplemented with PA at intervals of vigorous intensity. The aerobic modality can be further combined with resistance training. Because of the small number of studies and their intervention variability, additional research to strengthen the evidence is essential.

#### Methodologic Aspects of the Articles Reviewed

The number of participants in the included studies was relatively small, with the smallest including only 10 participants.

Analysis of the risk of bias showed a high risk of performance bias, which was expected because blinding of participants and personnel, for obvious reasons, is not possible in a supervised exercise intervention. All 3 CTs had high risk of selection bias, which negatively affects the external validity of the studies. This was expected because CTs are non-randomized. However, if the 3 CTs had been excluded from this review, the smaller number of studies would have led to a decreased insight into the variation of PA needed to treat ED.

#### Methodologic Aspects of Our Review

The strength of this review is the systematic literature search aimed at including all published RCTs and CTs regarding PA targeting ED. An additional strength is its strict adherence to the PRISMA guidelines. Moreover, all included trials used comparable measurements to evaluate changes of patient-reported erectile function (IIEF or IIEF-5). Further, the interventions in all studies were aerobic PA of moderate intensity.

A limitation of the review is that the effect of various PA levels is not directly comparable across the included studies because of variation in population groups, inclusion and exclusion criteria, and types of intervention. The limited number of eligible studies

is an obvious limitation, and a larger number of studies would have added strength to the results.

# CONCLUSION

Recommendations considering PA to decrease arterial ED should include supervised training consisting of aerobic exercise of moderate to vigorous intensity 4 times per week for 40 minutes. An overall weekly exercise dose of 160 minutes for 6 months contributes to a decrease of ED for men with arterial ED due to physical inactivity, obesity, HTN, MetS, and/or manifest CVD.

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