Review article

# Non-pharmacologic interventions for the prevention of erectile dysfunction

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Abstract

**Aim:** To describe the safety and effectiveness of non-pharmacologic preventive interventions for erectile dysfunction.

**Methods:** A systematic search was carried out electronically on the Medline (PubMed) and Embase databases for studies published from 2002 to 2018

**Results:** The studies showed that preventive interventions directed at risk factors, such as aerobic physical activity, the Mediterranean diet, and sex therapy, contributed to preventing the development of erectile dysfunction.

**Conclusions:** The findings suggest that carrying out the recommendations of increased physical activity and an adequate diet rich in fruits, vegetables, and dried fruits, from an early age, can help prevent the appearance of sexual dysfunction at more advanced ages.

**Keywords:** Sexual dysfunction, Mediterranean diet, physical activity, sex therapy, erectile dysfunction.

**Reference:** Herrera-Muñoz J.A., Preciado-Estrella D.A., Villalpando-Gómez L., Santana-Ríos Z., Martínez-Cervera P.F., Scavuzzo A., Jiménez-Ríos. Clinical characteristics and functional and oncologic results of patients with kidney tumors that underwent partial nephrectomy. Rev. Mex. Urol. 2019;79(1):pp. 1-17

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**Received:** July 21, 2018
**Accepted:** December 12, 2018

## Introduction

Erectile dysfunction (ED) is an important cause of reduced quality of life in men. Not only does it affect the individual, but it also has a negative impact at the family, psychologic, and sexual levels. ED is defined as the persistent inability to have and maintain an erection that enables satisfactory sexual performance.[1-2]

It is a common problem affecting more than 150 million men worldwide, and that figure is expected to double by 2025. ED was reported as the second most frequent sexual dysfunction in a group of Asian subjects, with an age-related increase in prevalence, and it was the most common disorder in advanced-age adults.[3]

Different studies have identified an association between ED and the risk factors of unhealthy lifestyle, smoking, a sedentary lifestyle, and inadequate diet. Those analyses support the management of lifestyle changes based on improving diet, performing physical activity regularly, reducing stress, and stopping smoking, given that all those factors share a similar pathophysiologic mechanism.[4]

Diabetes mellitus (DM), dyslipidemia, high blood pressure, heart disease, and depression have also been related to the development of ED.[5]

The World Health Organization (WHO) defines sexual health as a state of physical, emotional, mental, and social wellbeing related to sexuality that requires medical and public health interventions. Erectile dysfunction has been shown to cause physical, social, and emotional problems that lead to the development of frustration, anxiety disorder, and depression. Its negative impact on the couple can result in separation.[6]

Medical interventions include management with phosphodiesterase 5 inhibitors, intracavernosal injections, and the use of vacuum penile pump devices, among others. Studies have reported treatment abandonment due to inefficient results or interpersonal problems. Psychologic problems and unstable matrimonial or sexual relations appear to be involved in the development of ED, reflecting the importance of correctly identifying risk factors and creating a multidisciplinary approach to improve management results.[7] The focus of the present article is on non-pharmacologic interventions, as opposed to pharmacologic ones.

The aim of our review was to describe the safety and effectiveness of non-pharmacologic interventions for the prevention of erectile dysfunction.

## Methodology

A narrative review was conducted on non-pharmacologic interventions related to the Mediterranean diet, exercise, and sex therapy for the prevention of erectile dysfunction. Studies were chosen that were published from 2002 to 2018 and available in the Medline (PubMed) and Embase databases, utilizing the following keywords: sexual dysfunction, Mediterranean diet, physical activity, sex therapy, erectile dysfunction. Articles that were not in English or Spanish were excluded.

## Epidemiology

The Massachusetts Male Aging Study (MMAS) and the European Male Aging Study (EMAS) showed a 52% prevalence of erectile dysfunction in men 40-70 years of age.[8]

In addition, the South American DENSA study evaluated the prevalence of erectile dysfunction in Colombia, Ecuador, and Venezuela, in men above 40 years of age, and found a general age-adjusted prevalence rate for any grade of erectile dysfunction of 53.4%, in Colombia of 52.8%, in Ecuador of 52.1%, and in Venezuela of 55.2%. Nearly half of the study population presented with an alteration.[9]

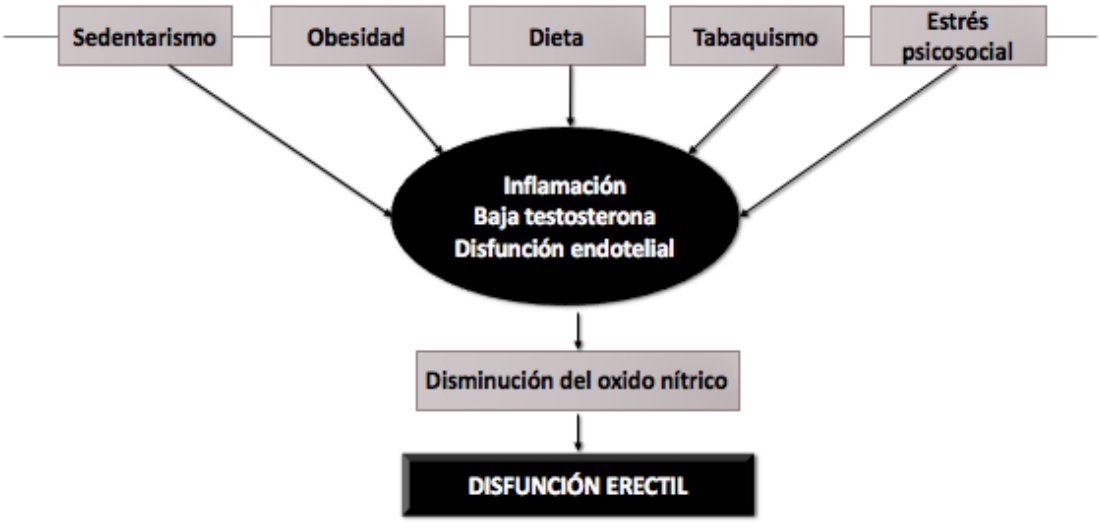
## Etiology

Different causes are known to alter erection and they are classified as organic (vasculogenic, neurogenic, anatomic, or endocrinologic) and psychogenic (generalized and situational).[10]

In a Turkish study whose aim was to determine the pathophysiology of factors causing erectile dysfunction, such as the risk factors in different age groups, the authors found that the primary etiology was psychogenic in 85.2% of men under 40 years of age, compared with 14.8% that presented with an organic cause of the pathology (arteriogenic, venogenic, neurogenic, endocrinologic, drug-induced, or mixed). In the comparison with the group of men above 40 years of age, the prevalence of psychogenic ED was 40.7% and the prevalence of organic ED was 59.3%.[11]

Risk factors reported to be associated with erectile dysfunction are age, smoking, dyslipidemia, high blood pressure, diabetes mellitus, metabolic syndrome, depression, and certain medications.[10] Table 1 describes those factors and the mechanisms of action through which they are related to the development of erectile dysfunction. Other lifestyle factors, such as obesity, physical activity, diet, and smoking, have been recognized as triggers for the onset and progression of the pathology (see figure 1).[12]

**Figure 1. Risk factors related to the development of erectile dysfunction. Image adapted and modified from Maiorino et al.[13]**



Endothelial dysfunction is considered the pathophysiologic mechanism that the different risk factors have in common for the development of erectile dysfunction. Therefore, it is important to recognize that the sequelae of the disease are far-reaching, affecting the physical, psychosocial, and psychologic spheres of the patient, as well as the relationship of the couple.[12]

**Table 1 Risk factors and the mechanisms through which they are associated with erectile dysfunction.**

| *RISK FACTOR* | *MECHANISM* |
|---|---|
| Metabolic syndrome | Endothelial dysfunction and low nitric oxide synthase regulation. |
| Benign prostatic hyperplasia | Probable decrease of nitric oxide in the penis, bladder, and prostate. |
| Cardiovascular disease | Endothelial dysfunction in the vasculature of the penis. |
| Smoking | Endothelial dysfunction associated with atherosclerosis. |
| Depression, social problems, or stressful marriage | Unknown. |
| Diabetes mellitus | Endothelial dysfunction, vasculopathy, and neuropathy. |
| Hypogonadism | Low androgen levels that lead to increased apoptosis of endothelial cells and smooth muscle cells. |

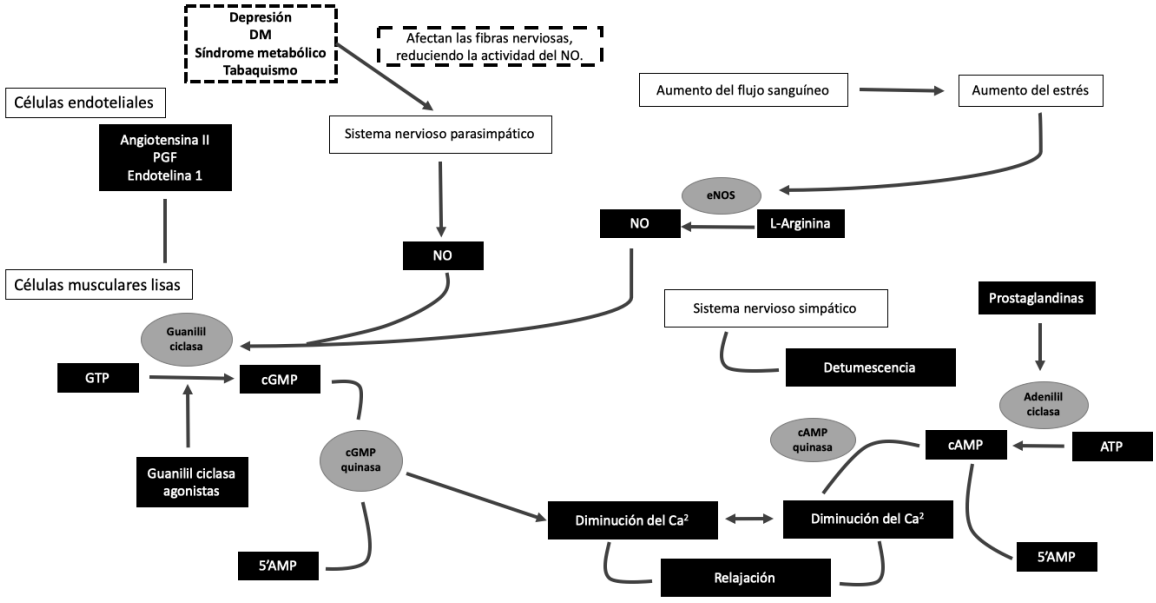
In 2009, the International Consultation on Sexual Medicine identified basic aspects for the management of sexual dysfunction in men and women, considering sexual health as an integral part of overall health. In addition, sexual dysfunctions were stated to have a great negative impact on quality of life and therefore they included lifestyle changes as a sexual function intervention in their treatment algorithm.[15]

Lifestyles have been identified as central factors in nitric oxide (NO) production, suggesting that its adequate control can have positive effects on preventing the development of sexual dysfunction. According to that information and the proposals from the international consultation, risk factor intervention would, in turn, be a preventive intervention for erectile dysfunction.[13]

## Pathophysiology

Under normal conditions, erections are the result of a combination of neurotransmitter and vascular smooth muscle responses that produce an increase of the arterial flow to the cavernous sinusoids and smooth muscle cells. Nitric oxide (NO) is the main factor involved in the process of erection and two NO production pathways are known. One is the stimulation of endothelial nitric oxide synthase (NOS), which increases NO production. That creates a decrease in intracellular calcium, with a consequent smooth muscle relaxation and increased blood flow (see figure 2).

**Figure 2. Molecular mechanisms and pathologies associated with ED. Image taken and modified from McVary, K. T. (2007). Erectile Dysfunction. New England Journal of Medicine.[16]**




The other pathway involves the parasympathetic system, in which noncholinergic and nonadrenergic nerve fibers trigger the relaxation of smooth muscle cells. Venous return is thus occluded by compression of the subtunical venules, and in consequence, producing erection.

Multiple pathologies have been observed to impact the pathophysiology, affecting nerve fibers, thus reducing NO activity. When that occurs, muscle relaxation is not produced, the diameter of the sinusoids decreases, and there is insufficient compression of the subtunical veins, resulting in erectile dysfunction.[16]

The mechanisms of action through which the risk factors cause erectile dysfunction have also been studied. They are related to inflammation production, reduced testosterone levels, and endothelial dysfunction, all of which lead to reduced nitric oxide and the development of the pathology.[13]

With the present knowledge of the pathophysiologic mechanisms that erectile dysfunction shares with the risk factors, preventive interventions should be directed at therapeutic measures that increase nitric oxide production.[13]

## Impact on quality of life

As with many diseases, erectile dysfunction should be comprehensively managed, given that not only does it affect the patient in an isolated, individual manner, but it also alters different spheres (psychosocial, sexual, couple relationships) in the patient's life.[8]

At the individual level, there is sexual performance dissatisfaction. As a result, men lose their self-confidence and present with depressive symptoms, anxiety, anguish and fears, and reach a point at which they avoid sexual activity. Approximately 69% of patients deny having

sexual dysfunction and delay seeking medical attention for an average of 2 years. Between 50-80% of patients interrupt treatment.[8]

Those psychologic disorders cause the individual to create thoughts that interfere with the process of erection, resulting in the inability to achieve or maintain erection due to the fears the individual develops about sexual intercourse.[8]

## Non-pharmacologic treatment

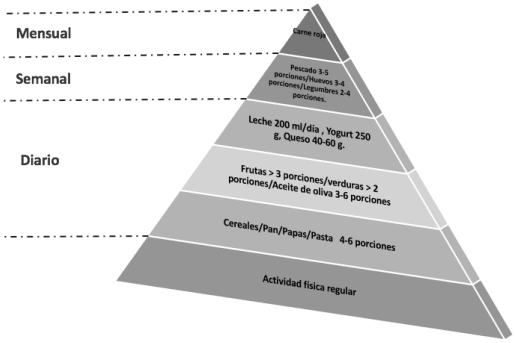
Risk factors associated with erectile dysfunction have been reported to produce consequences that affect the quality of life of the patient. Therefore, the treatment of the disease should be comprehensive, encompassing the totality of its pathophysiology, and include lifestyle changes that help improve sexual function.[17]

A description of the studies we found that evaluate the Mediterranean diet, physical activity, and sex therapy as non-pharmacologic interventions in erectile dysfunction is presented below.

## The Mediterranean diet

The United Nations Educational, Scientific and Cultural Organization (UNESCO) classified the Mediterranean diet as Intangible Cultural Heritage of Humanity, identified in the alimentary habits of certain populations (especially in Crete and southern Italy) in the mid-twentieth century, following the period of austerity in the wake of World War II. In those regions, the characteristic frugal diet consisted of a relatively high intake of cereals, vegetables, legumes, nuts, and dried fruits, with olive oil as the main source of fat, as well as moderate-to-high consumption of fish, moderate-to-low consumption of white meat (poultry and rabbit), dairy products (mainly yogurt or fresh cheese), low consumption of red meat, and moderate consumption of wine with meals (figure 3).[18]

**Figure 3. Mediterranean diet pyramid. Image adapted and modified from Mattioli et al.(18)**




Among the mechanisms of action of those foods, olive oil is known to increase the antioxidant capacity of plasma and reduce xanthine oxidase activity. Tomatoes are rich in vitamin C (carotenoids and polyphenols) and prevent the vascular dysfunction in erectile dysfunction through their anti-inflammatory properties, producing a positive effect on endothelial function, arterial rigidity, and cardiac remodeling.[4,18]

In their observational multicenter study, Ramírez et al. evaluated the prevalence of erectile dysfunction and its predictors, within the time frame of March 2010 to December 2012. Patients above 40 years of age being treated for dyslipidemia and other cardiovascular risk factors were included in the study. Anthropometric data, high blood pressure, dyslipidemia, obesity, physical activity, ischemic vascular disease, smoking, and dietary habits were assessed through a validated questionnaire of 14

items that provided a grade of dietary adequacy. ED was evaluated through the International Index of Erectile Function (IIEF) adapted to the Spanish population. A score of 6-10 points was considered severe ED, 11-16 moderate, 17-25 mild, and above 25 no ED. Patients with erectile dysfunction had an unhealthy lifestyle (smoking, alcohol consumption, and little physical activity). They also consumed fewer vegetables and dried fruits than the individuals that did not present with ED.[19]

Esposito et al. analyzed the effect of the Mediterranean diet on ED (evaluated through the IIEF-5 <21) in men with metabolic syndrome (Adult Treatment Panel III). Sixty-five men with metabolic syndrome met the inclusion criteria. Thirty-five of them were assigned to the Mediterranean diet intervention and thirty to the control diet. After two years, the men in the Mediterranean diet group consumed more fruit, vegetables, nuts, and legumes (P <0.001), olive oil (P <0.001), and omega 3 (P <0.001). The erectile function score was better in the Mediterranean diet group than in the control group, and sexual function improved in about one-third of the men in the intervention group.[20]

In a recent systematic review, evidence about the role of the Mediterranean diet in men with erectile dysfunction was analyzed through four clinical trials from 2010 to the present. The studies showed that the Mediterranean diet had an influence on sexual function in men. High consumption of olive oil, vegetables, and fruit, and moderate consumption of wine, whole grains, dried fruit, fiber, and fish, produced positive results. Those foods were associated with less risk and severity of erectile dysfunction.[21]

A randomized clinical trial on the primary prevention of sexual dysfunction through the Mediterranean diet in patients with type 2 diabetes evaluated the long-term effect of the Mediterranean diet on incident ED and female sexual dysfunction (FSD) in subjects with type 2 diabetes and the combined incidence of sexual dysfunction in men or women with worsening of sexual function in patients with baseline sexual dysfunction. A total of 108 patients were randomly assigned to the Mediterranean diet group and 107 subjects were assigned to the low-fat diet group, with a follow-up of 8.1 years.

Two validated questionnaires were employed:

1. the International Index of Erectile Function (IIEF)
2. he Female Sexual Function Index (FSFI)

They were applied at the beginning of the study, before the randomization, and every 6 months of the intervention. Incidence of the primary outcome (ED and FDS) throughout the entire follow-up was lower in the Mediterranean diet group (OR: 0.44, 95% CI: 0.19-1.00, p=0.045) and incidence of new ED and deterioration of preexisting ED was also lower in the Mediterranean diet group, compared with the low-fat diet group (OR: 0.41, 95% CI: [0.21-0.83], p=0.011).[22]

In a descriptive study, a questionnaire was applied to evaluate the association between fruit/vegetable consumption and erectile dysfunction (ED) in Canadian men with diabetes. ED was determined through the following question: Have you ever had any of the following conditions diagnosed by a health professional as erectile dysfunction? A total of 400 cases of ED were identified. There were also questions on food consumption (carrots, fruit, green leafy vegetables) that were answered: fewer than 5 servings per day, 5-10 servings per day, more than 10 servings per day, or not consumed. A

10% risk reduction for ED was found with each additional daily serving of fruit/vegetable consumed.[23]

Della Camera et al. correlated the Mediterranean diet, physical activity, body mass index (BMI), and depression with sexual dysfunction. ED was evaluated through the IIEF-5 questionnaire and the other instruments used were the Hamilton Depression Rating Scale, the MedDiet questionnaire, and the International Physical Activity Questionnaire (IPAQ). Two groups were assessed: 65 men without erectile dysfunction and 76 men with erectile dysfunction. Adherence to the Mediterranean diet and adequate weight were positive factors for sexual function.[24]

## Physical activity

Different mechanisms have been studied in relation to erectile dysfunction. Exercise has been shown to improve ED and its mechanism of action is the increase in systemic nitric oxide production that causes increased blood flow in the penis, heightening paraoxonase 1 (PON1) activity, which has an antioxidant mechanism associated with circulating HDL and reduces oxidative stress. Moderate physical activity reduces ED, whereas a sedentary lifestyle increases it two to ten-fold.[25

In a narrative systematic review, Maiorino et al. described the effects of lifestyle modifications related to physical activity, weight loss, diet, smoking, and alcohol on ED. With respect to physical activity, they reviewed a meta-analysis and found that high and moderate physical activity was associated with a lower risk for erectile dysfunction. Other prospective studies indicate that physical activity has a beneficial effect on the prevention and improvement of ED.[13]

In 2014, Leoni et al. reviewed several studies that included physical activity, cerebrovascular events, endothelial dysfunction, and erectile dysfunction, to verify their applicability for improving the health and quality of life in men with erectile dysfunction. In general, physical activity has produced improvement in erectile function, and thus is considered a protective factor for normal erectile function. The Massachusetts Male Aging Study, conducted on men 40 to 70 years of age, with an 8.8-year follow-up, showed that physically active men had a lower risk for ED, compared with men with a sedentary lifestyle.[26]

In a randomized clinical trial, the effect of a lifestyle modification program designed to improve erectile function in subjects with, or at risk for, erectile dysfunction was analyzed. Prevailing information was collected on healthy dietary options and general orientation toward increasing the physical activity of the participants. Changes in the erectile function score (IIEF-5) and the restoration of erectile function achieved through lifestyle changes were measured. Physical activity of more than 4 hours a week decreased body mass index ($P < 0.001$) and increased erectile function.[27]

La Vignera et al. evaluated the effects of a standard protocol of aerobic physical activity and Mediterranean diet in men with arteriogenic erectile dysfunction. They selected 50 patients with ED according to the IIEF-5, with a mean age of 57 years, and evaluated them at the baseline and after 3 months, with Doppler ultrasound and blood tests to determine the number of endothelial precursor cells (EPCs) and endothelial microparticles (EMPs). At the beginning of the study, there were no statistical differences in the number

of EPCs and EMPs between groups, but at 3 months, group A had a decrease in EPCs and EMPs from 15% to 6%, with a p = 0.05. The IIEF-5 score improved in group A, increasing to 16 points.[28]

In a clinical trial, the aim was to demonstrate whether increased physical activity was associated with improved erectile dysfunction. The study included patients between the ages of 18 and 40 years and excluded all patients that presented with a primary complaint or diagnosis of ED or Peyronie's disease. They used the validated IIEF-5 questionnaire to evaluate ED and the Paffenbarger questionnaire to assess energy expenditure during exercise (200 kcal/day). A sedentary lifestyle was associated with greater erectile dysfunction in the items evaluated in the IIEF-5: erectile function (P=0.04), orgasm (P=0.01), sexual satisfaction (P=0.04), and general satisfaction (P=0.02). There was a tendency toward greater dysfunction in the sedentary group reflected in the IIEF total score (P=0.057).[29]

Loprinzi et al. conducted a study in the United States on the association between objectively measured physical activity and ED in men aged 50 to 85 years. Physical activity was measured by accelerometry (moderate-to-vigorous) and prevalent sexual dysfunction was assessed with the question: How would you describe your ability to have and maintain adequate erection for satisfactory sexual intercourse? The response options were: always or almost always; usually; sometimes; and never. They also included the variables of age, ethnicity, waist circumference, the income-to-poverty ratio, cotinine (a biomarker of tobacco smoke exposure), and other diseases (ordinal variable ranging from 0 to 8 that indicated the number of physician-diagnosed conditions, including arthritis, coronary disease, cerebrovascular accident, congestive heart failure, heart attack, cancer, chronic obstructive pulmonary disease, and high blood pressure). For every daily 30-min increase in moderate-to-vigorous physical activity, the probability of presenting with ED was reduced by 43% (adjusted OR: 0.57; 95% CI).[30]

In a systematic review and meta-analysis, the effects of physical activity and exercise interventions were evaluated in adult men with erectile dysfunction. Seven controlled clinical trials (CCTs) were chosen that assessed erectile function through the IIEF, based on exercises (aerobics and specific pelvic floor exercises), and other studies evaluated physical activity plus pharmacologic treatment (PDE5 inhibitor, methyldopa). Four of those trials were based on supervised aerobic activity (Kafka 2013: 45 min 3 times a week; Marisca 2013: 30 min 3 times a week plus tadalafil; Lamina 2009: 45 min 3 times a week plus methyldopa; and Dorey 2004: pelvic floor exercises), and 3 trials were based on non-supervised exercise (Lin YH 2012: pelvic floor exercises for 10 seconds twice a day; Maio G 2010: 3 hours a week plus a PDE5 inhibitor; and Esposito K 2004: any activity such as walking, swimming, or playing that reduced weight by 10%). Statistically significant results of the meta-analysis showed that increased physical activity improved erectile function score by 3.85 points (95% CI: 2.33-5.37).[31]

## Sex therapy

All men should be educated at an early age about strategies for managing sexual dysfunction. There are currently many pharmacolo-

gic treatments available, such as the type 5 phosphodiesterase (PDE5) inhibitors, intracavernosal injections, vacuum devices (VPDs), or penile implants. Poor adherence to those treatments has been shown due to inadequate erections, disinterest on the part of the partner, adverse effects of the medications, mechanical failure of the implants, or discomfort from the device, all leading to treatment failure. Therefore, it is important to offer the patient other therapeutic measures and perform an intervention that includes the sexual partner, to provide adequate management of ED.[32]

William Masters and Virginia Johnson are considered pioneers in the field of sex therapy, the aim of which is to relieve symptoms and improve the sexual function of the patient, looking for the negative factors that do not allow good sexual health. It mainly provides information and suggestions for sexual tasks and communication, as well as teaching bodily, experience-based techniques, all of which improve the primary bonds of the couple, to achieve symptom remission.[33]

In a systematic review and meta-analysis, the effectiveness of psychologic interventions for treating ED was studied, in comparison with oral medications, local injections, vacuum devices, and other apparatuses. The participating patients were diagnosed with ED based on the DSM III, DSM IV, or CID 10 instruments, were above 18 years of age, and were of any ethnicity. Men already taking PDE5 inhibitors were excluded. Psychotherapeutic methods were employed for four weeks and sexual function was evaluated through the IIEF-5 questionnaire.

A total of eleven studies were selected and the psychotherapeutic interventions were organized by the authors:[34]

1. Rational emotive therapy (RET): based on a psychoeducational model and a cognitive, sexual intervention for reducing performance anxiety, resolving conflicts, improving the relationship, and training to prevent relapses.
2. Sex group therapy (GT): training in social skills and tasks assigned about anxiety in sexual situations, education and information on male sexuality in general, communication training, myths about male sexuality, non-demanding pleasures and permission to participate in self-pleasuring.
3. Modified Masters and Johnson technique: based on programs that combine education, tasks, and assessments.
4. Educational intervention: workshops focused on providing information on psychology and the physiologic changes that occur with the sexual response.
5. Systematic desensitization: behavior therapy focused on deep muscle relaxation to reduce anxiety caused by situations.

In two experimental studies (Price and Kilmann), the authors evaluated group sex therapy in different ways. Individually, no statistical significance was observed in any of the studies, but in the meta-analysis of those studies, sex group therapy favored sexual dysfunction improvement (RR: 0.13, 95% CI: 0.04-0.43). That same result was not observed with the other psychotherapies (RET, modified Masters and Johnson therapy, systematic desensitization).[34]

Banner et al. conducted a randomized clinical trial on men with psychogenic erectile dysfunction that received sildenafil, alone, or an integrative treatment protocol (ITP) with sildenafil and cognitive-behavior sex therapy (CBST) for 4 weeks. The subjects were evalua-

ted through the IIEF-5. There was significant improvement with both treatments for ED (P=0.007), but mean scores were higher in the men treated with the ITP (P=0.005) than in the men treated with sildenafil, alone (P=0.046). After 4 weeks of treatment, a higher percentage of men treated with the ITP (65.5%) had IIEF-5 scores above 6, compared with the men using sildenafil, alone (37.5%). Upon study completion, both groups showed additional improvement: 75% in the ITP group fit the success criteria and 45% in Group A, after adding CBST to the sildenafil regimen.[35]

In a randomized study, intracavernosal injection (ICI) therapy was evaluated with and without sexuality counseling (SC) in men with erectile dysfunction. They were interviewed by telephone after a mean follow-up of 11.3 months to determine their ICI use and reasons for its discontinuation. The data on that intervention were not statistically significant (P=0.24).[36]

To evaluate the vacuum constriction device (VCD), Wylie et al. compared that intervention with psychotherapy. Their results showed improvement in the psychotherapy group plus the VCD, versus psychotherapy, alone. Twenty-one couples reported improvement after psychotherapy and VCD sessions, compared with 12 couples that reported improvement with psychotherapy, alone. No differences were observed between the VCD plus psychotherapy results and those of psychotherapy, alone, after three weeks or after 6 weeks of management.[37]

A randomized clinical trial analyzed the efficacy of treatment with a PDE5 inhibitor versus its combination with sex therapy, for sexual function and cognition, couple intimacy and adaptation, and treatment satisfaction in patients with ED of mixed etiology. The results for treatment with sildenafil, alone, were statistically significant for men in the domains of sexual function (IIEF), erectile function (P<0.01), sexual desire (P <0.01), sexual satisfaction (p <0.01), general satisfaction (P <0.01), and general satisfaction total score (P<0.01). Men also stated they had fewer sexual doubts with respect to their partners (P <0.05). Results of treatment with the combined intervention were statistically significant in all the domains: erectile function (P <0.01), orgasmic function (P <0.01), sexual desire (P <0.01), sexual satisfaction (P ≤ 0.01), general satisfaction (P <.01), and total sexual scale (P <0.01). In addition, improvement was observed regarding doubts related to the partner, self-doubts, negativity, and increased sexual intimacy, all with statistical significance (P=0.01).[38]

In a randomized clinical trial on 30 men, treatments for 6 months with sildenafil, with PI, or with their combination, were analyzed. Data were evaluated at the study baseline, after treatment, and at month 3 of follow-up. There was statistical difference for group I (PI plus sildenafil) (P=0.0009) and group III (PI) (P=0.0002), but not for group II (sildenafil) (P=0.135).[39]

In a clinical study, Phelps et al. analyzed the addition of a psychoeducational component to oral sildenafil and sildenafil-only, in relation to sexual satisfaction and erectile function in psychogenic and organic ED. Fifty-five men, with a mean age of 61 years, and their partners were randomly assigned to the PDE5 inhibitor, alone, or combined with psychoeducational management. They received 10 doses per month of sildenafil for 6 months and attended 60 to 90-min workshops in groups of 6-8 patients, where they received information on the sexual response cycle, behavioral exercises, information on PDE5 inhibitor therapy, and self-help

material. Regarding erectile function, there were no statistically significant differences in the two groups at 6 months of treatment, but general satisfaction was higher in the sildenafil plus psychoeducation group (p=0.04) at 12 weeks.[40]

In another clinical trial from 2006, the authors studied honeymoon impotence in 100 patients, 20-28 years of age, that had erectile dysfunction from the beginning of their marriages. They were assigned to groups, according to the origin of their ED: the group with psychogenic cause received sildenafil (50 mg on-demand) plus concomitant sex therapy and the group with organic cause due to vascular alteration received a PDE5 inhibitor, alone. The results were measured through the IIEF-5. Of the patients with psychogenic cause, 74 achieved success with the combination treatment, 74% suspended treatment in less than 3 months, and 22% in less than one year. Only 4% required longer PDE5 inhibitor therapy. Of the 26 patients with ED of organic origin, 15 (58%) showed complete response after 3-6 months with PDE5 inhibitor management. Only 6% reported side effects and they were mild.[41]

Sex therapy has been evaluated and administered through the Internet in the form of self-help material, allowing the patient to have information and learn exercises that can be carried out weekly at home.[42]

Therapy via the Internet is cost-effective and can aid in cases involving long distances and can offer assistance to men that are afraid to seek help in person for their problem. In an Internet-guided randomized controlled trial on cognitive-behavioral therapy (ICBT) for erectile dysfunction, treatment was a 7-week online program with therapeutic support by email. The study included heterosexual and homosexual patients that had computer access to the Internet, were above 18 years of age, had an IIEF score < 21, and a stable sexual partner for at least 3 months. The treatment group received ICBT and the control group had access to an online discussion forum, both for 7 weeks. The participants were evaluated by telephone and used self-application online questionnaires at the follow-up at 6 months. Results showed improvement in the IIEF score in the treatment group. After the control group received ICBT, their erectile function score increased with statistical significance ($P < 0.01$).[43]

In a pilot study by McCabe et al., they evaluated the efficacy of the combination of an Internet program of psychologic therapy (PI) with PDE5 inhibitors and PI-only, through the Internet. The program focused on 3 aspects: sensory, communication exercises, and email contact with a therapist. It was presented in 5 modules and designed to be completed in 10 weeks. A multivariate mixed model showed a positive group result in sexual intercourse satisfaction and quality of sexual intercourse (P=0.05). The treatment group had significant improvement in sexual intercourse satisfaction (P=0.01) and quality of sexual intercourse (P=0.01), compared with the control group.[44]

And finally, in a 2015 review article in the Andrology Journal of Asia, intervention strategies on the risk factors associated with erectile dysfunction were described (sedentary lifestyle, obesity, unhealthy diet, alcohol consumption, and smoking). Those results are shown in Table 2.

**Table 2: Adaptation of the recommendations on risk factor changes, taken from the article: Maiorino et al.[13] (A: evidence from intervention studies; B: evidence from prospective cohort studies and case-control studies. * Few studies, and with small samples)**

| *RISK FACTOR* | *STRATEGY* | *RECOMMENDATION* | *LEVEL OF EVIDENCE* |
|---|---|---|---|
| Sedentary lifestyle | Physical activity | 30 min per day or 150 min per week of aerobic activity | A* |
| Obesity | Weight loss | 5-10% weight loss | A* |
| Unhealthy diet | Adequate diet | Increase the consumption of fruits, vegetables, grains, and legumes. Increase the consumption of monounsaturated and polyunsaturated fatty acids. Limit the consumption of processed foods and consume < 10% saturated fats | A* |
| Alcohol abuse | Suspend alcohol consumption | Maximum of 1-2 drinks per day | B |
| Smoking | Instruct how to stop the habit | Suspend | B* |

## Discussion

The scientific literature reviewed describes different interventions for making lifestyle changes that can prevent erectile dysfunction and reduce its progression. Patients diagnosed with ED evaluated in the majority of the studies through the International Index of Erectile Function (IIEF-5) had poor quality of life due to smoking, alcohol consumption, low physical activity, and low consumption of fruit and vegetables. Different clinical studies showed that a change in diet, in which the intake of fruit, vegetables, dried fruit, olive oil, and omega 3 was increased, improved sexual function. Those foods make up part of the Mediterranean diet and the studies reviewed showed a statistically significant reduction in the incidence and progression of ED through that diet, which was one of the aims of the present review.

In addition, a sedentary lifestyle was shown to be associated with greater erectile dysfunction in the items evaluated by the IIEF-5. The positive effect of physical exercise on erectile dysfunction was documented in a meta-analysis. Doing 30 to 45 min of aerobic physical exercise 3 times a week was statistically significant in increasing the erectile function score. In that study, the authors performed a sensitivity analysis, excluding the clinical trials that evaluated physical activity plus medications (sildenafil or methyldopa) as management, and found improvement of 3.30 points in erectile function with pelvic floor exercises or by simply carrying out any physical activity.

In addition, another clinical study measuring the cells involved in endothelial dysfunction confirmed that increasing physical exercise reduced their production, and in turn, the damage caused at the endothelial level, resulting in improved sexual function.

Due to the emotional and psychologic distress and the problems of intimacy between sexual partners that are caused by erectile dysfunction, a search was conducted for articles based on sex therapy as the intervention. In one of the meta-analyses found, the combination of sex therapy plus medications (sildenafil)

improved erectile function, orgasmic function, sexual desire, sexual satisfaction, self-doubts and negativity, and increased sexual intimacy. Positive results for improved sexual function were documented for sex group therapy, cognitive behavioral therapy, providing information on the sexual response cycle, behavioral exercises, information on PDE5 inhibitor therapy, and psychologic support via the Internet.

## Clinical practice implications

In different studies, thanks to evidence-based medicine, the importance that risk factors have on the diagnosis and treatment of different diseases has been found, and erectile dysfunction is no exception. As is clear in the present review, the evidence is in favor of carrying out lifestyle-changing interventions, and according to the results identified in the studies reviewed, they involve:

1. Emphasizing a Mediterranean-type diet and increasing the consumption of fruit, vegetables, omega 3, olive oil, and dried fruits.
2. Performing 30 to 45 min of aerobic physical exercise 3 times a week.
3. Providing sex therapy to improve the psychologic and marital alterations caused by the disease.

Therefore, health professionals should implement those recommendations as first-line therapy, carrying out a holistic approach to the patient, optimizing the preservation of sexual function and impeding the progression of erectile dysfunction.

## Conclusions

It is becoming increasingly important to perform comprehensive interventions in treating the pathologies patients suffer. As shown in the present review, there are positive results in both primary prevention and secondary prevention of erectile dysfunction. Carrying out the recommendations of increased physical activity and an adequate diet rich in fruit, vegetables, and dried fruit, from an early age, may prevent the appearance of sexual dysfunction at older ages. Likewise, the addition of sex therapy, associated with pharmacologic treatment, to the dietary and physical activity recommendations has a positive effect on the psychologic alterations caused by erectile dysfunction.

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