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# Impact of lifestyle on erectile dysfunction: literature review and educational recommendations

#### Konrad Wawszkowicz, MD

Medicover Medical Center in Cracow Fabryczna 1; 31-553 Cracow, Poland konrad.wawszkowicz@gmail.com

ORCID: https://orcid.org/0009-0003-0978-2280

## Liliana Dylag, MD

Stefan Żeromski Specialist Hospital in Cracow os. Na Skarpie 66; 31-913 Cracow, Poland liladylag@gmail.com

ORCID: https://orcid.org/0009-0009-0059-5204

#### Magdalena Graca, MD

Leszek Giec Upper-Silesian Medical Centre of the Medical University of Silesia in Katowice Ziołowa 45/47; 40-635 Katowice, Poland

magdalenagraca1995@gmail.com

ORCID: https://orcid.org/0000-0003-2948-286X

## Kinga Szopińska, MD

Provincial Specialist Hospital named after J. Gromkowski in Wroclaw

Koszarowa 5; 51-149 Wrocław, Poland

kingaszopinska97@gmail.com

ORCID: https://orcid.org/0000-0002-4552-8250

#### Weronika Łowicka, MD

Leszek Giec Upper-Silesian Medical Centre of the Medical University of Silesia in Katowice

Ziołowa 45/47; 40-635 Katowice, Poland

weronikalowicka22@gmail.com

ORCID: https://orcid.org/0009-0002-8725-8014

## Anna Szeliga, MD

Specialist Hospital named after Ludwik Rydygier in Cracow

os. Złotej Jesieni 1; 31-826 Cracow, Poland

ania.sz343@gmail.com

ORCID: https://orcid.org/0009-0003-3587-1877

## Agata Szostak, MD

Regional Specialized Hospital No. 4 in Bytom

Al. Legionów 10, 41-902 Bytom, Poland

agataszostak23@gmail.com

ORCID: https://orcid.org/0009-0004-7774-9068

## Karolina Korta, MD

Specialist Hospital named after Ludwik Rydygier in Cracow

os. Złotej Jesieni 1; 31-826 Cracow, Poland

karolina.anna.korta@gmail.com

ORCID: https://orcid.org/0009-0008-3494-9309

## Karolina Oluszczak, MD

Specialist Hospital named after Ludwik Rydygier in Cracow

os. Złotej Jesieni 1; 31-826 Cracow, Poland

karolinaoluszczak@outlook.com

ORCID: https://orcid.org/0009-0004-2159-0019

# Maria Janina Śmigielska-Mikołajczyk, MD

109. Military Hospital in Szczecin

Piotra Skargi 9/11; 70-965 Szczecin, Poland

marysia.smigielska@wp.pl

ORCID: https://orcid.org/0009-0006-4214-0097

#### **ABSTRACT**

*Introduction:* Erectile dysfunction (ED) represents a significant health problem that can have a negative impact on men's quality of life, intimate relationships and self-esteem. ED is a marker of overall health, requiring a comprehensive diagnostic and therapeutic approach. This article highlights the need for an integrated approach, in which lifestyle modifications are key to the successful treatment of erectile dysfunction.

**Aim of the study**: The aim of this article is to provide a comprehensive review of the literature on erectile dysfunction, with the intention of improving understanding of the condition and providing directions for future research and clinical practice.

*Materials and methods*: Electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar, were searched to identify studies and literature reviews on erectile dysfunction (ED).

The state of knowledge: This review examines the epidemiology, pathophysiology, and risk factors associated with ED, emphasizing the importance of lifestyle in prevention and treatment. The role of diet, physical activity, weight reduction, smoking cessation, and alcohol restriction in improving erectile function is discussed. The article also presents current diagnostic and therapeutic approaches, including pharmacotherapy, alternative therapies and psychological interventions.

*Conclusions:* Erectile dysfunction (ED) is a complex health issue that necessitates a comprehensive and interdisciplinary diagnostic and therapeutic approach. Lifestyle plays a pivotal role in the prevention and treatment of ED, and its modification should be an integral component of any treatment plan.

*Keywords:* "erectile dysfunction"; "risk factors"; "lifestyle modifications"; "physical activity"; "pharmacotherapy".

#### 1. INTRODUCTION

Erectile dysfunction (ED) is defined as the difficulty or inability to obtain and maintain a penile erection at a level that enables satisfactory sexual intercourse. [1] It is the most common sexual problem among men, causing serious distress and having a profound impact on intimate relationships, quality of life and overall self-esteem. [2,3,4] ED is not only a sexual problem but also an important indicator of general health [5], requiring a comprehensive diagnostic and therapeutic approach.

Erectile dysfunction is increasingly recognised as a significant public health challenge. Men suffering from ED often do not immediately recognise their problem. Deterioration in erectile quality occurs gradually, which can lead to uncertainty about the permanence or temporariness of erectile difficulties. A significant proportion of men delay seeking help, anticipating that the problem will resolve spontaneously. This is often due to the perception that it is a normal consequence of the ageing process, a lack of sexual activity, a failure to recognise ED as a medical issue, embarrassment about consulting a doctor, and stigma.

Consequently, the prevalence of ED is underestimated, and the problem is exacerbated by inappropriate clinical practice in which doctors do not address patients' sexual habits. [6,7] A comprehensive understanding of the multifaceted factors influencing erectile function and the implementation of efficacious interventions can markedly enhance the quality of life for men afflicted by this condition.

## 2. AIM OF THE STUDY

The objective of this thesis is to examine the epidemiology, pathophysiology and risk factors associated with erectile dysfunction (ED), which has a significant impact on men's quality of life, intimate relationships and self-esteem. It places particular emphasis on the role of lifestyle, including diet, physical activity, weight reduction, smoking cessation and alcohol restriction, as key factors in the prevention and treatment of ED. In addition, the paper presents an overview of current diagnostic and therapeutic approaches and makes recommendations for future research and clinical practice in this area.

## 3. MATERIALS AND METHODS

Electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar, were searched to identify studies and literature reviews on erectile dysfunction (ED). The review included studies published in English between 2000 and 2024 that addressed the epidemiology, pathophysiology, diagnosis and treatment of ED. Particular attention was paid to studies analysing the impact of lifestyle on ED. Studies with a limited study sample, studies without full texts available online and papers not subject to scientific peer review were excluded.

#### 4. STATE OF KNOWLEDGE

#### 4.1. Prevalence

Erectile dysfunction (ED) is the most common form of sexual dysfunction in men, with an estimated prevalence of 30% to 50% in the general population. [2,3] The condition affects up to one-third of men during their lifetime, with prevalence increasing with age. [8] A population-based study of US healthcare professionals revealed that the prevalence of erectile dysfunction (ED) was 12% in men under the age of 59, 22% in the 60-69 age group, and 30% in men over 69. [9] Epidemiological studies have demonstrated that the prevalence of erectile dysfunction is significantly elevated in populations with an increased risk of developing the condition, including those who are physically inactive, obese, hypertensive, affected by metabolic syndrome, atherosclerosis or overt cardiovascular disease. Moreover, the risk of erectile dysfunction is found to increase in proportion to the number of comorbid risk factors. [10]

#### 4.2. Normal erectile response

A normal erectile response is the result of a complex interaction between neurotransmitters, biochemical processes and vascular smooth muscle responses initiated by parasympathetic and sympathetic neuronal impulses. This process integrates physiological stimuli from the penis with sexual perception and desire.

Nitric oxide (NO), produced by endothelial cells in response to parasympathetic stimulation, initiates a molecular cascade leading to smooth muscle relaxation and increased arterial blood flow to the penile corpora cavernosa. This is followed by the compression of the outflow veins, which results in an erection. [11,12]

## 4.3. Causes of erectile dysfunction

Erectile dysfunction (ED) can have a variety of organic causes, including vascular, neurogenic, hormonal, anatomical, drug-induced, and psychological factors. It is often a combination of both. [13,14]

The following factors have been identified as potential contributors to erectile dysfunction:

- Age
- Smoking
- Sedentary lifestyle
- Obesity
- Cardiovascular diseases
- Hypercholesterolaemia
- Hypertension
- Diabetes
- Endocrine disorders (e.g. hypogonadism, hypothyroidism, hyperprolactinaemia)
- Drug use (e.g. cocaine, methamphetamine)
- Medications (e. g. antihistamines, benzodiazepines)
- Neurological diseases (e.g. Alzheimer's disease, multiple sclerosis, Parkinson's disease, paraplegia, tetraplegia, stroke)
- Mental health problems (e.g. anxiety, depression, guilt, past sexual abuse, relationship problems, stress)
- Radiotherapy or pelvic surgery, including radical prostatectomy

The majority of these risk factors are strongly associated with inflammation, which in turn leads to endothelial dysfunction and reduced nitric oxide (NO) availability and activity. As nitric oxide (NO) is a key element in the regulation of genital blood flow, it can be reasonably assumed that most cardiovascular risk factors are associated with erectile dysfunction in men. [15] The majority of men with vascular erectile dysfunction (ED) present with at least one significant cardiovascular risk factor. Erectile dysfunction is regarded as an early indicator of cardiovascular risk, with the potential to precede the clinical manifestations of atherosclerosis. Consequently, they may be regarded as an early indicator of vascular dysfunction. [16]

## 4.4. Diagnostics

**Medical history:** It is of great importance to gather detailed information on the patient's health history, including the presence of comorbidities, medications used and the patient's lifestyle and health habits. [17,18]

**Physical examination:** The physical examination plays an important role in identifying potential organic causes of erectile dysfunction, such as vascular or neurological problems. This includes the measurement of blood pressure, an assessment of the patient's hormonal status and an examination of the genitals. [17,19]

**Laboratory tests:** In men with erectile dysfunction, limited diagnostic testing is recommended, which may include fasting glucose levels, a lipid panel, a thyroid-stimulating hormone (TSH) test and morning total testosterone levels [17,19].

**Evaluation scales:** Questionnaires such as the International Index of Erectile Function (IIEF) and its shortened version the IIEF-5, also known as the SHIM (Sexual Health Inventory for Men) scale, are frequently employed to assess sexual function. Furthermore, these tools are employed to evaluate the efficacy of therapeutic interventions [20].

#### 4.5. Treatment

## 4.5.1. Pharmacotherapy

Phosphodiesterase type 5 (PDE5) inhibitors are the most effective oral drugs for the treatment of erectile dysfunction [21] and should be considered as first-line treatment alongside lifestyle modification. [17,22,23] This group of drugs includes sildenafil, tadalafil, vardenafil and avanafil. The mechanism of action of these drugs is to promote erection by enhancing the vasodilatory action of endogenous nitric oxide (NO) during sexual stimulation. All of the PDE5 inhibitors mentioned are effective within approximately an hour of administration and are typically used on an as-needed basis. They have no effect on improving libido. [24]

PDE5 inhibitors are generally well tolerated, but may cause mild and transient side effects such as headache, hot flashes, indigestion, runny nose and visual disturbances. It should be noted that these drugs are contraindicated in men using nitroglycerin or other nitrates due to the risk of significantly lowering blood pressure. In addition to its erectile effects, sildenafil affects the cardiovascular system by affecting heart rate, blood pressure, pulmonary and coronary circulation and endothelial function in patients with chronic heart failure. [25] Furthermore, PDE5 inhibitors demonstrate cardioprotective effects in the context of cardiac ischaemia, reducing infarct size, improving left ventricular function, reducing the frequency of ventricular arrhythmias and reducing myocardial necrosis. [26,27]

The growing body of evidence suggests the broad therapeutic potential of PDE5 inhibitors, which encompasses the cardiovascular, gastrointestinal, cutaneous and nervous systems. It is postulated that they may be beneficial in the treatment of various conditions, including Raynaud's phenomenon, heart failure, spontaneous hypertension and stroke. PDE5 inhibitors are therefore conceptually an attractive class of therapeutic agents with pleiotropic effects. [28]

Testosterone is of great importance in the achievement of an erection [29], as the pressure within the corpora cavernosa and the activity of the enzyme PDE5 are dependent on androgenic hormones. The estimated prevalence of hypogonadism in men with erectile dysfunction is between 5 and 10 per cent. [30,31]

In cases of hypogonadism, testosterone supplementation has been demonstrated to be more efficacious than a placebo in improving erectile function and sexual performance, resulting in enhanced erectile satisfaction and increased sexual desire. [32]

Testosterone supplementation necessitates the regular monitoring of haemoglobin, serum transaminase and prostate-specific antigen levels, as well as prostate examinations.

## 4.5.2. Alternative pharmacological therapies

In instances where conventional pharmacotherapy is ineffective or contraindicated, alternative therapies are considered. There is promising scientific evidence for the efficacy of herbal products such as Panax ginseng, Pygnogenol, Prelox and Tribulus terrestris, and dietary supplements containing L-arginine, in the treatment of erectile dysfunction. The precise mechanisms of action of these substances remain unclear. However, there is evidence to suggest that they may partially increase nitric oxide (NO) production. [33,34]

## 4.5.3. Psychological Therapy

It is increasingly recognized that a significant proportion of cases of erectile dysfunction in men have a psychological or interpersonal basis. [35] Psychogenic erectile dysfunction can occur at any age, although it is most commonly diagnosed in men under the age of 40. A number of factors may contribute to the development of psychogenic erectile dysfunction, including premature ejaculation, genital pain (dyspareunia), cultural or religious taboos and a history of sexual abuse. Cognitive-behavioral therapies, psychosexual therapies (including sensation-focused techniques) and interventions to improve interpersonal relationships have been demonstrated to significantly improve sexual function in patients. [36] In the case of co-occurrence of erectile dysfunction with depression or anxiety, it is of the utmost importance to prioritize treatment of the mood disorder. When prescribing antidepressants, it is recommended that substances with a lower potential for negative effects on erectile function be preferred. Phosphodiesterase type 5 (PDE5) inhibitors are an efficacious treatment option for men with depression, and can be employed in conjunction with psychotherapy for mood disorders. [37]

## 4.6. Lifestyle

It is evident that lifestyle and diet have a significant impact on vascular nitric oxide (NO) production and erectile function. It has been proposed that lifestyle modifications which reduce chronic low-grade inflammation may help to reduce problems with sexual dysfunction. [22] The link between modifiable behavioral factors and erectile dysfunction, particularly in men without other health issues, highlights the need for targeted interventions to prevent and enhance erectile function. Given the pivotal role of nitric oxide in vascular health, it is crucial to prioritize strategies that enhance its production within the vasculature.

Weight reduction: Epidemiological studies have indicated that overweight, obesity and metabolic syndrome are associated with a significant increase in the risk of erectile dysfunction. [38] Obesity is associated with a twofold increase in the risk of erectile dysfunction. [9] A study demonstrated that one-third of obese men exhibited improvements in erectile function following moderate weight loss and regular exercise. [22]

It is postulated that obesity-related reduced testosterone levels may contribute to impaired insulin resistance and endothelial function, which may further affect erectile dysfunction. [39]

**Healthy diet:** A diet comprising a high proportion of fruits, vegetables, whole grains, and healthy fats, such as those found in fish and nuts, and a low proportion of saturated fats and simple sugars is beneficial for cardiovascular health and may improve erectile function. [40] The Mediterranean diet, which is characterized by these properties, is particularly recommended for men with erectile dysfunction. [41,42] The beneficial effects of the Mediterranean diet on cardiovascular health and erectile dysfunction may be attributed to a multitude of biological mechanisms, including reduced oxidative stress, reduced subclinical inflammation, improved endothelial function and increased insulin sensitivity. [43,44]

**Smoking cessation:** It has been demonstrated that the risk of erectile dysfunction is 51% higher in current smokers and 20% higher in former smokers in comparison to men who have never smoked. [45] Both direct tobacco use and exposure to tobacco smoke are significant risk factors for erectile dysfunction. [46,47] Smoking cessation has been demonstrated to significantly improve both physiological and subjective assessments of sexual health in long-term smokers, regardless of the initial degree of erectile dysfunction. [48]

**Reducing alcohol consumption:** It has been postulated that excessive alcohol consumption may contribute to erectile dysfunction (ED) through damage to the nervous system and blood vessels. It has been demonstrated that moderate alcohol consumption may have a protective effect on erectile dysfunction (ED) in both the general population and in men with diabetes mellitus. [9,49,50] The beneficial effect of alcohol on erectile function may be partly due to the long-term benefits on high-density lipoprotein cholesterol and other variables that increase nitric oxide (NO) bioavailability.

Regular physical activity: Regular exercise has a significant impact on improving erectile function. Regular physical activity improves blood circulation, which is essential for achieving and maintaining an erection. The mechanisms by which physical activity alleviates ED include improved cardiovascular fitness and endothelial function [51], increased endothelial NO production [52], reduced oxidative stress [53] and increased numbers of regenerative endothelial progenitor cells (EPCs). [54] Furthermore, regular exercise has been shown to have a beneficial effect on self-esteem and mental health, which may have a positive impact on psychological aspects related to sexual dysfunction. [55] Studies have indicated that regular aerobic exercise at an intensity of approximately 800-1200 kcal per week is associated with beneficial changes in blood pressure [56], lipid and lipoprotein profiles [57], inflammatory markers [58], insulin sensitivity [56] and other chronic disease risk factors. [59, 60]

The scientific evidence indicates that physical activity of moderate to substantial intensity can help to prevent erectile dysfunction or improve existing dysfunction. [61-64] In order to reduce the risk of erectile dysfunction (ED), physical activity recommendations should include supervised workouts that consist of moderate to substantial intensity aerobic exercise performed four times a week for 40 minutes.

A total weekly exercise dose of 160 minutes for six months may help to reduce the incidence of erectile dysfunction in men affected by ED caused by physical inactivity, obesity, hypertension, metabolic syndrome and/or overt cardiovascular disease. [8,14, 65-67]

## 5. CONCLUSIONS

Erectile dysfunction (ED) is a prevalent health issue that negatively impacts the quality of life of affected males. The prevalence of ED increases with age and in populations with risk factors such as obesity, hypertension, diabetes and cardiovascular disease. The underlying mechanisms of ED are complex and include endothelial dysfunction, reduced nitric oxide bioavailability, inflammatory processes and psychogenic factors.

The primary modifiable risk factors for ED are:

- An unhealthy diet has been linked to an increased risk of ED, whereas a Mediterranean diet has been shown to improve erectile function.
- Regular aerobic exercise has been demonstrated to enhance cardiovascular fitness and erectile function.
- Weight reduction has been effective in treating ED in overweight or obese individuals.
- Smoking cessation has been linked to improved sexual health.
- Moderate alcohol consumption has been observed to have a beneficial effect on ED.

The early diagnosis of ED is of paramount importance for the effective treatment of the condition, which should include pharmacotherapy, alternative therapies, psychological interventions and lifestyle modifications. Lifestyle changes are fundamental to the prevention and treatment of ED, and their implementation should be an integral part of any treatment plan. Further research is needed to better understand the mechanisms of ED and to develop more effective therapeutic strategies.

#### **DISCLOSURES**

# **Author's contribution:**

Conceptualization: Liliana Dylag; Konrad Wawszkowicz; Karolina Oluszczak

Methodology: Kinga Szopińska; Agata Szostak; Maria Janina Śmigielska-Mikołajczyk Software: Weronika Łowicka; Anna Szeliga; Maria Janina Śmigielska-Mikołajczyk

Check: Magdalena Graca; Agata Szostak; Karolina Oluszczak

Formal analysis: Liliana Dyląg; Konrad Wawszkowicz;

Investigation: Kinga Szopińska; Anna Szeliga; Karolina Oluszczak

Resources: Weronika Łowicka; Karolina Korta; Maria Janina Śmigielska-Mikołajczyk

Data curation: Magdalena Graca; Konrad Wawszkowicz; Writing-rough preparation: Liliana Dyląg; Anna Szeliga; Writing-review and editing: Kinga Szopińska; Agata Szostak Visualization: Weronika Łowicka; Konrad Wawszkowicz;

Supervision: Magdalena Graca; Karolina Korta; Karolina Oluszczak

Project administration: Konrad Wawszkowicz; Karolina Korta

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#### **REFERENCES**

- 1. Muneer A, Kalsi J, Nazareth I, Arya M. Erectile dysfunction BMJ 2014; 348 :g129 doi:10.1136/bmj.g129
- 2. Johansen P.P., Zwisler A.D., Hastrup-Svendsen J.et al. The CopenHeartSF trial—comprehensive sexual rehabilitation programme for male patients with implantable cardioverter defibrillator or ischaemic heart disease and impaired sexual function: protocol of a randomised clinical trial. BMJ Open 2013;311: e003967.
- 3. Hehemann M.C., Kashanian J.A.Can lifestyle modification affect men's erectile function? Transl Androl Urol2016;52: 187-194.
- 4. Miner MM, Kuritzky L. Erectile dysfunction: a sentinel marker for cardiovascular disease in primary care. Cleve Clin J Med. 2007;74(suppl 3):S30-S37.
- 5. Liu L.H., Zhang T., Zhang Y.R.et al. Metabolic syndrome and risk for ED: a meta-analysis. Int J Impot Res2014;265: 196-200
- 6. Silva A.B., Sousa N., Azevedo L.F.et al. Physical activity and exercise for erectile dysfunction: systematic review and meta-analysis. Br J Sports Med2017;51: 1419- 1424
- 7. Eardley I. The incidence, prevalence, and natural history of erectile dysfunction. Sex Med Rev. 2013;1(1):3-16
- 8. Leoni, L. A. B., Fukushima, A. R., Rocha, L. Y., Maifrino, L. B. M. M., & Rodrigues, B. (2014). Physical activity on endothelial and erectile dysfunction: a literature review. The Aging Male, 17(3), 125–130. https://doi.org/10.3109/13685538.2014.923836
- 9. Bacon CG, Mittleman MA, Kawachi I, Giovannucci E, Glasser DB, Rimm EB. Sexual function in men older than 50 years of age: results from the health professionals follow-up study. Ann Intern Med. 2003;139(3):161-168.
- 10. Kendirci M, Nowfar S, Hellstrom WJ. The impact of vascular risk factors on erectile function. Drugs Today 2005;41:65–74
- 11. Panchatsharam PK, Durland J, Zito PM. Physiology, Erection. In: StatPearls. StatPearls Publishing, Treasure Island (FL); 2023. PMID: 30020650.

- 12. Annamaria Morelli, Sandra Filippi, Linda Vignozzi, Rosa Mancina, Mario Maggi, Physiology of Erectile Function: An Update on Intracellular Molecular Processes, EAU-EBU Update Series, Volume 4, Issue 3, 2006, Pages 96-108, ISSN 1871-2592, https://doi.org/10.1016/j.eeus.2006.03.003.
- 13. Shamloul R, Ghanem H. Erectile dysfunction Lancet. 2013;381:153–65
- 14. Calogero, A. E., Burgio, G., Condorelli, R. A., Cannarella, R., & La Vignera, S. (2018). Epidemiology and risk factors of lower urinary tract symptoms/benign prostatic hyperplasia and erectile dysfunction. The Aging Male, 22(1), 12–19. https://doi.org/10.1080/13685538.2018.1434772
- 15. Meldrum DR, Gambone JC, Morris MA, Meldrum DA, Esposito K, et al The link between erectile and cardiovascular health: the canary in the coal mine Am J Cardiol. 2011;108:599–606
- 16. Doumas M, Douma S. Sexual dysfunction in essential hypertension: myth or reality? J Clin Hypertens 2006;8:269–74
- 17. Montague DK, Jarow JP, Broderick GA, et al.; for the Erectile Dysfunction Guideline Update Panel. Chapter 1: The management of erectile dysfunction: an AUA update. J Urol. 2005;174(1):230-239
- 18. McVary KT. Clinical practice. Erectile dysfunction. N Engl J Med. 2007;357(24):2472
- 19. Jardin A, Wagner G, Khoury S, et al. Recommendations of the 1st International Consultation on Erectile Dysfunction. In: Jardin A, Wagner G, Khoury S, et al., eds. Erectile Dysfunction. Plymouth, U.K.: Health Publication Ltd, 2000:711–726.
- 20. Rosen RC, Cappelleri JC, Smith MD, Lipsky J, Peña BM. Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. *Int J Impot Res.* 1999;11(6):319-326.
- 21. Carson CC, Lue TF. Phosphodiesterase type 5 inhibitors for erectile dysfunction. BJU Int. 2005;96(3):257-280
- 22. Esposito K, Giugliano F, Di Palo C, et al. Effect of lifestyle changes on erectile dysfunction in obese men: a randomized controlled trial. JAMA. 2004;291(24):2978-2984
- 23. Vardi M, Nini A. Phosphodiesterase inhibitors for erectile dysfunction in patients with diabetes mellitus. Cochrane Database Syst Rev. 2007;1:CD002187.
- 24. Goldstein I, Lue TF, Padma-Nathan H, Rosen RC, Steers WD, Wicker PA for the Sildenafil Study Group. Oral sildenafil in the treatment of erectile dysfunction [published correction appears in N Engl J Med. 1998;239(1):59]. N Engl J Med. 1998;338(20):1397-1404
- 25. Raja SG, Nayak SH. Sildenafil: emerging cardiovascular indications. Ann Thorac Surg 2004;78:1496–506
- 26. Kontaras K, Varnavas V, Kyriakides ZS. Does sildenafil cause myocardial infarction or sudden cardiac death? Am J Cardiovasc Drugs 2008;8:1–7
- 27. Lee TM, Chen CC, Chung TH, Chang NC. Effect of sildenafil on ventricular arrhythmias in post-infarcted rat hearts. Eur J Pharmacol 2012;690:124–32
- 28. Vlachopoulos C, Terentes-Printzios D, Ioakeimidis N, et al. PDE5 inhibitors in non-urological conditions. Curr Pharm Des 2009;15:3521–39

- 29. DeLay KJ, Haney N, Hellstrom WJ. Modifying risk factors in the management of erectile dysfunction: a review. World J Mens Health. 2016;34:89–100.
- 30. Jain P, Rademaker AW, McVary KT. Testosterone supplementation for erectile dysfunction: results of a meta-analysis. J Urol. 2000;164(2):371-375
- 31. Earle CM, Stuckey BG. Biochemical screening in the assessment of erectile dysfunction: what tests decide future therapy?. Urology. 2003;62(4):727-731
- 32. Boloña ER, Uraga MV, Haddad RM, et al. Testosterone use in men with sexual dysfunction: a systematic review and meta-analysis of randomized placebo-controlled trials. Mayo Clin Proc. 2007;82(1):20-28
- 33. Leisegang, K., & Finelli, R. (2021). Alternative medicine and herbal remedies in the treatment of erectile dysfunction: A systematic review. Arab Journal of Urology, 19(3), 323–339. https://doi.org/10.1080/2090598X.2021.1926753
- 34. Hong B, Ji YH, Hong JH, Nam KY, Ahn TY. A double-blind crossover study evaluating the efficacy of korean red ginseng in patients with erectile dysfunction: a preliminary report. J Urol. 2002;168(5):2070-2073
- 35. Rosen RC. Psychogenic erectile dysfunction. Classification and management. Urol Clin North Am. 2001;28(2):269-278
- 36. Melnik T, Soares BGO, Nasselo AG. Psychosocial interventions for erectile dysfunction. Cochrane Database Syst Rev. 2007;3:CD004825
- 37. Makhlouf A, Kparker A, Niederberger CS. Depression and erectile dysfunction. Urol Clin North Am. 2007;34(4):565-574
- 38. Larsen SH, Wagner G, Heitmann BL. Sexual function and obesity Int J Obes (Lond). 2007;31:1189–98
- 39. Esposito K, Giugliano D. Obesity, the metabolic syndrome, and sexual dysfunction in men Clin Pharmacol Ther. 2011;90:169–73
- 40. Wang F, Dai S, Wang M, Morrison H. Erectile dysfunction and fruit/vegetable consumption among diabetic Canadian men Urology. 2013;82:1330–5
- 41. Giugliano F, Maiorino MI, Bellastella G, Autorino R, De Sio M, et al Adherence to Mediterranean diet and erectile dysfunction in men with type 2 diabetes J Sex Med. 2010;7:1911–7
- 42. Esposito K, Giugliano F, De Sio M, Carleo D, Di Palo C, et al Dietary factors in erectile dysfunction Int J Impot Res. 2006;18:370–4
- 43. Lopez-Garcia E, Hu FB. Nutrition and the endothelium Curr Diab Rep. 2004;4:253–9
- 44. Esposito K, Giugliano D. Diet and inflammation: a link to metabolic and cardiovascular diseases Eur Heart J. 2006;27:15–20
- 45. Johannes CB, Araujo AB, Feldman HA, Derby CA, Kleinman KP, McKinlay JB. Incidence of erectile dysfunction in men 40 to 69 years old: longitudinal results from the Massachusetts male aging study. *J Urol.* 2000;163(2):460-463
- 46. Polsky JY, Aronson KJ, Heaton JP, Adams MA. Smoking and other lifestyle factors in relation to erectile dysfunction BJU Int. 2005;96:1355–9
- 47. Kupelian V, Link CL, McKinlay JB. Association between smoking, passive smoking, and erectile dysfunction: results from the Boston Area Community Health (BACH) Survey Eur Urol. 2007;52:416–22

- 48. Harte CB, Meston CM. Association between smoking cessation and sexual health in men BJU Int. 2012;109:888–96
- 49. Kalter-Leibovici O, Wainstein J, Ziv A, Harman-Bohem I, Murad H, et al Clinical, socioeconomic, and lifestyle parameters associated with erectile dysfunction among diabetic men Diabetes Care. 2005;28:1739–44
- 50. Cheng JY, Ng EM, Chen RY, Ko JS. Alcohol consumption and erectile dysfunction: meta-analysis of population-based studies Int J Impot Res. 2007;19:343–52
- 51. Meldrum DR, Gambone JC, Morris MA, Esposito K, Giugliano D, et al Lifestyle and metabolic approaches to maximizing erectile and vascular health Int J Impot Res. 2012;24:61–8
- 52. Meldrum DR, Burnett AL, Dorey G, Esposito K, Ignarro LJ. Erectile hydraulics: maximizing inflow while minimizing outflow J Sex Med. 2014;11:1208–20
- 53. Esposito K, Ciotola M, Giugliano F, Maiorino MI, Autorino R, et al Effects of intensive lifestyle changes on erectile dysfunction in men J Sex Med. 2009;6:243–50
- 54. Van Craenenbroeck EM, Conraads VM. Endothelial progenitor cells in vascular health: focus on lifestyle Microvasc Res. 2010;79:184–92
- 55. Cooney GM, Dwan K, Greig CA, Lawlor DA, Rimer J, et al Exercise for depression Cochrane Database Syst Rev. 2013;9:CD004366 doi: 10.1002/14651858
- 56. Cornelissen VA, Fagard RH. Effects of endurance training on blood pressure, blood pressure-regulating mechanisms, and cardiovascular risk factors. *Hypertension*. 2005; 46: 667–675.
- 57. Durstine JL, Grandjean PW, Davis PG, Ferguson MA, Alderson NL, DuBose KD. Blood lipid and lipoprotein adaptations to exercise: a quantitative analysis. *Sports Med*. 2001; 31: 1033–1062.
- 58. Hamer M.. The relative influences of fitness and fatness on inflammatory factors. *Prev Med.* 2007; 44: 3–11.
- 59. Nelson ME, Rejeski WJ, Blair SN, Duncan PW, Judge JO, King AC, Macera CA, Castaneda-Sceppa C.; American College of Sports Medicine; American Heart Association. Physical activity and public health in older adults: Recommendation from the American College of Sports Medicine and the American Heart Association. *Circulation*. 2007; 116: 1094–105.
- 60. Autenrieth C., Schneider A., Döring A., Meisinger C., Herder C., Koenig W., Huber G., Thorand B.. Association between different domains of physical activity and markers of inflammation. *Med Sci Sports Exerc*. 2009; 41: 1706–1713.
- 61. Cheng JY, Ng EM, Ko JS, Chen RY. Physical activity and erectile dysfunction: meta-analysis of population-based studies Int J Impot Res. 2007;19:245–52
- 62. Feldman HA, Johannes CB, Derby CA, Kleinman KP, Mohr BA, et al Erectile dysfunction and coronary risk factors: prospective results from the Massachusetts male aging study Prev Med. 2000;30:328–38
- 63. Bacon CG, Mittleman MA, Kawachi I, Giovannucci E, Glasser DB, et al A prospective study of risk factors for erectile dysfunction J Urol. 2006;176:217–21
- 64. Ponholzer A, Temml C, Mock K, Marszalek M, Obermayr R, et al Prevalence and risk factors for erectile dysfunction in 2869 men using a validated questionnaire Eur Urol. 2005;47:80–5

- 65. Helle Gerbild, Camilla Marie Larsen, Christian Graugaard, Kristina Areskoug Josefsson, Physical Activity to Improve Erectile Function: A Systematic Review of Intervention Studies, *Sexual Medicine*, Volume 6, Issue 2, June 2018, Pages 75–89, https://doi.org/10.1016/j.esxm.2018.02.001
- 66. Mingming Zhang, Zichun Wang, Wanpeng Liu, Minglei Wang, Huaying Wu, Ruihua An, (2024) Association between the recommended volume of leisure-time physical activity and erectile dysfunction: A cross-sectional analysis of the national health and nutrition examination survey, 2001–2004, Heliyon, Volume 10, Issue 12, e32884, ISSN 2405-8440, https://doi.org/10.1016/j.heliyon.2024.e32884
- 67. La Vignera, S., Condorelli, R., Vicari, E., D'agata, R., & Calogero, A. (2011). Aerobic physical activity improves endothelial function in the middle-aged patients with erectile dysfunction. The Aging Male, 14(4), 265–272. https://doi.org/10.3109/13685538.2010.544344