Erectile Dysfunction

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Erectile Dysfunction (ED): Definition1

- “. . .the inability to attain and/or maintain penile erection sufficient for satisfactory sexual performance”
- A 3-month duration of these symptoms is accepted for establishing diagnosis

"The risk of having ED increases with age, but it affects men of all ages and ethnicities. As ED is actually a common male medical condition, it is surprising that a majority does not know what ED is," comments Prof. Christopher Chapple, Secretary General of the EAU.2

Ref 1:EAU Guidelines on Male Sexual Dysfunction – 2018
Ref 2: https://www.eurekalert.org/news-releases/699827

EVOLUTION OF TREATMENT
CHANGING MINDSET

	Timeline	Treatment	Goal
Desperation ↓	• Pre 1960s	Early surgery/ natural remedies	Any improvement ↓
↓	• 1960s	Pumps	
↓	• 1960s / 70s	Implants	
↓	• 1980s	Injections	Successful Erection ↓
↓	• Mid-1990s	Prescribed Injections	
	• 1998	Oral agents	
Expectation	• 21st	Future	Normal sex

Epidemiology

- It is estimated that ED has affected more than 150 million men worldwide and this number will reach approximately 322 million by 2025
- 11½ million men in Africa are diagnosed with ED
- In men attending primary care clinics in Western Cape, 70% had experienced some degree of ED
- Complete inability to attain and/or maintain an erection:

Age 40: 1 in 20 men

Age 70: 1 in 7 men

NEWS RELEASE 21-SEP-2020

European survey shows alarmingly low awareness of erectile dysfunction

Risk Factors

ED and IHD share the same risk factors. Endothelial dysfunction is the common link between ED and IHD.

Risk Factors include:

1. Age
2. Obesity
3. Smoking
4. Hypertension
5. Cholesterol
6. Psychological – Depression, low self esteem, social stresses
7. Diabetes

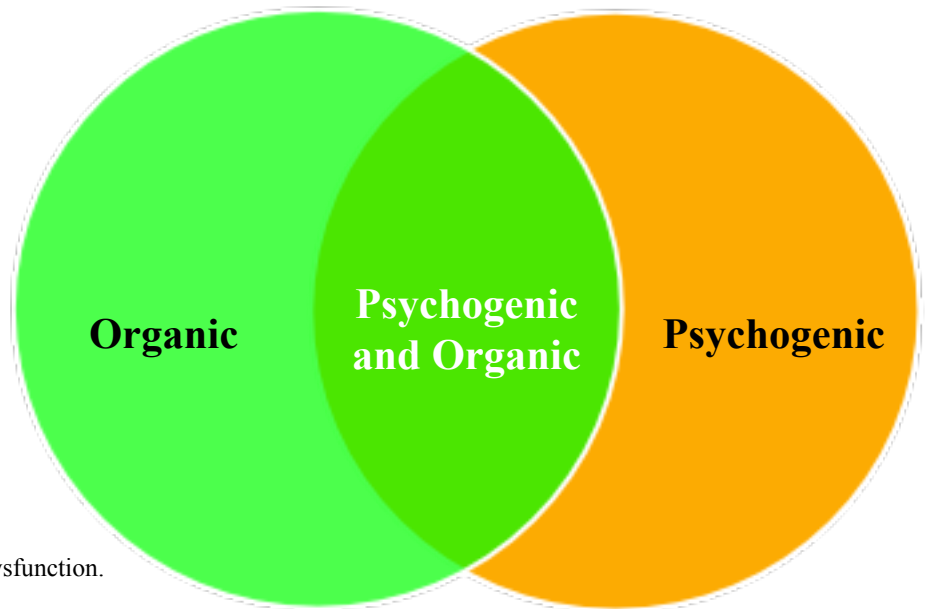
Why it is important to identify men with ED1,2

- ED can be associated with morbidity
  - anxiety and depression
  - decreased self-esteem
  - negative effect on relationships
- ED screenings may also uncover underlying diseases
  - diabetes
  - hypertension
  - dyslipidemia and CVD
  - certain malignancies
- Identifying ED can reveal medication and compliance issues

Ref 1: Goldstein I et al. N Engl J Med 1998; 338: 1397–1404
Ref 2: Shabsigh R et al. Urology 1998; 52: 848–852 NIH Consensus Development Panel. JAMA 1993; 270: 83–90

Etiology of ED: Psychogenic and Organic

- ED commonly involves a combination of psychogenic and organic factors



ED=Erectile dysfunction.

Tiefer L, Schuetz-Mueller D. *Urol Clin North Am* 1995;22:767-773.

Normal Male Sexual Function requires:

1) An intact Libido

2) Detumescence - the process of subsiding from a state of tension, swelling, or (especially) sexual arousal.

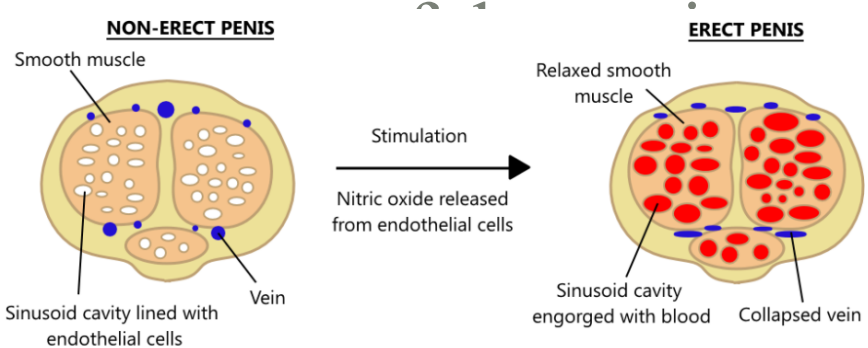
3) Ability to achieve and maintain penile Erection

4) Ejaculation :

- Parasympathetic nerves S2-4 mediate erection
- Sympathetic nerves T11-L2 control ejaculation and detumescence

Physiology of an erection

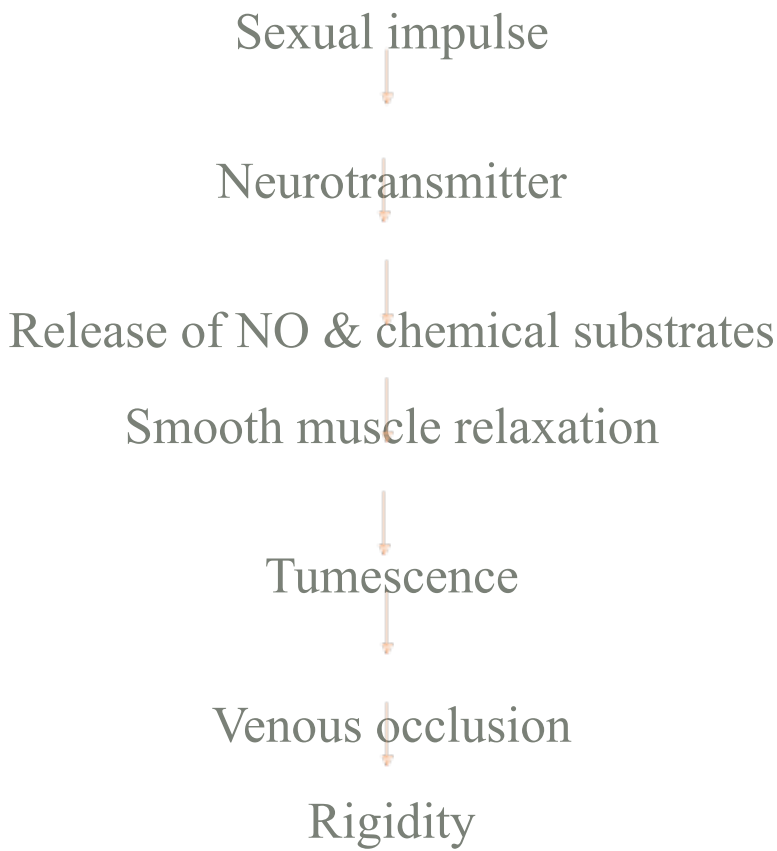
- Penile erection is a neurovascular event modulated by psychological factors and hormonal status.
- The corpora [illegible] ains a network of smooth mus [illegible] and sinusoid cavities



- When stimulated, endothelial cells release nitric oxide which causes smooth muscle cells to relax (dilate)
- Relaxed smooth muscle cells allow the sinusoids to fill

Reference: https://www.straighthealthcare.com/erectile-dysfunction.html

Normal Pathway to erection



Types of ED1

- ED can be primary or secondary
- Lack of sex hormone in the early developmental stage of male children is the major cause of primary ED.
- Secondary ED – a person develops ED after a period of normal function. 1
- The secondary cause of ED involves arteriosclerosis, diabetes or psychogenic disturbances. Other secondary factors may include hypertension, hyperlipidaemia, obesity and tobacco use.

Ref 1: Abdalla Ibrahim, Mohamed Ali, Thomas J Kiernan, Austin G Stack, Erectile Dysfunction and Ischaemic Heart Disease, *European Cardiology Review 2018;13(2):98–103.*https://doi.org/10.15420/ecr.2017.21.3

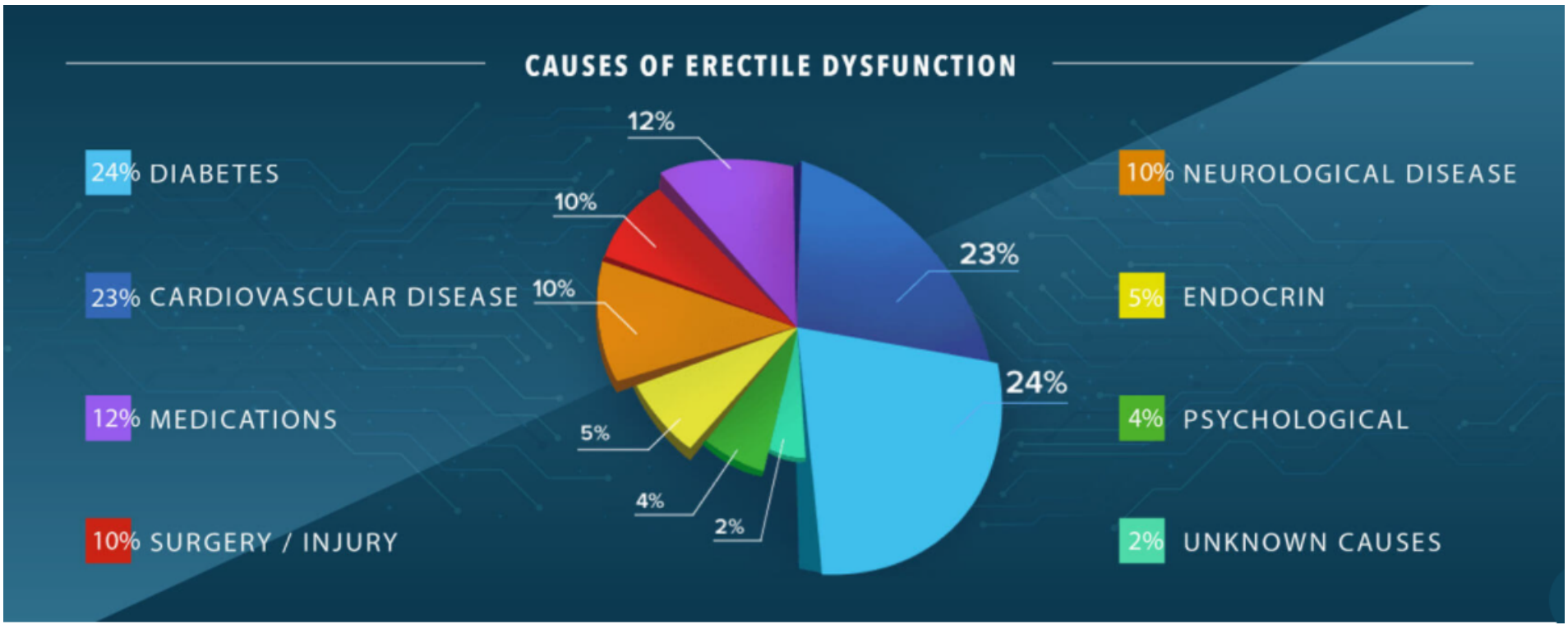
Organic Causes of ED1

- Vascular
- Neurogenic
- Hormonal
- Penile injury/disease
- Medications

ED=Erectile dysfunction.

Ref 1: Gratzke, C., et al. Anatomy, physiology, and pathophysiology of erectile dysfunction. J Sex Med, 2010. 7: 445.

CAUSES OF ED:



Reference : https://www.bostonmedicalgroup.com/erectile-dysfunction. Date accessed 18 January 2022

ED = a Marker for CVD

Penile Artery (1-2mm)

Coronary Artery (3-4mm)

Internal Carotid Artery (5-7mm)

Femoral Artery (6-8mm)

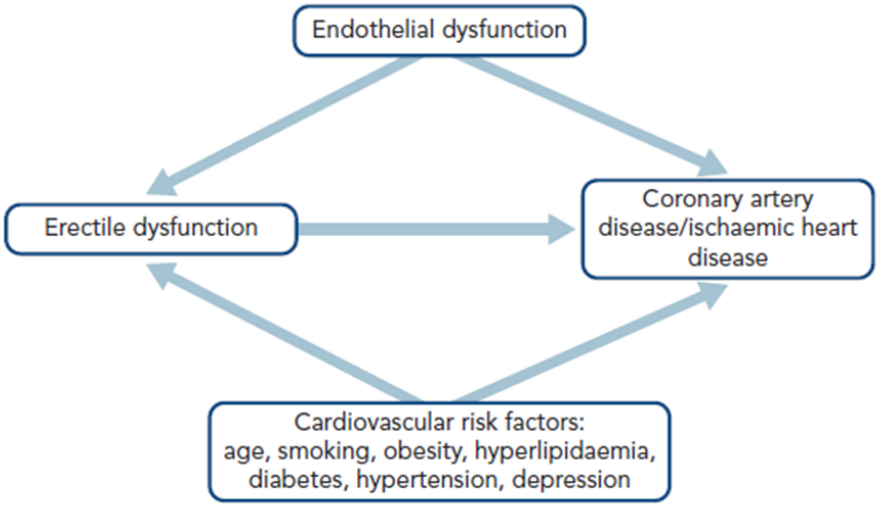
Montorsi et al, 2004

IHD & ED

- Ischaemic heart disease (IHD) or coronary artery disease (CAD), is a predominant manifestation of cardiovascular disease (CVD).
- ED and IHD are highly prevalent and occur concomitantly because they share the same risk factors, including diabetes, hypertension, hyperlipidaemia, obesity and smoking
- ED has been shown to occur at rates as high as 50 % in patients with CAD.2 A meta-analysis of 12 prospective cohort studies has provided evidence that ED is a predictor of IHD associated with an increased risk of CVD, stroke and all-cause mortality

Ref 1:Abdalla Ibrahim, Mohamed Ali, Thomas J Kiernan, Austin G Stack, Erectile Dysfunction and Ischaemic Heart Disease, European Cardiology Review 2018;13
103.https://doi.org/10.15420/ecr.2017.21.3
Ref 2 : Montorsi P, Ravagnani PM, Galli S, et al. Common grounds for erectile dysfunction and coronary artery disease. Curr Opinion Urol 2004;14:361–5.
PubMed

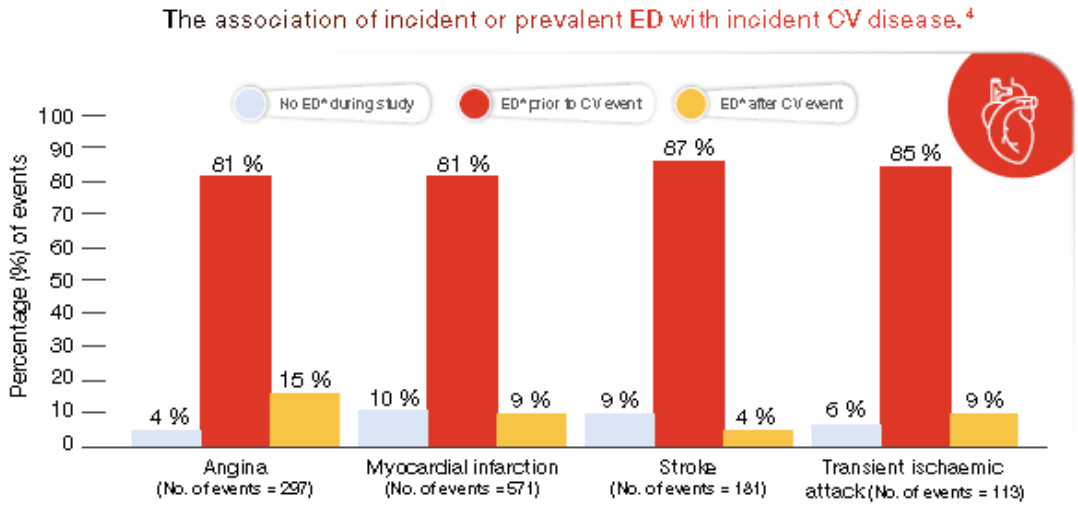
Figure 1: Risk Factors Associated with Erectile Dysfunction and Ischaemic Heart Disease



- A study that examined the association between ED and asymptomatic CAD showed that 67 % of patients had ED for a mean 38.8 months before developing symptoms of CAD.
- Interestingly, all patients with type 1 diabetes in this study had ED well before symptoms of CAD2

Ref 1: Abdalla Ibrahim, Mohamed Ali, Thomas J Kiernan, Austin G Stack, Erectile Dysfunction and Ischaemic Heart Disease, *European Cardiology Review 2018;13(2):98–103*.https://doi.org/10.15420/ecr.2017.21.3
Ref 2: Montorsi F, Briganti A, Salonia A, et al. Erectile dysfunction prevalence, time of onset and association with risk factors in 300 consecutive patients with acute chest pain and

In a study to examine the association of erectile dysfunction and subsequent cardiovascular disease, 9457 men were randomized to a placebo group in the Prostate Cancer Prevention Trial at 221 US centers. They were evaluated every 3 months for cardiovascular disease and erectile dysfunction between 1994 and 2003.



Conclusion Erectile dysfunction is an efficient predictor of coronary artery disease

ED Is Associated With Other Serious Treatable Disorders

- 60% of men with ED have dyslipidemia1,2
- 56% of men with ED have a positive cardiovascular stress test3
- 42% of men with ED have hypertension5
- 40% of men with ED have significant coronary occlusions2,3
- 20% of men with ED have diabetes mellitus4,5
- 11% of men with ED have depression5

ED=Erectile dysfunction.

1. Billups K, Friedrich S. *J Urol* 2000;163:Abstract 655.
2. Levine L, Kloner R. *Am J Cardiol* 2000;86:1210-1213 .
3. Pritzker MR. *Circulation* 1999;100(suppl I):I-711. Abstract 3751.

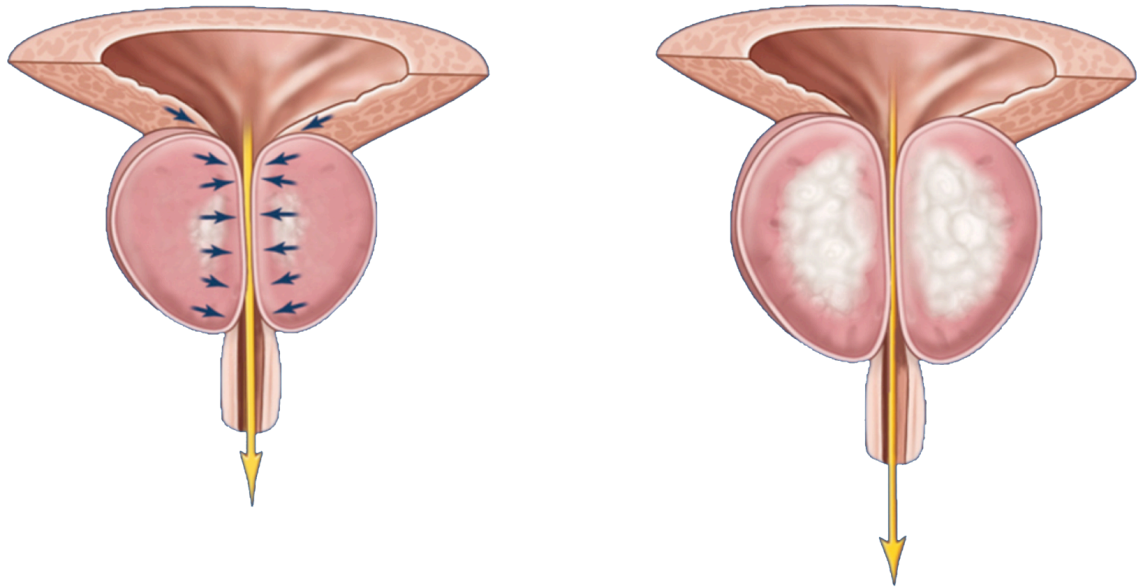
ED & Benign Prostatic Hyperplasia

- There are strong epidemiological data showing that LUTS/BPH is a risk factor for developing ED.1
- Phosphodiesterase 5 inhibitors (PDE5Is) increase intracellular cyclic G.M.P - Act by reducing smooth muscle tone of the detrusor, prostate and urethra. Several RCTs have demonstrated that PDE5I's reduce IPSS, storage and voiding LUTS

Ref 1: Glina S, Glina FP. Pathogenic mechanisms linking benign prostatic hyperplasia, lower urinary tract symptoms and erectile dysfunction. Ther Adv Urol. 2013 Aug;5(4):211-8. doi: 10.1177/1756287213488236. PMID: 23904860; PMCID: PMC3721438.

Ref 2: Lerner LB, McVary, KT, Barry MJ et al: Management of lower urinary tract symptoms attributed to benign prostatic hyperplasia: AUA Guideline part I, initial work-up and medical management. J Urol 2021; 206: 806.

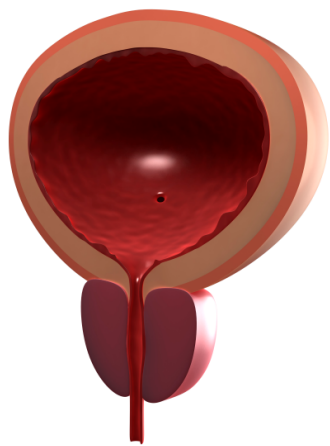
BPH Components – Static and Dynamic Obstruction

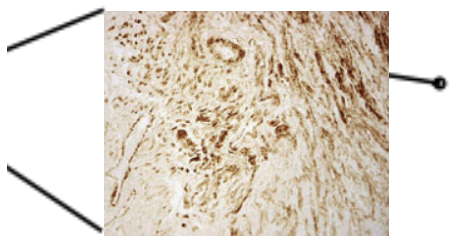


BPH = Benign Prostatic Hyperplasia

Localization of PDE5: Implications for BPH-LUTS

- PDE5 enzyme blocks nitric oxide mediated smooth muscle relaxation
- The PDE5 enzyme is found in tissues of the:1
- Penis
- Bladder
- Prostate
- Urethra



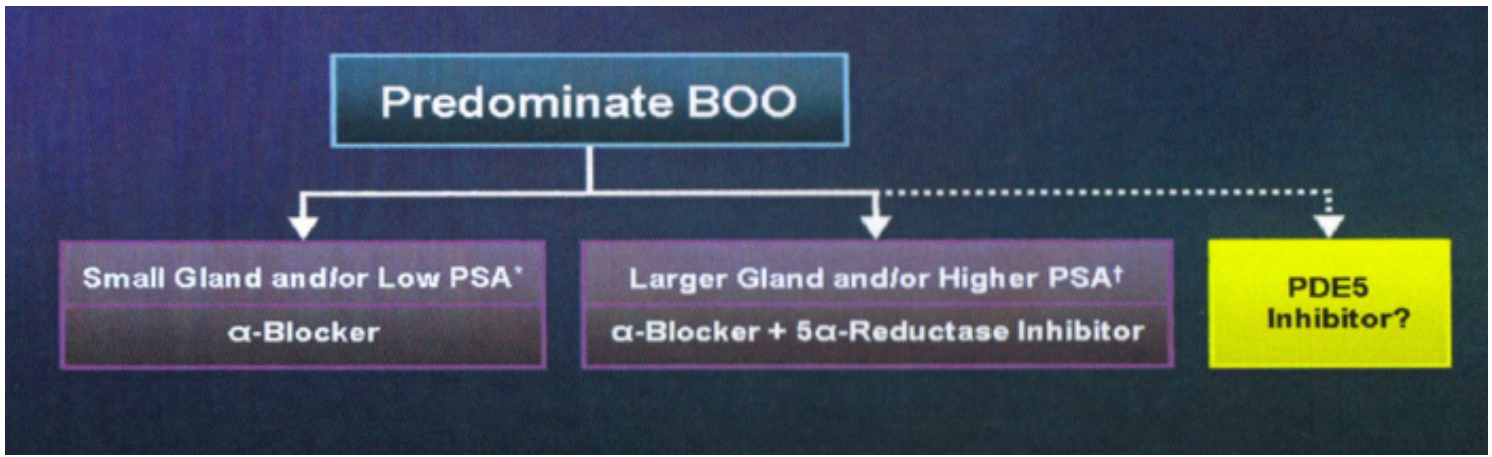


PDE5: phosphodiesterase 5.

1. Fibbi et al. *J Sex Med* 2010;7:59-69.

LUTS-BPH TREATMENT OPTIONS

Role of the PDE5-inhibitor



*PSA <1.5 ng/mL; †PSA >1.5 ng/mL
Crawford ED, et al. *Urology*. 2006;175(4):1422-1427; Roehrborn CG, et al. *Eur Urol*. 2009;55(2):461-471.

American Urological Association Guideline:

- *For patients with LUTS/BPH irrespective of comorbid erectile dysfunction (ED), 5mg daily tadalafil should be discussed as a treatment option1*

Ref `1: Lerner LB, McVary, KT, Barry MJ et al: Management of lower urinary tract symptoms attributed to benign prostatic hyperplasia: AUA Guideline part I, initial work-up and medical management. J Urol 2021; 206: 806

THORNY ISSUES

Gender differences in sexuality

Men

- **Genital-focused**
- **Performance-orientated**
- **Orgasm mandatory**
- **Visual stimulus has primacy**
- **Tactile stimulus often distracting**
- **Testosterone 8.4 – 28.7 nmol/L**

Women

- Intimacy-focused
- Sex viewed in a broader context
- Orgasm optional
- Visual stimulus often distracting
- Tactile stimulus (not exclusively genital) has primacy
- Testosterone 0.5 – 2.6 nmol/L

Gender and response to ED

Men

- Guilt
- Fear
- Loss of confidence
- Performance pressure
- Avoidance of sex
- Withdrawal from intimacy

Women

- Guilt
- Feels inadequate
- Feels less attractive
- Problem solving behaviour
- Feeling of rejection
- Sadness because of loss of intimacy

Difference in perception/needs between Females and Males

- **Females**
  - **Love**
  - **Communication**
  - **Intimacy**
  - **Appearance**
  - **Relationship oriented**
  - **In event of stress – need to communicate**
  - **Ego needs refer to pampering, understanding**
  - **Interpretation more on emotional levels**

- **Males**
  - **Competent**
  - **Control**
  - **Success**
  - **Power**
  - **Goal oriented**
  - **In event of stress – create distance**
  - **Ego needs refer to appreciation, acceptance**
  - **Interpretation more on factual basis**

Viljoen: Rome 2003

YOU DIDNT SAVE ANYTHING
FOR RETIREMENT DID YOU??

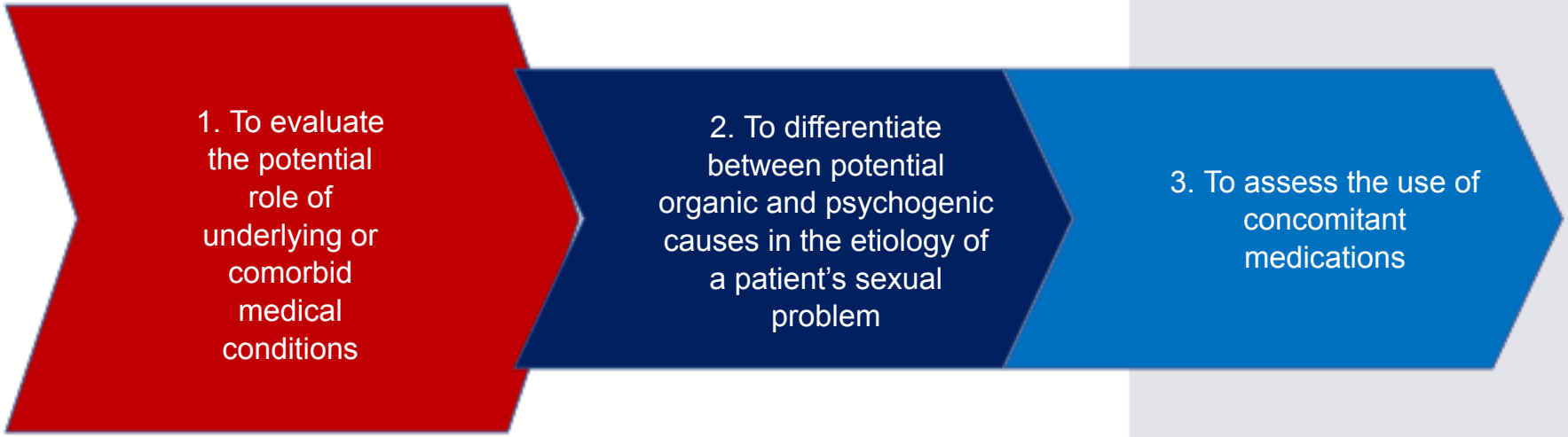
Diagnosis

1. History
   - Medical, surgical, psychiatric, medication, smoking, alcohol, drug use

2. Physical Exam- (includes the abdomen, penis, prostate, rectum, and testicles).
   - If the penis does not respond as expected to certain touch stimuli, there may be a problem with the nervous system.
   - Abnormal secondary sex characteristics, such as loss of armpit or pubic hair, can suggest problems in the endocrine system affecting hormone levels.
   - A circulatory problem might be indicated by, for example, an aneurysm in the abdomen (such as disease of the large artery, the aorta, which supplies blood to the abdomen and lower limbs).

3. Routine Lab
   - blood counts, urine analysis, lipid profile, and measurement of liver enzymes and creatinine (a waste product of protein metabolism). If sexual desire is low, the levels of testosterone in the blood may be measured to determine if there are any endocrine abnormalities

Goals of medical history



-https://www.aafp.org/afp/2016/1115/p820.html#:~:text=Tobacco%20cessation%2C%20regular%20exercise%2C%20weight,include%20alprostadil%20and%20vacuum%20devices.

Tests

- [redacted]
- [redacted]lominantly psychological or physical.
- [redacted]their sleep; if these occur, the cause is more likely to be psychological. However, these tests are not completely reliable, and have not been [redacted]t has reduced the indications for penile tumescence testing drastically.

2. T[redacted]ns.

- [redacted]rasound and angiography (a radiographic technique for examining the anatomy of a blood vessel).

3. F[redacted] not well standardised and are generally done only at major medical centres.

4[redacted]recommended when a major psychological cause is suspected.

Assessment

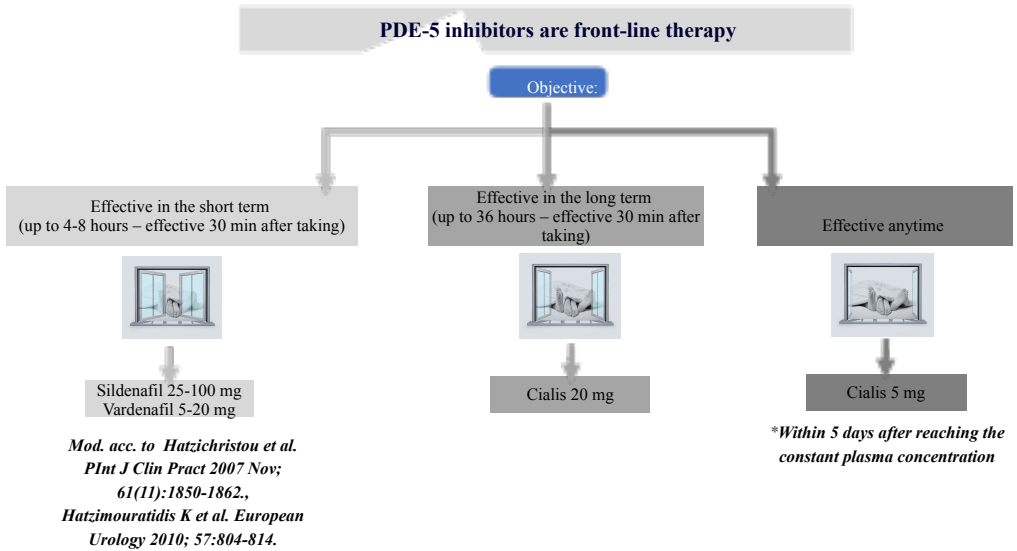
1. International Index of Erectile Function - IIEF 5

- The 15-question International Index of Erectile Function (IIEF) Questionnaire is a **validated, multi- dimensional, self-administered investigation** that has been found useful in the clinical assessment of erectile dysfunction and treatment outcomes in clinical trials.

Treatment of ED

- Identify and Treat Organic Comorbidities and other risk factors
- Counsel and Educate the Patient and Partner
- Identify and Treat any Psychosexual Dysfunctions
- Medications and Devices
- Surgery

Treatment Algorithm for Erectile Dysfunction (ED) (EAU guidelines) Which PDE5 ?



Comparison Of PDE-5 inhibitors

Medication	**Standard Dose**	**When to Take (h) Prior to Sex**	**Duration (h) of Action**	
Sildenafil	50-100 mg	1.0	≤ 4	
Tadalafil	10-20 mg	0.5 - 12	36	
Vardenafil	10-20	0.5-1.0	< 5	

Spontaneity and successful intercourse

Tadalafil, at doses from 5 mg to 20 mg versus placebo, significantly improved erectile function (EF) by all measures.

- 50%–65% of patients return to normal erectile function, irrespective of ED severity at baseline
- Almost 60%–90% of success rate at intercourse attempts during active treatment.

	Onset of action	Peak serum concentration	Elimination half-life
CIAVOR	15 minutes to 36 hours	2 hours post dose	18 hours
Other PDE5is	4-5 hours after dosing	1 hour post dose	5-6 hours

- Tadalafil is the only PDE-5 inhibitor that lasts up to 36 hours with a single dose[3]

	Earliest onset of action (min)	Duration of action (hours)
Tadalafil 20 mg	20	24-36 (up to 72)
Sildenafil 100 mg	30	4-6 (up to 12)
Vardenafil 20 mg	10	5-7 (up to 12)

Data from Raheem AA, *et al.*[4]

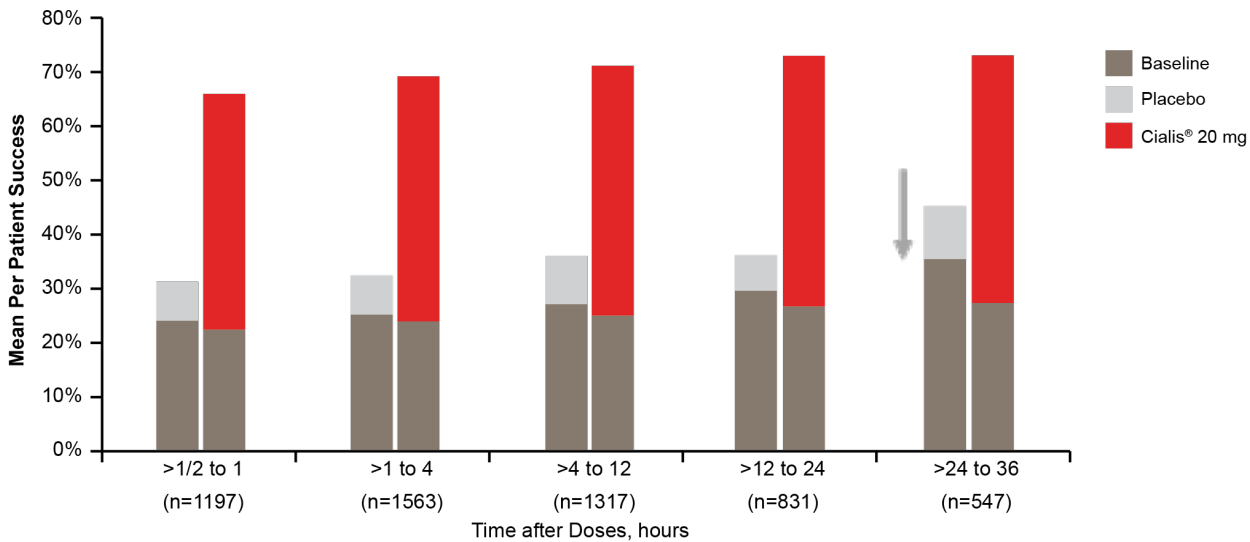
- Can conveniently be taken at any time of the day[5]

<u>Sexual spontaneity may be more easily restored</u>

- Long elimination half-life
- The rate and extent of absorption of tadalafil is not altered by food ingestion, age, diabetes, or mild to moderate hepatic insufficiency.

Success of Sexual Attempts Over Time (36 hours)

SEP3: "Did your erection last long enough for you to have successful intercourse?"



- Combined data from 11 multi-center, randomized, double blind, 12-week efficacy studies
- Men with ED were randomized to Cialis® 20 mg (n=1143) and placebo (n=638)

* <0.001 vs. placebo

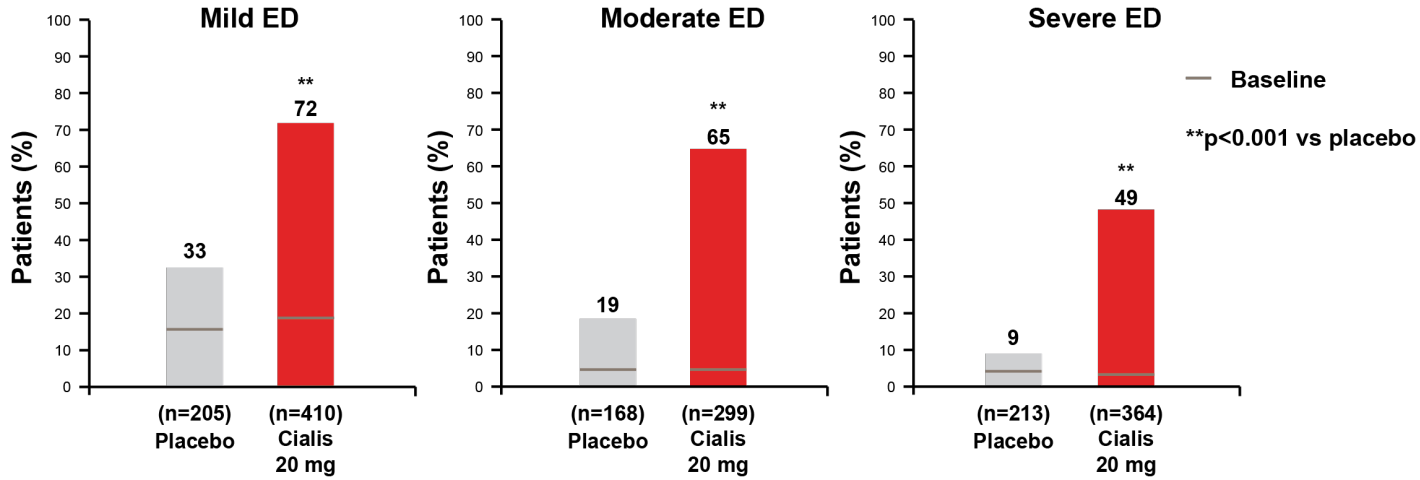
n=number of men attempting intercourse during each time frame

Tadalafil offers a broader window of opportunity for sexual encounters, i.e. up to 36 hours after dosing.1

1. Carson CC et al. *BJU Int*. 2004;93:1276-1281.

Satisfaction with Overall Sexual Experience Based on ED Severity

Moderately or Very Satisfied (IIEF Overall Satisfaction Domain)1



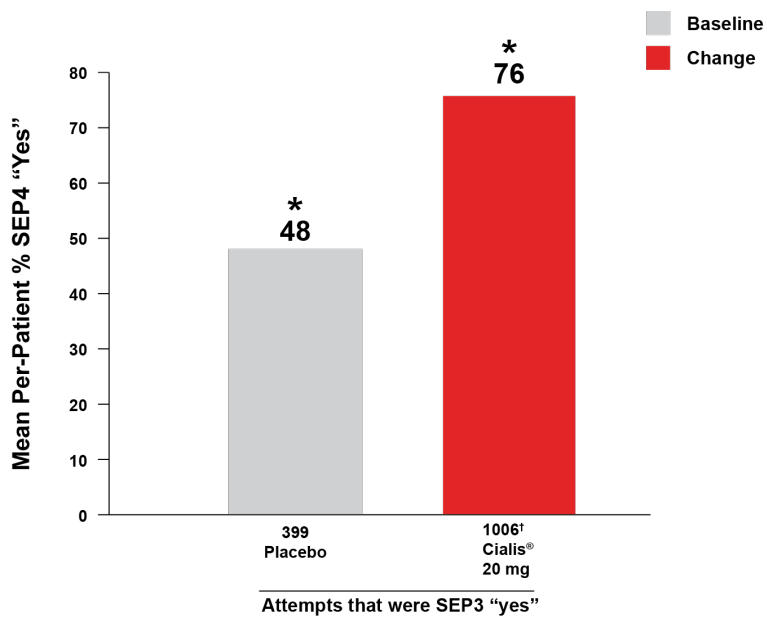
More Tadalafil-treated patients reported at least moderate overall satisfaction at endpoint compared with placebo-treated patients regardless of ED severity.

ED=Erectile dysfunction; IIEF=International Index of Erectile Function

1. Rosen RC et al. Curr Med Res Opin 2005;21:1701-1709.

Satisfaction with Overall Sexual Experience:

SEP5: were you satisfied overall with this sexual experience?



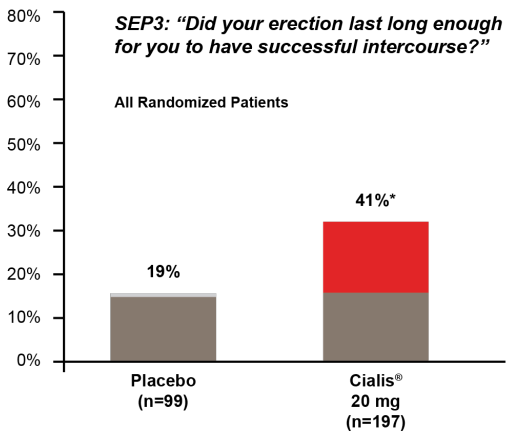
Men who reported successful intercourse with Tadalafil were significantly **more satisfied** with the **sexual experience** than the men who reported successful intercourse with Placebo.

* p<0.001 vs. placebo
† number of patients with
≥ 1 post-baseline success (SEP3)

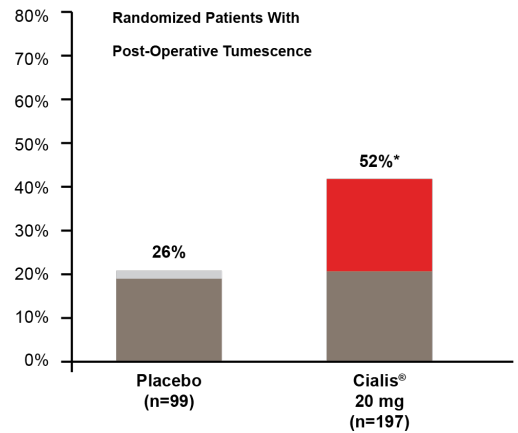
Porst H et al. J sex Med. 2005;2(SUPP 1):85.

Efficacy of Tadalafil 20 mg

Post-Prostatectomy



*p<0.001 vs. placebo



Dashed line within each bar represents baseline SEP3 score (% yes)

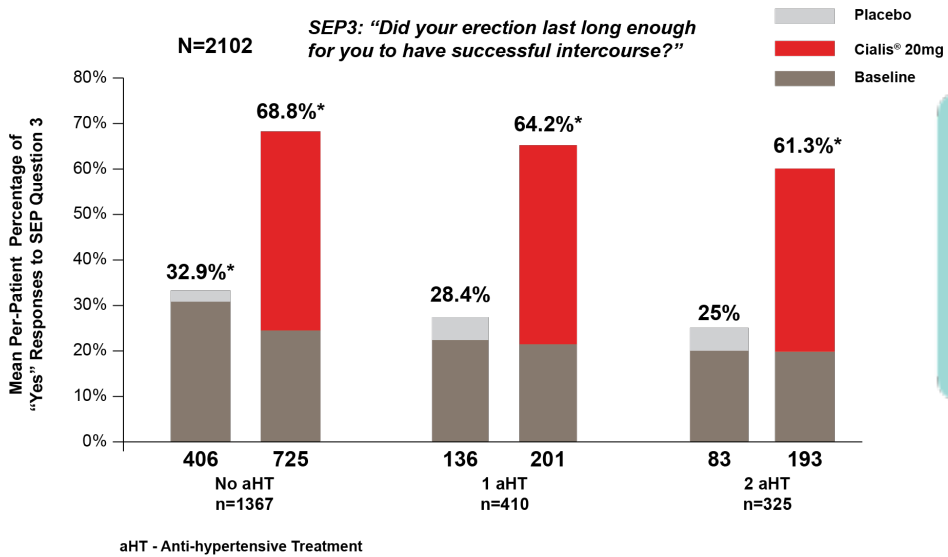
Tadalafil 20 mg taken on demand was an efficacious and well-tolerated treatment for ED following Bilateral Nerve-Sparing radical retropublic prostatectomy.

Montorsi et al, vol 172, 1036-1041, Sep 2004

See last page for important safety information about Cialis

Efficacy of Tadalafil 20mg

Men taking antihypertensive medications



Tadalafil 20mg worked equally well in patients whether they were taking none, one or multiple antihypertensives

*p<0.001 vs. placebo
**p=0.002 vs. placebo

‡Numbers shown below bus represent the number of patents in fiat category.

Number of subjects shown below each bar, dashed line within each bar represents baseline SEP3 score (% yes)

Lewis RW, et al. J Sex Med. 2005;2:517-531.

See last page for important safety information about Cialis


THANK
YOU!