CLINICAL PRACTICE GUIDELINES

2024

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Management of

ERECTILE DYSFUNCTION

Ministry of Health Malaysia

Malaysian Urological Association

Malaysian Family Medicine Specialists' Association

Academy of Medicine Malaysia

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https://www.acadmed.org.my

Also available as an app for Android and IOS platform: MyMaHTAS

STATEMENT OF INTENT
This clinical practice guidelines (CPG) is meant to be a guide for clinical practice based on the best available evidence at the time of development. The guideline should not override the responsibility of the practitioners to make decision appropriate to the circumstances of the individual. This should be done in consultation with the patients and their families or guardians, taking into account the management options available locally.

UPDATING THE CPG
These guidelines were issued in 2024 and will be reviewed in a minimum period of four years (2028) or sooner if there is a need to do so. When it is due for updating, the Chairman of the CPG or National Advisor of the related specialty will be informed about it. A discussion will be done on the need for a revision including the scope of the revised CPG. A multidisciplinary team will be formed and the latest systematic review methodology used by MaHTAS will be employed. Every care is taken to ensure that this publication is correct in every detail at the time of publication. However, in the event of errors or omissions, corrections will be published in the web version of this document, which is the definitive version at all times. This version can be found on the websites mentioned above.

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LEVELS OF EVIDENCE

Level	Study design
I	Properly powered and conducted randomised controlled trial; well-conducted systematic review or meta-analysis of homogeneous randomised controlled trials
II-1	Well-designed controlled trial without randomisation
II-2	Well-designed cohort or case-control analysis study
II-3	Multiple time series, with or without the intervention; results from uncontrolled studies that yield results of large magnitude
III	Opinions of respected authorities, based on clinical experience; descriptive studies or case reports; reports of expert committees

SOURCE: *U.S. Preventive Services Task Force. U.S. Preventive Services Task Force Procedure Manual. Rockville, MD: USPSTF; 2015.*

FORMULATION OF RECOMMENDATION

- In line with the new development in CPG methodology, the CPG Unit of MaHTAS is adapting **Grading Recommendations, Assessment, Development and Evaluation (GRADE)** in its work process. The quality of body of evidence and related effect size are carefully assessed/reviewed by the CPG DG.
- Recommendations are formulated based on **certainty of evidence** and the wording used denotes the **strength of recommendations**. This takes into account:
  - quality and level of the evidence
  - balance of benefits and harms of the options
  - patient's preference and values
  - resource implications
  - relevancy and applicability to the local target population
- The more criteria being fulfilled, the more certain is the evidence leading to strong recommendations using the word "**should**" being considered. Otherwise, weak recommendations use the word "**may**" in proposing an action to be made.
- In the CPG, a yellow box ☐ highlights important message(s) in the management while a blue box ☐ contains evidence-based recommendation(s) for the particular condition.

KEY RECOMMENDATIONS

The following recommendations are highlighted by the CPG DG as the key recommendations that answer the main questions addressed in the CPG and should be prioritised for implementation.

DIAGNOSIS AND ASSESSMENT

- A comprehensive medical, psychosocial and sexual history should be taken in every patient presenting with erectile dysfunction (ED).
- A validated questionnaire related to ED should be used to assess all sexual function domains (e.g. International Index of Erectile Function).
- A focused physical examination in the initial assessment of men with ED should be done to identify underlying medical conditions and co-morbid genital disorders that may be associated with ED.
- Routine laboratory tests should be performed to identify modifiable risk factors of ED.
- Patients with ED should have cardiac risk assessment and vice versa.

TREATMENT

- All patients with erectile dysfunction (ED) should be advised on lifestyle and risk factor modifications.
- Phosphodiesterase-5-inhibitor should be offered to all patients with ED unless contraindicated.
- Mechanical devices (e.g. using vacuum erection device or shockwave therapy) may be offered in ED. Low-intensity extracorporeal shockwave therapy should be performed by urologists for mild to moderate ED.
- Penile prothesis may be offered to patients with ED who have failed other interventions.
- An integrated and collaborative approach with psychological interventions should be considered in the treatment of ED.

GUIDELINES DEVELOPMENT AND OBJECTIVES

GUIDELINES DEVELOPMENT

The members of the DG for this CPG were from the Ministry of Health (MoH), the Ministry of Higher Education and the private sector. There was active involvement of a multidisciplinary Review Committee (RC) during the process of the CPG development.

A systematic literature search was carried out using the following electronic databases/platforms: mainly Medline via Ovid and others e.g. PubMed (refer to **Appendix 1** for **Example of Search Strategy**). The inclusion criteria are all adults at risk and with erectile dysfunction (ED) regardless of study design. The first search was limited to literature published in the last 15 years (2007 until 2022) for all clinical questions, on humans and in English. In addition, the reference lists of all retrieved literature and guidelines were searched to further identify relevant studies. Experts in the field were also contacted for studies related to the issues addressed. All searches were conducted from 2 to 17 August 2022. The literature search was repeated for all clinical questions at the end of the CPG development process allowing any relevant papers published before 9 January 2024 to be included. Future CPG updates will consider evidence published after this cut-off date. The details of the search strategy can be obtained upon request from the CPG Secretariat.

References were also made to other guidelines on ED as listed below:

- American Urological Association (AUA) - Erectile Dysfunction: AUA Guideline (2018)
- European Association of Urology (EAU) - EAU Guidelines on Sexual and Reproductive Health (2023)

A total of 12 main clinical questions were developed under different sections. Members of the DG were assigned individual questions within these sections. Refer to **Appendix 2** for **Clinical Questions**. The DG members met 21 times throughout the development of these guidelines. All literature retrieved was appraised by at least two DG members using the Critical Appraisal Skill Programme checklist, presented in evidence tables and further discussed in each DG meeting. All statements and recommendations formulated after that were agreed upon by both the DG and RC. Where evidence was insufficient, the recommendations were made by consensus of the DG and RC. Any differences in opinion are resolved consensually. The CPG was based largely on the findings of systematic reviews/meta-analyses and clinical trials, with local practices taken into consideration.

The literatures used in these guidelines were graded using the U. S. Preventive Services Task Force Level of Evidence (2015) while the grading of recommendation was done using the principles of GRADE as much as possible (refer to the preceding page). The writing of the CPG followed strictly the requirement of Appraisal of Guidelines for Research and Evaluation (AGREE) II.

Upon completion, the draft CPG was reviewed by external reviewers. It was also posted on the MoH Malaysia official website for feedback from any interested parties. The draft was finally presented to the Technical Advisory Committee for CPG and, the Health Technology Assessment (HTA) and CPG Council, MoH Malaysia, for review and approval. Details on the CPG development by MaHTAS can be obtained from the **Manual on Development and Implementation of Evidence-based Clinical Practice Guidelines** published in 2015 (available at https://www.moh.gov.my/moh/resources/CPG_MANUAL_MAHTAS.pdf).

OBJECTIVES

The objectives of the CPG are to provide evidence-based recommendations on the management of ED on the following aspects:
- risk and aggravating factors
- screening, diagnosis and assessment
- treatment
- monitoring and referral

CLINICAL QUESTIONS

Refer to **Appendix 2**.

TARGET POPULATION

Inclusion Criteria
- Patients with ED
- Special groups
  - ED patients with cardiac disease
  - ED patients with pelvic surgery or prostate cancer treatment
  - Spinal cord injury survivors

Exclusion Criteria
- Patients with disorders of ejaculation
- Patients with low sexual desire and male hypoactive sexual desire disorder
- Patients with genital anomalies or lesions

TARGET GROUP/USER

This document is intended to guide health professionals and relevant stakeholders in primary and secondary/tertiary care of both the public and private sectors in the management of ED including:
i. medical doctors
ii. allied health professionals
iii. trainees and medical students
iv. patients, partners and their advocates
v. professional societies
vi. policy makers

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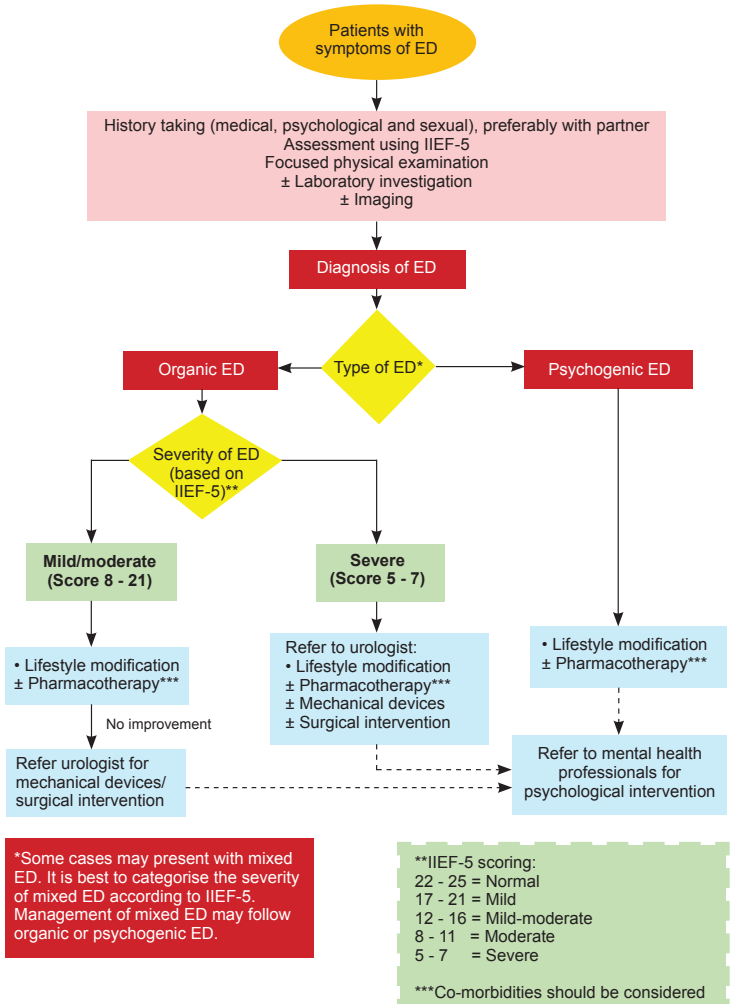
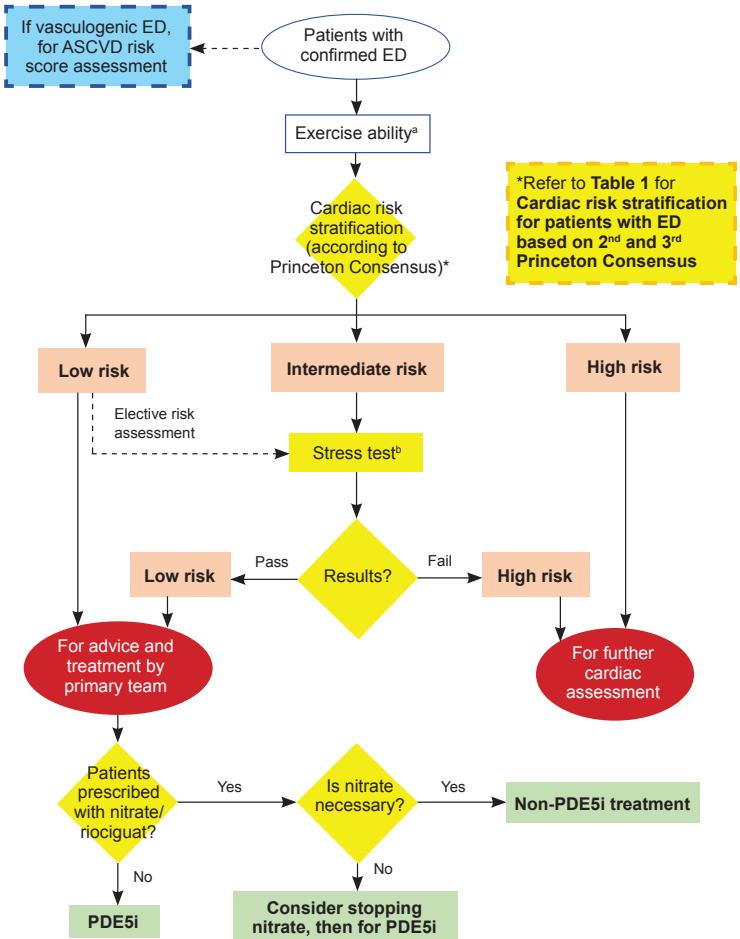
ALGORITHM 1: DIAGNOSIS AND TREATMENT OF ED



⋯⋯► May consider
ED = erectile dysfunction
IIEF-5 = 5-item version of International Index of Erectile Function

ALGORITHM 2: CLASSIFICATION FOR ED PATIENTS WITH CARDIOVASCULAR DISEASE



ASCVD = atherosclerotic cardiovascular disease; ED = erectile dysfunction; PDE5i = phosphodiesterase-5 inhibitors

[a] Exercise ability is used to guide physician estimating cardiovascular risk associated with sexual activity and should be established before the initiation of ED treatment. Sexual activity is equivalent to walking 1.6 kilometre (1 mile) on the flat in 20 minutes or briskly climbing two flights of stairs in 10 seconds.

[b] Sexual activity is equivalent to 4 minutes of the Bruce treadmill protocol. Pass is defined as completion of the test without symptoms, arrhythmias or a fall in systolic blood pressure.

1. INTRODUCTION

Erectile dysfunction (ED) is a prevalent and multifaceted medical condition characterised by the persistent inability to achieve or maintain an erection sufficient for satisfactory sexual performance. As a widespread health concern, ED substantially impacts the quality of life of affected individuals and their partners, leading to emotional distress, strained relationships and diminished overall well-being.[1, level III]

ED can manifest in various forms which can be due to organic, psychogenic and mixed aetiologies.[2] Organic ED may result from vascular, neurogenic, hormonal or anatomical factors, while psychogenic ED is often associated with psychosocial issues. Mixed ED involves a combination of both organic and psychogenic factors, making a comprehensive understanding of the condition crucial for effective management.

The pathophysiology of ED is complex, involving intricate interplay between vascular, neurologic, hormonal and psychological factors. Vascular insufficiency, endothelial dysfunction and altered smooth muscle tone are common contributors. Understanding these mechanisms is essential for tailoring therapeutic interventions to the specific needs of the patient.

In 1995, approximately 150 million men worldwide were estimated to be affected by ED and this is likely to double by 2025.[3, level III] Throughout Asia, there is variation in the prevalence rate of ED ranging between 2.0% and 81.8%.[4, level III] A local study at five government primary care clinics in Petaling District showed that the prevalence of ED for males aged 40 to 79 years old was 69.5%. It increased with age from 49.7% of men in their 40s to 66.5%, 92.8% and 93.9% of men in their 50s, 60s and 70s respectively.[5, level III] A recent study based on National Health and Morbidity Survey 2019 data revealed a prevalence of moderate to severe ED in men aged ≥18 years at 31.6% (95% CI 28.8 to 34.6).[6, level III]

The burden of ED extends beyond its physical manifestations, impacting the mental and emotional well-being of individuals. It is associated with co- morbidities e.g. diabetes mellitus (DM), cardiovascular diseases (CVDs) and depression. Moreover, ED is known to be an early marker of systemic vascular dysfunction, emphasising the importance of timely diagnosis and intervention.[2]

Clinical practices for the diagnosis and treatment of ED can vary significantly, reflecting differences in healthcare systems, cultural perceptions and access to resources. Recognising and addressing these variations is crucial to ensure equitable and effective care for the affected individuals.

In conclusion, this CPG on Management of ED endeavours to provide a systematic and culturally sensitive approach to the diagnosis and treatment of ED. It is hoped that this CPG can help in optimising resource utilisation by providing evidence-based recommendations for efficient and safe management of ED. Eventually, this will lead to standardised care, improved patient outcomes and reduced the burden of ED on affected individuals, their partners and the healthcare system.

2. RISK FACTORS

There are various risk factors associated with ED e.g. age, lifestyle behaviours, cardiovascular, metabolic, neurological, psychological and hormonal risks. A person may have more than one risk factor at a time.

2.1 Age

In a local study on moderate to severe ED, all age groups of patients above 18 years old and sexually active were substantially affected by the condition. The prevalence was 32.7% in those 18 - 30 years old, 26.3% in 31 - 59 years old and 64.1% in ≥60 years old. Men aged ≥60 years were strongly associated with moderate-to-severe ED with an OR of 3.04 (95% CI 2.27 to 4.10).[6, level III]

2.2 Lifestyle behaviours

a) Diet

In a meta-analysis on behaviour factors (including diet) in ED, fruit and vegetable consumption revealed mixed results on the risk of ED. Meanwhile, increased consumption of flavonoids reduced the risk.[7, level II-2]

A prospective cohort study on the association between the Mediterranean diet and ED reported highest category of Mediterranean Diet Score was inversely associated with incidence of ED in those aged <60 years (HR=0.78 95% CI 0.66 to 0.92) and 60 - 70 years (HR=0.82, 95% CI 0.76 to 0.89).[8, level II-2]

b) Physical activity

In males aged ≥20 years, a cross-sectional study showed physical activity of at least moderate intensity was associated with lower odds of ED compared with no physical activity in a week as demonstrated below:[9, level III]

- 1 - 2 days/week (OR=0.58, 95% CI 0.44 to 0.76)
- 3 - 4 days/week (OR=0.57, 95% CI 0.44 to 0.75)
- 5 - 7 days/week (OR=0.50, 95% CI 0.40 to 0.64)

The benefits of physical activity was shown in another cross-sectional study on diabetic patients where higher activity was inversely associated with moderate-to-severe ED and severe ED (OR=0.42, 95% CI 0.21 to 0.85 and OR=0.38, 95% CI 0.19 to 0.73 respectively).[10, level III]

A cross-sectional study showed that higher cardiovascular (CV) exercise levels (based on weekly metabolic equivalents time [MET]-hours) in physically active men were inversely associated with ED based on self-reported data of the respondents (p for trend=0.03).[11, level III]

However, a meta-analysis of five cross-sectional studies showed that cyclists had higher odds of having ED compared with non-cyclists (OR=2.00, 95% CI 1.57 to 2.55). Quality assessment showed that the primary studies were of fair to poor quality.[12, level III]

c) Obesity

A cross-sectional study in an andrology clinic showed that obese men (body mass index [BMI] ≥29 kg/m^2) had a higher risk of ED (OR=1.78, 95% CI 1.10 to 2.90) compared with those non-obese.[13, level III]

d) Smoking

A cross-sectional study among men showed that cigarette smoking was an independent risk factor for ED (OR=1.41, 95% CI 1.09 to 1.81). A dose-response was also exhibited (p=0.005).[14, level III]

e) Alcohol

In a meta-analysis of 24 cross-sectional studies, alcohol consumption was not associated with ED. Further analysis showed that when compared with non-drinkers, light to moderate consumption exhibited a beneficial effect on the risk of ED (OR=0.71, 95% CI 0.59 to 0.86) whereas high consumption did not. Heterogeneity in the analysis was significant.[15, level III] There was no report on quality assessment of primary papers.

f) Recreational drugs

A systematic review of behaviour factors in relation to ED showed that users of recreational drugs (amphetamine, cannabis, opioid and ecstasy) had an increased risk of ED compared with non-user. According to the Newcastle-Ottawa Scale, the primary papers scored moderate to high quality.[7, level II-2]

g) Pornography

A cross-sectional study on the association between problematic pornography consumption and ED using an internet-based questionnaire showed higher cyber pornography addiction test scores resulted in a higher probability of ED by 1.06 (95% CI 1.03 to 1.08).[16, level III]

In another cross-sectional study, the analysis demonstrated that men who preferred masturbation with pornography vs partnered sex without pornography were at a significantly increased risk of having ED.[17, level III]

h) Partner's sexual dysfunction

A meta-analysis was conducted to assess evidence on female sexual dysfunction (FSD) and its impact on male partners. The findings based on six cross-sectional studies revealed that the likelihood of ED is almost four times higher when the female partner had FSD compared with men who have partners without FSD (OR=3.80, 95% CI 1.96 to 7.38). Based

on McMaster Critical Review Form for Quantitative Studies, the risk of bias for the primary studies were scored 82 - 100%.[18, level III]

2.3 Co-morbidities

a) Diabetes mellitus

In a large meta-analysis on the prevalence of ED, the overall prevalence among diabetic patients was 59.1% (95% CI 55.5 to 62.7) while the odds of prevalence in diabetic patients vs healthy controls was 3.62 (95% CI 2.53 to 5.16).[19, level III]

b) Hypertension

In a meta-analysis of eight high-quality cross-sectional studies, hypertension was a risk factor for ED based on the International Index of Erectile Function (IIEF) (OR=1.61, 95% CI 1.30 to 2.00). However, the heterogeneity of primary studies was high.[20, level III]

c) Cardiovascular diseases

A local cross-sectional study reported a prevalence of various severity ED among patients with established ischaemic heart disease (IHD) at 90.4%. The mean age of patients was 60.5±9.58 years with two-thirds of them having moderate to severe ED.[21, level III]

In another cross-sectional study, the prevalence of ED among patients with post-myocardial infarction (MI) was 62%. Arterial hypertension (CVD risk) was significantly associated with ED.[22, level III]

d) End-stage renal disease

In a meta-analysis on the prevalence of ED in patients with end-stage renal disease (ESRD), the overall pooled prevalence was 71% (95% CI 67 to 74). Further subgroup analyses showed that pooled prevalence among patients with ESRD pre-dialysis (82%) was the highest compared with those who were on haemodialysis (79%), peritoneal dialysis (71%) and renal transplant recipients (59%).[23, level II-2]

e) Hyperuricaemia

A meta-analysis demonstrated an association between hyperuricaemia and risk of ED based on study design i.e.:[24, level II-2]

- five cohort studies (OR=1.45, 95% CI 1.11 to 1.89)
- six cross-sectional studies (OR=1.76, 95% CI 1.17 to 2.65)

The same meta-analysis of three cohort studies also reported that urate-lowering therapy reduced the risk among hyperuricaemic patients (OR=1.27, 95% CI 1.43 to 1.41).

f) Obstructive sleep apnoea

A systematic review of observational studies assessed the association between obstructive sleep apnoea (OSA) and ED. It reported the

prevalence of ED among patients with OSA ranged from 40.9% to 80%. There were mixed findings on the association between risk of ED and OSA severity (using Apnea-Hypopnea Index), oxygen saturation <90% during sleep or waketime sleepiness.[25, level II-2]

g) Chronic prostatitis/chronic pelvic pain syndrome

In a meta-analysis, a subgroup analysis based on observational studies showed chronic prostatitis/chronic pelvic pain syndrome had a higher risk of ED compared with controls (OR=2.68, 95% CI 2.23 to 3.22).[26, level II-2]

h) Depression and anxiety

In a meta-analysis of three cohort studies, the odds of having ED among depressed patients was 2.55 (95% CI 2.12 to 3.06) compared with non-depressed patients.[27, level II-2]

A systematic review of anxiety disorders found that the median prevalence of ED was 20.0% (IQR 5.1 to 41.2) based on IIEF-5, International Classification of Diseases, Ninth Revision (ICD-9) and Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) criteria and 17.6% (IQR 13.88 to 20.88) based on IIEF-5 alone.[28, level III]

i) Hypogonadism

In a cross-sectional study assessing the adverse health outcomes of testicular cancer survivors post-chemotherapy, those with secondary hypogonadism reported a higher risk of ED compared with those without the condition (19.6% vs 11.9%, p=0.018).[29, level III]

j) Traumatic brain injuries

A cohort study on the association of traumatic brain injuries (TBIs) and ED showed:[30, level II-2]

- incidence rate of ED was higher in the TBI group compared with the non-TBI group (24.66 per 100,000 vs 19.07 per 100,000) after a 10-year follow-up
- higher risk of ED for the TBI group after adjustment of confounding factors (HR=2.569, 95% CI 1.890 to 3.492)
- higher severity of TBI increased the risk of ED (dose-dependent) -
  - mild (HR=2.305, 95% CI 1.672 to 3.124)
  - moderate (HR=2.551, 95% CI 1.884 to 3.331)
  - severe (HR=5.467, 95% CI 2.452 to 7.706)

2.4 Medications

a) Antihypertensives

Thiazide diuretics and beta-blockers (β-blockers) are usually associated with drug-induced ED.[2]

However, a network meta-analysis showed NS difference in erectile function (EF) based on pairwise comparisons of all major antihypertensive classes (angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, β-blockers, calcium channel blocker and thiazide diuretics) and also with placebo. Further analysis of different β-blockers on EF demonstrated that:[31, level I]

- nebivolol had beneficial effect compared with non-vasodilatory β-blockers (OR=2.92, 95% CI 1.3 to 6.5)
- NS difference between carvedilol and non-vasodilatory β-blockers

b) Statins

In a meta-analysis that consisted of three randomised controlled trials (RCTs) on patients with established CVD or CVD risk factors, there was no association found between statins and the incidence of ED.[32, level I]

c) Finasteride

A meta-analysis of nine RCTs on androgenetic alopecia showed an increased risk of ED compared with placebo among patients who were on finasteride 1 mg/day (OR=1.99, 95% CI 1.10 to 3.60) but no association with dutasteride 0.5 mg/day.[33, level I]

A more recent meta-analysis showed that based on the safety profile, there was an NS difference in the risk of developing ED between finasteride and dutasteride.[34, level I]

Treatment for benign prostatic hyperplasia (BPH) includes 5-α-reductase inhibitors which are among the associated risk factors for drug-induced ED.[2]

d) Psychotropic agents

A large retrospective cohort study demonstrated that males with serotogenic antidepressants were associated with increased risk for ED compared with those without serotogenic antidepressants (OR=3.2, 95% CI 2.3 to 4.4).[35, level II-2]

Antidepressants (e.g. selective serotonin reuptake inhibitors and tricyclics) and antipsychotics are among the risk factors for drug-induced ED.[2]

3. DIAGNOSIS AND ASSESSMENT

Assessment and diagnosis of ED should always begin with a detailed medical, sexual and psychological history of the patients and, when available, their partners. The history should include information about past and current sexual relationships, previous consultations and treatments.

3.1 Medical History, Physical Examination and Laboratory Testing

a) History

A detailed history aided by validated questionnaires, e.g. the 15-item version of IIEF (IIEF-15), or its short version IIEF-5,[36, level III] help to assess the different sexual function domains (i.e. sexual desire, EF, orgasmic function, intercourse satisfaction and overall satisfaction), as well as the potential impact of a specific treatment modality. In a systematic review on the IIEF-15 and IIEF-5 measurement properties, both had comparable sensitivity and specificity at different cut-off points in evaluating ED.[37, level III]

Assessment of penile rigidity in practice and research can be supported by the use of the Erectile Hardness Score (EHS). A validation study of EHS showed that it had a fairly good correlation with IIEF in all domains (ranging between 0.63 to 0.86) except the sexual desire domain.[38, level III]

The assessment of IIEF-5 and EHS helps to determine severity of ED, hence guiding the physician in choosing the appropriate management.

Patients should always be screened for symptoms of possible hypogonadism, including decreased energy and libido. Potential risk factors for ED e.g. DM (refer to **Chapter 2**) should be screened for and identified.

Refer to **Appendix 3** for **Relevant History-taking in Patients with Symptoms of ED, Appendix 4** for **5-item Version of International Index of Erectile Function (IIEF-5)** and **Appendix 5** for **Erection Hardness Score**.

b) Physical examination

Patients should undergo physical examination focusing on the genitourinary (including prostate), endocrine, vascular and neurological systems. Blood pressure, heart rate and BMI or waist circumference should be measured during clinical examination as part of cardiovascular risk assessment.

A physical examination may reveal penile abnormalities, e.g. Peyronie's disease, pre-malignant or malignant genital lesions, prostatic enlargement and signs suggestive of hypogonadism (e.g. small testes or alterations in secondary sexual characteristics).[2]

c) Laboratory testing

Laboratory testing must be tailored to the patient's symptoms and risk factors. The tests are performed to identify and treat any modifiable risk factors. Fasting blood glucose or haemoglobin A1C (HbA1c) and lipid profile should be performed as part of the CV risk assessment.[2]

Additional laboratory tests may be considered on a case-to-case basis e.g. hormonal tests which include early morning total testosterone, total prostate-specific antigen (PSA), prolactin and luteinizing hormone.[2]

d) Advanced work-up

Most patients with ED can be managed based on their medical and sexual history; conversely, some patients may need specific diagnostic tests as discussed below.

i. Nocturnal penile tumescence and rigidity test

The nocturnal penile tumescence and rigidity (NPTR) device has to be worn by the patient overnight for at least two separate nights and gives the following information:

- number of erectile episodes
- tumescence (circumference change by strain gauges)
- maximal penile rigidity
- duration of nocturnal erections

An erectile event lasting ≥10 minutes and with at least 60% stiffness observed on the tip of the penis is indicative of a functional erectile mechanism. NPTR monitoring can help to differentiate between organic and psychogenic ED objectively; patients with psychogenic ED usually have normal findings. However, its routine use in the diagnosis of ED may be limited due to potential confounding factors (e.g. dreams) which may affect nocturnal erection.[2]

ii. Intracavernous injection test

The intracavernous injection test is performed with or without dynamic duplex Doppler ultrasound. The ultrasonography can help confirm potential vasculogenic aetiology of ED. Peak systolic blood flow >30 cm/s, end-diastolic velocity <3 cm/s and resistance index >0.8 are considered normal.[2]

iii. Arteriography

Patients who are being considered for penile revascularisation should have penile pudendal arteriography. For patients with ED and isolated penile artery stenosis, computed tomography angiography is advocated prior to penile artery angioplasty.[2]

The specific diagnostic tests for ED listed above are indicated for the following conditions:[2]

- primary ED (not caused by acquired organic disease or psychogenic disorder)
- young patients with a history of pelvic or perineal trauma suspected to have vasculogenic ED
- patients with penile deformities that might require surgical correction (e.g. Peyronie's disease and congenital penile curvature)
- patients with complex endocrine disorders
- patients with complex psychiatric or psychosexual disorders
- medico-legal reasons [e.g. implantation of penile prosthesis (PP) to document end-stage ED and sexual abuse]

3.2 Cardiovascular Risk Assessment

- ED could be the initial manifestation of a spectrum of clinical conditions that eventually lead to coronary artery disease (CAD) and peripheral vascular disease.
- The prevalence of ED is >70% among men with CVD.[39, level III]

A cohort study on patients with ED showed:[40, level II-2]

- severe ED predicted major adverse cardiac event (MACE) with HR of 1.75 (95% CI 1.10 to 2.78)
- lower penile blood flow before and after prostaglandin-E1 stimulation was associated with an increased risk of MACE -
  - in flaccid conditions (peak systolic velocity [PSV] <13 cm/s), the HR was 2.67 (95% CI 1.42 to 5.04)
  - in dynamic conditions (PSV <25 cm/s), the HR was 1.57 (95% CI 1.01 to 2.47)

A meta-analysis of cohort studies suggested that ED was associated with risk of:[41, level II-2]

- coronary heart disease (RR=1.46, 95% CI 1.31 to 1.63)
- stroke (RR=1.35, 95% CI 1.19 to 1.54)
- all-cause mortality (RR=1.19, 95% CI 1.05 to 1.34)

The above analysis showed NS heterogeneity. However, there was no report on the quality assessment of primary studies.

A cross-sectional study on three different CV risk engines among patients referred for sexual dysfunction showed that the AUC was 0.762, 0.716 and 0.667 for Progetto Cuore, Framingham and Prospective Cardiovascular Münster (PROCAM) engines respectively.[42, level III]

Patients with predominantly vasculogenic ED are suggested to be assessed using 2019 American College of Cardiology/American Heart Association atherosclerotic CVD (ASCVD) risk score based on recommendation by Princeton IV consensus guidelines. It provides estimation of patients with major CV events within the next 10 years and can be accessed online via https://tools.acc.org/ascvd-risk-estimator-plus/#!/calculate/estimate/. Depending on ASCVD score, patients may require for further cardiologist assessment.[43]

European Association of Urology (EAU) Guidelines 2023 categorise the cardiac risk stratification among patients with ED based on the 2nd and 3rd Princeton Consensus. The characteristics and management for each risk are as follows (**Table 1**).[2; 44]

Table 1: Cardiac risk stratification for patients with ED based on 2nd and 3rd Princeton Consensus

Cardiac risk	Low-risk category	Intermediate-risk category	High-risk category
Characteristics	Asymptomatic, <3 risk factors* for CAD (excluding sex)	≥3 risk factors* for CAD (excluding sex)	High-risk arrhythmias
	Mild, stable angina (evaluated and/or being treated)	Moderate, stable angina	Unstable or refractory angina
	Uncomplicated previous MI	Recent MI (>2, <6 weeks)	Recent MI (<2 weeks)
	LVD/CHF (NYHA class I or II)	LVD/CHF (NYHA class III)	LVD/CHF (NYHA class IV)
	Post-successful coronary revascularisation	Non-cardiac sequelae of atherosclerotic disease (e.g. stroke, peripheral vascular disease)	Hypertrophic obstructive and other cardiomyopathies
	Controlled hypertension		Uncontrolled hypertension
	Mild vascular disease		Moderate-to-severe valvular disease

Cardiac risk	Low-risk category	Intermediate-risk category	High-risk category
Management	Manage within a primary care setting Review treatment options with the patient and their partner (where possible)	Specialised evaluation recommended (e.g. exercise stress test for angina, echocardiogram for a murmur) Patient to be placed in high or low-risk category depending upon the outcome of testing	Refer for specialised cardiac evaluation and management Treatment for ED to be deferred until cardiac condition stabilised and/or specialist evaluation completed

CAD = coronary artery disease; CHF = congestive heart failure; ED = erectile dysfunction; LVD = left ventricular dysfunction; MI = myocardial infarction; NYHA = New York Heart Association
*Risk factors for CAD include high blood pressure, high low-density lipoprotein (LDL) cholesterol, DM, smoking and/or second-hand smoke exposure, obesity, unhealthy diet and physical inactivity.[45, level III]

3.3 Psychological and Sexual Assessment

Psychosocial and sexual history is important for thorough and comprehensive assessment. These can be assessed through clinical interviews and objective measurements on specific areas of history which include:[2; 46]

- current psychological state and co-morbid psychiatry conditions (e.g. anxiety, depression)
- relationship history - issues, dynamics, durations and partner history
- partner's sexual functioning (e.g. FSD)
- life stressors and coping abilities
- cognitive factors -
  - dysfunctional thinking style
  - expectations on sexuality and sexual performance, and treatment preferences
- sexual related factors -
  - education
  - trauma
  - experience (e.g. masturbation, pornography usage)
  - cultural and religious aspects
  - gender dysphoria and sexual orientation
- co-morbid sexual dysfunction (e.g. premature ejaculation)

Recommendation 1

- A comprehensive medical, psychosocial and sexual history should be taken in every patient presenting with erectile dysfunction (ED).
- A validated questionnaire related to ED should be used to assess all sexual function domains (e.g. International Index of Erectile Function).
- A focused physical examination in the initial assessment of men with ED should be done to identify underlying medical conditions and co-morbid genital disorders that may be associated with ED.
- Routine laboratory tests should be performed to identify modifiable risk factors of ED.
- Specific diagnostic tests may be performed when it is indicated*.
- Patients with ED should have cardiac risk assessment and vice versa.

*Refer to preceding text in **Subchapter 3.1** (d).

4. TREATMENT

ED can be treated with multiple therapeutic options. These include lifestyle modifications, pharmacological agents, mechanical devices, surgeries and psychological interventions. It should be a dynamic process resulting in a patient-centred treatment strategy that depends on the effectiveness, safety and cost of the treatment. In this context, shared decision-making (preferably with a partner) is essential throughout the management of ED.

4.1 Lifestyle Intervention

ED is strongly associated with lifestyle risk factors. Addressing these factors is important in the treatment of ED.

A systematic review of patients with ED ± treatment of ED showed that modifications of CV risk factors which included physical activity, Mediterranean diet and weight loss improved IIEF-5 score compared with those not receiving the interventions (MD=2.40, 95% CI 1.19 to 3.61). Overall, the studies had moderate to good methodological quality.[47, level I]

Another systematic review of 10 clinical trials demonstrated that aerobic exercise of moderate-vigorous intensity (≥3 times/week for ≥30 minutes/ session) improved IIEF or IIEF-5 for men with arterial ED due to physical inactivity, obesity, hypertension, metabolic syndrome and/or CVD compared with controls. In general, the risk of bias for each study was estimated to be moderate.[48, level I]

Weight loss regimen which included low-energy diet and physical exercises among overweight or obese man improved EF (MD of IIEF score=1.99, 95% 0.85 to 3.13) based on a meta-analysis of five moderate-to-high quality RCTs.[49, level I] In relation to weight loss, a pre-post study on ED patients with obesity (BMI ≥40 kg/m^2 or ≥35 kg/m^2 with other co-morbidities), bariatric surgery significantly improved their EF based on IIEF scores.[50, level II-3]

The male pelvic floor muscles have three major functions i.e. to support the abdominal content, coordinate contraction with sphincters for faeces and urine elimination, and to facilitate the erection and ejaculatory processes. A systematic review among patients with ED on pelvic floor muscle training under therapist supervision in 5 - 20 sessions for 3 - 4 months showed 35 - 47% of cure in ED from baseline. The mean methodological quality of the trials was 70% based on Crowe Critical Appraisal Tool score.[51, level II-3]

Another pre-post study on smoking cessation showed that quit smoking significantly improved ED irrespective of pack-years of smoking and severity of ED.[52, level II-3]

In a recent pre-post study on patients with alcohol use disorder and ED, IIEF-5 scores improved after three months of abstinence from alcohol ($p<0.001$). Multivariate analysis showed that age, alcoholic liver disease and number of standard drinks per day were associated with the improvement of ED.[53, level II-2]

A cross-sectional study found significantly higher perceived stress in patients with ED than healthy controls.[54, level III] In managing stress, counselling is helpful as an initial step to provide support and guidance regarding ED.

Psychotherapy, on the other hand, goes one step further and is directed towards gaining insights into chronic and recurrent emotional and cognitive patterns, and their contribution to ED (refer to **Subchapter 4.5**).[55, level III]

EAU Guidelines 2023 recommends to modify risk factors and commence lifestyle changes prior to or concurrently with ED treatments.[2]

Recommendation 2
- All patients with erectile dysfunction should be advised on lifestyle and risk factor modifications.

4.2 Pharmacological Treatment

The main pharmacological agents for ED are phosphodiesterase-5 inhibitors (PDE5is). These agents cause corporeal smooth muscle relaxation, increased arterial blood flow and compression of sub-tunical venous plexus leading to erection. Therefore, they are contraindicated in patients taking nitric oxide (NO) donors, organic nitrates or organic nitrites (e.g. glyceryl trinitrate). As they are not initiators of erection, PDE5is require environmental and psychological cues for sufficient sexual arousal and stimulation to facilitate an erection. The U. S. Food and Drug Administration (FDA)-approved PDE5is will be discussed below. Refer to **Appendix 6** for **Pharmacological Treatment in ED**.

a) Phosphodiesterase-5 inhibitor

i. Sildenafil

Sildenafil was the first available PDE5i in the market. The recommended initial dose is 50 mg and may be adjusted according to its responses and adverse events (AEs). The onset is 30 - 60 minutes and the effect persists up to 12 hours after administration.[2]

In a pre-post study on ED patients with DM and/or hypertension treated with flexible-dose sildenafil of 25 - 100 mg on-demand/ once daily, the medication significantly improved mean IIEF-5 score from 13.6±5.7 at baseline to 21.7±4.1 at week 12. Sildenafil was generally safe and well-tolerated. The most common reported AEs were headache (5.5%), flushing (1.9%) and nasal congestion (1.3%).[56, level II-3]

A meta-analysis of RCTs on the effectiveness and tolerability of sildenafil compared with placebo in patients with DM-associated ED showed that sildenafil:[57, level I]

- improved IIEF-5 Question 3 score (WMD=1.14, 95% CI 0.73 to 1.50) and IIEF-5 Question 4 (WMD=1.13, 95% CI 0.85 to 1.42)
- increased overall sexual performance satisfaction based on global efficacy question (RR=3.99, 95% CI 2.58 to 6.18)
- led to more successful intercourse (RR=3.34, 95% CI 2.10 to 5.31) with higher number of patients reporting at least one successful attempt of intercourse in the last four weeks of treatment (RR=2.86, 95% CI 2.25 to 3.65)

The most common AEs reported were headache, dyspepsia and flushing. Overall, the risk of bias of the primary studies was moderate to high.

A large network meta-analysis on the effectiveness and safety of PDE5i in ED showed that sildenafil at low doses (25 or 50 mg) followed by tadalafil (10 or 20 mg) were the first therapeutic options for ED.[58, level I]

ii. Tadalafil

In a meta-analysis of 13 RCTs on lower urinary tract symptoms (LUTS)/ BPH/ED, tadalafil 5 mg once daily was more effective than placebo in terms of:[59, level I]

- IIEF score (SMD=5.18, 95% CI 4.13 to 6.23)
- Sexual Encounter Profile (SEP)2 score (OR=5.46, 95% CI 3.53 to 8.46)
- SEP3 score (OR= 4.14, 95% CI 3.11 to 5.50)

Tadalafil was well tolerated although the AEs were not specified. The primary papers were of low risk of bias.

Two meta-analyses compared the effectiveness and safety of tadalafil 5 - 10 mg once-a-day and tadalafil 10 - 20 mg on-demand dosing regimen in ED patients. In the first meta-analysis, the once-a-day regimen improved IIEF-EF scores compared with on-demand at 12 weeks (WMD=1.82, 95% CI 0.85 to 2.80). A secondary sub-analysis on four RCTs showed that tadalafil 5 mg once-a-day was more effective in IIEF-EF than 20 mg on-demand at 12 weeks (WMD=1.51, 95% CI 0.49 to 2.53).[60, level I] However, the analysis showed NS differences in IIEF-EF scores between the two regimens regardless of different end-point

of study duration.[60 - 61, level I] There was NS difference in AEs between both groups.[61, level I] The quality of RCTs in both meta-analyses was variable.

A large meta-analysis of RCTs compared the effectiveness and safety of tadalafil vs sildenafil in the treatment of ED. The findings showed:[62, level I]

- NS differences in means of IIEF (IIEF-EF, IIEF-intercourse satisfaction, IIEF-overall satisfaction and IIEF-sexual desire)
- tadalafil had significantly better Self-Esteem and Relationship (SEAR) Confidence, SEAR Sexual Relationship and Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) total scores

Although there was NS difference in overall AEs between the two agents, tadalafil had significantly higher risk of myalgia and back pain, and lower risk of flushing. Most of the studies scored two on the Jadad score (low quality).

iii. Avanafil

Avanafil (100 mg and 200 mg) was compared with placebo in the meta-analysis of eight RCTs among patients with ED. It was more effective in terms of:[63, level I]

- higher IIEF-EF score (MD=4.57, 95% CI 3.68 to 5.46)
- successful vaginal penetration (RR=3.20, 95% CI 2.60 to 3.95)
- successful intercourse (RR=2.53, 95% CI 2.19 to 2.92)

In a sub-group analysis, the 200 mg dose was significantly better than 100 mg in IIEF score and successful intercourse. For AEs, avanafil had a higher risk compared with placebo (RR=1.78, 95% CI 1.38 to 2.31). However, there was NS difference in AEs between the two doses of avanafil. The methodological quality of primary studies was generally high.

In a 12-weeks, multi-centre, double-blind, placebo-controlled RCT of men with DM and ED, avanafil (100 and 200 mg) was more effective than placebo in improving IIEF score and successful intercourse which could be initiated in ≤15 minutes through >6 hours. The most commonly reported AEs with avanafil were headache, nasopharyngitis, flushing and sinus congestion.[64, level I]

iv. Vardenafil

The effectiveness of vardenafil vs placebo in ED was studied in a meta-analysis of RCTs. The former was significantly more effective in IIEF-overall satisfaction, SEP2 and SEP3 scores. No safety profile was reported. The mean Jadad score was 3.54, indicating that all included studies were of high quality.[65, level I] However, vardenafil is not registered yet in Malaysia.

- Patients with ED should stop PDE5i and seek immediate medical care when there is a sudden loss of vision in one or both eyes which could be a sign of non-arteritic anterior ischaemic optic neuropathy (NAION).[66, level III]
- However, patients with a history of NAION may be prescribed PDE5i with caution.

Recommendation 3
- Phosphodiesterase-5-inhibitor should be offered to all patients with erectile dysfunction unless contraindicated.
  - The choice of agent is individualised.

b) Combination therapy vs monotherapy

A meta-analysis showed that the combination of PDE5i with various agents (mainly alpha-blocker, testosterone and antioxidants) was more effective than PDE5i monotherapy in the subgroup of patients that have ED (WMD in IIEF score=1.76, 95% CI 1.27 to 2.24). However, there was NS difference in treatment-related AEs. GRADE gave a moderate quality assessment of the outcomes. The heterogeneity of the primary papers was significant.[67, level I]

On the treatment of ED, EAU Guidelines 2023 recommends PDE5is as a first-line therapeutic option for the specific condition. The choice of drug depends on the frequency of intercourse and the patient's personal experience.[2]

c) Other medications

- **Intracavernosal injection**

Intracavernosal injections (ICIs) were the first medical treatment for ED. The only FDA-approved preparation is alprostadil. There are many combination preparations that include either one or more of the following combinations of phentolamine, papaverine or atropine but none have obtained FDA approval, making standardisation of dosing difficult. Apart from that, patients and their partners need to learn the injection technique under supervision by trained medical personnel.

In a cohort study of Korean ED patients who received ICI at least twice, adequate penile rigidity was restored in 60.2% of patients. AEs occurred in 25.5% of patients which were due to:[68, level II-2]

- pain during self-injection (45.9%), longer erections than expected (23.0%), penile curvature (14.9%), palpable plaque (10.8%) and subcutaneous haematoma (5.4%) in the withdrawal group
- prolonged erection (44.4%) as the most common AE in the continuing group

There was no incidence of injection site infection. Overall satisfaction was 40.1%.

In patients on anticoagulation, caution should be exercised when ICI is used. A cross-sectional study found that the rate of bleeding events was higher on patients with anticoagulation compared with those not on the medication although it was NS.[69, level III] However, the study may be underpowered.

Novel intracavernosal therapies including stem cell and platelet-rich plasma have shown promising results but require more robust studies before they can be recommended.[2]

- **Intraurethral alprostadil**

For patients who are concerned with the AEs of PDE5is or refuse ICIs, intraurethral alprostadil is an alternative. There are two methods of administration. The first method is the Medicated Urethral System for Erection (MUSE) where a pellet of alprostadil is inserted into the urethra. A recent method uses topical cream that can be applied into the urethra meatus or onto the glans penis.

In a systematic review, five RCTs showed significant improvement in erection which was sufficient for intercourse in MUSE compared with placebo. However, MUSE was shown to be inferior to ICIs. In one of the RCTs on patients post-bilateral nerve sparing prostatectomy, MUSE was comparable to sildenafil in effectiveness but had lower compliance.[70, level I] There was no mention on quality assessment of the primary papers.

In a multi-centre pre-post study on ED, 74% of patients demonstrated overall improvement in EF with topical alprostadil. About 12% of patients discontinued the treatment due to hypo-/hyper-responsiveness while <5% did so because of AEs.[71, level II-3]

The most common AEs with topical alprostadil are local pain (29 - 41%) and dizziness with possible hypotension (1.9 - 14%). Penile fibrosis and priapism are rare (<1%). Urethral bleeding (5%) and urinary tract infections (0.2%) may occur if it is administered into the urethra.[2]

- ICI and intraurethral alprostadil are options in the treatment of ED. However, both are not available locally yet.

4.3 Mechanical Treatment

In the landscape of evolving treatment options for ED, mechanical devices have been used with success and safe to maintain an erection as discussed below. The common mechanical devices available are vacuum erection devices (VEDs) and low-intensity extracorporeal shockwave therapy (Li-ESWT). Refer to **Appendix 6** for M**echanical Treatment in ED**.

a) Vacuum erection device

A pre-post study to investigate satisfaction with VED for middle-aged and older male veterans with ED and their female partners showed:[72, level II-3]

- majority of patients achieved favourable outcomes i.e. -
  - 96.0% reported the ability to maintain an erection and 90.7% were able to engage with intercourse; however, the older age group (>65 years) was associated with significant difficulty in obtaining erections and engaging in sexual intercourse
  - 92.0% had improved intercourse
  - 93.9% mentioned that their sexual relationship with partner was satisfactory or very satisfactory
- 83.8% of female partners rated sex as better
- 23% of patients reported physical discomfort (e.g. difficulties placing the bands on the cylinder, sliding them on the penis, removing them after sex or pain)
- 9.1% reported having psychological discomfort (e.g. frustration and lack of spontaneity)

In an RCT of men with type 2 DM and ED treated with either combination of sildenafil 100 mg and VED, and sildenafil 100 mg alone, the former showed:[73, level I]

- significantly higher IIEF scores at one month (14.86±2.17 vs 12.41±2.63) and three months (17.53±2.95 vs 14.29±2.81)
- significantly higher rates of successful penetration (73.3% vs 46.6%) and successful intercourse (70.0% vs 46.6%) at three months

The AEs (e.g. penile bruising and numbness for VED) were mostly mild and did not affect the patients' daily life.

Refer to **Appendix 7** for **Application of Vacuum Erectile Device (VED)**.

b) Shockwave therapy

An RCT showed that Li-ESWT improved the EF of young patients with vasculogenic mild ED compared with placebo. The findings showed that Li-ESWT increased the mean IIEF-EF scores at three months follow-up (p=0.003) apart from successful penetration (SEP2) and intercourse

(SEP3) in >50% of attempts (p=0.001).[74, level I] There were limitations in the methodological quality of this RCT.

Two pre-post studies on moderate ED showed that Li-ESWT significantly improved EF post-treatment.[75 - 76, level II-3] It was also found to be safe as patients reported no irritative urinary symptoms and intracutaneous activity after undergoing the treatment.[75, level II-3]

A local technology review on the effectiveness and safety of Li-ESWT among patients with ED showed that the intervention:[77, level I]

- was mostly benefited in younger men with mild to moderate ED and those with fewer co-morbidities
- was effective from three to six months
- enhanced the medication responses in PDE5i non-responders
- when used with adjuvant daily therapy, increased its effectiveness and duration of effect
- was also safe and well tolerated with modest improvement

The treatment was recommended to be performed only by the urologists. This is because they are involved in the entire holistic management of the patients and understand the mechanisms of action to tailor the treatment plan.

Refer to **Appendix 8** for **Low-intensity Extracorporeal Shockwave Therapy**.

Recommendation 4

- Mechanical devices (e.g. using vacuum erection device or shockwave therapy) may be offered in erectile dysfunction (ED).
- Low-intensity extracorporeal shockwave therapy should be performed by urologists for mild to moderate ED.

4.4 Surgical Intervention

Surgical interventions in ED include penile revascularisation surgery and PP.

a) Penile revascularisation surgery

Vascular ED can be subcategorised as arterial insufficiency (AI), veno-occlusive disease (VOD) or mixed, with VOD being the most common finding. Generally, the affected patients tend to develop ED at a younger age and may have a history of preceding trauma. Penile revascularisation is usually done in a very specialised centre outside of Malaysia.

- **Arterial insufficiency**

AI occurs when there is inadequate arterial blood to the penis at the time of erection and may result if the artery cannot dilate appropriately after neurochemical signalling or if the upstream vascular flow is restricted.

Consensus guidelines by the International Consultation on Sexual Medicine (ICSM) recommend that men with ED who satisfy the criteria of the index patient (<55 years with recently acquired ED from focal arterial occlusive disease in the absence of other risk factors e.g. smoking, DM) can be considered for penile revascularisation procedures (microsurgery or endovascular intervention). However, current data do not support one procedure over another in terms of effectiveness.[78]

Short- and long-term complications of microsurgery include wound infection (2.8%), urinary tract infection (2.6%), inguinal hernias (2.8%), sepsis (3.5%), wound haematoma (7.8 - 25%), loss of penile length (28%), decreased penile sensitivity (24.7%) and glans hyperaemia (4 - 21%).[78]

Potential complications of endovascular treatment (balloon angioplasty with or without stent insertion) include vascular injury, puncture site aneurysm, infection, contrast-induced nephropathy. ICSM consensus guidelines reports NS AEs.[78]

- **Veno-occlusive disease**

VOD occurs when an erection cannot be achieved or maintained despite an adequate arterial supply. It is most likely results from endothelial and smooth muscle dysfunction leading to inadequate sinusoidal expansion and insufficient closure of emissary veins.

Both consensus guidelines of ICSM and EAU Guidelines 2023 do not recommend venous surgery or embolisation for VOD.[2; 78]

- Vascular ED should be suspected in patients with ED at a younger age with the absence of other risk factors.

b) Penile prosthesis

In Malaysia, PP is usually used when other treatment modalities have failed. There are several types including malleable, 2-piece inflatable and 3-piece inflatable systems.

In a pre-post study of ED patients with failure of medical treatment who received inflatable PP, overall patients' and partners' satisfaction was 85% and 76% respectively.[79, level II-3]

A meta-analysis with low-to-moderate risk of bias of primary studies on men with ED of any aetiology showed that 52.9% inflatable PP device survived at 20 years.[80, level II-3]

Main AEs include mechanical failure (<5% in five years) and infection (2 - 3% in low-risk patients). High-risk patients include patients undergoing revision surgery, those with impaired host defences (e.g. immunosuppression, DM or spinal cord injury [SCI]) or those with penile corporal fibrosis. Other AEs include implant erosion (1 - 6%) as well as glans ischaemia and necrosis.[2]

Refer to **Appendix 9** for **Examples of Penile Prosthesis**.

Recommendation 5
- Penile prothesis may be offered to patients with erectile dysfunction who have failed other interventions.

4.5 Psychological Intervention

Psychosocial intervention plays a vital role in ED treatment because both psychological and social factors predispose and perpetuate erectile problems. It is recommended to involve the partner in this management of ED as it may help to identify sexual difficulties among the partners.[18, level III; 55, level III] The main components of psychosocial treatment of ED include psychoeducation, cognitive and behavioural techniques, aimed at reducing anxiety, challenging dysfunctional beliefs, increasing sexual stimulation, disrupting sexual avoidance and, increasing intimacy and communication skills in a relational context. Sex therapy is a specific type of psychotherapy, focusing specifically on sexual experiences.[55, level III]

In a Cochrane systematic review on the effectiveness of psychosocial interventions for the treatment of ED, the findings were:[81, level I]
- focused sex-group therapy was more effective in reducing the persistence of ED than control (no treatment) (RR=0.13, 95% CI 0.04 to 0.43)
- group therapy with sildenafil showed increased reduction of persistent ED compared with sildenafil alone (RR=0.46, 95% CI 0.24 to 0.88)
- NS difference in effectiveness between psychosocial interventions vs local injection and vacuum devices

However, there were limitations in the methodological quality of the primary studies.
The above findings were supported by a later meta-analysis.[82, level I]

Another meta-analysis of RCTs looked into the effectiveness of the following comparisons in the treatment of ED:[83, level I]

- a specific psychological intervention vs wait-list
- two specific psychological interventions against each other
- a combination of psychological treatment and medication vs medication only

The psychological interventions included sex therapy, marital therapy, educational intervention and other psychotherapies. The findings revealed moderate improvement in the symptom severity and sexual satisfaction of ED participants, however it was not significant.[83, level I] The primary studies were of low-to-moderate quality.

A meta-analysis assessed the effectiveness of psychological interventions alone, PDE5i alone and their combination in the treatment of ED. The psychological intervention comprised of counselling, sex therapy, cognitive-behavioural sex therapy (CBST) and psychoeducation, delivered on an individual basis, with couples, in group settings or via the internet. The analysis was reported as below.[84, level I]

- Combined treatment had a superior effect on ED symptoms than PDE5i or psychological intervention alone (Cohen's d=0.45, 95% CI 0.02 to 0.89).
- There were NS differences between psychological intervention alone and PDE5is alone with respect to impact on ED symptoms.
- The effectiveness of the combined treatment remained consistent, regardless of the level of intensity in the psychological intervention.

However, the quality of the primary studies was low.

An umbrella review of meta-analyses on ED also supported the finding that combined treatment of PDE5i and psychological intervention was more effective than PDE5i alone (RR=2.26, 95% CI 1.04 to 4.92). Other findings were:[85, level I]

- group psychotherapy was superior to wait-list (RR=2.50, 95% CI 1.09 to 5.72)
- non-pharmacological treatments rarely reported any AEs

Based on GRADE, the quality of primary studies was very low.

In a recent systematic review of RCTs comparing the effectiveness of PDE5i alone, psychological intervention alone or a combination of both interventions in psychogenic ED, the combined interventions were more effective than the monotherapies in EF which was mainly based on IIEF scores. Examples of the psychological interventions assessed in the review were individual cognitive behaviour therapy (CBT)/CBST, group therapy and counselling and, couple CBST.[86, level I]

Qualitative findings in a mixed method study among patients with situational ED who received mindfulness-based group treatment

consisting of daily home-practice activities and, integrated elements of psychoeducation, sex therapy and mindfulness skills showed that patients:[87, level II-3]

- perceived the group treatment as safe and supportive, and validated their own experience which led to a reduction of stigmatisation for male sexual dysfunction
- were able to identify and reduce their performance anxiety
- reported improvements in self-efficacy and acceptance regarding their conditions
- had better insights into the significance of communicating and gaining support from their partners

A meta-analysis which included four RCTs on ED and one on both ED and premature ejaculation compared internet- and mobile-based psychological interventions (IMIs) with control. IMIs were more effective but with small effect sizes (Hedge's g=0.18) in improving sexual functioning in men. All IMIs were based on the principle of CBT together with elements of sexual therapy including treatment components e.g. psychosexual education, cognitive restructuring, sensate focus, communication, etc. Based on Risk of Bias 2 (RoB 2) tool by the Cochrane Collaboration, all five RCTs have some concerns risk of bias.[88, level I]

Recommendation 6

- An integrated and collaborative approach with psychological interventions should be considered in the treatment of erectile dysfunction.

5. TRADITIONAL AND COMPLEMENTARY MEDICINE

Traditional and complementary medicine (TCM) has been used for the prevention and treatment of ED for many years. The mechanisms of action remain unclear and warrant further clinical investigations.

A meta-analysis on nine RCTs comparing combination therapy of PDE5i and antioxidants (e.g. propionyl-L-carnitine or L-arginine) with PDE5i monotherapy in patients mainly with ED showed that the combination therapy was more effective based on IIEF score (WMD=1.99, 95% CI 1.34 to 2.63) without increasing AEs. The nine RCTs were mainly of low-risk of bias category.[67, level I]

A systematic review assessed various TCMs in the management of ED. A meta-analysis of seven RCTs demonstrated the effectiveness of red ginseng in the treatment of ED compared with placebo in:[89, level I]

- response rate (based on IIEF score) with RR of 2.40 (95% CI 1.65 to 3.51)
- psychogenic ED (based on global efficacy question) with RR of 2.05 (95% CI 1.33 to 3.16)
- sexual function (based on IIEF and Watts sexual function score) with SMD of 0.79 (95% CI 0.46 to 1.12)

However, the methodological quality of the included RCTs was averagely low.

Apart from the above, the other findings of the review were:[89, level I]

- yohimbine was a reasonable therapeutic option compared with placebo and, had infrequent and reversible AEs
- acupuncture was inconclusive in ED treatment due to scarce evidence

- There is insufficient evidence to recommend the use of TCM including Tongkat Ali in the treatment of ED.

6. FOLLOW-UP

The follow-up for a patient with ED depends on the individual case and the initial treatment plan. Generally:[2; 90, level III]

- short-term follow-up -

For patients initiating treatment with oral medications, a short-term follow-up within a few weeks to a couple of months may be appropriate to assess response and tolerance to the medication.

- long-term follow-up -

Once a treatment plan has been established, long-term follow-up may be scheduled at regular intervals. This allows for ongoing assessment of treatment effectiveness, potential adjustments to the treatment plan and monitoring for any emerging health issues.

- as needed follow-up -

For patients using on-demand treatments or lifestyle modifications, follow-up may be scheduled on an as-needed basis, depending on their progress and any changes in their health status.

- referral back to primary care -

If a urologist has been involved in the initial evaluation and management, the urologist may refer the patient back to his primary care physician for ongoing follow-up if the ED is stable and well-managed.

It is important to note that these are specific follow-up plans and will vary based on the patient's individual circumstances and response to treatment. Regular communication and collaboration between the primary care physician and the urologist, if involved, are key components of effective care for individuals with ED.

7. REFERRAL

Referring a patient with ED to a urologist or other relevant specialist is typically considered when/at:

- Primary care evaluation: The primary care physician has assessed the patient, taken a detailed medical history and performed a physical examination. If the underlying cause of ED is not evident or if there are concerns about specific urological issues, a referral may be appropriate.
- Treatment failure or complexity: If initial treatments, e.g. lifestyle changes, oral medications (like PDE5i) or other conservative measures, do not yield satisfactory results or if a case is complex and may require specialised interventions (e.g. penile injections, VEDs or surgical options), a urologist may be consulted.
- Underlying medical conditions: Presence of co-morbidities that might contribute to or exacerbate ED e.g. diabetes mellitus, CVD, or hormonal disorders, consultation with a urologist and/or endocrinologist/cardiologist may be warranted.
- Psychological factors: If psychological factors are suspected to be a significant contributor to the ED, collaboration with a mental health professional may be necessary. However, urologists may still play a role in addressing any physical aspects of the condition.

8. SPECIAL POPULATIONS

8.1 Patients with Cardiac Disease

Managing ED in patients with cardiac disease requires a comprehensive approach. Patients with atrial fibrillation showed an ED prevalence of 57% (95% CI 50 to 64) based on a meta-analysis.[91, level II-2]

In a cohort study among patients attending an exercise stress test (EST) clinic, it was found that patients with negative EST were less likely to have ED compared with those with positive EST (OR=0.18, p<0.001).[92, level II-2]

Based on a large network meta-analysis on PDE5i and its doses in ED, sildenafil 50 mg was the most effective (84% probability in SUCRA) in improving IIEF scores when compared with placebo among patients with CV disorders. In terms of safety, vardenafil and udenafil had the best benefit-risk profiles in these studies.[58, level I] Udenafil is not available locally yet.

In addition, a pre-post study among patients with ED with their CV risk based on Framingham risk score showed that tadalafil 10 mg on-demand improved IIEF scores in all risk groups (p<0.001). However, a few factors were associated with the failure of tadalafil to achieve complete responsiveness i.e.:[93, level II-3]

- increased high-density lipoprotein (HDL) level by every 1 mg/dL (OR=1.022, 95% CI 1.013 to 1.053)
- presence of hypertension (OR=2.217, 95% CI 1.015 to 2.987)
- higher Framingham score (OR=4.127, 95% CI 1.423 to 4.873)
- severe ED at the beginning of treatment (OR=3.102, 95% CI 1.325 to 5.450)

In an RCT comparing the effectiveness of sexual rehabilitation (physical exercise, pelvic floor exercise and psychoeducational consultation) with usual care among patients with ED and with either IHD and/or CAD, the former was superior in terms of:[94, level I]

- improved sexual function with a mean difference in IIEF score of 6.7 (95% CI 3.1 to 10.4) at four months and 6.7 (95% CI 3.2 to 10.1) at six months
- improved exercise capacity on cycle ergometer measured by Watt max (MD=10.3, 95% CI 3.6 to 16.9) and pelvic floor strength (p<0.01)

- Certain drugs used for the management of cardiac conditions may need to be assessed in patients with ED.
  - The use of PDE5i is contraindicated in patients taking nitrates for cardiac conditions due to the risk of hypotension.[66, level III; 95, level III]
- The appropriateness of using PDE5i is based on patient's cardiac status and medication regimen.
- A multidisciplinary team consisting of cardiologist, urologist, family medicine specialist, psychiatrist and/or rehabilitative physician are important in managing patients with ED and cardiac disease.

8.2 Patients with Diabetes Mellitus

The prevalence of ED among patients with DM is relatively high, thus they should be regularly screened for the medical condition and vice versa. Optimisation of glycaemic control and other risk factors should be advocated as the treatment of ED. Refer to CPG on Management of Type 2 Diabetes Mellitus (6th Edition).[96]

8.3 Patients with Pelvic Surgery or Prostate Cancer Treatment

ED is a well-known complication of pelvic surgery especially for cancers e.g. rectal, prostate and bladder cancer. Potential mechanisms include direct injury to the neurovascular bundles (e.g. fibrosis and ischaemia) that control the complex mechanism of the erectile response. Radical treatment for prostate cancer includes radical prostatectomy, brachytherapy and external beam radiotherapy (EBRT) which can damage the neurovascular bundles.

A cohort study on patients diagnosed with locoregional prostate cancer treated with surgery or radiation showed:[97, level II-2]

- ED was more prevalent in patients having prostatectomy compared with those receiving radiation (65.3% vs 33.8%, $p<0.001$)
- radiation group had a greater median time to ED diagnosis (346 vs 133 days, $p<0.001$)

A systematic review reported a prevalence of ED ranging from 25 - 100% post-radical prostatectomy.[98, level III] This is supported by a narrative review that showed that the incidence was between 29% and-88%.[99, level III] Factors predicting preservation of EF post-operatively include the patient's age, baseline EF and tumour size.[2]

Patients being considered for nerve-sparing radical prostatectomy should have good EF pre-operatively. Post-operative EF recovery can occur up to 48 months after radical prostatectomy. It has been suggested that post-operative therapy of any type should be initiated as soon as possible after the surgery.[2]

A Cochrane systematic review found that PDE5i was more effective than placebo in ED treatment post-nerve sparing open radical prostatectomy (OR=10.09, 95% CI 6.2 to 16.43). Analysis of two RCTs post-EBRT showed that PDE5i was also more effective than placebo in improving EF. However, the quality assessment for the RCTs on both outcomes was poor.[100, level I]

In another meta-analysis mentioned earlier, a subgroup analysis on the effectiveness of tadalafil 5 mg once-a-day and tadalafil 20 mg on-demand dosing regimen in post-treatment for prostate cancer reported NS in IIEF-EF domain score but significant difference favouring the once-a-day regimen in SEP2.[61, level I]

In an RCT on men treated for ED after bilateral nerve-sparing prostatectomy, combination of VED and tadalafil 20 mg vs tadalafil 20 mg alone was compared. It showed that the combination treatment had significantly higher:[101, level I]

- IIEF scores at 6 - 12 months
- penile hardness scores after 6 - 9 months
- percentage of successful vaginal penetration at 3 - 9 months
- percentage of ability to have intercourse to orgasm at six and 12 months

The AEs of VED were minor local discomfort and that of tadalafil was headache, flushing and muscle ache.

- Multimodal penile rehabilitation with nerve sparing approach may help to improve EF post-radical prostatectomy.

8.4 Spinal Cord Injury Survivors

SCI may lead to sensory, motor and autonomic abnormalities below the spinal lesion and complex urologic conditions. Approximately about 20 - 30% of SCI patients have either no erections or erection not sufficient for sexual intercourse.[102, level I] They are usually young individuals where sexuality and reproduction are important.

A systematic review outlined the following ED treatment options in patients with SCI:[102, level I]

Treatment option	Effectiveness	Safety
Phosphodiesterase-5-inhibitors (PDE5i)	Improved erection, frequency of sexual intercourse, satisfaction, enjoyment, sexual desire, overall sex life, sexual relationship and self-confidence in erection	Most common AEs were headache, dyspepsia, dizziness and rash
Intracavernosal injection (ICI)	82 - 100% rate of adequate penile erection for sexual intercourse	It is associated with a high incidence of AEs which include priapism, pain, penile bruising or swelling.
Vacuum erection device (VED)	Successful vaginal penetration at 70 - 93%	Issue with lack of spontaneity, uncomfortable and sensation of the cold penis
Penile prosthesis (PP)	Satisfaction rate up to 79%	Complications include infection and mechanical failures. Malleable implant is not recommended in men with spinal cord injury due to risk of erosion from lack of sensation.
Sacral neuromodulation	<50% effectiveness	No AEs have been reported

- All of the above treatments may trigger autonomic dysreflexia* which can potentially be life-threatening in SCI patients.

Autonomic dysreflexia is a dangerous syndrome involving an overreaction of the autonomic nervous system. It causes a sudden and severe rise of blood pressure in addition to other symptoms (unopposed sympathetic responses e.g. shortness of breath, chest tightness, flushing, throbbing headache and goosebumps).

9. IMPLEMENTING THE GUIDELINES

Implementation of this CPG is important as it helps in providing quality healthcare services based on the best and most recent available evidence applied to local scenario and expertise. Various factors and resource implications should be considered for the successful uptake of the CPG recommendations.

9.1 Facilitating and Limiting Factors

The facilitating factors in implementing the CPG are:

i) online availability of CPG on multiple websites for healthcare providers
ii) conferences and updates on the management of ED including those involving professional bodies (e.g. Malaysian Urological Association and Malaysian Society of Andrology and the Study of the Aging Male)
iii) public awareness campaigns on ED (e.g. Men's Health Day)

Limiting factors in the CPG implementation include:

i) different levels of expertise and wide variation in practice due to resource constraints
ii) limited awareness and knowledge in the management of ED among healthcare providers
iii) lack of confidence among healthcare providers in discussing ED with patients
iv) social stigmatisation of ED among patients

9.2 Potential Resource Implications

The prevalence of ED is increasing which renders it to become an emerging public health concern. This is made worse by the public and healthcare providers shying away from identifying and discussing the matter in the clinical practice. In diagnosing ED, healthcare providers require expertise (knowledge and skills) to elicit the problem and provide further management on it. Rigorous work-up and cardiovascular assessment further complicate diagnosing ED. Treatment-wise, the limited availability of pharmacotherapy and mechanical devices makes treating ED even more difficult. There is also an obvious lack of urologists and clinical psychologists especially in the public sector to help manage such cases.

In line with the key recommendations in this CPG, the following is proposed as clinical audit indicator for the quality management of ED:

Percentage of patients newly diagnosed with ED assessed using IIEF-5 = $\frac{\text{Number of newly diagnosed ED patients assessed with IIEF-5 in a period}}{\text{Total number of newly diagnosed ED patients in the same period}}$ x100%

Target of 100%

Percentage of ED patients with high cardiac risk based on Princeton Consensus referred to the cardiologist = $\frac{\text{Number of ED patients with high cardiac risk based on Princeton Consensus referred to the cardiologist in a period}}{\text{Total number of ED patients with high cardiac risk based on Princeton Consensus in the same period}}$ x100%

Target of 70%

Implementation strategies will be developed following the approval of the CPG by MoH which include Quick Reference and Training Module and they are available in the MoH and AMM websites after development.

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Appendix 1

EXAMPLE OF SEARCH STRATEGY

Clinical Question: What are the safe and effective pharmacological treatments in ED?

- phosphodiesterase-5-inhibitors

1. ERECTILE DYSFUNCTION/
2. (erectile adj1 dysfunction).tw.
3. impotence.tw.
4. (male adj1 impotence).tw.
5. (male adj2 sexual impotence).tw.
6. 1 or 2 or 3 or 4 or 5
7. PHOSPHODIESTERASE 5 INHIBITORS/
8. (phosphodiesterase 5 adj2 inhibitor*).tw.
9. ((pde5 or pde-5) adj1 inhibitor*).tw.
10. pde 5 inhibitor*.tw.
11. phosphodiesterase type 5 inhibitor*.tw.
12. SILDENAFIL CITRATE/
13. (sildenafil adj1 (citrate or lactate)).tw.
14. homosildenafil.tw.
15. hydroxyhomosildenafil.tw.
16. sildenafil.tw.
17. nglis.tw.
18. TADALAFIL/
19. nglis.tw.
20. VARDENAFIL DIHYDROCHLORIDE/
21. vardenafil.tw.
22. ((anhydrous or trihydrate) adj2 vardenafil hydrochloride).tw.
23. (vardenafil adj1 (dihydrochloride or hydrochloride)).tw.
24. nglish.tw.
25. avanafil.tw.
26. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25
27. 6 and 26
28. limit 27 to (nglish language and humans)
29. limit 28 to last 15 years
30. limit 29 to “systematic review”

Appendix 2

CLINICAL QUESTIONS

a) Risk factor, diagnosis and assessment

- What are the risk and aggravating factors for ED?
- What are the accurate screening tools for ED?
- What are the accurate methods used to assess ED?
- What are the accurate cardiovascular risk assessments in ED?
- How can the diagnosis of ED be accurately made?

b) Treatment

- What are the safe and effective non-pharmacological treatments in ED?
  - life-style changes to modify risk factors
    - smoking
    - diet
    - alcohol consumption
    - obesity
    - stress
    - physical activity
    - metabolic syndrome
  - device (second stage)
    - vacuum pump
    - shockwave therapy
  - psychosocial/psychopathological treatment
- What are the safe and effective pharmacological treatments in ED?
  - oral medications e.g. phosphodiesterase-5-inhibitors
  - topical/intraurethral alprostadil (vasoactive agents)
  - intra-cavernous penile injection with vasoactive agents
- What are the safe and effective surgical interventions in ED?
  - penile prosthesis
  - surgery for penile revascularisation

c) Traditional and complementary medicine

- What are the safe and effective treatment and complementary medicine (TCM) in ED?

d) Follow-up, monitoring and referral

- What is the effective follow-up and monitoring schedule for ED?
- When should patient with ED be referred for secondary/tertiary care?
  - urologist
  - cardiologist

- neurologist
- endocrinologist
- psychiatrist
- shared-care concept/multidisciplinary

e) Special Groups

- What are the safe and effective treatment modalities in ED for the following special groups?
  - patients with cardiac disease
  - patients with pelvic surgery or prostate cancer treatment
  - spinal cord injury survivors

Appendix 3

RELEVANT HISTORY TAKING IN PATIENTS WITH SYMPTOMS OF ED

History components	Questions
History of presenting complaint	Patients with suspected ED will primarily complain of difficulties initiating or sustaining an erection. Further details surrounding these issues should be explored: • Onset of sexual dysfunction (i.e. acute, gradual) • Duration of sexual dysfunction • Lack of libido • Rigidity of erection • Duration of sexual stimulation • Difficulties with ejaculation/orgasm • Absence of morning erection
Past medical/ surgical history	Previous sexual dysfunction, CVD, metabolic syndrome (i.e. hypertension, DM, obesity and dyslipidaemia) and pelvic surgery
Medication history	Antihypertensives, antidepressants, antipsychotics, anticonvulsants, nitrates and PDE5i
Psychiatric history	Current or previous psychological problems (e.g. depression, anxiety), stress, coping abilities, cognitive factors and previous trauma
Social history	Smoking, alcohol consumption, illicit drug use, diet, exercise, cultural and religious aspects
Sexual history	Current sexual partner(s), relationship status, partner's perception to ED, gender dysphoria or sexual orientation, sexual exposure and experience (e.g. masturbation, pornography consumption), plan for children

CVD = cardiovascular disease; DM = diabetes mellitus; ED = erectile dysfunction; PDE5i = phosphodiesterase-5-inhibitor

Appendix 4

5-ITEM VERSION OF INTERNATIONAL INDEX OF ERECTILE FUNCTION (IIEF-5)

A) English version

Patient Name: _____ Date of Birth: _____
Date Completed: _____

Over the past 6 months:					
1. How do you rate your **confidence** that you could get and keep an erection?	1 Very Low	2 Low	3 Moderate	4 High	5 Very high
2. When you had erections with sexual stimulation, **how often** were your erections hard enough for penetration?	1 Almost never/ Never	2 A few times (much less than half the time)	3 Sometimes (about half the time)	4 Most times (much more than half the time)	5 Almost always/ Always
3. During sexual intercourse, **how often** were you able to maintain your erection after you had penetrated (entered) your partner?	1 Almost never/ Never	2 A few times (much less than half the time)	3 Sometimes (about half the time)	4 Most times (much more than half the time)	5 Almost always/ Always
4. During sexual intercourse, **how difficult** was it to maintain your erection to completion of intercourse?	1 Extremely difficult	2 Very difficult	3 Difficult	4 Slightly difficult	5 Not difficult
5. When you attempted sexual intercourse, **how often** was it satisfactory for you?	1 Almost never/ Never	2 A few times (much less than half the time)	3 Sometimes (about half the time)	4 Most times (much more than half the time)	5 Almost always/ Always

IIEF-5 scoring

The IIEF-5 score is the sum of the ordinal responses to the 5 items.
22 - 25: No erectile dysfunction
17 - 21: Mild erectile dysfunction
12 - 16: Mild to moderate erectile dysfunction
8 - 11 : Moderate erectile dysfunction
5 - 7 : Severe erectile dysfunction

Total score: _____

Source: Rosen RC, Cappelleri JC, Smith MD, et al. 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):319-26.

B) Malay version

Nama Pesakit : _____ Tarikh Lahir : _____
Tarikh Penilaian : _____

Di sepanjang 6 bulan yang lalu:					
1. Pada penilaian anda, sejauh manakah **tahap keyakinan** anda, yang anda boleh mencapai serta mengekalkan ketegangan zakar (kemaluan atau 'batang' keras)?	1 Sangat rendah	2 Rendah	3 Sederhana	4 Tinggi	5 Sangat tinggi
2. Apabila anda mengalami ketegangan zakar (kemaluan atau 'batang' keras) menerusi rangsangan seks, **berapa kerap** ketegangan itu cukup keras untuk persetubuhan?	1 Tidak pernah atau hampir tidak pernah	2 Beberapa kali (kurang dari 50%)	3 Kadang-kadang (kira- kira 50%)	4 Sering kali (lebih dari 50%)	5 Setiap kali atau hampir setiap kali
3. Sewaktu bersetubuh, **berapa kerap** anda dapat mengekalkan ketegangan zakar (kemaluan atau 'batang' keras)?	1 Tidak pernah atau hampir tidak pernah	2 Beberapa kali (kurang dari 50%)	3 Kadang-kadang (kira- kira 50%)	4 Sering kali (lebih dari 50%)	5 Setiap kali atau hampir setiap kali
4. Sewaktu bersetubuh berapa sukarkah untuk mengekalkan ketegangan sehingga selesai persetubuhan?	1 Tersangat sukar	2 Sangat sukar	3 Sukar	4 Sukar sedikit	5 Tidak sukar
5. Apabila anda cuba melakukan persetubuhan, **berapa kerap** anda berasa puas hati?	1 Tidak pernah atau hampir tidak pernah	2 Beberapa kali (kurang dari 50%)	3 Kadang-kadang (kira- kira 50%)	4 Sering kali (lebih dari 50%)	5 Setiap kali atau hampir setiap kali

Pemarkahan IIEF-5:
Pemarkahan skor IIEF-5 adalah jumlah markah bagi 5 soalan di atas.
22 - 25: Tiada masalah lemah tenaga batin (erectile dysfunction)
17 - 21: Masalah lemah tenaga batin tahap ringan
12 - 16: Masalah lemah tenaga batin tahap ringan ke sederhana
8 - 11 : Masalah lemah tenaga batin tahap sederhana
5 - 7 : Masalah lemah tenaga batin yang serius

Jumlah markah: _____

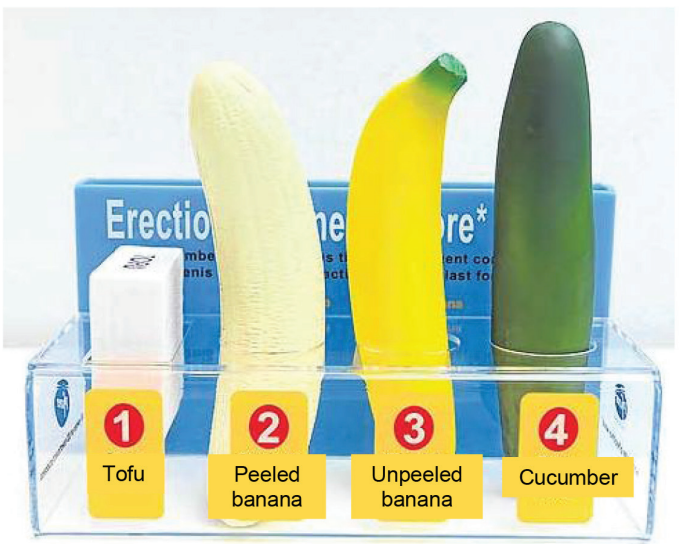
Adapted: Lim TO, Das A, Rampal S, et al. Cross-cultural adaptation and validation of the English version of the International Index of Erectile Function (IIEF) for use in Malaysia. Int J Impot Res. 2003;15(5):329-336.

Appendix 5

ERECTION HARDNESS SCORE (EHS)

Erection Hardness Score*
0 : Penis does not enlarge.
1 : Penis is larger but not hard.
2 : Penis is hard but not hard enough for penetration.
3 : Penis is hard enough for penetration but not completely hard.
4 : Penis is completely hard and fully rigid.

*"How would you rate the hardness of your erection?"



Source: Mulhall JP, Goldstein I, Bushmakin AG, et al. Validation of the erection hardness score. J Sex Med. 2007;4(6):1626-1634.

TREATMENT IN ED

A) Mechanical Treatment

Device	When/How to apply	Adverse events	Precautions
Vacuum Erectile Devices	5 - 10 minutes before intercourse	Issues with lack of spontaneity, uncomfortable and sensation of cold penis Priapism	Antiplatelets and anticoagulants - may cause bleeding and bruising
Low-intensity Extracorporeal Shockwave Therapy	20 - 30 minutes for each session, once or twice/week for at least 6 sessions	Pain at the site, bleeding and bruising, haematuria, skin infection, painful erection, worsening penile curvature	Antiplatelets and anticoagulants - may cause bleeding and bruising

Source:

1. Beaudreau SA, Van Moorleghem K, Dodd SM, et al. Satisfaction with a Vacuum Constriction Device for Erectile Dysfunction among Middle-Aged and Older Veterans. Clin Gerontol. 2020;44(3):307-315.
2. Ortac M, Ozmez A, Cilesiz NC, et al. The impact of extracorporeal shock wave therapy for the treatment of young patients with vasculogenic mild erectile dysfunction: A prospective randomized single-blind, sham controlled study. Andrology. 2021;9(5):1571-1578.
3. Salonia A, Bettocchi C, Capogrosso P, et al. EAU Guidelines on Sexual and Reproductive Health. EAU Guidelines Office, Arnhem, The Netherlands: European Association of Urology; 2023.

B) Pharmacological Treatment

Drug	Recommended Dose	Adverse events	Contraindications/Precautions
Sildenafil	**Initial dose:** 50 mg to be taken approximately 1 hour before sexual activity, effective 30 minutes to 4 hours after administration (Half-life: 4 hours)	**Common:** Headache, flushing, dyspepsia, nasal congestion, nasopharyngitis, back pain, myalgia, visual abnormalities **Rare:** NAION	Known hypersensitivity to PDE5i or any component of tablet Concurrent use of PDE5i with NO donors, organic nitrates or organic nitrites (e.g. glyceryl trinitrate)
	Dose range: 25 - 100 mg of maximum once a day		
	Dose adjustment: **Renal impairment:** CrCl <30 ml/min or HD - Starting dose 25 mg **Hepatic impairment:** Starting dose 25 mg **Geriatric use:** Starting dose 25 mg **Co-medications:** **Alpha-blockers -** Starting dose 25 mg **Ritonavir -** Maximum 25 mg over 48 hours **CYP3A4 inhibitors -** Starting dose 25 mg	Patients should seek emergency treatment if an erection lasts >4 hours. Use PDE5i with caution in patients predisposed to priapism. Patients to stop taking PDE5i and seek prompt medical attention in the event of sudden decrease or loss of hearing.	Time required from last dose to administration of a nitrate (e.g. glyceryl trinitrate): 24 hours
Tadalafil	**Initial dose:** <u>As needed:</u> 10 mg to be taken at least 30 minutes before sexual activity, effective for up to 36 hours after administration <u>Once daily use:</u> 2.5 mg once daily without regard to timing of sexual activity (Half-life: 17.5 hours)	**Common:** Headache, flushing, dyspepsia, nasal congestion, nasopharyngitis, back pain, myalgia, visual abnormalities **Rare:** NAION Patients should seek emergency treatment if an erection lasts >4 hours. Use PDE5i with caution in patients predisposed to priapism. Patients to stop taking PDE5i and seek prompt medical attention in the event of sudden decrease or loss of hearing.	Known hypersensitivity to PDE5i or any component of tablet Concurrent use of PDE5i with NO donors, organic nitrates or organic nitrites (e.g. glyceryl trinitrate) Time required from last dose to administration of a nitrate (e.g. glyceryl trinitrate): 48 hours Administration with guanylate cyclase (GC) stimulators e.g. riociguat
	Dose range: <u>As needed:</u> 5 - 20 mg of maximum once a day <u>Once daily use:</u> 2.5 - 5 mg		

Drug	Recommended Dose	Adverse events	Contraindications/Precautions
	Dose adjustment As needed: **Renal impairment:** CrCl 30 - 50 ml/min: Starting dose 5 mg, maximum dose 10 mg over 48 hours CrCl <30 ml/min or HD: Maximum 5 mg over 72 hours **Hepatic impairment:** Child Pugh Class A or B: Maximum dose 10 mg per day Child Pugh Class C: Not recommended CYP3A4 inhibitors: Maximum 10 mg over 72 hours		
	Once daily use: **Renal impairment:** CrCl <30 ml/min or HD: Not recommended **Hepatic impairment:** Child Pugh Class A or B: Caution is advised when prescribing Child Pugh Class C: Not recommended CYP3A4 inhibitors: Maximum 2.5 mg As needed & once daily dose: **Alpha-blockers:** Patient should be on stable dose prior to initiation of tadalafil and initiated at the lowest recommended dose		
Avanafil	**Initial dose:** 100 mg to be taken approximately 30 minutes before sexual activity (Half-life: 5 hours) **Dose range:** 50 - 200 mg of maximum once a day	**Common:** Headache, flushing, dyspepsia, nasal congestion, nasopharyngitis, back pain, myalgia, visual abnormalities **Rare:** NAION	Known hypersensitivity to PDE5i or any component of tablet Concurrent use of PDE5i with NO donors, organic nitrates or organic nitrites (e.g. glyceryl trinitrate)

Drug	Recommended Dose	Adverse events	Contraindications/Precautions
	Dose adjustment: **Renal impairment:** CrCl <30 ml/min or HD - Do not use **Hepatic impairment:** Child Pugh C - Do not use **CYP3A4 inhibitors:** Moderate inhibitors (e.g. erythromycin, diltiazem, fluconazole, verapamil) - Maximum 50 mg over 24 hours **Alpha-blockers:** Patient should be on stable dose prior to initiation of tadalafil and should be initiated at 50 mg dose	Patients should seek emergency treatment if an erection lasts >4 hours. Use PDE5i with caution in patients predisposed to priapism. Patients to stop taking PDE5i and seek prompt medical attention in the event of sudden decrease or loss of hearing.	Time required from last dose to administration of a nitrate (e.g. glyceryl trinitrate): 12 hours **CYP3A4 inhibitors:** Contraindicated in strong inhibitors (e.g. ketoconazole, ritonavir, itraconazole, clarithromycin)
Vardenafil	**Initial dose:** 10 mg to be taken approximately 60 minutes before sexual activity (Half-life: 4 - 5 hours)	**Common:** Headache, flushing, dyspepsia, nasal congestion, nasopharyngitis, back pain, myalgia, visual abnormalities **Serious:** QT prolongation **Rare:** NAION Patients should seek emergency treatment if an erection lasts >4 hours. Use PDE5i with caution in patients predisposed to priapism. Patients to stop taking PDE5i and seek prompt medical attention in the event of sudden decrease or loss of hearing.	Known hypersensitivity to PDE5i or any component of tablet Concurrent use of PDE5i with NO donors, organic nitrates or organic nitrites (e.g. glyceryl trinitrate) Time required from last dose to administration of a nitrate (e.g. glyceryl trinitrate): 24 hours Administration with GC stimulators, such as riociguat Patients with congenital QT syndrome or taking class IA (e.g. quinidine, procainamide) or class III (e.g. amiodarone, sotalol), antiarrhythmics
	Dose range: 5 - 20 mg of maximum once a day		
	Dose adjustment: **Renal impairment:** HD: Do not use **Hepatic impairment:** Child Pugh B: Starting dose 5 mg, maximum dose 10 mg Child Pugh C: Do not use **CYP3A4 inhibitors:** Ritonavir: Maximum 2.5 mg over 72 hours Indinavir, saquinavir, atazanavir, ketoconazole 400 mg daily, itraconazole 400 mg daily, clarithromycin: Maximum 2.5 mg over 24 hours Ketoconazole 200 mg daily, itraconazole 200 mg daily, erythromycin: Maximum 5 mg over 24 hours		

Drug	Recommended Dose	Adverse events	Contraindications/Precautions
	Alpha-blockers: Patient should be on stable dose prior to initiation of tadalafil and should be initiated at 5 mg dose **Geriatric populations (≥65 years of age): Starting dose 5 mg**		

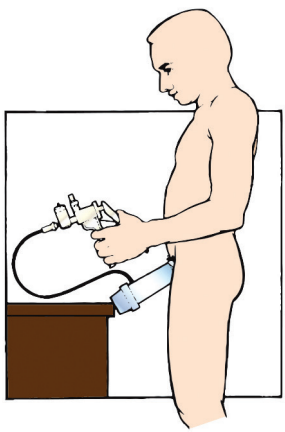
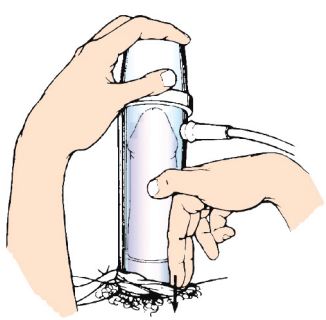
CrCl = creatinine clearance; ED = erectile dysfunction; HD = haemodialysis; GC = guanylate cyclase; mg = milligram; ml/min = millilitre per minute; NAION = non-arteritic anterior ischemic optic neuropathy; NO = nitric oxide; PDE5i = phosphodiesterase-5-inhibitors

Source:

1. Salonia A, Bettocchi C, Capogrosso P, et al. EAU Guidelines on Sexual and Reproductive Health. EAU Guidelines Office, Arnhem, The Netherlands: European Association of Urology; 2023.
2. U.S. Food & Drug Administration. PRESCRIBING INFORMATION: CIALIS®: USFDA; 2023.
3. U.S. Food & Drug Administration. PRESCRIBING INFORMATION: LEVITRA®: USFDA; 2015.
4. U.S. Food & Drug Administration. PRESCRIBING INFORMATION: STENDRA®: USFDA; 2012.
5. U.S. Food & Drug Administration. PRESCRIBING INFORMATION: VIAGRA®: USFDA; 2014.

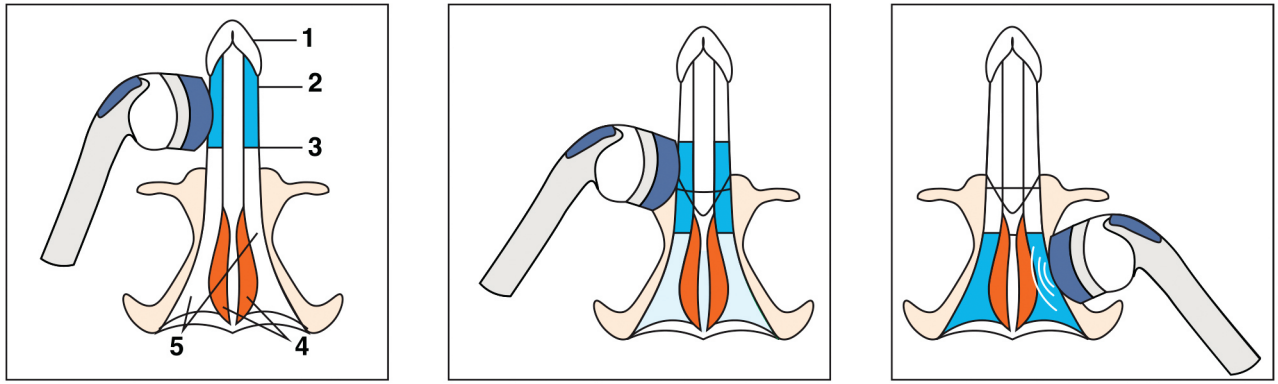
Appendix 7

APPLICATION OF VACUUM ERECTILE DEVICE (VED)

	• The equipment consists of a vacuum chamber, a vacuum pump, and a constricting ring or band. • The pump can be operated manually as shown, but usually battery-operated for easy use. • An elastic band is used to constrict the base of the penis to maintain erection after it is achieved.
	• Before the device is used, the constricting band is lubricated with a water-soluble jelly and placed around the chamber near its open end. • The jelly is next applied generously to the base of the penis to assure an air-tight seal. • The penis is placed in the chamber and the vacuum is applied for 3 - 6 minutes or until it becomes rigid.
	• The constricting band is slid off the end of the chamber to constrict the base of the penis. • The vacuum is then released and the chamber removed. Sexual intercourse can be performed immediately after. • The band should not be left on longer than 30 minutes.

Source: Nadig PW. Vacuum erection devices: a review. World J Urol. 1990;8:114-117.

LOW-INTENSITY EXTRACORPOREAL SHOCKWAVE THERAPY



1. Glans penis; 2. Corpus cavernosum; 3. Corpus spongiosum; 4. Bulbospongiosus muscle; 5. Ischiocavernosus muscle; Treatment area

How it works?

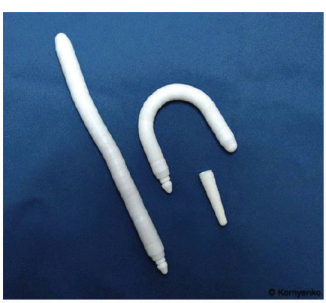
- While the patient is lying down, ultrasound gel is applied to the applicator head and/or the treatment area.
- The applicator head is applied to areas of the penile shaft and crus.
- The shockwave technology skilfully creates waves that treat a broad area from the superficial surface of the penile shaft to the deeper erectile tissues of the crura.
- It is currently recommended that this treatment to be conducted once or twice a week, for at least 6 sessions.
- The waves stimulate tissue and do not cause any pain or external scarring. Patients can resume daily regular activity after the procedure. Side effects (if any) are usually mild and temporary.
- Most patients report progress after 3 - 4 sessions.

Appendix 9

EXAMPLES OF PENILE PROSTHESIS

Three-piece inflatable penile prosthesis

Two-piece inflatable device



Malleable prosthesis

Source: Levine LA, Becher E, Bella A, et al. Penile prosthesis surgery: current recommendations from the international consultation on sexual medicine. J Sex Med. 2016;13(4):489-518.

LIST OF ABBREVIATIONS

AE	adverse event
AGREE	Appraisal of Guidelines for Research and Evaluation
AI	arterial insufficiency
ASCVD	atherosclerotic cardiovascular disease
AUA	American Urological Association
AUC	area under the curve
β-blocker	beta-blocker
BMI	body mass index
BPH	benign prostatic hyperplasia
CAD	coronary artery disease
CBST	cognitive-behavioural sex therapy
CBT	cognitive behaviour therapy
CDC	Centers for Disease Control and Prevention
CI	confidence interval
cm/s	centimetre per second
CHF	congestive heart failure
CPG	clinical practice guidelines
CrCl	creatinine clearance
CV	cardiovascular
CVD	cardiovascular disease
DG	development group
DM	diabetes mellitus
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th Edition
e.g.	for example
EAU	European Association of Urology
EBRT	external beam radiotherapy
ED	erectile dysfunction
EDITS	Erectile Dysfunction Inventory of Treatment Satisfaction
EF	erectile function
EHS	Erectile Hardness Score
ESRD	end-stage renal disease
EST	exercise stress test
FDA	Food and Drug Administration
FSD	female sexual dysfunction
GRADE	Grading Recommendations, Assessment, Development and Evaluation
HbA1c	haemoglobin A1C
HDL	high-density lipoprotein
HR	hazard ratio
HTA	Health Technology Assessment
i.e.	that is
ICD-9	International Classification of Diseases, Ninth Revision
ICI	intracavernosal injection
ICSM	International Consultation on Sexual Medicine
IHD	ischaemic heart disease
IIEF	International Index of Erectile Function
IIEF-5	5-item version of International Index of Erectile Function
IIEF-15	15-item version of International Index of Erectile Function
IIEF-EF	International Index of Erectile Function-erectile function
IMI	internet- and mobile-based psychological intervention

IQR	interquartile range
kg/m^2	kilogram per meter square
LDL	low-density lipoprotein
Li-ESWT	low-intensity extracorporeal shockwave therapy
LUTS	lower urinary tract symptoms
LVD	left ventricular dysfunction
MACE	major adverse cardiac event
MaHTAS	Malaysian Health Technology Assessment Section
MD	mean difference
MET	metabolic equivalents time
mg	milligram
mg/dL	milligram per decilitre
MI	myocardial infarction
MoH	Ministry of Health
MUSE	Medicated Urethral System for Erection
NAION	non-arteritic anterior ischemic optic neuropathy
NO	nitric oxide
NPTR	nocturnal penile tumescence and rigidity
NS	no significant
NYHA	New York Heart Association
OR	odds ratio
OSA	obstructive sleep apnoea
PDE5i	phosphodiesterase-5-inhibitor
PP	penile prosthesis
PROCAM	Prospective Cardiovascular Münster
PSA	prostate-specific antigen
PSV	peak systolic velocity
RC	review committee
RCT	randomised controlled trial
RoB	Risk of Bias
RR	relative risk / risk ratio
SCI	spinal cord injury
SEAR	Self-Esteem and Relationship
SEP	Sexual Encounter Profile
SMD	standardised mean difference
SUCRA	surface under the cumulative ranking curve
TBI	traumatic brain injury
TCM	traditional and complementary medicine
U.S.	United States
USPSTF	U. S. Preventive Services Task Force
VED	vacuum erection device
VOD	veno-occlusive disease
WMD	weighted mean difference

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