### Epidemiology and risk factors

- Erectile dysfunction (ED) has been defined as the persistent inability to attain and/or maintain an erection sufficient for sexual performance.
- The risk factors for ED (sedentary lifestyle, obesity, smoking, hypercholesterolaemia and the metabolic syndrome) are very similar to the risk factors for cardiovascular disease (CVD).
- It is clear ED may be associated with other causes of CVD such as hypertension, dyslipidaemia and endothelial dysfunction. ED may be the first presentation of serious medical conditions such as diabetes or hypertension.

### Laboratory testing

- The choice of investigations depends on the individual circumstances of the patient. Serum lipids and fasting plasma glucose should be measured in all patients.
- Hypogonadism is a treatable cause of ED that may also make men less responsive, or even non-responsive, to phosphodiesterase type 5 (PDE5) inhibitors; therefore, all men with ED should have serum testosterone measured on a blood sample taken in the morning between 08.00 and 11.00.
- Serum prostate specific antigen (PSA) should be considered if clinically indicated. It should certainly be measured before commencing testosterone therapy and at regular intervals during testosterone therapy.

### Cardiovascular system

- Coronary heart disease (CHD) is associated with many of the same risk factors as ED. Coronary artery disease (CAD) is often just one affected site in a generalised arteriopathy that is also likely to affect the arterial inflow to the corpora cavernosum of the penis.
- ED in an otherwise asymptomatic man may be a marker for underlying CAD. All men with unexplained ED should have a thorough evaluation and any risk factors for CHD that are identified should be addressed.
A man with ED and no cardiac symptoms is a cardiac patient until proven otherwise

Proactive management of ED in the cardiovascular (CV) patient provides an ideal and effective opportunity to address other CV risk factors and improve treatment outcomes

Men with previously-diagnosed CHD should be asked about ED as part of their routine surveillance and management; ED treatments should be offered to all who desire them

Current NICE guidance recommends that all men with type 2 diabetes be asked annually about ED, assessed, and offered oral treatment with the medication with the lowest acquisition cost

There is no evidence that currently licensed treatments for ED add to the overall CV risk in patients with or without previously-diagnosed CVD

Specialised investigations

Most patients do not need further investigations unless specifically indicated. However, some patients wish to know the aetiology of their ED and should be investigated appropriately. Other indications for specialist investigations include:
- young patients who have always had difficulty in obtaining and/or sustaining an erection
- patients with a history of trauma
- where an abnormality of the testes or penis is found on examination
- patients unresponsive to medical therapies that may desire surgical treatment for ED

Penile abnormalities

Surgical problems that cause ED, e.g. phimosis, tight frenulum and penile curvatures, should be diagnosed clinically and are usually simple to treat surgically, which results in a permanent cure of ED

Treatment

The primary goal of management of ED is to enable the individual or couple to enjoy a satisfactory sexual experience. This involves:

- identifying and treating any curable causes of ED
- initiating lifestyle change and risk factor modification
- providing education and counselling to patients and their partners

Reversible causes of ED

Hormonal:
- hypogonadism
- hyperthyroidism/hypothyroidism
- hyperprolactinaemia

Post-traumatic arteriogenic ED in young patients

Drug-induced ED – drugs may affect sexual response in a number of ways:
- drugs that cause sedation may affect sexual motivation and, indirectly, cause ED
- drugs that affect CV function, such as antihypertensive agents, may act centrally and may also affect penile haemodynamics
- some drugs affect endocrine parameters
- anti-androgens and oestrogens may affect both sexual desire and erection
- drugs that cause hyperprolactinaemia, such as phenothiazines, may also affect sexual desire and erection

Partner sexual problems

Psychosexual counselling and therapy

Radical prostatectomy

Lifestyle management

Lifestyle modifications can greatly reduce the risk of ED, and should accompany any specific pharmacotherapy or psychological therapy. However, pharmacotherapy should not be withheld on the basis that lifestyle changes have not been made

Lifestyle factors include:
- psychosocial issues
- adverse side-effects of non-prescription drugs
- influence of any co-morbidities, including those in the partner
Management algorithm according to graded cardiovascular risk

Sexual inquiry

Clinical evaluation

Low risk

Intermediate risk

High risk

Manage ED in primary care setting

Cardiovascular assessment and restratification

Sexual activity deferred until cardiac condition stabilised

Risk factors and CHD evaluation, treatment and follow-up for all patients with ED

**Grading of risk**

**Cardiovascular status upon presentation**

**ED management recommendations for the primary care physician**

**LOW RISK**

- Controlled hypertension
- Asymptomatic ≤3 risk factors for CAD – excluding age and gender
- Mild valvular disease
- Minimal/mild stable angina
- Post successful revascularisation
- CHF (NYHA class I)

- Manage within the primary care setting
- Review treatment options with patient and his partner (where possible)

**INTERMEDIATE RISK**

- Recent MI or CVA (i.e. within last 6 weeks)
- Asymptomatic but >3 risk factors for CAD – excluding age and gender
- LVD/CHF (NYHA class II)
- Murmur of unknown cause
- Moderate stable angina
- Heart transplant
- Recurrent TIA's

- Specialised evaluation recommended (e.g. exercise test for angina, echocardiogram for murmur)
- Patient to be placed in high or low risk category, depending upon outcome of testing

**HIGH RISK**

- Severe or unstable or refractory angina
- Uncontrolled hypertension
- (SBP >180 mmHg)
- CHF (NYHA class III, IV)
- Recent MI or CVA (i.e. within last 14 days)
- High risk arrhythmias
- Hypertrophic cardiomyopathy
- Moderate/severe valve disease

- Refer for specialised cardiac evaluation and management
- Treatment for ED to be deferred until cardiac condition established and/or specialist evaluation completed

ED=erectile dysfunction; CAD=coronary artery disease; NYHA= New York Heart Association; MI=myocardial infarction; CVA=cerebral vascular accident; LVD=left ventricular dysfunction; CHF=congestive heart failure; TIA=transient ischaemic attack; SBP=systolic blood pressure.
The potential advantages of lifestyle changes may be particularly pronounced in those with psychogenic ED, but patients with serious medical illnesses such as diabetes may also benefit from these changes, e.g. weight loss.

Hypogonadism and testosterone replacement therapy

The cause of hypogonadism should always be sought before treatment with testosterone is initiated, but this does not mean that treatment for ED should be deferred. Prior assessment and safety monitoring should be performed according to contemporary authoritative guidelines.

Men with a total serum testosterone that is consistently <12 nmol/l might benefit from up to a 6 months trial of testosterone replacement therapy for ED and should be managed according to current guidelines (see algorithm below).

A range of well-tolerated testosterone formulations is available
- long-acting (three-monthly) testosterone injection or daily application of a transdermal testosterone gel are acceptable to most men.

First-line treatment

- PDE5 inhibitors (e.g. sildenafil, tadalafil, vardenafil):
  - have proven efficacy and safety both in non-selected populations of men with ED and in specific sub-groups of patients (e.g. men with diabetes and those who have had a prostatectomy)
  - sildenafil and vardenafil are relatively short-acting drugs, having a half life of approximately 4 hours, whereas tadalafil has a significantly longer half life of 17.5 hours
  - are not initiators of erection but require sexual stimulation in order to facilitate an erection. It is currently recommended that patients should receive eight doses of a PDE5 inhibitor with sexual stimulation at maximum dose before classifying a patient as a non-responder
  - tadalafil is licensed for daily use at 2.5 mg and 5 mg for PDE5 responders who anticipate sexual activity more than twice per week.

This regime may be more cost effective in such cases and clinical trials suggest a marked reduction in reported adverse events.

- Vacuum erection devices:
  - are highly effective in inducing erections regardless of the aetiology of the ED
  - reported satisfaction rates vary considerably from 35% to 84%
  - long-term usage of vacuum devices also varies but is considerably higher than for self-injection therapy
  - most men who are satisfied with vacuum devices continue to use them long term
  - adverse effects include bruising, local pain, and failure to ejaculate. Partners sometimes report the penis feels cold
  - serious adverse events are very rare but skin necrosis has been reported

Second-line treatment

- Intracavernous injection therapy

- Intraurethral alprostadil

Third-line treatment

- Penile prosthesis:
  - should be offered to all patients who are unwilling to consider, failing to respond to, or unable to continue with medical therapy or external devices. All patients and their partners should be counselled pre-operatively, see and handle all the available devices and, if possible, speak to other patients who have had surgery
  - particularly suitable for those with severe organic ED, especially if the cause is Peyronie’s disease or post priapism. All patients should be given a choice of either a malleable or inflatable prosthesis.

Patient/partner education – consultation and referrals

- The primary reason for referral to the clinician should be elicited. The motivating factors and expectations should be clarified as well as the intention, or otherwise, of the partner.
to accept any specific pharmacological, physical or psychological therapies

- An understanding by the patient and partner of basic anatomy and physiology and the purpose of blood and specialist investigations is helpful
- An explanation of the principles of the treatment options is valuable
- Provision of educational information is valuable reinforcement for patients


- ED associated with the following medical conditions are deemed to qualify for prescription at NHS expense:
  - diabetes
  - multiple sclerosis
  - Parkinson’s disease
  - poliomyelitis
  - prostate cancer
  - prostatectomy
  - radical pelvic surgery
  - severe pelvic injury
  - renal failure treated by dialysis or transplant
  - single gene neurological disease
  - spinal cord injury
  - spina bifida
  - NHS drug treatment before 15th September 1998
  - if patient is suffering severe distress on account of their ED

- The GP is recommended to refer if severe distress is suspected. It is the role of the specialist to endorse that judgement. It is recommended that the following should be taken into account:
  - significant disruption to normal social and occupational activity
  - marked effect on mood, behaviour, social and environmental awareness
  - marked effect on interpersonal relationships

- After an initial titration period, 1 tablet per week is considered to be appropriate for the majority of patients, but when more is required the GP should prescribe that quantity at NHS cost

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**Algorithm for androgen therapy in a man presenting with ED**

**Male with ED**

First-time presentation

Screen all ED patients for T

- T normal
  - ED therapies (e.g. PDE5i)
  - Unsatisfactory response
  - Alternative therapies, e.g. injections, prosthesis

- T low
  - T therapy
  - Unsatisfactory response
  - Continue T therapy

- Satisfactory response

**Male with ED. Failure of PDE5i**

No previous T testing

Screen all ED patients for T

- T low
  - Combination therapy, e.g. T + PDE5i
  - Unsatisfactory response
  - Continue combination therapy

- T normal
  - Alternative ED therapies, e.g. injections, prosthesis
  - Satisfactory response