Introduction

The penile erection results from an integration of appropriate neurological, vascular and hormonal systems on phallic tissues. Erectile dysfunction is the inability to attain and or maintain an erection sufficient to permit satisfactory sexual performance. Normal erectile function relies on arterial dilatation, trabecular smooth muscle relaxation and veno-occlusion within the corpora. Erectile dysfunction prevalence increases with age and is often the earliest manifestation of cardiovascular disease.

The National Institute of Clinical Excellence (NICE) and the British Society of Sexual Medicine (BSSM) in the UK and the European Association of the Urology (EAU) have guidelines on the management of erectile dysfunction. This article will look at the similarities of the guidelines commenting where and how they differ.

Causes of erectile dysfunction

Both the UK and European guidelines agree that causative factors for erectile dysfunction (ED) include modifiable conditions of metabolic syndrome, lack of exercise and smoking. They agree these are also risk factors for cardiovascular disease (CVD) and that both conditions represent a disease of endothelial dysfunction.

The European Association of Urology (EAU) guidelines quote lifestyle modifications and cardiovascular optimization which can improve ED. These guidelines also note the need for prospective studies to determine the effects of exercise or other lifestyles changes on ED prevention. The British Society of Sexual Medicine (BSSM) discuss lifestyle changes for ED patients with psychogenic ED and mention patients with serious medical illness who might benefit from lifestyle modification. The National Institute of Clinical Excellence (NICE) guidelines emphasize weight loss and stopping smoking as well as alcohol reduction and increase in exercise in the overall management of ED. The dearth of evidence in this area has limited both guidelines on recommendations in lifestyle changes on a population with likely underlying CVD and ED.

The NICE guidelines specifically mention cycling and its association with ED. Cycling activity more than three times weekly increases the risk of ED, and the guidelines quote a trial of abstinence from cycling and reassessment of the symptoms of ED. They also mention the avoidance of herbal remedies, which can often contain sildenafil.

In the current economic climate of the NHS the adoption of lifestyle changes that would both prevent and...
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ameliorate ED and CVD are laudable goals but further evidence based studies are required in this domain.

**Assessment and evaluation of ED**

In evaluating risk factors of ED, the EAU and BSSM propose the use of validated questionnaires using the International Index of Erectile Function (IIEF) or its short form the Sexual Health Inventory for Men (SHIM). Here, the EAU guidelines are more detailed regarding penile rigidity scores and depression scales. These are based on clinical studies assessing the validity of hardness scales as an assessment tool in ED and other studies using focused questions to quantify depression. These extra levels of questioning do not appear in the UK guidance.

The BSSM and EAU guidelines require the patient to have a genital examination and assessment for signs of hypogonadism but digital rectal examination is not indicated in the absence of lower urinary tract symptoms. All the guidelines emphasize assessments of the cardiovascular system, to include blood pressure and heart rate, but the BSSM advises weight and waist circumference metrics. The EAU guidelines have been adapted from the published Princeton Consensus (Expert Panel) Conference which was dedicated to optimizing sexual function and preserving cardiovascular health. From this, three levels of cardiovascular risk were defined: Low (no significant cardiac risk factors), Intermediate (uncertain cardiac condition) and High risk (sufficiently severe cardiac condition). These categories form the basis for recommending initiating or resuming sexual activity (Figure 1). The BSSM/NICE guidelines have a similar algorithm based on recommendations from a BSSM panel. As all organic ED is thought to have endothelial dysfunction as its central mechanism, it is self-evident that new ED patients must be considered to be at risk of significant CVD.

This algorithm provides a useful tool for the clinician with an often comorbid patient and provides a rationale to refer the patient to cardiology for stabilization of any underlying CVD. There is no rational in either guideline for referral to bariatric services for a patient with obesity, even though there is evidence to support weight loss as a measure to improve ED.

**Treatment of hypogonadism**

BSSM/NICE use a value of testosterone (T) of less than 12 nmol/L as being hypogonadic. If the patient is symptomatic

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*Figure 1.* Treatment algorithm for determining level of sexual activity according to cardiac risk in erectile dysfunction, taken from European Association of Urology (EAU) Guidelines (based on the 3rd Princeton Consensus).
then a six-month trial of T with either three-monthly injections or a topical agent is recommended. The EAU guidelines discuss the hormonal causes of ED and primary or secondary hypogonadism and the need for treatment when clinically indicated but without giving parameters for treatment or duration of treatment.

**Treatment of ED**

All the guidelines agree on the involvement of the partner in consultations of diagnosis and treatments.15 In the BSSM/NICE guidelines, oral phosphodiesterase-5 inhibitors (PDE5i) are recommended as first-line therapy, with a response rate in about 75% of patients. Sildenafil, vardanafil and tadalafil are discussed. In the EAU guidelines, avanafil is also mentioned.

Sildenafil is useful in diabetics and post nerve sparing radical retropubic prostatectomy (NSRP). The EAU recommend starting at 50 mg and increasing to 100 mg, and importantly, avoiding fatty foods with administration and allowing 30–60 minutes for effect with simultaneous sexual stimulation. The UK guidelines recommend starting at the lower dose of 25 mg.

In post radical prostatectomy (RP) 25–75% of men develop ED.16 This is also seen following external beam radiotherapy and brachytherapy.17,18 Prescription of early versus delayed PDE5i in these patients potentially has a positive impact on natural healing of potency.19,20 Taking 100 mg of sildenafil every other day after NSRP has been shown to preserve intracavernosal smooth muscle21 and a greater return to spontaneous normal erectile function compared to placebo following bilateral nerve sparing in patients who were fully potent before the surgery.22 Sildenafil has shown a substantial increase in erectile function in a randomized parallel group double blind dose response study of sildenafil 25, 50 and 100 mg compared to placebo controls amongst a general population with ED. At 100 mg sildenafil, the benefit amounted to about 60% of patients over placebo. An improvement in the IIEF score was also shown with sildenafil.23 Given that sildenafil is now off patent and is no longer Schedule 2 listed, its usage is likely to increase in the UK given its reduced tariff.

Tadalafil is useful at 2.5–5 mg daily if sexual intercourse is greater than twice weekly. Tadalafil is 75% effective in improving erections with two men needing to be treated for one man to benefit (NNT=2). This is similar to other PDE5 inhibitors.24 It is also good in diabetics and after NSRP. Tadalafil has data showing that daily usage post NSRP results in increased patient satisfaction and erectile function and a reduced time to recover potency.19,25,26

Tadalafil is licensed for daily use at 2.5–5 mg daily for use in lower urinary tract symptoms in men with ED.27,28 The guidelines support the use of tadalafil, vardanafil and avanafil (EAU only) in all subgroups including diabetics. Each PDE5i has its own advantages: tadalafil and vardanafil have orodispersible formulations but avanafil is highly selective.

There is no triple blind trial comparing all four PDE5i and so patient preference and timing needs are used to decide on formulation choice. The EAU guidelines recommend at least six attempts with any drug and appropriate stimulation;29 the UK guidelines recommend up to eight, starting with the lowest dose.

In treatment failure, the presence of hypogonadism should be investigated. Twenty-five percent of men aged 65 years will have hypogonadism.30 This is easily corrected and will improve the success of PDE5i.2,31 PDE5i are dose dependent. If a selected dose fails, the dose should be increased. Different men will respond to different PDE5i and failure with one should signal a switch to a different agent by their clinician.32

**Payment of PDE5i in ED**

UK prescribing under HSC/177 1999 allows the free scheduling of prescriptions for ED if endorsed ‘selected list scheme (SLS)’ and the patient has any of the following conditions:

- Diabetes mellitus
- Parkinson’s disease
- Multiple sclerosis
- Polio
- Spinal cord injury
- Spina bifida
- Treatment was initiated before 1998
- Severe stress secondary to ED (as judged by a specialist)

If not eligible, a patient can obtain a private prescription. Generic sildenafil is now off patent and does not require ‘SLS’ endorsement.

**Treatment of ED – second-line therapy**

NICE/BSSM encourage the use of vacuum tumescence devices (VTD) quoting a 35–84% satisfaction rate. Intracavernosal and intraurethral alprostadil are listed as second-line therapy in all the guidelines. These are based on older studies in the literature. The newer agent topical alprostadil is only mentioned in the European guidelines and it is now licensed. It can be prescribed in the UK but has yet to appear on the guidance.

**Treatment of ED – third-line therapy**

For all the guidelines, third-line therapy consists of insertion of a penile prosthesis. This can be either a two or
three-piece inflatable penile prosthesis (IPP) or a malleable firm prosthesis. Nearly all IPPs are placed through a peno-scrotal incision.

The EAU guidelines report the highest satisfaction rate of 92–100% in patients with penile prostheses together with a satisfaction rate of up to 91–95% in partners.\textsuperscript{19,33–35} These high satisfaction rates compare better than any other prosthetic surgical procedures. (Table 1)

### Summary

In general, the UK and European guidelines have similar recommendations for the investigation and management of ED. They use similar bodies of evidence and the recommendations for coexistent CVD management are based on parallel expert groups.

The guidelines show best practice for the managing clinician, be they a general practitioner, endocrinologist, urologist or dedicated andrologist. The rise of metabolic syndrome and obesity puts the diagnosing clinician in a position to implement disease prevention, either through referral for cardiac optimization or bariatric referral to treat obesity. The guidelines also highlight the importance of addressing potential ED in prostate cancer patients before and after radical treatment as there is now a body of evidence to support early treatment with PDE5i.

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### References


