County Durham and Darlington

Guideline for the management of Erectile Dysfunction in adults ≥18 years

Contents

Guideline produced for use in Durham Dales, Easington and Sedgefield Clinical Commissioning Group (CCG), North Durham CCG and Darlington CCG areas.

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Introduction

This guidance is intended to inform management of erectile dysfunction (ED) in primary care and has been developed with reference to NICE 'Clinical Knowledge Summaries'[1] and national guidelines, as appropriate. The guidelines are intended to guide clinical management, but every patient should be assessed and managed individually.

These guidelines are intended for all clinicians in primary care in the County Durham and Darlington areas involved in managing patients with erectile dysfunction. This is the first iteration of these guidelines and any gaps should be identified for inclusion when the guideline is reviewed. These guidelines are not intended to provide a comprehensive overview of ED, but to inform decision making during a busy GP surgery.

How to use the guidelines

The BNF, the Durham and Darlington Formulary and the Durham and Darlington Erectile Dysfunction Commissioning Policy should be referred to as appropriate.

Goals

- Make a full assessment of physical, physiological, and psychological causes of erectile dysfunction
- Calculate and appropriately manage cardiovascular risk
- Provide advice on healthy lifestyle
- Treat people who require drug intervention with a phosphodiesterase-5 inhibitor
- Follow-up to assess satisfaction with treatment
- Refer all men who cannot be adequately managed in primary care

[1] https://cks.nice.org.uk/erectile-dysfunction#!topicsummary

Epidemiology and risk factors[2]

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, hypercholesterolemia 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

How should I assess a man with erectile dysfunction?

History

- Take a detailed account of the man's personal details and his interpretation of the problem, and ascertain whether the nature of dysfunction is physical (see Table 1) or psychological (see Table 2). This should include questions about his current and past medical, surgical, and psychiatric history; psychological (or emotional) factors; and medication for comorbidities (see Table 3). Ask about:
    - Relationship status (current and past) and sexual orientation.
    - Present and previous erection quality (including erections during sexual relations as well as awakening and masturbatory erections), and concomitant ejaculatory and orgasm dysfunction.
    - Issues with sexual aversion or pain, or issues for his partner (including menopause or vaginal pain).
    - Lifestyle, including use of alcohol, tobacco, and illicit drugs (including cannabis), and treatments already tried.
    - Energy levels, loss of libido, loss of body hair, or spontaneous hot flushes (symptoms of hypogonadism).
- The use of validated questionnaires, particularly the International Index of Erectile Function (IIEF) or the validated shorter version of the SHIM (Sexual Health Inventory for Men) may be helpful

Table 1**. Physical causes of erectile dysfunction.**

Disorder type	**Examples**
Vasculogenic	Generalized cardiovascular disease*, hypertension†, hyperlipidaemia, diabetes mellitus†, smoking

[2] https://www.guidelines.co.uk/BSSM/Erectile-dysfunction/247615.article

Disorder type	Examples
Neurogenic	Multiple sclerosis, multiple atrophy, Parkinson's disease, tumours, stroke, spinal disorders, diabetes mellitus, alcoholism, uraemia, polyneuropathy, surgery (of the pelvis or retroperitoneum)
Anatomical or structural	Peyronie's disease, penile fracture, congenital curvature of the penis, micropenis, hypospadias, epispadias
Hormonal	Hypogonadism, hyperprolactinaemia, hyperthyroidism, hypothyroidism, Cushing's disease, hypopituitarism following traumatic brain injury‡
Data from:[British Society for Sexual Medicine, 2009; Wespes et al, 2012] * The risk factors for erectile dysfunction are similar to the risk factors for CVD and include sedentary lifestyle, obesity, smoking, hypercholesterolaemia, metabolic syndrome, hypertension, endothelial dysfunction, and dyslipidaemia. Erectile dysfunction itself is a risk factor for CVD; it confers a 1.46 increased risk for cardiovascular disease, equivalent to the risk conferred by a moderate level of smoking [Hackett et al, 2008; British Society for Sexual Medicine, 2009] † Erectile dysfunction may be the first presentation of serious conditions like hypertension or diabetes mellitus [Hackett et al, 2008; British Society for Sexual Medicine, 2009] ‡ Erectile dysfunction is estimated to occur in 15–25% of survivors of traumatic head injury and is often unrecognized [Ghigo et al, 2005; Agha et al, 2007; Klose et al, 2007]	

Table 2. Psychological or emotional causes of erectile dysfunction. These can be predisposing (risk factors), precipitating (present), or maintaining (ongoing) causes.

Predisposing causes (risk factors)	Precipitating causes (present symptoms)	Maintaining causes (ongoing symptoms)
Lack of sexual knowledge	New relationship	Relationship problems
Past sexual problems	Acute relationship problems	Poor communication between partners
Relationship problems	Family or social pressures	Ongoing physical or mental health problems
Religious or cultural beliefs	Pregnancy and childbirth	Other sexual problems in the man or in his partner
Restrictive upbringing	Other life event	—
Unclear sexual or gender preference	Acute physical or mental health problems	—
Previous sexual abuse	Lack of knowledge about normal changes or ageing	—

Predisposing causes (risk factors)	Precipitating causes (present symptoms)	Maintaining causes (ongoing symptoms)
Physical or mental health problems	Other sexual problems in the man or in his partner	—
Other sexual problems in the man or in his partner	—	—
Adapted from: [Hackett et al, 2008]		

Table 3. Drugs that may cause erectile dysfunction.

Drug class	Examples
Diuretics*	Thiazides (for example bendroflumethiazide), spironolactone
Antihypertensives†	Methyldopa, clonidine, beta-blockers (for example propranolol), verapamil
Fibrates‡	Clofibrate, gemfibrozil
Antipsychotics	Phenothiazines (for example chlorpromazine), butyrophenones (for example haloperidol)
Antidepressants	Tricyclics (for example amitriptyline), monoamine oxidase inhibitors (for example phenelzine), selective serotonin reuptake inhibitors (for example fluoxetine), lithium
Histamine (H_2)-antagonists§	Cimetidine, ranitidine
Hormones and hormone-modifying drugs	Oestrogens (for example estradiol), progesterone, corticosteroids (for example prednisolone), cyproterone acetate, 5-alpha reductase inhibitors (for example finasteride)
Cytotoxics	Cyclophosphamide, methotrexate
Anti-arrhythmics and anticonvulsants	Disopyramide, carbamazepine
* Consider loop diuretics (for example furosemide). † Consider angiotensin-converting enzyme (ACE) inhibitors or other calcium-channel blockers (for example lisinopril). ‡ Consider statins (although these have also been linked to erectile dysfunction). § Consider proton pump inhibitors (for example omeprazole).		
Data from: [Hackett et al, 2008; British Society for Sexual Medicine, 2009; Wespes et al, 2012]		

Examination

- In all men, perform a focused physical examination with measurement of body weight, waist circumference, heart rate, and blood pressure as a minimum.
    - Examination of the genitalia may reveal hypogonadism or malformation such as Peyronie's disease (further detailed assessment is required if there is a history of rapid onset of pain or deviation of the erection). Also check for gynaecomastia and reduced body hair.
    - A digital rectal examination (DRE) is recommended if there are symptoms of an enlarged prostate, including obstructive urinary symptoms such as a weak and intermittent urinary stream. Rarely, the enlarged prostate obstructs the flow of ejaculate causing prolonged and intermittent ejaculation.

Investigations

- In all men:
    - Calculate the 10-year cardiovascular risk by measuring lipid and fasting glucose serum levels (see the CKS topic on CVD risk assessment and management).
    - HbA1c / lipids (if not done in the past 12 months)
    - Serum Prostate-specific antigen (PSA) should be considered if clinically indicated (men over 45). It should certainly be measured before commencing testosterone therapy and at regular intervals during testosterone therapy.[3]
    - Hypogonadism is a treatable cause of ED that may also make men less responsive, or even nonresponsive, 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 (an approximation can be made from total testosterone and sex hormone binding globulin levels at www.issam.ch/freetesto.htm; contact the biochemistry laboratory if there are doubts about availability of the analysis). If the free testosterone is low or borderline:
        - Repeat the testosterone measurement, and measure follicle-stimulating hormone, luteinizing hormone, and prolactin levels.
        - Consider referral to a specialist if these are abnormal.

[3] https://www.guidelines.co.uk/BSSM/Erectile-dysfunction/247615.article

What self-care advice should I give to a man with erectile dysfunction?

- Counsel the man that erectile dysfunction usually responds well to a combination of lifestyle changes and drug treatment. Advise, where applicable, that he should:
    - Lose weight (important), stop smoking, reduce alcohol consumption, and increase exercise.
    - Not stop prescribed medicine unless specifically advised to.
- **For men with coronary heart disease (CHD),** advise that most men with CHD can safely resume sexual activity and use phosphodiesterase-5 (PDE-5) inhibitors. The exception are men with:
    - Unstable heart disease.
    - A history of recent myocardial infarction.
    - Poorly compensated heart failure.
    - Unstable dysrhythmia.
    - Or if the patient is taking regular nitrates.
- **For men who cycle for more than 3 hours per week,** encourage a trial period without cycling to see if this improves their erectile function.
    - If it is not possible for them to stop cycling, preventative measures such as the use of a properly fitted bicycle seat and riding with the seat in a suitable position, may help prevent impairment of erectile function.
- Advise the man not to take unlicensed herbal remedies for erectile dysfunction as they may contain prescription-only medicines which may be contraindicated or interact with prescribed medication.
- Advice and support is also available from the Sexual Dysfunction Association www.sda.uk.net.

How should I treat a man with erectile dysfunction?

- If the man is taking medication that may cause erectile dysfunction, consider substituting it with another drug if a temporal link can be demonstrated (see Table 3 in History).
- Prescribe a phosphodiesterase-5 (PDE-5) inhibitor regardless of suspected cause (provided there are no contraindications). Generic sildenafil at the minimum effective dose is recommended for any man presenting with erectile dysfunction with a frequency of dosing of four times per month.
    - Other phosphodiesterase-5 (PDE-5) inhibitors (tadalafil[4] and avanafil) is only recommended for patients who meet the Government Selected

[4] Tadalafil once daily is not approved for use in County Durham and Darlington

Scheme (SLS) criteria AND where generic sildenafil is ineffective, with a frequency of dosing of four times per month[5] using the drug with the lowest acquisition cost.

  - Sildenafil works for about 4 hours. It is suitable for occasional or as required use.
  - Tadalafil acts for up to 17.5 hours. It is suitable for use for longer periods (for example over a weekend).

- Before prescribing, assess whether the man qualifies for an NHS prescription. If he does not, a private prescription can be issued.
  - Generic sildenafil can be prescribed without restriction on the NHS.
  - Viagra®, tadalafil[6] (Cialis®) and avanafil (Spedra®) are not prescribable on an NHS prescription except for men who:
    - Have diabetes, multiple sclerosis, Parkinson's disease, poliomyelitis, prostate cancer, severe pelvic injury, single-gene neurological disease (for example Huntington's disease), spina bifida, or spinal cord injury.
    - Are receiving renal dialysis for renal failure.
    - Have had radical pelvic surgery, prostatectomy[7] (including transurethral resection of the prostrate), or a kidney transplant.
    - Were receiving Caverject®, Erecnos®, MUSE®, Viagra®, or Viridal® at the expense of the NHS on 14 September 1998.
  - If prescribing tadalafil[8] (Cialis®), avanafil (Spedra®), or Viagra® on the NHS, endorse with 'SLS' (Selected List Scheme). Generic sildenafil does not need to be endorsed with 'SLS'.
- Prescribe the lower dose of the drug initially, and consider titrating upwards if this is ineffective (see Follow up).
  - Ensure the man is aware that PDE-5 inhibitors are not initiators of erection but require sexual stimulation in order to facilitate erection.
  - A man with erectile dysfunction should receive eight doses of a PDE-5 inhibitor at a maximum dose with sexual stimulation before being classified as a non-responder.

[5] County Durham and Darlington Erectile Dysfunction Commissioning Policy – maximum dosing frequency 4 times per month for NHS funded prescribing. A GP may issue a private prescription for any item in circumstances where the medicine is not available on the NHS. http://webarchive.nationalarchives.gov.uk/20130107105354/http:/www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4012086.pdf Health Service Circular HSC 1999/148 refers to research re frequency of treatment.

[6] Tadalafil once daily is not approved for use in County Durham and Darlington

[7] County Durham and Darlington Erectile Dysfunction Commissioning Policy does NOT cover post prostatectomy once daily prescribing of PDE5i

[8] Tadalafil once daily is not approved for use in County Durham and Darlington

- Advise the man not to take unlicensed herbal remedies for erectile dysfunction as they may contain prescription-only medicines which may be contraindicated or interact with prescribed medication.
- Sildenafil is now licensed for sale from pharmacies without a prescription as Viagra Connect, following a consultation with a pharmacist to check symptoms, general health and other medications. This may be an option for men who do not wish to consult their GP in the first instance or for those who require a dosage frequency of more than 4 a month.

How should I follow up a man with erectile dysfunction?

- Where possible, involve the man's partner in follow-up appointments (bearing in mind the sensitive nature of the condition).
- Ask about the effectiveness of treatment.
    - If treatment has not been satisfactorily effective:
        - Counsel about the appropriate use of phosphodiesterase-5 (PDE-5) inhibitors. Ensure that the man is aware that PDE-5 inhibitors are not initiators of erection but require sexual stimulation in order to facilitate erection.
        - Reconsider comorbidities and treat where possible. In particular, consider the possibility of hypogonadism (which makes PDE-5 inhibitors ineffective).
        - Consider increasing to the maximum dose, or switching to an alternative PDE-5 inhibitor. If this fails, consider referral.
    - A person with erectile dysfunction should receive eight doses of a PDE-5 inhibitor at a maximum dose with sexual stimulation before being classified as a non-responder.

Management of non-responders to PDE-5 inhibitors[9]

- The two main reasons why patients fail to respond to a PDE5i are either incorrect drug use or lack of efficacy of the drug. Data suggest that an adequate trial involves at least six attempts with a particular drug. The management of non-responders depends upon identifying the underlying cause.
- Check that the patient has been using a licensed medication. There is a large counterfeit market in PDE5is. The amount of active drug in these medications varies enormously and it is important to check how and from which source the patient has obtained his medication.

[9] https://uroweb.org/wp-content/uploads/EAU-Guidelines-Male-Sexual-Dysfunction-2016-3.pdf

- Check that the medication has been properly prescribed and correctly used. The main reason why patients fail to use their medication correctly is inadequate counselling from their physician. The most common causes of incorrect drug use are: i) failure to use adequate sexual stimulation; ii) failure to use an adequate dose; and, iii) failure to wait an adequate amount of time between taking the medication and attempting sexual intercourse.

Good practice principles

- Encourage an occasional drug holiday from PDE-5 inhibitors.
- Consider trial of 4 tablets and titrate to the maximum dose depending upon response. Move on to next tablet or stop if ineffective at max dose on at least 6 out of 8 attempts.
- To optimise response to PDE-5 inhibitors, ideally take before a meal, 30-60 minutes in advance of sexual activity and avoid taking after a heavy meal or excess alcohol.
- Encourage couples to engage in sexual intimacy and stimulation.
- Avoid PDE-5 inhibitors if the patient is taking regular nitrates or if the patient has unstable cardiac disease e.g. angina or heart failure or with unstable hypertension (SBP>180/DBP>100) or if hypotensive (SBP<100/DBP<70).
- 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.[10]
- 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.[11]

When should I refer a man with erectile dysfunction?

- **Admit to hospital** if there is priapism (persistent erection). Warn the man to seek advice if he has an erection lasting longer than 4 hours.
- **Refer to a specialist:**
    - Young men who have always had difficulty in obtaining or maintaining an erection.
    - Men with a history of trauma (for example to the genital area, pelvis, or spine).
    - If an abnormality of the penis or testicles is found on examination.
    - Men who do not respond to the maximum dose of at least two phosphodiesterase-5 (PDE-5) inhibitors (for people with diabetes, consider referral to diabetes clinic).

[10] https://uroweb.org/wp-content/uploads/EAU-Guidelines-Male-Sexual-Dysfunction-2016-3.pdf
[11] https://uroweb.org/wp-content/uploads/EAU-Guidelines-Male-Sexual-Dysfunction-2016-3.pdf

    - A person with erectile dysfunction should receive eight doses of a PDE-5 inhibitor with sexual stimulation at maximum dose before being classified as a non-responder.

- **Refer to a specialist or endocrinology,** men who have hypogonadism (characterized by abnormal testosterone, follicle-stimulating hormone, luteinizing hormone, or prolactin levels).
- **Refer to cardiology,** men who have severe cardiovascular disease that would make sexual activity unsafe, or contraindicates PDE-5 inhibitor use.
- **Consider referral for psychological assessment** for men with a psychogenic underlying cause of erectile dysfunction. There are no NHS funded services in County Durham and Darlington, however referrals can be made to private providers.
- **Vacuum erection devices** are only recommended for patients who meet the SLS criteria AND only if oral phosphodiesterase type-5 inhibitors are contraindicated or ineffective. VEDs may be the treatment of choice in well-informed older patients with infrequent sexual intercourse and comorbidity requiring non-invasive, drug-free management of ED but only after specialist initiation. These criteria also apply to NHS funded replacement of devices.

Referral Checklist

	✓
Full history (including lifestyle and sexual history)	
Examinations completed: penis/testes, BP, Peripheral pulses, plus rectal examination in men >50 years or with symptoms of an enlarged prostate	
Investigations completed: CVD Risk Assessment; HbA1c/Lipids (if not done in last 12 months); Testosterone – morning sample (repeated with SHBG if low), FSH/LFT/prolactin if testosterone low; PSA - Check	
Treatment: Patients have failed to respond to all three licenced oral (PDE5i) – which may take up to eight attempts at sexual activity at the maximum dose with appropriate instruction	
OR Suspected penile cancer, suspected prostate cancer, Peyronies Fibrosis, young men who have always had difficulty, h/o trauma to genital area/pelvis or spine, hypogonadism suspected, complex psychiatric/psychosexual disorders; severe cardiovascular disease	

Erectile Dysfunction Primary Care Pathway

History including sexual history:
Lifestyle – including use of alcohol, tobacco and illicit drugs; treatments already tried

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Examination:
BMI, waist circumference, heart rate and BP, check penis/testes, Peripheral pulses, plus rectal examination in men >50 years or with symptoms of an enlarged prostate

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Investigations:
Perform CVD Risk Assessment; HbA1c/Lipids (if not done in last 12 months); Testosterone – morning sample (and repeat with SHBG if low), FSH/prolactin if testosterone low; PSA – Check (men over 45 years)

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Treatment:
If medication is causing ED, consider substituting it with another drug if a temporal link can be demonstrated.

Lifestyle Advice: Smoking cessation, weight loss and exercise, alcohol and stress.

Prescribe a PDE-5 inhibitor regardless of suspected cause (provided there are no contraindications). Advise re side effects including Priapism.

Generic Sildenafil, at the minimum effective dose is recommended for any man presenting with erectile dysfunction with a frequency of dosing of four times per month*.
Initiate sildenafil at 50mg and if no response increase to maximum dose (100m).

All other PDE-5 inhibitors (tadalafil* and avanafil) are only recommended for patients who meet the Government Selected List Scheme (SLS) criteria AND where generic sildenafil is ineffective, with a frequency of dosing of four times per month** using the drug with the lowest acquisition cost.
Tadalafil: Initiate at 10mg and if no response increase to maximum dose (20mg) to be taken prn. Emphasise longer duration of response (36 hours)
Avanafil: 100mg taken on demand and aim to titrate up to 200mg if required.

If effective, continue to prescribe and review routinely at 12 month intervals. Encourage an occasional drug holiday from PDE5i. (See full guideline for further good practice principles)

** Daily dosing of PDE-5 inhibitors (e.g. tadalafil once daily) is not approved in County Durham and Darlington*
*** In accordance with County Durham and Darlington Erectile Dysfunction Commissioning Policy – NHS funded prescribing is restricted to a maximum frequency of dosing of four times per month. A GP may issue a private prescription for any item in circumstances where the medicine is not available on the NHS.*

Treatment with vacuum erection devices is **only recommended for patients who meet the SLS criteria AND only if oral phosphodiesterase type-5 inhibitors are contraindicated or ineffective**

NOTE: *Alprostadil cream is not approved for use in County Durham and Darlington and not routinely commissioned. Penile implants are commissioned by NHS England (Specialised Commissioning) for patients with end-stage ED who meet the criteria set out in their policy only via local commissioning teams.*

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Consider specialist referral:
Patients will typically have failed to respond to all three licenced oral (PDE5i) – which may take up to eight attempts at sexual activity at the maximum dose with appropriate instruction AND patient is keen to explore alternative treatment

Suspected penile cancer, suspected prostate cancer, Peyronies Fibrosis, young men who have always had difficulty, if h/o trauma to genital area/pelvis or spine, if hypogonadism suspected, if complex psychiatric/psychosexual disorders