A practical guide on the assessment and management of testosterone deficiency in adult men

Based on the 2017 British Society for Sexual Medicine (BSSM) guidelines on adult testosterone deficiency, with statements for UK practice[1]

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Why does it occur?

Testosterone deficiency (TD), also known as hypogonadism, may result from:[2–4]

- Problems with the testes [primary (hypergonadotropic) TD]
- Problems with the hypothalamus and pituitary gland [secondary (hypogonadotropic) TD]
- Problems with the hypothalamus/pituitary and testes (combined primary and secondary TD)
- Impaired action/suppression of testosterone

How is it diagnosed?

- The diagnosis of symptomatic TD requires the presence of characteristic signs and symptoms,[2,5–8] PLUS reduced serum concentrations of total testosterone (TT) or free testosterone (FT)[5]

Psychological

- Changes in mood (e.g. anger, irritability, sadness, depression)
- Decreased well-being/poor self-rated health
- Diminished cognitive function (including impaired concentration, verbal memory and spatial performance)

Cardiometabolic

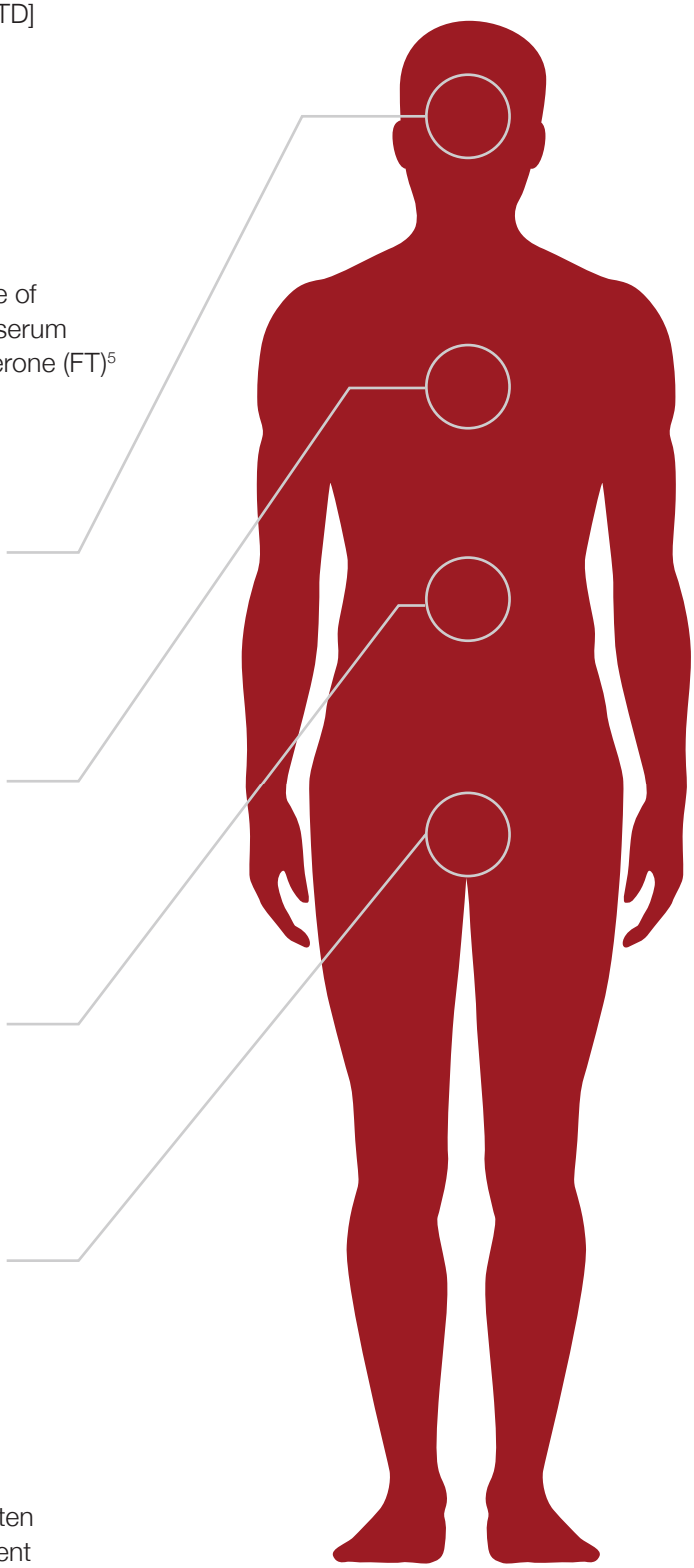
- Increased body mass index (BMI)/obesity
- Visceral obesity
- Metabolic syndrome
- Insulin resistance and type 2 diabetes

Physical

- Decreased body hair
- Gynaecomastia
- Decreased muscle mass and strength
- Hot flushes/sweats
- Sleep disturbances
- Fatigue
- Osteoporosis/height loss/ low trauma fractures

Sexual

- Delayed puberty
- Small testes
- Infertility
- Decreased sexual desire and activity
- Decreased frequency of sexual thoughts
- Erectile dysfunction (ED)
- Delayed ejaculation
- Decreased volume of ejaculate
- Decreased or absent morning/night-time erections



- The **3** most common symptoms of TD are ED, loss of early morning erections and low sexual desire – men often present with sexual dysfunction and a desire for treatment

Who should be screened for TD?

- Adult men with consistent and multiple signs of TD
- All men presenting with ED, loss of spontaneous erections or low sexual desire
- All men with type 2 diabetes mellitus, BMI >30 kg/m^2 or waist circumference >102 cm (40.2 inches)
- All men on long-term opiate, antipsychotic or anticonvulsant medication

History taking

- **Enquire** about previous and current prescription and non-prescription drug use[7]
- **Assess and exclude** systemic illness, ongoing acute disease, malabsorption and malnutrition[7]
- **Consider** the use of validated questionnaires, such as the Androgen Deficiency in the Ageing Male (ADAM) questionnaire (included in the Sexual Advice Association SMART SAA app, available at: http://sexualadviceassociation.co.uk/), or the Ageing Males' Symptoms (AMS) Scale (available at: http://www.issam.ch/AMS_English.pdf) – information on interpreting the scores can be found at: http://zeg-berlin.de/wp-content/uploads/2017/01/norm.pdf

Physical examination

- **Measure** height, weight, BMI and waist circumference[5]
- **Assess** the degree of body hair (including facial and pubic)[5]
- **Examine** for the presence and degree of breast enlargement, and abnormalities of the penis, testicles[5,7] and scrotum[5]
- **Check** the prostate via digital rectal examination (DRE)[7]
- **Arrange** blood investigations, including prostate-specific antigen (PSA), haematocrit, and appropriate tests according to physical findings and to determine cardiovascular (CV) risk

Laboratory diagnosis

Serum testosterone – measure between 7–11 am,[5,7] with a reliable method, on at least 2 occasions,[7] preferably 4 weeks apart. Fasting levels should be obtained where possible, as recommended by the European Association of Urology (EAU).[7]

If low/borderline, measure LH* and FSH,** plus SHBG to calculate FT.

FT – an online FT calculator and downloadable app, sponsored by the Primary Care Testosterone Advisory Group (PCTAG), can be found at http://www.pctag.uk/testosterone-calculator/

FSH – follicle-stimulating hormone, LH – luteinising hormone, SHBG – sex hormone-binding globulin
*LH to differentiate primary from secondary TD. **FSH is only necessary if fertility is an issue.

Main contraindications to testosterone therapy[7]

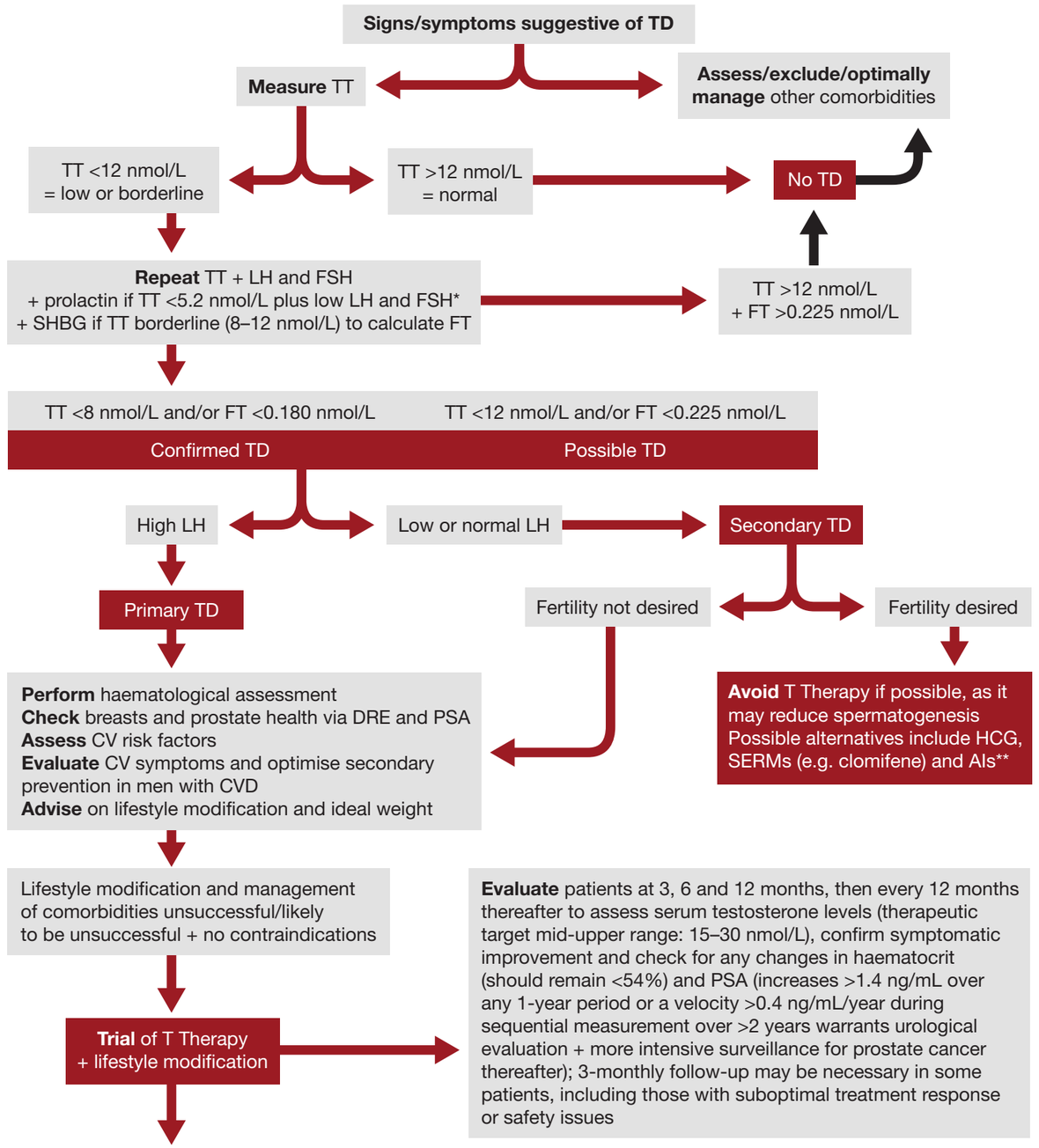
- Prostate cancer (locally advanced or metastatic)
- Male breast cancer
- An active desire to have children
- Haematocrit >54%
- Severe chronic heart failure [New York Heart Association (NYHA) class IV]

Testosterone therapy and ED

- Testosterone therapy (T Therapy) is appropriate for treating ED,[8,9] particularly at TT levels <8 nmol/L,[8] and for salvaging ED treatment failures with oral medication, particularly at TT levels <10.4 nmol/L[10]
- T Therapy reduces the need for more invasive and expensive second- and third-line treatments[11]
- A PDE5i can be prescribed for all men with ED when commencing T Therapy as long as there are no contraindications, because T Therapy can take many months to correct ED

PDE5i – phosphodiesterase type 5 inhibitor

Diagnosing and managing TD in adult men[2,7,9,12,13]



Adapted from Minhas and Mulhall, 2017.[13]
AI – aromatase inhibitor, CV – cardiovascular, CVD – cardiovascular disease, FSH – follicle-stimulating hormone, FT – free testosterone, HCG – human chorionic gonadotropin, LH – luteinising hormone, MRI – magnetic resonance imaging, PSA – prostate-specific antigen, SERM – selective oestrogen receptor modulator, SHBG – sex hormone-binding globulin, T Therapy – testosterone therapy, TT – total testosterone
*For men with TT levels <5.2 nmol/L plus low LH and FSH or increased prolactin levels, refer to endocrinology or arrange a pituitary MRI scan to exclude a pituitary adenoma.[2,14]
**These drugs should not be used if pituitary function is compromised. SERMs and AIs are not currently licensed for TD.

Testosterone therapy

- The patient should be fully informed about the expected benefits and side effects of T Therapy, to facilitate a joint decision on treatment choice

Testosterone therapy options[6,15]

Formulation	Route of administration	Frequency of administration	Advantages	Disadvantages
Testosterone 1%, 1.62%* and 2% gel available *1.62% = 16.2 mg/g	Transdermal gel 1% (sachets/tubes) 1.62%* (pump) 2% (pump) *1.62% = 16.2 mg/g	• Applied daily[16] • May require dose titration	• Fast onset • Provides uniform and normal serum levels for 24 hours[7]	• Skin irritation at application site • Potential for interpersonal transfer • Compliance may be an issue long-term
Testosterone undecanoate	Intramuscular injection	Every 10–14 weeks, adjusted to maintain trough testosterone >12 nmol/L	• Steady state levels • Reduced frequency of administration improves compliance	• Possible injection site pain/reaction[17]
Testosterone enantate	Intramuscular injection	Every 2–3 weeks	Can be administered every 3–6 weeks for maintenance, according to individual requirement[18]	• Levels fluctuate • Possible injection site pain/reaction[18]
Mix of 4 testosterone esters (including propionate) as Sustanon 250	Intramuscular injection	Usually administered every 3 weeks May cause a reaction at the injection site[19]		

Adapted from Hackett et al. (2017)[6] and Dohle et al. (2017)[15]

- When considering side effects and drug withdrawal times, physicians should bear in mind the pharmacodynamic and pharmacokinetic properties of the injectable versus the transdermal formulations

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