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# ISSM QUICK REFERENCE GUIDE ON TESTOSTERONE DEFICIENCY FOR MEN

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## What is testosterone deficiency?

**“Testosterone deficiency (TD) is a clinical and biochemical syndrome characterized by a deficiency of testosterone, or testosterone action, and relevant symptoms and signs.”**

**To make a diagnosis of TD, affected men must have symptoms of TD.** TD affects 2-6% of adult men, and may affect the function of multiple organ systems. TD may result in significant detriment in the quality of life due to alterations in sexual function, cardiovascular risk, glycemic control, bone health, and many other aspects of men’s health.

AND

**To make a diagnosis of TD, affected men must have a serum total testosterone that is consistently <8 nmol/l (231 ng/dl).**

BUT

**Men with a serum total testosterone that is consistently >8 nmol/l (231 ng/dl) but ≤ 12nmol/L (346ng/dL) may have TD** and may be offered a trial of testosterone replacement therapy (TRT); a sustained improvement in symptoms over a period of six months in response to TRT would confirm the diagnosis.

## What causes TD?

- Reduced testicular synthesis of testosterone due to impaired Leydig cell function (primary hypogonadism)
- Reduced testicular synthesis of testosterone due to inadequate gonadotropic stimulation of Leydig cells (secondary hypogonadism)

Medical conditions that may cause TD include:

*Primary TD:* Klinefelter’s syndrome, Noonan syndrome; testicular infarction; hemochromatosis; some drugs and surgeries; previous cryptorchidism, mumps orchitis, testicular trauma, torsion or irradiation.

*Secondary TD:* isolated hypogonadotropic hypogonadism; Kallmann’s syndrome; Prader-Willi syndrome; Pasqualini’s syndrome; primary and secondary CNS tumours; diabetes; obesity; hyperprolactinemia; some drugs; hypothalamic-pituitary irradiation or surgery.

TD always has a cause; this should be identified and documented, and reversible causes should be effectively treated.

## Clinical history

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In most men, symptoms are quite variable and onset is frequently very gradual. Common symptoms include: reduced muscle strength; physical frailty; impaired concentration; impaired verbal memory; fatigue; tendency to fall asleep during the day; insomnia; reduced sense of general well-being; reduced energy and motivation; anxiety; depression; irritability; reduced sexual desire; infrequent or absent nocturnal erections and erections on waking; impaired erectile, ejaculatory and orgasmic function. Currently available questionnaire instruments for the assessment of TD lack adequate specificity and their use is not recommended.

## Physical examination and signs

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Many men with TD have normal physical examination findings. Physical signs of the various health problems associated with TD may be present, particularly obesity. The following findings should be documented: assessment of general body habitus, including breast development (evidence of gynecomastia); nutritional state (height, weight, BMI, waist circumference); muscle development and strength; hair growth (body and facial hair; androgenic alopecia); inspection of the penis and testes to assess post-pubertal development; palpation of scrotal contents (evidence of testicular maldescent; size and consistency of testes and epididymes; evidence of scarring from

previous infection/inflammation). Digital rectal examination is not essential for the initial assessment of TD but, in men over 40, it must be performed before any treatment for TD is commenced.

## Laboratory diagnosis

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**Step 1:** Total testosterone (TT) assay on serum from a venous blood sample drawn between 08:00AM and noon.

- If TT  $\geq 12$ nmol/L (346ng/dL); TD is unlikely
- If TT is  $< 12$ nmol/L (346ng/dL), proceed to step 2

**Step 2:** TT assay on serum from a second venous blood sample drawn between 08:00AM and noon after an interval of at least one week, together with:

- Serum LH (to distinguish primary and secondary TD) and prolactin
- In case of obese and older men, sex-hormone binding globulin (SHBG)

## Treatment of TD

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Treatment of sleep apnea, weight reduction, and discontinuation of opioid medication may result in increased testosterone synthesis. Before offering drug treatment, the physician must identify men who wish to maintain their fertility and testicular volume, as prescription of testosterone is highly

likely to suppress spermatogenesis and fertility, and reduce testicular volume. Such men should be referred for specialist management.

At the time of publication, preparations of testosterone are the only pharmacological treatments approved for the indication of TD, regardless of its cause. There are differences between testosterone preparations in route of delivery, ease of use, pharmacokinetics and cost. Choice of treatment should be agreed on with patients to respect their preferences and promote long-term compliance.

### Treatment monitoring

Treatment effect on symptoms and inquiry about side effects should be made 3, 6, and 12 months after initiating TRT, and then annually thereafter.

The following issues should be covered during a follow-up visit:

*Laboratory work-up:* TT, hematocrit, lipid profile, PSA (men aged 40 and older).

*Clinical history:* inquire about therapeutic and adverse effects; inquire about changes in general health and medication usage; review compliance with dosing and administration instructions.

*Physical examination:* inspect body habitus for evidence of testosterone effect; assess weight/body mass index/waist

circumference and blood pressure; inspect and palpate testes, noting any change in size and consistency; in men aged 40 and older, perform digital rectal examination of prostate; for transdermal TRT users, inspect application sites.

The goal of TRT is to restore testosterone levels to the mid-normal range and to alleviate the signs and symptoms associated with TD. Hematocrit, PSA, and lipids should remain within laboratory reference ranges; out-of-range results should be managed according to authoritative local guidelines.

The absence of large-scale, long-term controlled studies with testosterone therapy precludes making definitive statements regarding TRT and cardiovascular risk. Equally, the weight of currently available evidence does not support the restriction of TRT, which, on balance, may benefit many men at risk of cardiovascular disease. TRT should not be given to men with prostate cancer except under specialist supervision.

## NEXT PAGE:

- Figure 1: Flow chart for the process of care for the assessment and management of testosterone deficiency in adult men
- Figure 2: Flow chart for the process of care for the assessment and management of testosterone deficiency in adult men wishing to maintain fertility

Figure 1: Flow chart for the process of care for the assessment and management of testosterone deficiency in adult men

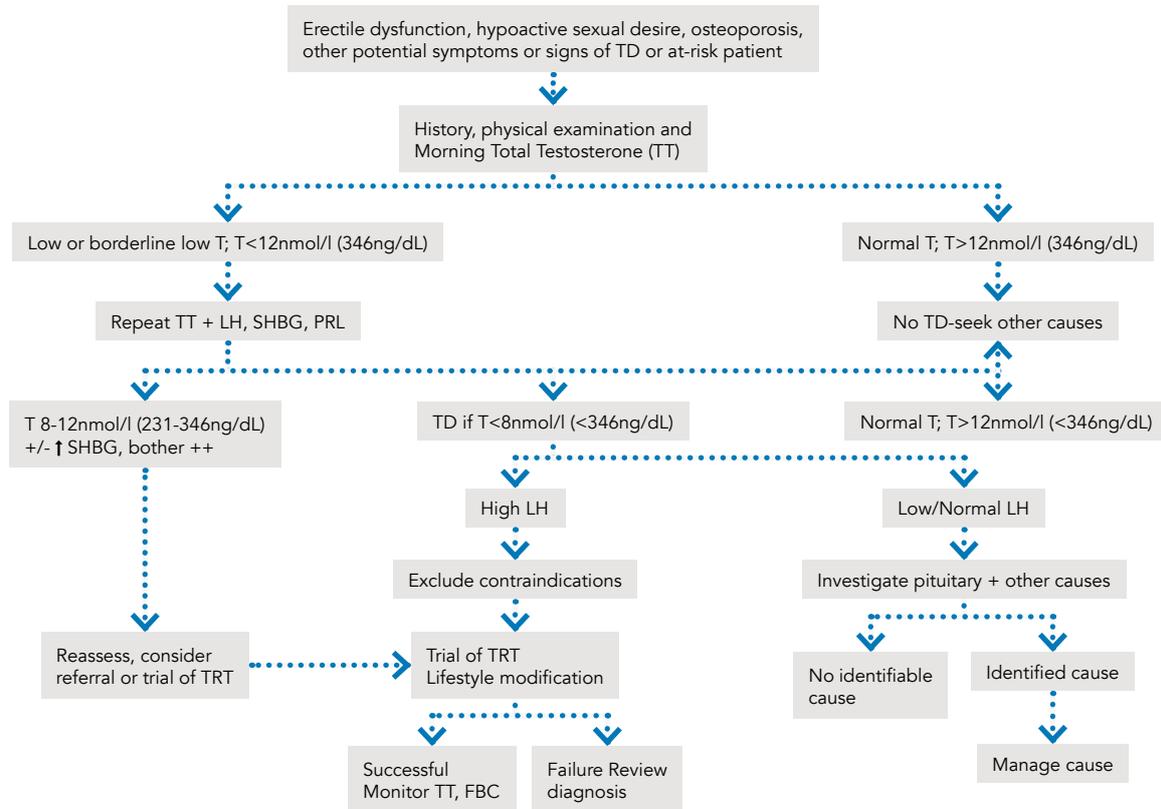
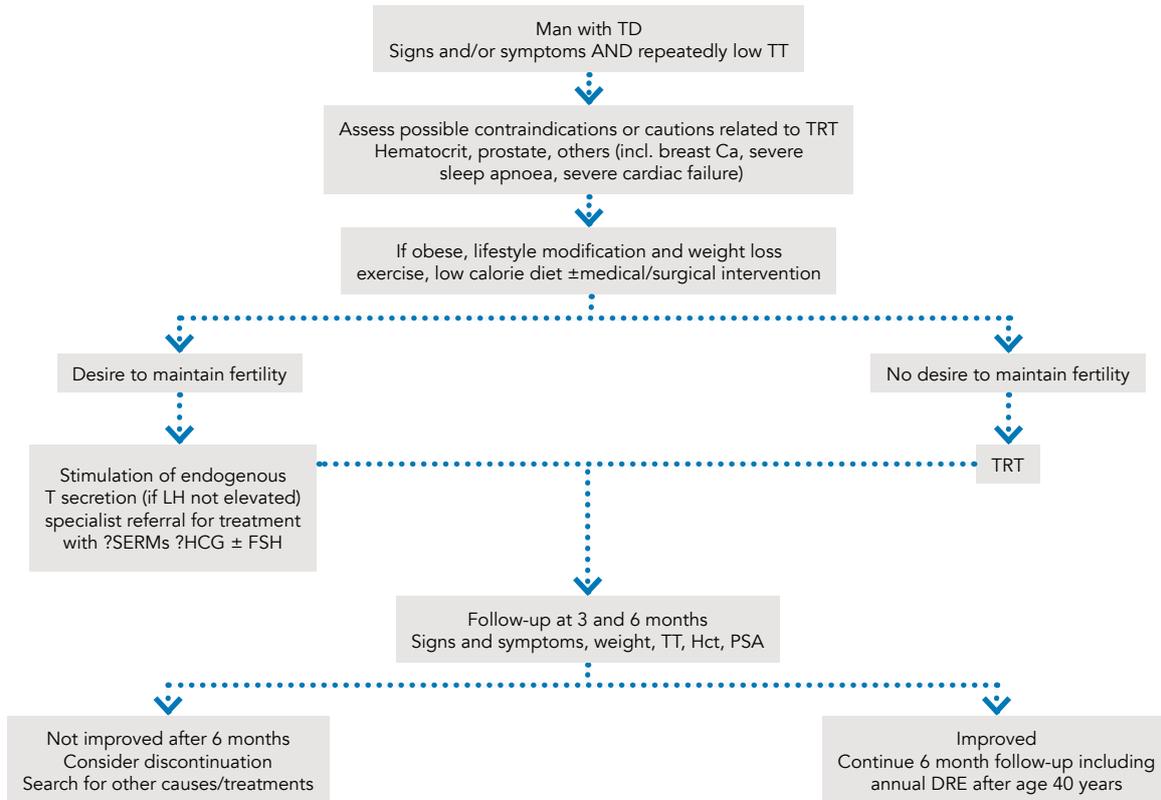


Figure 2: Flow chart for the process of care for the assessment and management of testosterone deficiency in adult men wishing to maintain fertility





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