

# Testosterone Deficiency: Case Study & British Society for Sexual Medicine Guidelines

Dr Jonny Coxon MA MD MRCS MRCGP DRCOG FECSM

GP Partner

Special Interest in Sexual & Gender Medicine

Clinical Assistant in Urology

Clinical Assistant (Endocrinology), Gender Identity Clinic

I have received recent honoraria from:

- Prostate Cancer UK
- Besins
- Bayer
- Ferring

# Mr Jonny Future, 55 years old



- Number of symptoms:
  - Fatigue
  - Decreased “zest for life”, irritable
  - Weight gain (BMI 35)
  - Low libido, poor erections
  - Spots on face
  - Night sweats, poor sleep
- PMH:
  - HT, ↑cholesterol, anaemia, back pain
- Meds:
  - Atorvastatin, losartan, tramadol

# What could be the diagnosis / cause?



Choose any that could apply:

1. Hypothyroidism
2. Vitamin D deficiency
3. Testosterone deficiency
4. Depression
5. Side effects of medication

# What could be the diagnosis / cause?



Choose any that could apply:

1. Hypothyroidism
2. ~~Vitamin D deficiency~~
3. Testosterone deficiency
4. Depression
5. Side effects of medication

## British Society for Sexual Medicine Guidelines on Adult Testosterone Deficiency, With Statements for UK Practice



Geoff Hackett, MD,<sup>1</sup> Michael Kirby, MD,<sup>2</sup> David Edwards, MD,<sup>3\*</sup> Thomas Hugh Jones, MD,<sup>4</sup> Kevan Wylie, MD,<sup>5</sup> Nick Ossei-Gerning, MD,<sup>6</sup> Janine David, MD,<sup>7</sup> and Asif Muneer, MD<sup>8,†</sup>

### ABSTRACT

**Background:** Testosterone deficiency (TD) is an increasingly common problem with significant health implications, but its diagnosis and management can be challenging.

**Aim:** To review the available literature on TD and provide evidence-based statements for UK clinical practice.

**Methods:** Evidence was derived from Medline, EMBASE, and Cochrane searches on hypogonadism, testosterone (T) therapy, and cardiovascular safety from May 2005 to May 2015. Further searches continued until May 2017.

**Outcomes:** To provide a guideline on diagnosing and managing TD, with levels of evidence and grades of recommendation, based on a critical review of the literature and consensus of the British Society of Sexual Medicine panel.

**Results:** 25 statements are provided, relating to 5 key areas: screening, diagnosis, initiating T therapy, benefits and risks of T therapy, and follow-up. 7 statements are supported by level 1, 8 by level 2, 5 by level 3, and 5 by

# Definition of Testosterone Deficiency

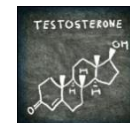
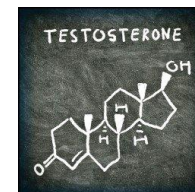
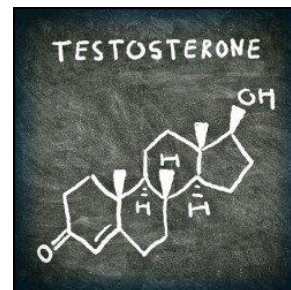
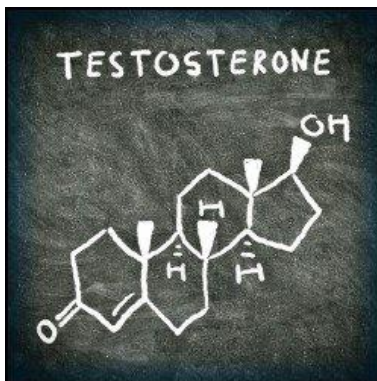
*“Testosterone deficiency (TD) is a **clinical** and **biochemical** syndrome characterized by a deficiency of testosterone, or testosterone action,*

**AND**

*relevant symptoms and signs”*



International Society  
for Sexual Medicine



- Estimates for prevalence vary
- Ranges from 2-12% of men over 40 / 50
- Increases with age



# Which features here are not linked to TD?



Choose any that apply:

1. Fatigue
2. Weight gain
3. Spots on face
4. Night sweats
5. Anaemia

# Which features here are not linked to TD?



Choose any that apply:

1. ~~Fatigue~~
2. ~~Weight gain~~
3. Spots on face
4. ~~Night sweats~~
5. ~~Anaemia~~

# Clinical *signs and symptoms* suggestive of TD



## **Depression**

- Depressed mood
- Cognitive impairment

## **Cardiovascular disorders**

- Hyperlipidaemia
- Hypertension

## **Physical decline**

- BMD: Loss of bone mineral density
- Fatigue: Decreased energy levels
- Sarcopaenia: Loss of muscle mass and strength

## **Metabolic disorders**

- Abdominal obesity
- Poor insulin regulation
- Poor glycaemic control<sup>2</sup>

## **Sexual dysfunction**

- Reduced sexual desire and activity
- Erectile dysfunction (ED)

- Sexual dysfunction symptoms prominent
- Also:
  - night sweats
  - sleep disturbance
  - other changes in mood

# Screening for TD



Recommendations—screening	LoE	Grade
Screen for TD in adult men with consistent and multiple signs of TD	3	C
Screen all men <u>presenting with ED, loss of spontaneous erections, or low sexual desire</u>	1	A
Screen for TD in all men with <u>T2DM, BMI &gt; 30 kg/m<sup>2</sup> or waist circumference &gt; 102 cm</u>	2	A
Screen for TD in all men on long-term <u>opiate, antipsychotic, or anticonvulsant medication</u>	2	B

# ADAM Questionnaire

Your answers to the following questionnaire will help to identify whether you have the features of Testosterone Deficiency Syndrome (TDS).

Please answer the questions honestly.

YES NO

- |                                                                            | YES                      | NO                       |
|----------------------------------------------------------------------------|--------------------------|--------------------------|
| 1. Do you have a decrease in libido (sex drive)?                           | <input type="checkbox"/> | <input type="checkbox"/> |
| 2. Do you have a lack of energy?                                           | <input type="checkbox"/> | <input type="checkbox"/> |
| 3. Do you have a decrease in strength and/or endurance?                    | <input type="checkbox"/> | <input type="checkbox"/> |
| 4. Have you lost height?                                                   | <input type="checkbox"/> | <input type="checkbox"/> |
| 5. Have you noticed a decreased "enjoyment of life"?                       | <input type="checkbox"/> | <input type="checkbox"/> |
| 6. Are you sad and/or grumpy?                                              | <input type="checkbox"/> | <input type="checkbox"/> |
| 7. Are your erections less strong?                                         | <input type="checkbox"/> | <input type="checkbox"/> |
| 8. Have you noticed a recent deterioration in your ability to play sports? | <input type="checkbox"/> | <input type="checkbox"/> |
| 9. Are you falling asleep after dinner?                                    | <input type="checkbox"/> | <input type="checkbox"/> |
| 10. Has there been a recent deterioration in your work performance?        | <input type="checkbox"/> | <input type="checkbox"/> |

If the answer is YES to question **1 or 7**, or **at least three** of the other questions:

Further evaluate for symptoms of TD & consider testing

Google "testosterone questionnaire"

# Investigations

- Mr JF comes in during his lunch break for blood tests
- Routine ‘fatigue bloods’ done: normal
- Recalling a great talk (😊!) about TD, you included these:

Serum testosterone level (XE2dr)	7.1 nmol/L [6.68 - 25.7]
Serum sex hormone binding globulin level (44CD.)	24 nmol/L [19.3 - 76.4]
Serum free testosterone level (XabD9)	168 pmol/L [163 - 473]



# *What do you advise him?*

Choose the best answer(s):

1. Reassure him bloods are normal this time
2. Test again, in another convenient lunch break
3. Test again, on a morning fasting sample
4. Diagnose testosterone deficiency

Serum testosterone level (XE2dr)	7.1 nmol/L [6.68 - 25.7]
Serum sex hormone binding globulin level (44CD.)	24 nmol/L [19.3 - 76.4]
Serum free testosterone level (XabD9)	168 pmol/L [163 - 473]

# What do you advise him?

Choose the best answer(s):

- ~~1. Reassure him bloods are normal this time~~
- ~~2. Test again, in another convenient lunch break~~
3. Test again, on a morning fasting sample
- ~~4. Diagnose testosterone deficiency~~

Serum testosterone level (XE2dr)	7.1 nmol/L [6.68 - 25.7]
Serum sex hormone binding globulin level (44CD.)	24 nmol/L [19.3 - 76.4]
Serum free testosterone level (XabD9)	168 pmol/L [163 - 473]



- Measure **testosterone**: fasting sample, before 11am
- Need at least 2 results, preferably 4 weeks apart

# Laboratory Diagnosis of TD



- If 1<sup>st</sup> test low/borderline:
  - repeat & measure **LH** (+/- FSH)
  - plus **SHBG** to calculate **free testosterone**
- Clinical symptoms more closely related to ***free testosterone*** than total

# Diagnosis of TD



www.pctag.uk/testosterone-calculator/



Google "testosterone calculator"

Contact us  
info@pctag.uk

HOME

ABOUT US

INFORMATION

NEWS

CONTACT US

FOLLOW US :



## FREE & BIOAVAILABLE TESTOSTERONE CALCULATOR

Welcome to the Free & Bioavailable Testosterone Calculator

Also available on [Apple Appstore](#) and [Google Play](#)



This website has been developed in part through an educational grant from Besins Healthcare (UK) Ltd. The company has no editorial control on its content.

**IMPORTANT LIMITATIONS:** This calculator is an educational tool and should not be solely relied upon in making any clinical decision. No responsibility whatsoever is assumed for its correctness or suitability for any given purpose. Please consult your health care provider first for any health concerns.

Additionally, the calculated free and bioavailable testosterone should not be relied upon in situations with potential massive interference by steroids binding to SHBG

### Free & Bioavailable Testosterone Calculator

Albumin\*:

Units:

SHBG:

Units:

Testosterone:

Units:

Free Testosterone:

- **BEWARE LABORATORY REFERENCES RANGES**
  - Vary considerably across the country
- Use **“action levels”** instead

# Thresholds for T Therapy



- Total T level **<8** nmol/L *or* free T **<180** pmol/L
  - Usually requires T Therapy
- Total T level **>12** nmol/L *or* free T **>225** pmol/L
  - Does not require T Therapy
- Total T **8-12** nmol/L *or* free T **180-225** pmol/L
  - May require a ***trial*** of T Therapy for a minimum of 6 months

# Diagnosis of TD

- If these low levels are confirmed, **in combination** with his symptoms, testosterone deficiency can be diagnosed

Serum testosterone level (XE2dr)	7.1 nmol/L [6.68 - 25.7]
Serum sex hormone binding globulin level (44CD.)	24 nmol/L [19.3 - 76.4]
Serum free testosterone level (XabD9)	168 pmol/L [163 - 473]

- Choice usually = **gel vs injection**
- No justification for selecting one over another except **patient choice**

# Testosterone *gels*

- Daily, may need titrating
- *Advantages:*
  - Fast onset
  - Levels peak 2-4 hours then slow ↓
- *Disadvantages:*
  - Skin irritation
  - Potential interpersonal transfer
  - Possible non-compliance long-term?





# Testosterone *injections*

## 1. Short-acting:

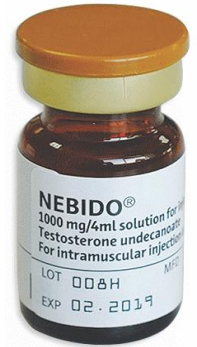
- Usually 3-weekly
- *Advantages:*
  - Low cost prescription (Sustanon)
  - Short duration allows quick withdrawal
- *Disadvantages:*
  - More frequent injections (cost?)
  - Fluctuating testosterone levels between injections



# Testosterone *injections*

## 2. Long-acting:

- Every 10-14 weeks
- *Advantages:*
  - Fewer injections – ↑ compliance
  - Maintains better steady state
- *Disadvantages:*
  - Slower drug withdrawal if needed
  - Possible painful injection site (4ml, needs to be SLOW)



# Does T therapy *work*?



- Good evidence cited in guidelines for improvements in:
  - Sexual desire, activity, erections
  - Waist circumference
  - BMI
  - Lean mass vs fat mass
  - Insulin resistance
  - Lipid profile
  - BP
  - Walking distances
  - Bone mineral density
  - Anaemia
  - Lower urinary tract symptoms
  - Depression scores

# *How long* to trial treatment?



- Different symptoms improve at different rates
- Should trial for **MINIMUM 6 MONTHS**
- Most commonly, **lifelong therapy**

# Follow-up and monitoring



Recommendations – Follow-up	LoE	Grade
Assess the response to therapy at <u>3, 6 and 12 months, and every 12 months</u> thereafter	4	C
Aim for a target level of <u>total testosterone 15-30 nmol/l</u> to achieve optimal response	4	C
Monitor <u>haematocrit</u> before treatment, at 3-6 months, 12 months and every 12 months thereafter. Decrease dosage, or switch preparation, if haematocrit >0.54. If haematocrit remains elevated, consider stopping and re-introduce at a lower dose.	4	C
Assess prostate health by PSA and DRE before commencing TRT followed by <u>PSA</u> at 3-6 months, 12 months and every 12 months thereafter	4	C
Assess cardiovascular risk before TRT is initiated and <u>monitor cardiovascular risk</u> factors throughout therapy	1b	A

# Risks of Testosterone Therapy



- 12 months after starting treatment, Mr JF is a “new man”:
  - Lost 4kg weight, 5cm waist circumference
  - BP & cholesterol improved
  - Better sexual function
  - Energy ↑
  - Hb ↑
- However, he says he thinks he might want to stop TT: he’s read about risks of heart disease and prostate cancer
- What can you tell him?

- BSSM Guideline gives full review of evidence
- Body of evidence links ***low T*** to **↑ *CV risk***

# Testosterone and CV risk



- Individual studies with TT cited:
  - ↓ major CV events
  - ↓ mortality
- Meta-analyses:
  - **No** increased CV risk with TT



- European Medicines Agency 2014
  - No concerns re CV risk



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

Hackett G et al. Int J Clin Pract 2016;70:244-53.

Sharma R et al. Eur Heart J. 2015;36:2706-15.

Baillargeon J et al. Ann Pharmacother 2014;48:1138-1144.

Wallis CJ, Lo K, Lee Y et al. Lancet Diabetes Endocrinol 2016;4:498-506.

Cheetham CT, An JJ & Jacobsen SJ. JAMA Intern Med 2017;177:491-499.

Corona G, Rastrelli G, Maggi M. Best Pract Res Clin Endocrinol Metab 2013;27:557-79.

[www.ema.europa.eu/docs/en\\_GB/document\\_library/Referrals\\_document/Testosterone\\_31/Position\\_provided\\_by\\_CMDh/WC500177617.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Testosterone_31/Position_provided_by_CMDh/WC500177617.pdf) (European Medicines Agency)



# Testosterone and prostate cancer

- Engrained belief that testosterone is linked to prostate cancer (pCa) growth
- Now think of **SATURATION MODEL**:
  - Beyond a low T level, receptors saturated, no further growth stimulated
- **No** evidence that T Therapy increases risk of pCa, or pCa progression



# Adverse effects of TT



- Changes in mood, energy, sexual desire
- Polycythaemia
- Acne
- ↓ fertility

# Adverse effects of TT

- Changes in mood, energy, sexual desire
  - Polycythaemia
  - Acne
  - ↓ fertility
- 
- ***Sustained supraphysiological levels should be avoided***





bssm.org.uk

[Home](#) [About](#) [Join](#) [Events](#) [Resources](#) [Contact Us](#)



The British Society for Sexual Medicine (BSSM) was founded to promote research and exchange of knowledge of impotence and other aspects of sexual function and dysfunction.

[Join BSSM](#)



[OUR NEXT EVENT](#)



[RESOURCES](#)

## Latest resources

### **A Practical Guide** – On The Assessment and Management of Testosterone Deficiency in Adult Men

2018



### British Society for Sexual Medicine Guidelines on Adult Testosterone Deficiency, With Statements for UK Practice

2018

### **A Practical Guide** – On Managing Erectile Dysfunction

2018

### British Society for Sexual Medicine Guidelines on the Management of Erectile Dysfunction in Men

2018

# 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<sup>1</sup>

## Why does it occur?

Testosterone deficiency (TD), also known as hypogonadism, may result from:<sup>2-4</sup>

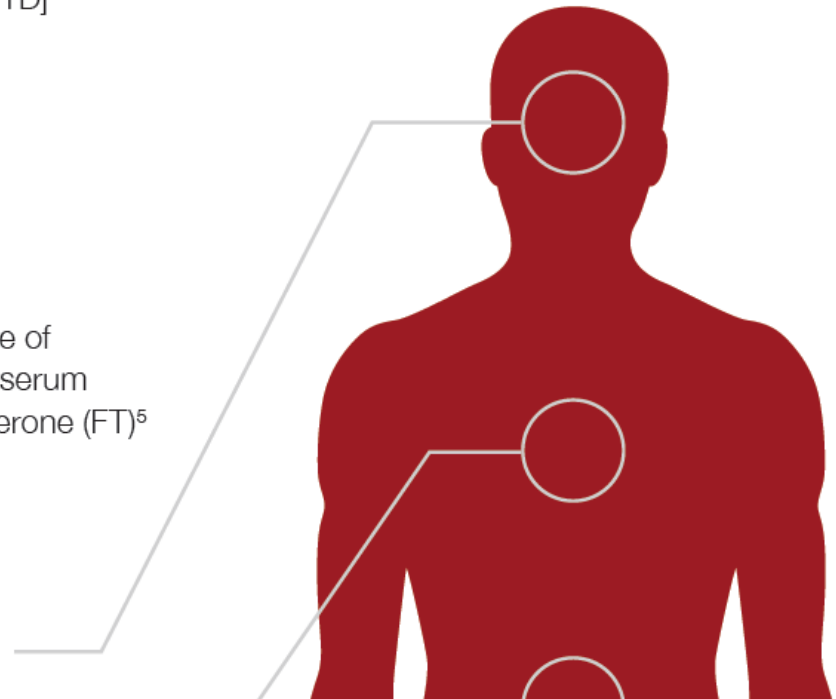
- Problems with the testes [primary (hypergonadotropic) TD]
- Problems with the hypothalamus and pituitary gland [secondary (hypogonadotropic) TD]
- Problems with the hypothalamus/pituitary and testes (combined primary and secondary TD)
- Impaired action/suppression of testosterone

## How is it diagnosed?

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

### Psychological

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



- TD is a **well-established and significant medical condition**, encompassing somatic, sexual and psychological effects
- Associated with **increased CV & all-cause mortality**
- Testosterone therapy is **evidence-based & effective** in TD, improving a number of clinical features