Quest Diagnostics®

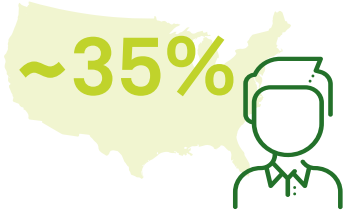
Diagnosing and managing **hypogonadism in men**

Evaluate testosterone deficiency with laboratory insights from Quest Diagnostics®

Get the insight you need to diagnose and manage **male reproductive disorders**

- Male hypogonadism is a clinical syndrome resulting from decreased testosterone and/or sperm production[1]
- Hypogonadism is a **common condition** in the male population[2]
- There is a **higher prevalence** of hypogonadism in older men, obese men, and men with type 2 diabetes[2]

It is estimated that



of men over 45 years of age have hypogonadism[2]

Laboratory testing for the **diagnosis and management of hypogonadism**

Laboratory testing is recommended for the diagnosis of men with suspected hypogonadism, especially when conditions associated with a high prevalence of low testosterone are present.[1,3]

Individuals suitable for testing:

- Men with symptoms, signs, or conditions associated with hypogonadism (Tables 1 & 2)[1,3]
- Men who are receiving testosterone replacement therapy (TRT)[1,3]

Table 1. Symptoms and signs of hypogonadism in men

Symptom type[3]		
Specific	**Suggestive**	**Nonspecific**
Incomplete or delayed sexual development[a]	Reduced libido[a]	Decreased energy, motivation, initiative, self-confidence
Loss of body hair	Decreased spontaneous erections	Depression
Very small testes (<6 mL)	Erectile dysfunction[a]	Poor concentration and memory
	Gynecomastia[a]	Sleep disturbances
	Eunuchoid body appearance[b]	Mild unexplained anemia (normochromatic, normocytic)
	Inability to conceive, low sperm count[a]	Reduced muscle bulk and strength
	Height loss	Increased body fat, BMI
	Osteoporosis or low-trauma bone fracture[a]	
	Low bone mineral density	
	Hot flashes, sweats	

BMI, body mass index.

[a] High-prevalence conditions of low testosterone for which serum testosterone measurements are suggested.[1]

[b] Eunuchoid body appearance is typical of hypogonadism occurring before epiphyseal fusion.

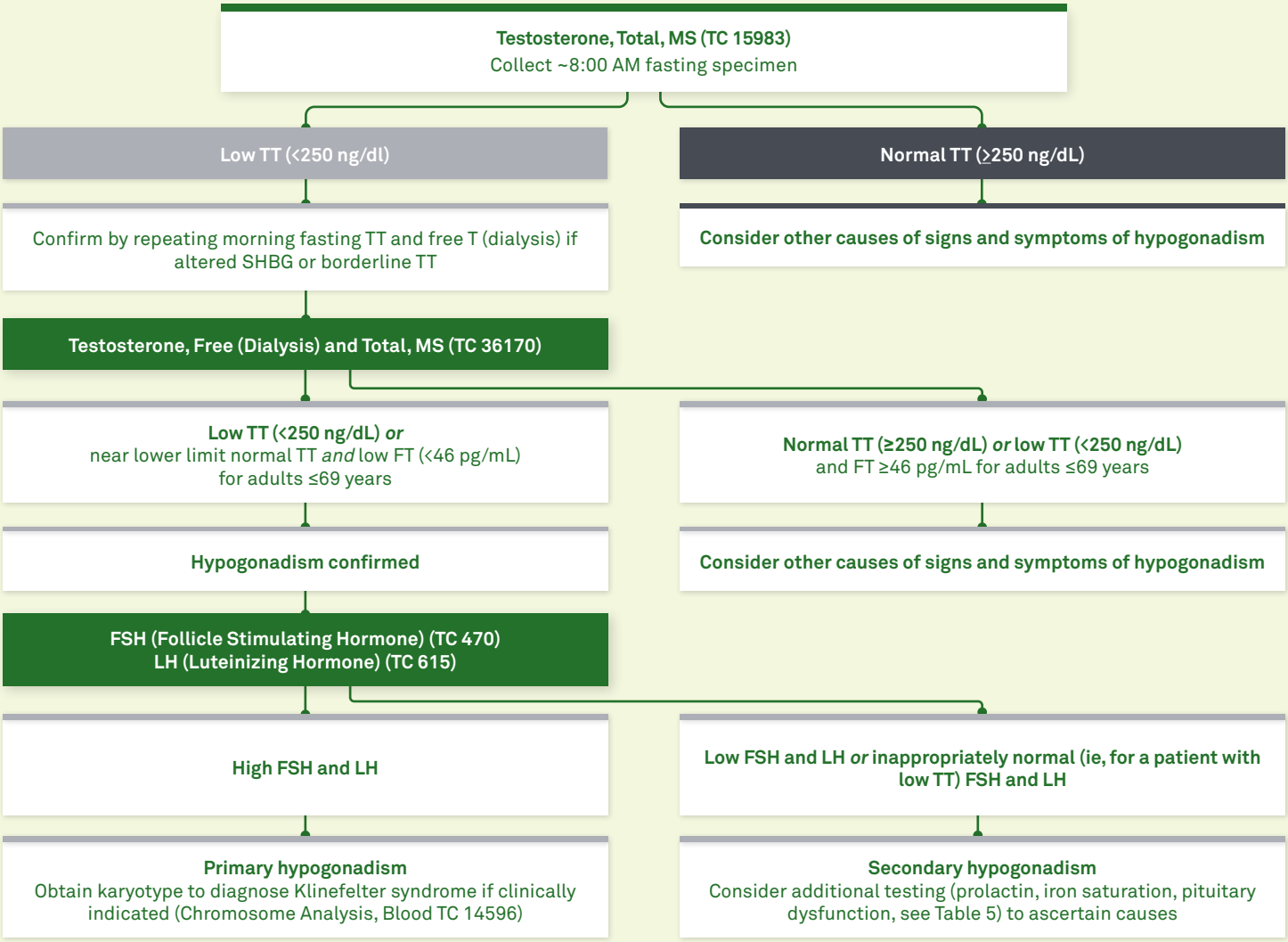
Table 2. Conditions associated with changes in SHBG

Conditions associated with decreased SHBG[1]
Insulin resistance
Obesity
Diabetes mellitus
Use of glucorticoids, some progestins, and androgenic steroids
Nephrotic syndrome
Hypothyroidsim
Acromegaly
Polymorphisms in the *SHBG* gene
Conditions associated with increased SHBG[1]
Aging
HIV disease
Cirrhosis and hepatitis
Hyperthyroidism
Use of some anticonvulsants
Use of estrogens
Polymorphism in the *SHBG* gene

SHBG, sex hormone binding globulin.

Figure 1. Adult male hypogonadism diagnostic algorithm

For adult male patients with signs and symptoms of hypogonadism in the absence of conditions that alter SHBG



FSH, follicle-stimulating hormone; FT, free testosterone; LH, luteinizing hormone; SHBG, sex hormone binding globulin; TC, test code; TT, total testosterone. This figure was developed by Quest Diagnostics based on reference 1. It is provided for informational purposes only and is not intended as medical advice. Test selection and interpretation, diagnosis, and patient management decisions should be based on the physician's education, clinical expertise, and assessment of the patient.

Types and causes of hypogonadism

Hypogonadism can occur in 3 forms: primary, secondary, and combined. If initial and confirmatory testing indicates low testosterone, FSH and LH should be measured to distinguish between primary and secondary hypogonadism.[1]

Primary hypogonadism (hypergonadotropic hypogonadism) is caused by abnormalities of the testes and is also characterized by high FSH and LH.

Secondary hypogonadism (hypogonadotropic hypogonadism) is caused by abnormalities of the hypothalamus and/or pituitary glands and, in contrast to primary hypogonadism, is characterized by low or inappropriately normal FSH and LH levels.

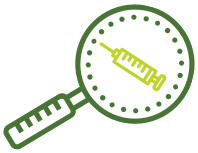
Combined hypogonadism, gonadotropin levels are variable depending on whether primary or secondary hypogonadism predominates.

When hypogonadism is diagnosed in men, additional diagnostic evaluation is recommended to determine the cause(s), which are classified as either organic or functional. Organic causes include congenital, structural, or destructive disorders like diabetes and obesity that suppress the hypothalamus, pituitary, or testis. Functional causes include conditions that suppress gonadotropins and testosterone concentrations.[1]

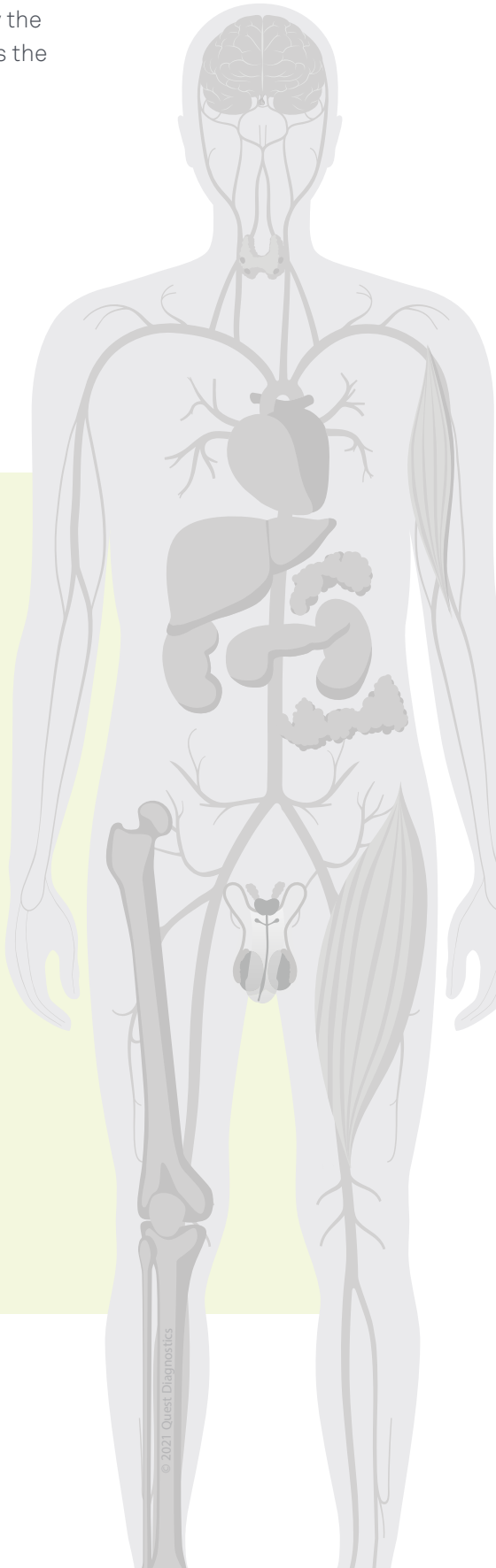
Guideline supported **testing recommendations**

LC-MS/MS provides a more precise and accurate measurement of TT at lower concentrations and is the recommended assay in Endocrine Society guidelines.[1]

Quest Diagnostics offers a Total Testosterone LC-MS/MS assay that is certified by the CDC Laboratory/Manufacturer Hormone Standardization (HoSt) Program, which is the assay recommended by the Endocrine Society for healthy men older than 18.[1,4]



FT should be measured if TT is reported near the lower limit of normal or if alterations in SHBG that affect TT are suspected (Table 2).[1] Guidelines recommend measuring FT by an equilibrium dialysis method.[1]



Diagnosis of hypogonadism (guideline-indicated, preferred)[1]

36170	Testosterone, Free (Dialysis) and Total, MS[a,b]	Diagnose androgen deficiency when TT is near lower limit of normal or alteration in SHBG is suspected
15983	Testosterone, Total, MS[a,b]	Diagnose hypogonadism

Table 3. Reference ranges for men

Analyte	Age	Reference range
TT	Adult	250-1100 ng/dL[a]
FT	18-69 years	46.0-224.0 pg/mL
	70-89 years	6.0-73.0 pg/mL

[a] Quest Diagnostics assays for TT have a reportable lower limit of 250 ng/dL. The reference range is based on the 2.5th percentile of a distribution of study results in a healthy population using specimens from healthy men across the age spectrum, including individuals up to age 90. For comparison, the lower limit of normal TT harmonized to the CDC standard for TT in healthy nonobese young men is 264 ng/dL (9.2 nmol/L).[4]

[b] Laboratory tests can provide 3 measurements of testosterone: free, bioavailable, and total. These measurements incorporate the 3 major forms of circulating testosterone: unbound (free), weakly bound to albumin, and tightly bound to SHBG. TT is the total concentration of bioavailable (free and weakly bound testosterone) and SHBG-bound testosterone.

Test interpretation

Quest Diagnostics Total Testosterone reference range (Table 3) is based on the 2.5th percentile of a distribution of study results in a healthy population using specimens from men across the age spectrum, including individuals up to age 90.

Testosterone therapy for **hypogonadism**

The Endocrine Society recommends testosterone therapy in hypogonadal men to induce and maintain secondary sex characteristics and correct symptoms of testosterone deficiency.[1]

Monitoring during testosterone therapy

- For men who have started TRT, monitoring of testosterone, hematocrit, prostate-specific antigen (PSA), and measurement of bone mineral density (BMD) is recommended[1]
- Hematocrit is assessed to evaluate for secondary erythrocytosis (ie, increase in hematocrit)[1]
- PSA levels may be increased in hypogonadal men who are receiving TRT[1]
- Endocrine Society guidelines recommend measuring TT and hematocrit from 3 to 6 months after initiation of TRT[1]
- Total Testosterone levels should be measured midway between injections when using intramuscular testosterone esters or 2 to 8 hours after application of a transdermal gel[1]

Table 4. Monitoring testosterone management[1,5,6]

Test code	Test name (component test codes for panels)	Clinical use
509	Hematocrit	
5363	PSA, Total	
15983	Testosterone, Total, MS[a,b]	

Get the answers you need with **testing from Quest**

Quest Diagnostics offers a comprehensive menu of laboratory insights that assists in diagnosing hypogonadism, distinguishing type and causes of hypogonadism, and monitoring and managing TRT.[1,3,7]

Panel components may be ordered separately.

Table 5. Available tests

Test code	Test name (component test codes for panels)	Clinical use
Diagnosis of hypogonadism (guideline-indicated, preferred)[1]		
36170	Testosterone, Free (Dialysis) and Total, MS[a,b]	Diagnose androgen deficiency when TT is near lower limit of normal or alteration in SHBG is suspected
15983	Testosterone, Total, MS[a,b]	Diagnose hypogonadism
Identifying type and cause of hypogonadism[1,3]		
8658	Alpha Subunit	Identify cause of secondary hypogonadism; elevated in patients with hypogonadism associated with a nonfunctioning pituitary tumor
14596	Chromosome Analysis, Blood	Diagnose Klinefelter syndrome as an organic cause of primary hypogonadism
4212	Cortisol, A.M.	Evaluate pituitary hormones if there is a clinical indication of hypopituitarism on imaging
38149	Cortisol Response to ACTH Stimulation test	
470	Follicle Stimulating Hormone (FSH)	Distinguish primary vs secondary hypogonadism
457	Ferritin	Diagnose and identify iron overload syndrome (ie, iron saturation) as an organic cause of male hypogonadism
5616	Iron, TIBC, and Ferritin Panel Includes iron, total (571), total iron binding capacity (7573), and ferritin (457).	
571	Iron, Total	
7573	Iron, Total and Total Iron Binding Capacity	
615	Luteinizing Hormone (LH)	Distinguish primary vs secondary hypogonadism
746	Prolactin	Diagnose and identify hyperprolactinemia as a functional cause of male hypogonadism
40049	Prolactin, Dilution Study	
16122	Prolactin, Total and Monomeric	
866	T4 Free (FT4)	Evaluate hypo- or hyperthyroidism, which are associated with changes in SHBG
35167	T4 Free, Direct Dialysis	
899	Thyroid Stimulating Hormone (TSH)	
Monitoring testosterone management[1,6,7]		
509	Hematocrit	
5363	PSA, Total	
15983	Testosterone, Total, MS[a,b]	
Other relevant tests		
30740	Sex Hormone Binding Globulin (SHBG)	Assess whether FT measurements are needed for diagnosis; useful if an equation is used to calculate FT
30741	Testosterone, Free, Bioavailable and Total, Males (Adult), Immunoassay[b,d]	Monitor response to testosterone therapy once levels have normalized
14966	Testosterone, Free, Bioavailable and Total, MS[a,b,c]	Diagnose androgen deficiency when TT is near lower limit of normal or alteration in SHBG is suspected
873	Testosterone, Total, Males (Adult), Immunoassay[b,d]	Monitor response to testosterone therapy once levels have normalized

ACTH, adrenocorticotropin hormone; FT, free testosterone; FT4, free thyroxine; LC/MS (LC-MS/MS), liquid chromatography/tandem mass spectrometry; MS, mass spectrometry; PSA, prostate-specific antigen; SHBG, sex hormone binding globulin, TRT, testosterone replacement therapy; TT, total testosterone.

[a] This test was developed and its analytical performance characteristics have been determined by Quest Diagnostics. It has not been cleared or approved by the FDA. This assay has been validated pursuant to the CLIA regulations and is used for clinical purposes.

[b] Laboratory tests can provide 3 measurements of testosterone: free, bioavailable, and total. These measurements incorporate the 3 major forms of circulating testosterone: unbound (free), weakly bound to albumin, and tightly bound to SHBG. TT is the total concentration of bioavailable (free and weakly bound testosterone) and SHBG-bound testosterone.

[c] As an alternative to FT measurement by dialysis, FT levels can be estimated from a formula based on TT, SHBG, and albumin measurements (test code 14966).[1] Quest uses a modified Sodergard equation[8] that accurately reflects FT as if it were measured by equilibrium dialysis[1]; however, FT measurement by dialysis is preferred (test code 36170).

[d] Direct immunoassays cannot accurately measure low serum testosterone levels found in hypogonadal men. For higher specificity, sensitivity, and precision testing of low TT, clinicians should consider using LC-MS/MS-based assays, preferably those certified by the Centers for Disease Control and Prevention (CDC).[1] The LC-MS/MS tests (test codes 15983, 36170) have been certified by the CDC Hormone Standardization Program.[4]

Get the insights you need from the lab that knows endocrinology

Count on actionable results to help you do your best for your patients.

- → Comprehensive test menu
- → Reliable and accurate result reporting
- → Endocrinology interpretation guides and algorithms
- → Medical and scientific expertise from Quest Diagnostics

Guidelines are a simplification provided as a convenience and should not be used as a substitute for the healthcare provider's professional judgment. The source materials and other information should be consulted when appropriate.

For more clinical information on hypogonadism testing, please visit the Quest Diagnostics Test Directory at **https://testdirectory.questdiagnostics.com**.

Contact your Quest Diagnostics sales representative for more information about testosterone testing.

To speak to an endocrinology specialist, call 1.866.MYQUEST (1.866.697.8378)

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