Polycystic Ovary Syndrome (PCOS)

Quest Diagnostics®

Diagnosing and managing **polycystic ovary syndrome**

Get the insights you need on this complex condition with testing from Quest Diagnostics

Know the signs and diagnostic tests for **polycystic ovary syndrome**

Diagnose and manage this complex disorder and comorbidities with testing from Quest.

Polycystic ovary syndrome (PCOS) is a common endocrine disorder that affects about 5 to18% of women, and is a condition with health impacts across the lifespan.[1-3] PCOS is also one of the most common causes of female infertility, affecting as many as 5 million women of reproductive age in the United States.[4]

PCOS is defined by a combination of signs and symptoms of androgen excess and ovarian dysfunction in the absence of other specific diagnoses.[1-3]

- → Hirsutism
- → Weight gain
- → Acne
- → Thinning hair/Androgenic alopecia
- → Ovulatory dysfunction/Menstrual irregularities
- → Enlarged polycystic ovaries
- → Infertility

Primary features of PCOS include:

Clinical presentations of PCOS encompass a wide spectrum, ranging from mild cases with normal androgens, ovulatory dysfunction, and polycystic ovaries, to severe instances that exhibit marked hirsutism, alopecia, obesity, and high testosterone.[1-3]

The exact cause of PCOS is unknown but is thought to involve complex genetic and environmental interactions. Insulin resistance, accompanied by compensating hyperinsulinemia, is believed to play a key role in PCOS pathophysiology by increasing androgen production.[1-3]

Diagnosing PCOS can be challenging

An estimated 75% of individuals with PCOS remain undiagnosed because of the variability in presentation and differences in published clinical diagnostic criteria.[5]

More than 1 in 3 women with PCOS may spend more than 2 years and see 3 or more healthcare professionals before the condition is diagnosed.[6]

No single criterion or test can be used to diagnose PCOS—diagnosis is primarily based on the exclusion of diseases with similar symptoms.[1-3] The 2003 Rotterdam criteria are the most-used approach for diagnosis of PCOS; the Rotterdam consensus defines PCOS based on the presence of at least 2 of 3 criteria:

- → hyperandrogenism
- → ovulatory dysfunction
- → polycystic ovarian morphology (PCOM)[1-3]

The use of 2 of 3 criteria for diagnosis of PCOS results in 4 recognized phenotypes (Table 1).[7] Notably, polycystic ovarian morphology (PCOM) on ultrasound is not necessary for diagnosis of PCOS (phenotype B).

Table 1. Polycystic Ovary Syndrome Phenotypes Based on Rotterdam Criteria

Criteria[1-3]	Phenotype[7]			
	A	B	C	D
Hyperandrogenism (clinical or biochemical)	✓	✓	✓	
Ovulatory dysfunction	✓	✓		✓
PCOM	✓		✓	✓

PCOM, polycystic ovarian morphology. ✓ Present

Many other disorders (eg, congenital adrenal hyperplasia [CAH], nonclassic CAH due to 21-hydroxylase deficiency, hyperprolactinemia, obesity, and hypothyroidism) also satisfy the criteria used to diagnose PCOS.[1-3] Some similar disorders have characteristics that can help distinguish them from PCOS (Table 2). *Importantly*, PCOS can only be diagnosed once other disorders have been excluded.[1-3,8]

Table 2. Potentially Distinguishing Characteristics Present in Disorders With Similar Clinical Features to PCOS

Disorder[1-3]	Potentially distinguishing characteristics
Acromegaly	Enlargement of hands, feet, and face
Cushing syndrome	Skin thinning, muscle weakness, hypertension
Hypothalamic amenorrhea	Low body weight, eating disorder, excessive exercise
Primary ovarian insufficiency	Hot flashes, mood swings, vaginal dryness
Virilizing tumors	Severe virilization with rapid onset

Accurately diagnosing—and ascertaining the cause—of the disorder is vital to determining appropriate treatment, ensuring effective disease management, and avoiding complications. Quest Diagnostics can help with a broad range of endocrine tests aligned to the most recent clinical practice guidelines for better disease management.

PCOS comorbidities and other considerations

Women with PCOS should also be assessed and treated for a number of serious comorbidities associated with PCOS.[1-3]

About half of all women with PCOS are obese.[1]

Compared to the general population, women with PCOS are:

4x as likely to develop type 2 diabetes mellitus[1]

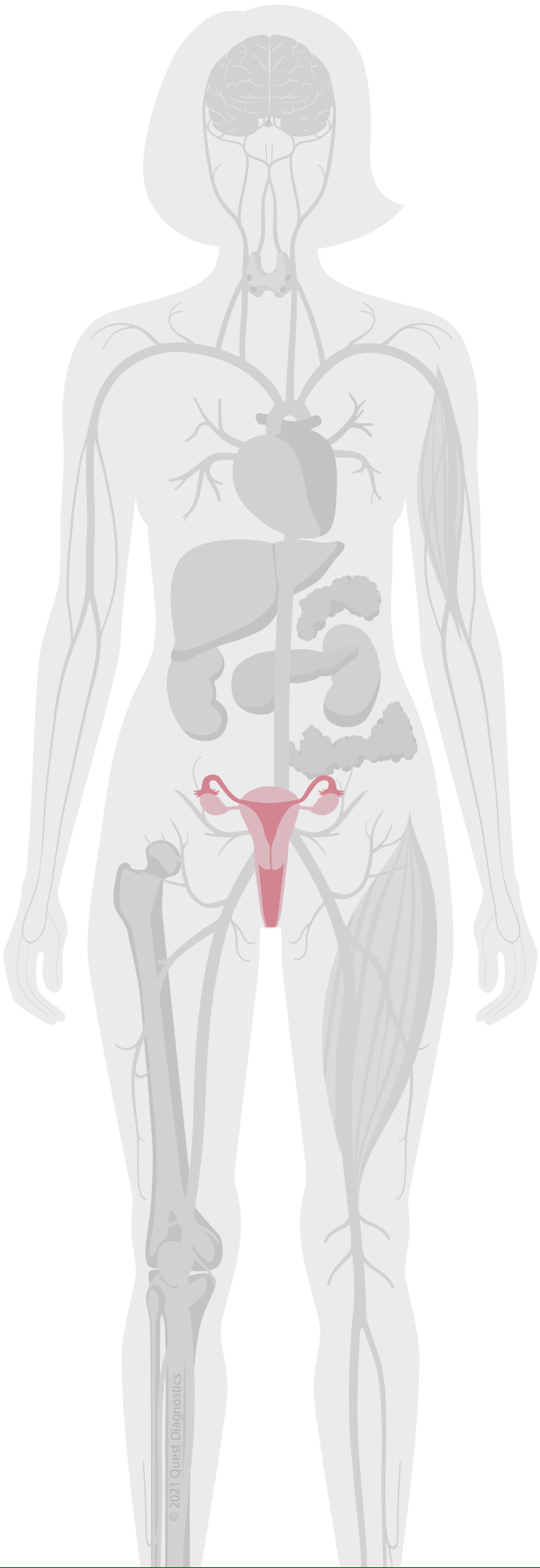
2x as likely to develop metabolic syndrome[3]

>50% of women with PCOS develop type 2 diabetes by age 40[4]

Women with PCOS are also at increased risk for[1-3,8,9]:

- Cardiovascular disease (CVD)
- Hypertension
- Metabolic syndrome
- Abnormal uterine bleeding
- Endometrial cancer
- Infertility and pregnancy complications
- Sleep apnea
- Nonalcoholic fatty liver disease (NAFLD)

Individuals with PCOS, particularly adolescents, also have higher rates of anxiety-related disorders and depression compared with the general population.[10]
The 2018 International Evidence-Based Guideline for the Assessment and Management of Polycystic Ovary Syndrome recommends that all women, especially adolescents, be screened for symptoms of anxiety and depression at the time of diagnosis; those with positive screening results should be referred to an appropriate healthcare provider.[11]



Laboratory tests for assessment of PCOS criteria and differential diagnosis of PCOS

Individuals suitable for testing:

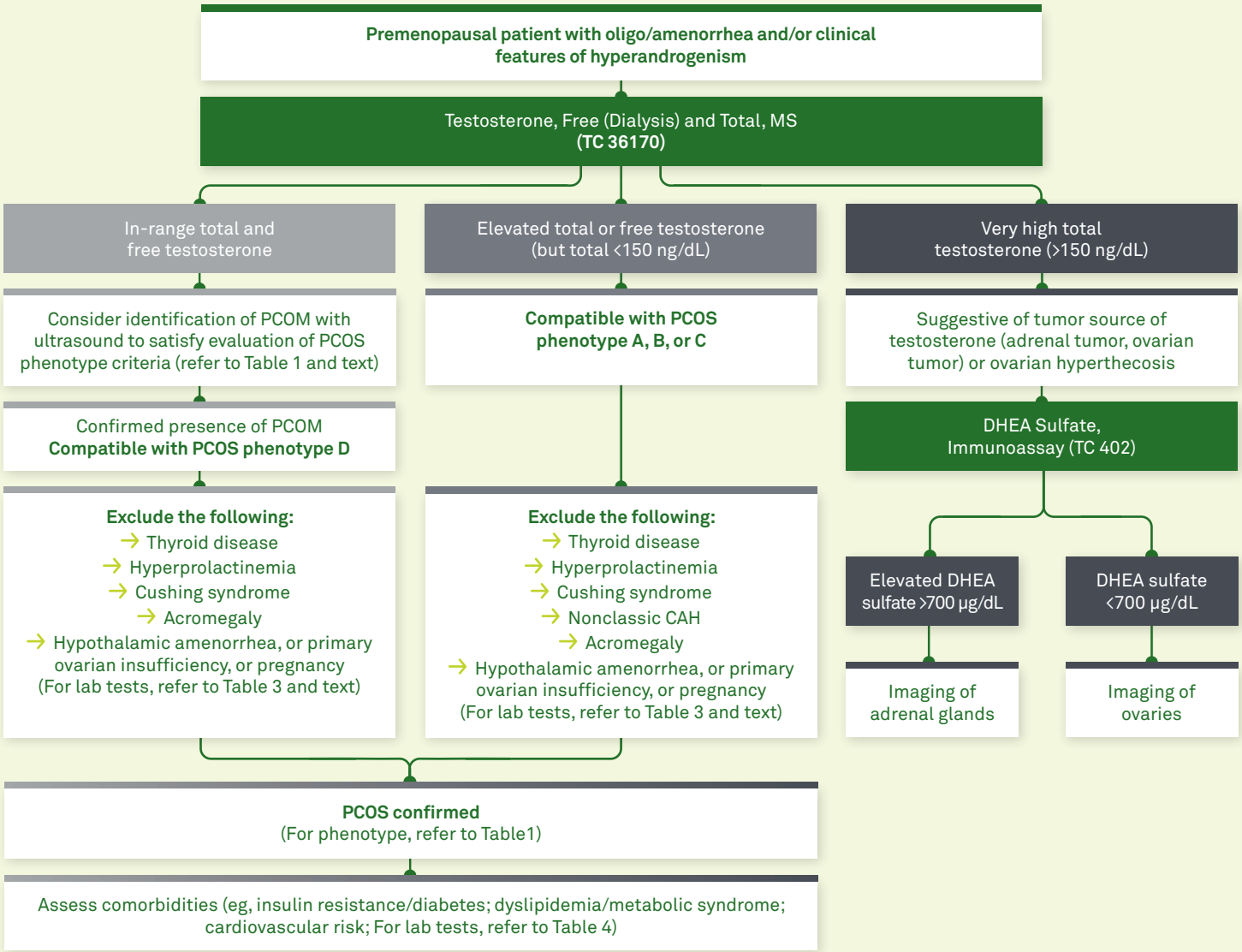
Women of reproductive age with ≥2 of the following criteria:

- → Hyperandrogenism (clinical or biochemical)
- → Ovulatory dysfunction
- → Polycystic ovaries

Adolescent girls with hyperandrogenism (clinical or biochemical) and persistent ovulatory dysfunction

Perimenopausal and menopausal individuals with a well-documented, long-term history of hyperandrogenism (clinical or biochemical) and ovulatory dysfunction

Figure 1. Polycystic Ovary Syndrome (PCOS) Diagnostic Algorithm



CAH, congenital adrenal hyperplasia; DHEA, dehydroepiandrosterone; FSH, follicle stimulating hormone; hCG, human chorionic gonadotropin; 17-OHP, 17-hydroxyprogesterone; LH, luteinizing hormone; PCOM, polycystic ovarian morphology; PCOS, polycystic ovary syndrome; TC, test code; TSH thyroid-stimulating hormone.

PCOM should be assessed by ultrasound. Excluding nonclassic CAH is not indicated for a diagnosis of PCOS phenotype D; testosterone is typically elevated in nonclassic CAH and in-range for PCOS phenotype D. If PCOS is suspected, ordering the following with testosterone may facilitate a quicker differential diagnosis: 17-Hydroxyprogesterone (TC 17180), hCG, Total, Quantitative (TC 8396) or hCG, Total with HAMA Treatment (TC 19720)—unnecessary if normal menstrual cycle; Prolactin (TC 746); TSH (TC 899) or TSH with HAMA Treatment (TC 19537); and FSH (TC 470) or FSH and LH (TC 7137). To exclude Cushing syndrome, consider initially ordering cortisol 24-hour urine (TC 14534), saliva (TC 19897), or low-dose DST (TC 6921).

This figure was developed by Quest Diagnostics based on references 1,2,7,12-16. 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.

Test availability

Quest Diagnostics offers tests and panels for PCOS criteria and differential diagnosis of disorders with overlapping features (Table 3).

Table 3. Laboratory Tests for Assessment of PCOS Criteria and Differential Diagnosis of PCOS

Test name (Component test codes for panels)	Test code	Description
PCOS criteria:		
Hyperandrogenism		
Androstenedione	17182	Diagnose hyperandrogenism
DHEA, (Dehydroepiandrosterone), Unconjugated	19894	Diagnose hyperandrogenism
DHEA Sulfate, Immunoassay[b]	402	Diagnose hyperandrogenism
Sex Hormone Binding Globulin (SHBG)	30740	Diagnose hyperandrogenism
Steroid Panel, Polycystic Ovary Syndrome (PCOS)[b,c] Includes androstenedione, DHEA, unconjugated, and total and free testosterone.	90424	Diagnose hyperandrogenism
Testosterone, Free, Bioavailable and Total, MS Includes total (15983) and free and bioavailable testosterone, sex hormone binding globulin (30740), and albumin (223).	14966	Diagnose hyperandrogenism
Testosterone, Free (Dialysis) and Total, MS Includes total (15983) and free testosterone.	36170	Diagnose hyperandrogenism
Testosterone, Total, MS	15983	Diagnose hyperandrogenism
Ovulatory dysfunction		
Progesterone, LC/MS[b]	17183	Assess ovulation
Polycystic ovaries		
Anti-Müllerian Hormone (AMH), Female[d]	37227	Diagnose polycystic ovaries
Differential diagnosis:		
Acromegaly[a]		
IGF-1, LC/MS[b]	16293	Diagnose acromegaly
Amenorrhea caused by hypothalamic amenorrhea or primary ovarian insufficiency		
Estradiol, Free[b]	36169	Diagnose hypothalamic amenorrhea or primary ovarian insufficiency
Estradiol, Ultrasensitive, LC/MS[b]	30289	Diagnose hypothalamic amenorrhea or primary ovarian insufficiency
FSH and LH Includes FSH (470) and LH (615)	7137	Diagnose hypothalamic amenorrhea or primary ovarian insufficiency
FSH (Follicle Stimulating Hormone)	470	Diagnose primary ovarian insufficiency
hCG, Total, Quantitative	8396	Rule out pregnancy
hCG, Total, with HAMA Treatment	19720	Rule out pregnancy in the presence of human anti-mouse antibodies (HAMA)
Cushing syndrome[a]		
Cortisol, Free, 24-Hour Urine with Creatinine[b]	14534	Diagnose cushing syndrome
Cortisol, Free, LC/MS, Serum	36423	Diagnose cushing syndrome
Cortisol, LC/MS, Saliva[b]	19897	Diagnose cushing syndrome
Cortisol, LC/MS, Saliva, 2 Samples[b]	93020	Diagnose cushing syndrome
Cortisol, LC/MS, Saliva, 4 Samples[b]	18921	Diagnose cushing syndrome
Dexamethasone Suppression Test (DST), 1 Specimen	6921	Diagnose cushing syndrome
Dexamethasone	29391	Assure adequate dosing during dexamethasone suppression
Hyperprolactinemia		
Prolactin	746	Diagnose hyperprolactinemia
Prolactin, Total and Monomeric	16122	Diagnose macroprolactinemia
Nonclassic CAH		
11-Deoxycortisol	30543	Diagnose nonclassic CAH
17-Hydroxyprogesterone[b]	17180	Diagnose nonclassic CAH
17-Hydroxyprogesterone Response to ACTH Stimulation	17682(X)	Diagnose nonclassic CAH
Steroid Panel, PCOS/CAH Differentiation[b,c] Includes 11-deoxycortisol, 17-hydroxyprogesterone, androstenedione, DHEA, unconjugated, and total and free testosterone.	90426	Diagnose nonclassic CAH
Thyroid disease		
TSH	899	Diagnose hyper- or hypothyroidism
TSH With HAMA Treatment	19537	Diagnose hyper- or hypothyroidism in the presence of HAMA
Tumors		
DHEA Sulfate, Immunoassay[b]	402	Diagnose virilizing tumors
Testosterone, Total, MS	15983	Diagnose virilizing tumors

ACTH, adrenocorticotropic hormone; CAH, congenital adrenal hyperplasia; DHEA, dehydroepiandrosterone; FSH, follicle stimulating hormone; HAMA, human anti-mouse antibody; hCG, human chorionic gonadotropin; IGF-1, insulin-like growth factor 1; LC/MS, liquid chromatography-(high resolution) mass spectrometry; LC/MS/MS, liquid chromatography-tandem mass spectrometry; LH, luteinizing hormone; PCOS, polycystic ovary syndrome; SHBG, sex hormone-binding globulin; TSH, thyroid-stimulating hormone.

[a] ACOG recommends screening for Cushing syndrome and other rare disorders such as acromegaly in symptomatic patients if nonclassical CAH has been ruled out (17-hydroxyprogesterone random level is <400 ng/dL or morning fasting level is <200 ng/dL).[10]

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

[c] Panel components (test code) may be ordered separately.

[d] AMH concentration in adult women reflects ovarian reserve (the number of primordial follicles remaining in the ovaries). AMH concentration is not considered a substitute for ultrasound in the diagnosis of PCOM. Levels, however, may predict the likelihood of women with PCOS achieving a live birth, as well as identify those less likely to ovulate and conceive on clomiphene therapy.[15]

Use testing from Quest Diagnostics to help manage comorbidities associated with PCOS

Quest also offers tests and panels for the diagnosis and management of comorbidities associated with PCOS. For example, testing related to cardiometabolic comorbidities (diabetes and CVD risk) is presented in Table 4.

Table 4. Laboratory Tests for the Diagnosis and Management of Cardiometabolic Comorbidities Associated with PCOS

Test name (Component test codes for panels)	Test code	Description
Cardio IQ® Insulin Resistance Panel with Score[e,f] Includes Insulin, Intact, LC/MS/MS (93103); C-peptide, LC/MS/MS; and insulin resistance (IR) score (calculated)	36509	Identify risk of insulin resistance
Glucose, Plasma	484	Diagnose diabetes and prediabetes based on fasting glucose in plasma
Glucose Tolerance Test, 3 Specimens (75g) Includes fasting, 1-hour, and 2-hour specimens	23475	Diagnose diabetes and prediabetes based on impaired glucose tolerance
Hemoglobin A1c	496	Diagnose diabetes based on HbA1c
Lipid Panel, Cardio IQ® Includes Cardio IQ Cholesterol, Total (91717), Cardio IQ HDL Cholesterol (91719), Cardio IQ Triglycerides (91718), Cardio IQ Non-HDL and calculated components	91716[f]	Diagnose dyslipidemia and assess risk of cardiovascular disease
Lipid Panel, Standard Includes total cholesterol (334), triglycerides (896), HDL cholesterol (608), calculated LDL cholesterol, cholesterol/HDL ratio, and non-HDL cholesterol	7600[f]	Diagnose dyslipidemia
Lipid Panel with Reflex to Direct LDL Same as 7600 plus direct LDL (8293) if triglyceride is >400 mg/dL	14852[f,g]	Diagnose dyslipidemia
Metabolic Risk Panel Includes Cardio IQ® Cholesterol, Total (91717), Cardio IQ HDL Cholesterol (91719), Cardio IQ Triglycerides (91718), Cardio IQ Non-HDL and calculated components, Cardio IQ Apolipoprotein B (91726), Cardio IQ Hemoglobin A1c (91732), Insulin, Intact, LC/MS/MS (93103), C-Peptide, LC/MS/MS and IR Score	39447[f]	Identify risk of insulin resistance, diabetes, and cardiovascular disease

HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; IR, insulin resistance; LC/MS/MS, liquid chromatography/tandem mass spectrometry; LDL, low-density lipoprotein; PCOS, polycystic ovary syndrome.

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

[f] Panel components (test code) may be ordered separately.

[g] Reflex tests are performed at an additional charge and are associated with an additional CPT code.

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The 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 PCOS and its associated tests, please visit the Quest Diagnostics Test Directory at https://testdirectory.questdiagnostics.com.

Please contact your Quest Diagnostics sales representative for more information about our PCOS testing.

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

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