

# Report to Congress: Polycystic Ovary Syndrome

A Report to the House Committee on Appropriations



U.S. Department of Health and Human Services  
Office of the Secretary  
Office on Women's Health

Rachel L. Levine, M.D.  
Assistant Secretary for Health

## Table of Contents

### Polycystic Ovary Syndrome at the National Institutes of Health: A Report to Congress

Introduction.....	3
Background and Incidence of PCOS In the United States .....	3
PCOS Diagnostic Criteria and Testing.....	4
PCOS Treatment.....	7
Economic Burden of PCOS.....	9
Ongoing PCOS Research and Agency Activities.....	11
Report Conclusion.....	16
References.....	16
Glossary of Terms.....	18

---

## Introduction

The Committee on Appropriations through House Report 117-96, which accompanied H.R. 2471 of the 117th Congress, requested a report, not later than one year after enactment of the Act, outlining the number of women in America currently suffering from polycystic ovary syndrome (PCOS); the annual cost to patients for treatment of PCOS; the annual cost to patients resulting from misdiagnosis or missed diagnosis of PCOS; the economic burden of PCOS on the United States; the effectiveness of current testing methods for PCOS; recommended ages for testing of PCOS; cost benefits of testing all women at recommended age; and feasibility of testing for PCOS before symptoms are present.

In collaboration, the National Institutes of Health (NIH) and the U.S. Department of Health and Human Services' Office on Women's Health (OWH) have included additional information on current and ongoing research and activities.

---

## Background and Incidence of PCOS In the United States

Polycystic ovary syndrome (PCOS) is a multifactorial chronic endocrine disorder generally diagnosed in women of reproductive age and characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovaries and is one of the most common causes of infertility.<sup>20</sup> Currently, there is not a universally accepted definition of PCOS.<sup>1</sup>

Although polycystic ovary syndrome is thought to be one of the most common endocrine disorders in women of reproductive age, reliable estimates of PCOS incidence do not currently exist. It is estimated that more than 105 million women worldwide and as many as 5 - 6 million U.S. women of reproductive age have been diagnosed with PCOS.<sup>3, 5, 10</sup> While prevalence estimates vary widely between studies, PCOS is estimated to impact between 4 and 26 percent of women,<sup>1, 8</sup> depending on diagnostic criteria applied and the population studied.

Higher prevalence has been associated with first-degree relatives with PCOS, prepubertal obesity, congenital adrenal disorders, above average or low birth weight for gestational age, premature adrenarche, and use of valproic acid as an antiepileptic drug.<sup>21</sup> Although race, ethnicity and provider type do not seem to have an impact on overall historical rates of PCOS, studies have suggested a higher prevalence among Hawaiian and Pacific Islander populations followed by Native American, Mexican Americans, then non-Hispanic Whites and African Americans.<sup>21</sup>

Incidence of diagnoses increased over time in younger and decreased over time in older age groups, likely related to changing practice patterns and increased practitioner awareness of PCOS's impact on long-term health outcomes and improved prevention efforts.<sup>21</sup>

Although the exact cause of PCOS is unknown, it is likely related to multiple diverse factors of this disorder working together. Evidence of genetic contribution to PCOS remains uncertain and although several susceptible genes have been identified as contributors to the pathophysiology of the disorder, there is currently no recommended genetic screening test.<sup>1</sup> No specific environmental substance has been identified as causing PCOS. Insulin resistance may be fundamental to the etiology of the syndrome.<sup>9</sup>

Multiple risk factors and comorbidities have been associated with PCOS, including infertility, metabolic syndrome, obesity, impaired glucose tolerance, type 2 diabetes, cardiovascular risk, depression, ovarian cancer, endometrial cancer, and obstructive sleep apnea. Pregnant women with PCOS appear to have higher rates of miscarriage, gestational diabetes, preeclampsia, premature delivery, and endometrial cancer.<sup>21</sup>

Women with PCOS generally present with diverse symptoms, including irregular menstrual cycles, excessive hair growth, subfertility, and pregnancy complications.<sup>20</sup> Additionally, PCOS is associated with psychological challenges such as anxiety, depression, and reduced self-esteem. With increasing age, the syndrome evolves from a reproductive disease to a metabolic disorder. The metabolic features include insulin resistance, impaired glucose tolerance, type 2 diabetes mellitus, dyslipidemia, and cardiovascular risk factors.<sup>20</sup> The diversity of the

phenotype highlights the need for individual health-risk estimation for patients with PCOS and their family members to receive appropriate clinical and supportive care.<sup>20</sup>

---

## PCOS Diagnostic Criteria and Testing

### Overview of Diagnostic Criteria

Four sets of diagnostic criteria for PCOS have been proposed over the years.<sup>6,18</sup> The NIH developed the first PCOS criteria in 1990, which required the presence of both hyperandrogenism, hyperandrogenemia and oligoovulation, with or without the presence of polycystic ovarian morphology (PCOM) on ultrasound, and excluding other disorders such as Cushing syndrome, hyperprolactinemia, and congenital adrenal hyperplasia. The second set of PCOS criteria was based on expert consensus reached at a meeting cosponsored by the European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine in Rotterdam, Netherlands, in 2003.<sup>11</sup> These criteria are commonly referred to as the Rotterdam criteria, and require two of the following three features to be present for the diagnosis: (1) oligo- or anovulation; (2) clinical and/or biochemical signs of hyperandrogenism; (3) PCOM on ultrasound, after the exclusion of other etiologies. Institution of the Rotterdam criteria broadened the PCOS diagnosis, significantly increasing the number of patients meeting the diagnosis of PCOS.<sup>18</sup>

In 2006, the Androgen Excess and PCOS Society (AE-PCOS)<sup>6</sup> published the third set of diagnostic guidelines based on recommendations from an expert task force. In contrast to the Rotterdam criteria, the AE-PCOS criteria made androgen excess requisite for the diagnosis, with either ovulatory disorder or PCOM as the second criterion.

Finally, in 2018, the fourth set of diagnostic guidelines was published by the International PCOS Network.<sup>3</sup> The PCOS Network published an international consensus guideline<sup>26</sup> on the assessment and management of PCOS based on an Appraisal of Guidelines for Research and Evaluation (AGREE)-compliant literature review and synthesis. This document endorsed the Rotterdam criteria for PCOS diagnosis in adults, heavily discouraged diagnosis in adolescents based on PCOM on ultrasound and provided more nuanced recommendations for

follicular count and menstrual cycle irregularity.<sup>26</sup> It is understood with all diagnostic approaches currently recommended that secondary causes such as adult-onset congenital adrenal hyperplasia, hyperprolactinemia, and androgen-secreting neoplasms, first be excluded.<sup>1</sup>

Criteria	NIH 1990	ESHRE/ASRM (Rotterdam) 2003	AE-PCOS 2006	NIH 2012 acceptance of Rotterdam 2003
Hyperandrogenism	✓	✓	✓	✓
Ovarian dysfunction	✓	✓	✓	✓
Polycystic ovarian morphology		✓	✓	✓
	2 of 2 required	2 of 3 required	2 of 3 required	2 of 3 required
Exclusion of conditions that mimic PCOS	✓	✓	✓	✓

Source: [NIH Office of Research on Women’s Health<sup>13</sup>](#)

## Testing

There is no single test for diagnosing PCOS, and it is considered a diagnosis of exclusion.<sup>21</sup> Disorders that mimic the clinical features of PCOS should be excluded such as thyroid disease, hyperprolactinemia, Cushing’s syndrome, and non-classic congenital adrenal hyperplasia with 21-hydroxylase deficiency.

Past medical history, weight changes, and symptoms of insulin resistance are essential considerations along with pelvic examination, a transvaginal ultrasound, and measuring hormone levels being among the most recommended investigations.<sup>24</sup>

## Recommended Age for Testing of PCOS

Diagnosing polycystic ovary syndrome during adolescence is often difficult because the polycystic ovary syndrome criteria include and overlap with normal physiological events that occur during puberty.<sup>24</sup> Although the presence of polycystic ovary morphology (PCOM) is a key diagnostic criterion of PCOS in adults, it is currently not recommended for the diagnosis in adolescents. As such, the diagnosis of PCOS in adolescents currently

hinges on evidence of ovulatory dysfunction and androgen excess.<sup>15</sup> The adolescent is likely to present with menstrual cycle concerns, unwanted hair growth or body weight and body image concerns that may significantly affect her self-concept. Care and management of the adolescent can be challenging for clinicians to treat the current physical state while preparing for and bringing awareness for proper management of the long-term needs, without compromising her evolution and self-identity.<sup>1</sup>

Review of available diagnostic criteria for adolescents outlined that PCOS can be diagnosed using two main criteria, 1) irregular menstrual cycles relative to number of years post-menarche and 2) hyperandrogenism after excluding other conditions that mimic PCOS. More advanced definitions of these two criteria will help to decrease current challenges with diagnosis and provide more timely diagnosis and management during adolescence.<sup>19</sup>

With increasing age, the syndrome evolves from a reproductive disease to a more metabolic disorder. Along with metabolic disturbances, including insulin resistance and abnormalities of energy expenditure, polycystic ovary syndrome is recognized as a major risk factor for the development of type 2 diabetes and cardiovascular disease in later life.<sup>1,19</sup>

The complexity of PCOS disorder, and overall impact on quality of life, requires a timely diagnosis in any woman that includes screening for complications with individualized treatment strategies for the long-term health issues associated with polycystic ovary syndrome. As a result of these complexities<sup>14</sup>, PCOS disorder remains underdiagnosed and undertreated and those with the condition often experience significant delays to diagnosis, increased cost burden, and often associated with significant psychological distress when receiving a diagnosis of this syndrome.

---

## PCOS Treatment

The management approach and selection of the best therapy option is dependent on patient priorities.

Treatment should be focused on both short and long-term features and tailored to the specific concerns and

needs of the individual.<sup>1</sup> Treatment can involve restoring fertility, treatment of the metabolic complaints, treatment of androgen excess, providing endometrial protection and psychological support.

Treatments targeting metabolic abnormalities generally include lifestyle changes, medication, and efforts for the prevention and management of obesity. Goals of therapy include fertility, decreased hirsutism and/or alopecia, and providing endometrial protection to avoid endometrial cancer.<sup>17</sup> Timely diagnosis and management strategies of the long-term health sequelae such as diabetes, hypertension, and risk factors for cardiovascular disease (CVD) are of paramount importance. Early identification of high-risk patients enables a thorough preventive screening and early treatment of adverse complications.<sup>17</sup>

Lifestyle modifications are thought to be the first-line therapy for women with PCOS and obesity in the form of diet and exercise. Strong associations exist among excessive weight, insulin resistance, glucose intolerance, menstrual irregularities, and infertility.<sup>17</sup> Modest lifestyle changes have been found to have a significant impact in reducing body weight and have been shown to restore ovulation and increase insulin sensitivity in obese women with PCOS.<sup>1,17</sup> Weight reduction has additional benefits and reduces the risk of comorbidities such as diabetes, hypertension, cardiovascular disease, obstructive sleep apnea and certain cancers.

In addition to lifestyle modifications, pharmacological treatment for PCOS should be targeted to each patient's individual disease characteristics, symptoms, personal goals and expectations and pregnancy planning.<sup>1,17</sup>

Oral contraceptives (OCs) are the most commonly used pharmacological treatment for regulating menstrual irregularities in women with PCOS. OCs have been found to be effective for treating hirsutism and acne by suppressing ovarian androgen production. However, women with PCOS who are obese and use OCs, are at an increased risk of thrombosis.<sup>1,17</sup>

Metformin improves the effectiveness of insulin produced by the body, as a treatment for type 2 diabetes and may be recommended for women with PCOS. Metformin is not usually recommended for women with PCOS who have hirsutism or difficulty becoming pregnant, because it is not as effective as other treatments for ovulation and antiandrogen excess concerns.<sup>1,17</sup>



There are several options available to treat obesity. These options are consistent with those recommended for women without PCOS and include diet and exercise, weight loss medications, and weight loss surgery. Bariatric surgery may be effective for patients with severe obesity, since significant weight loss following the procedure often resolves both metabolic disorders of PCOS and PCOS itself, restoring ovulatory function and fertility.

In patients who do not require fertility, statins can be used to treat dyslipidaemia.<sup>17</sup>

Ovulation induction with medications such as clomiphene citrate or letrozole have also been found effective for fertility treatment. For a patient who does not ovulate or is unable to conceive with ovulation induction medications, follicle-stimulating hormone (FSH) injections, are sometimes recommended. However, this treatment may cause multiple gestations, particularly in patients with PCOS. In vitro fertilization (IVF) has a lower risk of multiple gestations and is often recommended over FSH injections if clomiphene and letrozole do not result in a pregnancy.<sup>1,17</sup>

---

## Economic Burden of PCOS

Although PCOS is the most common hormone disorder affecting reproductive-aged women worldwide and in the United States, the immense nature of the various characteristics associated with the disorder and impact on the quality of life creates challenges in measuring the overall economic impact to determine an accurate assessment for public health priorities.<sup>25</sup>

A recently published report<sup>23</sup> by Riestenberg et al. concluded that the cost of PCOS in 2020 was \$8 billion U.S. Dollars (USD). The report arrived at this figure by utilizing a prior study<sup>3</sup> by Azziz et al. of the economic burden of PCOS conducted by the same authors, which considered the initial evaluation and treatment of reproductive endocrine disorders (increased androgen levels, menstrual irregularities, elevated luteinizing hormone levels, hypothalamic-pituitary dysfunction, ovarian dysfunction, infertility). The most current Riestenberg et al. report<sup>23</sup> included the economic burden of PCOS pregnancy-related comorbidities (gestational diabetes, severe gestational hypertension, and preeclampsia), combining the economic burden calculated in their first study with the economic burden of PCOS pregnancy-related costs arriving at \$8 billion USD in 2020.<sup>23</sup>

Researchers identified the most expensive aspects of PCOS care were the treatment of long-term metabolic health conditions, including stroke and type 2 diabetes, and reproductive health problems such as infertility, abnormal uterine bleeding, menstrual dysfunction, and hirsutism. Pregnancy complications such as gestational diabetes, gestational hypertension and preeclampsia made up about 5 percent of the estimated costs. The initial diagnostic process accounted for less than 2 percent of the total cost burden.<sup>23</sup> The findings in this analysis did not include increased risks of endometrial, breast and ovarian cancer and mental health disorders that women with PCOS face. Researchers excluded these conditions due to limited availability of data for these conditions.<sup>23</sup> The number of reproductive aged women in 2005 was calculated to be 4 million in the 2005 study<sup>3</sup>, and 5.46 million in the 2020 second study.<sup>23</sup>

The calculation from these two studies likely underestimates the actual economic burden. As the authors stated in these studies, their estimates are likely conservative, accounting for only the costs of evaluating and caring for the woman during her reproductive years, although much of the associated morbidity such as cardiovascular disease and diabetes may present in the post-reproductive years. Furthermore, only well-established complications associated with the disorder were included in the calculations excluding additional conditions such as the impact of mental health, obstetrical complications, and cancer. Given variation in the incidence range of women in the US is between 5% and 26%, and with the inclusion of additional known PCOS disorder factors, the \$8 billion dollar figure could realistically be as high as \$24 – \$30 billion USD annually.<sup>3,23</sup>

With improved understanding on how to diagnose and treat this common condition effectively, we may be able to reduce the economic burden as well as the impact on women's quality of life.<sup>23</sup> To support and prioritize public health interests, additional studies that include more reliable estimates of the economic burden of PCOS are needed.

---

## Ongoing PCOS Research and Agency Activities

The NIH supports scientific research to better understand the underlying pathophysiology and risk factors associated with PCOS, determine the short- and long-term health consequences associated with PCOS, assess the effectiveness of current treatment approaches, and develop new and innovative therapies.

Because PCOS affects an individual's function across multiple organs and systems, research on PCOS is supported by multiple Institutes, Centers, and Offices (ICOs) at NIH, including the National Cancer Institute (NCI); *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD); the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); the National Heart, Lung, and Blood Institute (NHLBI); the National Institute on Environmental Health Sciences (NIEHS); the National Institute of General Medical Sciences (NIGMS) and the National Center for Complementary and Integrative Health (NCCIH). In 2022, NIH developed a formal reporting category for PCOS using the [Research, Condition, and Disease Categorization \(RCDC\)](#) process, NIH's automated process to categorize and report the amount it funded in each of more than 280 reported categories of disease, condition, or research area, to facilitate tracking of and quantifying expenditures on PCOS research. RCDC data for fiscal year 2022 indicate that NIH funding for research on PCOS was approximately \$9.5M. Among all NIH ICOs, NICHD funds over half of the NIH portfolio on PCOS. NIDDK and NHLBI support research on conditions such as obesity and metabolic syndrome and cardiovascular disease for which individuals with PCOS are known to be at increased risk. In research on PCOS, as with all women's health research, the NIH Office of Research on Women's Health (ORWH) promotes a focus on the health of women across the life course and the biomedical research continuum.

### Pre-Clinical Research Opportunities

Pre-clinical studies provide a critical foundation for scientific discovery and generate new knowledge that can be moved into clinical realms. NIH supports pre-clinical research employing animal models as well as technology

development that has led to innovative platforms that mimic human organ systems relevant to PCOS. For example, NICHD-supported scientists are examining the origins and mechanisms underlying PCOS by studying how reproductive hormones affect the brain in a mouse model designed to resemble PCOS ([R01HD104345](#)). Another group of NICHD-supported researchers are studying how sex hormones called androgens and their receptors affect PCOS-associated ovarian dysfunction ([R01HD097321](#)). NIDDK-supported investigators have characterized a rat model of PCOS, and ongoing research using this model is investigating whether inhibition of androgen-induced mitochondrial dysfunction can improve renal and metabolic function ([F30DK127527](#)). Furthermore, NHLBI-funded research is examining how androgens and the sympathetic nervous system interact in blood pressure regulation using a rat model of excess androgen disorder, called hyperandrogenism ([R01HL135089](#)). Other NHLBI-supported researchers are investigating the relationship between *in utero* androgen exposure and cardiometabolic outcomes in a sheep model of developmental programming ([R01HL139639](#)).

### Clinical Research Opportunities

NIH supports clinical research to investigate factors that influence the risk of developing PCOS, as well as the development of improved diagnostics and therapeutics to improve the lives of patients with this condition. Additionally, efforts are underway to disseminate and implement research findings.

### PCOS Risk Factors

In a NICHD-supported project, two PCOS subtypes, each associated with distinct groups of gene variants, were identified.<sup>7</sup> NIEHS scientists are also examining how genetic factors may be implicated in the development of long-term health consequences related to PCOS. Multiple genetic variants have been identified that, when combined with stress, nutrition status, exercise, and other factors, may cause menstrual period disorders ([ZIAES103323](#)), and studies have shown that genomic interference with ovarian cell differentiation leads to abnormal ovary development associated with PCOS.<sup>33</sup> NHLBI-funded research is assessing whether maternal prenatal androgen

levels impact cardiometabolic risk ([K08HL132122](#)). Recently published NCI-funded research describes the relationship between 12 inflammatory-related exposures, including PCOS, and ovarian cancer mortality.<sup>32</sup>

## Diagnosis and Treatment of PCOS

Efforts are underway to test the effectiveness and feasibility of early detection of PCOS. Using state-of-the-art ultrasound imaging technology, NICHD-supported researchers are working to identify markers to improve the clinical evaluation of PCOS and related disorders that can predict clinical outcomes ([R01HD093748](#)). In addition, NIEHS is currently recruiting women ages 18 to 34 for the women's reproductive health study, [Demystifying a Girl's First Period](#)<sup>31</sup>, aimed at detecting early signs of the production of abnormal levels of androgens in women. NICHD recently issued a Notice of Special Interest (NOSI) to announce the opportunity for investigators to apply for funding to optimize treatments of comorbid conditions in adolescents and reproductive age women with PCOS ([NOT-HD-20-026](#)). Other NICHD-supported research is comparing two widely used medications, oral contraceptive pills, and metformin, to treat overweight and obese women with PCOS ([R01HD091350](#)). Efforts by NICHD-supported scientists have recently found that women with PCOS have less gut microbiome diversity compared to women without the disorder. NIDDK is supporting a clinical trial ([R01DK120612](#)) of 50 medication-naive obese girls with PCOS to investigate whether medication will directly improve their liver function. Another NIDDK-supported project ([R01DK107605](#)) supports a randomized double-blind placebo-controlled study of 90 women with PCOS who will receive an anti-inflammatory drug called salsalate or a placebo to investigate whether inflammation contributes to ovarian dysfunction independently of obesity or insulin resistance. Furthermore, NIDDK is supporting a clinical trial ([R01DK128205](#)) of overweight or obese adults with PCOS randomized to dietary interventions to compare changes in glycemic control. A randomized clinical trial supported by NCCIH ([R01AT009484](#)) is evaluating whether the dietary supplement inositol can reduce hyperandrogenism and improve glucose metabolism in women with PCOS.

## Other Activities

NIH has engaged the scientific and clinical research communities as well as a variety of collaborators to illuminate research gaps and clinical opportunities. On October 13 and 22, 2021, NHLBI, in collaboration with ORWH, NICHD, NIDDK and the NIH Office of Disease Prevention (ODP), led a virtual workshop titled “[Cardiovascular Risk Across the Lifespan for PCOS](#)” to evaluate current PCOS-related research needs and opportunities. This NIH workshop brought together a multidisciplinary team of scientists and practitioners to address critical research needs and highlight research questions at the interface between PCOS and CVD risk across the lifespan. The leadership and members of the PCOS Challenge, a patient advocacy group, also participated and provided important input for the workshop. This input was considered as NHLBI identified knowledge gaps and research opportunities. A summary manuscript is being developed for publication in the peer-reviewed medical literature to stimulate PCOS research.

Women who are affected by PCOS are at risk for chronic disease progression, which carries significant public health implications across the lifespan. Recognizing the need for plain language content and to enhance public outreach, ORWH published an informational booklet “Polycystic Ovary/Ovarian Syndrome (PCOS) – Underrecognized, Underdiagnosed and Understudied”.<sup>13</sup> This booklet includes definitions of PCOS through the years, signs of PCOS, risks and preventive measures, information for health care providers, and the economic impact of the disease and how NIH is addressing it.

### Additional Clinical Research Opportunities

The 2019–2023 Trans-NIH Strategic Plan for Women’s Health Research sets out an ambitious vision for a world where the biomedical research enterprise thoroughly integrates sex and gender influences; every woman receives evidence-based disease prevention and treatment tailored to her own needs, circumstances, and goals; and all women in scientific careers reach their full potential.<sup>12</sup> Multiple opportunities exist to engage collaborators, encourage research, and disseminate and implement findings to meaningfully improve outcomes for women with PCOS. Opportunities adapted from the aforementioned NHLBI workshop are outlined below.

## Preclinical Research Opportunities

- Determine biological underpinnings of PCOS (including genetic and genomic risk factors)
- Identify underlying mechanisms for increased cardiometabolic risk for patients with PCOS, including but also extending beyond obesity and metabolic syndrome
- Clarify possible pathways by which PCOS and related disorders may increase cancer risks.

## Clinical Research Opportunities

- Determine the role of underlying individual and environmental factors in the prevalence, phenotype, and economic burden of PCOS
- Expand the number of epidemiologic studies of PCOS in the context of related chronic conditions, including both gynecologic conditions and chronic long-term health conditions including obesity and cardiovascular risk
- Advance research on quality of life in women with PCOS, including research to advance understanding and treatment of mental health conditions such as anxiety and depression; development of treatments for hirsutism that do not interfere with fertility; and improved infertility treatments
- Conduct studies that evaluate long-term hormonal and metabolic changes, aging and menopause in women with PCOS, the influence of these factors on PCOS phenotype, and long-term health risks associated with PCOS.
  - Develop strategies for prevention, diagnosis, and treatment of chronic debilitating conditions in patients with PCOS
    - Use data science and systems biology approaches for disease subtyping, validation, and development of risk prediction models for the development of chronic conditions in patients with PCOS
    - Leverage existing cohorts to advance PCOS understanding through retrospective and prospective data collection
    - Conduct studies aiming to better understand adverse pregnancy outcomes related to PCOS and associated CVD later in life
    - Within cohort studies and clinical trials, expand inclusion of variables related to PCOS, such as menstrual and reproductive history
- Consider social determinants of health and include representation of diverse racial/ethnic (African American/Black, American Indian/Alaska Native, Hispanic, Asian), geographic, and age groups

(longitudinal cohorts, including children at risk and women aging with PCOS), as well as sexual and gender minority and global populations to understand the full spectrum of PCOS

- Characterize differences in biologic variations, long-term health risks across the lifespan, and social determinants of health in women with PCOS to resolve conflicting evidence

---

## Report Conclusion

PCOS is the most common endocrine disorder in women of reproductive age, affecting 5 percent to 26 percent of reproductive-aged women, depending on the diagnostic criteria used. It is undoubtedly one of the most perplexing disorders posing threat to women's health, probably due to various manifestations of the disorder and lack of uniformly accepted diagnostic criteria. There is no cure for the disorder, and hence the aim of treatment is to reduce the risk of complications and improve lifestyle.

PCOS is associated with multiple reproductive and psychological complications and represents a significant socioeconomic burden to women and to health care. Despite the prevalence of this syndrome, many clinicians are unfamiliar with the PCOS diagnostic criteria, and PCOS patients have a high level of dissatisfaction with their health care.<sup>26</sup>

Diagnosis of PCOS remains controversial and assessment and management are inconsistent. The needs of women with PCOS are not being adequately met and evidence practice gaps persist.<sup>26</sup> Additional resources would further support a more comprehensive response to PCOS, specifically considering the high prevalence and cost of the disorder. A clearer estimate in the economic burden and impact of PCOS on a woman's overall quality of life would allow for more accurate prioritization of the disorder as a national public health interest.

---

## References

1. [ACOG Practice Bulletin No. 194: Polycystic Ovary Syndrome](#), *Obstetrics & Gynecology* 136(3): p 638, September 2020. | DOI: 10.1097/AOG.0000000000004069



2. Amiri M, Fahimeh Ramezani Tehrani, Samira Behboudi-Gandevani, et. al.: Risk of hypertension in women with polycystic ovary syndrome: a systematic review, meta-analysis and meta-regression. *Reproductive Biological Endocrinology* 2020.
3. Azziz R, Marin C, Hoq L, et al. Health care-related economic burden of the polycystic ovary syndrome during the reproductive life span. *J Clin Endocrinol Metab* 2005; 90: 4650–4658.
4. Berni TR, Christopher L. Morgan, D. Aled Rees: Women with Polycystic Ovary Syndrome Have Increased Risk of Major Cardiovascular Events: A Population Study. *The Journal of Clinical Endocrinology & Metabolism* 2021, 106: e3369–e80.
5. CDC: PCOS (Polycystic Ovary Syndrome) and Diabetes. 2022.
6. Christ JP, Cedars MI. Current Guidelines for Diagnosing PCOS. *Diagnostics (Basel).* 2023 Mar 15;13(6):1113. doi: 10.3390/diagnostics13061113. PMID: 36980421; PMCID: PMC10047373.
7. Dapas M LF, Nadkarni GN, et. al.: Distinct subtypes of polycystic ovary syndrome with novel genetic associations: An unsupervised, phenotypic clustering analysis. *PLoS Med* 2020, 17:e1003132.
8. Deswal R, Narwal V, Dang A, Pundir CS. The Prevalence of Polycystic Ovary Syndrome: A Brief Systematic Review. *J Hum Reprod Sci.* 2020 Oct-Dec;13(4):261-271. doi: 10.4103/jhrs.JHRS\_95\_18. Epub 2020 Dec 28. PMID: 33627974; PMCID: PMC7879843.
9. Dunaif A. Insulin resistance and the polycystic ovary syndrome: mechanism and implications for pathogenesis. *Endocr Rev* 1997; 18: 774 – 800. (Level III)
10. Endocrine Society: Polycystic Ovary Syndrome. 2022.
11. Group REA-SPCW: Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Fertil Steril* 2004, 81:19-25
12. The 2019-2023 Trans-NIH Strategic Plan for Women’s Health Research. 2019.
13. NIH Office of Research on Women’s Health. Polycystic Ovary/Ovarian Syndrome (PCOS) Underrecognized, Underdiagnosed, and Understudied, 2019. Publication Number 19-OD-8095.
14. Hillman SC, Dale J. Polycystic ovarian syndrome: an under-recognised problem? *Br J Gen Pract.* 2018 May;68(670):244. doi: 10.3399/bjgp18X696101. PMID: 29700037; PMCID: PMC5916073.
15. Kamboj MK, Bonny AE. Polycystic ovary syndrome in adolescence: diagnostic and therapeutic strategies. *Transl Pediatr.* 2017 Oct;6(4):248-255. doi: 10.21037/tp.2017.09.11. PMID: 29184806; PMCID: PMC5682369.
16. Louwers YV, Laven JSE. Characteristics of polycystic ovary syndrome throughout life. *Ther Adv Reprod Health.* 2020 Mar 18;14:2633494120911038. doi: 10.1177/2633494120911038. PMID: 32518918; PMCID: PMC7254582.
17. Lua ACY, How CH, King TFJ. Managing polycystic ovary syndrome in primary care. *Singapore Med J.* 2018 Nov;59(11):567-571. doi: 10.11622/smedj.2018135. PMID: 30498839; PMCID: PMC6250763.
18. NIH NIOH: Evidence-based Methodology Workshop on Polycystic Ovary Syndrome December 3–5, 2012 2012
19. Peña AS, Codner E, Witchel S. Criteria for Diagnosis of Polycystic Ovary Syndrome during Adolescence: Literature Review. *Diagnostics (Basel).* 2022 Aug 10;12(8):1931. doi: 10.3390/diagnostics12081931. PMID: 36010282; PMCID: PMC9406411.
20. Rao, Manisha MSa; Broughton, K. Shane PhD; LeMieux, Monique J. PhD. Cross-sectional Study on the Knowledge and Prevalence of PCOS at a Multiethnic University. *Progress in Preventive Medicine ():p* e0028, June 2020. | DOI: 10.1097/pp9.0000000000000028

21. Rasquin Leon LI, Anastasopoulou C, Mayrin JV. Polycystic Ovarian Disease. [Updated 2022 Nov 15]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK459251/>
22. Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod. 2004 Jan;19(1):41-7. doi: 10.1093/humrep/deh098. PMID: 14688154.
23. Riestenberg C, Anika Jagasia, Daniela Markovic, et. al.: Health Care-Related Economic Burden of Polycystic Ovary Syndrome in the United States: Pregnancy-Related and Long-Term Health Consequences. The Journal of Clinical Endocrinology & Metabolism 2022, 107:575-85.
24. Sadeghi HM, Adeli I, Calina D, Docea AO, Mousavi T, Daniali M, Nikfar S, Tsatsakis A, Abdollahi M. Polycystic Ovary Syndrome: A Comprehensive Review of Pathogenesis, Management, and Drug Repurposing. Int J Mol Sci. 2022 Jan 6;23(2):583. doi: 10.3390/ijms23020583. PMID: 35054768; PMCID: PMC8775814.
25. Surabhi Yadav, Olivia Delau, Adam Bonner, Daniela Markovic, William Patterson, Sasha Ottey, Richard P. Buyalos, Ricardo Azziz: Direct Economic Burden of Mental Health Disorders Associated with Polycystic Ovary Syndrome: Systematic Review and Meta-analysis. medRxiv 2023.01.05.23284220; doi: <https://doi.org/10.1101/2023.01.05.23284220>
26. Teede HJ, M.B.B.S., Ph.D., FRACP, FAAHMS, Marie L. Misso, Ph.D., B.Sc., Michael F. Costello, M.B.B.S., M.Med.: Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Fertility and Sterility 2018, 110:364-79.
27. VanHise K, Jessica L Chan, Sahar Wertheimer, et. al.: Regional Variation Hormonal and Metabolic Parameters of White and Black Women with PCOS in the United States. The Journal of Clinical Endocrinology & Metabolism 2022.
28. Witchel SF, Oberfield SE, Peña AS. Polycystic Ovary Syndrome: Pathophysiology, Presentation, and Treatment with Emphasis on Adolescent Girls. J Endocr Soc. 2019 Jun 14;3(8):1545-1573. doi: 10.1210/js.2019-00078. PMID: 31384717; PMCID: PMC6676075.
29. Yin W FH, Yin L, Xu L, Ye W: Association Between Polycystic Ovary Syndrome and Cancer Risk. JAMA Oncology 2019, 5:106-7.
30. Yu O, Christ JP, Schulze-Rath R, et al. Incidence, prevalence, and trends in polycystic ovary syndrome diagnosis: a United States population-based study from 2006 to 2019. Am J Obstet Gynecol 2023;229:39.e1-12.
31. National Institute of Environmental Health Sciences (NIEHS), Study, Demystifying a Girl's First Period, 2023, in progress.
32. Katharine K. Brieger, Minh Tung Phung, et al., High Prediagnosis Inflammation-Related Risk Score Associated with Decreased Ovarian Cancer Survival. Cancer Epidemiol Biomarkers Prev 1 February 2022; 31 (2): 443–452. <https://doi.org/10.1158/1055-9965.EPI-21-0977>.
33. Nicol B, Rodriguez K, Yao HHC. Aberrant and constitutive expression of FOXL2 impairs ovarian development and functions in mice. Biol Reprod 2020 Oct 29;103(5):966-977. doi: 10.1093/biolre/ioaa146. PMID: 32945847; PMCID: PMC7609876.

---

## Glossary of Terms

- Alopecia: The absence or loss of hair in an area where it is expected to be present.

- [Androgen-secreting neoplasms](#): Tumors that make too much testosterone and can cause a masculinizing syndrome. In females, this can cause deepening of the voice, increased hair growth, acne, and ambiguous genitalia.
- [Congenital adrenal hyperplasia](#): Congenital adrenal hyperplasia (CAH) is an inherited disorder of the adrenal glands that can affect both boys and girls. These glands produce hormones your body needs to function properly. An imbalance in these hormones can cause symptoms affecting sexual development. Treatment includes various steroids to replace the hormones your body can't make.
- [Cushing syndrome](#): Cushing's syndrome is a disorder that occurs when the body makes too much of the hormone cortisol over a long period of time. Cortisol is sometimes called the "stress hormone" because it helps the body respond to stress. Cortisol also helps maintain blood pressure, regulates blood glucose, reduces inflammation, turns food into energy.
- [Dyslipidaemia](#): The imbalance of lipids such as cholesterol, low-density lipoprotein cholesterol, (LDL-C), triglycerides, and high-density lipoprotein (HDL). This condition can result from diet, tobacco exposure, or genetic and can lead to cardiovascular disease with severe complications.
- [Endometrial Hyperplasia](#): Hyperplasia is the increase in the production of cells in a healthy organ or tissue. Endometrial Hyperplasia is the thickening of the uterine lining, causing heavy or abnormal bleeding.
- [Hirsutism](#): A condition that causes excess hair to grow on certain parts of the body. Primarily affects women and people assigned female at birth.
- [Hyperandrogenemia](#): An excess amount of androgens in the body. Androgens are a group of sex hormones. They help start puberty and play a role in reproductive health and body development.
- [Hyperandrogenism](#): Hyperandrogenism happens when you have an excess amount of androgens (a group of sex hormones) in the body. It most commonly affects people assigned female at birth and can cause hirsutism, acne, and irregular periods.
- [Hyperprolactinemia](#): Higher-than-normal levels of prolactin in the blood. The most common cause is a prolactinoma, a benign (noncancerous) tumor in the pituitary gland.
- [Oligoovulation](#): A condition that causes infrequent or irregular ovulation. Most women have an ovulation every 21 to 35 days. In case of oligo-ovulation or infrequent ovulation, the cycle duration is more than 35 days, or less than 8 cycles per year.
- [Polycystic Ovary Syndrome](#): A common condition that affects hormones which causes irregular menstrual periods, excess hair growth, acne, and infertility.
- [Premature adrenarche](#): When the signs of puberty develop earlier than normal and other potential causes of early puberty have been ruled out.
- [Thrombosis](#): Condition where one or more blood clots form in blood vessels or the heart which can block blood flow where it formed, or it can break loose and travel elsewhere in your body. If a moving clot gets stuck in a critical area, it can cause life-threatening conditions like stroke and heart attack.