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Skeletal Muscle as a Therapeutic Target in Polycystic Ovary Syndrome (PCOS): Implications for Insulin Resistance, Ovulation, and Fertility

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Abstract

Background: Polycystic ovary syndrome (PCOS), recently predesignated polyendocrine metabolic ovarian syndrome (PMOS), affects approximately one in eight women of reproductive age. Insulin resistance is its cardinal metabolic feature, present across phenotypic subtypes and independent of body mass index. Skeletal muscle, responsible for approximately 80% of insulin-mediated postprandial glucose disposal, is the dominant tissue in which this insulin resistance is mechanistically expressed—yet skeletal muscle has received comparatively little attention in PCOS clinical practice and research frameworks organized around ovarian pathology.

Objective: *This narrative review synthesizes the peer-reviewed literature on skeletal muscle mass and quality, muscular fitness, structured exercise training, and their relationships with insulin resistance and reproductive outcomes in women with PCOS, with a comparative analysis of exercise versus pharmacological metabolic intervention and a secondary section on male reproductive parallels.*

Methods: *MEDLINE, Web of Science, and Scopus were searched from inception through April 2026 using the following primary search terms: PCOS, polycystic ovary syndrome, skeletal muscle, lean body mass, insulin resistance, exercise training, resistance training, ovulation, fertility, myokines, GLUT4, sarcopenic obesity, and male infertility. Randomized controlled trials, systematic reviews, meta-analyses, and mechanistic studies were prioritized. Reference lists of identified key papers were hand-searched for additional relevant publications. No language restriction was applied. Approximately 240 publications were reviewed, with primary emphasis on human RCTs, systematic reviews, meta-analyses, and mechanistic studies directly evaluating skeletal muscle function, exercise intervention, or body composition in women with PCOS. Animal and in vitro studies were included where they provide essential molecular context not yet available from human trials.*

Results: *Women with PCOS demonstrate an intrinsic, BMI-independent 27% reduction in whole-body insulin sensitivity, attributable to skeletal muscle signaling defects at IRS-1, PI3K-Akt, and GLUT4, compounded by intramuscular lipid accumulation and mitochondrial dysfunction. The lean PCOS phenotype insulin-resistant at normal BMI exemplifies the independence of muscle metabolic dysfunction from adiposity: lean women with PCOS demonstrate 25% lower insulin sensitivity by clamp, intramuscular lipid accumulation (40% higher triacylglycerol, 50% higher diacylglycerol, 300% higher ceramide), and reduced AMPK expression and activation compared with BMI-matched healthy controls. Sarcopenic obesity present in over 50% of women with PCOS in some cohorts amplifies metabolic and inflammatory burden in a pattern invisible to BMI-based assessment. Structured exercise training improves insulin sensitivity, reduces hyperandrogenemia, normalizes anti-Müllerian hormone (AMH), and restores ovulatory cyclicity. In the most direct fertility evidence available, six weeks of structured exercise tripled ovulation probability in obese clomiphene-resistant women with PCOS. Lifestyle modification and metformin produce comparable effects on pregnancy rate and menstrual cyclicity, while lifestyle intervention more effectively improves insulin resistance and SHBG. Physical activity's effect on ART live birth rate remains statistically uncertain in current meta-analytic evidence. In men, adequate muscle mass and favorable body composition are associated with higher endogenous testosterone and better semen parameters.*

Conclusions: *The available evidence supports skeletal muscle as an underrecognized metabolic organ in PCOS whose improvement through structured exercise including progressive resistance training may represent an important strategy for improving reproductive outcomes. These findings support integration of muscle-targeted lifestyle therapies as a key component of first-line management in PCOS fertility care. Adequately powered RCTs using live birth rate as a primary endpoint are needed to establish the full clinical scope of this benefit.*

Keywords: Polycystic Ovary Syndrome, Skeletal Muscle, Insulin Resistance, Resistance Training, Sarcopenic Obesity, GLUT4, Myokines, Irisin, Lean PCOS, Fertility, Ovulation, Spermatogenesis, Polyendocrine Metabolic Ovarian Syndrome

Note on Nomenclature

On May 12, 2026, The Lancet published a global consensus paper formally renaming polycystic ovary syndrome (PCOS) as polyendocrine metabolic ovarian syndrome (PMOS), following an eleven-year multistep international process involving more than 22,000 patients and health professionals across 56 organizations [1]. The core scientific rationale was that the term PCOS misrepresented the condition as primarily an ovarian structural disease, obscuring its defining endocrine and metabolic dimensions and contributing to delayed diagnosis, fragmented care, and inadequate metabolic screening [1]. This review uses PCOS as its primary terminology—the designation under which all cited studies were conducted and published—while noting PMOS at appropriate junctures. All citations retain their original PCOS language. The two terms describe the same clinical entity.

1. Introduction

Polycystic ovary syndrome (PCOS) is the most prevalent endocrine disorder in women of reproductive age, affecting approximately one in eight women worldwide—more than 170 million individuals [1]. Recently predesignated polyendocrine metabolic ovarian syndrome (PMOS) by an international consensus published in The Lancet in May 2026, the condition is defined by at least two of three Rotterdam criteria oligo or anovulation, clinical or biochemical hyperandrogenism, and polycystic ovarian morphology on ultrasonography or, in adults, elevated serum anti-Müllerian hormone (AMH) as a validated alternative [1-3]. Its disease burden extends well beyond reproductive dysfunction: women with PCOS carry substantially elevated lifetime risks of type 2 diabetes mellitus, metabolic syndrome, non-alcoholic fatty liver disease, obstructive sleep apnea, cardiovascular disease, and significant psychological morbidity [1]. The renaming from PCOS to PMOS reflects what decades of investigation have established: this condition is a systemic polyendocrine and metabolic disorder in which disrupted insulin signaling, androgen excess, neuroendocrine dysregulation, and chronic low-grade inflammation converge to produce reproductive dysfunction as one of several expressions of a broader metabolic phenotype [1]. As this review demonstrates, the metabolic organ most directly implicated in that disruption and most directly addressable by structured exercise is skeletal muscle.

Insulin resistance is a cardinal and intrinsic feature of PCOS, present across all phenotypic subtypes and demonstrably independent of obesity. A 2016 meta-analysis of gold-standard euglycaemic-hyperinsulinaemic clamp studies by Cassar and colleagues quantified an inherent 27% reduction in whole-body insulin sensitivity in women with PCOS compared with BMI-matched controls [4]. Skeletal muscle, responsible for approximately 80% of postprandial insulin-mediated glucose disposal, is the primary tissue in which this insulin resistance is mechanistically expressed yet skeletal muscle has historically received less investigative and clinical attention in PCOS than adipose tissue or the ovary [5]. This review addresses three interconnected questions. First, what is the nature and scope of skeletal muscle dysfunction in PCOS, and why has it been clinically underrecognized? Second, what does structure exercise training accomplish in terms of skeletal muscle metabolic function and reproductive outcomes? Third, how does exercise-based metabolic intervention compare with pharmacological approaches? A secondary section examines analogous mechanisms in male reproductive health. Throughout, we distinguish among established evidence, inferred mechanisms, and areas requiring further investigation.

2. Why Skeletal Muscle Has Been Overlooked in PCOS

Understanding why skeletal muscle has occupied a peripheral position in PCOS research and clinical practice helps explain why the evidence reviewed in this paper has not yet been fully translated into reproductive care. The first and most durable reason is diagnostic. The Rotterdam criteria, adopted in 2004 and still the prevailing diagnostic standard, are organized around three observable features: anovulation, hyperandrogenism, and ovarian morphology on ultrasound [1]. Each criterion foregrounds the reproductive tract and its immediate endocrine regulators. No metabolic measurement fasting insulin, HOMA-IR, body composition, or SHBG is required for diagnosis. The diagnostic framework thus directs clinical attention toward the ovary and away from the peripheral tissues where insulin resistance is mechanistically expressed. As the 2012 Amsterdam ESHRE/ASRM Consensus Workshop noted, in vivo insulin action is profoundly decreased in skeletal muscle in PCOS secondary to unique signaling defects—but this observation has not been incorporated into diagnostic or standard management algorithms [6]. The second reason is the dominance of the weight-loss paradigm. Because PCOS is strongly associated with overweight and obesity in many study populations—the US PCOS population in particular skews heavily toward overweight and obesity [7] the default treatment recommendation for metabolic features of the

condition has been weight reduction. When weight loss is the treatment target, adipose tissue becomes the implicit site of intervention. Skeletal muscle, whose functional state may improve substantially through exercise even in the absence of significant weight change, becomes invisible within this framing. The lean PCOS phenotype insulin-resistant at normal BMI sits entirely outside the weight-loss paradigm and has historically received less research attention as a result.

The third reason is measurement. Standard PCOS clinical assessment does not include body composition analysis. BMI is entirely blind to the sarcopenic obesity phenotype excess adiposity coexisting with relatively low functional muscle mass that affects more than half of women with PCOS in some cohorts [8,9]. Without tools that distinguish muscle from fat, the specific contribution of muscle deficits to reproductive and metabolic outcomes is invisible at the clinical level. Fourth, biopsy studies of skeletal muscle which provide the most mechanistically informative data on fiber type, intramuscular lipid, mitochondrial function, and insulin signaling are invasive, technically demanding, and costly, limiting their use to specialized research settings with small sample sizes. The result is that skeletal muscle molecular biology in PCOS has been characterized largely in studies involving ten to thirty participants, reducing statistical power and delaying the accumulation of consensus-forming evidence [10,11]. Together, these factors explain a persistent gap between biological evidence and clinical practice: skeletal muscle is mechanistically central to PCOS pathophysiology, but it is not where the diagnostic gaze has historically been directed.

3. The Nature of Skeletal Muscle Dysfunction In PCOS

3.1. Total Lean Body Mass: A Deceptive Metric

A systematic review and meta-analysis by Kazemi and colleagues (2021), pooling 45 observational studies comprising 3,676 participants, found that women with PCOS had a modest but statistically significant increase in total lean body mass (LBM) compared with controls (mean difference 0.83 kg; 95% CI 0.08–1.58 kg; $p = 0.03$; $I^2 = 72.0\%$) [12]. This apparent elevation was entirely attributable to excess body weight not to hyperandrogenism or insulin resistance per se: the PCOS subgroup with BMI ≥ 25 kg/m^2 demonstrated significantly greater total LBM than matched controls (mean difference 1.58 kg; 95% CI 0.82–2.34 kg; $p < 0.01$), while the lean PCOS subgroup showed no significant difference [12]. Appendicular lean mass and muscle strength data were contradictory across studies and could not be pooled signaling that functionally relevant dimensions of muscle—regional distribution, fiber composition, mitochondrial density, insulin signaling capacity—remain incompletely characterized in this population [12].

3.2. Muscle Quality: The More Consequential Dimension

Total lean body mass is a limited indicator of skeletal muscle metabolic health in PCOS. The qualitatively relevant variables fiber type composition, intramuscular lipid content, mitochondrial function, insulin signaling capacity, and metabolic flexibility are the mechanistically operative features. Proteomic analysis of skeletal muscle biopsies from women with PCOS has demonstrated a relative decrease in highly oxidative type I muscle fibers alongside increased extramyocellular lipid content; because type I fibers are the primary site of insulin-stimulated glucose oxidation, their relative depletion contributes directly to insulin resistance [11]. Skeletal muscle immunometabolism and transcriptomics data consistently demonstrate molecular dysfunction in intracellular insulin-signaling pathways, mitochondrial function, and fat oxidation in PCOS [13]. Metabolic inflexibility the impaired capacity to shift fuel substrate oxidation in response to substrate availability has been documented in PCOS skeletal muscle and is more pronounced at higher BMI, worsening insulin resistance and hyperandrogenemia [14].

3.3. Sarcopenic Obesity: The Invisible Phenotype

The sarcopenic obesity phenotype low appendicular skeletal muscle mass (>2 SD below the mean for healthy age-matched controls) coexisting with excess adiposity (body fat > 35%) is prevalent and systematically missed by BMI-based clinical assessment in PCOS. A case control study found that 53% of women with PCOS met criteria for sarcopenic obesity [9]. Within the PCOS group, appendicular skeletal muscle mass percentage correlated inversely with HOMA-IR ($r = -0.409$; $p < 0.01$), high-sensitivity C-reactive protein ($r = -0.608$; $p < 0.0001$), and HbA1c ($r = -0.430$; $p < 0.0001$), and positively with 25-hydroxyvitamin D ($r = 0.398$; $p < 0.0001$) [9]. Sarcopenic obesity represents a compound metabolic risk phenotype with direct hormonal and inflammatory implications for reproductive function, detectable only through body composition assessment beyond BMI.

3.4. The Lean PCOS Phenotype: Muscle Dysfunction Independent of Adiposity

Among the most scientifically instructive subgroups in PCOS research is the lean phenotype normal or low BMI with demonstrable insulin resistance and reproductive dysfunction. This subgroup directly dissociates skeletal muscle metabolic dysfunction from adiposity, providing in vivo evidence that muscle quality is an underrecognized determinant of insulin resistance in PCOS independently of fat mass. In a mechanistically definitive study by Hansen and colleagues published in the journal of clinical endocrinology & metabolism in 2019, thirteen lean (BMI ≤ 25 kg/m^2) hyperandrogenic women with PCOS and seven age- and BMI-matched healthy controls underwent a hyperinsulinemic-euglycaemic clamp with skeletal muscle biopsies [15]. Women with PCOS demonstrated 25% lower whole-body insulin sensitivity by clamp ($p < 0.05$) and significantly higher intramuscular lipid species: triacylglycerol (+40%; $p < 0.05$), sn-1,3-diacylglycerol (+50%; $p < 0.05$), and ceramide (+300%; $p < 0.05$) compared with controls [15]. Circulating adiponectin was 40% lower in PCOS women, and AMPK expression and activation were significantly reduced in skeletal muscle—providing a

mechanistic link between hypoadiponectinemia, impaired AMPK signaling, and lipotoxic intramuscular accumulation independent of total body fat [15]. Notably, this study found no defect in the canonical IRS-1/Akt insulin-signaling pathway in lean PCOS skeletal muscle distinguishing the lean phenotype from the obese phenotype where IRS-1 serine phosphorylation defects are more consistently demonstrated [15,16]. Step to and colleagues (2019) reviewing this mechanistic heterogeneity concluded that the PCOS-specific skeletal muscle insulin resistance defect is likely located distal to IRS1/2, at the level of Akt substrates such as AS160, or in alternative glucose-regulating pathways, with intramuscular lipid accumulation playing a modulatory rather than exclusively causal role [17]. This phenotypic heterogeneity may have implications for exercise prescription: the AMPK-centric mechanism in lean PCOS may be differentially responsive to different exercise modalities and intensities compared with the IRS-1 serine phosphorylation defect predominant in obese PCOS, a hypothesis warranting direct investigation.

3.5 Molecular Mechanisms: IRS-1, GLUT4, AMPK, and Mitochondria

In obese women with PCOS, constitutive activation of serine kinases within the MAPK-ERK pathway impairs insulin's metabolic actions in skeletal muscle while leaving the mitogenic pathway including insulin's co-gonadotropin action on ovarian theca cells at least partially intact [8]. This selective defect creates a self-reinforcing metabolic-reproductive loop: peripheral insulin resistance generates compensatory hyperinsulinism, which drives ovarian androgen overproduction through the preserved mitogenic pathway, and excess androgen further aggravates skeletal muscle insulin resistance through IRS-1 serine phosphorylation at Ser636/639, with downstream mTOR-S6K amplification [8.9]. GLUT4—the insulin-regulatable glucose transporter responsible for the majority of insulin-stimulated muscle glucose uptake—is the effector protein whose impaired translocation most directly mediates the glucose disposal deficit [5, 13]. Exercise training is the most potent non-pharmacological stimulus known to upregulate skeletal muscle GLUT4 expression, acting through AMPK and CaMKII activation of the HDAC4/5-MEF2 axis resulting in histone hyperacetylation at the GLUT4 gene promoter [18]. This molecular mechanism provides a direct rationale for why structured exercise training can partially compensate for GLUT4 trafficking deficiencies in PCOS skeletal muscle, independently of correction of upstream insulin receptor signaling.

Epigenetic modifications further compound the intrinsic signaling defects: changes in DNA methylation patterns alter the expression of nuclear-encoded genes involved in mitochondrial oxidative metabolism in PCOS skeletal muscle [19]. TGF-β–regulated tissue fibrosis in PCOS skeletal muscle, documented by Step to and colleagues (2020), is associated with impaired early insulin signaling and is partially reversed by aerobic exercise training [18]. Circulating MOTS-c—a mitochondria-derived peptide encoded within the mitochondrial genome that regulates skeletal muscle glucose metabolism—is significantly reduced in women with PCOS alongside broader markers of mitochondrial dysfunction in skeletal muscle suggesting that mitochondrial biology in PCOS extends beyond what standard respiratory assessments capture [20].

4. Exercise Training In PCOS: Evidence and Outcomes

4.1. Aerobic Exercise

Multiple systematic reviews and randomized controlled trials document improvements in whole-body insulin sensitivity, circulating androgens, menstrual cyclicity, and cardiometabolic risk following structured aerobic exercise in women with PCOS [1,21-25]. The mechanisms include GLUT4 upregulation, mitochondrial biogenesis, reduction of intramuscular lipid, and favorable shifts in the myokine secretory profile. A 2019 systematic review and meta-analysis (Patten et al.) confirmed that the most consistent improvements following exercise in PCOS are seen in cardiorespiratory fitness (VO_2 peak), BMI, waist circumference, fasting insulin, and HOMA-IR [26,27]. A pilot RCT by Benham and colleagues (2021) randomized 47 previously inactive women with PCOS aged 18–40 years to HIIT (n = 16), continuous aerobic exercise training (CAET; n = 14), or no-exercise control (n = 17), achieving 85% completion [14]. CAET produced significantly greater BMI reduction versus control (–1.0 kg/m^2; p = 0.01) and HIIT (–0.9 kg/m^2; p = 0.04) [22]. This trial used daily ovulation prediction kit testing as a primary reproductive endpoint, establishing ovulation assessment as feasible in exercise trials in PCOS [22].

Hutchison and colleagues (2012) enrolled sixteen overweight women with PCOS and thirteen non-PCOS controls in a 12-week structured exercise RCT with euglycaemic-hyperinsulinaemic clamp, mitochondrial enzyme activity, skeletal muscle gene expression and protein, and CT-estimated intramuscular lipid assessment [21]. Glucose infusion rate was significantly lower in PCOS at baseline (p = 0.01) and improved with exercise in both groups, with mitochondrial adaptations accompanying the insulin sensitivity improvement providing direct evidence that exercise-induced improvements in PCOS are at least partially mediated through mitochondrial remodeling in skeletal muscle [21].

4.2. Progressive Resistance Training: The Direct Muscle Intervention

Progressive resistance training (PRT) produces skeletal muscle adaptations mechanistically distinct from aerobic exercise: myofibrillar hypertrophy, increased absolute GLUT4 content per unit muscle mass, enhanced PI3K-Akt signaling capacity, type I fiber recruitment and maintenance, and direct augmentation of the tissue whose quantitative and qualitative deficits underpin PCOS metabolic dysfunction. These adaptations are particularly pertinent in the sarcopenic obesity phenotype excess

adiposity with relatively low functional muscle mass where aerobic exercise alone addresses cardiorespiratory fitness but not the muscle quantity and fiber-quality deficit. A 2016 pilot RCT by Vizza and colleagues (n = 15) demonstrated feasibility of PRT in PCOS, with supervised session adherence of 95% ± 6% and positive trends across physiological and psychological outcomes [26]. The systematic review and meta-analysis by Patten and colleagues (2020) reported positive effects of resistance training on insulin sensitivity, anthropometric measures, androgen concentrations, and AMH in women with PCOS [27]. The reduction in supraphysiologic ally elevated AMH through PRT is mechanistically important: pathologically elevated AMH inhibits FSH threshold sensitivity, contributing directly to anovulation, and its normalization may represent a specific reproductive mechanism of resistance training beyond insulin sensitization [27]. The 2023 comparative systematic review by Colombo and colleagues (prepared to inform the 2023 PCOS Guideline) found that combined aerobic and resistance training likely optimizes both metabolic and reproductive endpoints, though the limited evidence base precluded definitive modality superiority conclusions [28].

4.3. The Pivotal Ovulation Rate Evidence

The most directly fertility-relevant clinical trial evidence for exercise in PCOS comes from the RCT by Palomba and colleagues (2010; ClinicalTrials.gov: NCT01004680) [29]. Ninety-six consecutive overweight and obese CC-resistant women with PCOS were enrolled in a three-arm, parallel, controlled, assessor-blinded trial. Groups: CC alone (Group A; n = 32); hypocaloric diet followed by CC (Group B; n = 32); six weeks of structured exercise plus hypocaloric diet followed by CC (Group C; n = 32). Ovulation rate: 37.5% in Group C (12/32) versus 12.5% in Group A (4/32) and 9.4% in Group B (3/32; p = 0.008) approximately fourfold improvement relative to both comparators [29]. This trial demonstrates that structured exercise can overcome pharmacological resistance to ovulation induction, acting through improvements in skeletal muscle insulin sensitivity and downstream reduction of hyperinsulinism-driven androgen overproduction. Its primary limitation is that ovulation rate is an important intermediate endpoint pregnancy and live birth outcomes were not reported.

4.4. Myokines and the Muscle-Endocrine Axis

Skeletal muscle secretes bioactive peptides myokines in response to contraction and mechanical loading that communicate metabolically with multiple organ systems. Irisin, derived from proteolytic cleavage of FNDC5, augments insulin-induced PI3K/Akt signaling, promotes GLUT4 membrane translocation, upregulates GLUT4 and hexokinase 2 expression, and stimulates thermogenic browning of white adipose tissue through UCP1 induction [30,31]. Reduced irisin levels have been reported in some PCOS cohorts, potentially contributing to impaired skeletal muscle glucose metabolism [31]. Other exercise-induced myokines with metabolic relevance include IL-15 (which promotes fat-free mass and lipolysis), IL-6 (anti-inflammatory in the contracting muscle context), myostatin (whose exercise-mediated suppression enables hypertrophy), follistatin (which antagonizes myostatin and activin, the latter having ovarian folliculogenesis implications), and BDNF (relevant to hypothalamic energy homeostasis regulation) [30]. An important caveat is warranted: the myokine-reproductive axis in PCOS remains established primarily through mechanistic and animal studies rather than prospective human trials with reproductive endpoints. The distinction between demonstrated human evidence (improved insulin sensitivity and androgen profiles with exercise), inferred mechanisms (myokine-mediated reproductive benefits), and speculative pathways (BDNF-hypothalamic-ovarian communication) should be maintained when communicating findings to clinical or regulatory audiences.

Skeletal Muscle Dysfunction → Reduced GLUT4 expression and translocation; impaired PI3K-Akt-AMPK signaling; intramuscular lipid accumulation (↑ceramide, ↑IMTG); mitochondrial dysfunction; relative depletion of oxidative type I fibers

Systemic Insulin Resistance → Compensatory hyperinsulinism; reduced SHBG; elevated free androgen index; impaired hepatic insulin clearance

Ovarian Androgen Overproduction → Insulin's co-gonadotropin action on theca cells via preserved mitogenic signaling; elevated LH:FSH ratio; increased ovarian androgen biosynthesis

Follicular Arrest and Anovulation → Androgen excess suppresses follicular maturation; supraphysiological AMH inhibits FSH threshold sensitivity; dominant follicle selection fails

Exercise Intervention — Proposed Pathway of Benefit → GLUT4 upregulation via AMPK/CaMKII-HDAC/MEF2 axis; mitochondrial biogenesis; reduced intramuscular lipid; myokine secretion (irisin, IL-15, follistatin); improved insulin sensitivity → ↓hyperinsulinism → ↓ovarian androgen production → ↓AMH → restored ovulation

Figure 1: (Conceptual Schematic): The Proposed Muscle-Ovary Axis in PCOS

5. Exercise Versus Pharmacological Metabolic Intervention In PCOS

5.1. The Comparator Question

Any clinical argument for exercise as a fertility intervention must address the question of comparative effectiveness. The most widely used pharmacological metabolic intervention in PCOS is metformin an insulin sensitizer that reduces hepatic glucose production and, in some studies, improves ovulatory function and menstrual regularity. The following subsections address the available head-to-head evidence.

5.2. Lifestyle Modification Versus Metformin

A systematic review and meta-analysis by Nader poor and colleagues examined lifestyle modification (LSM) versus metformin alone and in combination in women with PCOS [32]. The meta-analysis found no statistically significant difference between LSM and metformin alone in menstrual cycle improvements (weighted MD 1.62) or pregnancy rates (MD 1.44), nor in BMI reduction (MD −0.11) [32]. However, LSM was superior to metformin for reducing insulin resistance (MD = −0.52) and increasing SHBG (MD = 8.27) both key markers of the metabolic substrate underlying PCOS androgen excess [32]. A 20-year review of metformin trial evidence found no sufficient basis to favor metformin or metformin plus CC over CC alone for ovulation induction in newly diagnosed PCOS and noted one trial reporting a higher though non-significant clinical pregnancy rate in a lifestyle modification group (20%) versus metformin (14.4%), CC (12.2%), or combined treatment (14.4%) [33]. A six-month double-blind RCT in 114 women with PCOS randomized to metformin or placebo within a concurrent lifestyle intervention found no statistically significant difference in ovulation rates between metformin and placebo-supplemented lifestyle, suggesting that the lifestyle component may be the primary metabolic driver in combination approaches [34]. These comparisons indicate that structured lifestyle intervention and metformin produce broadly comparable effects on ovulatory function and pregnancy rate in available trials, while exercise-based intervention may be superior for improving the underlying insulin resistance and SHBG. The available evidence supports positioning exercise alongside pharmacological approaches as a foundational first-line lifestyle intervention in PCOS fertility management, rather than as a secondary or preparatory recommendation.

5.3. The Live Birth Gap

The most clinically meaningful fertility endpoint live birth rate has not been demonstrated to improve with exercise intervention in adequately powered RCTs in women with PCOS. A systematic review examining maternal physical activity and IVF outcomes (10 cohort studies, 2 RCTs; 3,431 women) found statistically uncertain pooled evidence for the effect of physical activity on live birth rate per woman (OR 1.15; 95% CI 0.92–1.43; p = 0.23; I^2 = 61%) [35]. A meta-analysis of IVF outcomes in women with PCOS versus non-PCOS controls (95 studies; >21,289 PCOS patients) found comparable pregnancy and live birth rates per cycle, but significantly higher miscarriage (OR 1.44; 95% CI 1.20–1.72), biochemical pregnancy loss, and OHSS in PCOS women [36]. The Palomba ovulation rate trial demonstrates a clinically meaningful improvement in an important intermediate endpoint [29]. Whether that improvement translates proportionally into improvements in clinical pregnancy and live birth remains to be established in adequately powered prospective trials.

5.4. The Metabolic Case Beyond Ovulation

The argument for metabolic optimization through exercise extends beyond ovulation rate. Women with PCOS at high BMI face significantly worse IVF outcomes: a systematic review of 19 studies in 7,680 women found significantly higher odds of clinical pregnancy (OR 1.16; 95% CI 1.04–1.29) and live birth (OR 1.88; 95% CI 1.56–2.27) at normal versus high BMI in PCOS women undergoing IVF [37]. The excess adverse pregnancy outcomes miscarriage, gestational diabetes, hypertensive disorders, preterm birth disproportionately burdening obese women with PCOS undergoing ART provide additional rationale for metabolic optimization before and during fertility treatment, even in the absence of direct exercise-to-live-birth RCT evidence [38].

6. Body Composition, Anti-Müllerian Hormone, and Ovarian Reserve

AMH is secreted by granulosa cells of primary and small antral follicles and serves as the most clinically reliable marker of ovarian reserve, with negligible menstrual cycle variation [39]. In PCOS, AMH is characteristically supraphysiologic ally elevated, reflecting the excess of small antral follicles characteristic of the condition. This elevation is mechanistically active: pathologically elevated AMH inhibits FSH-stimulated follicular maturation, contributing to anovulation [39]. The observation that both aerobic exercise and progressive resistance training reduce elevated AMH in women with PCOS therefore carries direct mechanistic implications for restoration of ovulatory function [27]. A 2024 study by Wasilewski and colleagues found support for lifestyle factors including physical activity and body composition parameters influencing AMH levels and ovarian reserve in women with and without ovulatory infertility [40]. A large retrospective cohort of 30,746 IVF/ICSI cycles found significantly lower AMH in overweight and obese women with age-related AMH decline most pronounced at higher BMI indicating that body composition influences ovarian reserve trajectories and oocyte quality over time [41].

7. Clinical Measurement of Muscle Health In PCOS

After establishing that skeletal muscle quantity and quality are clinically relevant in PCOS, the practical question follows: how can muscle health be assessed in routine clinical practice? Several validated tools are available, each with distinct strengths and limitations.

7.1. Dual-Energy X-Ray Absorptiometry

DXA remains the gold-standard clinical method for body composition assessment, providing simultaneous

quantification of fat mass, appendicular skeletal muscle mass (ASM), fat-free mass, and regional fat distribution [42]. The appendicular skeletal muscle mass index (ASMI), calculated as ASM divided by height squared (kg/m^2), is the primary metric for diagnosing low muscle mass. The European Working Group on Sarcopenia in Older People (EWGSOP2) has established cutoff values for low ASMI by DXA of < 7.0 kg/m^2 for men and < 5.5 kg/m^2 for women, based on two standard deviations below the mean for young healthy reference populations [42]. DXA also characterizes gynoid and android fat distribution patterns, both of which are clinically relevant in PCOS given the association between central adiposity and insulin resistance. In research settings, DXA has been used to identify the sarcopenic obesity phenotype in PCOS and to track changes in body composition with exercise intervention [10,22]. Its primary limitations in clinical reproductive practice are cost, radiation exposure (minimal), and limited availability in outpatient gynecology settings.

7.2. Bioelectrical Impedance Analysis

BIA provides a portable, inexpensive, and radiation-free alternative for estimating body composition including ASMI. Emerging evidence supports BIA's validity as an ASMI estimation method relative to DXA as a reference standard, though BIA tends to overestimate skeletal muscle mass and validation equations should be population-specific [42]. Single-frequency and multi-frequency BIA devices are available for clinical use; multi-frequency devices (such as In Body systems) have demonstrated stronger concordance with DXA-derived ASMI. BIA-derived phase angle reflecting cellular hydration and membrane integrity has been proposed as a marker of overall muscle quality and has been associated with semen parameters in men suggesting potential utility as a surrogate for cellular health in both sexes. The primary limitations of BIA are sensitivity to hydration status, body temperature, and electrode placement, which can introduce measurement variability [41-50].

7.3. Handgrip Strength

Handgrip strength (HGS), measured by handheld dynamometry, is a validated, inexpensive, and rapid clinical surrogate for overall muscle strength and functional performance. It is strongly correlated with ASMI measured by DXA and with general physical function [42]. In women with PCOS, HGS has been studied as a clinical marker of muscular fitness; a case-control study of 170 women found that HGS correlated with body composition parameters measured by DXA, including lean mass distribution and fat percentage, across normal, overweight, and obese BMI categories [51]. HGS is particularly attractive as a clinical tool because it requires no specialized equipment beyond a dynamometer, takes less than two minutes to administer, and produces a continuous quantitative output that can be tracked longitudinally. Its limitation as a PCOS-specific muscle quality marker is that it reflects primarily upper extremity muscle function and may not fully capture lower-extremity or core muscle deficits relevant to insulin sensitivity.

7.4. Cardiorespiratory Fitness

Cardiorespiratory fitness (CRF), most precisely quantified as VO_2 peak or VO_2 max by cardiopulmonary exercise testing (CPET), is an independent predictor of metabolic health, insulin sensitivity, and cardiovascular risk. A study assessing CRF and muscular strength in 31 women with PCOS and 13 controls matched for age, body composition, androgenic pattern, and insulinemic pattern found that the PCOS group demonstrated significantly higher VO_2 max per kg (30.9 ± 7.6 vs. 24.8 ± 4.1 mL/kg/min; p = 0.010) and higher handgrip strength per kg of fat-free mass compared with controls, suggesting that PCOS per se does not impair exercise capacity and that women with PCOS can achieve high levels of physical fitness [52]. This finding underscores that exercise prescription for PCOS is not limited by the biology of the condition itself but by historical underinvestment in targeted exercise programming for this population. A recent systematic review and meta-analysis (2026, BMC Women's Health) confirmed that exercise interventions across intensities improve insulin resistance and VO_2 max in women with PCOS, with high-intensity training showing particular benefit for VO_2 max and insulin levels [53].

7.5. Clinical Integration: A Proposed Assessment Hierarchy

Based on the available evidence and clinical practicability, a tiered muscle health assessment framework for women with PCOS presenting to fertility care may include: (1) BIA as a first-line, cost-effective screen for ASMI and phase angle in all women with PCOS undergoing fertility evaluation; (2) DXA for women in whom BIA identifies low ASMI or whose phenotype (normal BMI with metabolic features) raises concern for sarcopenic obesity; (3) handgrip dynamometry as a rapid, inexpensive functional test that can be repeated at each visit to track change; and (4) a standardized physical activity history tool (such as the Global Physical Activity Questionnaire, GPAQ) to estimate current activity level and inform exercise prescription. VO_2 max testing through CPET is valuable for research contexts and may be considered in women for whom cardiorespiratory fitness is a specific clinical concern.

8. Male Reproductive Health: Body Composition and Spermatogenesis

Male factor infertility or subfertility is present in approximately 40–50% of infertile couples. The metabolic disruptions that impair female fertility through insulin resistance and hyperandrogenism have directly analogous effects on male reproductive function through the HPG axis.

8.1. Muscle Mass, Testosterone, and Spermatogenesis

Testosterone acts through pulsatile GnRH-driven pituitary LH and FSH secretion to support Leydig cell testosterone production and Sertoli cell-mediated spermatogenesis [36]. Adequate skeletal muscle mass is associated with higher endogenous testosterone, and men performing regular

heavy physical labor have demonstrated 46% higher sperm concentration and 44% higher total sperm count compared with sedentary men in observational data [37].

8.2. Adiposity, Aromatization, and Sperm Quality

Excess adipose tissue in men drives aromatase-mediated conversion of testosterone to estradiol, suppressing the HPG axis, reducing intratesticular testosterone, and impairing spermatogenesis [28]. A cross-sectional study of 483 male partners of subfertile couples found that BMI ≥ 35 kg/m^2 was associated with significantly lower total sperm count (adjusted median difference −86 × 10^6 sperm; 95% CI −134, −37), lower inhibin B, higher estradiol, lower testosterone and SHBG, and significantly greater sperm DNA fragmentation [39]. BIA-based body composition studies show that lower skeletal muscle mass and reduced phase angle are associated with worse semen parameters [40].

8.3. The Exogenous Androgen Caveat

Exogenous anabolic-androgenic steroids and testosterone replacement therapy suppress pituitary LH and FSH through negative HPG feedback, reducing intratesticular testosterone to levels insufficient for spermatogenesis and producing oligospermia or azoospermia [41]. Men with hypogonadism who wish to preserve fertility should be managed with clomiphene citrate or HCG rather than testosterone therapy [41].

9. Clinical Implications

9.1. Metabolic Assessment in PCOS Fertility Evaluation

The evidence in this review supports expanding PCOS fertility assessment to include a metabolic profile: fasting insulin and glucose, HOMA-IR, fasting lipids, SHBG, body composition analysis including ASMI (by BIA or DXA), handgrip strength, and physical activity history. Women with sarcopenic obesity at any BMI, and lean women with elevated HOMA-IR, represent priority groups for muscle-building intervention. These evaluations should be conducted without weight stigmatizing language, consistent with the 2023 International PCOS Guideline's explicit emphasis on avoiding stigmatization of body weight [1].

9.2. Exercise Prescription Framework

Based on the available evidence and the 2023 International PCOS Guideline and ESSA position statement [1,23], the following framework is supported for women with PCOS and infertility. Aerobic exercise at moderate-to-vigorous intensity for a minimum of 150 minutes per week is foundational, with evidence for improvements in insulin sensitivity, cardiometabolic risk, VO_2 peak, and ovulatory frequency [1,21-25]. Progressive resistance training targeting major muscle groups at 60–80% of one-repetition maximum, at least twice weekly with progressive overload, is supported as a complement to aerobic exercise for its direct effects on skeletal muscle mass, GLUT4 expression, type I fiber recruitment, and AMH normalization [26,27]. For obese, CC-resistant women, a minimum six-week structured exercise and dietary pre-treatment period warrants consideration given the fourfold ovulation improvement demonstrated by Palomba and colleagues with the explicit caveat that live birth benefit has not been established in adequately powered trials. Combined aerobic and resistance training protocols appear to provide additive metabolic benefit and are endorsed by the 2023 comparative systematic review [28,29].

9.3. Positioning Exercise Relative to Pharmacotherapy

The available evidence supports structured exercise, including progressive resistance training, as a foundational first-line lifestyle intervention to be considered alongside pharmacological approaches in PCOS fertility management. Lifestyle modification and metformin produce comparable effects on pregnancy rate and menstrual cyclicity in available trials, while lifestyle intervention may be superior for improving the underlying insulin resistance and SHBG [32]. In women for whom metformin is indicated, exercise may complement its metabolic effects; in women for whom it is contraindicated or not tolerated, exercise-based metabolic conditioning provides an evidence-supported alternative pathway.

10. Limitations and Future Research Directions

This narrative review is subject to the inherent limitations of the review method: study selection was not conducted with PRISMA-level rigor and narrative synthesis is susceptible to selective emphasis. The underlying evidence base carries additional limitations: most exercise intervention trials in PCOS involve small samples (typically fewer than 50 participants per arm), short durations (12–16 weeks), and heterogeneous outcome measures. No adequately powered RCT has used live birth rate as a primary endpoint for a skeletal muscle-focused exercise intervention in women with PCOS. The most directly fertility-relevant trial uses ovulation as its primary outcome—an important but intermediate endpoint. The comparative efficacy of aerobic versus resistance versus combined training modalities for specific reproductive outcomes has not been resolved [28,29]. The lean PCOS phenotype is underrepresented in exercise intervention trials. The myokine-reproductive axis is established primarily through mechanistic and animal data. Body composition normative data for ASMI cutoffs in reproductive-aged women with PCOS remain underdeveloped relative to older adult sarcopenia literature.

An important structural reason why resistance training RCTs in PCOS are small and sparse deserves explicit acknowledgment: historically, PCOS research funding and clinical trial infrastructure have been organized around ovarian and reproductive endpoints, with limited investment in exercise science trials in this population. The invasiveness of muscle biopsy protocols, challenges with long-term exercise trial adherence, and the difficulty of powering trials on live birth outcomes (requiring large samples and long follow-up) compound this structural limitation. Addressing these barriers—through dedicated

PCOS exercise trial funding mechanisms, pragmatic trial designs, and collaboration between reproductive medicine and exercise science communities—is a prerequisite for the next generation of evidence in this field. Future research priorities: adequately powered RCTs with live birth and pregnancy rate as co-primary endpoints for structured exercise in PCOS infertility; trials specifically enrolling lean PCOS phenotypes; longitudinal studies examining ASMI, AMH trajectories, and ART outcomes; mechanistic trials directly testing the myokine-reproductive axis; couple-level intervention studies with couple-level pregnancy rates as primary outcomes; and head-to-head trials comparing standardized resistance training versus metformin for reproductive outcomes in parallel-group designs.

11. Conclusions

Skeletal muscle is an underrecognized metabolic organ in polycystic ovary syndrome whose improvement through structured exercise including progressive resistance training may represent an important strategy for improving reproductive outcomes in affected women. The mechanistic case is multiply supported: intrinsic skeletal muscle signaling defects and intramuscular lipid accumulation drive the hyperinsulinism that fuels ovarian androgen overproduction and anovulation; these defects are present in the lean PCOS phenotype at normal BMI, establishing their independence from adiposity; sarcopenic obesity amplifies the metabolic and inflammatory burden in a pattern invisible to standard clinical assessment; and exercise training corrects the GLUT4 deficit, partially reverses mitochondrial dysfunction, reduces supraphysiological AMH, and restores ovulatory cyclicity.

The available evidence supports structured exercise, including progressive resistance training, as a key component of first-line lifestyle management and a potentially important adjunct to fertility-directed therapies in PCOS. Lifestyle modification and metformin produce comparable effects on pregnancy rate in available trials, while lifestyle intervention may be superior for improving the underlying metabolic substrate. Live birth rate following exercise intervention has not been established in adequately powered trials—the most important unresolved research question in this field. The formal renaming of PCOS to polyendocrine metabolic ovarian syndrome in May 2026 provides institutional context for the metabolic reorientation of clinical care that the evidence has long supported, foregrounding the endocrine and metabolic dimensions of this condition and thereby the interventions—including building metabolically efficient skeletal muscle that target those dimensions most directly.

Acknowledgement

All studies cited below were published under the designation polycystic ovary syndrome (PCOS), reflecting the nomenclature current at their time of publication. PCOS has been formally redesignated PMOS (The Lancet, May 12, 2026; see Ref. A1). DOIs and PMIDs are provided for independent verification.

References

1. Teede, H. J., Khomami, M. B., Morman, R., Laven, J. S., Joham, A. E., Costello, M. F., ... & Piltonen, T. (2026). Polyendocrine metabolic ovarian syndrome, the new name for polycystic ovary syndrome: a multistep global consensus process. *The Lancet.*
2. Endocrine Society. Polyendocrine metabolic ovarian syndrome: new name to improve diagnosis and care [press release]. May 12, 2026.
3. Teede, H. J., Tay, C. T., Laven, J. J., Dokras, A., Moran, L. J., Piltonen, T. T., ... & Joham, A. E. (2023). Recommendations from the 2023 international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *European journal of endocrinology, 189*(2), G43-G64.
4. Cassar, S., Misso, M. L., Hopkins, W. G., Shaw, C. S., Teede, H. J., & Stepto, N. K. (2016). Insulin resistance in polycystic ovary syndrome: a systematic review and meta-analysis of euglycaemic–hyperinsulinaemic clamp studies. *Human reproduction, 31*(11), 2619-2631.
5. Richter, E. A., & Hargreaves, M. (2013). Exercise, GLUT4, and skeletal muscle glucose uptake. *Physiological reviews*.
6. Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. Consensus on women's health aspects of polycystic ovary syndrome (PCOS). Fertil Steril. 2012;97(1):28–38.
7. Carmina, E., & Lobo, R. A. (2022). Comparing lean and obese PCOS in different PCOS phenotypes: Evidence that the body weight is more important than the Rotterdam phenotype in influencing the metabolic status. *Diagnostics, 12*(10), 2313.
8. Diamanti-Kandarakis, E., & Dunaif, A. (2012). Insulin resistance and the polycystic ovary syndrome revisited: an update on mechanisms and implications. *Endocrine reviews, 33*(6), 981-1030.
9. Skov, V., Glintborg, D., Knudsen, S., Jensen, T., Kruse, T. A., Tan, Q., ... & Højlund, K. (2007). Reduced expression of nuclear-encoded genes involved in mitochondrial oxidative metabolism in skeletal muscle of insulin-resistant women with polycystic ovary syndrome. *Diabetes, 56*(9), 2349-2355.
10. McBreairty, L. E., Chilibeck, P. D., Gordon, J. J., Chizen, D. R., & Zello, G. A. (2019). Polycystic ovary syndrome is a risk factor for sarcopenic obesity: a case control study. *BMC endocrine disorders, 19*(1), 70.
11. Stepto, N. K., Hiam, D., Gibson-Helm, M., Cassar, S., Harrison, C. L., Hutchison, S. K., ... & Teede, H. J. (2020). Exercise and insulin resistance in PCOS: muscle insulin signalling and fibrosis. *Endocrine connections, 9*(4), 346-359.
12. Stener-Victorin, E., Eriksson, G., Mohan Shrestha, M., Rodriguez Paris, V., Lu, H., Banks, J., ... & Benrick, A. (2024). Proteomic analysis shows decreased type I fibers and ectopic fat accumulation in skeletal muscle from women with PCOS. *Elife, 12*, RP87592.
13. Kazemi, M., Pierson, R. A., Parry, S. A., Kaviani, M., & Chilibeck, P. D. (2021). Obesity, but not hyperandrogenism or insulin resistance, predicts

skeletal muscle mass in reproductive-aged women with polycystic ovary syndrome: A systematic review and meta-analysis of 45 observational studies. *Obesity Reviews, 22*(8), e13255.

14. Manti, M., Stener-Victorin, E., & Benrick, A. (2020). Skeletal muscle immunometabolism in women with polycystic ovary syndrome: a meta-analysis. *Frontiers in Physiology, 11*, 573505.
15. McDonnell, T., Cussen, L., McIlroy, M., & O'Reilly, M. W. (2022). Characterizing skeletal muscle dysfunction in women with polycystic ovary syndrome. *Therapeutic Advances in Endocrinology and Metabolism, 13*, 20420188221113140.
16. Hansen, S. L., Svendsen, P. F., Jeppesen, J. F., Hoeg, L. D., Andersen, N. R., Kristensen, J. M., ... & Kiens, B. Molecular mechanisms in skeletal muscle underlying insulin resistance in lean women with polycystic ovary syndrome. *The Journal of Clinical Endocrinology & Metabolism.*
17. Allemand, M. C., Irving, B. A., Asmann, Y. W., Klaus, K. A., Tatpati, L., Coddington, C. C., & Nair, K. S. (2009). Effect of testosterone on insulin stimulated IRS1 Ser phosphorylation in primary rat myotubes—a potential model for PCOS-related insulin resistance. *PloS one, 4*(1), e4274.
18. Stepto, N. K., Moreno-Asso, A., McIlvenna, L. C., Walters, K. A., & Rodgers, R. J. (2019). Molecular mechanisms of insulin resistance in polycystic ovary syndrome: unraveling the conundrum in skeletal muscle?. *The Journal of Clinical Endocrinology & Metabolism, 104*(11), 5372-5381.
19. Skov, V., Glintborg, D., Knudsen, S., Jensen, T., Kruse, T. A., Tan, Q., ... & Højlund, K. (2007). Reduced expression of nuclear-encoded genes involved in mitochondrial oxidative metabolism in skeletal muscle of insulin-resistant women with polycystic ovary syndrome. *Diabetes, 56*(9), 2349-2355.
20. Kutuk, I. S., Akin, S., Demirel, H., Mumusoglu, S., Ciftci, T., & Yildiz, B. O. (2026). Reduced serum and skeletal muscle MOTS c levels in women with polycystic ovary syndrome are associated with mitochondrial dysfunction. Scientific reports.
21. Hutchison, S. K., Teede, H. J., Rachoń, D., Harrison, C. L., Strauss, B. J., & Stepto, N. K. (2012). Effect of exercise training on insulin sensitivity, mitochondria and computed tomography muscle attenuation in overweight women with and without polycystic ovary syndrome. *Diabetologia, 55*(5), 1424-1434.
22. Holmes, B. F., Kurth-Kraczek, E. J., & Winder, W. W. (1999). Chronic activation of 5′-AMP-activated protein kinase increases GLUT-4, hexokinase, and glycogen in muscle. **Journal of applied physiology, 87**(5), 1990-1995.
23. Benham, J. L., Booth, J. E., Corenblum, B., Doucette, S., Friedenreich, C. M., Rabi, D. M., & Sigal, R. J. (2021). Exercise training and reproductive outcomes in women with polycystic ovary syndrome: a pilot randomized controlled trial. *Clinical endocrinology, 95*(2), 332-343.
24. Shushan, T., Lovell, R., McLaren, S. J., Buchheit, M., Iacono, A. D., Arguedas-Soley, A., & Norris, D. (2024). Assessing criterion and longitudinal validity of submaximal heart rate indices as measures of cardiorespiratory fitness: A preliminary study in football. *Journal of Science and Medicine in Sport, 27*(8), 565-571.
25. Vizza, L., Smith, C. A., Swaraj, S., Agho, K., & Cheema, B. S. (2016). The feasibility of progressive resistance training in women with polycystic ovary syndrome: a pilot randomized controlled trial. *BMC sports science, medicine and rehabilitation, 8*(1), 14.
26. Patten, R. K., Boyle, R. A., Moholdt, T., Kiel, I., Hopkins, W. G., Harrison, C. L., & Stepto, N. K. (2020). Exercise interventions in polycystic ovary syndrome: a systematic review and meta-analysis. *Frontiers in physiology, 11*, 606.
27. Colombo, G. E., Bouzo, X. D., Patten, R. K., Mousa, A., Tay, C. T., Pattuwage, L., ... & Sabag, A. (2023). Comparison of selected exercise training modalities in the management of PCOS: a systematic review and meta-analysis to inform evidence-based guidelines. *JSAMS Plus, 2*, 100024.
28. Palomba, S., Falbo, A., Giallauria, F., Russo, T., Rocca, M., Tolino, A., ... & Orio, F. (2010). Six weeks of structured exercise training and hypocaloric diet increases the probability of ovulation after clomiphene citrate in overweight and obese patients with polycystic ovary syndrome: a randomized controlled trial. *Human Reproduction, 25*(11), 2783-2791.
29. Bowman, R. W., Jordahl, E. M., Davis, S., Hedayati, S., Barsouk, H., Ozbaki-Yagan, N., ... & O'Donnell, A. F. (2022). TORC1 signaling controls the stability and function of α-arrestins Aly1 and Aly2. *Biomolecules, 12*(4), 533.
30. Kim, H. J., Lee, H. J., So, B., Son, J. S., Yoon, D., & Song, W. (2016). Effect of aerobic training and resistance training on circulating irisin level and their association with change of body composition in overweight/obese adults: a pilot study. *Physiological research, 65*(2), 271.
31. Naderpoor, N., Shorakae, S., de Courten, B., Misso, M. L., Moran, L. J., & Teede, H. J. (2015). Metformin and lifestyle modification in polycystic ovary syndrome: systematic review and meta-analysis. *Human reproduction update, 21*(5), 560-574.
32. Hashim, H. A. (2016). Twenty years of ovulation induction with metformin for PCOS; what is the best available evidence?. *Reproductive biomedicine online, 32*(1), 44-53.
33. Hoeger, K. M., Kochman, L., Wixom, N., Craig, K., Miller, R. K., & Guzick, D. S. (2004). A randomized, 48-week, placebo-controlled trial of intensive lifestyle modification and/or metformin therapy in overweight women with polycystic ovary syndrome: a pilot study. *Fertility and sterility, 82*(2), 421-429.
34. Kakargia, E., Mamalakis, E., Frountzas, M., Anagnostou, E., & Siristatidis, C. (2023). The role of maternal physical activity on in vitro fertilization outcomes: a systematic review and meta-analysis. *Archives of Gynecology and Obstetrics, 307*(6), 1667-1676.
35. O'Neill, D., Pounds, R., Scully, N., Marriott, N., Balega, J.,

Ganesan, R., ... & Yap, J. (2021). The impact on obstetric outcomes following complete amputation of the cervix uteri in fertility preservation surgery for cervical neoplasm. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 260*, 171-176.

36. González-Santos, S., Mugabure, B., Granell, M., Aguinagalde, B., López, I. J., Aginaga, A., ... & Herreros-Pomares, A. (2024). Analgesic efficacy and safety of intrathecal morphine or intercostal levobupivacaine in lung cancer patients after major lung resection surgery by videothoracoscopy: a prospective randomized controlled trial. *Journal of clinical medicine, 13*(7), 1972.
37. Xie, N., & Zhao, W. (2025). Adverse pregnancy and perinatal outcomes in women with polycystic ovary syndrome undergoing assisted reproductive technology: a systematic review and meta-analysis. *Frontiers in Medicine, 12,* 1656389.
38. Broer, S. L., Broekmans, F. J., Laven, J. S., & Fauser, B. C. (2014). Anti-Müllerian hormone: ovarian reserve testing and its potential clinical implications. *Human reproduction update, 20*(5), 688-701.
39. Skowrońska, M., Pawłowski, M., Buczyńska, A., Wiatr, A., Dyszkiewicz, A., Wenta, A., ... & Milewski, R. (2024). The relationship between body composition parameters and the intake of selected nutrients, and serum anti-Müllerian Hormone (AMH) levels in the context of ovulatory infertility. *Nutrients, 16*(23), 4149.
40. Li, Y. L., Yan, E. Q., Zhao, G. N., Jin, L., & Ma, B. X. (2024). Effect of body mass index on ovarian reserve and ART outcomes in infertile women: a large retrospective study. *Journal of Ovarian Research, 17*(1), 195.
41. Cruz-Jentoft, A. J., Bahat, G., Bauer, J., Boirie, Y., Bruyère, O., Cederholm, T., ... & Zamboni, M. (2019). Sarcopenia: revised European consensus on definition and diagnosis. *Age and ageing, 48*(1), 16-31.
42. Beaudart, C., Rolland, Y., Cruz-Jentoft, A. J., Bauer, J. M., Sieber, C., Cooper, C., ... & Fielding, R. A. (2019). Assessment of muscle function and physical performance in daily clinical practice.
43. Skowrońska, M., Pawłowski, M., Buczyńska, A., Wiatr, A., Dyszkiewicz, A., Wenta, A., ... & Milewski, R. (2024). The relationship between body composition parameters and the intake of selected nutrients, and serum anti-Müllerian Hormone (AMH) levels in the context of ovulatory infertility. *Nutrients, 16*(23), 4149.
44. Li, Y. L., Yan, E. Q., Zhao, G. N., Jin, L., & Ma, B. X. (2024). Effect of body mass index on ovarian reserve and ART outcomes in infertile women: a large retrospective study. *Journal of Ovarian Research, 17*(1), 195.
45. Nassar, G. N., & Leslie, S. W. (2026). Physiology, testosterone. In StatPearls [Internet]. StatPearls Publishing.
46. Gaskins, A. J., Mendiola, J., Afeiche, M., Jørgensen, N., Swan, S. H., & Chavarro, J. E. (2015). Physical activity and television watching in relation to semen quality in young men. *British journal of sports medicine, 49*(4), 265-270.
47. Broughton, D. E., & Moley, K. H. (2017). Obesity and female infertility: potential mediators of obesity's impact. *Fertility and sterility, 107*(4), 840-847.
48. Chavarro, J. E., Toth, T. L., Wright, D. L., Meeker, J. D., & Hauser, R. (2010). Body mass index in relation to semen quality, sperm DNA integrity, and serum reproductive hormone levels among men attending an infertility clinic. *Fertility and sterility, 93*(7), 2222-2231.
49. Liprino, A., Giacone, F., Lombardo, D., Asmundo, M. G., Russo, G. I., Abdelhameed, A. S., ... & Chamayou, S. (2024). Phase angle at bioelectric impedance analysis is associated with detrimental sperm quality in idiopathic male infertility: a preliminary clinical study. *Frontiers in Endocrinology, 15*, 1354733.
50. Durairajanayagam, D. (2018). Lifestyle causes of male infertility. *Arab journal of urology, 16*(1), 10-20.
51. Kogure, G. S., Ribeiro, V. B., de Oliveira Gennaro, F. G., Ferriani, R. A., Miranda-Furtado, C. L., & Dos Reis, R. M. (2020). Physical performance regarding handgrip strength in women with polycystic ovary syndrome. *Revista Brasileira de Ginecologia e Obstetrícia/RBGO Gynecology and Obstetrics, 42*(12), 811-819.
52. Baioccato, V., Quinto, G., Rovai, S., Conte, F., Dassie, F., Neunhäeuserer, D., ... & Mioni, R. (2022). Do androgenic pattern, insulin state and growth hormone affect cardiorespiratory fitness and strength in young women with PCOS?. *Biomedicines, 10*(9), 2176.
53. Sámano Sánchez, M., Floridia Rietmann, L. M., Magallanes Bajana, A., Rodriguez, C. F. C., Moreno Díaz, T. A., Sultana, S., ... & Calderón Martínez, E. (2026). Comparative cardiometabolic effects of high, moderate, and low intensity exercise in polycystic ovary syndrome: a systematic review and network meta-analysis of randomized controlled trials. *BMC Women's Health, 26*(1), 89.