Metabolism Open 25 (2025) 100341

Contents lists available at ScienceDirect

Metabolism Open

journal homepage: www.sciencedirect.com/journal/metabolism-open

# The impact of intermittent fasting on fertility: A focus on polycystic ovary syndrome and reproductive outcomes in Women-A systematic review

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ARTICLE INFO

*Keywords:*
Intermittent fasting
Time-restricted feeding
Fertility
Pregnancy outcomes
Reproductive health

ABSTRACT

*Introduction:* Polycystic Ovary Syndrome (PCOS) is a prevalent endocrine disorder characterized by hyperandrogenism, insulin resistance, and menstrual irregularities, leading to infertility in many women. Emerging evidence suggests intermittent fasting (IF), particularly time-restricted feeding (TRF), may improve reproductive and metabolic outcomes in women with PCOS by addressing core pathophysiological mechanisms. This systematic review examines the impact of IF on fertility and reproductive hormones in women with PCOS.

*Methods:* A systematic search was conducted in PubMed, Scopus, and Cochrane Library using predefined search terms related to intermittent fasting, fertility, and PCOS. Eligible studies published between 2014 and 2024 were identified following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Inclusion criteria targeted primary research evaluating the effects of IF on reproductive outcomes, menstrual irregularities, and metabolic parameters in women with PCOS. Data extraction and quality assessment were performed using the Caldwell framework.

*Results:* Three studies were included in the review. TRF interventions led to significant improvements in menstrual regularity, with 33–40 % of participants reporting normalized cycles. Reductions in total testosterone, free androgen index, anti-Müllerian hormone (AMH), and luteinizing hormone (LH) levels were observed, alongside increased sex hormone-binding globulin (SHBG). TRF also improved insulin sensitivity, reduced body weight, and decreased inflammatory markers, all of which contribute to enhanced reproductive outcomes. Key outcomes included a 9 % reduction in testosterone levels, 26 % reduction in the free androgen index (FAI), and significant improvements in menstrual regularity (33–40 %).

*Conclusions:* Intermittent fasting, particularly TRF, shows potential as a non-pharmacological intervention to improve reproductive health and fertility in women with PCOS. By targeting hyperandrogenism, insulin resistance, and menstrual irregularities, TRF offers a promising lifestyle approach. However, larger randomized controlled trials with long-term follow-up are needed to confirm these findings and establish IF as a standard therapeutic option for PCOS management.

## 1. Introduction

Polycystic Ovary Syndrome (PCOS) is a prevalent and complex endocrine disorder affecting women of reproductive age, characterized by hyperandrogenemia, anovulation, and polycystic ovarian morphology [1]. It represents one of the most common causes of menstrual irregularities, infertility, and metabolic dysfunctions in this population. Epidemiological data suggest that its prevalence ranges globally from 6 % to 21 %, with significant variations due to differences in diagnostic criteria, genetic predispositions, and environmental factors [2]. Clinically, PCOS manifests with a constellation of reproductive and metabolic symptoms. Reproductive complications include oligo-ovulation or anovulation, clinical and biochemical hyperandrogenism, and infertility, which affects approximately 70 % of women with PCOS [3].

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https://doi.org/10.1016/j.metop.2024.100341
Received 22 December 2024; Received in revised form 28 December 2024; Accepted 29 December 2024
Available online 6 January 2025

Beyond reproductive concerns, PCOS is strongly associated with several metabolic disturbances, including obesity, insulin resistance (IR), hyperinsulinemia, and a predisposition to type 2 diabetes mellitus (T2DM). Obesity exacerbates the underlying pathophysiology of PCOS by increasing hyperinsulinemia, which, in turn, stimulates ovarian androgen production, contributing to hyperandrogenism and further impairing ovulatory function [3]. These interrelated metabolic abnormalities highlight the importance of lifestyle interventions in the management of PCOS. Dietary modifications, in particular, have been shown to play a pivotal role in addressing both the reproductive and metabolic sequelae of PCOS, offering a non-pharmacological, sustainable treatment option [4].

In recent years, intermittent fasting (IF) has emerged as a promising dietary strategy for managing metabolic disorders and improving hormonal balance in PCOS. IF involves alternating periods of fasting and feeding without necessarily imposing strict caloric restrictions, thus providing a flexible approach to dietary interventions. IF is hypothesized to improve insulin sensitivity, reduce body weight, and regulate reproductive hormones—key targets in the management of PCOS pathophysiology [5].

Conventional treatments for PCOS, including pharmacological interventions like metformin or clomiphene, often target insulin resistance and ovulatory dysfunction but are associated with side effects and variable adherence rates [6]. Similarly, dietary interventions such as caloric restriction have demonstrated efficacy in improving metabolic parameters [7]. IF stands out as a novel strategy due to its potential to align with physiological circadian rhythms while avoiding the challenges of continuous caloric restriction [5].

The most widely studied forms of intermittent fasting include alternate-day fasting (ADF), time-restricted feeding (TRF), and the 5:2 diet [8]. In ADF, fasting days, during which energy intake is restricted to water alone or minimal caloric intake, are interspersed with feeding days that allow unrestricted food consumption. This regimen has shown potential for reducing body weight, fasting glucose levels, and improving insulin sensitivity—factors that are crucial in PCOS management [9,10].

TRF, on the other hand, confines food intake to specific time windows, typically 4–10 h, with unrestricted food and beverage intake during the eating window. Outside this period, only non-caloric beverages such as water, unsweetened tea, or black coffee are allowed. TRF has garnered significant attention due to its practicality and the ability to align feeding schedules with circadian rhythms, which are intrinsically linked to metabolic and endocrine regulation [11,12].

The 5:2 diet represents a variation of ADF, involving two non-consecutive fasting days per week where caloric intake is restricted to 20%–25 % of total daily energy requirements, while normal food intake is maintained on the remaining five days. This approach balances caloric restriction with sustainability, reducing the metabolic and psychological stress of continuous dieting [13,14].

Another noteworthy form of intermittent fasting is Ramadan fasting, which is practiced by Muslims globally. During Ramadan, fasting occurs daily from sunrise to sunset, prohibiting the consumption of both food and fluids during daylight hours. This unique pattern of fasting provides an opportunity to study the physiological effects of prolonged fasting windows on metabolic, endocrine, and reproductive parameters [15].

Given the complex relationship between metabolic dysfunction and reproductive health in women with PCOS, intermittent fasting has emerged as a promising therapeutic approach. By addressing core aspects of PCOS, such as insulin resistance, hyperinsulinemia, and hyperandrogenism, intermittent fasting has the potential to restore hormonal balance, improve menstrual regularity, and support ovulatory function. Furthermore, its positive effects on weight loss and metabolic outcomes may contribute to enhanced reproductive health. Despite this theoretical promise, the current understanding of how different intermittent fasting protocols specifically impact PCOS-related mechanisms and fertility outcomes remains incomplete. A systematic exploration of the available evidence is necessary to clarify the role of intermittent fasting in improving reproductive and metabolic parameters in women with PCOS and to evaluate its potential as a sustainable, non-pharmacological intervention for managing the condition.

## 2. Methods

This systematic review of the literature was conducted following the guidelines outlined by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [16]. This systematic review has been registered in the International Prospective Register of Systematic Reviews (PROSPERO) with ID number 628793.

### 2.1. Search strategy

To identify the studies for inclusion, a structured literature search was carried out in the following electronic databases: PubMed/Medline, Scopus, and Cochrane Library. The search process was initially broad and subsequently refined into three specific search algorithms to enhance precision. The search terms focused on the following concepts: i) Intermittent fasting; ii) Time-restricted feeding; iii) Fertility and iv) Infertility.

The detailed search strategies for each database were as follows: a) PubMed/Medline: (intermittent-fasting OR maternal-intermittent-fasting OR fasting-effects OR time-restricted-feeding OR time-restricted-eating OR intermittent-fasting-protocols OR fasting-regimens OR fasting-periods OR prolonged-fasting) AND (fertility OR prolificity OR fertilization-rate OR pregnancy-outcomes OR pregnant OR reproductive-health OR pregnancy-health OR ovulation OR conception OR pregnancy OR pregnancy-results OR pregnancy-impacts OR pregnancy-effects OR IVF OR in-vitro-fertilization OR IVF-results OR IVF-outcomes OR pregnancy-complications OR infertility OR IVF-infertility OR female-fertility OR female-infertility); b) Scopus: (“intermittent fasting" OR “maternal intermittent fasting" OR “fasting effects" OR “time restricted feeding" OR “time restricted eating" OR “intermittent fasting protocols" OR “fasting regimens" OR “fasting periods" OR “prolonged fasting") AND (fertility OR prolificity OR “fertilization rate" OR “pregnancy outcomes" OR pregnant OR “reproductive health" OR “pregnancy health" OR ovulation OR conception OR pregnancy OR “pregnancy results" OR “pregnancy impacts" OR “pregnancy effects" OR IVF OR “in vitro fertilization" OR “IVF results" OR “IVF outcomes" OR “pregnancy complications" OR infertility OR “IVF infertility" OR “female fertility" OR “female infertility") and c) Cochrane Library: (Intermittent AND fasting OR maternal AND intermittent AND fasting OR fasting AND effects OR time AND restricted AND feeding OR time AND restricted AND eating OR intermittent AND fasting AND protocols OR fasting AND regimens OR fasting AND periods OR prolonged AND fasting) AND (Fertility OR prolificity OR fertilization AND rate OR pregnancy AND outcomes OR pregnant OR reproductive AND health OR pregnancy AND health OR ovulation OR conception OR pregnancy OR pregnancy AND results OR pregnancy AND impacts OR pregnancy AND effects OR IVF OR in AND vitro AND fertilization OR IVF AND results OR IVF AND outcomes OR pregnancy AND complications OR infertility OR IVF AND infertility OR female AND fertility OR female AND infertility).

### 2.2. Inclusion and exclusion criteria

To determine the eligibility of studies, the Population-Intervention-Comparison-Outcome-Studies-Timeliness (PICOST) framework [17] was employed. Each component of PICOST corresponds to specific inclusion and exclusion criteria as follows: a) Population (P): Studies involving women undergoing intermittent fasting were included; b) Intervention (I): Intermittent fasting and its impact on fertility; c) Comparison (C): Studies evaluating fertility outcomes in women who did not follow intermittent fasting protocols; d) Outcome (O): Studies reporting on the impact of intermittent fasting on fertility outcomes; e)

Study Design (S): Inclusion was restricted to primary research studies and f) Timeliness (T): Studies published between November 8, 2014, and November 8, 2024 were included to ensure relevance. Research conducted outside this time frame was excluded.

### 2.3. PRISMA process

The Flow diagram of the PRISMA selection process is illustrated in Fig. 1.

### 2.4. Identification

The literature search was conducted across PubMed/Medline, Scopus, and the Cochrane Library electronic databases. A total of 402 records were initially identified through the search process. Specifically, 229 records were retrieved from PubMed/Medline, 136 from Scopus, and 37 from the Cochrane Library.

### 2.5. Screening

To ensure rigor in the selection process, duplicate records were first removed. Upon examination of the dataset, 81 duplicate entries were identified and subsequently removed, yielding a final count of 321 unique records. These records were then screened for relevance by reviewing their titles and abstracts. Articles unrelated to the topic—specifically the impact of intermittent fasting on fertility and pregnancy—were excluded at this stage.

After this initial screening process, 312 articles were excluded as they did not meet the inclusion criteria. Consequently, 9 articles were considered eligible for full-text evaluation.

### 2.6. Eligibility and Inclusion

At the next stage, efforts were made to retrieve the full text of the 9 selected studies. All 9 articles were successfully retrieved. Upon further evaluation, 7 articles were excluded because they did not constitute primary research. As a result, the number of eligible studies was reduced to 2.

To ensure comprehensive coverage, an additional relevant article was identified through reference list searches, bringing the total number of studies included in the systematic review to 3.

### 2.7. Quality assessment of included studies

The quality of the included studies was independently evaluated by two reviewers using the Caldwell framework [18]. This framework systematically assesses the methodological rigor of research across critical domains, including a) Study Design; b) Sample Size; c) Measurement Methods; d) Data Analysis, and e) Identification of Limitations.

The quality assessment is provided in Supplementary File 1.

### 2.8. Data extraction

From the selected studies, the following variables were extracted to ensure a comprehensive analysis and synthesis of the findings: a) First Author: The name of the primary author of the study; b) Year of Publication: The year in which the study was published; c) Type of Research: The research design (e.g., randomized controlled trial, observational study); d) Sample Size for Target Population: The specific sample size related to the population of interest; e) Overall Sample Size: The total number of participants included in the study; f) Measurement and Data Collection Methods: The tools, instruments, and processes used to gather the data; g) Comparison Group (if applicable): Whether a comparison or control group was included in the study; h) Key Findings: The primary results and outcomes reported in the study; i) Specific Findings Regarding the Research Question: Results relevant to the research question, specifically regarding childbirth methods; j) Follow-up with the Sample (if applicable): Whether follow-up data collection occurred and details of such efforts; k) Limitations: The reported limitations and

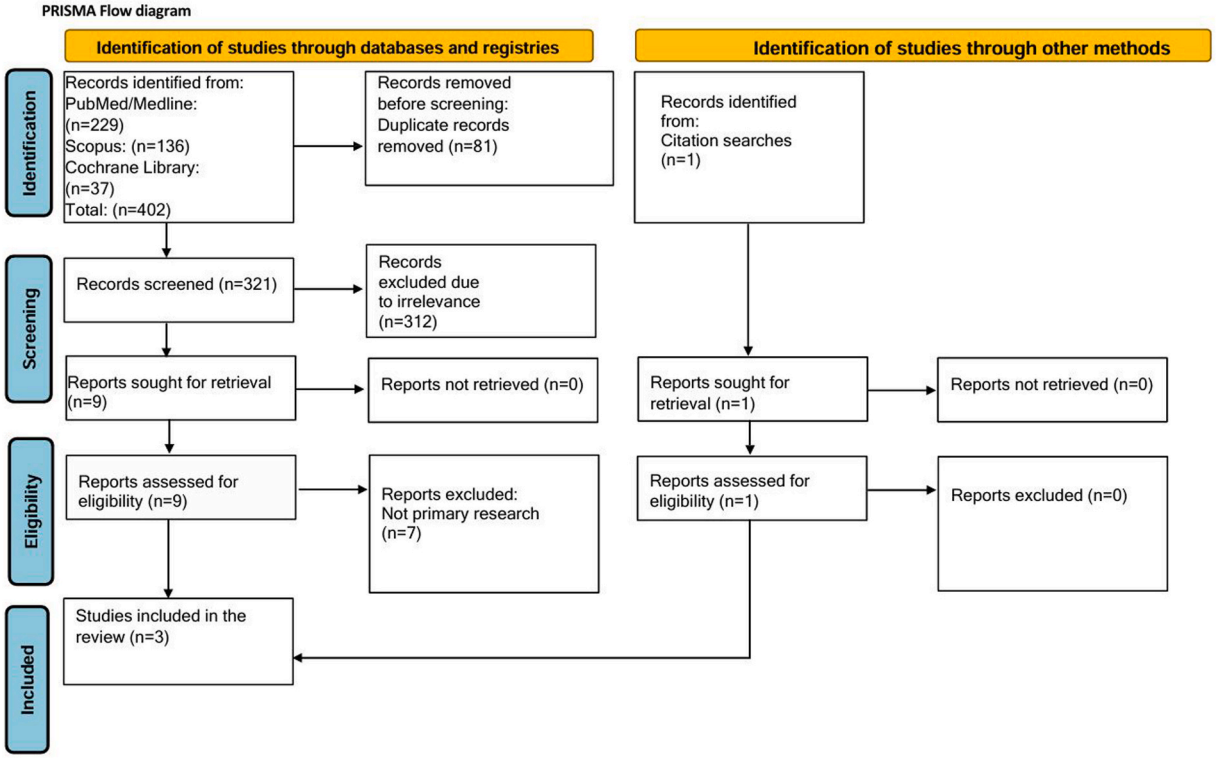


**Fig. 1.** PRISMA flowchart illustrating the study selection process.

**Table 1**
Summary of the study characteristics.

| First Author | Title | Year | Journal | Country | Type of Research | Participants | Focus Group | Measurement and Data Collection | Comparison Group | Measured Outcome | Key Findings | Specific Fertility Findings | Follow-up | Study Limitations |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Chunzhu Li | Eight-hour time-restricted feeding improves endocrine and metabolic profiles in women with anovulatory polycystic ovary syndrome [19] | 2021 | Journal of Translational Medicine | China | Prospective cohort study | 18 women with PCOS, 18–31 years, BMI ≥24 kg/m2 | 18 women with PCOS, 18–31 years, BMI ≥24 kg/m2 | Clinical trial (6 weeks) | None | TRF (8-h): body weight, BMI, BFM, BF%, VFA, TT, SHBG, FAI, FINS, HOMA-IR, AUCIns, AUCGlu, ALT, hsCRP, IGF-1 | ↓ body weight, BMI, BFM, BF %, VFA, FINS, AUCIns, HOMA-IR, hsCRP, ALT; ↑ IGF-1; menstrual cycle irregularities improved | Improvement in menstrual irregularities; ↑ SHBG, ↓ TT, FAI; unchanged LH, FSH, LH/FSH | None | Non-randomized, small sample size, short duration (6 weeks), non-standardized diets, adherence issues |
| Bihter Senem Feyzioglu | Eight-Hour Time-Restricted Feeding: A Strong Candidate Diet Protocol for First-Line Therapy in Polycystic Ovary Syndrome [20] | 2023 | Nutrients | Turkey | Retrospective study | 63 women with PCOS, TRF as first-line therapy | 63 women with PCOS, TRF as first-line therapy | 6-week TRF program as first-line therapy | None | Anthropometric indices, insulin resistance, inflammatory markers, lipid profile, reproductive hormones | ↓ AMH, FSH, LH, E2, PRL, total & free testosterone, DHEA-S, FAI; ↑ SHBG | Improvement in reproductive hormone levels; ↑ SHBG, ↓ AMH, FSH, LH | None | Small sample size, no control group, short duration (6 weeks), limited exclusion criteria, lack of inflammatory parameter assessment |
| Sepide Talebi | The effects of time-restricted eating alone or in combination with probiotic supplementation in comparison with a calorie-restricted diet on endocrine and metabolic profiles in women with polycystic ovary syndrome: A randomized clinical trial [21] | 2024 | Wiley | Iran | Randomized clinical trial | 90 women, 18–40 years, BMI 25–35 kg/m2 with PCOS | 90 women, 18–40 years, BMI 25–35 kg/m2 with PCOS | Parallel, double-blind, placebo-controlled clinical trial (8 weeks) | 30 women with calorie-restricted diet and placebo supplementation | Body weight, hirsutism, acne, insulin resistance, safety and side effects, menstrual cycle, gonadal parameters | ↓ AMH in TRE (14:10) group with probiotics; menstrual regularity improved across all groups | No significant differences in metabolic, menstrual, or gonadal parameters | None | Self-reported compliance, physical activity self-reported, adherence issues with 10-h TRE, short duration, limited participants |

potential biases in the study methodology; l) Journal of Publication: The scientific journal where the study was published; m) Country of Study: The geographical location where the research was conducted.

## 3. Results

Three scientific articles were analyzed to examine the impact of IF on fertility [19–21].

The studies were conducted in various countries, including China (n = 1), Turkey (n = 1), and Iran (n = 1).

Table 1 summarizes the key points of the three reviewed studies.

**ADF**: Alternate-Day Fasting; **ALT**: Alanine Aminotransferase; **AMH**: Anti-Müllerian Hormone; **AUCIns**: Area Under the Curve for Insulin; **AUCGlu**: Area Under the Curve for Glucose; **BF%**: Body Fat Percentage; **BFM**: Body Fat Mass; **BMI**: Body Mass Index; **DHEA-S**: Dehydroepiandrosterone Sulfate; **E2**: Estradiol; **FAI**: Free Androgen Index; **FINS**: Fasting Insulin; **FSH**: Follicle-Stimulating Hormone; **HOMA-IR**: Homeostatic Model Assessment of Insulin Resistance; **hsCRP**: High-Sensitivity C-Reactive Protein; **IGF-1**: Insulin-Like Growth Factor 1; **IF**: Intermittent Fasting; **IVF**: In Vitro Fertilization; **LH**: Luteinizing Hormone; **PCOS**: Polycystic Ovary Syndrome; **PRL**: Prolactin; **SHBG**: Sex Hormone-Binding Globulin; **TRE**: Time-Restricted Eating; **TRF**: Time-Restricted Feeding; **TT**: Total Testosterone; **VFA**: Visceral Fat Area.

The findings from the included studies indicate that IF exerts a substantial and beneficial effect on menstrual cyclicity and reproductive hormones, both of which are directly correlated with fertility.

### 3.1. Menstrual cycle improvements

Regarding menstrual irregularities, 73.3 % of women (11 out of 15) showed improvements in menstrual cycle abnormalities following an 8-h TRF protocol [19]. Similarly, in another study, menstrual regularity improved across all intervention groups, with a 33.3 % improvement observed in the group adhering to TRF with placebo supplementation, and a higher rate of 40 % reported in the group following TRF combined with daily probiotic intake [21].

### 3.2. Anti-Müllerian Hormone (AMH)

A significant reduction in AMH levels was observed in the group following a 14:10 TRF protocol combined with probiotics [19]. This finding is corroborated by another study, which also reported a significant decrease in AMH levels among women following TRF [20].

### 3.3. FSH and LH levels

Regarding gonadotropic hormones, which play a key role in reproductive health, one study noted reductions in follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels [18]. In contrast, another study reported no significant changes in FSH, LH, or the LH/FSH ratio following a 6-week TRF intervention [17].

### 3.4. Sex hormone-binding globulin (SHBG)

SHBG levels, which regulate the bioavailability of androgens, showed a 2 % increase following the TRF protocol [19]. This finding is consistent with results from another study, which also reported elevated SHBG levels [20].

### 3.5. Testosterone levels

A notable 9 % decrease in total testosterone (TT) was observed, indicating a reduction in overall androgen levels [19]. Similar reductions in both total and free testosterone were reported in a separate study, further supporting the positive effects of TRF on androgen regulation [20].

### 3.6. Free androgen index (FAI)

The free androgen index (FAI), which reflects the biologically active androgens in the body, showed a significant reduction in one study [20]. In another study, FAI levels were reduced by 26 %, further highlighting the potential of TRF in reducing hyperandrogenism [19].

### 3.7. Estradiol (E2) and prolactin

Estradiol (E2), the primary estrogen responsible for reproductive health, and prolactin, a hormone linked to lactation that can influence reproductive function, both showed a reduction following the TRF intervention [20].

### 3.8. DHEA-S levels

Finally, the levels of dehydroepiandrosterone sulfate (DHEA-S), a steroid hormone produced by the adrenal glands and associated with androgen activity, were also significantly reduced [20].

## 4. Discussion

The menstrual cycle and reproductive hormones are critical factors for fertility and the overall physiological function of the body. Consequently, any changes in these hormone levels directly influence reproductive capacity. This study represents the first systematic review investigating the association between IF and fertility. The findings from this review demonstrate significant positive outcomes on hormonal regulation and menstrual irregularities, particularly improving reproductive health among women with PCOS [19–21].

Several animal studies have reported positive effects of intermittent fasting, such as improved follicular development, oocyte maturation, and overall offspring health, particularly in obese mice [22]. IF not only enhances ovulation frequency and increases follicle numbers but also strengthens the meiotic activity of oocytes and embryonic development. These benefits extend to both nuclear and cytoplasmic maturation of maternal-aged oocytes [8]. Moreover, time-restricted feeding (TRF), which involves equal caloric intake within a defined window, has been found to prevent obesity-related complications [23].

The current findings suggest that TRF can restore hormonal balance, thereby improving menstrual regularity and reproductive health. Specifically, all three studies included in this review highlight reductions in androgen levels and AMH levels, alongside an increase in SHBG production [19–21]. However, further research is needed to elucidate the effects of intermittent fasting on FSH and LH, which are pivotal for menstrual cycle regulation and reproduction. While one study reported reductions in FSH and LH [20], another found no significant changes in these hormone levels [19].

For overweight or obese women, as well as those with PCOS, both the 5:2 diet and TRF have shown significant reductions in androgenic markers such as testosterone and FAI, while simultaneously increasing SHBG levels. These changes improve menstrual cycle regulation and fertility outcomes [24]. Existing evidence indicates that IF can effectively address hyperandrogenism in women with PCOS, reducing testosterone and FAI levels while increasing SHBG, thereby improving fertility and menstrual regularity [25].

Cumulative findings suggest that TRF or TRE, either as a standalone intervention or combined with probiotic supplementation, leads to reductions in body weight and body mass index (BMI) among women with PCOS. Both dietary interventions—TRE and calorie-restricted diets—demonstrated equivalent efficacy in weight loss, indicating no superiority of one approach over the other [21]. Furthermore, studies concur that TRE positively influences insulin resistance, which is a key factor in the pathophysiology of PCOS [19–21]. The observed improvements in menstrual regularity and reductions in androgen levels can be attributed to enhanced insulin sensitivity during fasting periods,

which reduces hyperinsulinemia—a primary driver of ovarian androgen production. Furthermore, aligning feeding windows with circadian rhythms may optimize endocrine function, as circadian disruptions have been linked to menstrual irregularities and hormonal imbalances [26].

Therefore, TRE emerges as a promising first-line therapeutic strategy for PCOS management [19]. These findings position IF, particularly TRF, as a practical and non-invasive alternative to conventional pharmacological treatments, such as metformin or clomiphene, which are often associated with side effects. By improving metabolic parameters like insulin resistance and hyperandrogenism, TRF directly targets the core pathophysiology of PCOS, presenting a sustainable first-line strategy for long-term reproductive health improvements.

This systematic review provides a comprehensive synthesis of the current evidence on the effects of IF, particularly TRF, on reproductive and metabolic outcomes in women with PCOS. The study highlights the emerging role of IF as a practical and non-invasive intervention, addressing critical aspects of PCOS pathophysiology, such as hyperandrogenism, insulin resistance, and menstrual irregularities. By consolidating findings from recent studies, the review offers valuable insights into the efficacy of TRF in improving fertility-related outcomes, which have been understudied in comparison to pharmacological interventions. Additionally, the study incorporates a robust methodological approach following PRISMA guidelines and identifies key areas requiring further investigation.

While this systematic review provides meaningful insights, several limitations must be acknowledged. The inclusion of only three studies with small sample sizes (18–90 participants) limits the generalizability of the findings and raises concerns about the robustness of the conclusions. Small sample sizes reduce statistical power and increase the risk of Type II errors, potentially overlooking significant effects. Another notable limitation is the heterogeneity in study designs, including variations in fasting protocols, participant demographics, and the absence of control groups in some studies. Differences in fasting durations, dietary adherence, and baseline characteristics of participants may contribute to inconsistent results and complicate the synthesis of findings. Such variability underscores the challenges in deriving unified conclusions and highlights the need for future studies to adopt standardized protocols and include control groups to enhance comparability and the reliability of outcomes. Self-reported adherence to TRF protocols may introduce bias, as compliance with fasting regimens can vary. The results of the Caldwell framework's quality assessment highlight key methodological limitations of the included studies, such as small sample sizes, limited use of randomization, and the absence of control groups. These factors reduce confidence in the findings and highlight the need for caution when interpreting the results. For instance, non-randomized designs may introduce selection bias, and short intervention durations limit insights into the long-term efficacy of intermittent fasting. A critical limitation of the reviewed studies is their short duration, ranging from 6 to 8 weeks. While these studies provide valuable insights into the immediate effects of time-restricted feeding (TRF) on metabolic and reproductive outcomes in women with PCOS, they do not address the sustainability or long-term impacts of these interventions. The absence of long-term follow-up data limits the ability to assess whether the observed improvements in hormonal balance, insulin sensitivity, and menstrual regularity persist over extended periods. Future research should prioritize longitudinal studies with extended follow-up to evaluate the durability of these benefits and explore potential challenges in maintaining adherence to TRF protocols over time. Finally, most studies did not include control groups or standardize dietary intake outside the fasting windows, potentially confounding the observed outcomes.

The findings of this review have significant clinical implications for the management of PCOS. TRF emerges as a promising, cost-effective, and patient-friendly alternative to conventional treatments such as metformin and clomiphene, which are often associated with adverse side effects and low adherence. By improving insulin sensitivity, reducing hyperandrogenism, and enhancing menstrual regularity, TRF addresses the core metabolic and reproductive challenges of PCOS. Clinicians can consider recommending TRF as a first-line lifestyle intervention for women with PCOS, particularly those who are overweight or insulin-resistant. Importantly, TRF's ability to align feeding schedules with circadian rhythms provides an additional mechanism for optimizing endocrine function, further supporting its clinical utility.

Advancing IF, particularly TRF, as a standardized therapeutic intervention for PCOS necessitates comprehensive research across multiple essential domains. Future studies must address these pivotal areas to establish the efficacy of this approach. Large-scale, well-powered randomized controlled trials (RCTs) involving diverse populations are essential to validate the efficacy and safety of TRF protocols. Long-term follow-up studies are needed to assess the sustained effects of TRF on reproductive hormones, menstrual regularity, and fertility outcomes over extended periods. Standardized fasting regimens across studies will be crucial to improve the comparability and reproducibility of results. Additionally, mechanistic studies exploring the effects of TRF on circadian rhythms, insulin signaling pathways, and ovarian function will provide deeper insights into its physiological benefits. Research should also investigate the synergistic effects of TRF when combined with other lifestyle interventions, such as physical activity or dietary supplementation, to optimize PCOS management. Finally, evaluating the feasibility, acceptability, and long-term adherence to TRF in real-world clinical settings is necessary to facilitate its practical implementation as a sustainable intervention for improving reproductive and metabolic outcomes in women with PCOS.

## 5. Conclusions

In conclusion, intermittent fasting, particularly TRF, demonstrates promising benefits in improving reproductive and metabolic parameters in women with PCOS. This systematic review highlights that TRF effectively reduces hyperandrogenism, as evidenced by decreased testosterone and free androgen index levels while increasing SHBG production. Improvements in menstrual regularity, reductions in AMH, and enhanced insulin sensitivity further underscore TRF's potential as a sustainable, non-invasive intervention for managing PCOS. However, the small sample sizes, short durations, and methodological variability across studies emphasize the need for larger, well-designed randomized controlled trials with long-term follow-up to confirm these findings. By addressing core pathophysiological mechanisms, TRF emerges as a practical first-line strategy to improve fertility outcomes and metabolic health in women with PCOS, offering an alternative to conventional pharmacotherapy.

## CRediT authorship contribution statement

**Maria Velissariou:** Writing – original draft, Software, Investigation, Data curation. **Chrysoula Rozalia Athanasiadou:** Methodology, Investigation. **Athina Diamanti:** Visualization, Software. **Aikaterini Lykeridou:** Validation. **Antigoni Sarantaki:** Writing – review & editing, Visualization, Supervision.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.metop.2024.100341.

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