

Time-Restricted Feeding in Women With Polycystic Ovary Syndrome and Insulin Resistance: Metabolic Effects, Dynamic Adherence, and Longitudinal Weight Response

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Abstract

Background

Time-restricted feeding (TRF) may provide metabolic benefits for women with polycystic ovary syndrome (PCOS), but longitudinal adherence patterns and their associations with clinical outcomes remain unclear. We characterized TRF adherence over time and examined its relationships with body weight and metabolic and reproductive outcomes.

Methods:

Thirty-six PCOS patients with hyperinsulinemic-euglycemic clamp-confirmed IR underwent a 20-week 8-h TRF (30 completed). Anthropometric, metabolic, reproductive endocrine, and mental health outcomes were assessed before and after the intervention, TRF adherence was recorded weekly. Segmented regression assessed temporal adherence patterns, and linear mixed-effects models evaluated associations between adherence and weight trajectories. Participants subsequently entered a 1-year unsupervised follow-up.

Results

TRF significantly reduced body weight (-8.42%) and improved insulin sensitivity (elevated GDR, decreased HOMA-IR). Menstrual regularity improved in 83.3%, optimized reproductive hormones (increased SHBG; decreased TT, FAI, LH, LH/FSH and AMH). Improvements were also observed in CRP, hepatic metabolic burden (ALT, AST, GGT, TC, TG, LDL-C) and potentially anxiety, depression, and sleep quality. Mean adherence was 5.45 ± 0.74 days/week. A change point occurred at week 11; adherence was stable beforehand (slope, -0.019 days/week; $P=0.265$) but declined thereafter (-0.137 days/week; $P<0.001$). Greater weekly adherence was associated with more favorable weight trajectories (week-by-adherence $\beta=-0.0368$ kg/week per additional adherent day; 95% CI -0.0503 to -0.0234; $P<0.001$), with consistent sensitivity analyses. Associations between mean adherence and changes in several metabolic or reproductive outcomes were not evident. During follow-up, 11 participants continued TRF, and three with pregnancy intentions conceived spontaneously and delivered at term. No significant adverse events occurred.

Conclusions

TRF improved weight, insulin sensitivity, metabolic parameters, and reproductive endocrine profiles in PCOS with IR. Adherence varied over time, and greater weekly adherence was associated with favorable weight trajectories. Long-term TRF management should emphasize adherence monitoring and support. Larger controlled studies should confirm long-term metabolic and reproductive benefits.

Trial registration Chinese Clinical Trial Registry, ChiCTR2300077501, registered November 10, 2023,

<https://www.chictr.org.cn/bin/project/edit?pid=196341>

Background

Polycystic ovary syndrome (PCOS) is one of the most common endocrine-metabolic disorders in women of reproductive age and is frequently accompanied by metabolic abnormalities and reproductive dysfunction(1). Lifestyle modification remains the cornerstone of first-line management, particularly for those who are overweight or have metabolic abnormalities(2). Insulin resistance (IR) is a central pathophysiological feature of PCOS, approximately 75% of lean women and 95% of women with obesity, and contributes substantially to both metabolic and reproductive dysfunction(3). Although the homeostatic model assessment of insulin resistance (HOMA-IR) is commonly used in clinical practice to evaluate IR, the hyperinsulinemic-euglycemic clamp remains the reference standard for the direct assessment of insulin sensitivity(4). Therefore, dietary strategies that can improve metabolic health while remaining sustainable over time are of particular clinical relevance for women with PCOS and IR.

Time-restricted feeding (TRF) is a form of intermittent fasting characterized by a restricted daily eating window, with or without concomitant caloric restriction.

Early studies in women with PCOS reported reductions in body weight and insulin resistance, along with favorable changes in hyperandrogenism following short-term TRF interventions. Subsequent randomized trials have further investigated this approach; however, the patterns and magnitude of benefit have varied across studies.

Talebi et al. reported that early TRF offered no additional weight or metabolic benefits over caloric restriction(5). However, a 6-month randomized trial found that 6-h TRF without caloric restriction achieved weight loss comparable to strict caloric restriction, while significantly improving IR and hyperandrogenemia(6). A 16-week randomized controlled trial showed that TRF plus a calorie-restricted diet yielded greater weight loss and metabolic improvements than caloric restriction alone(7). Floyd et al. reported that 6-h TRF effectively reduced weight and improved glycemic parameters in women with PCOS without prescribed dietary changes(8). Another randomized controlled trial found that both early and mid-day TRF improved glycemic control and reduced adiposity(9).

Current research on TRF in PCOS has largely focused on intervention efficacy, whereas the temporal pattern of adherence and its relationship with longitudinal treatment response remain insufficiently characterized. To address this gap, we enrolled women with PCOS and IR confirmed by the hyperinsulinemic-euglycemic clamp and prospectively recorded weekly adherence during a 20-week TRF intervention. The principal analyses were designed to (1) characterize the temporal trajectory of TRF adherence and (2) examine the association between weekly adherence and longitudinal body-weight change. Pre–post changes in metabolic and reproductive endocrine measures, and participant-level associations between mean adherence and selected clinical changes, were treated as supportive or exploratory analyses.

Methods

Participants

Participants were recruited from outpatients with PCOS and IR at the Department of Endocrinology and Metabolism, Affiliated Hospital of Zunyi Medical University, between November 2023 and November 2025. The inclusion criteria were: (1) age 18–40 years; (2) diagnosis of PCOS based on the Rotterdam diagnostic criteria; (3) diagnosis of IR confirmed by a glucose disposal rate (GDR) < 6.0 mg/kg/min as assessed by the euglycemic-hyperinsulinemic clamp test. The exclusion criteria were: (1) presence of other endocrine disorders that may cause androgen elevation, such as androgen-secreting tumors, pituitary tumors, congenital adrenal hyperplasia, Cushing's syndrome, hyperprolactinemia, or thyroid dysfunction; (2) use of medications that improve insulin resistance (e.g., metformin, pioglitazone) within the past 3 months; (3) use of medications that regulate hormone secretion within the past 3 months; (4) confirmed pregnancy or lactation; (5) use of weight-loss medications (e.g., semaglutide, liraglutide) within the past 3 months; (6) body weight fluctuation > 5% within the past 3 months.

Study design

This study was approved by the Ethics Committee of the Affiliated Hospital of Zunyi Medical University (KLL-2023-483). This was a prospective single-arm intervention study with a pre–post design and was registered in the Chinese Clinical Trial Registry (ChiCTR2300077501). The study was conducted in accordance with the Declaration of Helsinki and its later amendments, and written informed consent was obtained from all participants. Enrollment data included general characteristics, menstrual and reproductive history, medical history, and questionnaire assessments. Anthropometric measurements were obtained at enrollment and repeated immediately before initiation of the 20-week TRF intervention. Enrollment measurements are presented in Table 1 to characterize the completer cohort, whereas pre-intervention measurements were used as baseline values for all pre–post analyses. During the TRF intervention period, participants adhered to a daily eating window from 8:00 AM to 4:00 PM, with only water permitted outside of this period. Total daily caloric intake was restricted to 1200–1500 kcal. Participants were required to upload photographs of their meals online for documentation and calorie assessment. A TRF-adherent day was defined as a day on which all caloric intake occurred within the prespecified 8-h eating window; weekly adherence was calculated as the number of adherent days per week. Participants were instructed to measure their body weight at home every Monday morning after waking and voiding, in a fasting state, wearing light clothing and no shoes, and using the same household scale throughout the intervention whenever possible. Supervisors provided remote monitoring, dietary guidance aimed at maintaining a balanced dietary pattern, and adverse-event surveillance. Menstrual cyclicity and weekly TRF adherence were recorded during the intervention. After 20 weeks, baseline assessments were repeated in the morning after an overnight fast. Participants then entered a 1-year observational follow-up without active supervision, during which fertility outcomes and adverse events were recorded among those who independently chose to continue TRF.

Table 1
Characteristics of participants at enrollment who completed the 20-week intervention

Enrollment characteristics	
Total number of participants	30
Age (years)	24.9 ± 4.83
Height (cm)	156.80 ± 6.54
Weight (kg)	75.70 ± 12.34
BMI (kg/m ²)	30.83 ± 4.19
Waist Circumference (cm)	90.92 ± 8.57
Hip Circumference (cm)	104.82 ± 7.70
Waist-to-Height Ratio (WHtR)	0.58 ± 0.05
Educational Level	
Bachelor's degree or higher	25
High school	4
Junior high school or below	1
Marital Status	
Married	12
Unmarried	18
Reproductive and Menstrual History	
Gravidity (Number of Pregnancies) (Number of Pregnancies)	
Gravidity (Number of Pregnancies)	
≥2	2
1	3
0	25
Parity (Number of Deliveries)	
0	29
1	1
Menstrual Cycle	
Prolonged (> 35 days)	25

Enrollment characteristics	
Shortened (< 21 days)	4
Regular (21–35 days)	1
Smoking History	
Yes	1
No	29
Alcohol Consumption	
Yes	7
No	23
Self-Rating Anxiety Scale (SAS)	33.90 ± 5.96
Self-Rating Depression Scale (SDS)	42.23 ± 6.73
Pittsburgh Sleep Quality Index (PSQI)	6.58 ± 2.67
Glucose Disposal Rate (GDR, mg/kg/min)	3.43 ± 1.29

Blood sampling and analysis

Blood samples were collected from the antecubital vein of participants in a fasting state, both before and after TRF intervention. For the assessment of sex hormone-related indicators, fasting blood samples were obtained during the early follicular phase (menstrual cycle days 2–4) in participants with regular menstrual cycles, following an 8–12 hour fast. For those with irregular menstrual cycles or amenorrhea, fasting blood samples were collected upon transvaginal ultrasound confirmation of the absence of dominant follicles (i.e., a basal state) to evaluate baseline sex hormone levels. The levels of luteinizing hormone (LH) (mIU/mL), follicle-stimulating hormone (FSH) (mIU/mL), sex hormone-binding globulin (SHBG) (nmol/L), estradiol (E₂) (pmol/L), prolactin (PRL) (mIU/L), dehydroepiandrosterone (DHEA) (umol/L), progesterone (P) (nmol/L), total testosterone (TT) (nmol/L), anti-Müllerian hormone (AMH) (ng/mL), and fasting insulin (FINS) (μU/mL) were measured using an electrochemiluminescence immunoassay on a Beckman Coulter Unicel Dxl 800 analyzer. Total cholesterol (TC) (mmol/L) was determined by the cholesterol oxidase method, Triglycerides (TG) (mmol/L) were measured by the glycerol phosphate oxidase method, Low-density lipoprotein cholesterol (LDL-C) (mmol/L) was assessed using the direct surfactant clearance method, alanine aminotransferase (ALT) (U/L), aspartate aminotransferase (AST) (U/L) and gamma-Glutamyl Transferase (GGT) (U/L) were measured by NADH method, C-reactive protein (CRP) (mg/L) were measured separately by rate nephelometry method on ci 16200 Abbott Architect analyzer. Homeostasis model assessment-insulin resistance (HOMA-IR) was calculated according to the formula “FINS (μU/mL) × FPG (mmol/L)/22.5”. Free androgen index (FAI) (%)

was calculated according to the formula “TT (nmol/L) ×100/SHBG (nmol/L)”. Glucose disposal rate (GDR) (mg/kg/min) was assessed by the euglycemic-hyperinsulinemic clamp test.

Hyperinsulinemic-euglycemic clamp

Peripheral insulin sensitivity was assessed using a hyperinsulinemic-euglycemic clamp following an overnight fast. human regular insulin was infused at a constant rate of 40 mU/m²/min. A variable infusion of 20% dextrose was administered to maintain a target blood glucose level of 4.4–5.0 mmol/L, monitored every 5 minutes using arterialized venous blood. The glucose disposal rate (GDR, mg/kg/min) was calculated based on the mean glucose infusion rate during the steady state of the final 30 minutes of the 120-minute clamp.

Questionnaires

All participants completed the Self-rating Depression Scale (SDS), Self-rating Anxiety Scale (SAS), and Pittsburgh Sleep Quality Index (PSQI) before and after the intervention to assess depressive symptoms, anxiety symptoms, and sleep quality.

Statistical analysis

All data were subjected to the Shapiro-Wilk normality test. Data with a normal distribution were presented as the mean ± standard deviation (mean ± SD), whereas non-normally distributed data were expressed as the median (25-75th percentiles). The normality of change scores was assessed using the Shapiro–Wilk test. Paired Student’s t tests were applied for normally distributed data, and Wilcoxon signed-rank tests for non-normally distributed data, to compare parameters before and after the 20-week TRF intervention. Longitudinal TRF adherence was analyzed using segmented regression with candidate change points from weeks 4 to 17 in 0.5-week increments. Participant-specific fixed effects were included, and participant-clustered robust standard errors were used for inference. The optimal change point was selected by minimum AICc, with $\Delta AICc \leq 2$ used to define the supported range. Pre- and post-change slopes were estimated from the segmented model. Robustness was assessed using a random-intercept segmented mixed-effects model fitted by maximum likelihood. Repeated body weight was analyzed using a linear mixed-effects model including centered intervention week, centered weekly adherence, and their interaction as fixed effects, with participant-specific random intercepts and week slopes. The final model was fitted using restricted maximum likelihood, with the week-by-adherence interaction as the primary parameter of interest. To separate between-participant differences from within-participant fluctuations, weekly adherence was decomposed into participant-mean adherence and week-specific deviations from that mean; their respective interactions with week were examined in a secondary mixed-effects model. For each participant, overall adherence was defined as the mean weekly adherence across the 20-week intervention. Associations between mean adherence and changes in selected clinical outcomes were explored using Spearman rank correlations with permutation-based P

values and bootstrap 95% confidence intervals; multiple comparisons were controlled using the Benjamini–Hochberg false discovery rate procedure. Statistical analyses were performed using SPSS (version 27.0), GraphPad Prism software (version 8.0.1) and R software (version 4.6.1). All statistical tests were two-sided, with $P < 0.05$ considered statistically significant.

Results

Participants

A total of 42 participants were recruited in this study, six women were excluded: two were taking medication for menstrual regulation, two were using weight-loss drugs, and two refused to participate for work reasons. Finally, 36 participants were enrolled in the intervention. Thirty participants completed the 20-week TRF intervention. Six participants dropped out: three because of job transfers, two after one week due to intolerance, and one could not be contacted after 4 weeks (Fig. 1). The participants were aged between 19 and 40 years. All participants were confirmed to have IR by the euglycemic-hyperinsulinemic clamp test. Among them, 26 participants presented with hyperandrogenemia; 8 were overweight, and 22 were obese. 29 participants presented with menstrual disorders, including 25 with oligomenorrhea and 4 with shortened menstrual cycles. In terms of sleep and emotional status, 8 participants were identified as having poor sleep quality based on Pittsburgh Sleep Quality Index (PSQI) scores. Furthermore, based on the Self-Rating Anxiety Scale (SAS) and Self-Rating Depression Scale (SDS), none of the participants met the cut-off criteria for anxiety or depression (Table 1). During the intervention, 9 participants reported prominent hunger during the first 2 weeks, and 11 experienced gastrointestinal discomforts such as abdominal distension and constipation during the initial intervention period (weeks 1–3). No severe adverse events, such as hypoglycemia, were observed throughout the study.

Anthropometric Outcomes and Overall Weight Loss

Following the 20-week TRF intervention, the mean body weight of the 30 participants decreased significantly from a baseline of 75.70 ± 12.34 kg to 69.31 ± 11.66 kg ($p < 0.001$). The mean weight loss was 6.39 ± 3.41 kg, with an overall total weight loss (%TWL) of $8.42\% \pm 4.2\%$, meeting the criterion for clinically significant weight loss ($> 5\%$). BMI, waist circumference, hip circumference and waist-to-height ratio were all significantly decreased (all $p < 0.001$). The results are presented in (Table 2).

Table 2

Changes in Body Weight and Biochemical Indicators Before and After 20 Weeks of Intervention

WC (cm)	Pre-TRF	Post-TRF	P-value
	90.56 ± 9.31	87.07 ± 7.50	<0.001
HC (cm)	103.97 ± 8.33	102.23 ± 8.97	<0.001
WHtR	0.58 ± 0.05	0.55 ± 0.05	<0.001
Weight (kg)	75.70 ± 12.34	69.31 ± 11.66	<0.001
BMI (kg/m ²)	30.83 ± 4.19	28.09 ± 3.82	<0.001
CRP (mg/L)	2.75(1.88,5.19)	2.24(1.56,2.90)	<0.001
ALT (IU/L)	34.50(23.50,52.00)	18.50(14.00,25.00)	<0.001
AST (IU/L)	28.50 (23.25,33.75)	20.00 (16.50,23.00)	<0.001
GGT (IU/L)	24.00(18.00,38.00)	16.00(13.00,22.00)	<0.001
HDL-C (mmol/L)	1.12 ± 0.19	1.07 ± 0.16	0.159
LDL-C (mmol/L)	3.03 ± 0.77	2.82 ± 0.79	0.008
TC (mmol/L)	4.63 ± 1.18	4.42 ± 1.04	0.005
TG (mmol/L)	2.85 (2.56,3.20)	2.70 (2.38,3.03)	<0.001

WC: Waist Circumference; HC: Hip Circumference; WHtR: Waist-to-Height Ratio; BMI: body mass index; CRP: C-reactive protein; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma-glutamyltransferase; TG: triglyceride; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol;

Glucose metabolism parameters and Insulin Sensitivity

FPG, FINS, HbA1c and HOMA-IR (all $p < 0.001$) were all significantly decreased. Furthermore, the repeated euglycemic-hyperinsulinemic clamp test showed a significant improvement in the GDR ($p < 0.001$). The data are presented in Table 3.

Table 3

Comparison of FPG, FINS, HbA1C, HOMA-IR and GDR Before and After 20 Weeks of Intervention

FPG (mmol/L)	Pre-TRF	Post-TRF	P-value
(mmol/L)	5.08(4.69,5.40)	4.33(3.98,4.60)	<0.001
FINS (μU/mL)	20.80(16.85,28.27)	15.54(10.53,18.58)	<0.001
(Umol/L)			
HbA1C (%)	5.63 ± 0.64	5.20 ± 0.43	<0.001
HOMA-IR	4.74(3.57,7.02)	2.91(2.21,3.61)	<0.001
GDR (mg/kg/min)	3.43 ± 1.29	5.10 ± 1.50	<0.001
FBG: fasting blood-glucose; FINS: fasting insulin; HbA1C: Hemoglobin A1c ; HOMA-IR: homeostasis model assessment-insulin resistance; GDR: glucose disposal rate.			

Menstruation and gonadal parameters

Menstrual cycle irregularities improved in 83.3% (25/30) of participants. Regarding gonadal parameters, SHBG was significantly increased ($p<0.001$), FAI ($p<0.001$), TT ($p<0.001$), LH ($p = 0.031$), LH/FSH ($p = 0.034$) and AMH($p = 0.030$) were decreased. No significant changes were observed in FSH, P, E2, PRL and DHEA. Data are shown in Table 4.

Table 4
Comparison of sex hormone levels before and after 20 weeks of intervention.

Menstrual Cycle (day)	Pre-TRF	Post-TRF	P-value
	116.64 ± 90.9	42.83 ± 16.51	<0.001
AMH (ng/mL)	5.92(4.24,8.92)	6.07(3.59,8.67)	0.030
SHBG (nmol/L)	16.28(13.11,19.93)	22.16(18.32,29.82)	<0.001
FAI (%)	11.96 ± 6.71	7.68 ± 4.21	<0.001
TT (nmol/L)	2.00 ± 0.84	1.57 ± 0.73	<0.001
LH (mIU/mL)	12.00 (7.90,14.7)	10.20 (5.80,13.10)	0.031
FSH (mIU/mL)	5.45(4.75,6.75)	5.45(4.55,6.40)	0.418
LH/FSH	2.22 (1.53,2.82)	1.79 (1.37,2.37)	0.034
P (nmol/L)	0.54(0.35,0.90)	0.61(0.33,0.87)	0.911
E2 (pmol/L)	187.85 (147.62,231.15)	191.90 (154.78,272.17)	0.076
PRL (mIU/L)	315.40(258.62,410.15)	334.25(239.75,430.62)	0.080
DHEA (umol/L)	6.53 ± 3.12	6.34 ± 3.47	0.559
AMH: anti-Müllerian hormone; FAI: free androgen index; SHBG: sex hormone-binding globulin; FSH: follicle-stimulating hormone; LH: luteinizing hormone; TT: total testosterone; E2: estrogen; P: progesterone; PRL: prolactin; DHEA: dehydroepiandrosterone			

Biochemical metabolism parameters

Significant reductions were observed in CRP ($p<0.001$), ALT ($p<0.001$), AST ($p<0.001$), GGT ($p<0.001$), TG ($p<0.001$), TC ($p = 0.005$), and LDL-C ($p = 0.008$), There was no significant changes in HDL-C. The results are presented in Table 2.

Questionnaires

According to the results of SAS, SDS, and PSQI, although none of the participants met the diagnostic criteria for anxiety or depression, improvements in these scores and sleep quality were observed after the intervention. Data are presented in Table 5.

Table 5
Comparison of SAS, SDS, PSQI Before and After 20 Weeks of Intervention

SAS	Pre-TRF	Post-TRF	P-value
	33.90 ± 5.96	32.53 ± 5.95	0.035
SDS (Umol/L)	42.23 ± 6.73	39.47 ± 8.95	0.002
PSQI	6.58 ± 2.67	5.58 ± 2.62	0.011
SAS: Self-rating Anxiety Scale; SDS: Self-rating Depression Scale; PSQI: Pittsburgh Sleep Quality Index.			

Weekly adherence trajectory

Complete adherence data were available for 30 participants (600 participant-weeks), with a mean adherence of 5.45 ± 0.74 days/week. Segmented regression identified an optimal change point at week 11, with an AICc-supported range of weeks 9.5–11.5. Adherence was stable before the change point (slope = 0.019 days/week, 95% CI = 0.053 to 0.015; $P = 0.265$) but declined thereafter (slope = 0.137 days/week, 95% CI = 0.178 to – 0.095; $P < 0.001$), with a significant change in slope (– 0.118 days/week, 95% CI = 0.181 to – 0.054; $P < 0.001$). Sensitivity analysis using a random-intercept segmented mixed-effects model yielded the same optimal change point and similar effect estimates, supporting the robustness of the week-11 transition. (Fig. 2)

Adherence and Longitudinal Weight Loss Trajectory

Greater weekly TRF adherence was associated with a more favorable longitudinal body-weight trajectory. In the linear mixed-effects model, the week-by-adherence interaction was significant ($\beta = -0.0368$ kg/week per additional adherent day, 95% CI = 0.0503 to – 0.0234; $P < 0.001$). In the within-between decomposition model, both the week-by-participant-mean-adherence interaction ($\beta = -0.0938$; $P = 0.019$) and the week-by-within-person-deviation interaction ($\beta = -0.0351$; $P < 0.001$) were significant, supporting contributions from both between-participant adherence differences and within-participant fluctuations (Fig. 3).

Mean adherence and representative clinical changes

In the exploratory participant-level analysis, higher mean adherence showed nominal positive associations with greater GGT reduction (Spearman $\rho = 0.41$; permutation $P = 0.025$), greater WHtR reduction ($\rho = 0.39$; $P = 0.033$), and greater weight loss ($\rho = 0.37$; $P = 0.045$). FINS reduction ($\rho = 0.35$) and TG reduction ($\rho = 0.33$) were in the same direction but did not meet the nominal 0.05 threshold. Mean adherence was not materially associated with GDR increase, FPG reduction, SHBG increase, FAI reduction, or AMH change. None of the 12 associations remained statistically significant after Benjamini-Hochberg correction (Fig. 4; Supplementary Table S1).

One-Year Observational Follow-up

During the 1-year observational follow-up after the 20-week intervention, TRF was self-selected and unsupervised. Of the 30 participants who completed the initial trial, 19 resumed their habitual dietary patterns, while the remaining 11 continued TRF independently. Among these, three women with fertility intentions conceived spontaneously at 3, 12, and 32 weeks post-intervention and subsequently delivered full-term live births; all three had demonstrated high adherence during the intervention phase (mean weekly TRF frequencies: 5.75, 5.50, and 4.30 days, respectively). Of the other eight, seven maintained self-managed TRF, and one discontinued at 17 weeks owing to occupational constraints. No significant adverse events were reported throughout the extended follow-up.

Discussion

In this study, a 20-week 8-h TRF intervention was implemented in patients with PCOS and IR confirmed by hyperinsulinemic-euglycemic clamp. The intervention significantly improved body weight, insulin resistance, glucolipid metabolism, and reproductive endocrine parameters. Adherence to TRF fluctuated dynamically over the intervention period, and higher weekly adherence was associated with a more favorable longitudinal trajectory of weight loss; this association was supported by both conventional mixed-effects models and within-between decomposition models. However, improvements in certain metabolic outcomes were not significantly correlated with overall adherence. During the 1-year unsupervised follow-up, some participants voluntarily continued TRF, and spontaneous pregnancies and full-term deliveries were observed, suggesting that long-term TRF providing exploratory observations regarding reproductive outcomes. Nevertheless, further studies are warranted to validate these findings.

The findings of this study are generally consistent with previous TRF research, demonstrating that TRF can effectively reduce body weight and improve insulin sensitivity, glucolipid metabolism, and reproductive endocrine disturbances(10–12).IR and compensatory hyperinsulinemia are central to the metabolic dysfunction of PCOS; hyperinsulinemia may not only exacerbate abnormalities in glucose and lipid metabolism but also disrupt reproductive endocrine function by stimulating ovarian androgen production and reducing SHBG, thereby contributing to menstrual irregularity and infertility(2, 13, 14). Therefore, improving insulin sensitivity is an important therapeutic target in PCOS. In the present study, Using the euglycemic-hyperinsulinemic clamp test, we found that insulin sensitivity was significantly enhanced following the TRF, whereas the magnitude of improvement was not clearly associated with overall adherence, suggesting that these metabolic benefits may not be entirely dependent on adherence intensity. Beyond the effects mediated by weight loss, TRF may confer additional metabolic benefits by prolonging the daily fasting duration and improving the synchronization of food intake with circadian rhythms(15–17). However, the mechanisms underlying these effects remain to be elucidated.

One notable finding of this study was that adherence to TRF exhibited marked temporal dynamism rather than remaining a stable individual trait. The average weekly adherence was 5.45 ± 0.74 days per week. Segmented regression analysis further revealed that adherence remained relatively stable during the first

approximately 11 weeks, followed by a significant and accelerated decline thereafter, suggesting a potential period of increased vulnerability to adherence decline during which adherence begins to wane in long-term TRF interventions. As the intervention extended, maintenance of TRF might be increasingly challenged by work schedules, social obligations, and other daily life demands, thereby compounding the difficulty of sustaining compliance in the later stages. Consequently, assessing intervention exposure solely based on mean adherence or end-of-intervention adherence may obscure important temporal variations. Continuous monitoring of adherence, coupled with reinforced behavioral support during the mid-to-late intervention period, may be instrumental in sustaining long-term adherence and enhancing the overall sustainability of TRF interventions.

Previous studies of TRF have primarily focused on overall intervention efficacy(18–20). Although several studies have reported overall adherence rates or feasibility measures(21–23), the longitudinal dynamics of adherence and their relationship with weight-loss responses remain insufficiently characterized(24). In the present study, weekly TRF adherence was significantly associated with the longitudinal trajectory of body weight. Linear mixed-effects modeling showed that greater weekly adherence was associated with a steeper decline in body weight over time, with model-predicted trajectories progressively diverging across different levels of adherence. This pattern suggests that relatively modest differences in weekly adherence may accumulate over the course of a prolonged intervention and translate into distinct weight trajectories. Within-between decomposition further showed that both higher participant-level mean adherence and increases in adherence relative to an individual's own average were associated with more favorable longitudinal weight trajectories. These findings suggest that the observed adherence–weight association may not be explained solely by relatively stable differences between individuals, but may also reflect time-varying changes in adherence within individuals. Collectively, the degree to which TRF is implemented in practice may represent an important behavioral factor contributing to heterogeneity in weight-loss responses, underscoring the value of longitudinal adherence assessment and management during sustained TRF. Nevertheless, because adherence was not randomly assigned and residual confounding by time-varying factors such as total energy intake, physical activity, and other lifestyle behaviors cannot be excluded, these findings should be interpreted as associative rather than causal. Larger studies with more comprehensive assessment and control of time-varying confounders are warranted to further clarify the causal relationship between TRF adherence and weight loss.

Notably, in contrast to the relatively clear adherence–response relationship observed for body weight, improvements in several metabolic and reproductive endocrine outcomes were not significantly associated with mean TRF adherence over the 20-week intervention, suggesting that sensitivity to the degree of TRF adherence may differ across clinical outcomes. As a cumulative consequence of long-term energy balance, body weight may more directly reflect differences in adherence. By contrast, insulin sensitivity, glucose and lipid metabolism, and reproductive endocrine function may be influenced by multiple mechanisms related to TRF, including the duration and timing of fasting, circadian alignment, and changes in body weight(10, 25–27). Previous controlled studies have also shown that TRF can improve insulin sensitivity and glycemic regulation even in the absence of substantial weight loss, supporting the possibility that some metabolic effects of TRF may not be entirely mediated by weight

reduction(25, 26). Accordingly, these outcomes may not exhibit a simple linear relationship with the average number of adherent days per week. It is also possible that some metabolic responses to TRF follow threshold or nonlinear patterns, whereby benefits emerge once a sufficient level of exposure is achieved; however, this hypothesis remains to be tested. Given the modest sample size of the present study, the absence of statistically significant associations should not be interpreted as evidence that adherence is unrelated to these outcomes. Future studies incorporating more granular measures of intervention exposure, including actual fasting duration, timing of the eating window, total energy intake, and dietary composition, together with larger sample sizes, are needed to better characterize adherence–response relationships across metabolic and reproductive outcomes.

The 1-year observational follow-up provided preliminary insights into the long-term sustainability of TRF and its potential reproductive benefits. In the absence of continued guidance or supervision from the study team, 11 of the 30 participants who completed the intervention voluntarily chose to continue TRF, and most were able to maintain the regimen through self-management. This finding is consistent with previous evidence suggesting that time-restricted eating is generally feasible and acceptable over extended intervention periods, although sustained adherence may require individualized behavioral support(22). Notably, three participants who intended to conceive became pregnant spontaneously at 3, 12, and 32 weeks after completion of the intervention, respectively, and all subsequently delivered at term. Insulin resistance and compensatory hyperinsulinemia are closely intertwined with the metabolic and reproductive disturbances of PCOS, including hyperandrogenism, ovulatory dysfunction, and infertility(2, 13). Previous preliminary evidence in women with anovulatory PCOS has also suggested that TRF may improve body weight, insulin resistance, hyperandrogenemia, and menstrual regularity. Thus, the improvements in body weight, insulin sensitivity, and reproductive endocrine profiles observed with TRF may provide a biologically plausible metabolic context for recovery of reproductive function. However, continuation of TRF during follow-up was entirely self-selected, and the number of pregnancy events was small; therefore, no causal relationship between TRF and restoration of ovulation or pregnancy outcomes can be inferred. These observations should be regarded as hypothesis-generating and warrant confirmation in prospective controlled studies with prespecified reproductive outcomes, including ovulation, spontaneous pregnancy, and live birth. In addition, no significant adverse events were reported during follow-up, providing preliminary support for the long-term safety of TRF, although confirmation in larger cohorts with longer follow-up is needed.

This study has several limitations. First, the non-randomized design lacks a parallel control group, with statistical analyses restricted solely to pre- and post-intervention data. Second, the relatively small sample size and short intervention period preclude definitive conclusions regarding the long-term efficacy, safety, and potential risks of TRF. Third, the 1-year observational follow-up data were derived from a self-selected subgroup, without parallel tracking of the participants who resumed their habitual diets. This may introduce selection bias and limit the generalizability of the observed reproductive benefits. Future large-scale, randomized controlled trials with extended follow-up are required to systematically evaluate the long-term impact of TRF, as well as varying levels of adherence, on metabolic parameters, reproductive function, and quality of life in patients with PCOS.

Overall, our findings further support the potential value of TRF for improving metabolic and reproductive endocrine abnormalities in women with PCOS and insulin resistance, while also highlighting adherence as a clinically relevant, time-varying behavioral factor. Greater weekly adherence was associated with more favorable longitudinal weight trajectories, whereas improvements in several metabolic and reproductive endocrine outcomes did not show clear linear relationships with mean adherence, suggesting that adherence–response patterns may differ across clinical outcomes. These findings underscore that the clinical implementation of TRF should extend beyond simply prescribing the intervention to include longitudinal monitoring of adherence and individualized support during periods when adherence is more likely to decline. Moreover, the voluntary continuation of TRF and reproductive outcomes observed during the long-term unsupervised follow-up provide exploratory evidence regarding its potential long-term applicability. Larger prospective controlled studies incorporating more granular assessments of dietary exposure and lifestyle behaviors are needed to validate the relationships between adherence and metabolic and reproductive outcomes and to further define the role of TRF in the long-term management of PCOS.

Conclusions

TRF significantly reduced body weight and improved insulin sensitivity, metabolic profiles, and reproductive endocrine function in women with PCOS and IR. TRF adherence showed a clear time-varying pattern, and greater weekly adherence was associated with more favorable longitudinal weight trajectories. Long-term TRF management should therefore emphasize continuous adherence monitoring and support. Larger controlled studies are needed to confirm its long-term metabolic and reproductive benefits.

Abbreviations

PCOS
Polycystic ovary syndrome
TRF
Time-restricted feeding
IR
Insulin-resistance
BMI
Body mass index
FPG
fasting plasma glucose
FINS
fasting insulin
HbA1c
Hemoglobin A1c
GDR

glucose disposal rate
HOMA-IR
Homeostasis model assessment-insulin resistance
HDL-C
high-density lipoprotein cholesterol
LDL-C
Low - density lipoprotein cholesterol
TC
Total cholesterol
TG
Triglycerides
AMH
anti-Müllerian hormone
FAI
free androgen index
SHBG
sex hormone-binding globulin
FSH
follicle-stimulating hormone
LH
luteinizing hormone
TT
total testosterone
E2
estrogen
P
progesterone
PRL
prolactin
DHEA
dehydroepiandrosterone
CRP
C-reactive protein
ALT
Alanine aminotransferase
AST
Aspartate aminotransferase
GGT
gamma-glutamyltransferase
SAS

Self-rating Anxiety Scale
SDS
Self-rating Depression Scale
PSQI
Pittsburgh Sleep Quality Index.

Declarations

Ethics approval and consent to participate

All patients provided written informed consent before the beginning of the study. The study was approved by the Ethics Committee of the Affiliated Hospital of Zunyi Medical University, (reference: KLL-2023-483). This study was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments.

Consent for publication

Written informed consent has been obtained from the patients to publish this paper

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

DL and ZT: Dietary management, supervision, data analysis, data collection and writing original draft; HZ, XY, QZ and LZ: dietary management and dietary guidance; ZT, YD, HZ, YL and YY: glucose-hyperinsulinic clamp assay, QH and XL: manuscript writing and revision.

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References

1. Salari N, Nankali A, Ghanbari A, Jafarpour S, Ghasemi H, Dokaneheifard S, et al. Global prevalence of polycystic ovary syndrome in women worldwide: a comprehensive systematic review and meta-analysis. *Archives of gynecology and obstetrics*. 2024;310(3):1303-14.
2. Teede HJ, Tay CT, Laven JJE, Dokras A, Moran LJ, Piltonen TT, et al. Recommendations from the 2023 international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *European journal of endocrinology*. 2023;189(2):G43-g64.
3. Stepto NK, Cassar S, Joham AE, Hutchison SK, Harrison CL, Goldstein RF, et al. Women with polycystic ovary syndrome have intrinsic insulin resistance on euglycaemic-hyperinsulinaemic clamp. *Human reproduction (Oxford, England)*. 2013;28(3):777-84.
4. Cassar S, Misso ML, Hopkins WG, Shaw CS, Teede HJ, Stepto NK. Insulin resistance in polycystic ovary syndrome: a systematic review and meta-analysis of euglycaemic-hyperinsulinaemic clamp studies. *Human reproduction (Oxford, England)*. 2016;31(11):2619-31.
5. Talebi S, Shab-Bidar S, Moini A, Mohammadi H, Djafarian K. 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. *Diabetes, obesity & metabolism*. 2024;26(10):4468-79.
6. Corapi S, Runchey MC, Lyons J, Alonso de Leon M, Pavlou V, Lin S, et al. Time-restricted eating for body weight management in women with polycystic ovary syndrome: a randomized controlled trial. *Nature medicine*. 2026;32(6):2155-63.
7. Zheng S, Chen Y, Zheng X, Ma D, Yan X, Zhang J, et al. Time-restricted eating plus calorie-restricted diet versus calorie-restricted diet in women with polycystic ovary syndrome. *iScience*. 2025;28(11):113654.
8. Floyd R, Dyer A, Gibney J, Alawami F, Owens L, Phelan N, et al. Time-Restricted Eating to Improve Metabolic Abnormalities in Polycystic Ovarian Syndrome (TimeMAP). *Clinical endocrinology*. 2026;104(4):327-42.
9. Aminian M, Hajshafiha M, Heidari M, Daneghian S. Effect of two types of time-restricted eating on glycemic, lipid indices, and weight in women with polycystic ovary syndrome: a randomized controlled trial. *European journal of nutrition*. 2026;65(5).
10. Manoogian ENC, Chow LS, Taub PR, Laferrère B, Panda S. Time-restricted Eating for the Prevention and Management of Metabolic Diseases. *Endocrine reviews*. 2022;43(2):405-36.
11. Naous E, Achkar A, Mitri J. Intermittent Fasting and Its Effects on Weight, Glycemia, Lipids, and Blood Pressure: A Narrative Review. *Nutrients*. 2023;15(16).

12. Sukkriang N, Buranapin S. Effect of intermittent fasting 16:8 and 14:10 compared with control-group on weight reduction and metabolic outcomes in obesity with type 2 diabetes patients: A randomized controlled trial. *Journal of diabetes investigation*. 2024;15(9):1297-305.
13. Joham AE, Norman RJ, Stener-Victorin E, Legro RS, Franks S, Moran LJ, et al. Polycystic ovary syndrome. *The lancet Diabetes & endocrinology*. 2022;10(9):668-80.
14. Zhao H, Zhang J, Cheng X, Nie X, He B. Insulin resistance in polycystic ovary syndrome across various tissues: an updated review of pathogenesis, evaluation, and treatment. *Journal of ovarian research*. 2023;16(1):9.
15. Xia J, Guo W, Hu M, Jin X, Zhang S, Liu B, et al. Resynchronized rhythmic oscillations of gut microbiota drive time-restricted feeding induced nonalcoholic steatohepatitis alleviation. *Gut microbes*. 2023;15(1):2221450.
16. Marjot T, Tomlinson JW, Hodson L, Ray DW. Timing of energy intake and the therapeutic potential of intermittent fasting and time-restricted eating in NAFLD. *Gut*. 2023;72(8):1607-19.
17. Petersen MC, Gallop MR, Flores Ramos S, Zarrinpar A, Broussard JL, Chondronikola M, et al. Complex physiology and clinical implications of time-restricted eating. *Physiological reviews*. 2022;102(4):1991-2034.
18. Li C, Xing C, Zhang J, Zhao H, Shi W, He B. Eight-hour time-restricted feeding improves endocrine and metabolic profiles in women with anovulatory polycystic ovary syndrome. *Journal of translational medicine*. 2021;19(1):148.
19. Lowe DA, Wu N, Rohdin-Bibby L, Moore AH, Kelly N, Liu YE, et al. Effects of Time-Restricted Eating on Weight Loss and Other Metabolic Parameters in Women and Men With Overweight and Obesity: The TREAT Randomized Clinical Trial. *JAMA internal medicine*. 2020;180(11):1491-9.
20. Jamshed H, Steger FL, Bryan DR, Richman JS, Warriner AH, Hanick CJ, et al. Effectiveness of Early Time-Restricted Eating for Weight Loss, Fat Loss, and Cardiometabolic Health in Adults With Obesity: A Randomized Clinical Trial. *JAMA internal medicine*. 2022;182(9):953-62.
21. O'Neal MA, Gutierrez NR, Laing KL, Manoogian ENC, Panda S. Barriers to adherence in time-restricted eating clinical trials: An early preliminary review. *Frontiers in nutrition*. 2022;9:1075744.
22. Termannsen AD, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: A systematic scoping review. *Obesity (Silver Spring, Md)*. 2023;31(6):1463-85.
23. Wu B, White K, Maw MTT, Charleston J, Zhao D, Guallar E, et al. Adherence to Diet and Meal Timing in a Randomized Controlled Feeding Study of Time-Restricted Feeding. *Nutrients*. 2022;14(11).
24. O'Connor SG, Boyd P, Bailey CP, Shams-White MM, Agurs-Collins T, Hall K, et al. Perspective: Time-Restricted Eating Compared with Caloric Restriction: Potential Facilitators and Barriers of Long-Term Weight Loss Maintenance. *Advances in nutrition (Bethesda, Md)*. 2021;12(2):325-33.
25. Sutton EF, Beyl R, Early KS, Cefalu WT, Ravussin E, Peterson CM. Early Time-Restricted Feeding Improves Insulin Sensitivity, Blood Pressure, and Oxidative Stress Even without Weight Loss in Men with Prediabetes. *Cell metabolism*. 2018;27(6):1212-21.e3.

26. Jamshed H, Beyl RA, Della Manna DL, Yang ES, Ravussin E, Peterson CM. Early Time-Restricted Feeding Improves 24-Hour Glucose Levels and Affects Markers of the Circadian Clock, Aging, and Autophagy in Humans. *Nutrients*. 2019;11(6).

27. Adafer R, Messaadi W, Meddahi M, Patey A, Haderbache A, Bayen S, et al. Food Timing, Circadian Rhythm and Chrononutrition: A Systematic Review of Time-Restricted Eating's Effects on Human Health. *Nutrients*. 2020;12(12).

Figures

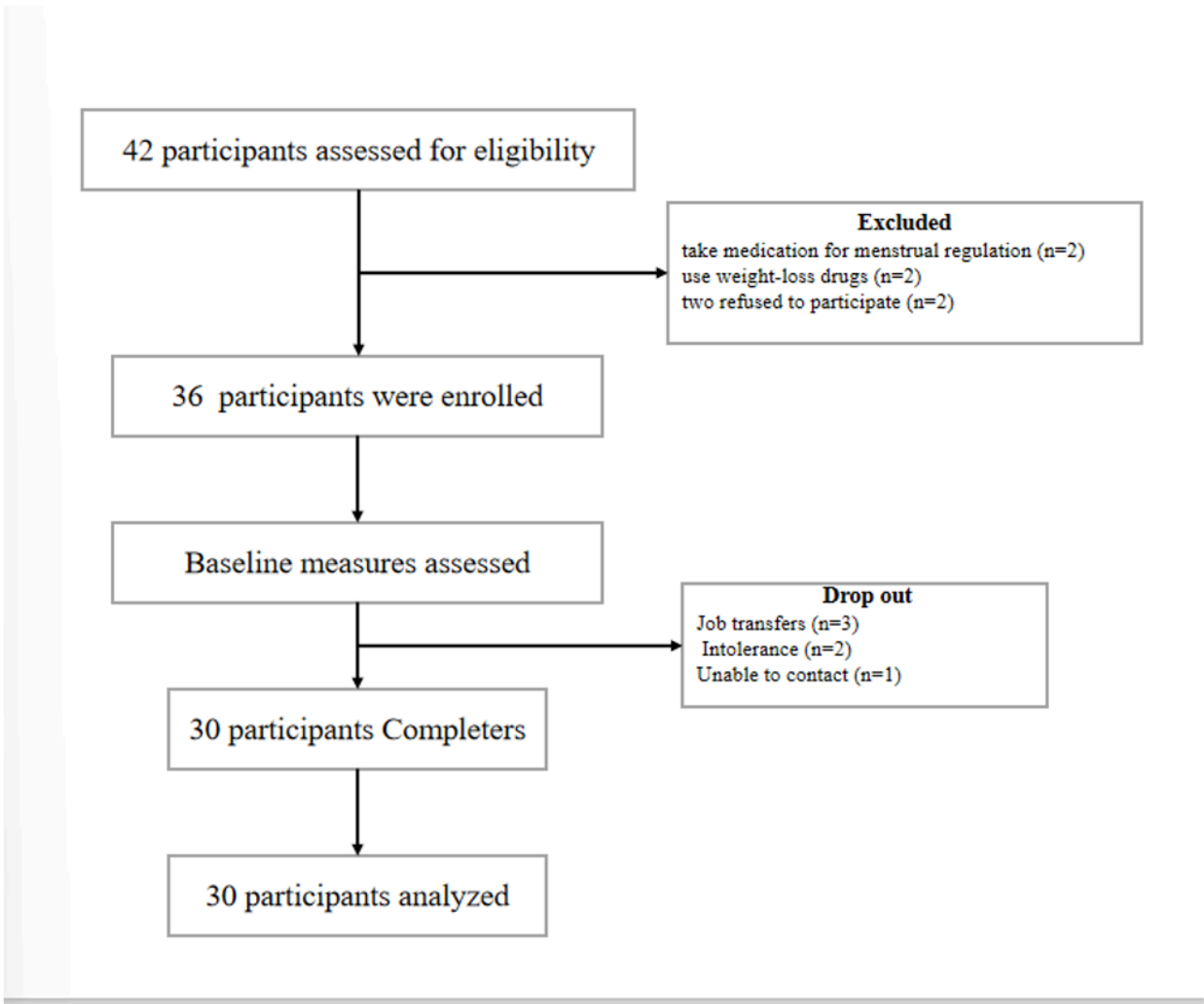


Figure 1

Flow chart from the study design

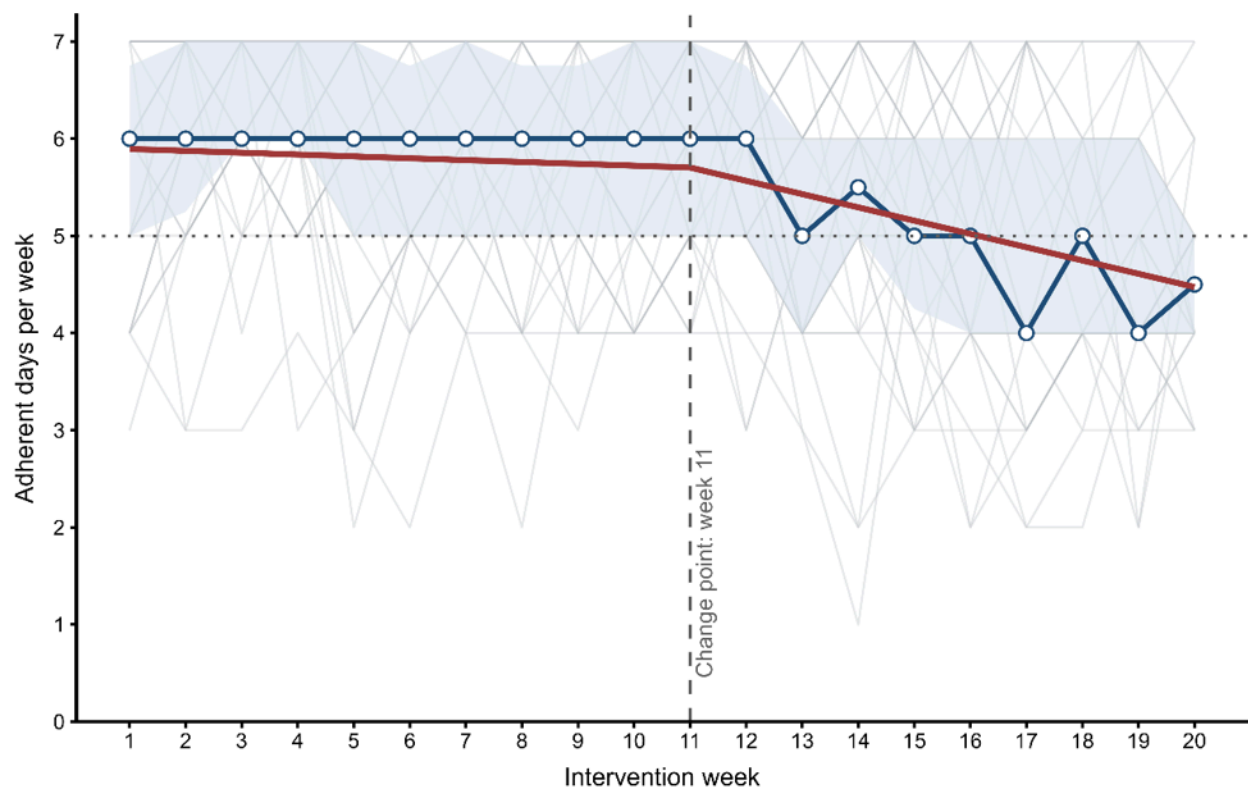


Figure 2

Weekly TRF adherence during the 20-week intervention. Individual trajectories, weekly medians, interquartile ranges, and the segmented regression fit are shown. The model-selected change point occurred at week 11.

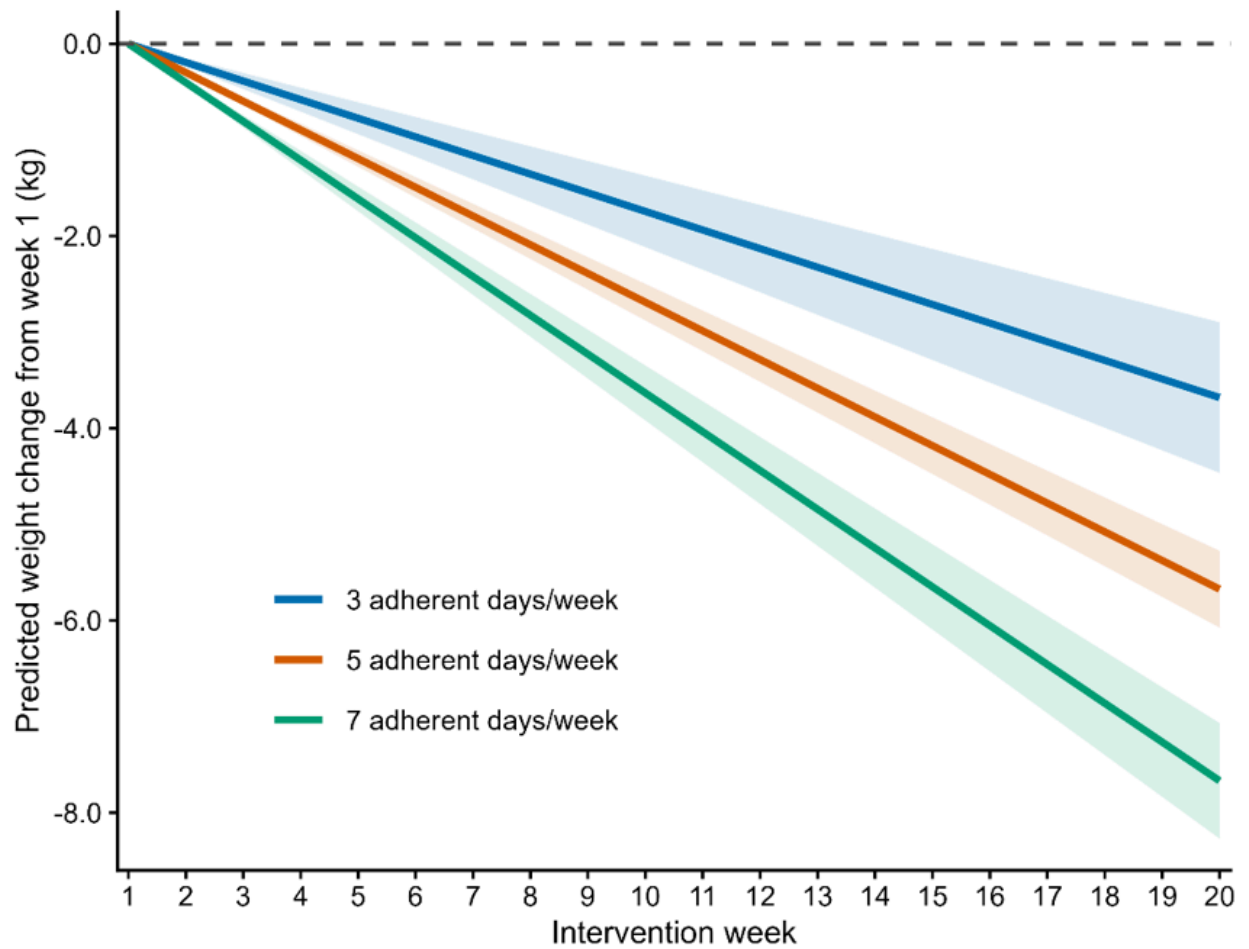


Figure 3

Model-predicted longitudinal body-weight changes at representative weekly TRF adherence levels of 3, 5, and 7 days/week. Shaded areas indicate 95% confidence intervals from the linear mixed-effects model.

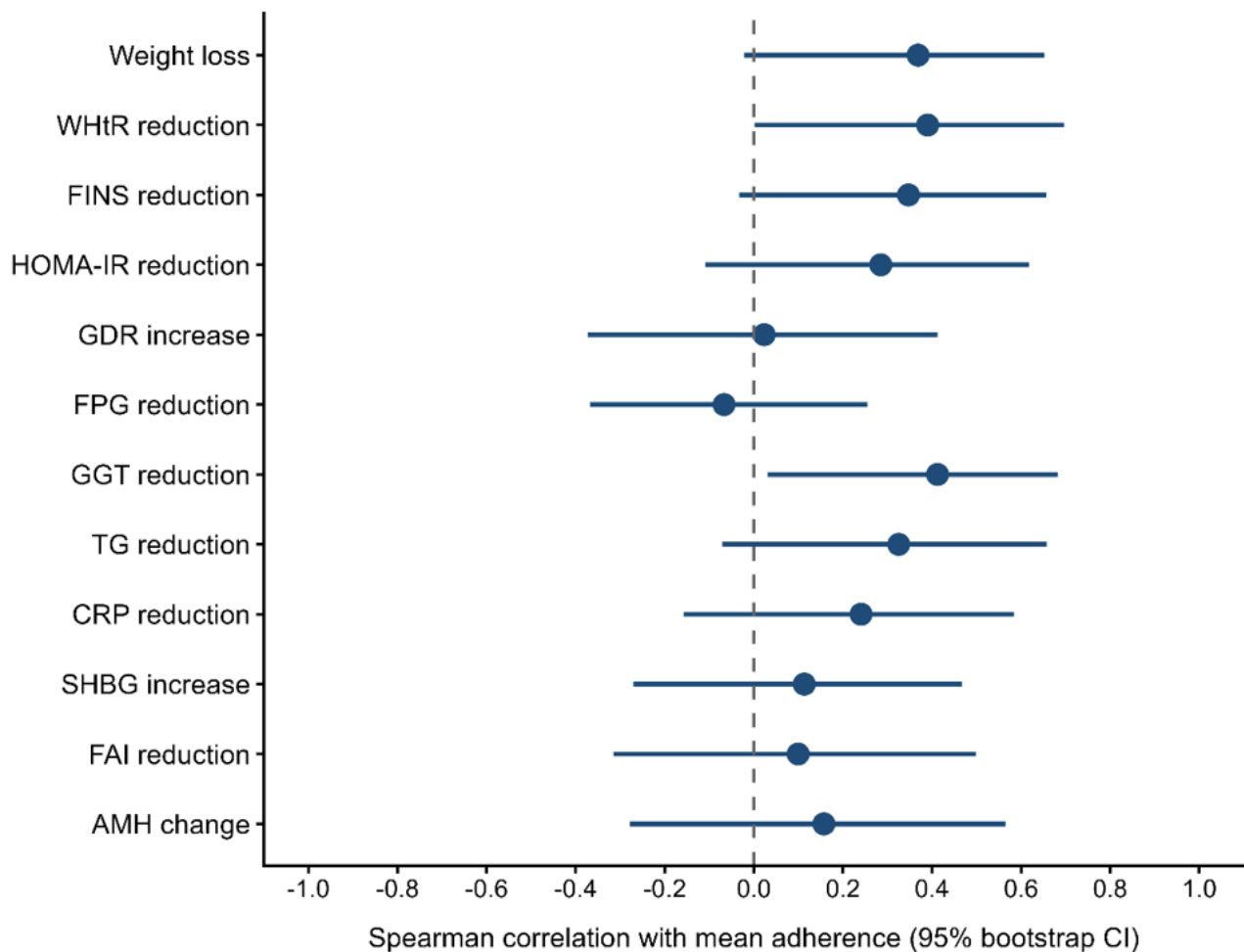


Figure 4

Associations between mean weekly TRF adherence and selected clinical changes among 30 completers. Points show Spearman correlation coefficients and horizontal bars show 95% bootstrap confidence intervals; multiplicity was controlled using the Benjamini-Hochberg procedure.

Supplementary Files

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- [SupplementaryTableS1.docx](#)