Mediterranean vs. Ketogenic Diets

Comparing Effect on Various Disease condition &
PCOS, Endometriosis & Reproductive Outcomes

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DIETARY PROFILES

Mediterranean Diet: Core Profile & Nutritional Architecture



Nutritional Architecture & Bioactive Components

Carbohydrate Quality (45–50% total energy): Unrefined, complex low-glycemic index grains, legumes, whole fruits, and vegetables rich in dietary fiber.

Fat Breakdown (35–40% total energy): Predominantly Monounsaturated Fatty Acids (MUFAs) derived from Extra Virgin Olive Oil (EVOO), supplemented by PUFAs from nuts and fish.

Protein Distribution (15–20% total energy): Moderate-to-high fish and seafood intake, low-to-moderate poultry and dairy, and minimal red/processed meats.

Micronutrient & Antioxidant Density: High intake of polyphenols (oleocanthal, hydroxytyrosol), resveratrol, carotenoids, and vitamins C and E.

DIETARY PROFILES

Ketogenic Diet: Core Profile & Ketotic Mechanics



Macronutrient Distribution & Metabolic Ketosis

Severe Carbohydrate Restriction (<5–10% total energy): Targeting <20–50g net carbohydrates per day to exhaust hepatic glycogen reserves.

Lipid-Dominant Intake (70–80% total energy): High proportion of saturated and unsaturated fats to drive hepatic mitochondrial beta-oxidation.

Moderate Protein Intake (15–20% total energy): Calibrated protein to maintain muscle mass while preventing excess gluconeogenesis from amino acid precursors.

Systemic Ketone Substrates: Hepatic production of acetoacetate, acetone, and primary signaling molecule β-hydroxybutyrate (BHB).

METHODOLOGICAL COMPARISON

Side-by-Side Physiological & Structural Comparison

Domain	Mediterranean Diet 	Ketogenic Diet 
Primary Mechanism	Anti-inflammatory pathways, polyphenol bioavailability, endothelial repair.	Hepatic ketogenesis switch, suppressed insulin, BHB signaling.
Carbohydrate Strategy	Unrefined complex carbs (High Fiber, Low Glycemic Index).	Severe restriction (<50g/day) to deplete hepatic glycogen.
Satiety Signaling	Gastric distension via dietary fiber & complex meal volume.	Direct central appetite suppression via BHB & suppressed ghrelin.
Microbiome Impact	Enhances SCFA-producing bacteria (e.g., Roseburia, Faecalibacterium).	Alters gut taxa; potential decrease in Bifidobacteria & fiber species.
Adherence & Feasibility	High long-term retention in real-world clinical and trial settings.	High short-term compliance; higher long-term attrition rate.

Important: ketosis ≠ calorie deficit. Weight loss can occur on either diet when energy intake is reduced.

Included papers at a glance

Paper 1

KD vs Mediterranean diet: obesity/metabolic outcomes meta-analysis
Rev Endocr Metab Disord • 21 Sep 2026

Paper 2

Diet macronutrient content after matched weight loss: randomized trial
Cell Metabolism • online 27 Aug 2026

Paper 3

Ketogenic diet and adult lipid profile: systematic review/meta-regression
Endocrine Practice • May 2026

Paper 4

Ketogenic diet–induced lipid changes: systematic review/meta-regression
BMC Cardiovascular Disorders • 30 Apr 2026

Paper 5

Keto-Med randomized crossover trial
American Journal of Clinical Nutrition • 2022

Paper 6

Dietary patterns in type 2 diabetes: systematic review/meta-analysis
Frontiers in Nutrition • 12 Oct 2026

Paper 1 | Direct KD vs Mediterranean meta-analysis

Xu K, Roostaee A, Safarpour Lima Z, Rohani P. Rev Endocr Metab Disord. Published 21 Sep 2026.

Research question

Among adults, does a ketogenic diet outperform a Mediterranean diet for anthropometric and metabolic outcomes?

Methods

Systematic review and meta-analysis of randomized controlled trials; database search from inception through March 2026; random-effects models.

Design caveats

Pooled estimates depend on included trial quality, diet definitions, adherence and duration; publication bias detected for LDL-C and triglycerides.

- Primary focus: weight, BMI, waist circumference, body fat, insulin and cardiometabolic biomarkers.
- Useful because it directly compares KD with Mediterranean diets, rather than comparing each with unrelated control diets.



DOI: 10.1007/s11154-026-10086-x | https://pubmed.ncbi.nlm.nih.gov/42766067/

Paper 1 | Results and interpretation

Body weight

−3.56 kg
95% CI −5.62 to −1.49

BMI

−1.86 kg/m^2
95% CI −2.73 to −0.98

Waist circumference

−4.25 cm
95% CI −7.46 to −1.04

Body fat

−2.09 percentage points
95% CI −3.98 to −0.20

No significant difference

Fasting glucose, HbA1c, LDL-C, HDL-C, triglycerides, blood pressure and CRP.

Interpretation

Anthropometric outcomes favored KD in this synthesis; several metabolic outcomes were comparable. Long-term superiority is not established.

Negative weighted mean differences are reported as KD minus Mediterranean diet and favor KD for these outcomes.

Paper 2 | Matched weight-loss randomized clinical trial

Petersen MC, Smith GI, Farabi SS, et al. Cell Metabolism. Online 27 Aug 2026.

Population

People with metabolically unhealthy obesity: obesity with prediabetes and hepatic steatosis.

Interventions

Very-low-carbohydrate ketogenic diet vs Mediterranean diet vs very-low-fat plant-forward diet.

Design strengths

Targeted ~10% weight loss; provided meals and weekly dietitian support to improve adherence and compare responses after similar weight loss.

- Outcomes included muscle and hepatic insulin sensitivity, intrahepatic triglyceride, hepatic de novo lipogenesis, HbA1c, serial glucose/insulin and lipids.
- ClinicalTrials.gov registration: NCT02706262.



Paper 2 | Key results and appraisal

Liver metabolism

Intrahepatic triglyceride, hepatic de novo lipogenesis, HbA1c and 24-hour glucose/insulin decreased most in the very-low-carbohydrate group.

Insulin sensitivity

Muscle insulin sensitivity improved by ~50% in all groups; hepatic insulin sensitivity increased 2–3 times more in the ketogenic group ($p < 0.001$).

Lipids

No between-group differences in LDL-C, ApoB or 24-hour plasma triglycerides after matched weight loss.

- Strength: food provision and weekly support reduce some adherence uncertainty.
- Limitations: selected metabolic phenotype, intensive intervention, moderate weight-loss target and mechanistic/biomarker outcomes.
- Take-home: macronutrient composition may affect hepatic outcomes beyond the amount of weight lost; replication and longer clinical follow-up are needed.

Source: Cell Metabolism, corrected proof / clinical and translational report; DOI above.

Paper 3 | Ketogenic diet and adult lipid profile

The Impact of the Ketogenic Diet on the Lipid Profile in Adults: A Comprehensive Review and Meta-Regression Analysis of RCTs. Endocrine Practice, May 2026.

Methods

Systematic review and meta-regression of 62 randomized trials comparing ketogenic diets with control diets.

Triglycerides / HDL-C

Triglycerides decreased by 19.96 mg/dL; HDL-C increased by 3.61 mg/dL.

LDL-C / total cholesterol

LDL-C increased by 8.49 mg/dL; total cholesterol increased by 8.14 mg/dL.

- Authors reported reductions in triglycerides and TG/HDL-C ratio alongside increases in HDL-C, LDL-C and total cholesterol.
- Clinical interpretation should not treat a lower triglyceride level or higher HDL-C as cancelling out an increase in atherogenic lipoproteins.
- Study-level heterogeneity, control diet composition and intervention duration matter.

DOI: 10.1016/j.eprac.2026.01.009 | https://doi.org/10.1016/j.eprac.2026.01.009



Paper 4 | KD-induced lipid changes: 53 RCTs

Zhao J, Wei C, Gong F, Pang Z, et al. BMC Cardiovascular Disorders. Published 30 Apr 2026;26:520.

Evidence base

53 randomized controlled trials included; search began with 2,127 records, with 1,289 unique records after deduplication.

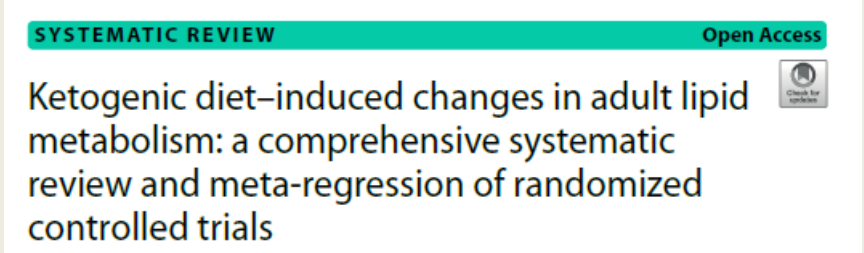
Pooled pattern

KD was associated with lower triglycerides and higher HDL-C, but also higher LDL-C and total cholesterol than control diets.

How to use it

Supports the need to assess the whole lipid profile, not just triglycerides or HDL-C, when considering KD.

- Do not assume all individuals have the same LDL response: the response varies by baseline characteristics, weight change, food sources and adherence.
- Follow-up should include LDL-C and non-HDL-C; ApoB can be useful where clinically appropriate.
- Meta-analysis evaluates lipid biomarkers, not whether KD changes heart attack, stroke or mortality rates.


SYSTEMATIC REVIEW Open Access

Ketogenic diet–induced changes in adult lipid metabolism: a comprehensive systematic review and meta-regression of randomized controlled trials

Paper 5 | Keto-Med randomized crossover trial

Gardner CD et al. American Journal of Clinical Nutrition. 2022;116(3):640–652.

Question

In adults with prediabetes or type 2 diabetes, how do a well-formulated ketogenic diet and a Mediterranean-plus diet compare?

Design

Randomized crossover trial; 40 adults enrolled and 33 completed primary analysis; each diet for 12 weeks in random order.

Comparator detail

Both patterns limited added sugar and refined grains; the Mediterranean-plus diet allowed legumes, fruit and whole grains that were more restricted on KD.

- Direct comparison is valuable because the same participants experienced both interventions.
- Crossover designs can reduce between-person confounding but remain limited by duration, adherence and potential carryover effects.



Paper 5 | Keto-Med findings

HbA1c / weight

Both diets improved HbA1c; there was no significant between-diet difference. Weight loss was similar: about 8% on KD vs 7% on Mediterranean-plus.

Triglycerides

Greater reduction with KD: approximately −16% vs −5% on Mediterranean-plus.

LDL cholesterol

LDL-C increased about 10% on KD and decreased about 5% on Mediterranean-plus.

- KD provided less fiber and several micronutrients in the trial diet.
- Participants tended to favor the Mediterranean-plus pattern after the intervention.
- Interpretation: comparable glycemic improvement can coexist with different lipid and nutrient-quality trade-offs.

Source: Gardner et al., Am J Clin Nutr. 2022;116:640–652. https://doi.org/10.1093/ajcn/nqac154

Paper 6 | Dietary patterns in type 2 diabetes

Effect of different dietary patterns on patients with type 2 diabetes: a systematic review and meta-analysis of RCTs. Frontiers in Nutrition, 12 Oct 2026.

Question / methods

Compared Mediterranean, ketogenic, intermittent fasting and energy-restricted diets in adults with T2D; 25 RCTs included.

Findings

Pooled estimates suggested improvements in fasting glucose and HbA1c across dietary approaches, but heterogeneity was substantial.

Relative ranking

KD and energy-restricted diets showed numerically larger weight reductions; MD showed stable glycemic improvement and favorable safety.

- Prediction intervals crossed zero for key pooled glycemic outcomes, limiting claims about which diet is superior.
- Authors note variable trial quality, incomplete adherence reporting and limited long-term follow-up.
- Safety signal: ketogenic approaches may produce more mild adverse events and require closer supervision in people with diabetes.


SYSTEMATIC REVIEW article

Front. Nutr., 12 October 2026

Sec. Clinical Nutrition

Volume 13 - 2026 | https://doi.org/10.3389/fnut.2026.1929818

Effect of different dietary patterns on patients with type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials

Cross-paper synthesis: what is consistent?

Weight

Some pooled analyses favor KD for short-term weight and waist reduction. Effect sizes are modest in some energy-matched comparisons and certainty may be low.

Glycemia / liver

Both patterns can improve glycemic control. A 2026 controlled trial suggests a larger short-term hepatic metabolic response to KD in a selected population.

Lipids / prevention

KD often lowers triglycerides but may raise LDL-C and total cholesterol. Mediterranean-style eating has broader evidence for long-term cardiovascular prevention.

- Direct trials are fewer and shorter than the evidence base for many individual diet patterns.
- Clinical context matters: baseline LDL-C/ApoB, medication use, diabetes phenotype, liver disease, patient preferences and adherence.
- Do not infer fewer cardiovascular events or longer survival from changes in weight, HbA1c, triglycerides or liver fat alone.

Clinical application and monitoring

If choosing KD

- Clarify goal and expected duration
- Prefer olive oil, nuts, seeds, fish and non-starchy vegetables
- Monitor LDL-C / non-HDL-C (± ApoB)
- Review glucose-lowering medication
- Avoid unsupervised use with SGLT2 inhibitors due to ketoacidosis risk

If choosing Mediterranean

- Emphasize vegetables, legumes, whole grains, nuts, fish and olive oil
- Limit processed meat, refined grains and added sugars
- Set energy target if weight loss is the goal
- Monitor weight, HbA1c and lipids as appropriate

For either pattern

- Individualize to medical history and preferences
- Review adherence and food access
- Monitor clinically relevant outcomes
- Adjust the plan if side effects, poor adherence or worsening biomarkers emerge

Evidence hierarchy: what can each study design tell us?

Use the right level of inference for each outcome

Mechanistic / biomarker studies

Can support plausibility and identify pathways.

Cannot establish that patients conceive more often or have more live births.

Observational studies

Can identify associations with diet adherence and ART outcomes.

Confounding, selection and healthy-user effects may explain some associations.

Randomized comparative trials

Best suited to estimating causal effects of one dietary strategy versus another.

Need adequate sample size, adherence assessment and live-birth endpoints.

Key distinction: within-group pre–post change is not the same as superiority over a comparator.

PCOS: outcome-by-outcome comparison

Qualitative evidence synthesis—not a direct head-to-head trial

Outcome	Mediterranean pattern	Ketogenic pattern
Weight loss	Effective if a sustainable energy deficit is achieved	Promising short-term results in selected populations
Insulin resistance	Potential benefit via food quality and weight management	Encouraging short-term evidence; heterogeneous
Androgen markers	Potential indirect improvement	Some promising short-term changes
Ovulation / cycle	Direct evidence limited	Promising signals; certainty remains low
Clinical pregnancy	No established causal benefit	Insufficient robust evidence
Live birth	Not established as superior	Insufficient robust evidence

Most important gap: adequately powered trials reporting live birth.

Sources: International PCOS Guideline 2023; ketogenic diet reviews 2025–2026

Ketogenic diet in PCOS: promising short-term signals

2026 systematic review and meta-analysis; studies searched through February 2025

Pooled pre–post mean changes reported in the review

Body weight

−10.77 kg

BMI

−3.38 kg/m^2

Waist circumference

−8.93 cm

Insulin resistance

−2.43 units*

Interpretation: these are pooled changes after ketogenic interventions—not estimates of superiority over a Mediterranean diet, and not estimates of pregnancy or live-birth benefit.

*Insulin-resistance outcome had very high heterogeneity (I^2 = 95%); populations and protocols differed.

Source: Clinical Nutrition 2026;56:106535. DOI: 10.1016/j.clnu.2025.11.019

How strong is the ketogenic evidence?

Promising signals should not be overstated

- Many studies are small, short, heterogeneous or uncontrolled.
- Pre–post changes do not isolate the diet effect from weight loss or energy restriction.
- Ketogenic protocols and comparator diets differ across studies.
- Menstrual regularity and hormone concentrations are surrogate outcomes.
- Pregnancy and live-birth data are sparse compared with metabolic data.

Defensible conclusion

Ketogenic diets may be an option for selected women with PCOS—especially with overweight/obesity—seeking short-term metabolic improvement.

They are not proven superior for fertility.

The 2023 international PCOS guideline does not endorse one dietary composition as universally superior.

Sources: 2023 International PCOS Guideline; Clinical Nutrition 2026 meta-analysis

Mediterranean diet in PCOS: a strong long-term foundation

Benefits are plausible and consistent with general cardiometabolic guidance

Diet quality

Fiber-rich plant foods, unsaturated fats, nuts, legumes and minimally processed carbohydrates support overall dietary quality.

Metabolic pathway

Weight management and improved dietary quality may improve insulin sensitivity and indirectly support androgen-related outcomes.

Evidence boundary

Guidelines do not establish Mediterranean eating as superior to all other healthy dietary patterns for reproductive outcomes.

Clinical implication: choose a sustainable, nutritionally adequate pattern that fits phenotype, preferences and goals.

Source: 2023 International Evidence-based Guideline for PCOS

Endometriosis: do not extrapolate from PCOS

Different disease biology, different evidence base

Disease context

Estrogen-dependent lesions, chronic inflammation, pelvic pain and possible impairment of fertility.

Mediterranean pattern

Reasonable supportive nutritional strategy for general health; symptom-specific findings are preliminary and not definitive.

Ketogenic pattern

Proposed metabolic/anti-inflammatory rationale, but clinical evidence for lesion control or fertility benefit is insufficient.

Neither diet is established as a treatment for endometriosis-associated infertility or as a way to increase live birth.

Sources: 2025 review of nutrition in endometriosis; 2026 clinical nutrition position paper

Assisted reproduction: association is not causation

Mediterranean diet adherence and ART outcomes

What some studies suggest

Observational studies have reported associations with selected embryo, pregnancy or live-birth outcomes.

Results are inconsistent across studies.

What we cannot conclude

The diet causes improved live birth, doubles the chance of success, or is superior to keto.

Confounding and selection bias remain important.

A 2022 meta-analysis reported an association with live birth in two studies (OR 1.98, 95% CI 1.17–3.35; n=355), but the evidence was limited and at risk of bias.

Do not translate this odds ratio into a claim that the diet doubles an individual patient's probability.

Clinical decision framework

Individualize the diet; do not prescribe a universal winner

PCOS + overweight / insulin resistance

Offer structured lifestyle care. Mediterranean-style eating is a strong default; keto may be considered selectively.

PCOS + normal BMI

Prioritize nutritional adequacy, activity and metabolic health; weight loss or ketosis is not automatically indicated.

Endometriosis + pain

Use dietary care as supportive, not disease-modifying treatment. Individualize for GI tolerance and nutrition.

Active conception / fertility treatment

Coordinate with reproductive care; consider pregnancy possibility, folate and micronutrient adequacy; avoid unnecessary restriction.

For anovulatory infertility due to PCOS, diet complements—not replaces—evidence-based ovulation induction. Letrozole is guideline-recommended first-line pharmacologic therapy when appropriate.

Sources: International PCOS Guideline 2023; ASRM guidance

Safety, implementation and research priorities

What a responsible recommendation should include

Ketogenic diet: clinical checks

- Dietary fiber and micronutrient adequacy
- Lipid response and gastrointestinal tolerance
- Sustainability and patient preference
- Preconception and pregnancy context
- Avoid assuming ketosis is necessary for PCOS care

What future trials need

- Direct Mediterranean-versus-keto randomized comparisons
- Clear intervention and adherence measures
- Stratification by BMI, insulin resistance and PCOS phenotype
- Adequate duration and sample size
- Ovulation, time to pregnancy, miscarriage and live birth

The best diet is not simply the one that changes a biomarker most—it is the one that is safe, sustainable and supported by outcomes relevant to the patient.

TAKE-HOME MESSAGES

No proven universal winner for fertility.

- Ketogenic diets: promising short-term metabolic and hormonal signals in selected women with PCOS.
- Mediterranean diet: a flexible, nutrient-dense long-term foundation for cardiometabolic and preconception health.
- Endometriosis: neither diet is established as a fertility treatment.
- Live birth—not weight loss or a biomarker—is the outcome that matters most



Individualized nutrition + evidence-based reproductive medicine

Journal-club take-home points

01 KD can produce greater short-term reductions in body weight in some direct comparisons.

02 Both diets can improve glycemic control; direct evidence does not consistently show KD is better for HbA1c.

03 Triglyceride reduction with KD must be interpreted alongside LDL-C, non-HDL-C and/or ApoB.

04 New mechanistic findings for liver fat are promising but do not yet establish long-term clinical superiority.

05 Mediterranean eating remains a strong default for broad cardiometabolic health; individualization and sustainability are central.

Thank you