ISRCTN48060037 https://doi.org/10.1186/ISRCTN48060037

Mediterranean diet adherence, testicular function and fertility

Submission date	Recruitment status	[X] Prospectively registered
23/12/2025	Recruiting	[_] Protocol
Registration date	**Overall study status**	[X] Statistical analysis plan
30/12/2025	Ongoing	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
30/12/2025	Nutritional, Metabolic, Endocrine	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Mediterranean Diet (MedDiet) health benefits are well-documented and several randomly allocated clinical trials (RCT) and observational studies have proven that it is effective in reducing the risk of cardiovascular diseases, diabetes, and overall mortality but no clear associations/effects were observed on testicular function and fertility outcomes. The main objective of this study is to assess the associations/effects of a MedDiet on testicular function and fertility. The study hypothesizes that adherence to a MedDiet improves testicular function and reduces the risk of infertility.

This project will be the first to observationally and prospectively assess the role of a food pattern (MedDiet) in the primary prevention of infertility by assessing the diet-testicular function-fertility axis and the possible mechanisms implicated. Built on three well-conducted cohort studies and a newly designed RCT, the MEDFERTYL project will lead to translatable dietary interventions and contribute to the paradigm shift towards precision nutrition for fertility programs.

Who can participate?
Healthy male volunteers at reproductive age (18-40 years old).

What does the study involve?
The study will assess the associations between MedDiet adherence, testicular function, and fertility using international cohorts of individuals or couples. To assess the effect of the MedDiet on testicular function (seminogram and peripheral hormone level) and possible mechanisms implicated (sperm DNA integrity, sperm chromatin condensation, and sperm methylation).

What are the possible benefits and risks of participating?
Benefits: It is possible that you may not obtain any health benefits from participating in this study. The aim of the study is to deepen knowledge of male infertility in order to improve its detection, diagnosis, and treatment. In the short term, the results obtained in the study are not expected to directly benefit the participant, but rather to benefit the general population.

Risks: The study does not involve any risk beyond that associated with blood collection. Drawing the blood sample may cause a stinging sensation at the point where the needle is inserted into the skin and may result in a small bruise that disappears after a few days. More rarely, it may cause transient dizziness.

Where is the study run from?
Carlos III Health Institute, Spain.

When is the study starting and how long is it expected to run for?
January 2026 to December 2028.

Who is funding the study?
Strategic Action in Health-Strategic Lines of Health Research, Carlos III Health Institute, Spain.

Who is the main contact?
Dr. Albert Salas-Huetos, albert.salas@urv.cat

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Dr Albert Salas Huetos

ORCID ID
https://orcid.org/0000-0001-5914-6862

Contact details
C/Sant Llorenç, 21
Reus
Spain
43201
+34 977759379
albert.salas@urv.cat

Additional identifiers

Strategic Action in Health-Strategic Lines of Health Research, Carlos III Health Institute, Spain.
AES-LEIS 2024-2027

Protocol serial number
PI25/00603

Study information

Scientific Title
Mediterranean diet adherence, testicular function and fertility

Acronym

MedFertyl

Study objectives
Main: To assess the effects of a Mediterranean diet (MedDiet) on testicular function.
1. To assess the effect of a MedDiet, compared to the usual diet, on 1) semen parameters (primary endpoint), and 2) peripheral levels of reproductive hormones.
2. To assess the effect of a MedDiet, compared to the usual diet, on the main possible mechanism of the changes: 1) sperm DNA integrity, 2) sperm chromatin condensation, and 3) sperm methylation.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 18/12/2025, Comité Ético de Investigación con Medicamentos IISPV (Hospital Universitario Sant Joan de Reus, Avda. Josep Laporte, 2, Reus, 43204, Spain; +34 977779946; ceim@iispv.cat), ref: 338/2025

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Parallel

Purpose
Prevention

Study type(s)
Prevention, Quality of life

Health condition(s) or problem(s) studied
Primary prevention of infertility.

Interventions
The trial will be a two-group parallel randomized single-blind intervention study of 14 weeks duration that will be performed on healthy subjects (18-40 years) who, at baseline, followed a Western-style nutritional pattern. The trial will randomly assign participants (in a 1:1 ratio using computer-assisted randomization) to one of the following two interventions: 1) changing the usual Western-style diet to a Mediterranean diet (intervention group); or 2) following the usual Western-style diet (control group).

Intervention Type

Mixed

Primary outcome(s)
1. Semen quality parameters: sperm vitality, sperm motility, sperm morphology, and sperm count and concentration measured using the CASA System according to the 2010 WHO protocols at baseline (V0) and the end of the intervention period (V3, after 14 weeks)

Key secondary outcome(s)
1. Peripheral blood levels of reproductive hormones (total testosterone (pool), free testosterone, estradiol, inhibin B, prolactin (pool), LH, FSH, and SHBG) measured using standardized protocols of the hospital and/or using ELISA at baseline (V0) and the end of the intervention period (V3, after 14 weeks)

2. Blood count, glycemic profile, lipid profile, and liver and renal function measured using standardized protocols of the hospital and/or using ELISA at baseline (V0) and the end of the intervention period (V3, after 14 weeks)

3. Plasma folate and red blood cell folate (RBCF) concentrations measured using microbiological assay with Lactobacillus casei, and plasma cobalamin by Lactobacillus leichmannii at baseline (V0) and the end of the intervention period (V3, after 14 weeks)

4. Total fasting plasma homocysteine (tHcy) measured using IMx fluorescence polarization immunoassay at baseline (V0) and the end of the intervention period (V3, after 14 weeks)

5. Riboflavin and pyridoxine status measured using erythrocyte glutathione reductase activation coefficient (EGRAC) and erythrocyte aspartate aminotransferase activation coefficient (EASTAC), respectively. Polymorphisms were determined on leukocyte-extracted DNA by matrix-assisted laser desorption/ionization/time-of-flight MS at baseline (V0) and the end of the intervention period (V3, after 14 weeks)

6. Sperm DNA integrity in semen samples: The analysis of double-stranded DNA breaks (DSB) measured using the Neutral Comet assay at baseline (V0) and the end of the intervention period (V3, after 14 weeks)

7. Sperm chromatin condensation in semen: Analysis of sperm chromatin condensation measured using labeling with chromomycin A3 (CMA3) at baseline (V0) and the end of the intervention period (V3, after 14 weeks)

8. Sperm DNA methylation in semen: Sperm DNA methylation profiles measured using pyrosequencing at baseline (V0) and the end of the intervention period (V3, after 14 weeks)

Completion date
31/12/2028

Eligibility

Key inclusion criteria
1. Healthy subjects
2. Aged 18-40 years
3. Male
4. Follow a Western-style nutritional pattern

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
Yes

Age group
Adult

Lower age limit
18 Years

Upper age limit
40 Years

Sex
Male

Total final enrolment
0

Key exclusion criteria
1. Allergy to foods typical of the Mediterranean diet (nuts or traces thereof, extra virgin olive oil).
2. Presence of alcoholism, active drug dependence, or smoking (>5 cigarettes per day or equivalent).
3. Known history of hepatitis B or C, or HIV antibodies.
4. Any serious illness.
5. Cancer diagnosed within the last five years.
6. Active infectious disease.
7. High-grade inflammatory disease.
8. Scheduled surgery within the next 2 months after randomization.
9. Use of plant sterols, antihypertensive or antidiabetic medications, mineral supplements, fiber supplements, fish oil, or antioxidants.
10. Following vegetarian, macrobiotic, vegan, or similar diets for weight loss at the start of the study.
11. Weight loss of more than 5 kg in the past month.
12. Any type of disease in the reproductive history or vasectomy.
13. Use of medications associated with sperm abnormalities: antidepressants (paroxetine, citalopram, fluoxetine, sertraline, bupropion); calcium channel blockers (diltiazem, nifedipine); alpha-adrenergic blockers (tamsulosin, alfuzosin); antiepileptics (phenytoin, carbamazepine, valproate); antiretrovirals (HAART, saquinavir), etc.
14. Other medical or social conditions that may hinder adherence to the intervention or follow-up.

Date of first enrolment
01/01/2026

Date of final enrolment
31/12/2028

Locations

Countries of recruitment
Spain

Study participating centre
Universitat Rovira i Virgili
C/Sant Llorenç, 21
Reus
Spain
43201

Sponsor information

Organisation
Instituto de Salud Carlos III

ROR
https://ror.org/00ca2c886

Funder(s)

Funder type
Not defined

Funder Name
Instituto de Salud Carlos III

Alternative Name(s)
SaludISCIII, InstitutodeSaludCarlosIII, Instituto de Salud Carlos III | Madrid, Spain, Carlos III Institute of Health, Institute of Health Carlos III, Carlos III Health Institute, La misión del Instituto de Salud Carlos III (ISCIII), ISCIII

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Spain

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be available upon reasonable request to the PI: Albert Salas-Huetos (albert.salas@urv.cat).

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Statistical Analysis Plan			30/12/2025	No	No