ISRCTN13218128 https://doi.org/10.1186/ISRCTN13218128

Integrated lifestyle interventions for reducing accelerated aging: A randomized controlled clinical trial in a Mediterranean population

Submission date
17/12/2024

Recruitment status
Recruiting

Registration date
18/12/2024

Overall study status
Ongoing

Last Edited
18/12/2024

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Research on the aging process has become increasingly important due to growing sociological and economic concerns about a rapidly aging global population. Likewise, the association between age and multiple diseases has stimulated basic research on the mechanisms of aging and strategies to mitigate its impact. Although we do not yet fully understand the causes of human aging, understanding these factors could transform biomedical research, given the age of the world's population. Currently, there are several biomarkers that can measure biological age and analyze its change after lifestyle interventions (mainly healthy diet, non-smoking, healthy sleep, physical activity, stress reduction, and time-restricted eating patterns). Emerging biomarkers based on omics parameters are more robust in determining biological aging, suggesting that a multi-omics panel of biomarkers may be more informative, representing a promising area for research that could soon be translated into clinical practice. Therefore, the main objective of the project is to analyze whether an intervention combined with healthy lifestyles (increased adherence to the Mediterranean diet, increased physical activity, healthy sleep, smoking restriction, stress reduction and time-restricted eating) has a favorable effect on biomarkers of aging based on DNA methylation (also called first, second and third generation biological clocks) after a 6-month intervention, taking into account possible confounding factors and also examining the specific effects of sex, its association with other aging biomarkers such as metabolomics, proteomics, genomics, transcriptomics and metagenomics, as well as changes in cardiometabolic health parameters. We will also assess other secondary objectives related to aging.

Who can participate?
Overweight or obese (Body Mass Index (BMI >=25 kg/m2 and less than 40 kg/m2) volunteers from the general population aged from 20 to 85 years old

What does the study involve?
In this study participants will be randomly assigned to either the intervention group or the control group. The intervention will include healthy lifestyle advice such as following the Mediterranean diet, time-restricted eating, reducing smoking, improving sleep, and reducing

stress, and will last for six months. The main outcome will be the effect on aging markers, tested after six months, with a follow-up evaluation at one year. The trial will involve 250 participants, half of whom will be women, with 125 in each group. The study will measure DNA methylation clocks across three generations using standardized protocols, and will also analyze sex-specific data and associations with other biomarkers like genomics, metabolomics, and transcriptomics.

What are the possible benefits and risks of participating?
In the intervention group, some benefits associated with the healthy lifestyle intervention may be observed in aging biomarkers. However, in the control group, no additional benefits are expected. Participants will be informed that no risk will be expected.

Where is the study run from?
University of Valencia, Spain

When is the study starting and how long is it expected to run for?
January 2024 to December 2027

Who is funding the study?
1. University of Valencia, Spain
2. CIBEROBN (Biomedical Research Network Center, Obesity Pathophysiology and Nutrition), Spain
3. Ministry of Science, Innovation and Universities, Spain

Who is the main contact?
Prof Dolores Corella, sorli@uv.es

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS_02412

Study information

Scientific Title
Combined lifestyle strategies to reduce accelerated aging: A randomized controlled clinical trial in a Mediterranean population: The LOVeMyAGE trial

Acronym
LOVeMyAGE

Study objectives
Currently, there are several biomarkers available that can measure biological age and analyze its change after lifestyle interventions. Although several omic biomarkers have recently been proposed to measure biological aging based on the genome, proteome, transcriptome, microbiome, or metabolome, epigenomics, particularly DNA methylation, is emerging as one of the most robust biomarkers of biological aging. The hypothesis is that a combined intervention with a healthy lifestyle over 6 months, consisting of increased adherence to the Mediterranean diet, increased physical activity, healthy sleep, smoking restriction, stress reduction, and time-restricted eating, will have a favorable effect on reducing accelerated aging primarily using methylomic biomarkers and also in combination with other genomic, metabolomic, proteomic, transcriptomic, and metagenomic biomarkers. Additionally, differences by sex may be obtained and the effect may persist after the intervention.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 10/12/2024, The Ethics Committee of Research in Humans of the Ethics Commission of University of Valencia, (Avda. Blasco Ibañez, 13, Valencia, 46010, Spain; +34963864109; vicerec.investigacio@uv.es), ref: 2024-MED-3730906

Study design
Interventional randomized controlled trial (single-centre)

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Prevention of accelerated aging in subjects with overweight or obesity

Interventions

A randomized, controlled clinical trial of a combined lifestyle intervention will be conducted. It will be a parallel trial in which people will be randomized 1:1 to the intervention group or the control group (no intervention). A simple randomization procedure based on a single sequence of random assignments generated by computer software will be used for the assignment of a person to the intervention or the control group. The estimated sample size will be 250 participants (125 assigned to the intervention group and 125 participants to the control group). The duration of the intervention will be 6 months. Participants will be followed up for six additional months, but no intervention will be carried out. Both the control and the intervention group, baseline, 3 months and 12 months visits and data collection will be carried out.

Interventions:
1. Intervention group: In this group a combined intervention with healthy lifestyle advice will be carried out during 6 months. This combined intervention will consist of advice to increase adherence to the Mediterranean diet; reduce tobacco consumption; increase the days of time-restricted eating (increasing the days by following an 8-hour eating and 16-hour fasting schedule, adapted to their schedules); increase physical activity; increase/decrease sleep hours to have a healthy recommendation adapted to age (7 to 9 hours) and improve sleep quality; and an intervention will also be carried out to reduce stress levels. Specialized personnel, including registered dietitians for dietary interventions, psychologists for stress reduction interventions, and specialized healthcare professionals for sessions on tobacco consumption reduction, healthy sleep, and physical activity enhancement, will carry out these interventions. After signing informed consent and randomization, individuals assigned to the intervention group will receive an intensive initial in-person session of 1.5–2.5 hours with all healthcare professionals to explain the combined interventions for a healthy lifestyle. The University of Valencia's Faculty of Medicine will host it. Afterwards, the medical school will host group sessions on specific aspects of a healthy lifestyle once a month during the 6-month intervention. Individual intervention sessions will be held every 15 days, either in person or online, to tailor the interventions to each participant's specific lifestyle aspect that requires improvement (diet, sleep, stress, and/or physical activity). The goal protocol will be used throughout the interventions and monitor compliance with various instruments. Validated questionnaires on adherence to the Mediterranean diet, diet logs with meal times to monitor time-restricted eating, questionnaires on physical activity and sleep quality, accelerometers in a subsample, and questionnaires on stress and tobacco consumption will be used. Participants will receive small gifts during the visits. They will not receive payment for their participation.

2. Control group: There will be no lifestyle intervention in the control group. The individuals will continue with their usual lifestyle. They will attend the 3-month follow-up visit, the end-of-intervention visit at 6 months, and the final follow-up visit at 12 months, just like the intervention group. They will receive small gifts during these visits. They will not receive payment for their participation.

Intervention Type
Behavioural

Primary outcome(s)
DNA methylation (epigenomic biomarker of aging) in isolated blood measured using the EPIC v.2 Illumina array at baseline and 6 months

Key secondary outcome(s))
1. Omics biomarkers, including metabolomics (measured in plasma/serum by magnetic nuclear resonance), transcriptomics (measured in RNA isolated from blood and analyzed with a human

transcriptome array), proteomics (measured in blood in a subsample), and metagenomics (measured in DNA from feces in a subsample using metatatoxonomics), at 6 months
2. Epigenomics and the other biomarkers (in a subsample) measured using the described methods at baseline and 3 months
3. The effects on aging markers and cardiometabolic health parameters after a year of follow-up (6 months intervention and 6 months after the intervention and after the combined intervention) using the same methodology for the omics analysis.
4. Association with cardiometabolic health parameters, including antropometric parameters (weight, % fat mass measured by bioimpedance, waist circumference), biochemical parameters (fasting glucose, plasma lipids, liver function biomarkers, kidney function biomarkers, measured by standard procedures) and autophagy biomarkers (polyamines, reporters in isolated leukocytes in a subsample). In addition, chronotype (MEQ questionnaire), cognitive function (by validated tests including minimental, fluency test and spacial memory tests) at 6 months and at 3 and 12 months in a subsample.
5. The main lifestyle variables associated with the combined intervention consisting on diet (adherence to the Mediterranean diet measured by the MEDAS-14 and MEDAS-17 validated questionnaire and food frequency questionnaires), physical activity (measured by validated questionnaires and accelerometers in a subsample), healthy sleep (sleep duration and quality measured by validated questionnaires), tobacco consumption, stress (measured by validated questionnaires), and restricted meal time (measured by specific time-restricted questionnaires and 24h-recalls including timing of foods) from baseline to 6 months of intervention compared to the control group. These parameters will also be measured at 3 and 12 months.

Completion date
31/12/2027

Eligibility

Key inclusion criteria
1. Volunteers from the general population
2. Overweight or obese (Body Mass Index (BMI >=25 kg/m2 and less than 40 kg/m2)
3. Aged from 20 to 85 years old
4. With at least one other risk factor related to aging (sedentary, low adherence to the Mediterranean Diet, smoker, unhealthy sleep patterns or very frequent eating patterns)
5. Caucasian origin of the Spanish population
6. 50% women

Participant type(s)
Healthy volunteer, Population

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
20 years

Upper age limit
85 years

Sex
All

Key exclusion criteria
1. Pregnancy or breastfeeding
2. Diabetes type 1 or 2
3. Taking medications to lose weight
4. Consumption of psychoactive substances or alcohol abuse.
5. Existing cardiovascular diseases, active cancer, active infections and other acute diseases (respiratory, intestinal, liver, kidney)
6. Allergies or problems related to the interventions

Date of first enrolment
30/12/2024

Date of final enrolment
28/02/2026

Locations

Countries of recruitment
Spain

Study participating centre
University of Valencia
Blasco Ibanez, 15
Valencia
Spain
46010

Sponsor information

Organisation
University of Valencia

Organisation
CIBEROBN

Funder(s)

Funder type
University/education

Funder Name
Universitat de València

Alternative Name(s)
University of Valencia, UV

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Spain

Funder Name
CIBEROBN

Funder Name
Ministerio de Ciencia, Innovación y Universidades

Alternative Name(s)
Ministry of Science, Innovation and Universities, MCIU

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Spain

Results and Publications

Individual participant data (IPD) sharing plan
Data will not be available outside the core research group as the informed consent form signed by participants stated that individual-level data will not be publicly available. Researchers who are interested in this study can contact the main investigator (Dra. Dolores Corella Piquer) if they have any questions regarding the data or are interested in further collaborations. The

participants will receive written information about what the study involves and sign a consent form before entering the study.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes