

# Effects of lifestyle changes in an obese metabolically healthy elderly population

<b>Submission date</b> 11/11/2021	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
<b>Registration date</b> 29/11/2021	<b>Overall study status</b> Completed	<input checked="" type="checkbox"/> Protocol
<b>Last Edited</b> 20/12/2023	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Metabolically Healthy Obese individuals (MHO) are special, seemingly protected from the cardiometabolic disorders associated with excess body fat. The aim of this study is to test whether the change of lifestyle by promoting physical exercise and recommendations of a healthy Mediterranean-style diet (without caloric restriction) in elderly MHO is associated with changes in insulin sensitivity and metabolomic mechanisms.

### Who can participate?

Persons aged over 65 years, with a body mass index of 30-40 kg/m<sup>2</sup> and one or fewer common health issues associated with obesity.

### What does the study involve?

Participants will be encouraged to follow a Mediterranean diet based on the Trichopoulou index and practice regular adapted physical activity for 24 months. During the follow-up, 4 visits are planned: baseline and at 4, 12, and 24 months.

### What are the possible benefits and risks of participating?

There are no other potential risks from participating in this study other than discomfort from taking blood samples. The potential benefits derive from following a healthy Mediterranean diet and practicing adapted physical activity, which have been shown to prevent cardiovascular disease.

### Where is the study run from?

Regional University Hospital of Malaga (Spain)

### When is the study starting and how long is it expected to run for?

July 2018 to March 2022

### Who is funding the study?

Institute of Health Carlos III (Spain)

Who is the main contact?

Dr. M Rosa Bernal-Lopez, robelopajiju@yahoo.es.

## Contact information

### Type(s)

Scientific

### Contact name

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## Additional identifiers

### Clinical Trials Information System (CTIS)

Nil known

### Protocol serial number

PI18/00766

# Study information

## Scientific Title

Obese metabolically healthy elderly population: -omic studies (epigenetics, metabolomics, metagenomics) and its relationship with environmental pollutants

## Study objectives

H1. It is postulated that the maintenance and/or weight loss produced by a change in lifestyle, mediated by changes in dietary habits and physical activity, and undertaken at the community level in the elderly Metabolically Healthy Obesity (MHO), will improve insulin sensitivity, compared to the non-responder group. Environment factors such as diet are able to modify the profile of epigenetic changes and, consequently, influence the development of obesity-associated diseases such as insulin resistance.

H2. It is postulated that epigenetic modifications (on histones and in the promoter region) in genes involved in insulin resistance in obesity (epiobesigenes) are responsible for the development of the same, through the regulation of gene expression of genes regulating expansion ability, adipose tissue differentiation, adipogenesis, lipogenesis and inflammation.

H3. It is postulated that the components of the microbiota have an immune function, a trophic function and digestive function. For this, interindividual variability exists depending on the composition of the flora, which can modify the energy value of food.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Approved 26/07/2018, Comité de Ética de la Investigación Provincial de Málaga (Hospital Regional Universitario de Málaga, Avnda. Carlos Haya s/n, Pabellón A, 7º planta, Málaga, Spain; +34 951 29 19 77; gloria.luque.exts@juntadeandalucia.es), ref: PI18/00766-260718

## Study design

Interventional cross-sectional open study

## Primary study design

Interventional

## Study type(s)

Other

## Health condition(s) or problem(s) studied

Lifestyle intervention in metabolically healthy obese older adults

## Interventions

Participants will be encouraged to follow a Mediterranean diet advised by a nutritionist based on the Trichopoulou index and practice regular adapted physical activity for 24 months. The recommended caloric intake is 1500-1750 kcal/day, distributed as follows: 30% from fats (5-8% from saturated fatty acids, 15-18% from monounsaturated fatty acids, 5-8% from polyunsaturated fatty acids and <300 mg of cholesterol/day), 55% from carbohydrates (<10% from simple sugars, 40% from complex sugars and low glycemic index) and 15% from protein. The recommended Mediterranean diet is based on the Trichopoulou criteria, prioritizing olive oil as the main cooking fat, consuming poultry or rabbit meat preferably rather than red meat and

encouraging the consumption of fish, fruits, legumes and vegetables. Similarly, participants are encouraged to practice daily physical activity adapted to their age and physical condition, following the internationally-accepted physical activity guidelines (Physical Activity Guidelines for Americans. Chapter 5. Available at <https://health.gov/our-work/physical-activity/current-guidelines>). The intervention will last 24 months. Visits will be made at baseline and then at 4 and 12 months to reinforce the intervention and monitor the study variables and at 24 months to monitor the study variables for the last time. Lipid profile, inflammatory biomarkers (hsPCR, IL6, TNFa, fibrinogen) and adipokines (adiponectin, leptin) will be analyzed. Epigenetic (methylation), metabolomic, and metagenomic (gut microbiota) studies will be carried out and their possible relationship with different environmental pollutants will be analyzed.

## **Intervention Type**

Behavioural

## **Primary outcome(s)**

The primary outcome is a composite outcome where the researchers will analyze the effectiveness of a multidisciplinary and multicomponent intervention carried out in the community setting, aimed at modifying the lifestyle (use of a Mediterranean diet and promotion of physical activity) to prevent the incidence of cardiometabolic alterations in elderly healthy metabolically obese subjects. This has been quantified as an improvement in Mediterranean diet adherence through food frequency questionnaires (baseline and 4, 12 and 24 months) and improvement in physical activity intensities, measured by accelerometry (minutes/day).

1. Nutritional assessment and monitoring: food intake analyzed using questionnaires at baseline and at 4, 12 and 24 months:
  - 1.1. A non-consecutive, 3-day dietary record (two workdays and one weekend day), containing detailed information about food composition and cooking recipes over 72 hours
  - 1.2. A food frequency questionnaire (number of times/day, number of days/week, number of days/14 days, number of days/month, rarely, or never)
  - 1.3. Adherence to Mediterranean diet assessed by a validated 14-item food consumption frequency questionnaire
2. Physical activity monitored using a GENEActiv Actigraph GT3X+ accelerometer at baseline and at 4, 12 and 24 months. The accelerometer should be worn under the chest with a tight elastic belt to ensure close contact with the body. Recordings are made every day for at least 7 days (weekdays and the weekend) to take their hours of physical activity and sleep, except during water activities. Physical activity is also evaluated using the Rapid Assessment of Physical Activity (RAPA) questionnaire, a validated 7-item questionnaire at baseline and at 4, 12 and 24 months

## **Key secondary outcome(s)**

1. Anthropometric variables measured by trained personnel at baseline and at 4, 12 and 24 months:
  - 1.1. Weight measured using an electronic scale: TANITA Body Composition Analyzer. Type TBF-300 MA. (TANITA Corporation; 1-14-2 Maeno-cho, Itabashi-ku. Tokyo, Japan)
  - 1.2. Height measured with no shoes using a wall stadiometer (Stadiometer Barys Electra Model. 511-300-A0A. ASIMED)
  - 1.3. BMI calculated by dividing weight (kg) by height squared (m<sup>2</sup>)
  - 1.4. The waist/hip index (WHI) calculated as the ratio of abdominal circumference (at the level of the mid-point between the anterosuperior iliac crest and the last costal arch, parallel to the ground and upon exhalation) and hip, both in cm
  - 1.5. Blood pressure measured with a validated automated electronic sphygmomanometer

(OMRON M7 (HEM-780-E, OMRON Healthcare Co. Ltd, Kyoto, Japan) after 5 minutes of rest while the participant is in a seated position

2. Serum adipokine and inflammatory biomarkers levels (IL-6 and TNF $\alpha$ ) measured using an enzyme-linked immunosorbent assay (ELISA) (R&D Systems, Inc., Minneapolis, MN, USA) on blood samples collected after an overnight fast at baseline and at 4, 12 and 24 months

3. High-sensitivity CRP levels measured using ELISA (DRG Instruments GmbH, Germany) on blood samples collected after an overnight fast at baseline and at 4, 12 and 24 months

**Completion date**

31/03/2022

## Eligibility

**Key inclusion criteria**

1. Aged >65 years
2. BMI  $\geq 30$ -<40 kg/m<sup>2</sup>
3. One or none of the following four cardiometabolic disorders:
  - 3.1 Systolic blood pressure  $\geq 140$  mmHg and/or diastolic blood pressure  $\geq 90$  mmHg
  - 3.2 Triglycerides  $\geq 150$  mg/dl
  - 3.3 HDL-C <40 mg/dl in men and <50mg/dl women
  - 3.4 Fasting blood glucose  $\geq 100$  mg/dl, following the WHO criterion of MHO

**Participant type(s)**

Healthy volunteer

**Healthy volunteers allowed**

No

**Age group**

Senior

**Lower age limit**

65 years

**Sex**

All

**Total final enrolment**

169

**Key exclusion criteria**

1. Diabetes
2. Hypertension
3. Previous cardiovascular disease (coronary, cerebrovascular or peripheral; aortic aneurysm, heart failure)
4. Severe associated disease (advanced organ failure, dementia, cancer)
5. Immobilized or terminally ill individuals
6. Alcoholism or drug addiction
7. Severe psychiatric illness
8. Weight loss  $\geq 5$  kg in the last 6 months of unknown cause.

**Date of first enrolment**

01/11/2018

**Date of final enrolment**

10/03/2020

## Locations

**Countries of recruitment**

Spain

**Study participating centre****Regional University Hospital of Málaga**

Avda. Carlos Haya, s/n

Málaga

Spain

29007

## Sponsor information

**Organisation**

Instituto de Investigación Biomédica de Málaga

**ROR**

<https://ror.org/05n3asa33>

## Funder(s)

**Funder type**

Government

**Funder Name**

Instituto de Salud Carlos III

**Alternative Name(s)**

SaludISCI, 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 (ISCI), ISCI

**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 analysed during the current study are available upon request from María Rosa Bernal-López (robelopajiju@yahoo.es). Data is already partially available and will be stored for the next 10 years. Each participant gave their written consent and data was anonymized by giving each participant an identification number code. Data are available if the study results need to be checked.

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		01/09/2022	10/10/2022	Yes	No
<a href="#">Results article</a>		13/11/2021	10/10/2022	Yes	No
<a href="#">Results article</a>		09/06/2022	10/10/2022	Yes	No
<a href="#">Participant information sheet</a>			15/11/2021	No	Yes
<a href="#">Protocol (other)</a>		09/06/2022	20/12/2023	No	No