

Cardiometabolic effect of weight loss in metabolically healthy obese subjects

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Registration date 26/07/2016	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 18/08/2023	Condition category 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

Obesity is a growing concern worldwide, which can lead to serious health problems such as diabetes, heart disease and even cancer. Many obese patients experience changes to their metabolism (chemical process in the body to maintain life), which increases their risk of developing cardiovascular disease (disease of the heart and/or blood vessels). Metabolically healthy obesity (MHO) is a type of obesity in which there are no disruptions to metabolism. Currently, there are many discussions about whether MHO patients have a lower risk of developing diabetes or cardiovascular disease and if weight-loss can help further lower this risk. The Mediterranean diet is considered to be one of the healthiest diets worldwide, and particularly effective at helping prevent obesity. In addition, exercise has been shown to be extremely effective at helping people to lose weight as well as protecting against death and disease. The aim of this study is to find out whether weight-loss in MHO patients can help to prevent diabetes and cardiovascular disease.

Who can participate?

Adults aged between 35 and 55 with MHO.

What does the study involve?

Participants are randomly allocated to one of two groups. Participants in the first group consume a Mediterranean diet for two years. This diet involves using olive oil as the main source of dietary fat, increasing consumption of fruits, vegetables and fish, reducing consumption of red meat, and cutting out dairy products, sugary drinks and confectionery. Participants are also encouraged to practice daily exercise, which involves walking on average for 150 minutes every week for the two years of the study. Participants in the second group continue as normal for the duration of the study. Participants in both groups have their blood sugar measured at the start of the study and then after 3, 6, 12, 18 and 24 months in order to test for diabetes. Additionally, participants provide further blood samples to test levels of chemicals in the body which are important for metabolism and have their weight and blood pressure measured.

What are the possible benefits and risks of participating?

If participants continue the healthy lifestyle they adopt during this study, then it is likely to have long term benefits for their heart health. There are no notable risks involved with participating in this study.

Where is the study run from?

1. Regional University Hospital of Malaga (Spain)
2. Hospital Virgen de la Victoria (Spain)

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

January 2012 to June 2016

Who is funding the study?

1. Instituto de Salud Carlos III (Spain)
2. FEDER Funds (Spain)

Who is the main contact?

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Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

Protocol serial number

HRM-MHO/12-01373

Study information

Scientific Title

Cardiometabolic effect of weight loss in metabolically healthy obese subjects (MHO)

Study objectives

The aim of this study is to investigate assess whether significant weight loss induces short-term metabolic benefits in metabolically healthy obese (MHO) individuals and whether the rate of weight loss influences the metabolic response to the intervention.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Ethics approval by the institutional ethical committee (Comité Coordinador de Ética de la Investigación Biomédica de Andalucía), 20/04/2012, ref: 140402

Study design

Multi-centre randomized controlled trial

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Obesity

Interventions

Participants are randomly allocated to one of two groups using a computer-generated sequence of random numbers.

Intervention group: Participants take up a Mediterranean diet for two years, which is based on the use of olive oil as the main source of visible fat and regular consumption of vegetables (≥ 2 servings / day), fruits (≥ 3 servings / day), legumes (≥ 3 servings / week) and fish (≥ 3 times a week), reducing the consumption of red meat or sausage (< 2 times a week) and eliminating (or reducing to < 1 time / week) the consumption of dairy products, sugary drinks and confectionery. The recommended diet provide a calorie deficit of 600 Kcal/day. Participants are also encouraged to practice daily exercise, with a minimum target walk an average of 150 minutes a week for the two year duration of the study.

Participants receive nine medical visits throughout the study (every three months during the first year, then every six months) by the specialist physician and a nurse visit every four weeks during the first semester and then every 3 months until the end of the study (16 visits throughout the study). Checkups include general hygiene and dietary recommendations and clinical assessment.

Control group: Participants receive a minimum of four medical consultations and four nursing visits annually, which may be extended at the discretion of the physician or nurse responsible according to the associated pathology presented by the patient, according to standard clinical practice in these cases will be made. Checkups include general recommendations on heart-healthy diet and exercise, and identical clinical and analytical assessments as in the experimental group. During nursing visits (individual, 10 minutes) participants receive written information about diet and exercise without specific individual recommendations.

Participants are followed up at 3, 6, 12, 18 and 24 months for the intervention group and at 12, 18 and 24 months in the control group.

Intervention Type

Behavioural

Primary outcome(s)

Type 2 diabetes and/or prediabetes incidence is determined by measuring:

1. Fasting plasma glucose levels at baseline, 3, 6, 12, 18 and 24 months
2. Oral glucose tolerance test at baseline, 12 and 24 months
3. Glycated hemoglobin (HbA1c) at baseline, 3, 6, 12, 18 and 24 months

Key secondary outcome(s)

1. Anthropometric variables are measured at baseline, 3, 6, 12, 18 and 24 months for the intervention group and at baseline, 12, 18 and 24 months in the control group.

- 1.1. Weight measured in kg on a scale
- 1.2. Waist circumference is measured in cm
- 1.3. BMI is calculated as the ratio between weight and height (kg/m²)
- 1.4. Blood pressure is measured using a validated automatic sphygmomanometer (OMRON M4-I) when the participant is in a sitting position.
2. Insulin resistance is calculated using the HOMA-IR index and proinsulin/insulin ratio at baseline, 12, 18 and 24 months
3. Serum lipid profile (HDL-cholesterol, LDL-cholesterol, Triglycerides) is measured using commercial equipment (Dimension®, Dade Behring, Germany) at baseline, 12, 18 and 24 months
4. Inflammatory parameters (leucocytes, fibrinogen, hs-CRP, IL-6, TNF- α) are measured using an Enzyme-Linked ImmunoSorbent Assay at baseline, 12, 18 and 24 months
5. Metabolic hormone (adiponectin and resistin) levels are measured using an Enzyme-Linked ImmunoSorbent Assay at baseline, 12, 18 and 24 months
6. Liver function is measured through serum liver function tests (AST, ALT, GGT) and Fatty Liver Index (FLI) at baseline, 12, 18 and 24 months

Completion date

30/06/2016

Eligibility

Key inclusion criteria

1. Aged 35-55 years
2. Metabolically healthy obese (MHO)*
3. BMI between 30-45 kg/m²

*A participant is considered to have MHO status when meeting ≤ 1 of these four metabolic syndrome criteria: fasting plasma glucose ≥ 100 mg/dL, blood pressure $\geq 135/85$ mmHg (or use of blood pressure-lowering agents), HDL-cholesterol ≤ 50 mg/dL, and triglycerides ≥ 150 mg/dL (or use of lipid-lowering therapies).

Participant type(s)

Healthy volunteer

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

35 years

Upper age limit

55 years

Sex

All

Key exclusion criteria

1. Diabetes or impaired glucose tolerance
2. Hypertension
3. Pregnancy or planning to become pregnant during the study
4. Cardiovascular disease
5. Severe systemic disease (advanced organ failure, dementia, cancer)
6. Immobilized individuals
7. Alcohol or drug abuse
8. Severe psychiatric illness
9. Patients who self-initiated a program of physical activity or started a diet in the past three months
10. Weight loss ≥ 5 kg in the last 6 months of unknown cause

Date of first enrolment

15/06/2013

Date of final enrolment

15/04/2014

Locations

Countries of recruitment

Spain

Study participating centre

Regional University Hospital of Malaga

Avda. Hospital Civil s/n

Málaga

Spain

29010

Study participating centre

Hospital Virgen de la Victoria
Campus de Teatinos s/n
Malaga
Spain
29010

Sponsor information

Organisation

Fundación Pública Andaluza para la Investigación de Málaga en Biomedicina y Salud (FIMABIS)

ROR

<https://ror.org/002nw1r81>

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

Funder Name

Federación Española de Enfermedades Raras

Alternative Name(s)

Spanish Federation for Rare Diseases, FEDER

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

Spain

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/07/2017		Yes	No
Results article		09/04/2019	18/08/2023	Yes	No
Other publications	Substudy results	12/02/2018	18/08/2023	Yes	No