

# Effect of extra virgin olive oil versus refined olive oil in alleviating obesity-induced inflammation in obese people with pre-diabetes

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| <b>Submission date</b><br>31/12/2019   | <b>Recruitment status</b><br>No longer recruiting              | <input type="checkbox"/> Prospectively registered<br><input checked="" type="checkbox"/> Protocol |
| <b>Registration date</b><br>10/02/2020 | <b>Overall study status</b><br>Completed                       | <input type="checkbox"/> Statistical analysis plan<br><input checked="" type="checkbox"/> Results |
| <b>Last Edited</b><br>04/07/2023       | <b>Condition category</b><br>Nutritional, Metabolic, Endocrine | <input type="checkbox"/> Individual participant data  |

## Plain English summary of protocol

### Background and study aims

The purpose of this clinical trial is to verify whether the consumption of extra virgin olive oil (which has high levels of polyphenols) improves the inflammatory profile in people with low-grade inflammation, also known as meta-inflammation, and that it is common in people obese with prediabetes, compared to an olive oil with tiny amounts of polyphenols. Likewise, other important aspects for health such as body weight and metabolic profile (fasting glucose, insulinemia, insulin resistance, beta cell functionality, glycosylated hemoglobin, lipidemia, etc.) will also be evaluated.

The improvement of these parameters is associated with a delay in the development of cardiovascular disease and diabetes, and could lead to the use of extra virgin olive oil, high in polyphenols, as a substitute for the natural source of dietary fat, as well as elaborate functional foods based on extra virgin olive oil.

### Who can participate?

Adults (45 – 60 years old) who are obese (BMI 30 – 40) not diagnosed with diabetes

### What does the study involve?

Participants will be randomly allocated to receive a one-month consumption of one type of olive oil (extra-virgin olive oil or refined olive oil) followed by a wash period of 15 days and a second one-month consumption of the second olive oil (refined olive oil or extra-virgin olive oil)

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

Expected benefits could include amelioration of metabolic alterations, such as fasting glucose, insulin resistance and weight loss. There are no expected risk for participants as they are just asked for substituting cooking oil at home for the one provided (blinded commercially available olive oil with low/high polyphenols content).

### Where is the study run from?

Hospital Regional de Malaga, Spain

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

March 2018 to June 2019

Who is funding the study?

1. Consejería de Salud y Familias, Junta de Andalucía (Ministry of Health and Families, Junta de Andalucía), Spain
2. Instituto de Salud Carlos III, Ministerio de Sanidad, Gobierno de España (Carlos III Health Institute, Ministry of Health, Government of Spain)

Who is the main contact?

Dr Francisco-Javier Bermudez-Silva

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## Contact information

**Type(s)**

Scientific

**Contact name**

Dr Francisco-Javier Bermudez-Silva

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## Additional identifiers

**EudraCT/CTIS number**

Nil known

**IRAS number**

**ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

PI-0247-2016

## Study information

**Scientific Title**

Randomized double-blind cross-over interventional trial to assess the beneficial effects of extra-virgin olive oil versus refined olive oil in meta-inflammation

**Acronym**

APRIL

**Study objectives**

Extra virgin olive oil improves obesity-related meta-inflammation in obese people with pre-diabetes when compared to refined olive oil

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Approved 29/11/2017, Ethics Committee for Clinical Research (CEI) of Malaga (Ethics Research Committee Provincial de Málaga, 7ª planta, Pabellón A, Hospital Regional Universitario, Avda Carlos Haya s/n, 29010-Málaga, Spain; + 34 951291977; [eticainvestiga.hch.sspa@juntadeandalucia.es](mailto:eticainvestiga.hch.sspa@juntadeandalucia.es)), ref:11/2017-PI1

**Study design**

Randomized single-centre double-blind cross-over interventional trial

**Primary study design**

Interventional

**Secondary study design**

Randomised cross over trial

**Study setting(s)**

Home

**Study type(s)**

Treatment

**Participant information sheet**

See trial outputs table

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

Obesity and pre-diabetes

**Interventions**

One-month consumption of one type of olive oil (extra-virgin olive oil or refined olive oil) followed by a wash period of 15 days and a second one-month consumption of the second olive oil (refined olive oil or extra-virgin olive oil)

Randomisation process: 1:1 randomisation without stratification.

**Data collection:**

The nurse in charge of the study collects during each visit data on social status, habits, clinical, nutritional habits and semi-quantitative food frequencies, physical activity and anthropometrics.

Fasting urine and blood samples are also collected, for measuring standard biochemical parameters, inflammatory parameters, oxidative stress markers, hormones, polyphenols levels. Patients are asked to bring with them a faeces sample for microbiota analysis.

## **Intervention Type**

Supplement

## **Primary outcome measure**

Inflammatory markers measured from serum/plasma samples by multiplex assay (IL-6, IL-1B, TNF- $\alpha$ , Leptin, adiponectin, CXCL-1, IFN- $\gamma$ , IL12p40, IL-4, IL-10, IL-13, IL-RA, hs-CRP) before and after each treatment

## **Secondary outcome measures**

1. Body weight (kg) measured before and after each treatment
- Measured from serum/plasma samples by multiplex assay before and after each treatment:
2. Metabolic status (fasting glucose, insulinemia, HOMA-IR, HOMA-B, HbA1C, lipid profile)
3. Standard biochemical analysis (Urea, uric acid, albumin, Fe<sup>2+</sup>, ferritin, bilirubin, FA, Vit D, hemogram)
4. Oxidative status (LOOH, AOPP, TAS, Total thiol, Glutathione reductase)
5. Lipidomic profile by DOSY-NMR
6. Microbiota profile

## **Overall study start date**

13/07/2016

## **Completion date**

13/06/2019

# **Eligibility**

## **Key inclusion criteria**

1. Adult (40 - 65 years old)
2. Obese: BMI 30 - 40 kg/m<sup>2</sup>
3. Glycated hemoglobin (HbA1c): 5.7 - 6.4
4. Signed informed consent

## **Participant type(s)**

Patient

## **Age group**

Adult

## **Lower age limit**

40 Years

## **Upper age limit**

65 Years

## **Sex**

Both

**Target number of participants**

130

**Total final enrolment**

91

**Key exclusion criteria**

1. Previous diagnosis of diabetes mellitus
2. Pregnant women
3. Diagnosis of some type of neoplasia
4. Inflammatory diseases in progress (Crohn's disease, ulcerative colitis, arthritis) and/or anti-inflammatory treatments
5. Women in hormone replacement therapy
6. Eat regularly more than 3 meals/week away from home (lunch or dinner, unless it is homemade food prepared with the provided oil)

**Date of first enrolment**

08/03/2018

**Date of final enrolment**

27/02/2019

**Locations****Countries of recruitment**

Spain

**Study participating centre**

**Hospital Regional de Malaga**

Plaza del Hospital Civil s/n Pabellon 2

Sotano Lab Investigacion-Hormonas

Malaga

Spain

29009

**Sponsor information****Organisation**

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

**Sponsor details**

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fimabis@fimabis.org

**Sponsor type**  
Government

**Website**  
<http://www.fimabis.org/>

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

## **Funder(s)**

**Funder type**  
Government

**Funder Name**  
Consejería de Salud y Familias, Junta de Andalucía

**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, ISCI

**Funding Body Type**  
Government organisation

**Funding Body Subtype**  
National government

**Location**  
Spain

## **Results and Publications**

### **Publication and dissemination plan**

The results will be presented in national/international congresses in the field of obesity and diabetes.

The whole study will be published in a peer-reviewed international scientific journal.

The findings will be disseminated to citizens through the official channels and social media of

the sponsor's research institution and through the social media of the members of the research group.

## Intention to publish date

01/12/2020

## Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request. Dr. Javier Bermudez-Silva, (javier.bermudez@ibima.eu); specifically, raw data for published variables; data are expected to be available late 2020/early 2021 and during at least 10 years; data will be shared with researchers from public/non-profit research organizations upon reasonable request, allowing analysis of health variables related to the aims of this trial; consent from patients was obtained, patients were code converted, being the principal investigator the only person who guards the file (protected by password) encoding personal data of the participants; samples will be stored in the public biobank of the Consejería de Salud de la Junta de Andalucía (Biobanco del Sistema Sanitario Público de Andalucía (BBSSPA), biobancomalaga.fps@juntadeandalucia.es) under specific MTA agreement between BBSSPA and the principal investigator and signed consent from patients; surplus samples will be available to other researchers from public/non-profit research organizations upon reasonable request to the principal investigator (Dr. Javier Bermudez-Silva, javier.bermudez@ibima.eu); Biological samples and associated clinical data will be used in accordance to Ley 14/2007, of 3rd July, of Biomedical Research (Spain); Personal data collected will be considered confidential and managed according to Ley Orgánica 15/1999, of 13th December (Spain), of personal data protection.

## IPD sharing plan summary

Available on request

## Study outputs

| Output type                                   | Details   | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|--------------|------------|----------------|-----------------|
| <a href="#">Protocol file</a>                 | version 3   | 28/11/2017   | 13/09/2022 | No             | No              |
| <a href="#">Preprint results</a>              |   | 29/03/2023   | 31/03/2023 | No             | No              |
| <a href="#">Participant information sheet</a> | Sample donation informed consent in Spanish<br>version v.03 | 30/06/2017   | 28/04/2023 | No             | Yes             |
| <a href="#">Participant information sheet</a> | Spanish   | 31/10/2017   | 28/04/2023 | No             | Yes             |
| <a href="#">Results article</a>               |   | 27/06/2023   | 04/07/2023 | Yes            | No              |