# PROTOCOL

# An intervention program on dietary and physical activity using new technologies in food-insecure elderly

**Contents**

## 1. Investigator Signature

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|---|---|
| Title | An intervention program on dietary and physical activity using new technologies in food-insecure elderly |
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| Date of finalization of this current version of the protocol | 8th May 2015 |

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## 2. Title Page

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|---|---|
| Title | An intervention program on dietary and physical activity using new technologies in food-insecure elderly |
| Sponsor | Sociedade Portuguesa de Reumatologia |
| Sponsor's address | Av. de Berlim, 33 B<br>1800-033 Lisboa<br>Portugal |
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## 3. Synopsis

The first United Nations' Millennium Development Goal is to eradicate extreme poverty and hunger. Following this objective, European Union has been developing programs and funding research projects to assess and fight food insecurity. WHO's European Food and Nutrition Action Plan (2015-2020) aims to reduce inequalities targeting vulnerable populations. In Portugal, the aim of the National Health Plan is to maximize health gains and to improve health in all individuals, reducing inequalities. Because of decreased financial resources, increased comorbidities and poor physical strength with ageing, older adults are more likely to face needs making them more vulnerable to adverse health conditions. Food insecurity is a worldwide problem. The concept is mainly focused on limited or uncertain food accessibility, and availability due to lack of resources. However, the elderly experiences nutritional deficits and limited or uncertain food use due to function impairments and health problems. Food insecurity has been a risk factor for poor nutritional status and low muscle power especially in those with physical disabilities, increasing hospitalizations and dead.

The lack of epidemiological information, valid and useful to support decision-making, constitutes a major public health challenge in Portugal. Moreover, there is a lack of population management programs in old people targeting nutrition, balance, muscle strength and clinical outcomes in order to optimize health status and reduce health resources consumption.

Taking into account the principles above, we will conduct a randomized control trial with personalized, cheap and easily affordable dietary and physical exercise programs, in 200 elderly with food insecurity, selected from the EpiReumaPt study. Subjects will be followed over 6 months year and intervention will last 3 months. The intervention will be based on new ICT –TV interactive programs that will be available as intervention tools, developed by our team, that aim to improve knowledge regarding healthy food acquisition and confection at low prices and implement regular physical exercise in elderly. The primary outcome will be the improvement of food security among elderly. The clinical endpoints will be the improvement of dietary patterns, indicators of nutritional status, serological markers of cardiovascular risk, body composition balance, muscle

strength, balance and control postural, physical activity habits and quality of life contributing to falls prevention. Our consortium is composed by a group of leading experts on different fields. The knowledge and experience exchange among partners will assure goal attainment. We will be able to accomplish the schedule and answer the relevant research questions addressed in the project.

Our project will develop new sustainable and easy to disseminate ICT tools tailored to change behaviors and improve health. Ultimately, it will contribute to the improvement of health status, decrease of morbidity and health related costs of a main vulnerable group in the Portuguese population.

## 4. Background and rationale

Nutritional status is a key indicator of poverty, hunger, poor health, inadequate education and social condition [1]. The first United Nations' Millennium Development Goal is to eradicate extreme poverty and hunger. According to the European Parliament, the estimated losses linked to health inequalities had cost around 1.4% of GDP within the European Union in 2011 [2-4]. Following this objective, the European Union has been developing programs and funding research projects to assess and fight food insecurity. The new WHO's European Food and Nutrition Action Plan (2015-2020) established the reduction of inequalities in access to healthy food as a priority goal for food and nutrition policies in the European context [5]. In Portugal, the aim of the National Health Plan [6] is to maximize health gains by involving all social partners at national, regional and local levels in the promotion of healthy policies and to improve health in all individuals, reducing inequalities. Moreover, the Portuguese Program for the Promotion of Healthy Eating (PNPAS), also consider the reduction of inequalities in diet as a one of its main challenges [7].

Defining the concept of food insecurity attributes include uncertainty or worry about food, inadequate quality of food, inadequate quantity of food, food acquired through socially unacceptable means, and lack of consistent access to adequate food [8]. Rates of food insecurity have been rising worldwide [8]. In fact, while the United States is one of the wealthiest nations in the world with a rich and abundant supply of food and resources, 14.3% of U.S. households were food insecure at some point during 2013 [9].

A study in Portuguese primary care centers attendees in 2012 showed that 49.0% were food insecure [10]. Furthermore, more than one third of Portuguese adults with food insecurity are overweight (41.0% in moderate food insecurity and 37.7% in severe food insecurity categories) [11]. In other countries, food insecurity showed to be associated with poor self-rated health, and several non-communicable chronic diseases such as diabetes, hypertension, fibromyalgia and osteoporosis [12-16].

Because of decreased financial resources, increased comorbidities and poor physical strength and balance with ageing, older adults are more likely to face needs making them more vulnerable to adverse health conditions. For older

adults, who generally require special attention for optimal nutrition, food insecurity has been a risk factor for poor nutritional status and low muscle power especially in those with physical disabilities, increasing hospitalizations and dead [17, 18]. The concept of food insecurity in elderly persons includes nutritional deficits and other relevant aspects related with limited or uncertain food use (inability to use food) due to functional impairments and health problems as well as inadequate availability, affordability and accessibility of food [19, 20].

Research on food insecurity and health-related conditions among older adults is limited. Furthermore, less is known about the effectiveness of interventions to reduce food insecurity and to improve the nutritional status among elderly populations.

For this study, we hypothesized that an intervention program on dietary and physical activity that uses information and communication technologies (ICTs) tools will improve food security, as well as, some clinical endpoints such as nutritional status, body composition, balance, strength and quality of life in the elderly population.

## 5. Objective and endpoints

### 5.1 General objective

- To improve nutritional status, body composition, balance, strength and quality of life among older Portuguese subjects with food insecurity.

### 5.2 Primary objective

- To improve food security among older Portuguese population (evaluated by Household Food Insecurity Scale adapted from the USDA Household Food Security Survey Module).

### 5.3 Secondary objectives

To improve several clinical endpoints, such as:

- Dietary habits (evaluated by Food Frequency Questionnaire)
- Indicators of nutritional status (BMI and MNA)
- Muscle strength (evaluated by dynamometer)
- Quality of life (EQ5D V2)
- Serological markers of cardiovascular risk (insulin resistance, cholesterol levels, haemoglobin A1c, hs-CRP, adipocytokines, IL1, IL6, and TNF)
- Balance and postural control (by a force plate (Bertec Corporation – USA)
- Physical activity (by an actimeter and a walking test (locometrix TD))
- Body composition balance evaluated by DXA.

### 5.4 Primary endpoint

- Changes from baseline in food insecurity score among older Portuguese population at 6 months.

### 5.5 Secondary endpoints

- Changes from baseline in dietary habits among older Portuguese population at 6 months.

- Changes from baseline in indicators of nutritional status (BMI and MNA) among older Portuguese population at 6 months.

- Changes from baseline in muscle strength improvement among older Portuguese population at 6 months.
- Changes from baseline in quality of life among older Portuguese population at 6 months.
- Changes from baseline in serological markers of cardiovascular risk (insulin resistance, cholesterol levels, haemoglobin A1c, hs-CRP, adipocytokines, IL1, IL6, and TNF) among older Portuguese population at 6 months.
- Changes from baseline in balance and postural control among older Portuguese population at 6 months.
- Changes from baseline in physical activity habits among older Portuguese population at 6 months.
- Changes from baseline in body composition balance among older Portuguese population at 6 months.

## 6 Project design

We will perform an interventional study (randomized controlled study) on dietary and physical activity in the elderly subjects with food insecurity, identified in the EpiReumaPt study. Furthermore, new information and communication technologies (ICTs) will be develop to support this interventional program.

About 200 elderly with food insecurity from the EpiReumaPt study will be invited to participate in a randomized controlled study with a personalized dietary and exercise program that uses new information and communication technologies (ICTs) –TV programs available in a TV interactive platform and mobile phone's text messages, as intervention tools. Subjects will be followed over 6 months and intervention will last 3 months. Our aim is to determine the short and long-term improvement in food security situation, as well as, in some clinical endpoints (dietary habits, nutritional status (BMI, body composition balance evaluated by DXA and MNA), muscle strength, physical activity habits and quality of life (EQ5D)). We will also assess biomarkers of health improvement associated with the nutritional and exercise intervention in elderly with food insecurity.

EpiReumaPt [21] is a national population-based survey developed by Jaime Branco and Helena Canhão as principal investigators. The main aim of this project was to determine rheumatic diseases (RD) prevalence and its burden. We included 10,661 subjects across the country (mainland, Azores and Madeira Islands), who were interviewed by trained interviewers at their homes [22]. 3886 out of them were observed in a clinical appointment performed in several primary Health Care Centers across the country. Clinical appointments were conducted by a multidisciplinary team (rheumatologist, nurse, X-ray technician) with the support of a mobile unit (with digital X-ray, DXA and equipped for sample collection and short-term storage), between Sep 2011 and December 2013. Data management and analysis is ongoing. In EpiReumaPt, 3184 elderly were interviewed and data on sociodemographic, economic, life style, nutrition patterns, physical exercise, therapies, chronic noncommunicable diseases, health status and mental status were collected. In the second wave of follow-up of EpiReumaPt, household food insecurity will be assessed according to the

objectives of the ProFooSe Project, a project funded by EEA Grants that will be conducted between June and December 2015.

The randomized controlled study (interventional study) aims to change and improve short and long term food security situation, specific energy balance-related behaviors, body composition, balance and strength. The secondary outcomes will be the identification of serological markers of health improvement. Baseline, 3 months and 6 months multidisciplinary appointments will be conducted to collect clinical data (blood pressure, abdominal perimeter, weight and height), blood samples (insulin resistance, cholesterol levels, haemoglobin A1c, adipocytokines, hs-CRP, IL1, IL6, and TNF), body composition by DXA, muscle strength using a dynamometer, balance and postural control by a force plate (Bertec Corporation - USA) and physical activity by an actimeter and a walking test (locometrix TD).

For the experimental group, nutritional and physical exercise programs will be prescribed at baseline. Moreover, nutritional and physical exercise programs will also be delivered through ICTs. In fact, interactive Tv programs with tips regarding healthy food acquisition and confection at low prices and regular physical exercise will be delivered once a week during 3 months. The videos content will be based on the book *"Alimentação Inteligente – Coma melhor, poupe mais"*, a book published by the Directorate-General of Health on how to eat healthy on a low budget. Moreover, experienced researchers from "Faculdade de Motricidade Humana" will develop videos with exercise programs specific adjusted for elderly. This videos accessed by TV interactive are very helpful to teach nutritional and exercise programs in older people. Also text messages are powerful in recalling and stimulating study participants to adhere. Tv interactive will also be used to collect data and a protocol will be developed in order to have regular data regarding some eating habits, blood pressure and falls. Pushing TV bottoms in interactive programs and using mobile phones can be used to easily collect simple information. ICT are very useful to transmit information, monitor and increase study's adherence and to collect real-time information. Finally, adherence to the program will be monitor using the tv interactive data.

Early impact in behavior and health will be assessed throughout the intervention. Also delayed impact will be assessed, using the same assessment

tools, 3 months after the end of the intervention.

Validated questionnaires will be applied to representative samples. Our expert team in large database analysis will apply robust statistical methods. The trial will follow the principles of best clinical practices, all subjects will sign an informed consent and all procedures will be submitted to Ethics Committee.

Given the vast expertise of the team members and institutions involved in handling large-scale surveys and trials, nutrition, exercise, muscle and frailty assessment and database analysis, this study has a higher likelihood of success. We will build upon the partners' experience to gather data on food insecurity and frailty and to develop for the first time in Portugal, innovative tools, easy to disseminate at a low cost, which will contribute to identify and change behaviors with the aim of reducing diet inequalities and improving nutrition patterns, balance and muscle power in insecure and disadvantage elderly.

To accomplish our aims this project is composed by 3 main tasks:

**Task 1 –** Development of specific information and communication technology (ICT) tools to support the interventional randomizes controlled study, that aims to improve food security, nutritional status, body composition, balance and strength, contributing to falls prevention in elderly.

**Task 2 –**Recruitment and follow-up of subjects for the randomized control study with a personalized and affordable dietary and physical activity program that uses new information and communication technologies (ICTs).

**Task 3 –** Identification of serological markers of nutritional and muscle power improvement in elderly with food insecurity.

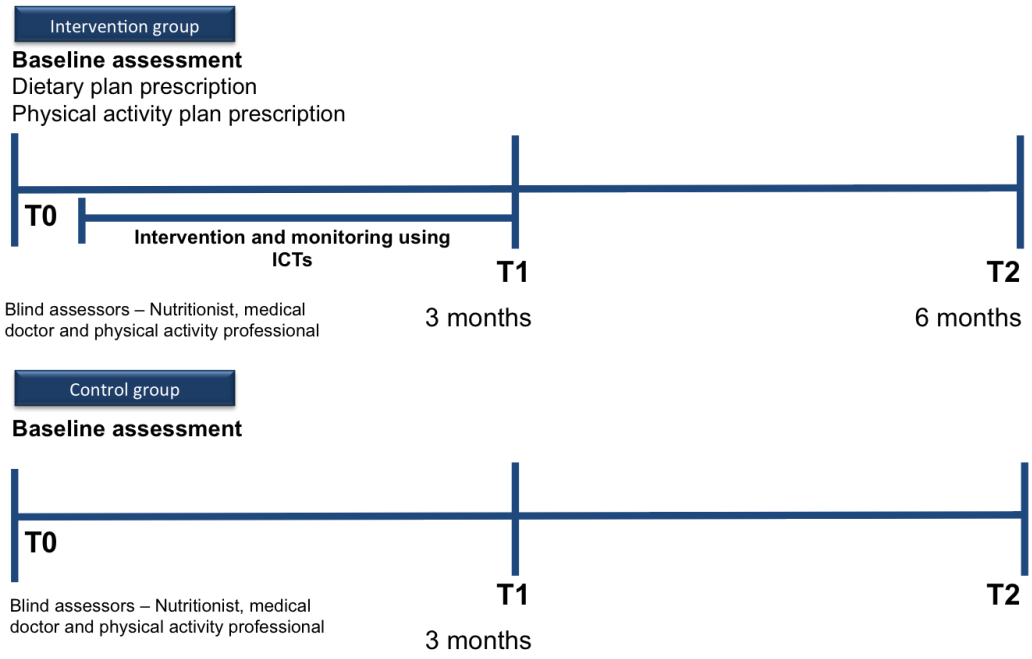


**Figure 1.** Project design diagram.

# 7 Study population

## 7.1 Overview

This randomized controlled study (interventional study) will include elderly (≥ 65 years old) subjects from EpiReumaPt sample who are food insecure.

Taking into account a prevalence of food insecurity among elderly of 9% estimated in the NHANES III study and considering a refusal / dropout rate of 33% we expect to include and randomize 100 experimental and 100 control elderly with food insecurity from the representative EpiReumaPt sample. The exclusion criteria are those illiterate, having hearing/visual loss, significant cognitive impairment and functional impairment as defined by a Barthel Index (BI) ≤ 35.

If we have recruitment difficulties we are prepare to apply food insecurity questionnaires to elderly that attend primary care centers at Lisbon region and invite the ones that are food insecure to attend this RCT. This recruitment will be developed under the Infofamília Project, a national survey on household food insecurity conducted by the Directorate-General of Health (DGS).

## 7.2 Inclusion criteria

To be eligible for this randomized controlled study, subjects must fulfill all of the following inclusion criteria.

Each subject must be/have...

- Able and willing to give written informed consent and comply with the requirements of the study protocol.

- Age ≥ 65 years old.

- Identified as food insecure according to the second wave of follow-up of EpiReumaPt.

## 7.3 Exclusion criteria

A subject meeting any of the exclusion criteria listed below must be excluded

from participating in the trial.

The subject is/has....

- Illiterate.
- Hearing/visual loss.
- Significant cognitive impairment.
- Functional impairment as defined by a Barthel Index (BI) ≤ 35.
- Dependence upon others for food acquisition and food preparation.

## 8. Project tasks and assessments

This project is composed by 3 main tasks:

**Task 1 –** Development of specific information and communication technology (ICT) tools to support the interventional randomizes controlled study, that aims to improve food security, nutritional status, body composition, balance and strength, contributing to falls prevention in elderly.

**Task 2 –** Recruitment and follow-up of subjects for the randomized control study with a personalized and affordable dietary and physical activity program that uses new information and communication technologies (ICTs).

**Task 3 –** Identification of serological markers of nutritional and muscle power improvement in elderly with food insecurity.

### 8.1 Task 1 - Development of specific information and communication technology (ICT) tools to support the interventional randomizes controlled study, that aims to improve food security, nutritional status, body composition, balance and strength, contributing to falls prevention in elderly.

Task 1 will include the development of specific information and communication technology (ICT) tools to support an interventional randomized controlled study (Task 2) that aims to improve food security, nutritional status, body composition, balance and strength contributing to falls prevention in elderly.

New health ICT is broadly defined as the use of information and communication technology in health care to support the delivery of patient or population care or to support patient self-management. Health ICT can support patient care related

activities such as order nutritional programs, communications, results reporting, care planning and clinical or health documentation. Health IT applications or systems can use a variety of platforms, such as desktop computers, tablet computers, cellular phones, smart phones, and others. The use of health ICT has been demonstrated to improve health care quality. New health ICT can be used to support chronic disease management, adherence to clinical guidelines, and increased appropriate preventive screening. ICT are key to improve the well known 4 P - personalized, participatory, preventive and predictive medicine.

In Task 1, our team will develop new health ICTs to deliver and support the nutritional and exercise programs and also to allow data collection in real-time. The tools are able to register their use pattern such as number of hours, time of use and subject preferences which will allow us to measure adherence to the program.

- We will develop videos based on the book *"Alimentação Inteligente – Coma melhor, poupe mais"*, published by the Directorate-General of Health that will be delivered at weekly basis. Moreover, experienced researchers from "Faculdade de Motricidade Humana" will develop videos with exercise programs specific adjusted for elderly that will be delivered 3 times per week. This videos accessed by TV interactive are very helpful to teach nutritional and exercise programs in older people. Text messages will be sent with reminders for the physical exercise program and water intake. Tv interactive will also be used to collect data and a protocol will be developed in order to have regular data regarding some eating habits, blood pressure, falls and health resources consumption (outpatient clinical appointments, hospitalizations).

### 8.2 Task 2 – Recruitment and follow-up of subjects for the randomized control study with a personalized and affordable dietary and physical activity program that uses new information and communication technologies (ICTs).

In Task 2 we will use the acquired knowledge and clinical expertise of our team to efficiently enroll 200 elderly with food insecurity, selected from the

EpiReumaPt study to participate in a randomized control study with a personalized and affordable dietary and physical activity program that uses new information and communication technologies (ICTs). Subjects will be followed over 6 months and intervention will last 3 months.

Baseline, 3 months and 6 months multidisciplinary evaluations will be conduced to collect clinical data (blood pressure, abdominal perimeter, weight and height, MNA questionnaire, EQ5D and SF36, comorbilities, anxiety and depression symptoms, risk of falls), blood samples (insulin resistance, adipokines, cholesterol levels, haemoglobin A1c, hs-CRP, IL1, IL6, and TNF), body composition by DXA, muscle strength using a dynamometer, balance and postural control using a force plate (Bertec corporation) and physical activity by a walking test (Locometrix TD). Participants will be asked to wear an actimeter. Variables will also be collected using ICT tools, such as regular physical activity information, weight registries, food frequency questionnaire, food security assessment, health resources consumption (outpatient clinical appointments, hospitalizations), and drug intake. ICT tools will be applied to each subject according to his/her ICT profile in the baseline outpatient clinical visit.

A personalized and affordable dietary and the physical activity program will be developed for the experimental group. This study will focus on increasing the water intake and promoting fruit and vegetable consumption as well as meat or fish by the elderly. The nutrition program will teach to create simple and low cost meals taking into account their physical disabilities. For the experimental group, nutrition tips and culinary recipes will be available through videos on the interactive TV platform. Nutrition tips will be based on the book *"Alimentação Inteligente – Coma melhor, poupe mais"*, a book published by the Directorate-General of Health on how to eat healthy on a low budget. Moreover the experimental group subjects will be instructed to take a structured exercise course of one hour, 3 times per week for 6 months, delivered by interactive TV. Text messages with reminders on physical activity and water intake will be sent to participants. Phone calls and ICT deliveries will be used to assure compliance to the program.

In conclusion, we consider that our intervention will contribute to the improvement of food security situation, health, nutritional status and muscle

strength among elderly with food insecurity.

### 8.3 Task 3 – Identification of serological markers of nutritional and muscle power improvement in elderly with food insecurity.

In Task 3 we will identify serological markers of nutritional and muscle power improvement in elderly with food insecurity. Those subjects will participate in a randomized control trial (Task 2) that will have a nutritional and exercise program delivered by ICT tools (Task 1). We will also assess serum biomarkers of health improvement associated with the nutritional and exercise interventions.

Inflammatory cytokines (IL1, IL6 and TNF) increasing with age and are significantly associated with metabolic syndrome and cardiovascular risk. On the other hand, adipokines possess insulin sensitizing, anti-atherosclerotic and anti-inflammatory properties. A number of epidemiological studies on adipokines (adiponectin, leptin, visfatin, resistin) have been conducted in aged populations. Adipokine levels were significantly associated with high-density lipoprotein cholesterol (HDLPLOS C) concentrations in postmenopausal women, which suggested that high adipokine levels might have a protective effect against atherosclerosis, when the HDL-C concentrations are high. The inverse relationship between regional fat depots and the risk of the metabolic syndrome may be partially mediated by adipokine levels and the inflammatory status of the middle-aged and elderly.

We hypothesize that plasma inflammatory cytokines (TNF, IL1 and IL6) are increased in elderly with food insecurity as compared with elderly with no food insecurity and that the improvement of the nutritional status and muscle strength of these subjects will be associated with a significant decrease of these inflammatory cytokines. Moreover, adiponectin levels will be lower in elderly with food insecurity and will significantly increase after intervention and in the ones that have significantly improve their body composition, nutritional status and muscle strength.

This task will have two main steps. First, blood samples will be collected. Subjects will be divided in two groups- elderly with food insecurity versus elderly with no food insecurity. Serum levels of inflammatory cytokines (TNF,

IL1 and IL6), adipokines, insulin resistance, cholesterol, hs-CRP and hemoglobin A1c will be determined and comparisons will be made between the two groups. Socioeconomic and demographic (age, gender, region, income, employment status, educational level) and clinical variables will be included in the analysis.

Secondly, serum levels of the proteins mentioned above will be determined in subjects with food insecurity who will be recruited to a randomized control trial (Task 2) with a personalized cheap and easily affordable dietary and physical exercise programs delivered by ICTs (Task 1). The intervention aims to improve nutritional status, body composition, balance and strength in Portuguese elderly food insecure. The secondary aim presented in this Task is to identify serological markers of nutritional and muscle power improvement. In this trial, blood samples will be collected at baseline, 6 months and 1 year. Comparisons between the group of elderly with food insecurity that were under the program of nutrition and physical exercise and the control group (elderly with food insecurity with no intervention) will be made. Finally, we will also compare serum levels of inflammatory cytokines, adipokines, hs-CRP, insulin resistance, cholesterol and hemoglobin A1c between elderly that achieved the primary outcome and the ones who do not.

In summary, with this task we will identify markers of food insecurity in elderly and also of nutrition and muscle strength improvement.

Biological samples will be collected with the aim described above, as well as, with the aim to build a Biobank to support a diverse range of research projects intended to improve prevention and to promote health. This Biobank will take into account all the ethical issues and law requirements.

## 9. Potential risks and benefits

Each clinical trial has its own benefits and risks, although for this project are not expected so many risks.

During this study, two blood samples will be collected (10ml for each one). In general, these procedures are quite well tolerated. The risks of taking blood include pain, a bruise at the point where the blood is taken, redness and swelling of the vein and infection, and a rare risk of fainting.

Balance and postural control assessment will be conducted using a force plate (Bertec Corporation) and physical activity will be assessed by a walking test (Locometrix TD). During these assessments, it is possible to have a small fall risk, although this risk will be minimized with the presence of lateral protections in the equipments.

The radiation dose from DEXA is estimated of 0,1-0,4 μSV (0.01-0.04 mrem), which are the common levels of radiation that we are exposed in the urban areas. Other risks are not expected.

The other diagnosis methods are in general well tolerated, with no risks described,

The participation in this study might also have some benefits for its participants. This study will provide relevant information on healthy eating and physical activity. Thus, it might contribute for health improvements of the participants.

## 10. Project schedule

This project is planned to start June 2015 and its baseline evaluation planned for September 2015. The planned data for completion the last follow-up evaluation is February 2016.

## 11. Statistical and analytical plan

### 11.1 Sample size calculation

Taking into account a prevalence of food insecurity among elderly of 9% estimated in the NHANES III study and considering a refusal / dropout rate of 33% we expect to include and randomize 100 experimental and 100 control elderly with food insecurity from the representative EpiReumaPt sample.

### 11.2 Statistical methods

Analysis will be performed with STATA. Prevalence estimates and confidence intervals will be calculated. Continuous variables will be reported as mean and standard deviation (or in case of non-normal distribution as median and interquartile range). Categorical variables will be displayed as frequencies or proportions. The association between each outcome and the candidate covariables will be performed using generalized models. We will use multivariate logistic and linear (according to the outcome) regression models. The candidate covariates will be first analyzed by univariate regression. Covariates will enter the multivariate models if their p-value<0.25 in univariate analysis or considered clinically relevant in this setting. The selection of covariates will be stepwise by backward selection, according to the level of significance<0.05. Multilevel analysis and sensitive analysis will be performed when appropriate.

## 12. Ethical conduct

### 12.1 Independent Ethics Committee or Institutional Review Board

Prior to initiation of the project at any site, the project, including the protocol, informed consent, and other project documents must be approved by an appropriate IRB/IEC. The IRB/IEC must be constituted according to applicable regulatory requirements.

In the event that the IRB/IEC requires changes in the protocol, the sponsor shall be advised and must approve the changes prior to implementation. The investigator shall not modify the project described in the protocol once finalized and after approval by the IRB/IEC without the prior written approval of sponsor.

### 12.2 Subject Information and Consent

The details of the protocol must be provided in written format and discussed with each potential subject, and written informed consent must be obtained for all subjects before any project-related procedure is performed. In obtaining informed consent, the information must be provided in language and terms understandable to the subject. The subject, or the subject's legal representative, must give their written consent to participate in the interventional study. The signed and dated consent form itself must be retained by the investigator as part of the project records. A copy of the signed and dated consent form must be given to the subject. The consent form must include all of the required elements of informed consent in accordance with ICH Guidelines E6 and local laws.

The consent form must be approved by the appropriate IRB/IEC and sponsor before trial initiation at a project site. Any subsequent changes to the approved informed consent form must be reviewed and approved by the appropriate IRB/IEC and sponsor before implementation.

### 12.3 Protection and confidentiality of participants' data

The confidentiality of participants' data will be ensured. Identification numbers will be used for logistic reasons, although they will be saved independent of other data. These data will be not divulgated by other institutions without involvement in the project.

All the participants' data will be encrypt to preserve the anonymity of each

individual, according to the obligations described in the Law dispatch 20510/2008, of July 24th. In the transference of the clinical data to a database from the SPR, the data encryption process will enable the guarantee of the confidentiality and anonymity of each individual. It will be available a code number to decode the subjects' identity. This code number will be just available for the principal investigator, in a different place of the other data. The computer where the data will be centralized will be available in the SPR, with restrict access (with an username and password) for the principal investigator, or other person designated for that propose.

### 12.4 Biobank data collection and protection

This study is committed with the requirements of the Deliberation nº 227/2007 of the National Commission of Data Protection. It will be guaranteed for the participants that their participation in this intervention project and in the Biobank is distinctive. Participants will be not required to integrate the Biobank if they agree to participate in the intervention study.

The Biobank constitution will be committed to protecting the confidentiality of data and samples. Systems will be in a place for secure data flow and for protecting confidentiality, (reversibly) anonymising data and samples and enforcing security. During enrolment, the assessment centre will need to hold identifying information (such as name, or other elements of identification) together with information collected from the participant during the assessment visit, and this information will be encrypted for security.

All identifying information will be held centrally by SPR in a restricted-access database that is controlled by principal investigator. Only a few people within Biobank will have access to the "key" to the code for relinking the participants' identifying information with their data and samples (i.e. "reversible anonymisation"). It is necessary to retain this link with identifying information to allow follow-up of participants' health; to eliminate redundant data (e.g. duplicate cases); to verify correctness and completeness of data against original records; to establish correct linkages among databases; and to find specific data or samples if participants withdraw.

Regarding to the sample collection, it will be collected 10 ml of blood for each subject. The biological samples will be collected to an appropriate bottle. Bottles with biological samples will be transported, as soon as possible, for the Biobank of the *Instituto de Medicina Molecular da Faculdade de Medicina da Universidade de Lisboa* (IMM/FMUL). Exceptionally, biological samples might be saved up to one week in a refrigerator.

All bottles should be identified with the following information: date and local of data collection, contact of the person responsible for the sample collection, identification code of the participant (without the participants' name or other element of identification).

## 13. Participants' insurance

An insurance will be provided for each participant in this study.

## 14. Publications and other rights

### 14.1 Rights to publish by investigator

The investigator has the right to publish or publicly present the results of the project in accordance with this Section 12.1 of the protocol.

The investigator agrees not to publish or publicly present any interim results of the project without the prior written consent of the sponsor. The investigator further agrees to provide to the sponsor 45 days prior to submission for publication or presentation, review copies of abstracts or manuscripts for publication (including, without limitation, slides and texts of oral or other public presentations and texts of any transmission through any electronic media, eg, any computer access system such as the Internet, World Wide Web, etc) that report any results of the project. The sponsor shall have the right to review and comment with respect to publications, abstracts, slides, and manuscripts and the right to review and comment on the data analysis and presentation.

If the parties disagree concerning the appropriateness of the data analysis and presentation, and/or confidentiality of the sponsor's confidential information, investigator agrees to meet with the sponsor's representatives at the project site or as otherwise agreed, prior to submission for publication, for the purpose of making good faith efforts to discuss and resolve any such issues or disagreement.

### 14.2 Use of Proprietary or Confidential Information in a Publication

No publication or manuscript shall contain any trade secret information of the sponsor or any proprietary or confidential information of the sponsor and shall be confined to new discoveries and interpretations of scientific fact. If the sponsor believes there is patentable subject matter contained in any publication or manuscript submitted for review, the sponsor shall promptly identify such subject matter to investigator. If sponsor requests and at sponsor’s expense, investigator shall use its best efforts to assist sponsor to file a patent application covering such subject matter with the USA Patent and Trademark Office or through the Patent Cooperation Treaty prior to any publication.

### 14.3 Use of Project Information in a Publication

Investigator is granted the right subject to the provisions of this protocol to use the results of all work provided by investigator under this protocol, including but not limited to, the results of tests and any raw data and statistical data generated for investigator's own teaching, research, and publication purposes only. Investigator/Institution agrees, on behalf of itself and its employees, officers, trustees, and agents, not to cause said results to be knowingly used for any commercial purpose whatsoever except as authorized by the sponsor in writing.

### 14.4 Authorship of Publications

Authors of publications must meet the International Committee of Medical Journal Editors (ICMJE) guidelines for authorship and must satisfy the 3 criteria that follow:

a) Authors must make substantial contributions to the conception and design of the project, acquisition of data, or analysis of data and interpretation of results;

b) Authors must draft the publication or, during draft review, provide contributions (data analysis, interpretation, or other important intellectual content) leading to significant revision of the manuscript with agreement by the other authors;

c) Authors must provide written approval of the final draft version of the publication prior to submission.

All contributors who do not meet the 3 criteria for authorship should be listed in an acknowledgments section within the publication, if allowed by the journal, per the ICMJE guidelines for acknowledgment.

## 15. Investigators and project administrative structure

### 15.1 Sponsor

The sponsor of this project is indicated in Section 1, Investigator Signature Page and Section 2, Title Page.

The sponsor is Sociedade Portuguesa de Reumatologia as Institution and Helena Cristina de Matos Canhão principal investigator.

## 15.2 Investigators

### 15.2.1 Selecting Investigators

Only investigators qualified who have the knowledge, skills and experience to successfully achieve the project's goals are selected.

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