The effect of a combined caloric restriction and exercise intervention on phenotypic profiles of offspring of families with exceptional longevity and their partners

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON41285

Source
ToetsingOnline

Brief title
Growing Old Together

Condition

- Other condition

Synonym
body composition, energy metabolism, fat metabolism, glucose metabolisme

Health condition

lichaamsgewicht, lichaamssamenstelling, bloeddruk, metabole markers gerelateerd aan glucose- en vetstofwisseling

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: NWO

Intervention

Keyword: caloric restriction, exercise, metabolic profiles, middle-aged

Outcome measures

Primary outcome

Primary outcome measure is the change in fasting insulin level.

Secondary outcome

Secondary outcome measures are blood parameters (metabolic/metabolomics), parameters measured in biopsies of muscle and fat (proteomics/epigenetics), anthropometrics, body composition, blood pressure, 24-hour glucose monitoring, glucose load, energy metabolism (resting metabolic rate), and psychological factors (cognitive performance, mood, quality of life, sleep, hunger) parameters Magnetic Resonance (MR) scan (leg, brain, knee cartilage) and activity levels.

Study description

Background summary

In animals caloric restriction (CR) is the most effective intervention known to extend lifespan and to delay the onset or reduce the incidence of many age-related diseases. A similar effect is seen in multiple nutrient signaling pathways that have been connected to CR and longevity regulation, implying that aging is a regulated process and that certain genes govern the rate of aging. This has been shown in a variety of species including mammals and is also an

interesting observation from the perspective of human aging. However, the evidence on the effectiveness of caloric restriction on biomarkers of healthy aging in humans is limited and lacking in middle-aged individuals. It can also be questioned in the genetic heterogeneous human population, whether dietary restriction improves the metabolism of all individuals. In the Leiden Longevity Study we have two groups of individuals to compare in this sense: a healthy ageing group (members of long-lived families) that display a beneficial profile of many metabolic markers and a normative ageing group (the partners of these members) with an average metabolic profile. The longevity families were included by selecting for living nonagenarian sibships (sibpairs or larger sibships) and recruiting these individuals, their offspring and the partners of that offspring (The Leiden Longevity Study). The existing contrast of healthy and normative ageing, the fact that we have numerous metabolic baseline phenotypes of these study participants and the fact that they are middle aged (the group of individuals that are likely to improve life expectancy by healthy behavior) prompted us to initiate a study into the health effects of dietary restriction and physical exercise specifically in these contrasting groups of middle aged individuals.

Study objective

The main objective of this study is to examine whether an intervention of dietary restriction and exercise can bring the phenotypic profiles (with respect to biomarkers of metabolic health) of the normative ageing controls (*partners*) towards those of their healthy aging spouses (*offspring* of families with exceptional longevity). We also examine if such an intervention could still improve the phenotypic profile of the offspring and which (clinical, biochemical, molecular) baseline mediators determine response to treatment. Additional objectives are to assess compliance (and its determinants) to the intervention, to determine implementation possibilities to stimulate healthy aging in middle-aged couples and to assess if possible health benefits last by reassessing the biomarkers of metabolic health 1 year after the intervention (for this aim budget still has to be raised).

Study design

Intervention study.

Intervention

3 months (13 weeks) intervention with 25% lowered energy expenditure by 12.5% caloric restriction and a 12.5% increase in physical activity.

Study burden and risks

Main study:

Eligible participants will first undergo a screening to determine fulfilment to in- and exclusion criteria. Prior to the baseline measurements habitual dietary intake (online FFQ) and habitual physical activity (accelerometer and physical activity questionnaire) will be assessed. In total participants will be visited at home twice (screening and pre-baseline assessment) and visit the study centre twice (baseline and after 13 weeks) after an overnight fast. At baseline and after 13 weeks of intervention the following biomaterials will be collected: blood, a fat biopsy and a muscle biopsy. Furthermore, at baseline and after 13 weeks of intervention, anthropometrics, body composition, blood pressure, 24-hour glucose, energy metabolism, and psychological factors will be assessed. Home visits will take about 45 minutes and visits to the study centre will take about 3 hours each time. Except the pre-baseline measurement, all visits will include collection of blood samples, which may cause a small hematoma. Furthermore, for the biopsies a small incision has to be made, which will be done by an experienced physician and which will heal completely. All other tests and measurements performed are non-invasive. During the 13 weeks of intervention participants will follow a dietary regime of 12.5% caloric restriction and 12.5% increased physical activity. To fulfil this program participants have to adhere to previously determined individual guidelines, will record their dietary behaviour and physical activity in a diary and will weekly be in contact with a dietician and/or physiotherapist.

Validation study:
Eligible participants will first undergo a screening to determine fulfilment to in- and exclusion criteria.
Participants are asked to fill out at home a questionnaire on their daily physical activity, taking around 15 minutes. At the LUMC, participants will fill out their age and sex on a form, and will have their weight assessed by means of a weighing scale. After attaching the activity sensors to the participant, a calibration of the COSMED K4b2 will be performed, as well as a sensor synchronisation by lightly jumping up and down for 20 seconds, and a step test in which the participant steps up and down a small step 20 times at a self-selected pace.
Subsequently, participants are to perform a series of daily-life activities: sitting, standing, lying down, performing household chores, walking and cycling. Activities will be performed both inside and outside of the LUMC. The DirectLife Activity monitor, Activ8, Polar Electro, experimental Philips activity monitor and GENEActiv are small and lightweight, and only burden participants minimally. The Equivital belt and COSMED K4b2 do not hinder participants* freedom of movement. The COSMED K4b2 is lightweight (<1kg) and the participant can remove its facemask at any time during the trial. All activities, both indoors as well as outdoors, are monitored and supervised at all times by a researcher. The entire trial at and around the LUMC will take approximately two hours.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Main study:
• Middle-aged (<75years) couples consisting of offspring from long-lived siblings and his/her current partner. In incidental cases they can participate as singles.
• BMI >=23 and <=35 kg/m2;Validation study:
• Middle-aged persons (age >= 60 and <= 70).
• BMI >=23 and <=35 kg/m2
• Participants must bring their own bike

Exclusion criteria

Main study:

• Type I or type II diabetes (on diabetic medication)
• Individuals who have lost or gained >=3 kg over the past 6 months
• Individuals engaged in heavy/intensive physical activity (top sport or physically heavy work)
• Any disease or condition that seriously affects body weight and/or body composition including active types of cancer, heart failure (NYHA III/VI), COPD (GOLD III/VI)
• Recent (3 months prior to intervention) immobilisation for longer than 1 week
• Psychiatric or behavioral problems (eg, history or clinical manifestation of any eating disorders, vegan dietary lifestyle, major depression)
• Medication: thyroid medication, immunosuppressive drugs (e.g. prednisone, methotrexat, biologicals (TNF-alpha antagonists etc))
use of anticoagulantia (e.g. coumarines, carbaspirin calcium): only excluded for biopsies
• Concurrent participation in any other intervention study or weight management program;Magnetic Resonance (MR) exclusion criteria (3 tesla and 7 tesla):
• Claustrophobia
• Pacemakers and defibrillators
• Nerve stimulators
• Intracranial clips
• Intraorbital or intraocular metallic fragments
• Cochlear implants
• Ferromagnetic implants (e.g. thoracic implant for scoliosis)
• Inability to lie supine during for 1 hour
• not having a general practitioner;Validation study:
• Any conditions that may inhibit free movement
• Individuals engaged in heavy/intensive physical activity (top sport or physically heavy work)

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-03-2012
Enrollment:	194
Type:	Actual

Ethics review

Approved WMO Date:	06-02-2012
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	25-03-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL38332.058.11