# Effects of almond consumption on chronic glucose regulation, vascular function and cognitive performance: The AL-INCLUSIVE trial

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Glucose metabolism disorders (incl diabetes mellitus) |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON50723

**Source**
ToetsingOnline

**Brief title**
Almonds and Health

### Condition

- Glucose metabolism disorders (incl diabetes mellitus)

**Synonym**
diabetes, glucose metabolism

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Universiteit Maastricht

**Source(s) of monetary or material Support:** californian almond board

## Intervention

**Keyword:** Almonds, Glucose metabolism, Nutrition, Vascular function

## Outcome measures

### Primary outcome

The primary endpoint is glucose infusion rate (GIR) determined during a hyperinsulinemic euglycemic clamp, as measure for whole body insulin sensitivity.

### Secondary outcome

* To investigate if improved chronic glucose metabolism in subjects with prediabetes after long-term almond consumption translates into improved peripheral and brain vascular function, and enhanced cognitive performance.

* To examine to what extent improved chronic glucose metabolism in subjects with prediabetes after long-term almond consumption can be explained by (combined) effects of lowered hepatic lipid accumulation and inflammation, skeletal muscle characteristics, visceral and subcutaneous fat accumulation, pancreatic function or fecal microbiota composition.

# Study description

### Background summary

Almond consumption is associated with ameliorations in various factors associated with cardiovascular disease (CVD) risk such as hyperglycemia, hyperlipidemia, and hypertension. Most of the intervention studies described were well-controlled, but relatively short. Therefore the question is whether

these effects are sustained over longer time. An additional question is how the protective effects on glycemic control and CVD risk can be explained mechanistically. Therefore in the current study we will combine a long-term intervention study with a panel of state of the art techniques to understand the potential mechanisms underlying the observed health effects.

**Study objective**

The primary objective of the proposed study is to examine and understand the impact of long-term almond consumption on chronic glucose metabolism in subjects with prediabetes (either impaired glucose tolerance (IGT) and/or impaired fasting glucose (IFG), as measured by whole body insulin sensitivity. Secondary objectives are to investigate if improved chronic glucose metabolism in subjects with prediabetes after long-term almond consumption translates into improved peripheral and brain vascular function, and enhanced cognitive performance. In addition, we will address to what extent improved chronic glucose metabolism in subjects with prediabetes after long-term almond consumption can be explained by (combined) effects of lowered hepatic lipid accumulation and inflammation, skeletal muscle characteristics, visceral and subcutaneous fat accumulation, pancreatic function or fecal microbiota composition.

**Study design**

The proposed study will be a 12 months randomized, well-controlled trial with a cross-over design. Two experimental periods of five months will be separated by a two months wash out period.

**Intervention**

During the intervention period of 5 months, subjects will receive daily 50 gr almonds, but not in the 2 months washout and 5 months control periods.

**Study burden and risks**

Subjects will be screened to determine eligibility during two visits of 150 and 15 minutes. During these screening visits, anthropometric measurements will be performed and blood pressure will be determined. In addition, a venous blood sample (9.0 mL) will be drawn and IGT and IFG status will be determined via an OGTT test (4.0 ml blood sampled two hours after drinking a standardized 250 mL glucose solution). During the study there will be 6 separate blood sampling moments and 4 test days (2x postprandial test and 2x clamp test). No direct health benefit for the study participants is expected. Investigational products are safe, i.e. the almonds and all ingredients to prepare the mixed meals for the postprandial test are commercially available and approved for human consumption. There are no side effects for the almonds as well as the mixed

meals. In total during the entire study 496 mL blood will be sampled (two screenings of each 13 mL, six times 15 mL fasting, 2 postprandial test days of 105 mL each, and two clamp test days of 85 mL each). Some study subjects may report pain during venipuncture. Insertion of the cannula can cause some discomfort and possible a hematoma or bruise. Some subjects may also report pain during the insertion of the cannula. Sampling adipose and skeletal muscle tissue biopsies is performed under local anaesthesia, a hematoma can occur due to invasive method for taking the fat biopsy, and muscle pain can occur due to invasive method for taking muscle tissue biopsy. In principle, all measurements are routine in our metabolic research unit (MRUM) and are not expected to lead to physical side effects. Time investment for the participants is approximately 32 hours, excluding travel time.

# 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

- Aged between 40-75 years
- Men and women
- BMI between 25-40 kg/m2 (overweight and obese)
- Being classified as having prediabetes, either having impaired glucose tolerance (IGT) and/or having impaired fasting glucose (IFG). IGT is defined according the criteria of the WHO and American Diabetes Association (ADA) as two-hour glucose concentrations of 7.8 to 11.0 mmol/l (140 to 199 mg per dL) during the 75-g oral glucose tolerance test. IFG is defined as having a fasting plasma glucose between 6.1 and 7.0 mmol/l (110 to 125 mg per dL) and a two-hour glucose concentration below 7.8 mmol/l (140 mg per dL).
- Serum total cholesterol < 8.0 mmol/L (further testing is recommended for excessive hyperlipidemia [serum total cholesterol * 8.0 mmol/L] according to the Standard for cardiovascular risk management of the Dutch general practitioners community [NHG])
- Serum triacylglycerol < 4.52 mmol/L
- No current smoker
- No diabetic patients
- No familial hypercholesterolemia
- No abuse of drugs
- Not more than 4 alcoholic consumption per day with a maximum of 21 per week??
- Stable body weight (weight gain or loss < 3 kg in the past three months)
- No use of medication known to treat blood pressure, lipid or glucose metabolism
- No use of an investigational product within another biomedical intervention trial within the previous 1-month
- No severe medical conditions that might interfere with the study, such as epilepsy, asthma, kidney failure or renal insufficiency, chronic obstructive pulmonary disease, inflammatory bowel diseases, auto inflammatory diseases and rheumatoid arthritis
- No active cardiovascular disease like congestive heart failure or cardiovascular event, such as an acute myocardial infarction or cerebrovascular accident
- Willingness to give up being a blood donor from 8 weeks before the start of the study, during the study and for 4 weeks after completion of the study
- No difficult venipuncture as evidenced during the screening visit
- Willing to comply to study protocol during study
- Informed consent signed

## Exclusion criteria

- Allergy or intolerance to almonds

- Serum total cholesterol * 8.0 mmol/L
- Serum triacylglycerol * 4.52 mmol/L
- Current smoker, or smoking cessation <12 months
- Diabetic patients
- Familial hypercholesterolemia
- Abuse of drugs
- More than 4 alcoholic consumptions per day or 21 per week
- Unstable body weight (weight gain or loss > 3 kg in the past three months)
- Use medication known to treat blood pressure, lipid or glucose metabolism
- Use of an investigational product within another biomedical intervention trial within the previous 1-month
- Severe medical conditions that might interfere with the study, such as epilepsy, asthma, kidney failure or renal insufficiency, chronic obstructive pulmonary disease, inflammatory bowel diseases, auto inflammatory diseases and rheumatoid arthritis
- Active cardiovascular disease like congestive heart failure or cardiovascular event, such as an acute myocardial infarction or cerebrovascular accident
- Not willing to give up being a blood donor from 8 weeks before the start of the study, during the study or for 4 weeks after completion of the study
- Not or difficult to venipuncture as evidenced during the screening visit
- Use of over-the-counter and prescribed medication or supplements, which may interfere with study measurements to be judged by the principal investigator;
- Use of oral antibiotics in 40 days or less prior to the start of the study;
- Blood donation in the past 3 months before the start of the study
- Not willing to comply to study protocol during study or sign informed consent

# Study design

## Design

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| Study type: | Interventional |
| Intervention model: | Crossover |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |

**Primary purpose:** Prevention

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 02-02-2018 |

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| Enrollment: | 84 |
| Type: | Actual |

## Ethics review

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| Approved WMO Date: | 19-07-2017 |
| Application type: | First submission |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |
| Approved WMO Date: | 22-11-2017 |
| Application type: | Amendment |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |
| Approved WMO Date: | 03-10-2018 |
| Application type: | Amendment |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |
| Approved WMO Date: | 24-07-2019 |
| Application type: | Amendment |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |

## 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 |
| --- | --- |
| ClinicalTrials.gov | NCT03419702 |
| CCMO | NL61425.068.17 |