

# The effect of a magnesium supplement on arterial calcification and arterial stiffness in individuals with type 2 diabetes

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<b>Registration date</b> 28/07/2023	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 21/01/2025	<b>Condition category</b> Circulatory System	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

People with type 2 diabetes have an increased risk of heart disease. Vascular calcification is common in people with type 2 diabetes and is associated with a higher risk of heart disease. However, people with type 2 diabetes have calcium builds up on the medial layer of the artery. This form of vascular calcification causes stiffening of the blood vessel wall. This stiffening of the arteries is undesirable because it increases the risk of cardiovascular disease. For example, stiffening of the arteries can cause the heart muscle to stiffen, which can lead to heart failure. The stiffening of the arteries must therefore be controlled and preferably even be reduced. This may be possible by taking three magnesium capsules per day. The aim of this study is to find out whether taking magnesium daily in a supplement can reduce vascular calcification and stiffness in people with type 2 diabetes. The knowledge gained from this research may contribute to improved treatment of vascular calcification and stiffness in people with type 2 diabetes.

### Who can participate?

Patients who have participated in the SMART-ARTEMIS study or the Early-HFpEF study (both Dutch cohort studies), aged 50-80 years, with type 2 diabetes and medial arterial calcification

### What does the study involve?

The study involves a total of four visits over a period of 6 months. Overall, the visits will take about 1.5 hours. Oral magnesium citrate supplements or placebo supplements have to be taken daily for 6 months. At screening and at the first follow-up after 3 months, participants will undergo a blood sampling for plasma magnesium concentrations and measurement of arterial stiffness. At baseline and at the second follow-up after 6 months, participants will undergo blood sampling for magnesium as well as cardiovascular biomarkers, will hand in a 24-hour urine collection and will undergo measurements of arterial stiffness. Dietary intake of magnesium will be assessed by a short food frequency questionnaire at the start of the study and the second follow-up after 6 months.

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

Oral magnesium citrate supplements have a good safety profile and previous studies reported a

low rate of side events (mainly gastrointestinal such as diarrhea, nausea, and vomiting) that usually only occur when used in very large doses. Blood sampling may cause discomfort and may result in bruising that continues up to a few days after the examinations. Determination of arterial stiffness is a non-invasive procedure method and no discomfort is expected. Participants gain no individual benefit from their participation in the study. However, the study is expected to increase the understanding of arterial stiffness and arterial calcification as a mechanism for increased heart disease risk in type 2 diabetes, and may ultimately lead to a new treatment.

Where is the study run from?

Diabetes Research Centre (Netherlands)

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

November 2021 to October 2024

Who is funding the study?

Netherlands CardioVascular Research Committee (CVON) (Netherlands)

Who is the main contact?

Romain Meer

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## Contact information

### Type(s)

Principal Investigator

### Contact name

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## Additional identifiers

### EudraCT/CTIS number

Nil known

### IRAS number

### ClinicalTrials.gov number

Nil known

## Secondary identifying numbers

Nil known

# Study information

## Scientific Title

Magnesium supplementation as a strategy to reduce serum calcification propensity and vascular stiffness in people with type 2 diabetes: a double-blind, randomized, placebo-controlled parallel trial

## Acronym

Mg-MAC

## Study objectives

Oral magnesium supplementation could improve calcification propensity and reduce vascular stiffness in people with type 2 diabetes, thereby representing a novel preventive strategy that may reduce their risk of cardiovascular disease.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

1. Approved 15/05/2023, Amsterdam UMC Medical Research Ethics Committee (Amsterdam UMC MREC) (Van der Boechorststraat 7, Amsterdam, 1081BT, Netherlands; +31 (0)20-4445585; metc@amsterdamumc.nl), ref: 2022.0524 - Mg-MAC
2. Approved 15/05/2023, Medical Ethics Committee of Amsterdam UMC, location VUmc (postal address: not available due to working from home due to the COVID-19 pandemic; +31 (0)20-44 45585; metc@vumc.nl), ref: 2022.0524 - NL81281.029.22

## Study design

Single-center interventional double-blind randomized placebo-controlled parallel trial

## Primary study design

Interventional

## Secondary study design

Randomised controlled trial

## Study setting(s)

Other therapist office, Other

## Study type(s)

Treatment

## Participant information sheet

Not available in web format, please use contact details to request a participant information sheet

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

Vascular stiffness in people with type 2 diabetes

## **Interventions**

The goal is to investigate the effect of daily intake of 350 mg of magnesium citrate oral supplementation over a period of 6 months on serum calciprotein particle maturation time (T50), a measure of calcification propensity, and on vascular stiffness, in people with type 2 diabetes (T2D). The trial will be performed in a double-blind fashion (blinding for participants, investigators and outcome assessors) with two equal groups of 37 participants. To ensure the double-blind design, optically similar capsules will be packed and coded by the laboratory, which will provide the study medication (magnesium supplements and placebo). The randomization will be performed by a statistician not involved in the study by using a randomization list. Blocked randomization (blocks of 4) will be used to ensure good balance of participant characteristics in each group. Randomization will be stratified on sex, two strata of age and on two strata of the carotid-femoral pulse wave velocity (c-f PWV) to prevent misbalance of age and baseline c-f PWV values at randomization. Allocation will be determined by using a computerized random number generation process. All study products will be sequentially numbered.

## **Intervention Type**

Supplement

## **Primary outcome measure**

1. Serum T50 measured using nephelometry at 3 and 6 months after baseline
2. Carotid-femoral pulse wave velocity (c-f PWV) measured using applanation tonometry at 3 and 6 months after baseline

## **Secondary outcome measures**

1. Total magnesium measured in heparin vials using standard laboratory tests at the Dijklander Hospital Laboratory at 3 and 6 months after baseline
2. Sodium measured in heparin vials using standard laboratory tests at the Dijklander Hospital Laboratory at 6 months after baseline
3. Potassium measured in heparin vials using standard laboratory tests at the Dijklander Hospital Laboratory at 6 months after baseline
4. Calcium measured in heparin vials using standard laboratory tests at the Dijklander Hospital Laboratory at 6 months after baseline
5. Phosphate measured in heparin vials using standard laboratory tests at the Dijklander Hospital Laboratory at 6 months after baseline
6. Urea measured in heparin vials using standard laboratory tests at the Dijklander Hospital Laboratory at 6 months after baseline
7. Total protein measured in heparin vials using standard laboratory tests at the Dijklander Hospital Laboratory at 6 months after baseline
8. Creatinine measured in heparin vials using standard laboratory tests at the Dijklander Hospital Laboratory at 6 months after baseline
9. Triglycerides measured in heparin vials using standard laboratory tests at the Dijklander Hospital Laboratory at 6 months after baseline
10. Total cholesterol measured in heparin vials using standard laboratory tests at the Dijklander Hospital Laboratory at 6 months after baseline
11. LDL-cholesterol measured in heparin vials using standard laboratory tests at the Dijklander Hospital Laboratory at 6 months after baseline
12. HDL-cholesterol measured in heparin vials using standard laboratory tests at the Dijklander Hospital Laboratory at 6 months after baseline
13. Fasting plasma glucose measured in NaF vials using standard laboratory tests at the Dijklander Hospital Laboratory at 6 months after baseline

14. HbA1C measured in EDTA vials using standard laboratory tests at the Dijklander Hospital Laboratorium at 6 months after baseline

**Overall study start date**

01/11/2021

**Completion date**

11/10/2024

## **Eligibility**

**Key inclusion criteria**

1. Age 50-80 years
2. T2D
3. Presence of a predominantly MAC pattern on the CT scan
4. c-f PWV >12 m/s
5. Ability to provide informed consent prior to initiating screening visit procedures

**Participant type(s)**

Healthy volunteer

**Age group**

Adult

**Lower age limit**

50 Years

**Upper age limit**

80 Years

**Sex**

Both

**Target number of participants**

74

**Total final enrolment**

74

**Key exclusion criteria**

1. Myasthenia gravis
2. Use of medications that might interact with magnesium supplements (levothyroxine, osteoporosis medications tiludronate and alendronate, warfarin)
3. Advanced diabetes complications:
  - 3.1. Proliferative retinopathy
  - 3.2. Disabling polyneuropathy
  - 3.3. Nephropathy with an estimated glomerular filtration rate (eGFR), calculated with the Jaffé method according to the Chronic Kidney Disease Epidemiology Collaboration equation <15 ml/min/1.73 m<sup>2</sup> or chronic dialysis
  - 3.4. cardiac complications

4. Uncontrolled hyperthyroidism or active parathyroid disease
5. Chronic diarrheal disease or inflammatory bowel diseases
6. Congestive heart failure, bradycardia with a resting heart rate below 60 mmHg and systolic blood pressure less than 90 mmHg
7. Atrial fibrillation
8. Previous aortic surgery
9. Severe hepatic insufficiency
10. Malignancy or other non-cardiac conditions limiting life expectancy to <3 years
11. Using food supplements that contain magnesium, or unwilling to stop 2 weeks before randomization
12. Mental or legal incapacitation to provide informed consent
13. Plasma magnesium concentration <1.5 mg/dl or >2.6mg/dl at screening

**Date of first enrolment**

06/09/2023

**Date of final enrolment**

11/04/2024

## Locations

**Countries of recruitment**

Netherlands

**Study participating centre**

**Diabetes Research Centre Hoorn**

Maelsonstraat 7

Hoorn

Netherlands

1624 NP

## Sponsor information

**Organisation**

Amsterdam UMC Location VUmc

**Sponsor details**

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**Sponsor type**

Hospital/treatment centre

**Website**

<http://www.vumc.nl/>

**ROR**

<https://ror.org/00q6h8f30>

## **Funder(s)**

**Funder type**

Research organisation

**Funder Name**

Netherlands CardioVascular Research Committee (CVON)

## **Results and Publications**

**Publication and dissemination plan**

Planned publication in a high-impact peer-reviewed journal

**Intention to publish date**

01/03/2025

**Individual participant data (IPD) sharing plan**

The data will be stored at the Diabetes Research Centre in Hoorn and at the Department of Epidemiology & Data Science of the Amsterdam UMC. First, all desired analyses will be carried out by the involved researchers. Once these analyses are finished and the articles are published, the research group is open to collaborations and the data may be shared in a confidential and anonymized matter.

**IPD sharing plan summary**

Available on request