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# Magnesium deficiency and vascular complications in type 1 diabetes

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| **Submission date**<br>08/01/2026 | **Recruitment status**<br>Recruiting | [_] Prospectively registered<br>[_] Protocol<br>[_] Statistical analysis plan<br>[_] Results<br>[_] Individual participant data<br>[X] Record updated in last year |
| **Registration date**<br>09/06/2026 | **Overall study status**<br>Ongoing | |
| **Last Edited**<br>09/06/2026 | **Condition category**<br>Nutritional, Metabolic, Endocrine | |

## Plain English summary of protocol

Background and study aims
This study aims to investigate whether replacing magnesium in Type 1 diabetes mellitus (T1DM) patients could offer a safe and cost-effective approach to reduce cardiovascular complications.

Who can participate?
Adult patients aged over 18 with T1DM.

What does the study involve?
The study involves a screening visit at which bloods are given and the participants magnesium level is checked. If the magnesium level is above the study reference range they will be eligible for the reference group and no further participation or study visits is required. If the participant has a magnesium level that is below the study reference range they will qualify for the intervention arm. The intervention group will be asked to attend for 4 additional visits.
Visit 1 - Randomly assigned to take either the magnesium supplement or the placebo (empty tablet) which is blinded (The participant will not know which tablet is given). The participant will be provided with questionnaires to complete. The participant will take the magnesium supplement or placebo once a day for 2 weeks.
Visit 2 - Bloods taken and asked to stop taking the supplement/placebo for 2 weeks. The participant will also be provided with questionnaires to complete.
Visit 3 - Blood samples will be taken and swapped to either the supplement or placebo to be taken every day for 2 weeks. The participant will also be provided with questionnaires to complete.
Visit 4 - Blood samples will be taken together with the collection of completed questionnaires.

What are the possible benefits and risks of participating?
Taking part in the study may not benefit the participant; however, the information collected may help to improve future routine diabetes clinical care. Taking blood causes very little discomfort with minimal risk but some patients may experience fainting and the possibility of a small bruise. Magnesium supplementation has no reported major side effects, but some participants may experience mild gastrointestinal discomfort.

Where is the study run from?
All study visits will occur at the Manny Cussins Centre, Beckett Wing, St James's University Hospital, Leeds, UK.

When is the study starting and how long is it expected to run for?
The study started on 3rd September 2025 and is expected to run until February 2027.

Who is funding the study?
Diabetes UK.

Who is the main contact?
1. Prof Ramzi (Consultant in Diabetes and Endocrinology), Ajjan r.ajjan@leeds.ac.uk
2. Julie Bailey (Senior Research Nurse), Julie.bailey10@nhs.net

# Contact information

### Type(s)
Scientific, Principal investigator


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Public


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# Additional identifiers

### Integrated Research Application System (IRAS)
337472

### Central Portfolio Management System (CPMS)
62927

### Protocol number
2024-NCT11

# Study information

### Scientific Title
Magnesium deficiency as a reversible driver of vascular complications in type 1 diabetes

### Acronym
MAGVASC

### Study objectives
Type 1 diabetes (T1D) is associated with vascular complications that increase mortality risk, underpinned by extensive vascular disease coupled with an enhanced thrombotic environment. We have found that individuals with T1D have lower plasma magnesium concentrations than in age/sex-matched controls and that these reduced levels associate with impaired fibrin clot lysis. Hypofibrinolysis predicts cardiovascular outcomes in diabetes and targeting this pathway has the potential to reduce thrombosis risk. We hypothesise that adequate plasma magnesium concentrations are important for normal haemostasis. We propose to examine the role(s) of magnesium in regulating fibrinolysis using in vitro/in vivo approaches and employing a clinical study of magnesium supplementation in deficient T1D individuals. We will analyse the effects of magnesium on thrombotic/fibrinolytic potential, glycaemic and insulin resistance measures as well as patient well-being. We also will determine whether magnesium deficiency (and subsequent supplementation) induces molecular changes in coagulation factors that may influence fibrinolysis. This work will provide a mechanistic understanding of how magnesium controls fibrinolysis and will determine the usefulness of monitoring plasma magnesium in T1D and correcting abnormally low levels. In turn, this may pave the way to new T1D management strategies that reduce the mortality risk using a safe and affordable supplementary therapy.

### Ethics approval required
Ethics approval required

### Ethics approval(s)
Approved 31/07/2024, West of Scotland REC 1 (Ward 11, Dykebar Hospital, Grahamston Road, Paisley, PA2 7DE, United Kingdom; +44 0141 314 0212; WoSREC1@ggc.scot.nhs.uk), ref: 24/WS/0084

### Primary study design
Interventional

### Allocation
Randomized controlled trial

### Masking

Blinded (masking used)

## Control
Placebo

## Assignment
Crossover

## Purpose
Treatment

## Study type(s)
Prevention, Treatment

## Health condition(s) or problem(s) studied
Magnesium deficiency as a reversible driver of vascular complications in patients with type 1 diabetes

## Interventions
Magnesium supplement - 360mg magnesium bisglycinate. This will correspond to 2 ‘active magnesium-rich’ tablets/capsules per day (will be taken orally, in a single sitting).
Placebo - This will correspond to 2 magnesium-naïve placebo tablets/capsules per day (will be taken orally, in a single sitting) in the same way as instructed for the magnesium-rich tablets.

Questionnaires –
• PHQ-9 - objectifies and assesses the degree of depression severity
• Leeds dyspepsia questionnaire - measure the presence, frequency, and severity of dyspepsia symptoms
• Diabetes treatment satisfaction (DTSQs and DTSQc) questionnaire - measure absolute levels of satisfaction (status version: DTSQs) and changes over time in satisfaction (change version: DTSQc)
• Food Frequency Questionnaire - a dietary assessment tool designed to estimate a person's habitual magnesium intake.

Crossover design. Individuals in the intervention group will be randomised to Arm 1 or Arm 2, prior to commencing supplementation, using sealenvelope.com (random permuted blocks, 1:1 randomisation). Ineligible participants will continue to reference group.
The supplementation period on each arm will be 2 weeks, interspersed with a 2-week wash-out period to allow for residual supplementation to be excreted.

A further two-week supplementation period will then follow, with individuals receiving the alternative treatment.
• Citrated plasma will be collected immediately before and after each supplementation period and retrospectively analysed for total plasma magnesium concentrations.
• Supplements (magnesium and placebo) will be provided at Day 0 and Day 28.
• PHQ-9, Leeds Dyspepsia Questionnaire and DTSQs will be completed at Day 0, Day 14, Day 28 and Day 42. DTSQc will be completed on day 42.
• Food Frequency Questionnaire will be completed at Screening, Day 14 and Day 42.

Diabetologists and Diabetes Research Nurses run the study with face-to-face visits and compliance SMS reminders at Manny Cussins Diabetes Centre, Leeds Teaching Hospitals NHS Trust.

There are 4 x clinic visits over 42 days. Visits are at Day 0, Day 14, Day 28 and Day 42. Each visit will last approx. 1 hour.

### Intervention Type
Supplement

### Primary outcome(s)
1. Lysis time measured using a validated turbidimetric assay at visit 1 - day 0, visit 2 – day 14, and visit 3 – day 28

### Key secondary outcome(s)
1. Fibrin network structure measured using turbidimetric analysis, confocal and electron microscopy at visit 1 - day 0, visit 2 – day 14, visit 3 – day 28

2. Plasma levels of thrombotic and fibrinolytic proteins, Fibrinogen, plasminogen, complement C3 and PAI-1 measured using ELISA techniques at visit 1 - day 0, visit 2 – day 14, visit 3 – day 28

3. Glycaemia and insulin resistance, assessed using Time in Range (TIR) and estimated glucose disposal rate (eGDR) measured using standard clinical data and a validated eGDR formula at visit 1 - day 0, visit 2 – day 14, visit 3 – day 28

4. Patient reported outcomes, including mental health issues and gastrointestinal symptoms measured using the Patient Health Questionnaire (PHQ-9) and the Leeds Dyspepsia Questionnaire (LDQ) at visit 1 - day 0, visit 2 – day 14, visit 3 – day 28, visit 4 – day 42

5. General response to magnesium therapy measured using the Diabetes Treatment Satisfaction Questionnaire (DTSQ), status version (DTSQs) and change version (DTSQc) at visit 1 - day 0, visit 2 – day 14, visit 3 – day 28, visit 4 – day 42 for DTSQs; and at visit 4 – day 42 for DTSQc only

### Completion date
16/02/2027

## Eligibility

### Key inclusion criteria
1. Type 1 diabetes for a minimum of 3 years (supported by clinical history and antibody testing (if available)).
2. Not on any other repeated prescription treatment other than insulin with the exception of stable adjunctive therapy for at least 3 months (including metformin, GLP-1 receptor agonists and gliflozins), long term contraceptive, long term hormonal therapy (including but not limited to thyroxine and hydrocortisone) or vitamin D and B12 supplementation. Treatment with any lipid lowering agents (such as statins) and any antihypertensive agents will also be allowed.
3. Aged 18 and over.
4. Has capacity to consent

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Mixed

### Lower age limit
18 Years

### Upper age limit
110 Years

### Sex
All

### Total final enrolment
0

### Key exclusion criteria
1. Significant microvascular or macrovascular complications (any retinopathy other than grade I, significant and persistent microalbuminuria, estimated glomerular filtration rate <60 ml/kg/min or clinical neuropathy)
2. Any treatment other than insulin, metformin, GLP-1RA, gliflozin, lipid or blood pressure lowering agents, long term contraceptive, long term hormonal therapy (including but not limited to thyroxine and hydrocortisone) or vitamin D and B12 supplementation.
3. Pregnancy (or planning pregnancy)
4. Any diabetes other than T1D
5. Individuals with a history of clinically symptomatic coronary artery, cerebrovascular or peripheral vascular disease will also be excluded.
6. History of cancer (active or previous)
7. History of deep venous thrombosis and/or pulmonary embolism within 6 months of study enrollment.
8. Evidence of thrombophilia.

### Date of first enrolment
14/11/2025

### Date of final enrolment
31/12/2026

## Locations

### Countries of recruitment
United Kingdom

England

### Study participating centre

**Leeds Teaching Hospitals NHS Trust**
St. James's University Hospital
Beckett Street
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# Sponsor information

**Organisation**
University of Leeds

**ROR**
https://ror.org/024mrxd33

# Funder(s)

**Funder type**
Not defined

**Funder Name**
Diabetes UK

# Results and Publications

**Individual participant data (IPD) sharing plan**
The datasets generated during the current study will be stored in a non-publicly available repository and will be available upon request from Prof Ramzi Ajjan or Julie Bailey (leedsth-tr.diabetesresearch@nhs.net)
All data will be recorded and stored in accordance with GCP in an ISO compliant environment. Electronic data will be stored on encrypted NHS computers/laptops and password protected. Information pertaining to participants' medical records will be kept separately (electronically) from patient identifiable information (a separate spreadsheet will be used with a participant study number). Paper records, namely the data capture form used at the baseline visit will be kept in a locked, secure area of the diabetes centre at the host institution.
University computers will only store unidentified patient data. Analysis of pseudonymised data may be undertaken on University computers, identifiers will be removed and study ID used in its place
Statistical analysis will be undertaken using pseudonymised data, individuals involved in this will not have access to the identifiable data or the study key.
A study statistician will ensure appropriateness of the various statistical analyses and will take responsibility for the integrity of generated data. We will analyse data using a number of

software packages including Excel (Microsoft), Prism (Graphpad), SPSS (IBM Statistics), and R (RStudio).

### IPD sharing plan summary

Available on request, Stored in non-publicly available repository