ISRCTN34875079 https://doi.org/10.1186/ISRCTN34875079

The Glucose Lowering In Non-diabetic hyperglycaemia Trial (GLINT) - Glucose lowering in those at risk of diabetes

Submission date
13/12/2012

Recruitment status
No longer recruiting

Registration date
18/12/2012

Overall study status
Completed

Last Edited
16/12/2024

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Cardiovascular disease (CVD), heart attack and stroke are the most common long term condition in the UK, and is associated with significant disability and premature death. Currently most people become aware that they have CVD when they experience a heart attack or stroke. Therefore, finding and treating people at high risk before they have an event is an important strategy. Elevated blood glucose levels define diabetes. However, even in people without diabetes, higher than desirable glucose levels are associated with increased CVD risk. We know that early intensive treatment of blood glucose with a well-established, safe and cheap tablet (metformin) is effective at reducing CVD in people with diabetes, and may also reduce cancer risk. Metformin can also delay the onset of diabetes among the larger numbers of people with high glucose levels who do not have diabetes. However, it is unknown whether metformin can prevent CVD in this group. This study will address this critical issue.

Who can participate?
Initially this study (GLINT) aims to recruit 250 individuals aged 40 years or over for a pilot (initial study) and feasibility trial. These individuals will be from a multi-ethnic population who are at high CVD risk and have high blood glucose levels (Non-Diabetic Hyperglycaemia - NDH) but not diabetes. The pilot will allow us to address uncertainties about feasibility and acceptability prior to continuing into the larger main trial including 12,834 people. Individuals from different regions of the UK will be invited to take part via the national NHS Health Checks programme, existing registers of research participants and directly via their general practitioner (GP).

What does the study involve?
Following informed consent and a baseline health check, participants will be allocated by chance to receive metformin or a placebo tablet. The effect of metformin on CVD, cancer, and health status will be checked via medical records.

What are the possible benefits and risks of participating?
Metformin is associated with substantial beneficial effects on CVD risk factors and risk of diabetes. Common side effects include gastrointestinal (GI) upset (stomach upset) and diarrhea.

Where is the study run from?
MRC Epidemiology Unit in Cambridge with collaborating sites at the Universities of Oxford and Leicester (UK)

When is the study starting and how long is it expected to run for?
GLINT is anticipated to start in April 2013 and will continue until June 2016 (for the feasibility) and December 2024 for the full trial

Who is funding the study?
National Institute for Health Research Health Technology Assessment Programme

Who is the main contact?
Prof. Simon Griffin
ProfGP@medschl.cam.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Simon Griffin

Contact details
Medical Research Council - Epidemiology Unit
Institute of Metabolic Science
Box 285
Addenbrooke's Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Additional identifiers

Clinical Trials Information System (CTIS)
2012-005570-56

Protocol serial number
HTA 09/01/48, R121127/147

Study information

Scientific Title
Glucose Lowering In Non-diabetic hyperglycaemia Trial (GLINT) - a randomised controlled trial to establish the effectiveness and cost-effectiveness of metformin in preventing cardiovascular events in people with non-diabetic hyperglycaemia at high risk over five years

Acronym

GLINT

Study objectives
Metformin is superior to placebo with regard to the risk of developing a confirmed event in the primary CVD composite endpoint.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 28/01/2014, NRES Committee East of England - Cambridge South (The Old Chapel, Royal Standard Place , Nottingham , NG1 6FS, United Kingdom; +44 115 8839437; nrescommittee.eastofengland-cambridgesouth@nhs.net), ref: 13/EE/0415

Study design
Multi-centre randomised double-blind parallel group primary prevention trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Metabolic, Cardiovascular, Cancer, Type 2 diabetes.

Interventions
Slow-release metformin (Glucophage®) 1500mg (3 x 500mg tablet/day) or Placebo (3 x 500mg tablet/day).

Participants will receive study medication until a median of five years of follow-up has been reached. Provision of study medication will not be continued beyond the trial period. After the study ends, participants should follow up with their usual care physician to determine appropriate future treatment.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Metformin

Primary outcome(s)
Time to first confirmed event in the primary composite macrovascular endpoint (cardiovascular mortality, nonfatal myocardial infarction, and nonfatal stroke)

Key secondary outcome(s)
1. Time to event for each of the components of the primary composite endpoint (e.g. cardiovascular mortality, nonfatal myocardial infarction, nonfatal stroke)

2. All-cause mortality (supplied by Office of National Statistics)
3. Time to first non-melanoma cancer (supplied by the National Cancer Registry)
4. Death due to a non-melanoma cancer cause according to primary/underlying cause of death on death certificate (supplied by the Office of National Statistics)
5. Incident diabetes (physician diagnosed)
6. Patient satisfaction with treatment (adapted DTSQ)
7. Functional status (SF-8)
8. Health utility (EuroQol EQ-5D)

Completion date
01/12/2024

Eligibility

Key inclusion criteria
Participants must meet all of the following criteria to participate in the study:
1. Men and women with non-diabetic hyperglycaemia (HbA1c equal to or greater than 5.5% but <6.5% within 6 months prior to enrolment), aged 40 years or older
2. Estimated 10-year cardiovascular disease (CVD) risk equal to or greater than 20% (Framingham / QRISK2)
3. Estimated glomerular filtration rate (eGFR) >45ml/min as determined by the MDRD-4 method and measured within 6 months prior to enrolment
4. Participant understands the study procedures, alternative treatments available, and the risks involved with the study, and voluntarily agrees to participate by providing written informed consent
5. Participant agrees to allow study staff to contact his or her General Practitioner and/or consultant to notify them of study participation and to obtain all medical records necessary for complete data ascertainment during the follow-up period.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
40 years

Sex
All

Total final enrolment
249

Key exclusion criteria
The participant may not enter the study if ANY of the following apply:
1. Prior history of physician-diagnosed diabetes.

Note: Participants with a history of gestational diabetes which resolved after pregnancy are permitted to enrol.
2. Prior history of CVD, defined as:
2.1. Myocardial infarction, surgical or percutaneous coronary revascularisation procedure
2.2. Stroke (haemorrhagic or ischemic)
Note: Participants with prior transient ischemic attack or unstable angina are NOT excluded and may be enrolled
3. Participant has a planned or anticipated revascularisation procedure within 6 months following enrolment
Note: Participants with previous peripheral revascularisation procedure are NOT excluded and may be enrolled
4. Participant is pregnant
5. History of cirrhosis of the liver or other significant hepatic impairment, as assessed by medical history
6. End-stage renal disease
7. In the investigators opinion, participant has a medical history that indicates a life expectancy of <2 years or might limit the individual's ability to take the trial treatments for the duration of the study
8. Any other significant disease or disorder which, in the opinion of the Investigator, may either put the participant at risk because of participation in the study, or may influence the result of the study, or the participant's ability to participate in the study.
9. Participant is enroled in or has participated within 12 weeks prior to enrolment in another experimental protocol involving the use of an investigational drug or device or an intervention that would interfere with the conduct of the trial.

Date of first enrolment
01/02/2015

Date of final enrolment
01/11/2015

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
MRC Epidemiology Unit
University of Cambridge
Cambridge
United Kingdom
CB2 0QQ

Study participating centre

Leicester Diabetes Centre
University of Leicester
United Kingdom
LE5 4PW

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust and the University of Cambridge

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme (grant code: 09/01/48)

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from University of Cambridge

IPD sharing plan summary
Stored in non-publicly available repository, Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/04/2018		Yes	No