ISRCTN16890855 https://doi.org/10.1186/ISRCTN16890855

Effectiveness of a holistic intervention to address multimorbidity in adults with early-onset type 2 diabetes

Submission date
12/04/2023

Recruitment status
No longer recruiting

Registration date
22/05/2023

Overall study status
Ongoing

Last Edited
06/02/2025

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Type 2 diabetes is a condition where the body struggles to process blood glucose, causing a higher chance of problems like heart attacks and strokes. Type 2 diabetes is becoming more common and adults are getting it earlier (aged under 40). This 'early-onset' type 2 diabetes is worrying because health problems can develop faster and people can die younger. Early-onset type 2 diabetes often occurs with other health conditions, including obesity, high blood pressure and mental health problems, like anxiety or depression. The good news is that early treatment and diabetes self-management can reduce the risk of health problems developing. Currently, early-onset type 2 diabetes care is delivered in the same way as for older adults. However, attendance tends to be low, probably because younger adults have very different lives and needs. Several things may help younger people with type 2 diabetes care for their health, including making sure it:
• is holistic, meaning that it includes lots of different things which will help improve health
• is organised to suit the person's life and work
• focuses on what is important to them
• uses technology where needed
The M3 intervention will bring all of these together to create a new, individualised approach to supporting younger people with type 2 diabetes. This study aims to see whether the M3 intervention can improve the health of younger people with type 2 diabetes compared to the standard care which is currently offered.

Who can participate?
People can take part if they:
• are aged 16 to 45 years
• were diagnosed with type 2 diabetes before their 40th birthday
• have an HbA1c ≥6.0% within 3 months of starting the trial
• can provide informed consent

What does the study involve?
Participants will be randomly allocated to one of two groups. The control group will continue to

receive their standard care. The M3 intervention group will receive a multifactorial care package that is tailored specifically to the needs of young adults with type 2 diabetes. The care will be delivered over 24 months by a team of healthcare practitioners who have received bespoke training. The intervention involves several components, including person-centred care which focusses on what matters most to the participant, personalised drug reviews and the earlier use of newer therapies where appropriate, personalised strategies for dietary, psychology, and physical activity support, and the use of novel technology, including wearable devices (glucose sensors and physical activity monitors), online health monitoring reports, and an online health management system, to help facilitate a flexible approach to care and allow easier communication between the participant and the care team.

All participants will undergo a series of assessments which take place in the laboratory at the beginning of the study (baseline), at 26 weeks, 52 weeks, and 104 weeks. Participants will also have reviews every 3 months either over telephone, video call, or face-to-face (according to their preference), to monitor and discuss progress.

What are the possible benefits and risks of participating?
During the study, participants will receive close monitoring of their diabetes. The study will also provide detailed results from a range of health and wellbeing assessments. The researchers will be happy to review the results with them after the study is completed. The M3 intervention could potentially benefit participants in this group in several ways, including support to do more physical activity and improve diet, earlier access to medications that may be beneficial, psychosocial support to help manage stress, anxiety, and distress, education around what causes diabetes and how to manage overall health in the long term, and care that is tailored specifically to needs and preferences.

There may be an additional time commitment for people in the M3 intervention group, as they will complete both the study assessments and some extra assessments used to personalise and tailor the treatment to their needs. The functional tests in the 52-week and 104-week visits are not strenuous, but can make some people feel uncomfortable or unsteady. A trained member of staff will always supervise the tests the participant can stop the test whenever they wish. Finally, giving blood can cause mild pain and discomfort. Trained research staff will take the blood samples and the comfort of the participant will be prioritised. Every attempt will be made to make the procedure as pain free as possible.

Where is the study run from?
University of Leicester (UK)

When is the study starting and how long is it expected to run for?
June 2020 to February 2027

Who is funding the study?
This study is funded by the National Institute for Health and Care Research (NIHR) (UK) under its Programme Grants for Applied Research Programme (NIHR201165).

Who is the main contact?
Trial Manager: Lisa Moyes, lisa.moyes@uhl-tr.nhs.uk

Contact information

Type(s)

Public

Contact name
Miss Lisa Moyes

Contact details
Leicester Diabetes Centre
Leicester General Hospital
Gwendolen Road
Leicester
United Kingdom
LE5 4PW
+44 116 258 4251
lisa.moyes@uhl-tr.nhs.uk

Type(s)
Public

Contact name
Dr Tommy Slater

ORCID ID
https://orcid.org/0000-0003-2764-3148

Contact details
Leicester Diabetes Centre
Leicester General Hospital
Gwendolen Road
Leicester
United Kingdom
LE5 4PW
-
tommy.slater@leicester.ac.uk

Type(s)
Scientific

Contact name
Dr Jack Sargeant

ORCID ID
https://orcid.org/0000-0003-0395-7329

Contact details
Leicester Diabetes Centre
Leicester General Hospital
Gwendolen Road
Leicester
United Kingdom

LE5 4PW
+44 116 258 8624
jack.sargeant@uhl-tr.nhs.uk

Type(s)
Scientific

Contact name
Prof Melanie Davies

ORCID ID
https://orcid.org/0000-0002-9987-9371

Contact details
Leicester Diabetes Centre
Leicester General Hospital
Gwendolen Road
Leicester
United Kingdom
LE5 4PW
+44 116 258 6481
melanie.davies@uhl-tr.nhs.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
322040

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 55295, IRAS 322040, NIHR201165, 0827

Study information

Scientific Title
The impact of a holistic multifactorial management intervention in adults with early-onset type 2 diabetes (aged 16 to 45 years): the M3 randomized controlled trial

Acronym
M3

Study objectives
A multifactorial intervention tailored specifically for young adults with type 2 diabetes will result in greater improvements in HbA1c when compared to standard care.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/04/2023, East Midlands - Nottingham 1 Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 207 104 8271; Nottingham1.rec@hra.nhs.uk), ref: 23/EM/0032

Study design
Randomized; Interventional; Design type: Treatment, Process of Care, Complex Intervention

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Type 2 diabetes

Interventions
Following the completion of their baseline assessment, the participant will be randomly allocated equally to one of two groups using a secure web-based service. Randomisation will be stratified by trial site, sex, age (≤/>25 years), and baseline HbA1c (≤/>8.5% [≤/>69mmol/mol]):

The M3 Intervention – will be delivered by a multidisciplinary team of healthcare practitioners trained specifically by members of the central research team. The intervention will utilise a hybrid approach of digital and face-to-face contacts to reduce participant burden. A designated care coordinator at each site will act as a central point of contact for each participant, helping to facilitate consistent, continuous care across the multidisciplinary team. The intervention will be person centred, focusing on what matters most to the participant, which may include traditional (e.g., glucose levels and body weight) and non-traditional risk factors (e.g., psychosocial/mental wellbeing, self-management support, and lifestyle). Healthcare professionals will perform personalised drug reviews and may promote the earlier use of newer therapies such as glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and sodium-glucose co-transporter-2 inhibitors (SGLT2is), where appropriate, alongside personalised strategies for dietary, psychological, and physical activity support. Finally, the M3 intervention will make use of novel technology, including wearable devices (glucose sensors and physical activity monitors), online health monitoring reports, and an online health management system, which will facilitate a flexible approach to care and allow easier communication between the participant and the care team.

Ongoing standard care – participants will continue receiving standard care under their usual diabetes service providers

Intervention Type
Other

Phase
Not Specified

Primary outcome(s)

Change in HbA1c from baseline to 52 weeks collected by venous blood sampling.

Key secondary outcome(s))

Current secondary outcome measures as of 02/01/2024:
Measured at baseline, week 26, week 52, and week 104, unless specified otherwise
1. Glycaemic level: Change in HbA1c from baseline to 26 weeks and baseline to 104 weeks collected by venous blood sampling
2. Multimorbidity management and burden: Treatment burden using the Multimorbidity Treatment Burden Questionnaire (MTBQ)
3. Cardiometabolic and renal risk:
3.1. Total cholesterol and high-density lipoprotein collected by venous blood sampling
3.2. Kidney function measured using estimated glomerular filtration rate (eGFR) by venous blood sampling
3.3. Anthropometry and body composition (body weight, height, body mass index, lean body mass, and fat mass) measured by bioelectrical impedance
3.4. Systolic and diastolic blood pressure measured using an automated sphygmomanometer
4. Psychosocial wellbeing and self-management support:
4.1. Self-compassion measured using the Self-Compassion Scale (SCS)
4.2. Distress measured using the Problem Areas in Diabetes (PAID) questionnaire
4.3. Depression measured using the Patient Health Questionnaire (PHQ-9)
4.4. Stigma measured using the type 2 Diabetes Stigma Assessment Scale (DSAS-2)
4.5. Self-efficacy measured using the Diabetes Management Self-Efficacy Scale (DMSES)
5. Self-reported quality of life:
5.1. Health status and quality of life using the EQ-5D-5L questionnaire
5.2. Health-related quality of life across multiple domains using the Short Form 36 Health Survey Questionnaire (SF-36)
6. Health service resource utilisation and work productivity:
6.1. Healthcare service utilisation using the Modular Resource Use Measure (ModRUM)
6.2. Work productivity using the Work Productivity and Activity Impairment (WPAI) questionnaire
7. Physical activity: Device-measured daily steps using a wrist-worn accelerometer (optional to minimise participant burden)

Exploratory measures:
Measured at baseline and week 26 (* selected outcomes only), week 52, and week 104
1. Other measures related to glycaemic level
1.1. Percentage of time spent within range (% of readings and time between 3.9–10.0 mmol/L) measured using a continuous glucose monitor (optional to minimise participant burden)*
1.2. Percentage of time spent above range (% of readings and time >10.0 mmol/L) measured using a continuous glucose monitor (optional to minimise participant burden)*
1.3. Percentage of time spent below range (% of readings and time <3.8 mmol/L) measured using a continuous glucose monitor (optional to minimise participant burden)*
1.4. Fasting plasma glucose by venous blood sampling (optional if willing to fast)*
1.5. Fasting plasma insulin by venous blood sampling (optional if willing to fast)*
1.6. Fasting circulating c-peptide by venous blood sampling (optional if willing to fast)*
2. Other cardiometabolic and renal risk factors
2.1. Low density lipoprotein by venous blood sampling*
2.2. Fasting triglyceride by venous blood sampling (optional if willing to fast)*
2.3. Circulating inflammatory profile (including c-reactive protein) by venous blood sampling*
2.4. Kidney function measured using urine albumin-to-creatinine ratio (UACR) through urine sampling, new-onset albuminuria, and progression of albuminuria
2.5. Body fat percentage measured by bioelectrical impedance*

3. Liver function: Liver panel enzymes by venous blood sampling*
4. Other lifestyle related outcomes
4.1. Self-reported use of glucose-lowering therapies by medical review*
4.2. Self-reported change in multimorbidity status by medical review*
4.3. Self-reported sleepiness measured using the Epworth Sleepiness Scale
4.4. Self-reported obstructive sleep apnoea measured using the Stop-Bang questionnaire)
4.5. Self-reported habitual dietary intake measured using the UK Diabetes and Diet Questionnaire (UKDDQ)
4.6. Habitual alcohol consumption and smoking status measured by clinical review
5. Other assessments of physical activity, inactivity, function, or disability risk
5.1. Device-measured time spent performing moderate-to-vigorous intensity physical activity using a wrist-worn accelerometer (optional to minimise participant burden)*
5.2. Device-measured time spent sedentary using a wrist-worn accelerometer (optional to minimise participant burden)*
5.3. Device-measured sleep quality and duration using a wrist-worn accelerometer (optional to minimise participant burden)*
5.4. Physical function measured using the short physical performance battery (SPPB)
5.5. Hand grip strength measured using handgrip dynamometry
5.6. Disability and life participation measured using the World Health Organisation Disability Assessment Schedule (WHODAS 2.0)

———

Previous secondary outcome measures:
Measured at baseline, week 26, week 52, and week 104, unless specified otherwise
1. Glycaemic level: Change in HbA1c from baseline to 26 weeks and baseline to 104 weeks collected by venous blood sampling.
2. Multimorbidity management and burden: Treatment burden using the Multimorbidity Treatment Burden Questionnaire (MTBQ).
3. Cardiometabolic and renal risk:
3.1. Total cholesterol and high-density lipoprotein collected by venous blood sampling.
3.2. Kidney function measured using estimated glomerular filtration rate (eGFR) by venous blood sampling.
3.3. Anthropometry and body composition (body weight, height, body mass index, lean body mass, and fat mass) measured by bioelectrical impedance.
3.4. Systolic and diastolic blood pressure measured using an automated sphygmomanometer.
4. Psychosocial wellbeing and self-management support:
4.1. Self-compassion measured using the Self-Compassion Scale (SCS).
4.2. Distress measured using the Problem Areas in Diabetes (PAID) questionnaire.
4.3. Depression measured using the Patient Health Questionnaire (PHQ-9).
4.4. Stigma measured using the type 2 Diabetes Stigma Assessment Scale (DSAS-2).
4.5. Self-efficacy measured using the Diabetes Management Self-Efficacy Scale (DMSES).
5. Self-reported quality of life:
5.1. Health status and quality of life using the EQ-5D-5L questionnaire.
5.2. Health-related quality of life across multiple domains using the Short Form 36 Health Survey Questionnaire (SF-36).
6. Health service resource utilisation and work productivity:
6.1. Healthcare service utilisation using the Modular Resource Use Measure (ModRUM).
6.2. Work productivity using the Work Productivity and Activity Impairment (WPAI) questionnaire.
7. Physical activity: Device-measured daily steps using a wrist-worn accelerometer (optional to minimise participant burden).

Exploratory measures:
Measured at baseline and week 26 (* selected outcomes only), week 52, and week 104
1. Other measures related to glycaemic level
1.1. Percentage of time spent within range (% of readings and time between 3.9–10.0 mmol/L) measured using a continuous glucose monitor (optional).
1.2. Percentage of time spent above range (% of readings and time >10.0 mmol/L) measured using a continuous glucose monitor (optional).
1.3. Percentage of time spent below range (% of readings and time <3.8 mmol/L) measured using a continuous glucose monitor (optional).
1.4. Fasting plasma glucose by venous blood sampling (optional if willing to fast)*.
1.5. Fasting plasma insulin by venous blood sampling (optional if willing to fast)*.
1.6. Fasting circulating c-peptide by venous blood sampling (optional if willing to fast)*.
2. Other cardiometabolic and renal risk factors
2.1. Low density lipoprotein by venous blood sampling*.
2.2. Fasting triglyceride by venous blood sampling (optional if willing to fast)*.
2.3. Circulating inflammatory profile (including c-reactive protein) by venous blood sampling*.
2.4. Kidney function measured using urine albumin-to-creatinine ratio (UACR) through urine sampling, new-onset albuminuria, and progression of albuminuria.
2.5. Body fat percentage measured by bioelectrical impedance*.
3. Liver function: Liver panel enzymes by venous blood sampling*.
4. Other lifestyle related outcomes
4.1. Self-reported use of glucose-lowering therapies by medical review*.
4.2. Self-reported change in multimorbidity status by medical review*.
4.3. Self-reported sleepiness measured using the Epworth Sleepiness Scale.
4.4. Self-reported obstructive sleep apnoea measured using the Stop-Bang questionnaire).
4.5. Self-reported habitual dietary intake measured using the UK Diabetes and Diet Questionnaire (UKDDQ).
4.6. Habitual alcohol consumption and smoking status measured by clinical review.
5. Other assessments of physical activity, inactivity, function, or disability risk
5.1. Device-measured time spent performing moderate-to-vigorous intensity physical activity using a wrist-worn accelerometer (optional to minimise participant burden)*.
5.2. Device-measured time spent sedentary using a wrist-worn accelerometer (optional to minimise participant burden)*.
5.3. Device-measured sleep quality and duration using a wrist-worn accelerometer (optional to minimise participant burden)*.
5.4. Physical function measured using the short physical performance battery (SPPB).
5.5. Hand grip strength measured using handgrip dynamometry.
5.6. Disability and life participation measured using the World Health Organisation Disability Assessment Schedule (WHODAS 2.0).

Completion date
28/02/2027

Eligibility

Key inclusion criteria
1. Age 16 to 45 years, inclusive
2. Type 2 diabetes diagnosed before the age of 40 years; confirmed by medical history with

/without specialist investigations (e.g., antibodies)
3. HbA1c >= 6.0% (>= 42 mmol/mol) within 3 months of trial enrolment
4. Able to provide informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
16 years

Upper age limit
45 years

Sex
All

Key exclusion criteria
1. Diagnosed with other forms of diabetes (e.g., type 1 diabetes, monogenic diabetes [MODY], gestational diabetes or latent autoimmune diabetes in adults [LADA])
2. Serious illness or event with life-expectancy <1 year or other significant illness which, in the opinion of a study clinician, precludes involvement
3. Planned major surgery
4. Requirement for renal replacement therapy
5. Current pregnancy, or actively trying to conceive
6. Unable or unwilling to provide informed consent
7. Current participation in a competing clinical trial (CTIMP, as determined by the study investigator)

Date of first enrolment
13/09/2023

Date of final enrolment
28/02/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre

University Hospitals of Leicester NHS Trust
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
University Hospitals of Derby and Burton NHS Foundation Trust
Royal Derby Hospital
Uttoxeter Road
Derby
United Kingdom
DE22 3NE

Study participating centre
Imperial College Healthcare NHS Trust
The Bays
St Marys Hospital
South Wharf Road
London
United Kingdom
W2 1BL

Sponsor information

Organisation
University of Leicester

ROR
https://ror.org/04h699437

Funder(s)

Funder type
Government

Funder Name
NIHR Central Commissioning Facility (CCF)

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request from Dr Jack Sargeant (jack.sargeant@uhl-tr.nhs.uk)

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			20/09/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes