ISRCTN15394285 https://doi.org/10.1186/ISRCTN15394285

Manchester Intermittent and Daily diet Diabetes App Study

Submission date	Recruitment status	[X] Prospectively registered
08/01/2018	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
30/01/2018	Ongoing	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
11/04/2024	Nutritional, Metabolic, Endocrine	

Plain English summary of protocol

Background and study aims
Currently in the UK 1 in 12 people are living with Type 2 diabetes, and this figure continues to rise.
Diet, maintaining a healthy weight and physical activity are the cornerstone of Type 2 diabetes treatment and can significantly reduce the need for medications and long term complications of the condition. Studies in the UK have shown that an 8 week low calorie diet consisting of 800 calories/day, which has become known as the “Newcastle Diet” can be highly effective in producing significant weight loss and normalisation of blood glucose (sugar levels). This study compares the standard daily 800 kcal low calorie diet for eight weeks to an intermittent low calorie diet which involves two 800 kcal days/week spread over 27 weeks. The aim of this study is to see if diet is more effective at helping participants lose weight and achieve better blood glucose control. This study also tests whether patients can be successfully supported with these diets remotely using a novel app/web based programme, rather than normal face to face appointments.

Who can participate?
The study is including adults diagnosed with type 2 diabetes in the last 8 years who are currently overweight or obese (BMI >27 Kg/m2.

What does the study involve?
Participants are randomly allocated to one of two low calorie diets. Participants in group one complete the standard daily low calorie diet of 800 calories/day for eight weeks. Participants in group 2 complete the intermittent low calorie diet invovling two 800 kcal days each week spread over 27 weeks. Participants from both groups are supported by healthcare progessions using a smartphone/tablet app or regular telephone calls. The 800 calorie days on both diets involve a liquid meal replacement product called Optifast. Participants have an initial appointment which includes a three hour screening and assessment to check eligibility of the study. Participants are assessed for their weight and body fat, measurements, blood tests, blood pressure, short questionnaires and pregnant. They are then randomly allocated to their group for their diet. PArticipants receive individuals exercise advice from a diabetes exercise specialist via telephone or video call for around 30-45 minutes. Participants are asked to attend follow up face to face appointments at Wythenshawe hospital at two, three, six and 12 months. The six and 12 month

appointments last 1.5 hrs and will involve a repeat of the assessments and questionnaires done at your initial appointment. The two and three month appointments lasts one hour as they involve fewer tests and questionnaires. For the first three months participants are contacted at least weekly by their diabetes specialist dietitian and periodically by their diabetes specialist nurse if you are (or were before the study) on specific diabetes medications including insulin. Between three and 12 months the frequency of contact with their diabetes specialist dietitian are reduced to fortnightly and then monthly as participants settle into self-managing their diet, and their contact with the diabetes specialist nurse is monthly. Participants complete questionnaires such as the Binge Eating Scale, Audit of Diabetes Dependent Quality of Life questionnaire, weight efficacy lifestyle questionnaire, and anxiety.

What are the possible benefits and risks of participating?
Patients are expected to benefit from participating in the study and to have their weight reduced. Patients may benefit from reduced mortality and morbidity associated with obesity and complications of type 2 diabetes. Participants in both arms of the study will receive individual tailored advice and support to undertake an energy restricted diet and support which are not routinely available to patients on standard care. This includes remote support from the study dietician and diabetes specialist nurse, clinical psychologist and exercise specialist . The very low energy diet drinks used in the weight loss programme are provided free of charge to the patients home during the trial.

Where is the study run from?
1. Wythenshawe Hospital (UK)
2. Northenden Group Practice (UK)
3. Bowland Road Practice (UK)
4. Washway Road Practice (UK)

When is the study starting and how long is it expected to run for?
May 2017 to January 2029

Who is funding the study?
OVIVA UK LIMITED (UK)

Who is the main contact?
Dr Sian Hanison (Scientific)
basil.issa@uhsm.nhs.uk

Contact information

Type(s)
Scientific

Contact name
Dr Sian Hanison

Contact details
R&D Directorate, NIHR Building
Manchester University NHS Foundation Trust Wythenshawe Hospital
Southmoor Road
Manchester
United Kingdom

-
+44 1612912399
basil.issa@uhsm.nhs.uk

Additional identifiers

ClinicalTrials.gov (NCT)
NCT04674384

Protocol serial number
34397

Study information

Scientific Title
A Pilot randomised controlled trial comparing efficacy of Continuous Very Low Energy Diet (C-VLED) to Intermittent Very Low Energy Diet (I-VLED) in patients with Type 2 Diabetes

Acronym
MIDDAS

Study objectives
This study will assess the efficacy of daily very low energy diets to a an intermittent very low energy diet incorporating high-frequency remote follow-up with a novel app for achieving significant weight loss (1- 2 stone or more) and blood sugar control amongst patients with type 2 diabetes. The findings in this trial will inform the feasibility of a large scale trial in the UK comparing the two different diets.

The primary objectives of this trial are:
1. To assess enrolment rate to a randomized trial of continuous (daily) very low energy diet to an intermittent very low energy diet amongst patients with type 2 diabetes
2. To assess the proportion of participants in both groups who successfully lose and maintain >15% weight loss at 12 months using an intention to treat analysis
3. To assess the proportion of participants in both groups who achieve good blood sugar control defined as an HbA1c of <48 mmol/mol at 12 months using an using an intention to treat analysis

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West- Preston Research Ethics Committee, 14/08/2017, ref: 17/NW/0389

Primary study design
Interventional

Study design
Randomised; Interventional; Design type: Treatment, Dietary

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Specialty: Diabetes, Primary sub-specialty: Type 2; UKCRC code/ Disease: Metabolic and Endocrine/ Diabetes mellitus

Interventions
Participants are randomly allocated to one of two low calorie diets. Participants in group one complete the standard daily low calorie diet of 800 calories/day for eight weeks. Participants in group 2 complete the intermittent low calorie diet invovling two 800 kcal days each week spread over 27 weeks. Participants from both groups are supported by healthcare progessions using a smartphone/tablet app or regular telephone calls. The 800 calorie days on both diets involve a liquid meal replacement product called Optifast.

The trial intervention is delivered through a combination of the following programmes:
1. Dietary Programmes
2. Dietary support by Diabetes Dietitian
3. Clinical Support by Diabetes Specialist Nurse mainly for participants who are:
3.1. Currently prescribed insulin, sulphonyureas, gliptin, SGLT2 or GLP1
3.2. Previously prescribed insulin, sulphonyureas, gliptin, SGLT2 or GLP1 before commencing the study
3.3. Patients with abnormal glucose results (>7 mmol fasting and > 11 mmol non-fasting) during the study
4. Exercise therapy
5. Psychological Support
6. Clinical Support through MDT and scheduled visits and remote monitoring via Milestones DM2 app

Participants have an initial appointment which includes a three hour screening and assessment to check eligibility of the study. Participants are assessed for their weight and body fat, measurements, blood tests, blood pressure, short questionnaires and pregnant. They are then randomly allocated to their group for their diet. PArticipants receive individuals exercise advice from a diabetes exercise specialist via telephone or video call for around 30-45 minutes.

Participants are asked to attend follow up face to face appointments at Wythenshawe hospital at two, three, six and 12 months. The six and 12 month appointments last 1.5 hrs and will involve a repeat of the assessments and questionnaires done at your initial appointment. The two and three month appointments lasts one hour as they involve fewer tests and questionnaires.

For the first three months participants are contacted at least weekly by their diabetes specialist dietitian and periodically by their diabetes specialist nurse if you are (or were before the study) on specific diabetes medications including insulin.

Between three and 12 months the frequency of contact with their diabetes specialist dietitian are reduced to fortnightly and then monthly as participants settle into self-managing their diet, and their contact with the diabetes specialist nurse is monthly.

Participants complete questionnaires such as the Binge Eating Scale, Audit of Diabetes Dependent Quality of Life questionnaire, weight efficacy lifestyle questionnaire, and anxiety.

Intervention Type
Other

Primary outcome(s)
1. Enrolment rate is measured using the data collected on numbers of patients at end of recruitment window (6 months)
2. Proportion of participants who lose and maintain 15% weight loss is measured using ITT analysis (intention to treat (ITT) analysis) at 12 months
3. Proportion of participants who achieve good blood sugar levels are measured using an intention to treat analysis at 12 months

Key secondary outcome(s)
1. Quality of life is measured using the EQ-5D-3L and Audit of Diabetes-Dependent Quality of Life questionnaires at weeks 27 and 52
2. Body composition is measured using the Tanita 180 at weeks 8,12, 27 and 52 weeks and fasting blood glucose levels weeks 8,12,27,52
3. Cardiovascular risk markers measured using blood pressure, weight, waist circumference at baseline weeks 8,12, 27, 52 and lipid profile at baseline, weeks 27 and 52
4. Reduction in diabetes medicine is measured using data collected on treatments and current treatments as per the study protocol at the end of the study
5. Feasibility is measured using a qualitative interview at weeks 8, weeks 27 and 52

Completion date
31/01/2029

Eligibility

Key inclusion criteria
1. Patients aged 18–75 years
2. Patients with diagnosis of T2DM for less than 8 years , based on 2 recorded diagnostic-level tests, HbA1c and/or blood glucose or OGTT
3. HbA1c ≥ 48 mmol/mol within last 12 months
4. Body Mass Index (BMI) >27 kg/m2 and <50kg/m2 or >25 kg/m2 and <50kg/m2 in high-risk minority ethnic groups (specifically South Asian, Black African and African Caribbean people)
5. Patients should have access and able to use a smartphone or tablet running iOS or Android to be able to use the Oviva app OR access and ability to use a telephone
6. Participants must be willing to give written informed consent and be able to adhere to the study
schedules and procedures
7. Patients should be willing to follow the VLED using Optifast drinks
8. Female participants of childbearing age must agree to maintain highly effective contraception during their participation in the study and must have negative pregnancy test at screening and each study visit where there is a possibility they could be pregnant

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit

18 Years

Sex
All

Total final enrolment
79

Key exclusion criteria
1. Patients with recent routine HbA1c > = 108 mmol/mol (last 3 months) or at screening
2. Patients with non-stable retinopathy, or grade R2 or later, or had no retinopathy screen within 12 months
3. Patients presenting with severe systemic or organ disease, or active cancer
4. Patients who experienced unintentional weight loss of > 5 kg within the last 6 months
5. Patients who lack capacity or are unable to read or understand written or verbal instructions in English or those diagnosed with learning difficulties
6. Patients intend to become pregnant during the study or pregnancy confirmed by pregnancy test during the trial.
7. Patients with a history of self- harm and previous diagnosis of borderline personality disorder or bipolar disorder history. Diagnosis of substance abuse or harmful alcohol use or dependency, OR a positive AUDIT Alcohol Screen with an AUDIT total score of above 15 (high risk or harmful level).
8. Patients with score of 35 or below as assessed with a Weight Efficacy Lifestyle Questionnaire Short-Form (WEL-SF)
9. Patients who are diagnosed with eating disorder, OR a score of score of 27 or more (severe binge-eating using Binge Eating Scale (BES)
10. Patients with moderate to severe depression assessed with the Patient Health Questionnaire-9 (PHQ-9) of 16 or more.
Patients with severe anxiety assessed with a general anxiety disorder (GAD-7) scale 16 or more.
11. Patients who are on lithium carbonate or other psychotropic medications
12. Patients who are currently on treatment with Orlistat
13. Patients who have previously had bariatric surgery for weight loss including gastric bypass and sleeve gastrectomy
14. Patients who are on chronic use of steroids (more than 20mg daily of prednisolone or its equivalent) .
15. Patients with known hypersensitivity to any of the ingredients of Optifast® diet i.e lactose intolerance
15. Other medical conditions which in the opinion of the treating physician will put the patient at risk of deterioration in their conditions or use of VLED is contraindicated such as:
15.1. Recent (within the last 3 months) cardiovascular diseases (e.g. acute myocardial infarction, unstable angina, stroke or transient ischemic attack, active thrombophlebitis
15.2. Gastrointestinal conditions such as liver cirrhosis/ failure, active hepatitis, gall bladder disease, acute pancreatitis, active peptic ulcer
15.3. Metabolic disorders such as porphyria
15.4. Advance renal diseases (eGFR < 30 mL/min./sq.m)
15.5. Major bone fractures (e.g. pelvis or hip) in the past 6 months
16. Patients who are currently in a diabetes therapy trial

Date of first enrolment
31/01/2018

Date of final enrolment
01/06/2018

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Wythenshawe Hospital
Manchester University NHS Foundation Trust
Southmoor Road
Wythenshawe
Manchester
United Kingdom
M23 9LT

Study participating centre
Northenden Group Practice
489 Palatine Road
Wythenshawe
Manchester
United Kingdom
M22 4DH

Study participating centre
Bowland Road Practice
52 Bowland Road
Wythenshawe
Manchester
United Kingdom
M23 1JX

Study participating centre
Washway Road Practice
67 Washway Road
Sale
United Kingdom
M33 7SS

Sponsor information

Organisation
University Hospital of South Manchester NHS Foundation Trust

ROR
https://ror.org/00he80998

Funder(s)

Funder type
Industry

Funder Name
OVIVA UK LIMITED

Results and Publications

Individual participant data (IPD) sharing plan
Patient trial files and copies of consent forms will be held in secure locked filing cabinet in both the diabetes and
research and development departments at Manchester University NHS Foundation Trust Wythenshawe Hospital. The trial database will be stored on a password protected desktop and backed up on the hospital server.

Manchester University NHS Foundation Trust Wythenshawe Hospital MIDDAS research team will have access to patients' personal data Manchester University NHS Foundation Trust Wythenshawe Hospital R&D department are the sponsor and they may request permit trial-related monitoring, audits,and regulatory inspection(s), providing direct access to source data /documents. Nestle Health Care will have access to patients name and address for the purpose of delivering Optifast directly to their home address. Consent will be sought for this disclosure. Oviva UK ltd have the patients e mail to enable them have a log in for the app, patients are made aware of this on the patient information sheet. No medical records will be shared with Nestle or Oviva. Patient entered information about their health will be stored on Oviva server in a secure anonymised format. Neither Oviva nor Nestle will be able to use patient data in non-anonymised form. Anonymised audio recordings will be sent to a UK based external transcription company for transcription. The MIDDAS research team at Wythenshawe Hospital will receive trial ID identified data from Oviva.co.uk to assess use of the app which is one of the exploratory endpoints of the trial. Data will be analysed by the MIDDAS research team at Manchester University NHS Foundation Trust Wythenshawe Hospital and will not be transferred elsewhere.

Essential documents (consent/case report forms) will be kept for 10 years for possible audit or inspection. Documents should be securely stored and access restricted to authorised personnel. The Sponsor will archive the documents on to appropriate media for the long term accessible

storage. Hard copies of data will be boxed and transferred to specifically designated storage premises with unique reference numbers to enable confidentiality, tracking and retrieval if necessary. Audio recordings will be destroyed after transcription has taken place and been checked by the qualitative researcher.

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		19/03/2021	22/03/2021	Yes	No
HRA research summary			28/06/2023	No	No