# Investigating the limits of reversibility of type 2 diabetes

Submission date 08/08/2012	<b>Recruitment status</b> No longer recruiting	[X] Prospectively registered	
		[_] Protocol	
Registration date 09/08/2012	<b>Overall study status</b> Completed	Statistical analysis plan	
		[X] Results	
Last Edited 04/08/2015	<b>Condition category</b> Nutritional, Metabolic, Endocrine	Individual participant data	

## Plain English summary of protocol

#### Background and aims

Type 2 diabetes is regarded as an irreversible disease of the pancreas. It is now known that this is not true. A study performed in Newcastle has shown that people with short duration type 2 diabetes can regain normal blood sugar (glucose) control after a period of strict dieting. This study will examine whether the reversal of diabetes using a very low calorie diet is possible in individuals with long duration diabetes as well as short duration disease. It will establish the sustainability of the reversal of type 2 diabetes, and the best approach to maintaining the beneficial effects of this period of dieting using longer term lifestyle modification. Finally, the mechanisms behind the reversal of diabetes will be defined, looking in particular at the effect of fat on the pancreas. By using MRI scans of the pancreas and liver, along with tests using glucose and insulin, the effect of fat in the 'wrong' place will be defined. Together, this information would be of enormous importance to all people with type 2 diabetes, improving our understanding of the condition and exploring the potential of a medication-free treatment strategy.

#### Who can participate?

People aged between 25 and 80 years who have type 2 diabetes of less than 4 years or more than 8 years duration.

#### What does the study involve?

The research involves an 8-week period of very low calorie dieting to induce weight loss and improve blood glucose control. Participants will then be asked to follow a weight maintaining diet and physical activity plan for 6 months with education and support throughout. Detailed metabolic tests and magnetic resonance imaging (MRI) scans will be performed on three occasions with more regular, shorter visits throughout the 8-month study.

What are the possible benefits and risks from taking part in this study? The weight loss achieved during the study is likely to bring substantial benefits to health. Participants will gain a better understanding of type 2 diabetes and its management. There are no major risks from taking part in this study. The very low calorie diet is safe under medical supervision. The intense dieting and longer term lifestyle change are challenging but full support will be given. Occasionally there may be some mild discomfort at the sites of the plastic tubes for a few hours after removal. The MRI scans are non-invasive, safe and do not use X-rays or any other harmful radiation. It makes a high-pitched sound and you will be given ear-muffs to wear. There is a very small risk (less than one in a million) of an allergic reaction to a substance used in the study called Intralipid. This only occurs in people who are allergic to soy protein or eggs so if you have these allergies you will not be able to take part in the study.

Where is the study run from? Newcastle University (UK).

When is the study starting and how long is it expected to run for? The study started in August 2012 and will run for 2 years.

Who is funding the study? Novo Nordisk UK Research Foundation and the Newcastle NIHR Biomedical Research Centre.

Who is the main contact? Dr Sarah Steven sarah.steven@ncl.ac.uk

# **Contact information**

**Type(s)** Scientific

**Contact name** Dr Sarah Steven

## **Contact details**

Newcastle University Institute for Ageing and Health Campus for Ageing and Vitality Newcastle upon Tyne United Kingdom NE4 5PL

# Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

**Secondary identifying numbers** 12627

# Study information

**Scientific Title** Characterisation of the principle determinants of long term reversal of type 2 diabetes

#### **Study objectives**

Restated hypothesis as of 31/07/2015:

Prevalence of Type 2 diabetes increases sharply with age. Our recent work has shown that the twin defects of insulin resistance and inadequate insulin secretion can be entirely reversed by short term calorie restriction resulting in long term withdrawal of oral hypoglycaemic agents and insulin. Three distinct questions must now be answered:

1. What is the interaction of duration of type 2 diabetes with reversibility?

2. Does dietary modification over 6 months protect the return to normal blood glucose control and beta cell function in the group achieving restoration of normality?

3. Does increased daily physical activity or increased monounsaturated fat intake enhance this protection?

#### Previous hypothesis:

Prevalence of Type 2 diabetes increases sharply with age. Our recent work has shown that the twin defects of insulin resistance and inadequate insulin secretion can be entirely reversed by short term calorie restriction resulting in long term withdrawal of oral hypoglycaemic agents and insulin. Three distinct questions must now be answered:

1. What is the interaction of duration of type 2 diabetes with reversibility?

2. Does dietary modification protect the beta cells from longer term deterioration of function after restoration of normality, as seen in vitro?

3. Does increased daily physical activity enhance this protection?

On 31/07/2015 the overall trial end date was changed from 01/09/2013 to 30/06/2014.

#### Ethics approval required

Old ethics approval format

#### Ethics approval(s)

Newcastle and North Tyneside 2 Research Ethics Committee, 22/06/2012, ref: 12/NE/0208

#### Study design

Randomised interventional trial

#### **Primary study design** Interventional

Secondary study design Randomised controlled trial

**Study setting(s)** Hospital

**Study type(s)** Treatment

#### Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

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

#### Diabetic Control, Nutrition, Obesity

#### Interventions

#### Restated interventions as of 31/07/2015:

Dietary modification, Very low calorie diet; Physical activity, Increased physical activity levels. The weight maintenance interventions are of 6 months duration and primarily involve a level of calorie intake to maintain weight steady. The randomised sub-study tests involve either a high monounsaturated fat diet or usual diet, and increased physical activity or usual physical activity.

#### Previous interventions:

Dietary modification, Very low calorie diet; Physical activity, Increased physical activity levels. The weight maintenance interventions are of 6 months duration and involve either a high monounsaturated fat diet or usual diet, and increased physical activity or usual physical activity.

#### Intervention Type

Behavioural

#### Primary outcome measure

Restated primary outcome measures as of 31/07/2015: Fasting plasma glucose at 6 months in the group achieving non-diabetic levels at 10 weeks (following VLCD and return to normal eating)

Previous primary outcome measures: Beta cell function measured at baseline, 8 weeks and 8 months

#### Secondary outcome measures

Added 31/07/2015: Change in beta cell function from 10 weeks to 6 months

## Overall study start date

20/07/2012

#### **Completion date**

30/06/2014

# Eligibility

## Key inclusion criteria

Type 2 diabetes of < 4 years or > 8 years duration
 HbA1c < 80 mmol/l / 9.5%</li>
 BMI 28-40kg/m2
 Age 25-80 years
 Stable weight for previous 6 months (within 5kg)
 Male and female participants

Participant type(s) Patient

## Age group

Adult

**Sex** Both

**Target number of participants** UK Sample Size: 34

#### Key exclusion criteria

- 1. Current treatment with thiazolidinediones, GLP-1 agonists or steroids
- 2. Renal or hepatic dysfunction
- 3. Contraindications to MRI
- 4. Alcohol consumption > 3 units per day for women and > 4 units per day for men
- 5. Allergy to soybean or eggs
- 6. Highly restrictive diet

Date of first enrolment 31/08/2012

Date of final enrolment 11/09/2013

# Locations

**Countries of recruitment** England

United Kingdom

#### Study participating centre Newcastle University

Newcastle upon Tyne United Kingdom NE4 5PL

# Sponsor information

**Organisation** Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

**Sponsor details** Midwifery Research Department Leazes Wing Queen Victoria Road Newcastle upon Tyne England United Kingdom NE1 4LP

**Sponsor type** Hospital/treatment centre

Website http://www.newcastle-hospitals.org.uk/

ROR https://ror.org/05p40t847

# Funder(s)

**Funder type** Government

**Funder Name** National Institute of Health Research [NIHR] - Biomedical Research Centre (UK)

Funder Name Novo Nordisk UK Research Foundation

Alternative Name(s) The Novo Nordisk UK Research Foundation, ovo Nordisk Research Foundation UK, NNUKRF

**Funding Body Type** Private sector organisation

**Funding Body Subtype** Trusts, charities, foundations (both public and private)

**Location** United Kingdom

# **Results and Publications**

**Publication and dissemination plan** Not provided at time of registration

Intention to publish date

## Individual participant data (IPD) sharing plan

## IPD sharing plan summary

Data sharing statement to be made available at a later date

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<u>Results article</u>	results	01/09/2015		Yes	No