

# REVISE-Diabetes: Randomisation to Endobarrier alone Versus with Incretin analogue in SustainEd Diabetes

<b>Submission date</b> 31/07/2013	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
<b>Registration date</b> 31/07/2013	<b>Overall study status</b> Completed	<input type="checkbox"/> Protocol
<b>Last Edited</b> 17/05/2021	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Effective treatment options for combined diabetes and obesity, sometimes called diabetes, are fairly limited. There are diet and exercise lifestyle options, oral and injectable medications including insulin and Liraglutide (Victoza). Despite current treatment options, diabetes and weight often remain uncontrolled with high blood sugars and obesity. Surgery to reduce stomach size or bypass the intestine may be considered radical. The aim of this study is to find out if a new device called the Endobarrier is an effective treatment option for diabetes either alone or in combination with diabetes medications. We are also seeking to find out how the device works in reducing weight and improving diabetes control.

### Who can participate?

Adult patients with type 2 diabetes and obesity can take part if they have tried at least 6 months' treatment with Liraglutide. Participants should be able to attend their local study centre (King's College Hospital, London; Guy's and St Thomas' Hospitals, London; City Hospital, Birmingham, Glasgow Royal Infirmary), so distance from these centres is a factor which may affect participation.

### What does the study involve?

Participants will be randomly allocated to one of the following three treatments:

1. Endobarrier alone: Endobarrier implanted for 1 year, inserted and removed by endoscopic procedure. Liraglutide stopped for 2 years.
2. Endobarrier + Liraglutide: Endobarrier implanted for 1 year, inserted and removed by endoscopic procedure. Liraglutide continued for 2 years.
3. Liraglutide alone.

The hospital visits will take place at: City Hospital, Birmingham, King's College Hospital, London or Glasgow Royal Infirmary for routine diabetes care including checks of weight, body mass index, and blood tests. Additional tests will include blood tests, a telephone interview of dietary habits, and stool and urine tests that will be done to better determine how the device works. All patients will be asked to follow a standard diet (liquid/puree food) for the first 2 weeks written in a dietary information sheet that we will provide. For patients in the Endobarrier treatment

groups, they will fast on the day preceding the insertion, which will be done under general anaesthetic. During the procedure, the endoscopy doctor will gently pass an endoscope (a flexible telescope with a light at the end) through the patient's mouth until it is just beyond the stomach. X-rays will also be used to ensure the Endobarrier's position.

What are the possible benefits and risks of participating?

The possible benefits of taking part include an improvement in diabetes and reduction in weight in all treatment groups. It is possible that these benefits may be considerable. However, this cannot be guaranteed. The information we get from this study may help us to treat future patients with diabetes better. There are risks that the device may fail, move, become blocked, block the intestine, or cause bleeding or pain. The overall risk for this is low (<5%). If this occurs, another endoscopic procedure will be required to remove the device. Bleeding or perforation complications will usually become evident within a few hours of the procedure (abdominal pain) so patients will be observed following the procedure. If there is severe pain, bleeding or black tarry stool in the days following the procedure, the Emergency Department should be contacted (and inform the research team but this should not delay you attending the Emergency Department). It is possible that if the treatment is given to a pregnant woman it will harm the unborn child. Pregnant women must not therefore take part in this study, neither should women who plan to become pregnant during the study. Women who are at risk of pregnancy may be asked to have a pregnancy test before taking part to exclude the possibility of pregnancy. Women who could become pregnant must use an effective contraceptive during the course of this study. Any woman who becomes pregnant during the study should immediately tell her research doctor. In this trial, x-rays will be used to guide the Endobarrier device into place and check its position after insertion. We are all exposed to a background level of radiation from natural and artificial sources; the radiation received as part of this trial is equivalent to about 3 years' worth of this background radiation. It is similar to the maximum dose that someone working with radiation is allowed to receive each year. There is a small risk to patients from this radiation: the likelihood of detrimental effects is estimated to be 1 in 2,500. This small risk is considered to be acceptable when compared with the potential benefits from having the device fitted.

Where is the study run from?

The lead site is City Hospital, Birmingham (the sponsor is Sandwell and West Birmingham Hospitals NHS Trust, which is organising and overseeing it). Other locations are London and Glasgow.

When is the study starting and how long is it expected to run for?

The study began recruiting patients in June 2013 and the first study-related Endobarrier insertion procedure was done in July 2013. The study is expected to finish in November 2015.

Who is funding the study?

The research is funded by the Association of British Clinical Diabetologists (ABCD). The research team is not funded by the device manufacturers.

Who is the main contact?

Dr Piya Sen Gupta - Research Fellow  
piya.sengupta@nhs.net

## Contact information

Type(s)

Scientific

**Contact name**

Dr Piya Sen Gupta

**Contact details**

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Diabetes Centre  
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United Kingdom  
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+44 (0)79 6690 9046  
piya.sengupta@nhs.net

**Additional identifiers**

**ClinicalTrials.gov (NCT)**

NCT02055014

**Clinical Trials Information System (CTIS)**

2012-004988-42

**Protocol serial number**

14147

**Study information**

**Scientific Title**

REVISE-Diabesity: Randomisation to Endobarrier alone Versus with Incretin analogue in SustainEd Diabetesity

**Acronym**

REVISE-Diabetesity

**Study objectives**

Methodology: open label multicentre randomised controlled clinical trial (RCT) involving the use of a novel device (Endobarrier) that achieves 60cm of duodeno-jejunal exclusion and can improve metabolic and weight control without surgery in obese type 2 diabetic (T2DM) patients failing to achieve treatment targets with their current therapy.

Seventy-two patients with T2DM and obesity ( $HbA1c \geq 7.5\%$ ,  $BMI \geq 35\text{kg/m}^2$ ) with at least 6 months' liraglutide treatment, will be recruited from the following NHS centres: City Hospital, Birmingham; Kings College Hospital; Guys and St Thomas Hospitals and Glasgow Royal Infirmary. Enrolled patients will be studied over 24 months (seen every 3 months) and randomised to receive one of:

1. Control group: increase Liraglutide dose 1.2mg to 1.8mg
2. Endobarrier alone group: stop Liraglutide therapy, undergo Endobarrier insertion
3. Endobarrier+Liraglutide group: continue Liraglutide 1.2mg, undergo Endobarrier insertion

We will establish the mechanisms of action and their time course by repeated measures of: 1. glycated haemoglobin; weight; BMI, waist and neck circumference; 2. fasting glucose, insulin, c-peptide and HOMA-IR; 3. Imaging of liver and pancreas fat stores (MRI, ultrasound, dual energy CT) and 4. the insulin, c-peptide, incretin and bile acid response to a mixed meal challenge; 5. Stool microbiota; calprotectin and intestinal permeability and absorption.

#### Objectives:

1. To assess, in an NHS setting, the metabolic effectiveness of Endobarrier alone versus combined Endobarrier-Liraglutide therapy in patients with obesity and type 2 diabetes mellitus (T2DM) who remain overweight and with suboptimal glycaemic control despite Liraglutide treatment
2. To understand the mechanisms of action of Endobarrier by assessing the biological response to its placement.

Hypothesis: the combined Endobarrier-Liraglutide treated patients will maintain lower HbA1c better than the Endobarrier without Liraglutide patients.

#### Ethics approval required

Old ethics approval format

#### Ethics approval(s)

NRES Committee West Midlands - Edgbaston, First MREC approval date 02/01/2013, ref: 12/WM/0408

#### Primary study design

Interventional

#### Study design

Interventional open label multicentre randomised controlled clinical trial; Design type: Treatment

#### Study type(s)

Treatment

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

Topic: Diabetes Research Network; Subtopic: Type 2; Disease: Diabetic Control, Device studies, Metabolic, Obesity

#### Interventions

1. Endobarrier alone, Endobarrier implanted for 1 year, inserted and removed by endoscopic procedure. Liraglutide stopped for 2 years.
2. Endobarrier+Liraglutide, Endobarrier implanted for 1 year, inserted and removed by endoscopic procedure. Liraglutide continued for 2 years (for the first year, combined with Endobarrier).
3. Liraglutide 1.8mg, Active Control Group

Follow Up Length: 24 months

Study Entry : Single Randomisation only

Secondary address for contact:

King's College London  
Research Fellow Office  
3rd Floor - Diabetes  
WEC, 10 Cutcombe Road  
London SE5 9RS  
United Kingdom

## **Intervention Type**

Drug

## **Phase**

Phase IV

## **Drug/device/biological/vaccine name(s)**

Liraglutide

## **Primary outcome(s)**

HbA1c; Timepoints: End of Study & interim 0, 6, 12 months

## **Key secondary outcome(s)**

1. Fasting Insulin Resistance; Timepoints: Day 0, 2, 4, 7 implant; day 0, 2, 4, 7 explant and end of study
2. Gut microbiota, stool calprotectin, intestinal permeability and absorption; Timepoints: 0, 6 & 18 months
3. Hepatic and pancreatic fat stores; Timepoints: 0, 3 months
4. Insulin, Bile Acids, Gut Peptides, Adipokines response to meal; Timepoints: Day 0, 7 implant; Day 0, 7 explant & end of study
5. Nutrition & Food Group Evaluation; Timepoints: 0, 1 year & end of study
6. Quality of Life Evaluation (EQ-5D); Timepoints: 0, 1 year & end of study
7. Weight, BMI; Timepoints: End of Study & interim at 6 months and 1 year

## **Completion date**

30/11/2015

## **Eligibility**

### **Key inclusion criteria**

1. Participation in the Association of British Clinical Diabetologists' Nationwide Liraglutide Audit with data for at least 6 months
2. Type 2 diabetes with latest HbA1c  $\geq 7.5\%$
3. Obesity with body mass index (BMI)  $\geq 35\text{kg/m}^2$  (or  $\geq 30\text{kg/m}^2$  for South Asian origin patients)
4. Treatment with liraglutide for at least 6 months with baseline and follow-up HbA1c and weight data available\*. Stable weight and HbA1c in preceding 3 months ( $< 3\text{kg}$  reduction in weight and  $< 0.3\%$  reduction in HbA1c).
5. Target Gender: Male & Female ; Lower Age Limit 18 years

### **Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

All

**Key exclusion criteria**

1. <18 years of age
2. Abnormal intestinal anatomy
3. Contraindication to oesophago-gastroduodenoscopy
4. Previous bariatric surgery or bowel surgery
5. Active infection or C-reactive protein (CRP)>10mg/dL
6. Anticoagulation therapy which cannot be discontinued/ coagulopathy INR>1.3
7. Estimated Glomerular Filtration Rate (eGFR)<30
8. Known portal hypertension
9. Previous pancreatitis or amylase >3 times the upper limit of normal
10. Uncontrolled cardiovascular disease
11. Lactating or pregnant females
12. Patients taking aspirin in whom it should continue (e.g. active ischaemic heart disease or cerebrovascular disease)

**Date of first enrolment**

10/06/2013

**Date of final enrolment**

30/11/2014

**Locations****Countries of recruitment**

United Kingdom

England

Scotland

**Study participating centre**

**City Hospital Birmingham**

Birmingham

United Kingdom

B18 7QH

**Study participating centre**  
**King's College Hospital**  
London  
United Kingdom  
SE5 9RS

**Study participating centre**  
**Guy's and St Thomas' Hospital**  
London  
United Kingdom  
SE1 7EH

**Study participating centre**  
**Glasgow Royal Infirmary**  
Glasgow  
United Kingdom  
G4 0ET

## **Sponsor information**

**Organisation**  
Sandwell and West Birmingham Hospitals NHS Trust (UK)

**ROR**  
<https://ror.org/05mzf3276>

## **Funder(s)**

**Funder type**  
Research council

**Funder Name**  
Association of British Clinical Diabetologists (ABCD)

## **Results and Publications**

**Individual participant data (IPD) sharing plan**

## IPD sharing plan summary

Not expected to be made available

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes