

# Evaluation of the efficacy and safety of endoscopically achieved proximal intestinal exclusion as an adjunct to glucagon-like peptide-1 therapy in diabetes: REVISE-Diabetes clinical trial

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## Background and Aims:

Innovative and effective treatments are needed to combat the global diabetes pandemic. Aims were to evaluate 1. efficacy and safety of endoscopic proximal intestinal exclusion, using Endobarrier (Fig. 1), added to GLP-1RA therapy compared to either treatment alone, 2. maintenance following device removal.

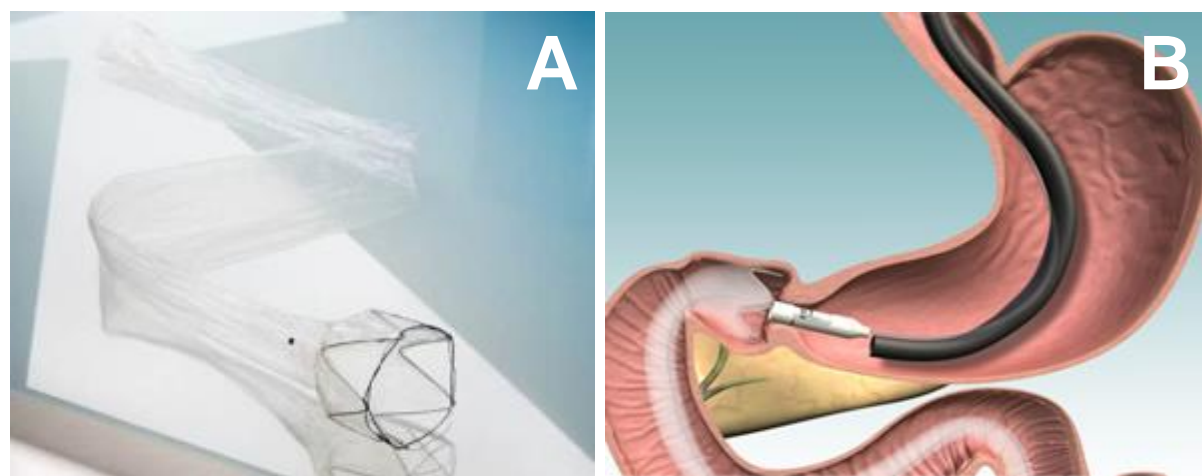


Fig. 1A. Photograph of Endobarrier with crown anchor in foreground and tubing posteriorly. 1B shows the device released from a capsule (white) under endoscopic (black) guidance.

## Methods:

In this UK multicentre, open-label trial (ISRCTN00151053), adults with suboptimally controlled type 2 diabetes (T2D, HbA1c $\geq$ 7.5%) and obesity (BMI $\geq$ 35kg/m<sup>2</sup>) despite GLP-1RA (liraglutide 1.2mg daily) therapy were randomised as follows in Fig. 2:

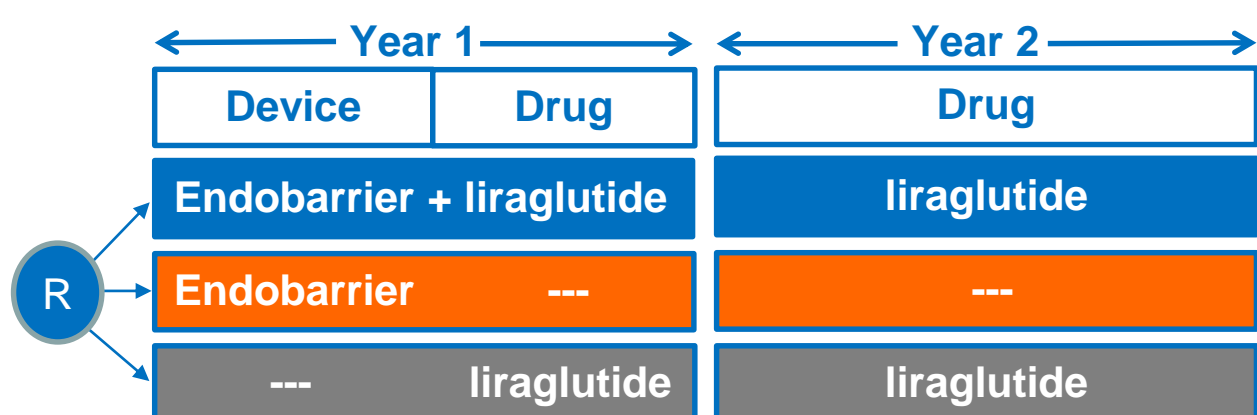


Fig. 2. Study schedule. Participants were seen 3-monthly.

## Results

The baseline characteristics are shown in Table 1.

Parameter	Endobarrier + liraglutide n=24	Endobarrier n=24	liraglutide n=22
Age (years)	52.0 $\pm$ 11.7	50.7 $\pm$ 8.4	54.0 $\pm$ 10.1
Sex (%male)	41.7	29.2	36.4
Caucasian(%)	66.7	70.8	72.7
*Diabetes duration (yrs)	11.2(6.7-17.1)	10.3(7.8-12.7)	13.3(9.0-18.4)
HbA1c (%)	9.6 $\pm$ 1.4	9.3 $\pm$ 1.7	9.7 $\pm$ 1.7
BMI (kg/m <sup>2</sup> )	40.3 $\pm$ 4.8	41.7 $\pm$ 4.9	40.6 $\pm$ 4.4
Weight (kg)	112.8 $\pm$ 20.4	115.6 $\pm$ 19.4	113.9 $\pm$ 14.9

All participants completed the 12-month visit. Data were available in 65 at the end of the study (1-year post-device removal, Fig. 3). HbA1c reduction of >1% was maintained in 14/22 (63.6%) (EL), 10/20 (50.0%) (E) and 10/21 (47.6%) in L groups. There were 5 (10.4%) early device removals due to gastrointestinal symptoms and 5 Endobarrier-treated patients (10.4%) had serious device-related adverse events (bleed, obstruction, complex removal, liver abscess) with resolution in all cases.

## Conclusion:

This is the first study to demonstrate combination proximal intestinal exclusion with GLP-1RA therapy is effective and has an acceptable safety profile. In patients with diabetes, treatment with Endobarrier is augmented by GLP-1RA therapy, with clinical benefit and advantage over either treatment alone.

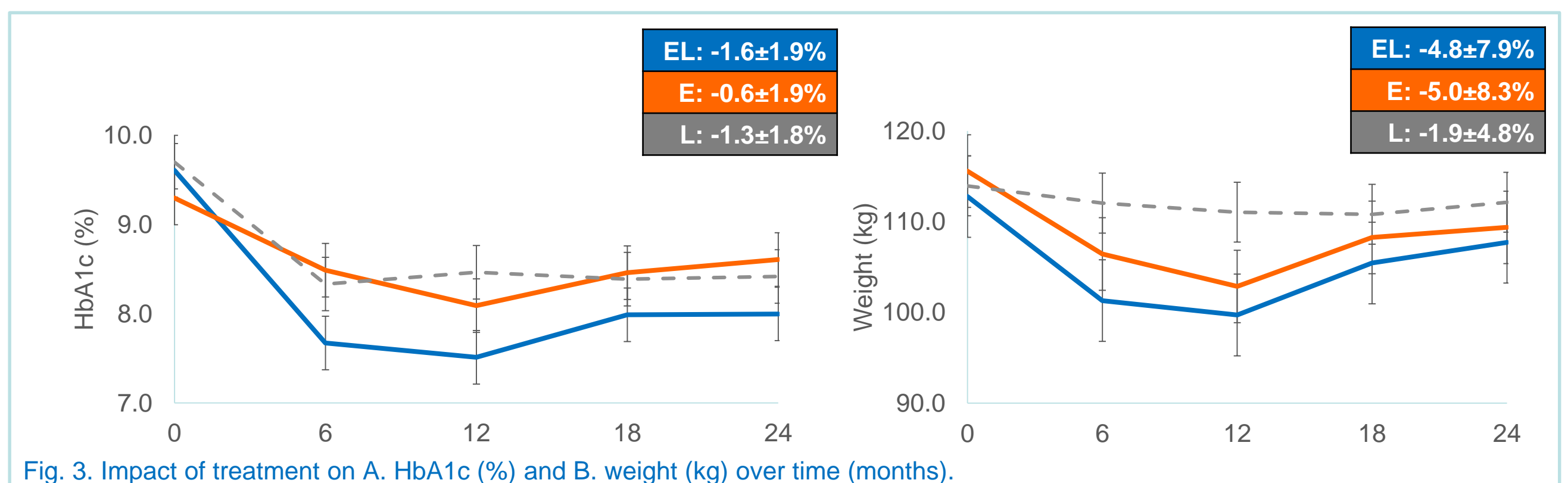


Fig. 3. Impact of treatment on A. HbA1c (%) and B. weight (kg) over time (months).