

# The interaction of endoscopic proximal intestinal exclusion therapy using Endobarrier with GLP-1 therapy rapidly improves type 2 diabetes by increasing fasting and postprandial satiety



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## BACKGROUND

Endoscopically-delivered proximal intestinal exclusion therapy using Endobarrier (Fig. 1), a 60cm polyethylene tubing device, is effective at weight and glycaemic lowering in type 2 diabetes, particularly in combination with GLP-1 receptor agonist therapy. The mechanisms in achieving this remain unclear.

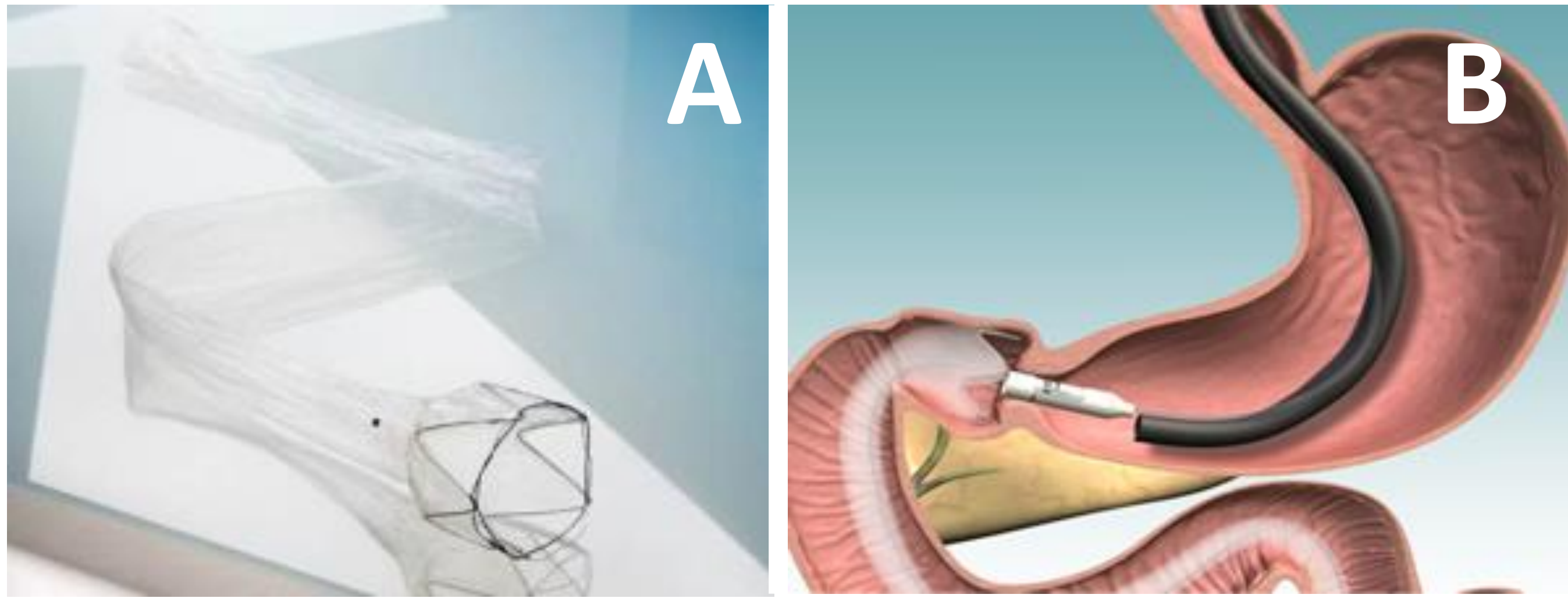


Fig. 1A. Photograph of Endobarrier with crown anchor in foreground and tubing posteriorly; 1B shows the device implanted with endoscope (black) being used to guide capsule (white) containing Endobarrier. Once sited in the duodenum instruments are used to deploy the Endobarrier.

## AIM

To evaluate the acute effect of proximal intestinal exclusion with and without GLP-1RA therapy, on hunger, satiety and associated peptides.

## METHOD

A subset of 70 adults with type 2 diabetes mellitus (HbA1c $\geq$ 58mmol/mol) and obesity (BMI $\geq$ 35kg/m<sup>2</sup>) despite GLP1-RA (liraglutide) therapy randomised to one of:

- Endobarrier + liraglutide 1.2mg
- Endobarrier (and stop liraglutide)
- Liraglutide 1.8mg (and no endobarrier)

underwent meal tests (400kcal, carbohydrate 31.1g, fat 26.7g, and protein 7.4g, using vanilla flavour Häagen-Dazs<sup>®</sup> ice cream) at baseline, 1 week and 1 year post-intervention (REVISE-Diabetes, ISRCTN00151053).

Simultaneous visual analogue scores (VAS, 10cm linear scale) for hunger and satiety were recorded and blood sampled at regular intervals post-ingestion as indicated in Fig. 2.

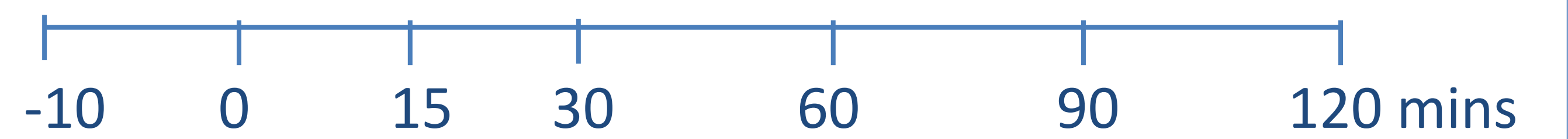
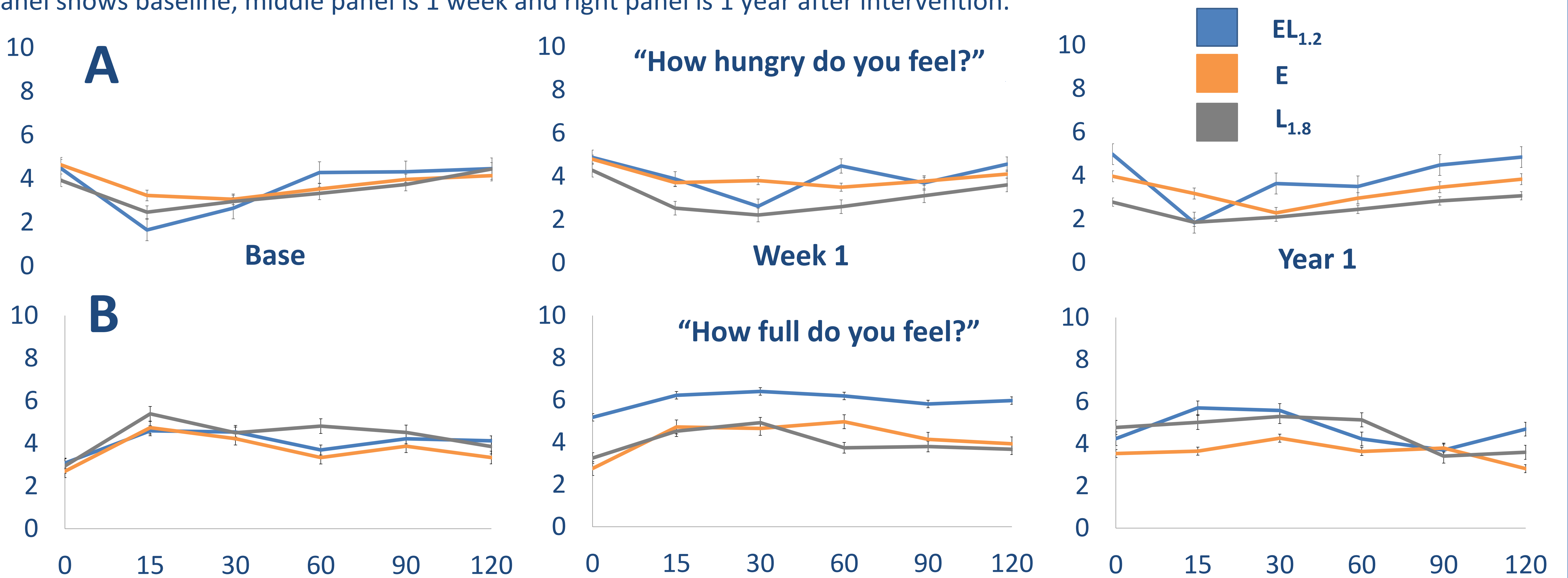


Fig. 2. protocol for hunger, satiety VAS completion and blood sampling.

## RESULTS

Fig. 3A-B. Impact of treatment on hunger and satiety scores. A shows hunger scores and B satiety scores over time (minutes). The left panel shows baseline, middle panel is 1 week and right panel is 1 year after intervention.



There were 44 participants (age 50.2 $\pm$ 10.7 years, 45.5% male, 63.6% Caucasian, type 2 diabetes duration 12.4 $\pm$ 7.7 years, BMI 40.8 $\pm$ 4.7kg/m<sup>2</sup>, HbA1c 78.5 $\pm$ 15.4mmol/mol). Fasting satiety rose from 31.4 $\pm$ 18.0 to 50.8 $\pm$ 27.3 at 1 week in the E+L group (P=0.017, n=17) but did not significantly change in the other groups. E+L also increased post-prandial satiety at 1 week (total AUC 476.2 $\pm$ 201.9 at baseline, to 736.2 $\pm$ 248.8 (P=0.001), sustained at 1 year to 606.3 $\pm$ 231.1 (P=0.03, n=11). There were no corresponding changes in hunger or total GLP-1 responses.

## CONCLUSION

- Increased satiety, without changes in hunger, contributes to improved glycaemic control when proximal intestinal exclusion is combined with GLP-1RA therapy.
- This increased satiety is sustained up to 1 year.
- The key mediator for this is not GLP-1 and alternatives are sought with planned analyses including PYY and GIP.