Early (6 month) metabolic and body weight effects of proximal intestinal exclusion as an adjunct to GLP-1 therapy in suboptimally controlled type 2 diabetes

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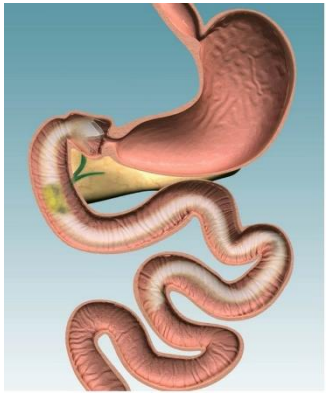


ABCD Autumn meeting
6th November 2015

Background: NICE guidelines GLP-1RA in type 2 diabetes

Issue date: May 2009

Type 2 diabetes: newer agents

Type 2 diabetes: newer agents for blood glucose control in type 2 diabetes

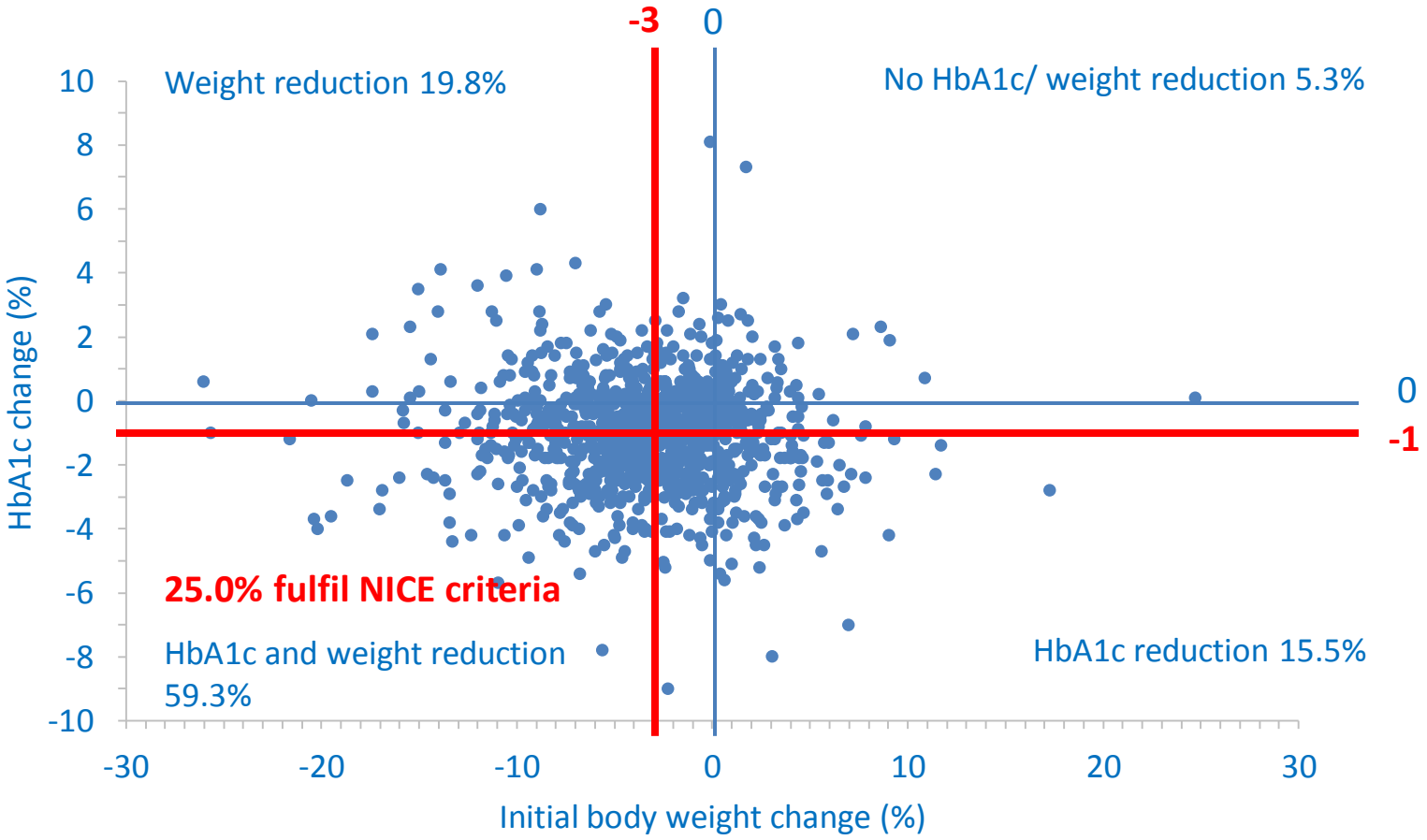
NICE clinical guideline 87

Recommendation 1.1.15

Only continue GLP-1 mimetic (exenatide) therapy if the person has had a beneficial metabolic response (a reduction of at least 1.0 percentage point in HbA_{1c} and a weight loss of at least 3% of initial body weight at 6 months).

Background: failure rate of GLP-1RA = 75%

Scatterplot of HbA1c and initial body weight change at 6 months (±6 weeks)
ABCD liraglutide audit data (2009-14), n1023



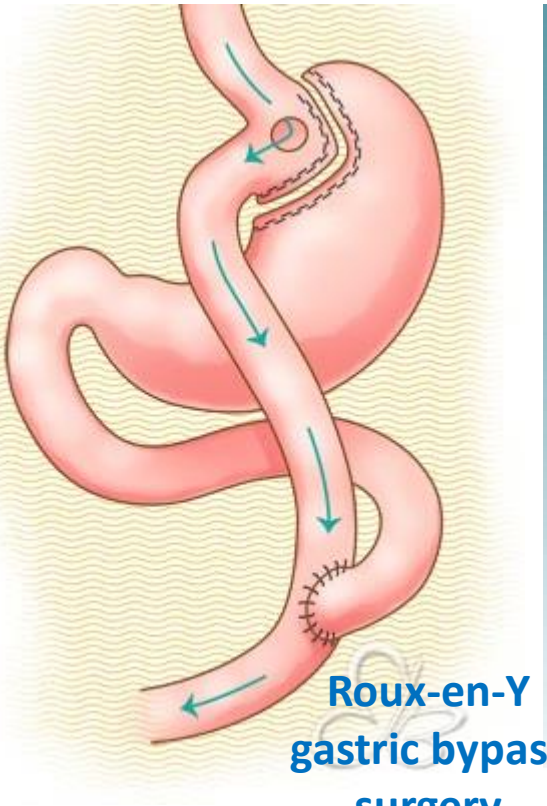
1. Thong KY, Sen Gupta P et al. GLP-1RAs in type 2 diabetes – NICE guidelines versus clinical practice. BJDVD 2014 (14), 2:52-59.

Background:
New effective therapies for diabesity are needed

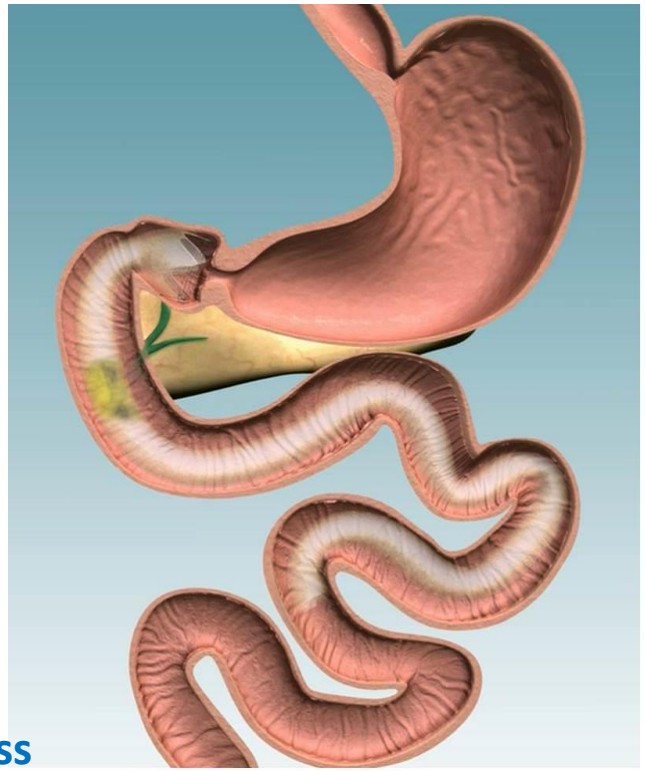
Endobarrier – an implantable duodenal-jejunal liner device

Nitinol Anchor

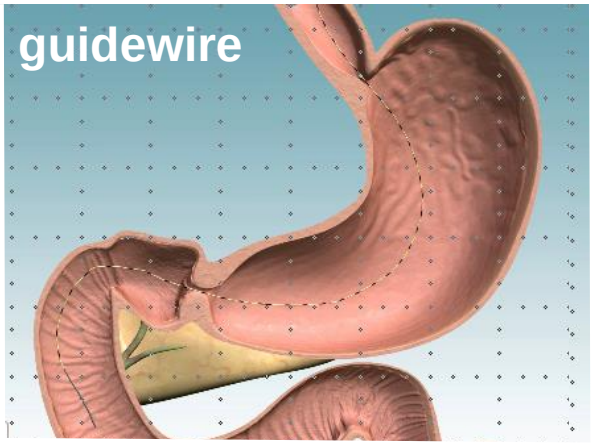
Fluoropolymer wall

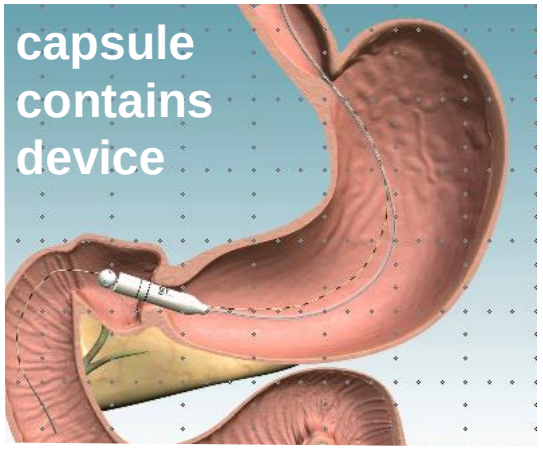


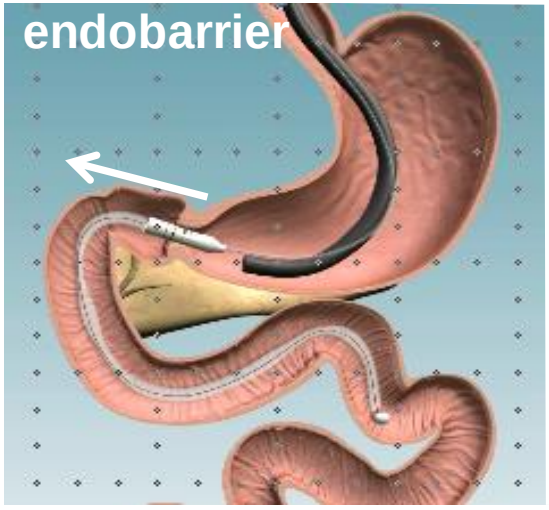
Roux-en-Y gastric bypass surgery

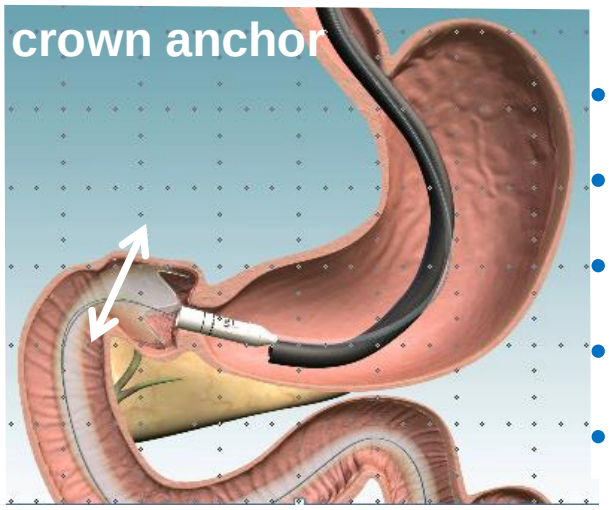


Endobarrier – endoscopic implant procedure









- general anaesthetic
- 2-week diet for placement
- implant for 1 year
- reversible
- endoscopic explant

Aim

To investigate the early effects of adding proximal intestinal exclusion to GLP-1RA therapy not achieving targets, on weight and HbA1c compared to either treatment alone

Study design: Selection Criteria

INCLUSION CRITERIA:

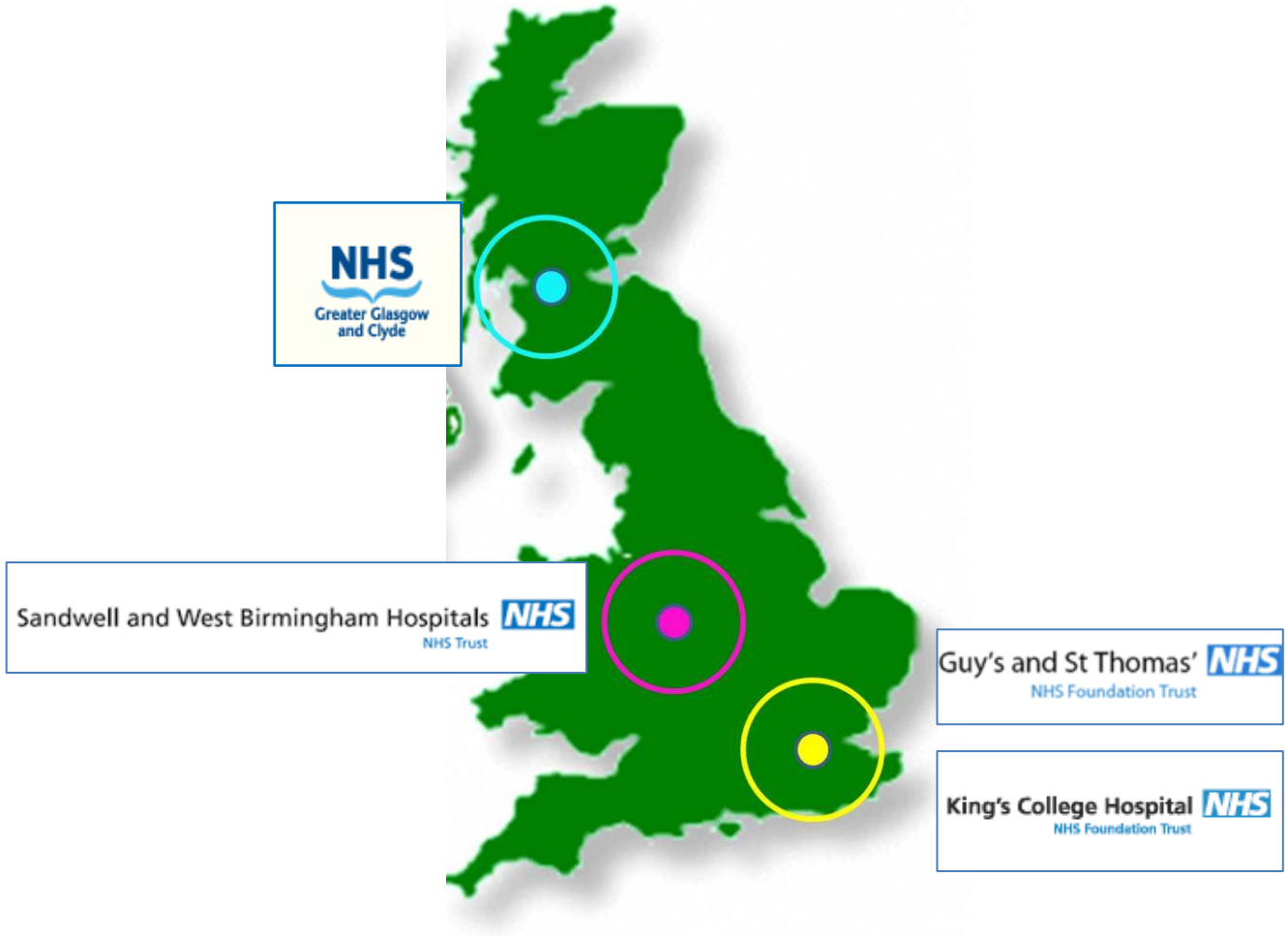
- Type 2 Diabetes
- Liraglutide treated for ≥6 months
- HbA1c ≥7.5%
- Obesity, BMI ≥35kg/m^2
- Stable weight, HbA1c (3 months)

EXCLUSION CRITERIA:

- Safety considerations:
- Bleeding risk: aspirin, warfarin
- Infection
- Pregnancy
- Conditions interfering with endobarrier placement/ findings

Study design:

Open label, multicentre, parallel group, randomised controlled trial



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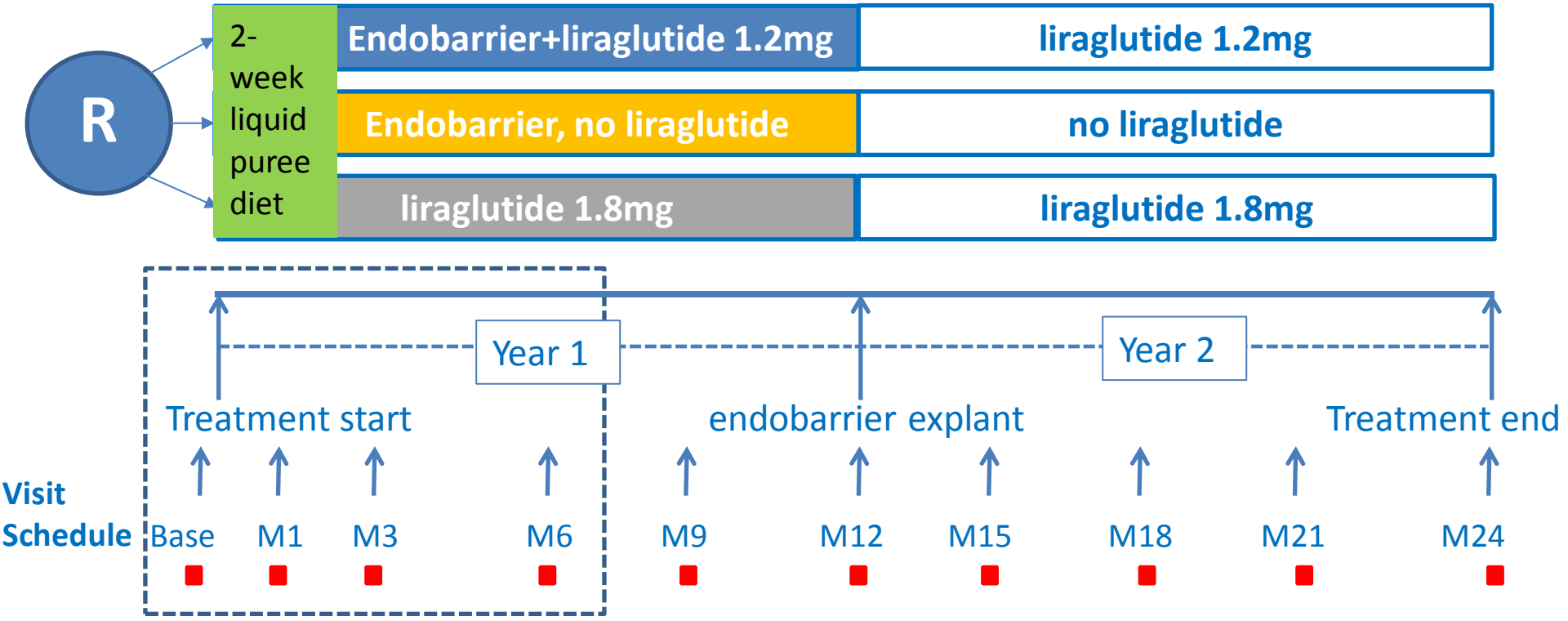
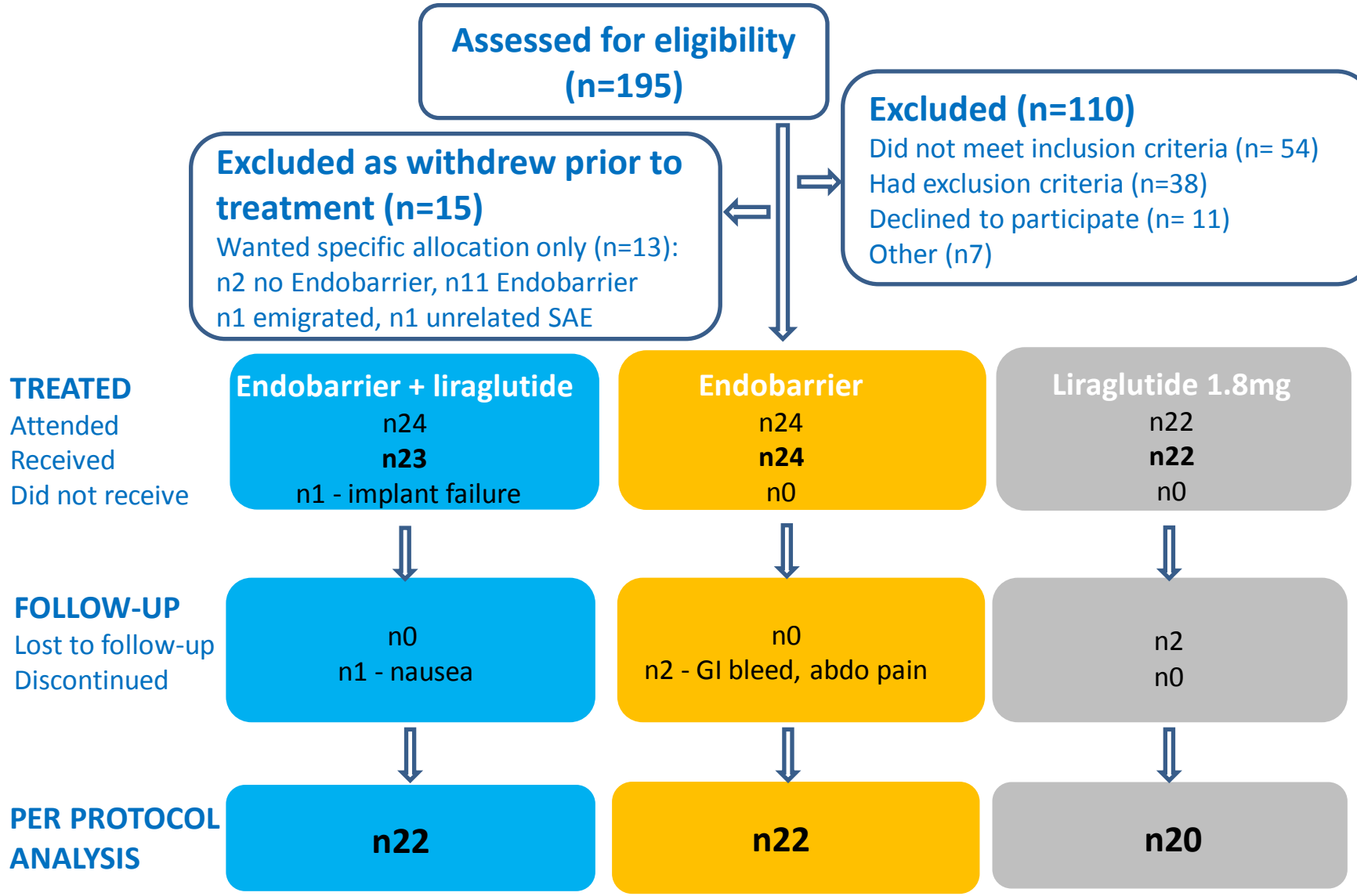


3-monthly visits:

- Interview: compliance, diet, safety checks, adverse symptoms, drug changes
- Anthropometry
- Blood tests: fbc, u&e, lft, amylase, lipids, HbA1c

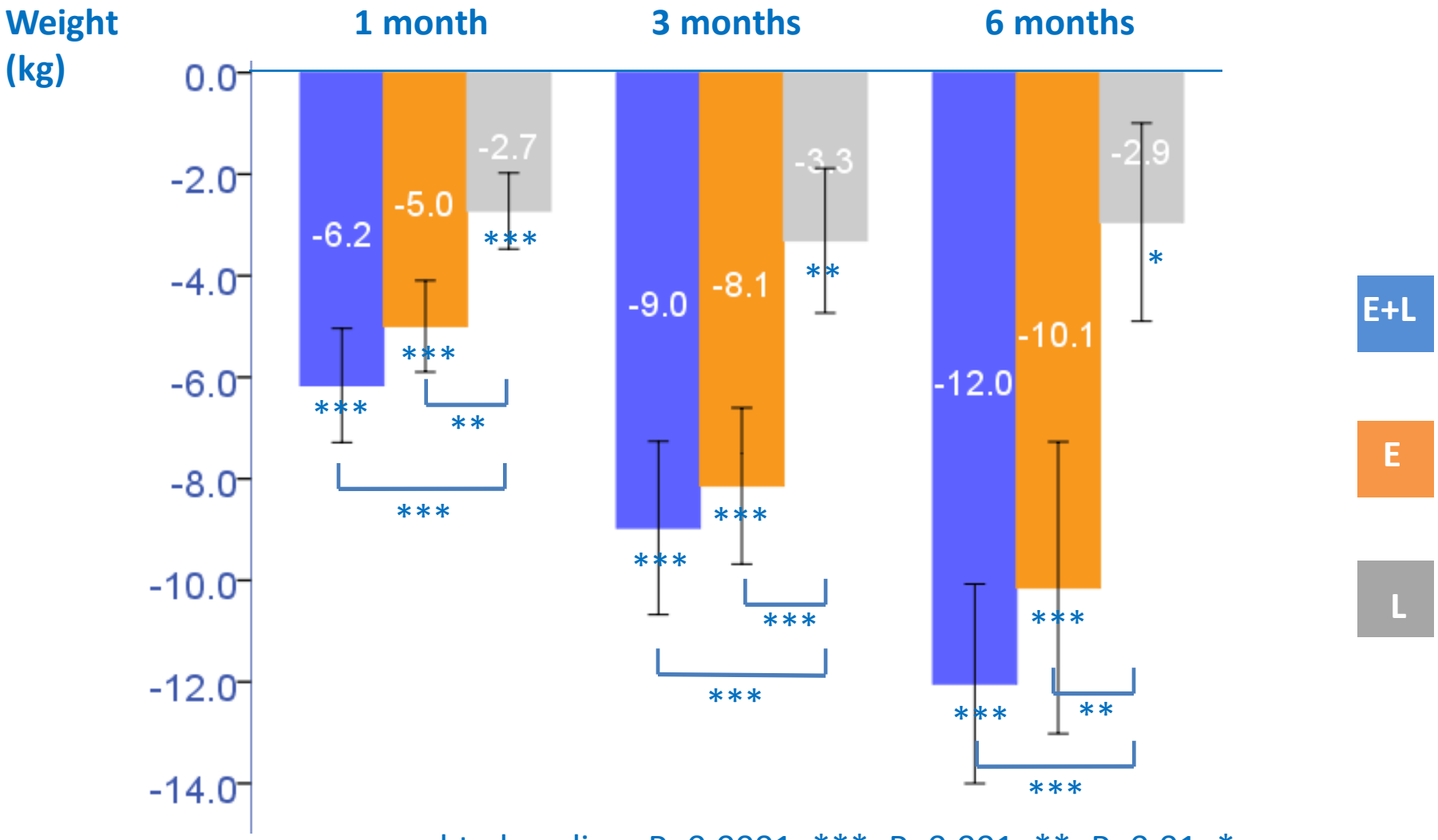
Flowsheet of study subjects (n70 treated, 97.2% target)



Baseline characteristics n64

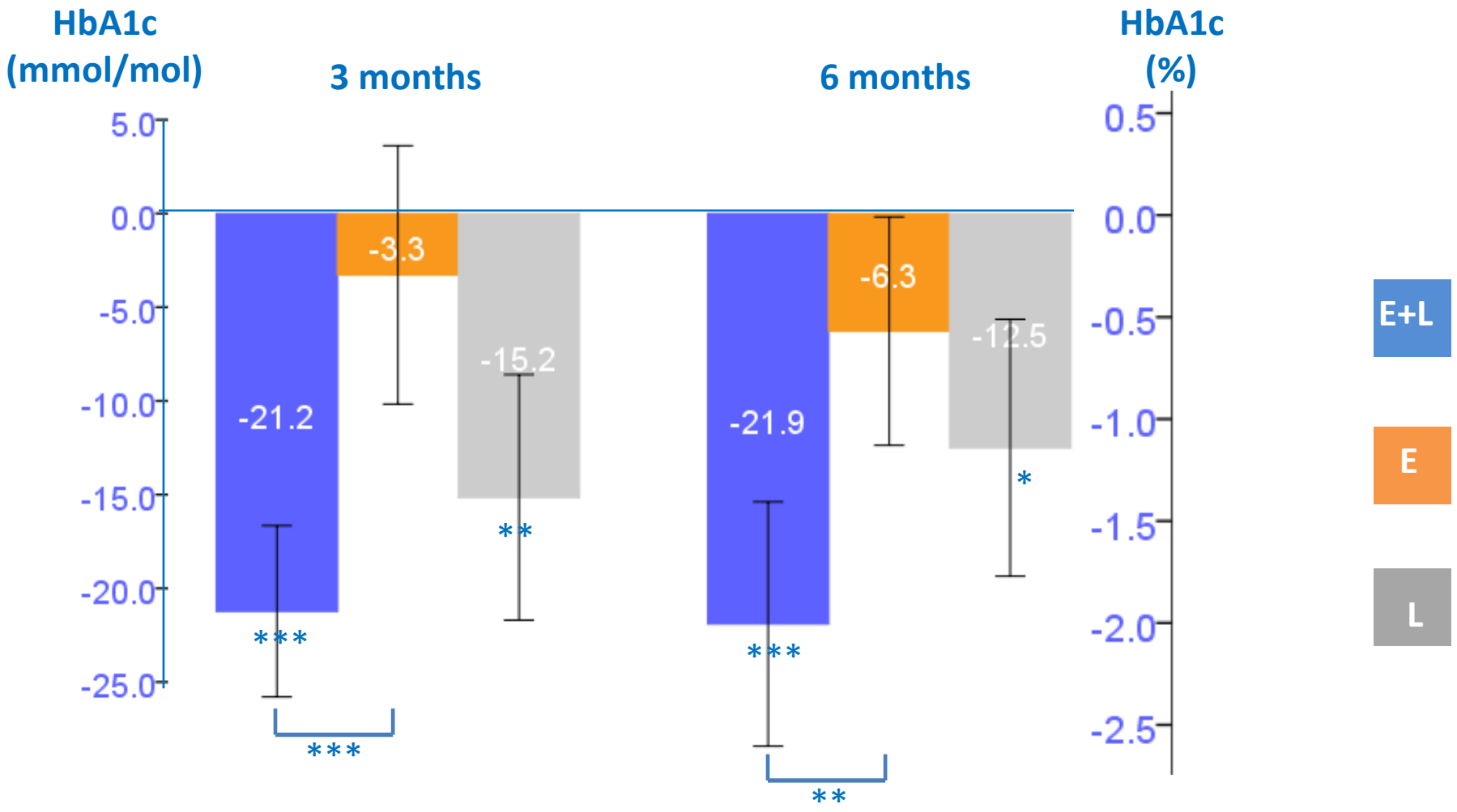
Parameter		Endobarrier +liraglutide	Endobarrier	liraglutide
Number		22	22	20
Age (years)		51.8±12.2	50.1±8.5	54.9±6.6
Sex (% male)		45.5	31.8	31.8
Ethnicity	Caucasian (%)	68.2	68.2	75.0
	South Asian (%)	18.2	13.6	15.0
	Afro-Caribbean (%)	0.0	13.6	5.0
	Other (%)	13.6	4.5	5.0
BMI (kg/m^2)		40.4±4.8	41.9±5.0	41.0±4.5
Weight (kg)		113.2±21.3	117.6±18.	115.2±14.8
HbA1c (mmol/mol)		82.1±15.4	78.1±19.8	81.4±15.9
HbA1c (%)		9.7±1.4	9.3±1.8	9.6±1.5

Results: weight change over time



compared to baseline: P<0.0001=***, P<0.001=**, P<0.01=*

Glycaemic control: HbA1c change over time



compared to baseline: P<0.0001=***, P<0.001=**, P<0.01=*

Summary

- Both endobarrier groups produced largest reduction in weight
- Both liraglutide groups produced largest reduction in HbA1c
- E+L group is superior at reducing both weight and HbA1c at 6-months
  - weight reduction of 12.0±4.6kg
  - HbA1c reduction of 21.9±15.3mmol/mol (2.0±1.4%)

Conclusion

These data suggest that adding proximal intestinal exclusion to suboptimally performing GLP1-RA therapy has a useful role in the management of refractory diabetes and obesity.

Acknowledgements

All study participants

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Data monitoring committee: Cliff Bailey, John McClure, Parth Narendran

Association of British Clinical Diabetologists

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