

Case study: Medical Management

**2022 EASO Obesity Masterclass Summer School
Les Pensieres of the Fondation Merieux
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Bariatric Surgery: Medical Management

Luca Busetto – Disclosures

- Novo Nordisk
- Bruno Farmaceutici
- Rythm
- Pronokal
- Therascience
- Enzymmanagement

The case of Gianpietro



- Severe long-standing obesity with a BMI $>50 \text{ kg/m}^2$
- Insulin-treated T2DM requiring >100 units of insulin per day
- Arterial hypertension controlled by 3 drugs
- Severe OSA treated by C-PAP
- Divorced, living alone, mildly depressed
- Nibbling during the day, sometimes night eating
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Medical management before and after BS: T2DM

Peri-operative complications related to type 2 diabetes

- Surgical stress is associated with exacerbation of hyperglycemia in patients with type 2 diabetes and with “stress hyperglycemia” in non-diabetic patients.
- Among hospitalised patients, adverse outcomes (hospital mortality, infection, heart failure after myocardial infarction, need for ICU admission, and increased length of hospital stay) are more frequent in patients with hyperglycemia compared to those with normal glucose levels [Moghissi ES. Addressing hyperglycemia from hospital admission to discharge. Curr Med Res Opin 2010;26:589-98].
- Both before and after adjustment for several possible confounding variables, an HbA1c level of more than 7% was found to be associated with a two-fold increased rate of infectious complications (pneumonia, wound infection, urinary tract infection, or sepsis) in 490 diabetic patients undergoing several types of surgical procedures at a tertiary referral US centre [Dronge AS, Perkal MF, Kancir S, et al. Long-term glycemic control and postoperative infectious complications. Arch Surg 2006;141:375-80].

Medical management before and after BS: T2DM

Main goals for glucose controls in bariatric patients

Pre-operative phase

Identification of patients with type 2 diabetes
Optimisation of metabolic control

HbA1c value of 6.5%-7.0% or less, a fasting blood glucose level of ≤ 110 mg/dL, and a 2-hour postprandial blood glucose concentration of ≤ 140 mg/dl.

More liberal preoperative targets, such as a HbA1c of 7-8%, should be considered in patients with advanced micro-vascular or macro-vascular complications, extensive co-morbid conditions, or long-standing diabetes in which the general goal has been difficult to attain despite intensive efforts.

AACE/TOS/ASMBS. Obesity 2013;21:S1-S27.

Medical management before and after BS: T2DM

Table 7. List of graded clinical practical recommendations for the management of major obesity-related comorbidities after bariatric surgery

Recommendations	Level of evidence	Grade of recommendation*
<i>Type 2 diabetes</i>		
Bariatric surgery has profound effects on diabetes and can lead to prompt modifications and adjustments of medical therapy.	1	A
Metabolic control should be optimized in preparation for a bariatric procedure. HbA1c levels of 6.5–7%, fasting glucose levels <110 mg/dl and 2 h post-load glucose <140 mg/dl should be targeted. In patients with long lasting diabetes, diabetes complications and poor glucose control, HbA1c levels <8% are considered acceptable.	2	C
Glitazones, glinides and dipeptidyl-dipeptidase 4 inhibitors (DDP4i) should be discontinued 24 h before surgery with a reduction of basal insulin dosage to 0.3 units/kg. Metformin should be discontinued on the day of surgery.	3	D

Medical management before and after BS: T2DM

Table 7. List of graded clinical practical recommendations for the management of major obesity-related comorbidities after bariatric surgery

Recommendations	Level of evidence	Grade of recommendation*
On the day of surgery, glucose levels should be targeted at <140 mg/dl and short acting insulin should be used according to a correction factor of one unit of insulin for every 40 mg/dl above the level of 140 mg/dl.	3	D
In hospital, target glucose values should be 140–180 mg/dl. if values are >180 mg/dl in two consecutive tests basal insulin at a dose of 0.1 units/kg should be prescribed.	3	D
Metformin can be reassumed from the 3rd day after surgery providing that renal function has been controlled at a dosage of 850 mg, 1–2 times daily. After gastric bypass surgery, biological availability of metformin increases by 50%, and therefore reduced dosages should be prescribed.	3	D

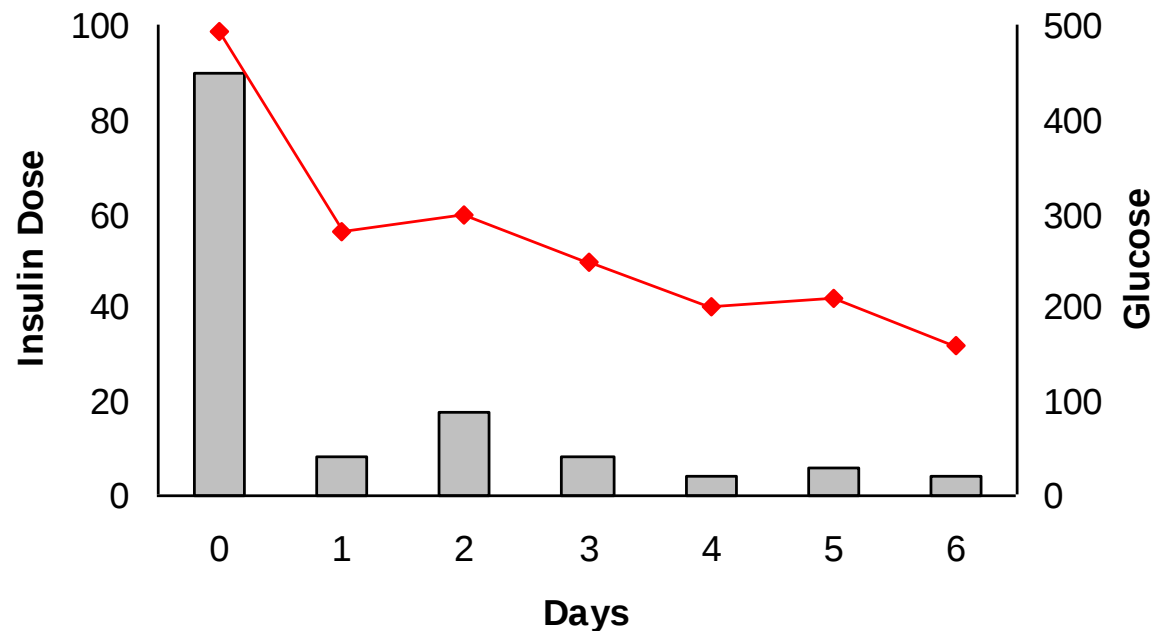
Obesity Facts
The European Journal of Obesity

Obes Facts 2017;10:597–632

Medical management before and after BS: T2DM

- **Peri- and Post-operative phase**

Adjustment of glucose-lowering to the new therapeutic needs
Continued surveillance and preventive diabetes care



Medical management before and after BS: T2DM

Table 7. List of graded clinical practical recommendations for the management of major obesity-related comorbidities after bariatric surgery

Recommendations	Level of evidence	Grade of recommendation*
In the first 7–10 days after surgery, treatment should be directed toward fasting glucose values and patients should be instructed to test sugar at least twice a day fast in the morning (target values: 100–120 mg/dl) and during the day (less than 180 mg/dl 2 h after a meal).	3	D
In the first 7–10 days after surgery, use of sulfonylureas and medications that increase the risk of hypoglycaemia should be avoided.	3	D
For patients still requiring insulin during their post-operative hospital staying, basal insulin should be continued at discharge, with strict glucose monitoring and tapering of insulin units for avoidance of hypoglycaemia.	3	D
In cases of complicated glucose control in the early post-operative phase, consultation with an endocrinologist should be considered.	3	D

Obesity Facts

The European Journal of Obesity

Obes Facts 2017;10:597–632

Medical management before and after BS: T2DM

Table 8. A simple scheme for basal insulin prescription at discharge after bariatric surgery

Basal insulin needs before discharge	Dose of basal insulin prescribed at discharge
10 units or less of basal insulin	the same dose should be continued at discharge
10–19 units of basal insulin	10 units should be continued at discharge
20–29 units of basal insulin	15 units should be continued at discharge
30–39 units of basal insulin	20 units should be continued at discharge
40–49 units of basal insulin	30 units should be continued at discharge
50 units or more of basal insulin	40 units should be continued at discharge

Medical management before and after BS: T2DM

Patient Body weight: ____ kg Estimated total daily insulin dose (*): ____ UI/die
Type of pre-prandial bolus insulin: _____ Type of basal insulin : _____

Daily prescription:

Days	1		2		3	
	Bolus Insulin	Basal Insulin	Bolus Insulin	Basal Insulin	Bolus Insulin	Basal Insulin
Breakfast						
Lunch						
Dinner						
Bedtime	NO		NO		NO	

Guidelines for the correction of bolus pre-prandial dose according to the glucose pre-prandial level (**):

Low Dose Algorithm Total insulin dose ≤50 U/die		Medium Dose Algorithm Total insulin dose 50-90 U/die		High Dose Algorithm Total insulin dose >90 U/die	
Pre-prandial glycemia	Insulin unit modification	Pre-prandial glycemia	Insulin unit modification	Pre-prandial glycemia	Insulin unit modification
70-90	-1	70-90	-2	70-90	-2
150-199	1	150-199	1	150-199	2
200-249	2	200-249	3	200-249	4
250-299	3	250-299	5	250-299	7
300-349	4	300-349	7	300-349	10
>349	5	>349	8	>349	12

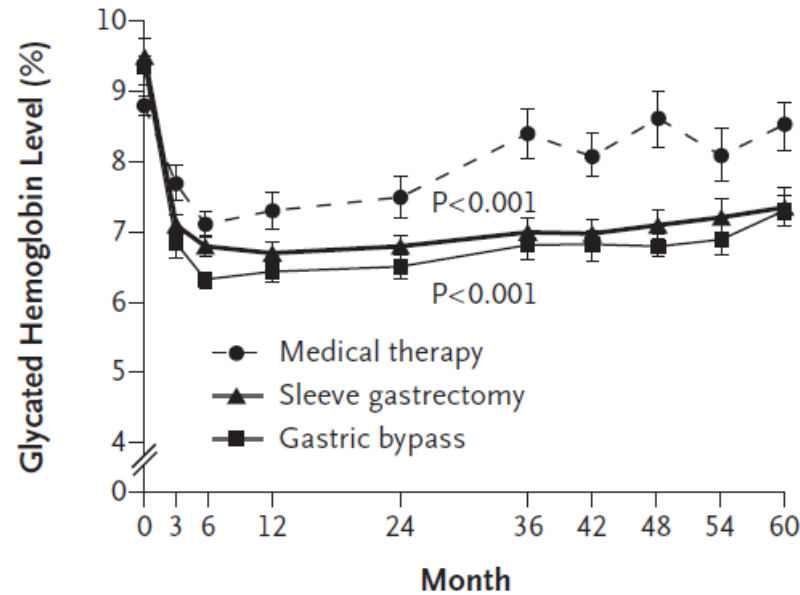
(*): Estimated total daily insulin dose may be calculated as 0,3-0,7 UI/die per Kg of body weight.

(**): Guidelines for the correction of bolus pre-prandial dose according to the glucose pre-prandial level may be used by nurses in the hospital and by patients at home.

**Algorithm for
basal-bolus insulin
after surgery**

Medical management before and after BS: T2DM

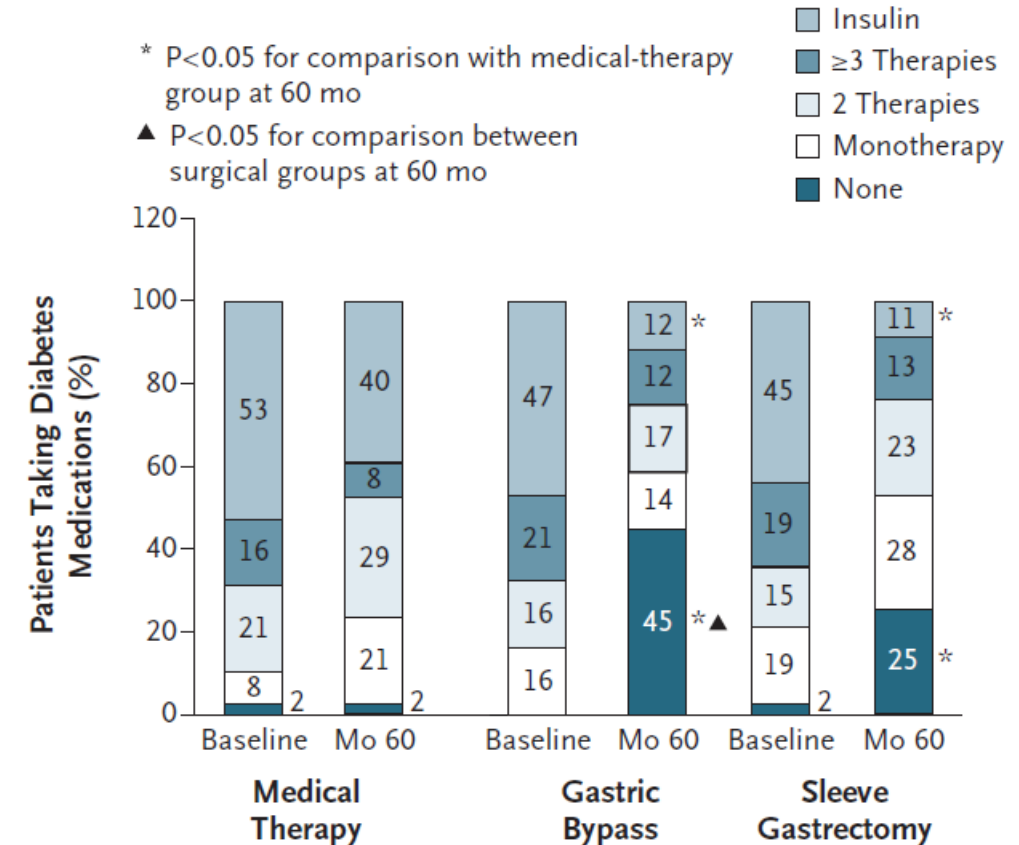
A Glycated Hemoglobin



Mean (median)
Value at Visit

Medical therapy	8.8 (8.6)	7.3 (6.8)	7.5 (7.2)	8.4 (7.7)	8.6 (8.2)	8.5 (8.0)
Gastric bypass	9.3 (9.4)	6.4 (6.2)	6.5 (6.4)	6.8 (6.6)	6.8 (6.8)	7.3 (6.9)
Sleeve gastrectomy	9.5 (8.9)	6.7 (6.4)	6.8 (6.8)	7.0 (6.7)	7.1 (6.6)	7.4 (7.2)

B Diabetes Medications



Bariatric Surgery versus Intensive Medical Therapy for Diabetes — 5-Year Outcomes

Schauer PA. NEJM 2017;376:641

Medical management before and after BS: T2DM

Reviews/Commentaries/ADA Statements
CONSENSUS STATEMENT

How Do We Define Cure of Diabetes?

Definitions

Partial remission

- Hyperglycemia below diagnostic thresholds for diabetes
- At least 1 year's duration
- No active pharmacologic therapy or ongoing procedures

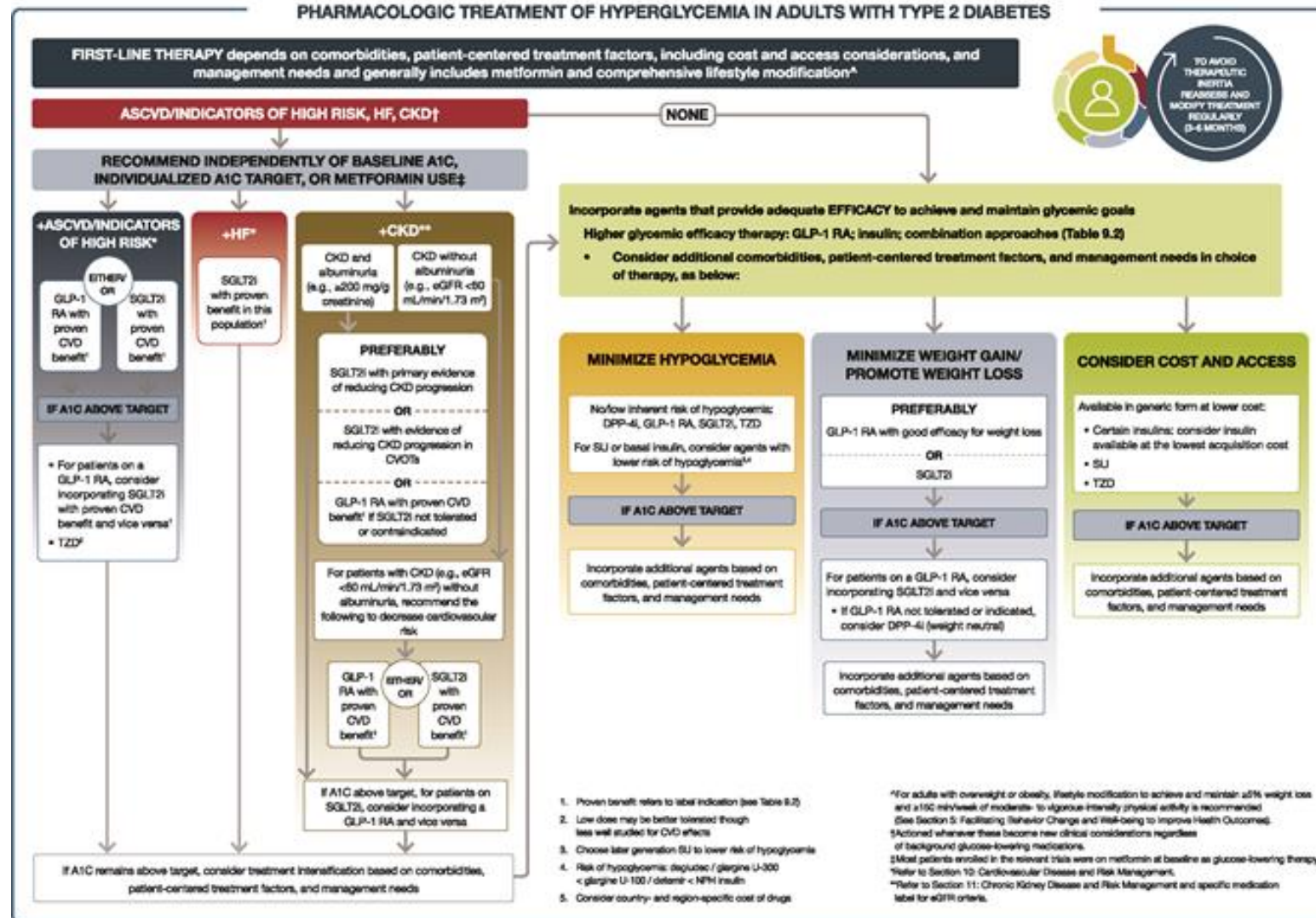
Complete remission

- Normal glycemic measures
- At least 1 year's duration
- No active pharmacologic therapy or ongoing procedures

Prolonged remission

- Complete remission of at least 5 years' duration

Medical management before and after BS: T2DM



Clin Diabetes. 2022;40:10-38.

Medical management before and after BS: T2DM

Reviews/Commentaries/ADA Statements

CONSENSUS STATEMENT

How Do We Define Cure of Diabetes?

Recommendations

Treatment goals for comorbid conditions

Same as those for patients with diabetes for patients with partial or complete remission of less than 5 years' duration

With prolonged remission, could consider goals appropriate for patients without diabetes, as long as there is no recurrence of diabetes and no cardiovascular disease

Screening for microvascular complications

Same protocols as those for patients with diabetes for patients with partial or complete remission of less than 5 years' duration

With prolonged remission, could consider screening at reduced frequency depending on the status of each complication

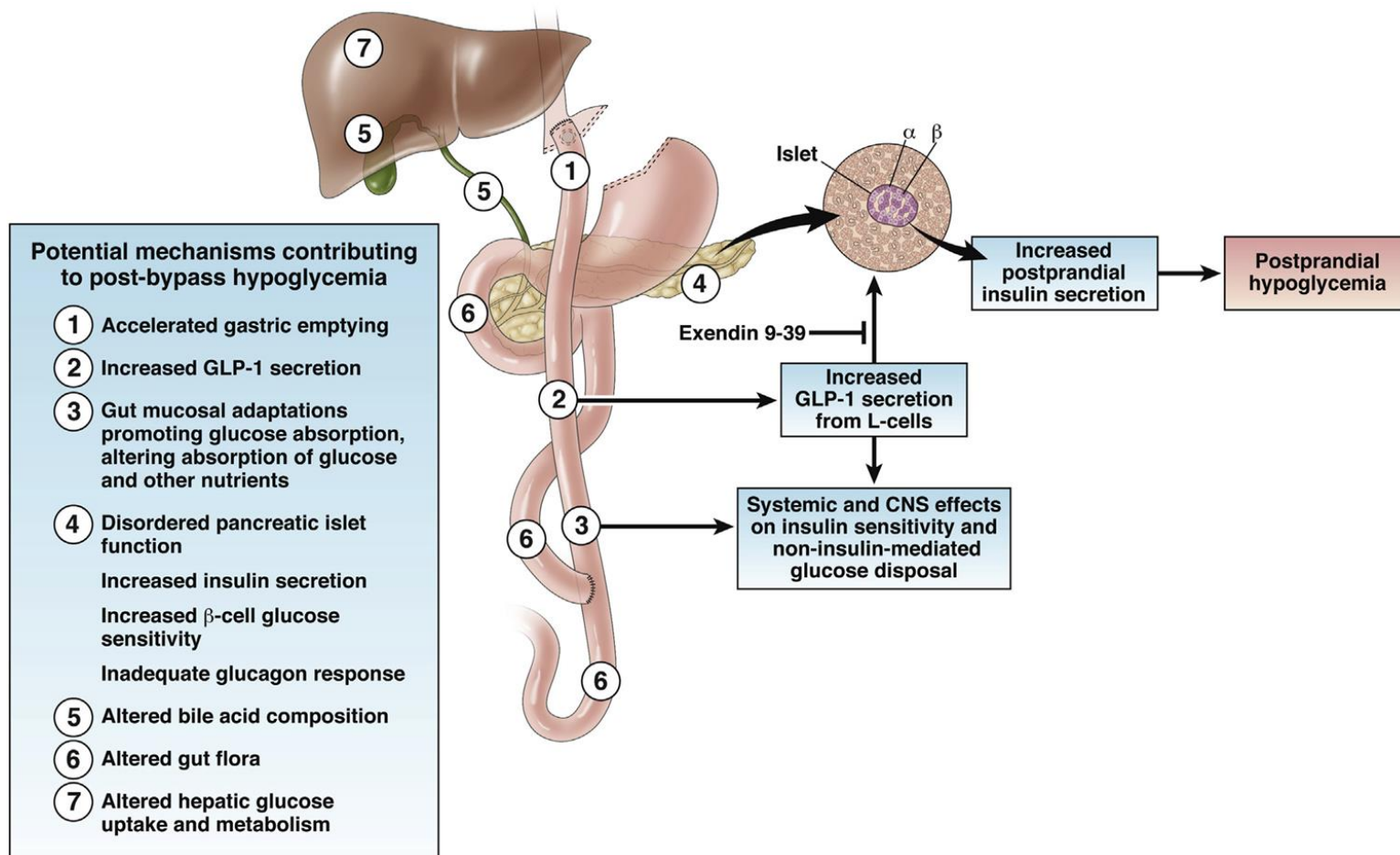
With prolonged remission, only consider stopping screening for a particular complication completely if there is no history of that complication

Medical management before and after BS: T2DM

Table 7. List of graded clinical practical recommendations for the management of major obesity-related comorbidities after bariatric surgery

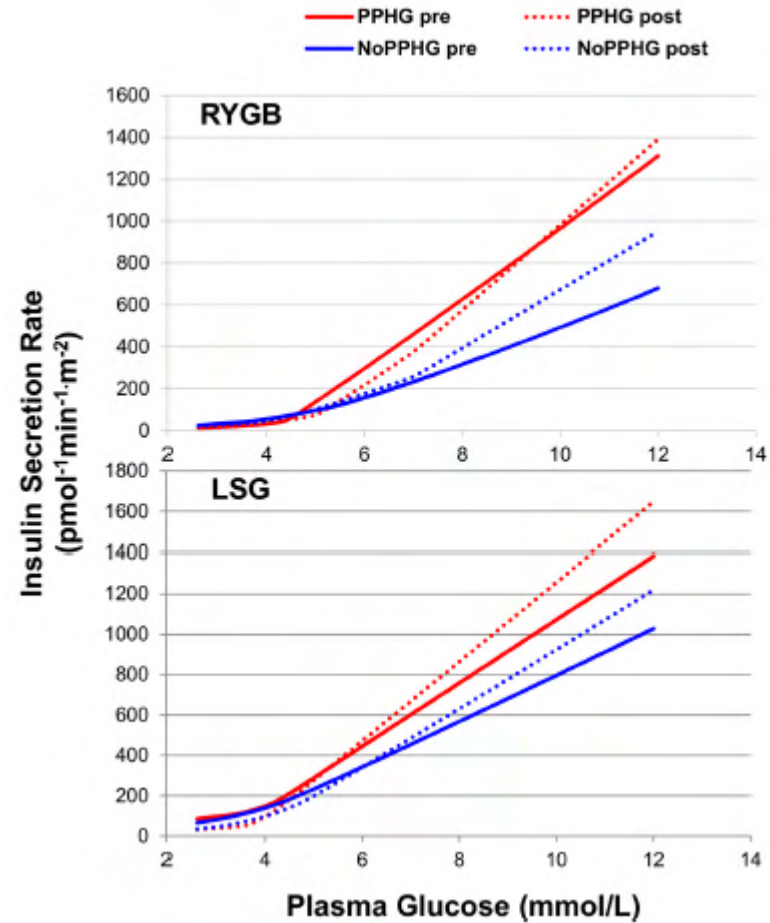
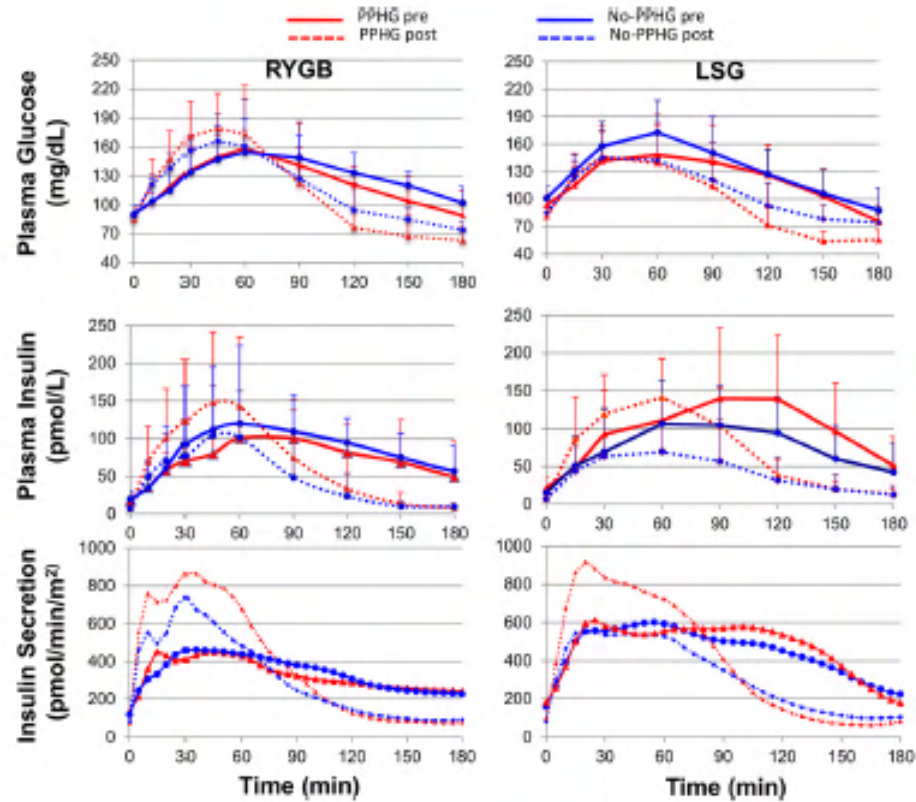
Recommendations	Level of evidence	Grade of recommendation*
After the first early post-operative period, standard diabetes guidelines should be followed for the management of patients still requiring pharmacologic anti-diabetic treatment after bariatric surgery.	4	D

Post-bariatric hypoglycaemia



Post-bariatric hypoglycaemia

Risk factors for spontaneously self-reported postprandial hypoglycemia after bariatric surgery

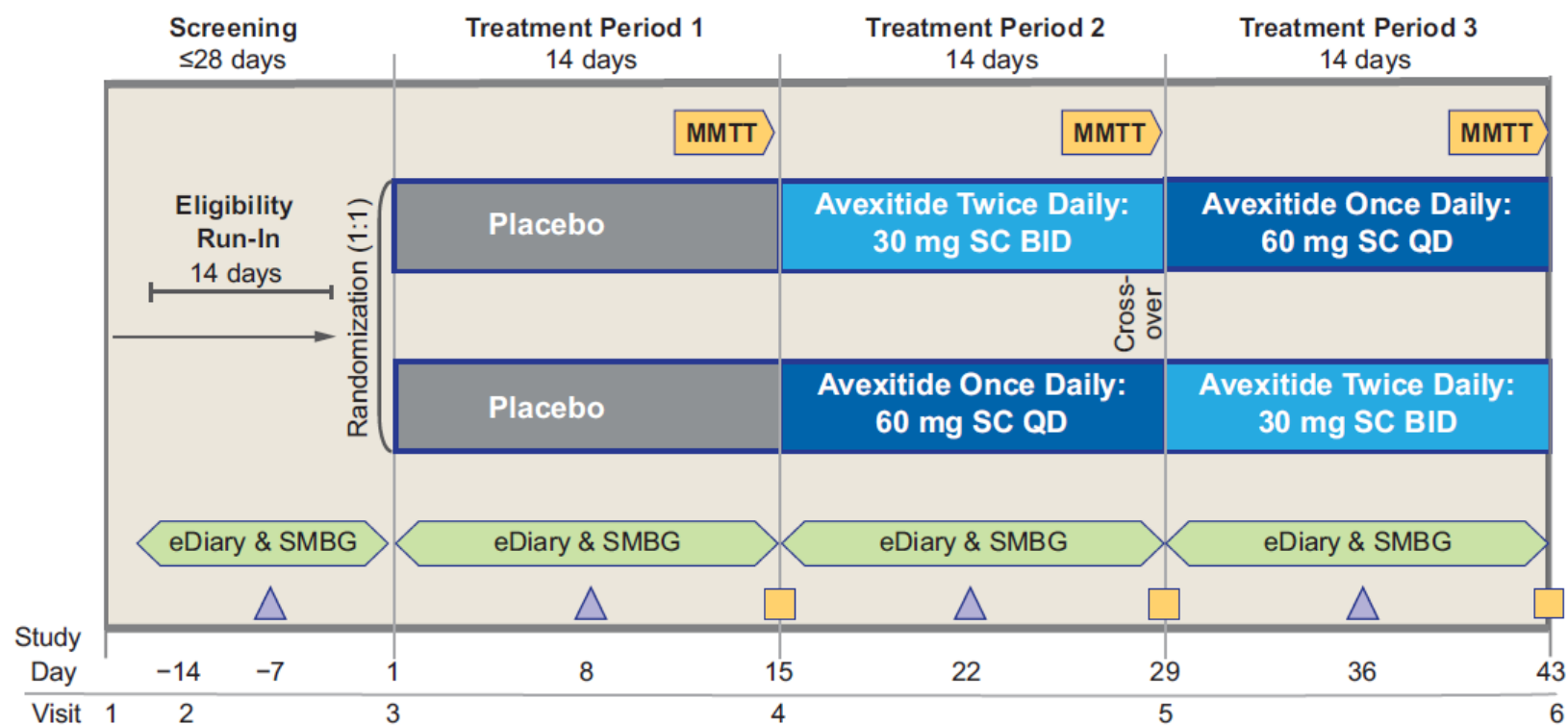


Post-bariatric hypoglycaemia

Nutritional advice:

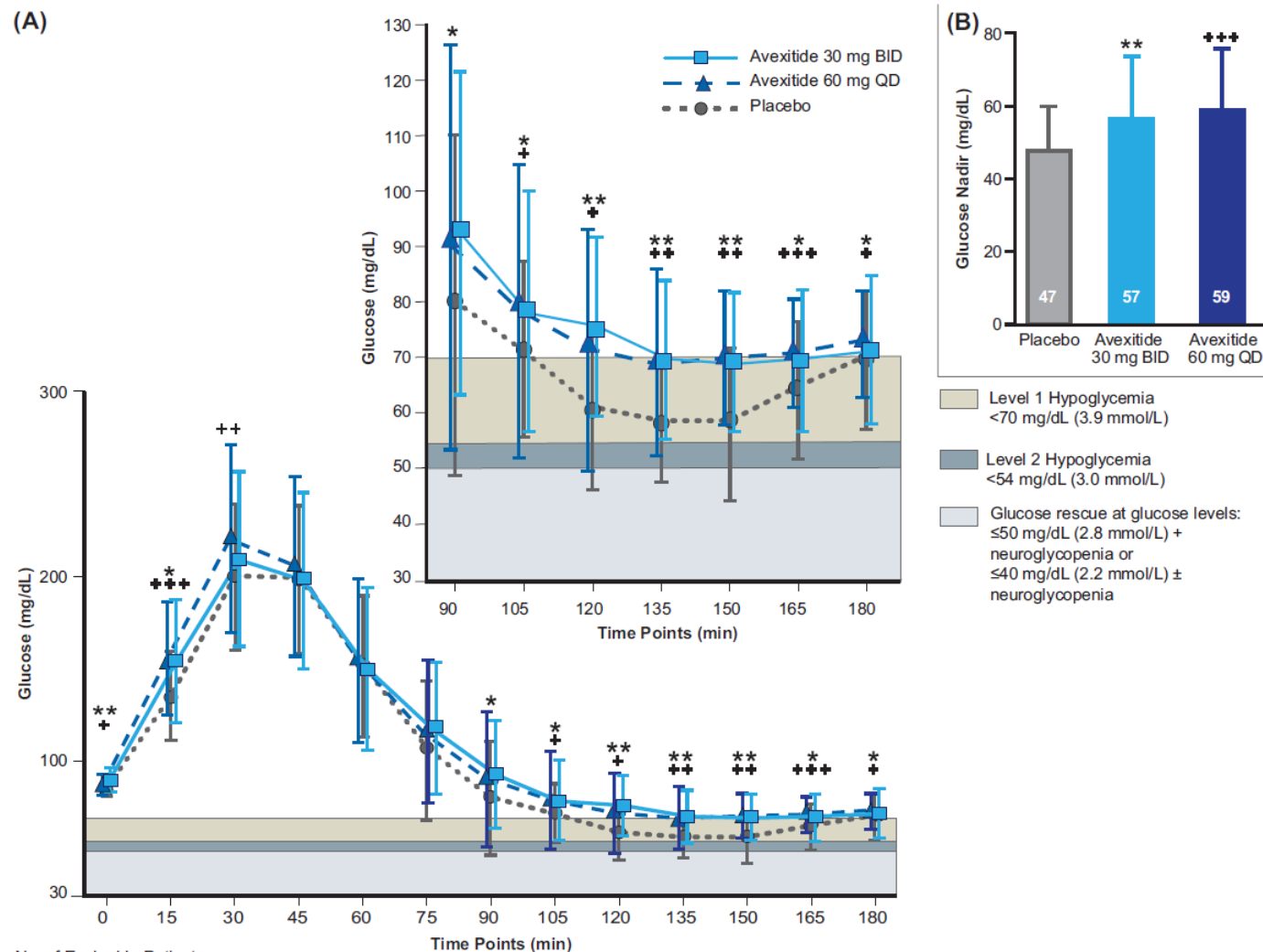
- **Eat smaller meals with snacks between meals and at bedtime.** Eat five to six small meals or snacks a day
- **Avoid foods high in simple carbohydrates, maintain intake of complex carbohydrates** (starches).
- **Have protein foods and healthy fats** (olive oil, nuts and seeds) **at each meal and snack.**
- **Increase intake of fiber.**
- **Avoid foods and beverages containing caffeine** often produces the same symptoms as hypoglycemia and may make you feel worse.
- **Avoid alcoholic beverages.** Alcohol lowers blood sugar levels, especially on an empty stomach.

PREVENT: A Randomized, Placebo-controlled Crossover Trial of Avexitide for Treatment of Postbariatric Hypoglycemia



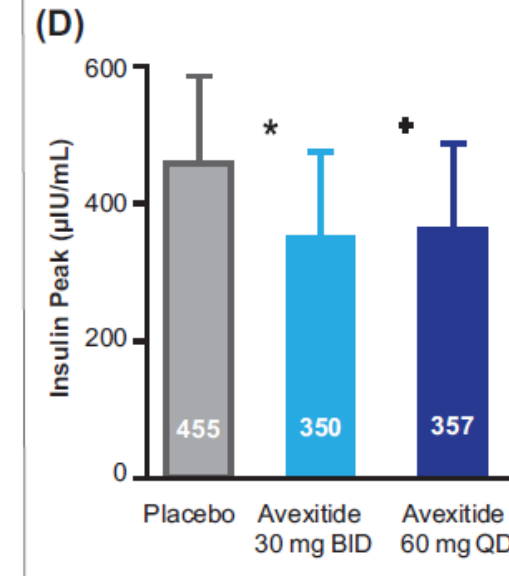
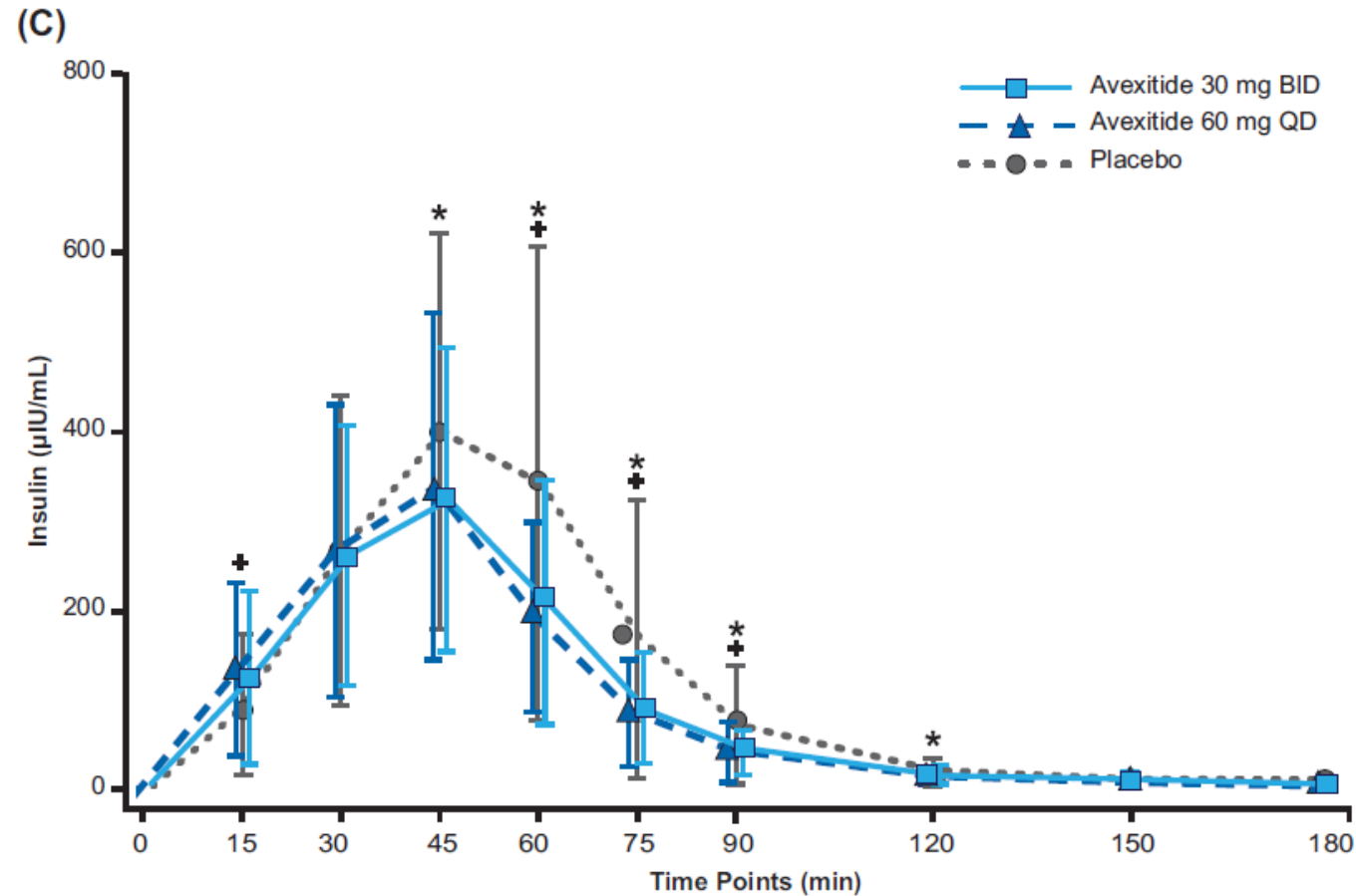
EXENDIN 9-39
GLP1R blocker

Post-bariatric hypoglycaemia



Craig CM et al. JCEM 2021;106:e3235

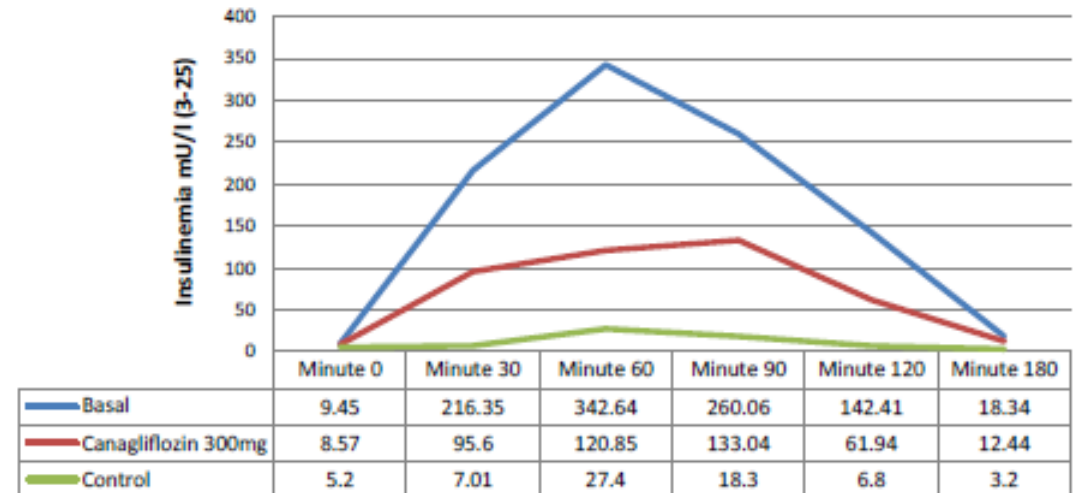
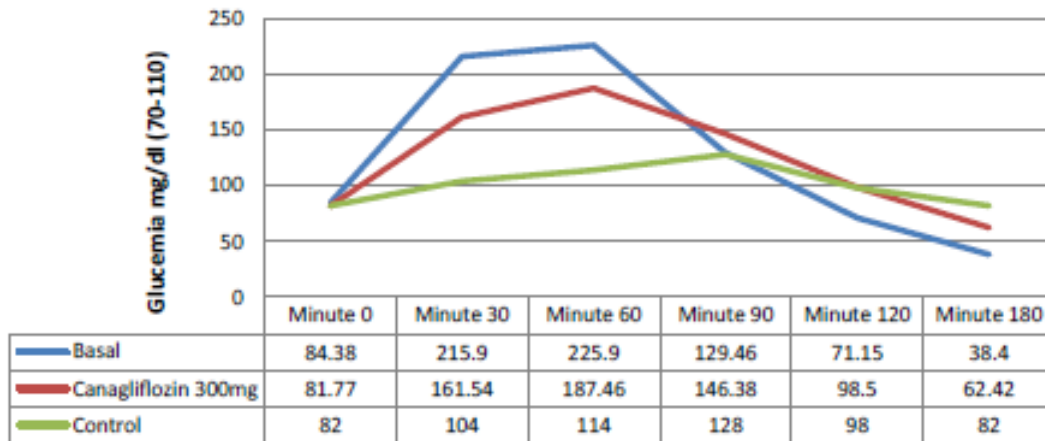
Post-bariatric hypoglycaemia



Craig CM et al. JCEM 2021;106:e3235

Post-bariatric hypoglycaemia

**Canagliflozin: A New Therapeutic Option
in Patients That Present Postprandial
Hyperinsulinemic Hypoglycemia after Roux-en-Y
Gastric Bypass: A Pilot Study**



Ciudin A et al. Obes Facts 2021;14:291

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Pre-operative weight loss

Systematic Review and Meta-Analysis of the Effectiveness of Insurance Requirements for Supervised Weight Loss Prior to Bariatric Surgery

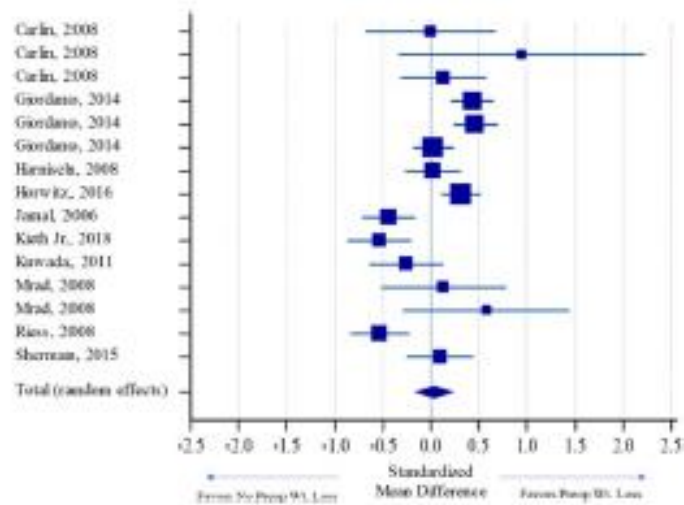


Fig. 2 Forest plot and meta-analysis of prospective and retrospective cohort studies included evaluating mean percent excess weight loss (%EWL) at 12 months for cohorts undergoing preoperative weight loss versus no preoperative weight loss

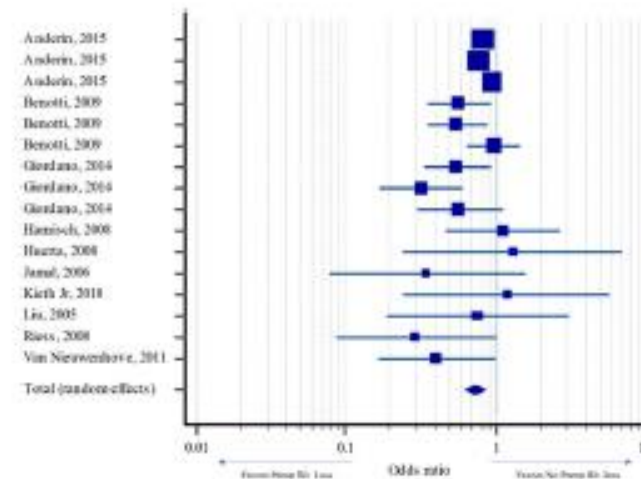
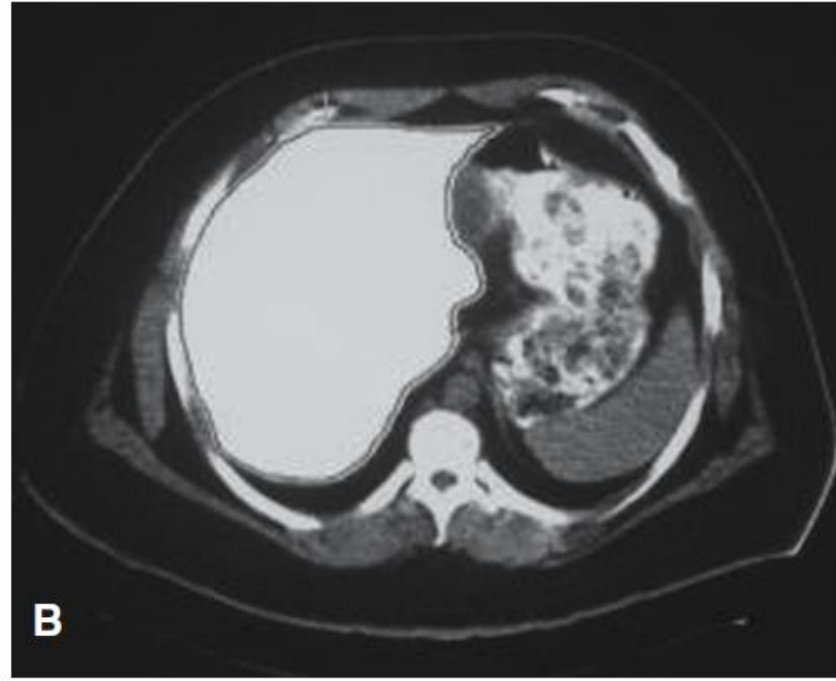
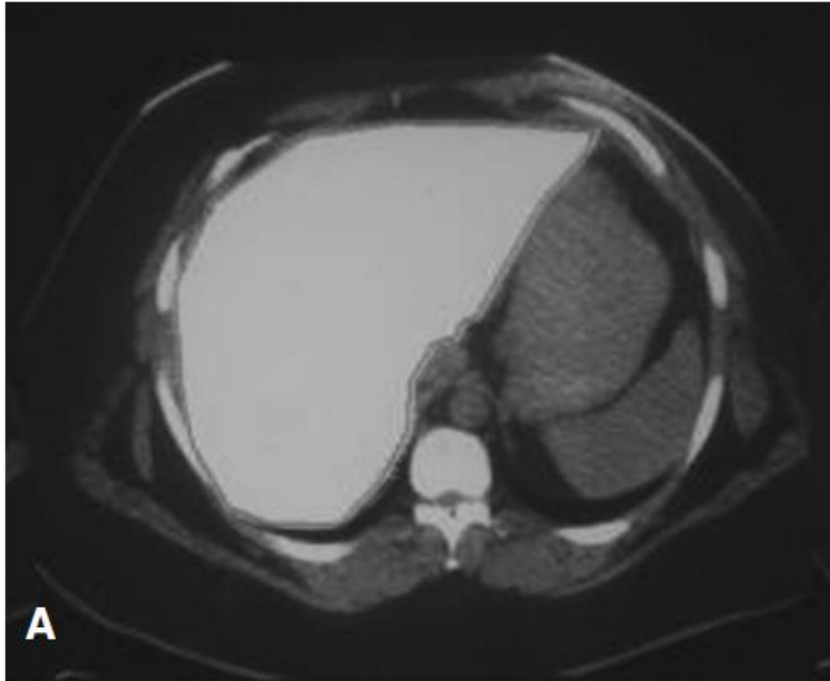


Fig. 3 Forest plot and meta-analysis of studies evaluating perioperative complications (perioperative to 90 days) for cohorts undergoing preoperative weight loss versus no preoperative weight loss

Pre-operative weight loss

Intragastric Balloon Reduces Liver Volume in Super-Obese Patients, Facilitating Subsequent Laparoscopic Gastric Bypass



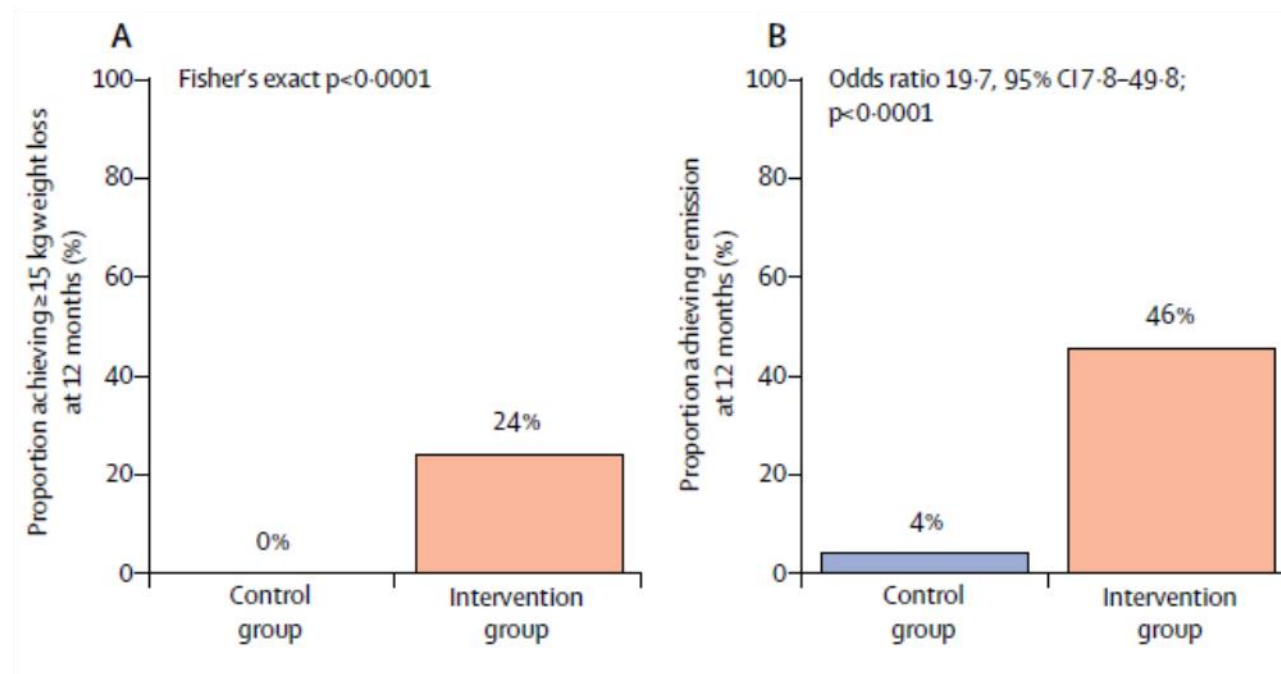
Frutos MD et al. Obes Surg. 2007;17:150

Pre-operative weight loss

Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial

Control group (N. 149 with T2DM): Best practice care by guidelines in 49 primary care practices in Scotland.

Intervention group (N. 149 with T2DM): Weight management programme in 49 primary care practices in Scotland.



Pre-operative weight loss

European Guidelines for Obesity Management in Adults with a Very Low-Calorie Ketogenic Diet: A Systematic Review and Meta-Analysis

Muscogiuri G et al. Obes Facts 2021;14:222

Conclusions and Recommendations

After a careful systematic review and meta-analysis of the current evidence, and considering the potential side effects, VLCKD can be recommended as an effective dietary treatment for individuals with obesity, in particular for patients with severe obesity and/or comorbidities (joint diseases, preoperative period of bariatric surgery, and cardiovascular and metabolic diseases) who need immediate and substantial weight loss. Therefore, VLCKD can be prescribed targeting a specific population of patients with obesity after consideration of the potential contraindications and under medical surveillance. However, it is important to personalize the diet, based on the patient's preferences, allowing food choices within the VLCKD protocol. After achievement of the weight target with VLCKD, implementation of long-term lifestyle strategies (physical activity and nutritional counselling) is strongly recommended to reduce the risk of weight regain in the long term.

Pre-operative weight loss

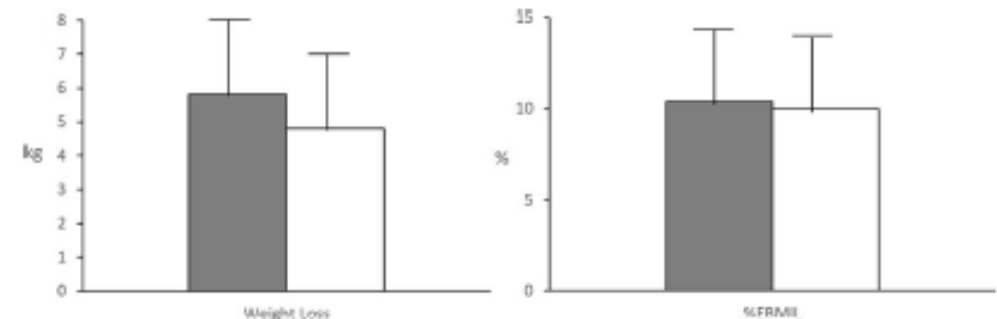
Pre-operative Very Low Calorie Ketogenic Diet (VLCKD) vs. Very Low Calorie Diet (VLCD): Surgical Impact

Table 1 Baseline characteristics in the two groups

	VLCKD	VLCD
Male (n)	12	27
Female (n)	60	79
Body weight (kg)	125.5 ± 19.5	120.9 ± 22.6
BMI (kg/m ²)	46.0 ± 6.3	43.6 ± 6.9
Mean age (years)	43.4 ± 12.1	43.5 ± 11.8

VLCKD very low calorie ketogenic diet, VLCD very low calorie diet

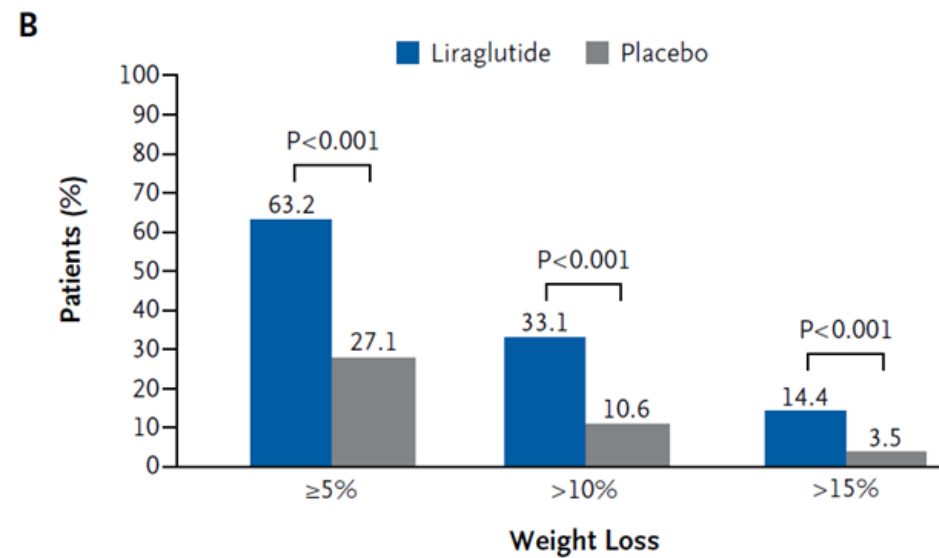
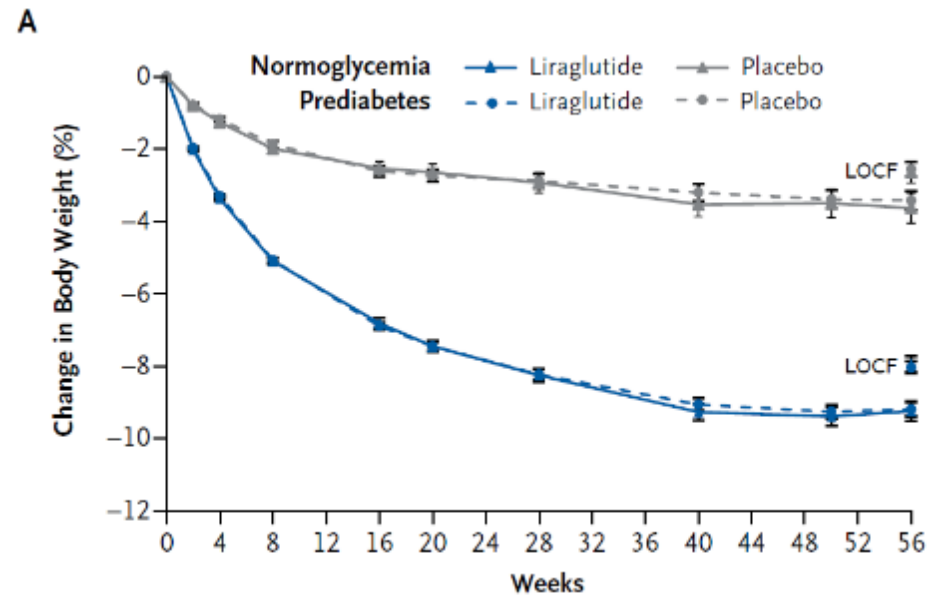
Fig. 1 Absolute weight loss (left panel) and %EBMIL (right panel) in the group of patients receiving a very low calorie ketogenic diet (VLCKD) (gray bars) and in the group of patients receiving a very low calorie diet (VLCD) (white bars)



Mean operative time and hospital stay were slightly but not significantly shorter in the VLCKD group (59.8 ± 18.7 vs. 69 ± 31.7 min, $p = 0.28$; 3.0 ± 0.2 vs. 3.2 ± 2.4 days, $p = 0.31$). The percentage of patients requiring a hospital stay longer than anticipated (> 3 days) was 2.8% in the VLCKD group and 10.4% in the VLCD group ($p = 0.048$ by chi-square test).

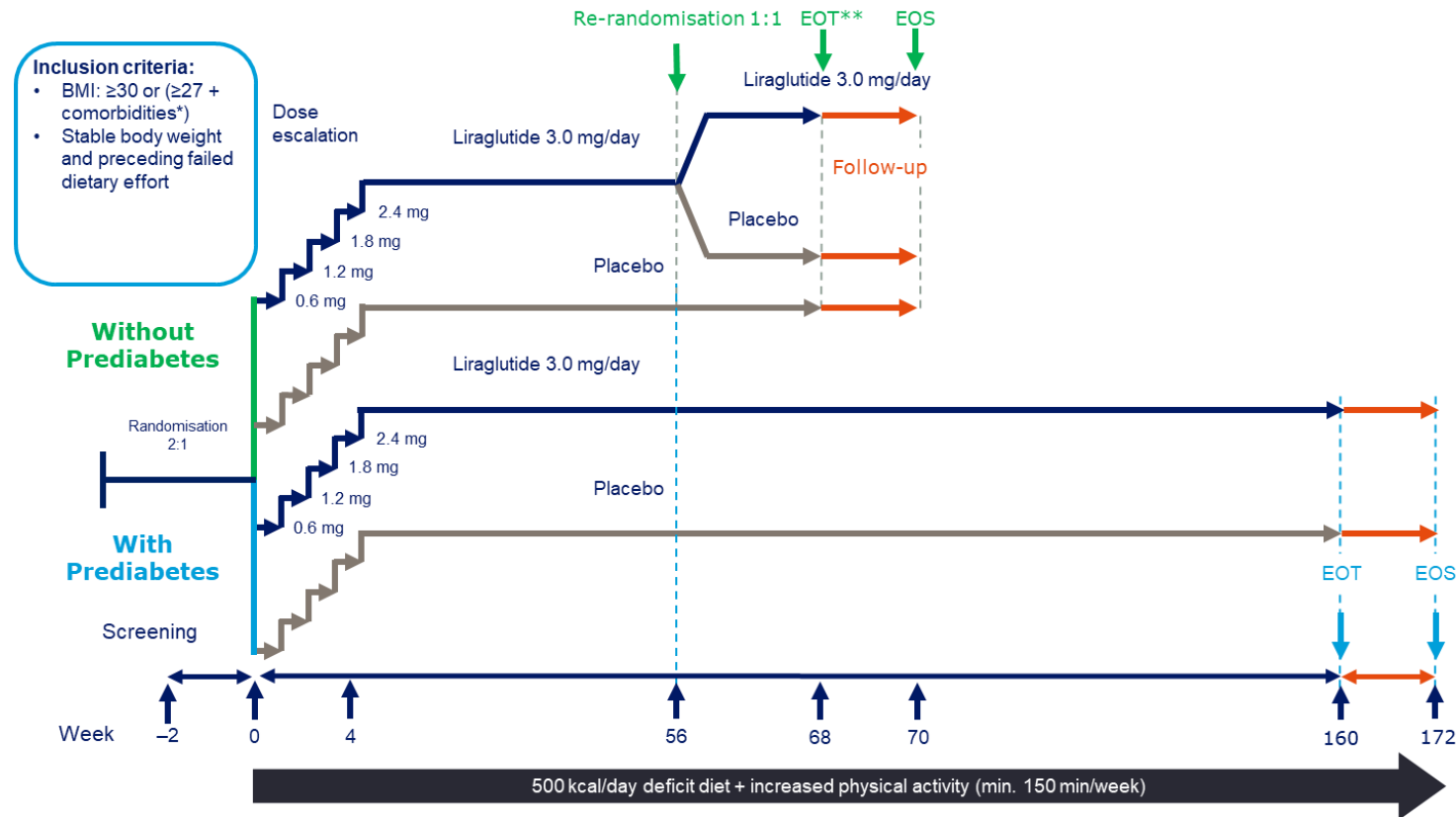
Post-operative hemoglobin levels in g/l were greater in the VLCKD group (13.1 ± 1.2 vs. 12.7 ± 1.49 g/l, $p = 0.04$). Drainage output resulted also less in the VLCKD group (141.2 ± 75.8 vs. 190.7 ± 183.6 ml, $p = 0.032$). No gastric leaks were registered in both groups.

Pre-operative weight loss

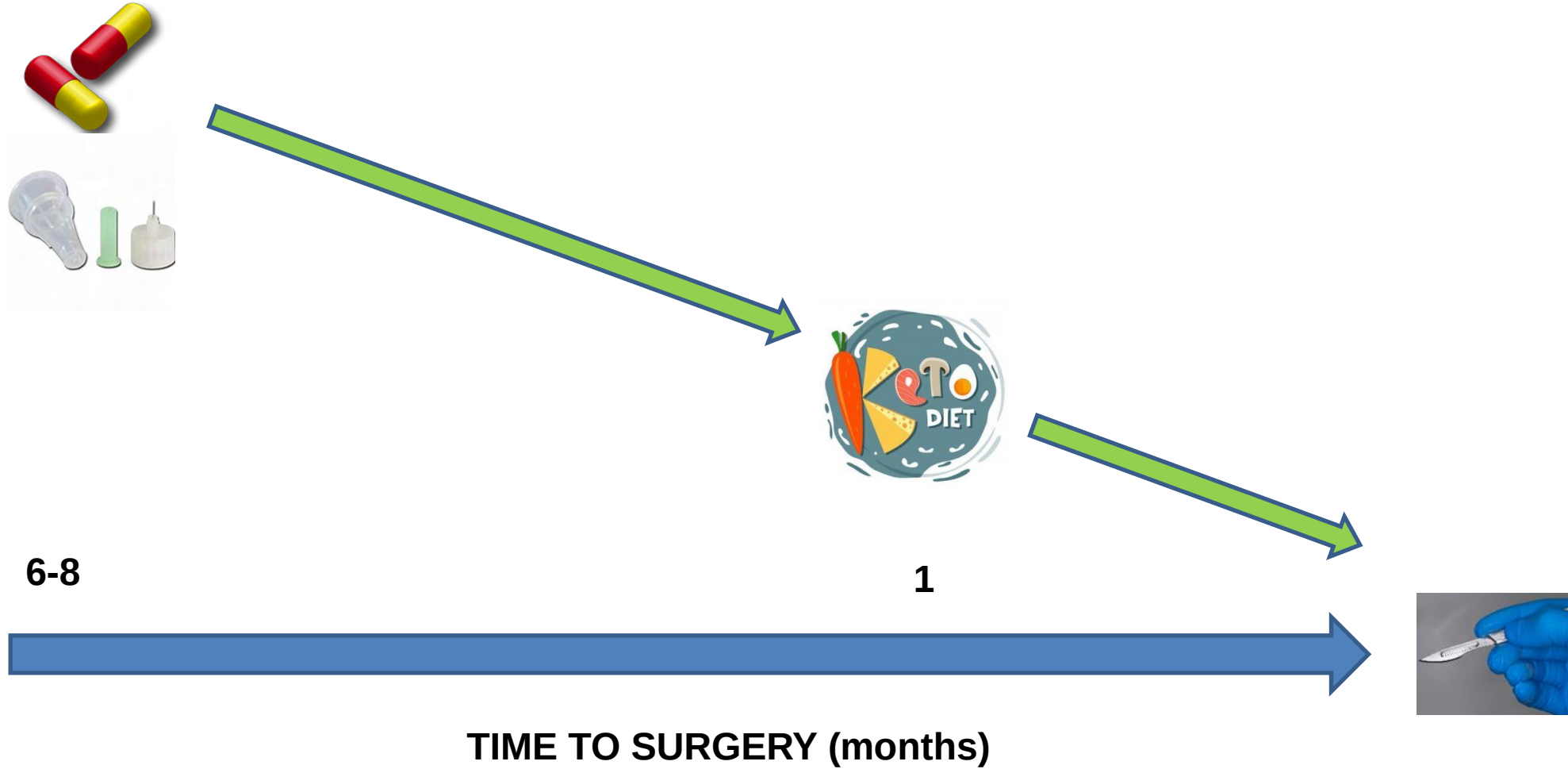


Pre-operative weight loss

A Randomized, Controlled Trial of 3.0 mg of Liraglutide in Weight Management



Pre-operative weight loss



Post-bariatric surgery follow-up



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Post-bariatric surgery follow-up



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Post-bariatric surgery follow-up

Grazie !!!



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