



How do I Manage Obesity in people with Type 1 Diabetes?

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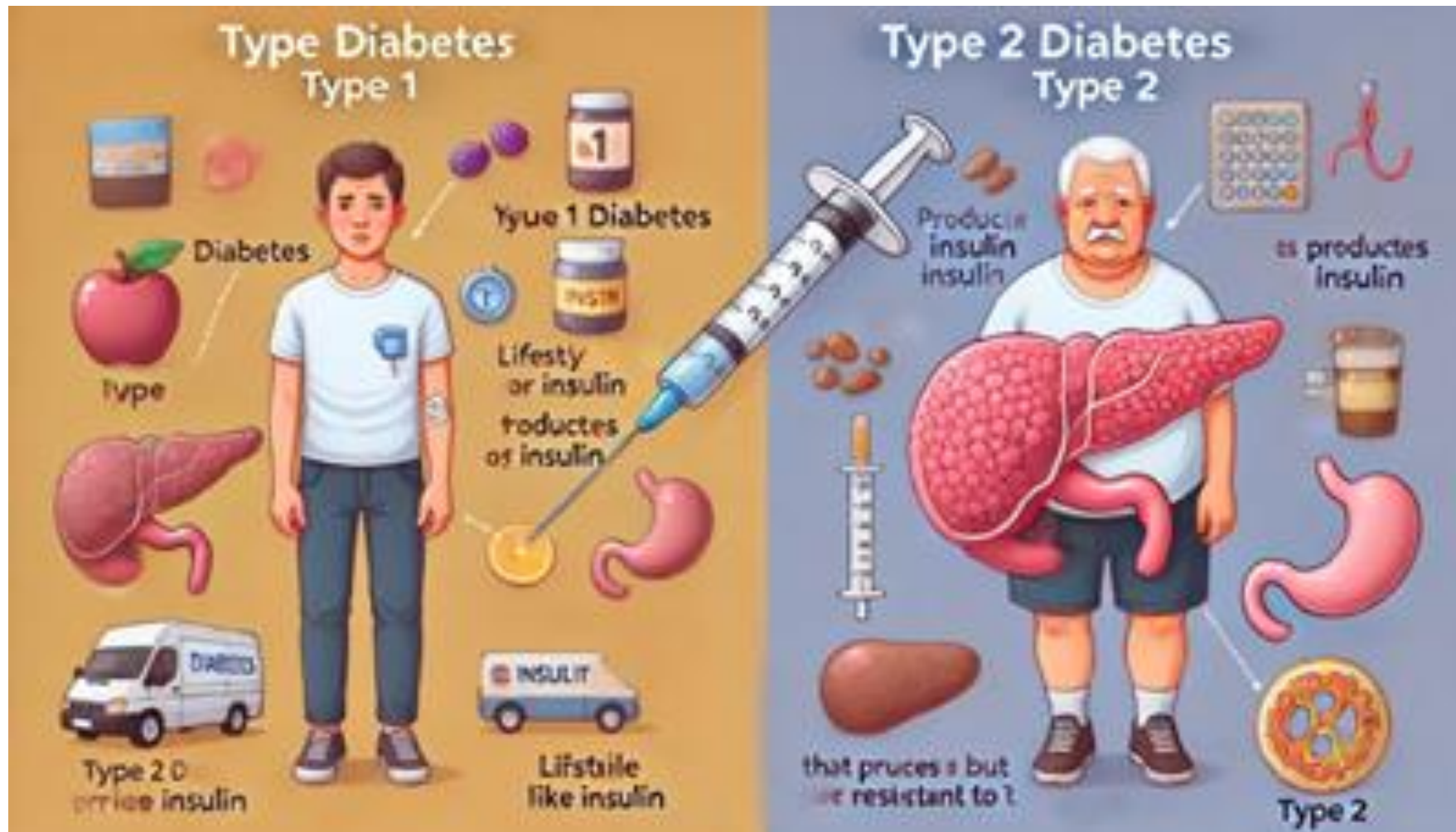
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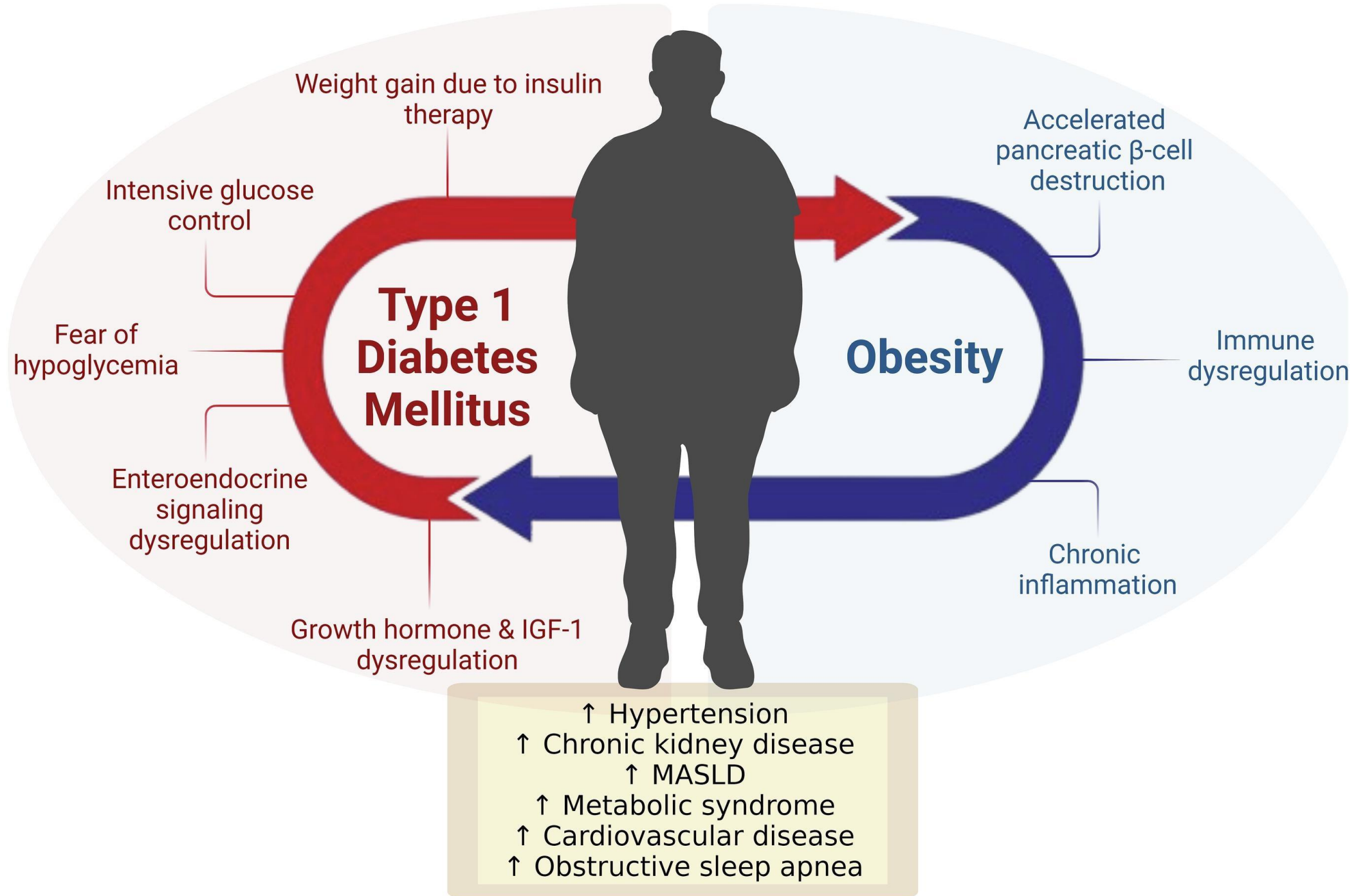


OBESITY IN TYPE 1 DIABETES

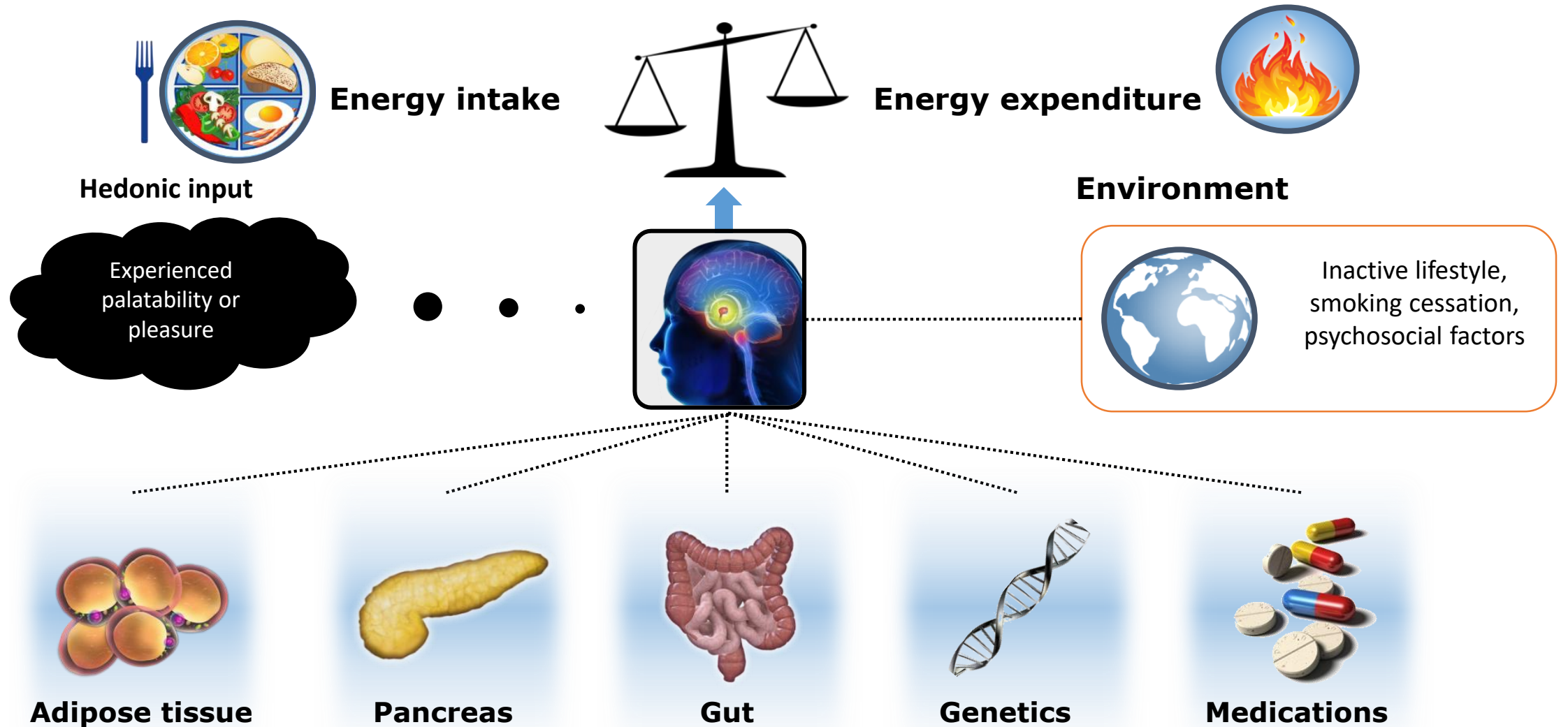


US adults with T1DM, the prevalence of overweight and obesity are estimated at 34 % and 28 %, respectively

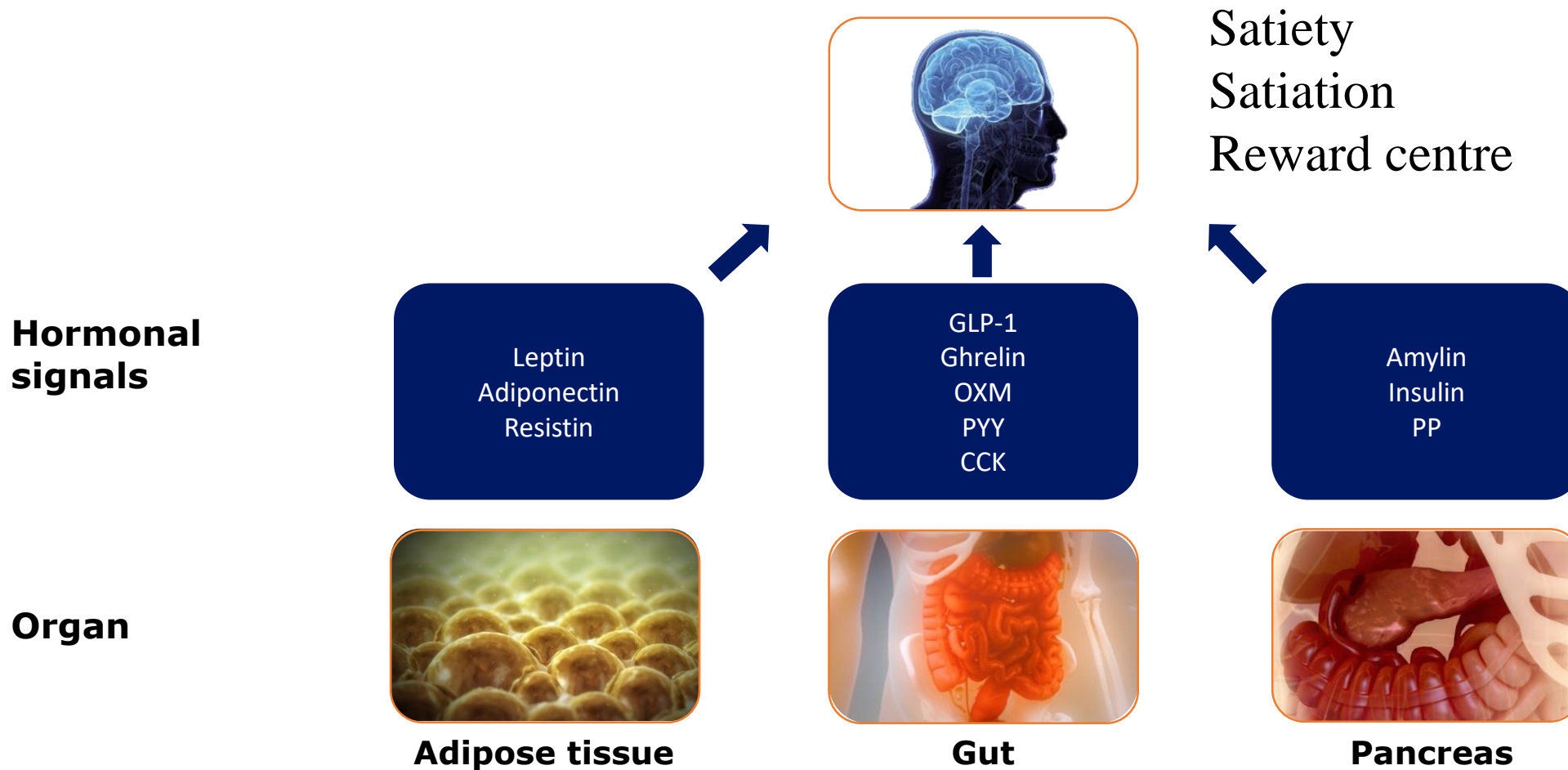
25–40 % of people with T1DM have hypertension, 20–40 % have metabolic syndrome, 6–12 % have metabolic dysfunction-associated liver disease, 16 % have chronic kidney disease, and 10–46 % have obstructive sleep apnea



Obesity is a complex and multifactorial disease



Multiple hormonal signals influence appetite



CCK, cholecystokinin; GLP-1, glucagon-like peptide 1; OXM; oxyntomodulin; PP, pancreatic polypeptide; PYY, peptide YY

Weight loss may improve obesity related comorbidities

Benefits of 5–10% weight loss

Reduction in risk of type 2 diabetes¹



Reduction in CV mortality²



Improvements in blood lipid profile³



Improvements in blood pressure⁴



Improvements in severity of obstructive sleep apnea^{5,6}



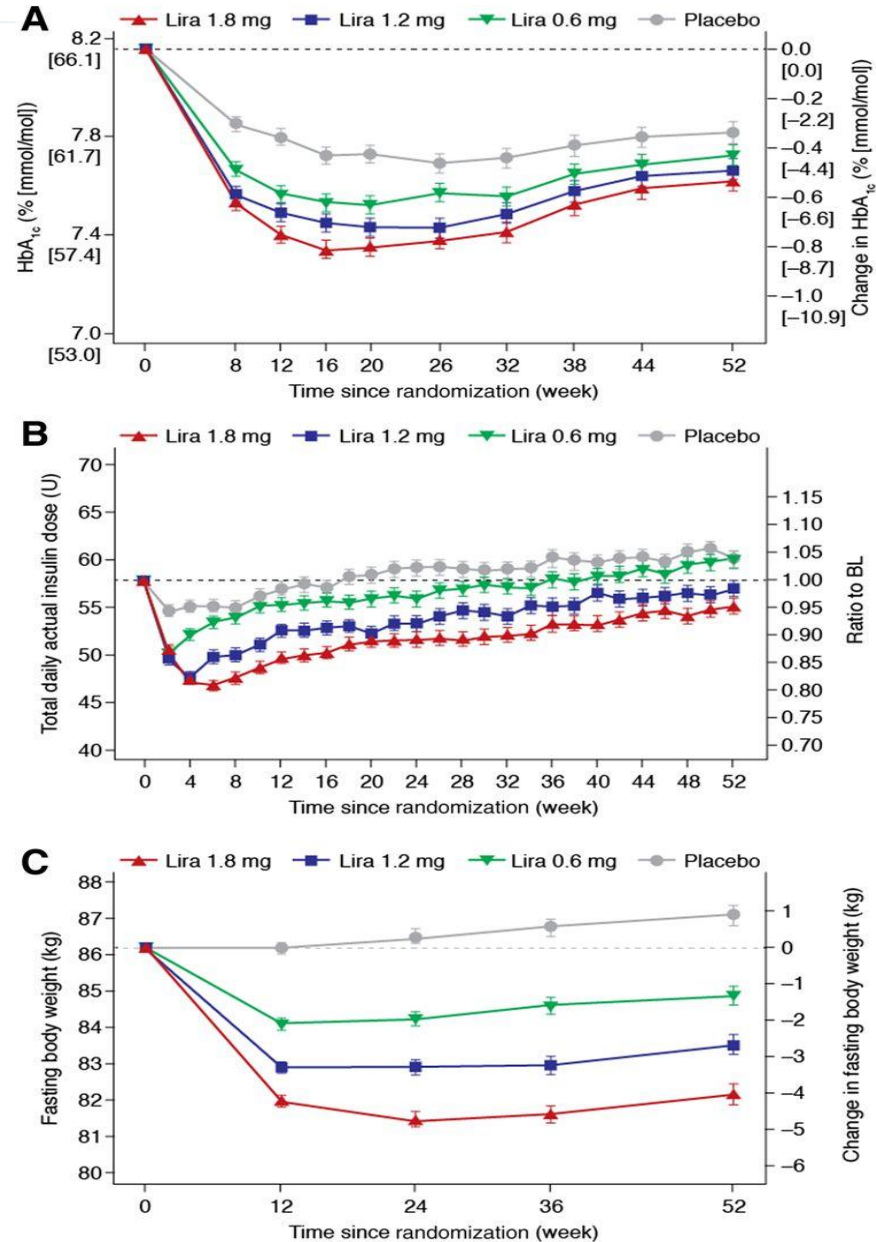
Improvements in health-related quality of life^{7,8}



Weight loss in type 1 diabetes – basic concept

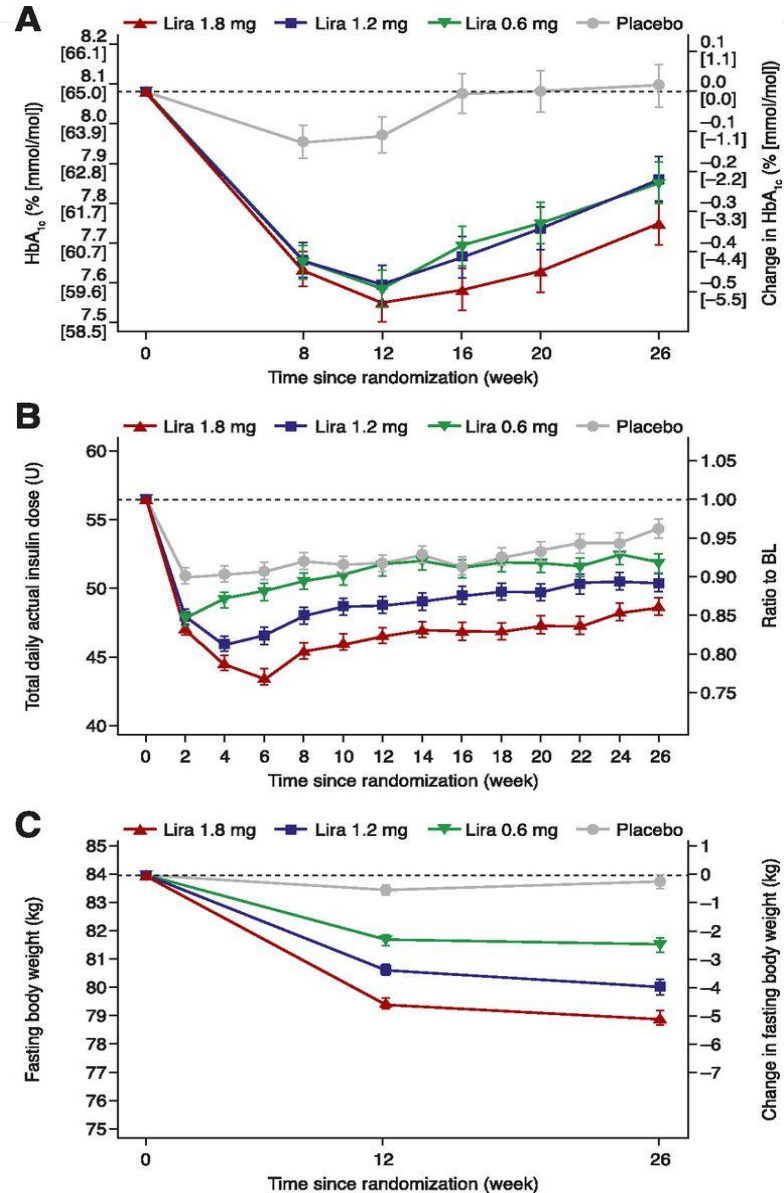
- Provide nutritional education to accurately count carbohydrates and fine-tune their basal and prandial insulin concentrations
- Low carbohydrate (ADA define as 60-130g/day)
- Use of technology (CGM, pump, HCL) – to support dietary and exercise intervention
- Behavioural intervention – identifying fear of hypoglycaemia
- Weight gain analogue insulin < regular insulin
- Avoidance of weight promoting medications

Efficacy and Safety of Liraglutide Added to Insulin Treatment in Type 1 Diabetes: The ADJUNCT ONE Treat-To-Target Randomized Trial



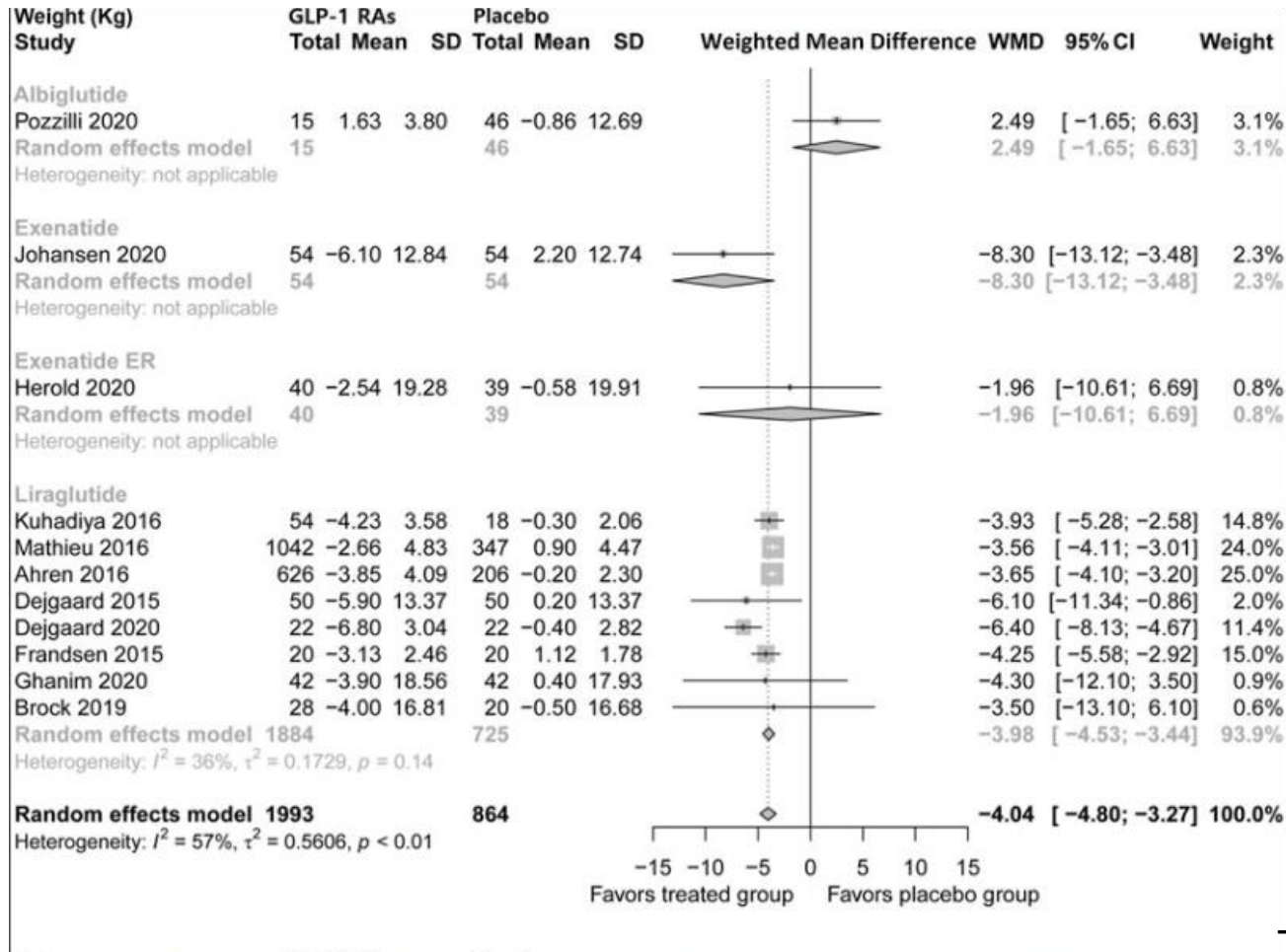
~4.6% weight loss

Efficacy and Safety of Liraglutide Added to Capped Insulin Treatment in Subjects With Type 1 Diabetes: The ADJUNCT TWO Randomized Trial



~6.1% weight loss

Incretin based therapy in Type 1 diabetes - Meta-analysis

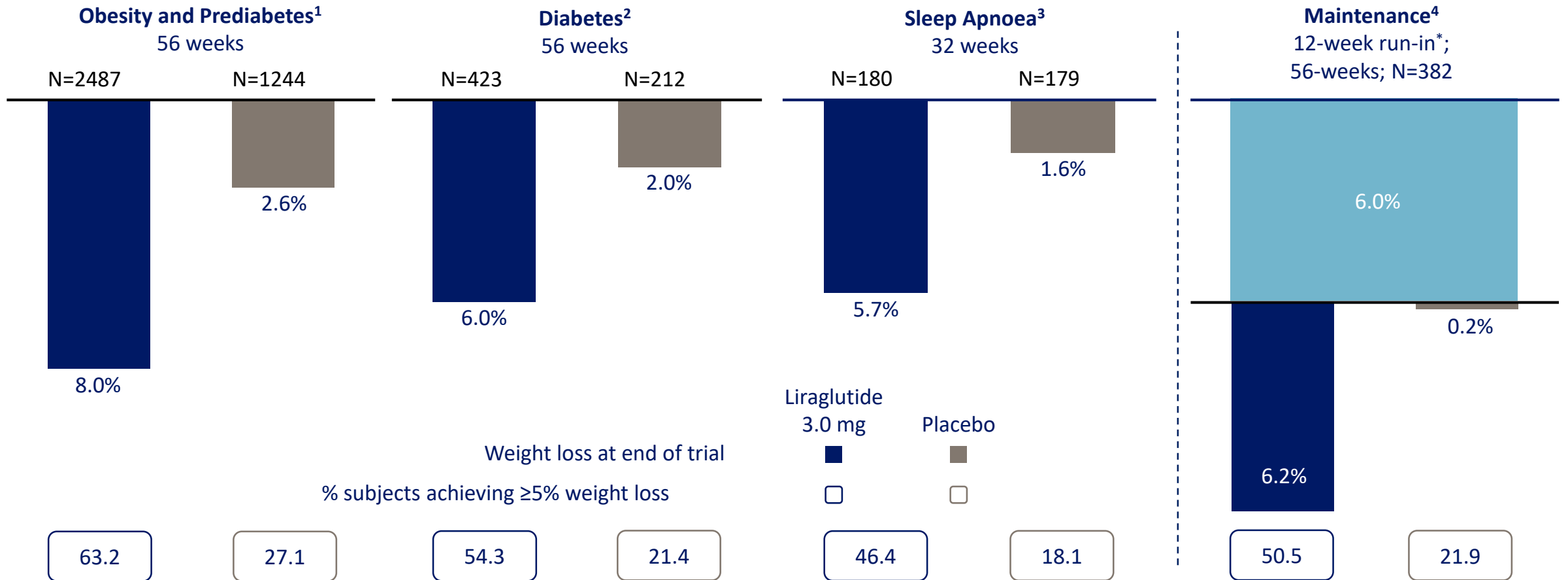


11 trials
N=2859

-4.04kg weight loss
HbA1c reduction by -0.21%
Reduction in prandial and basal insulin

No increased risk of DKA
No increased risk of severe hyperglycaemia
No increased risk of severe adverse events

Weight loss across SCALE trials



Data are observed means/proportions (except SCALE Diabetes estimated LS means/proportions); LOCF at end of trial.

*, low calorie diet (total energy intake 1200–1400 kcal/day); LOCF, last observation carried forward; LS, least-squared; N, number contributing to the analysis

1. Pi-Sunyer *et al.* *N Engl J Med* 2015;373:11–22; 2. Davies *et al.* *JAMA* 2015;314:687–99; 3. Blackman *et al.* *Int J Obes (Lond)* 2016;doi:10.1038/ijo.2016.52;

4. Wadden *et al.* *Int J Obes (Lond)* 2013;37:1443–51

Adjunct 1 and Adjunct 2 learning points

- Hypoglycaemia events occurred in > 90% of cases
- Capping insulin – total daily insulin dose <15% of baseline – driven mainly by reduction in prandial insulin. Some Hba1c relapse but comparable to ADJUNCT1
- No difference in hyperglycaemia rate between Lira and Placebo
- Hyperglycaemia & ketosis occurred in ~11% (dose dependent - higher compared to placebo) mainly in the first 8 weeks of treatment. This increase corresponded to a dose-dependent increase in nausea and an increase in the reduction of insulin dose
- Adjudicated DKA is uncommon (no difference with placebo)
- Almost all ketosis occurred in those with undetectable c peptide
- No increased risk of severe hypos compared to placebo (no compromise of glucagon level in type 1 diabetes)
- Difficulties in bolusing ; especially pre-bolusing.

Practical aspects of GLP-1 in type 1 diabetes

- Consistent 10% reduction in bolus insulin
- To consider injecting insulin after eating
- Close ketones monitoring especially in the first 8 weeks of GLP-1 treatment
- Use C peptide level as a predictor of risks of hypos and hyperglycaemia
- Watch for HbA1c relapse
- Dietetic advice on optimal carbohydrate intake
- Use of technology to optimise insulin dosing and hypoglycaemia prevention

Semaglutide in Type 1 Diabetes

Subcutaneous weekly semaglutide with automated insulin delivery in type 1 diabetes: a double-blind, randomized, crossover trial (N=28)

- Increase in TiR; Hba1c reduction (0.5%); Placebo deducted weight loss (-5.3kg ~7.6%); reduction in daily insulin use (-11.3 units), no DKA, No retinopathy progression

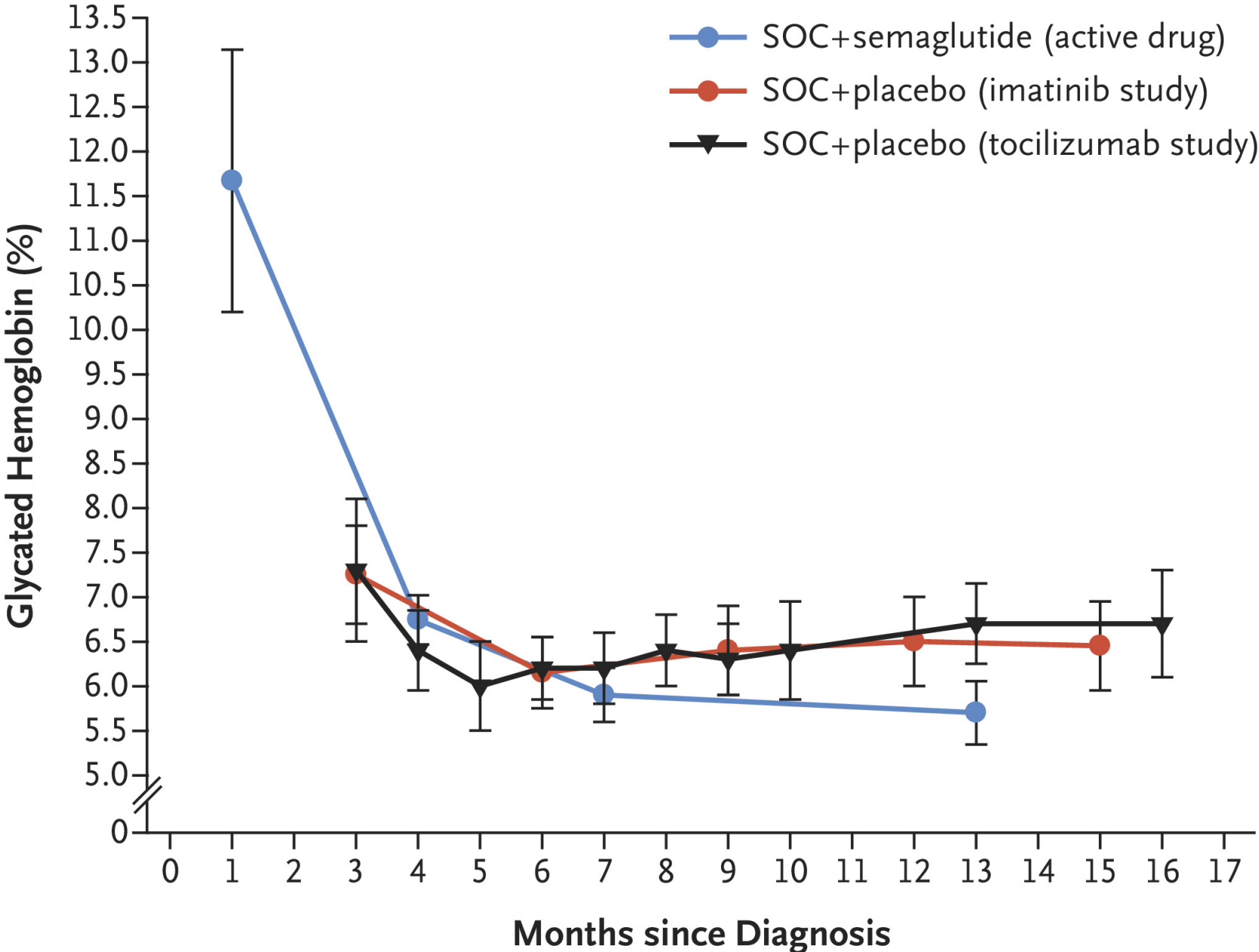
Pasqua et al. Nature Medicine 2025

Effect of low dose Semaglutide in people with Type 1 Diabetes and excess weight (N=11, sensor augmented pump) – 0.5mg weekly

- Weight loss of ~11%; reduction in basal insulin over FU proportion with weight loss, bolus insulin reduce with reduce carb intake.

Grassi et al. Diab Res Cline Prac, 2024

Semaglutide Early in Type 1 diabetes



Glucagon-like Peptide-1 Receptor Agonism

Glucose-dependent Insulinotropic Polypeptide Receptor Agonism

Central Nervous System

- ↑ Satiety
- ↓ Food Intake
- ↑ Nausea
- ↓ Body Weight

Pancreas

- ↑ Insulin
- ↓ Glucagon

Stomach

- ↓ Gastric Emptying

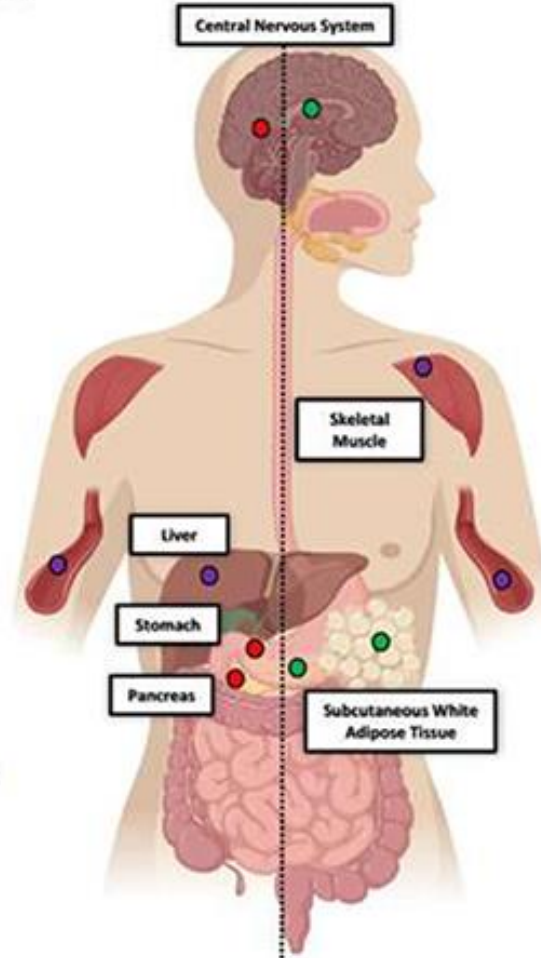
Systemic

- ↓ Hyperglycemia

Liver

- ↑ Insulin Sensitivity
- ↓ Hepatic Glucose Production
- ↓ Ectopic Lipid Accumulation

- Glucose-dependent Insulinotropic Polypeptide Receptor Agonism
- Glucagon-like Peptide 1 Receptor Agonism
- Indirect Action



Central Nervous System

- ↓ Food Intake
- ↓ Nausea
- ↓ Body Weight

Pancreas

- ↑ Insulin
- ↑ Glucagon

Subcutaneous White Adipose Tissue

- ↑ Insulin Sensitivity
- ↑ Lipid Buffering Capacity
- ↑ Blood Flow
- ↑ Storage Capacity
- ↓ Proinflammatory Immune Cell Infiltration

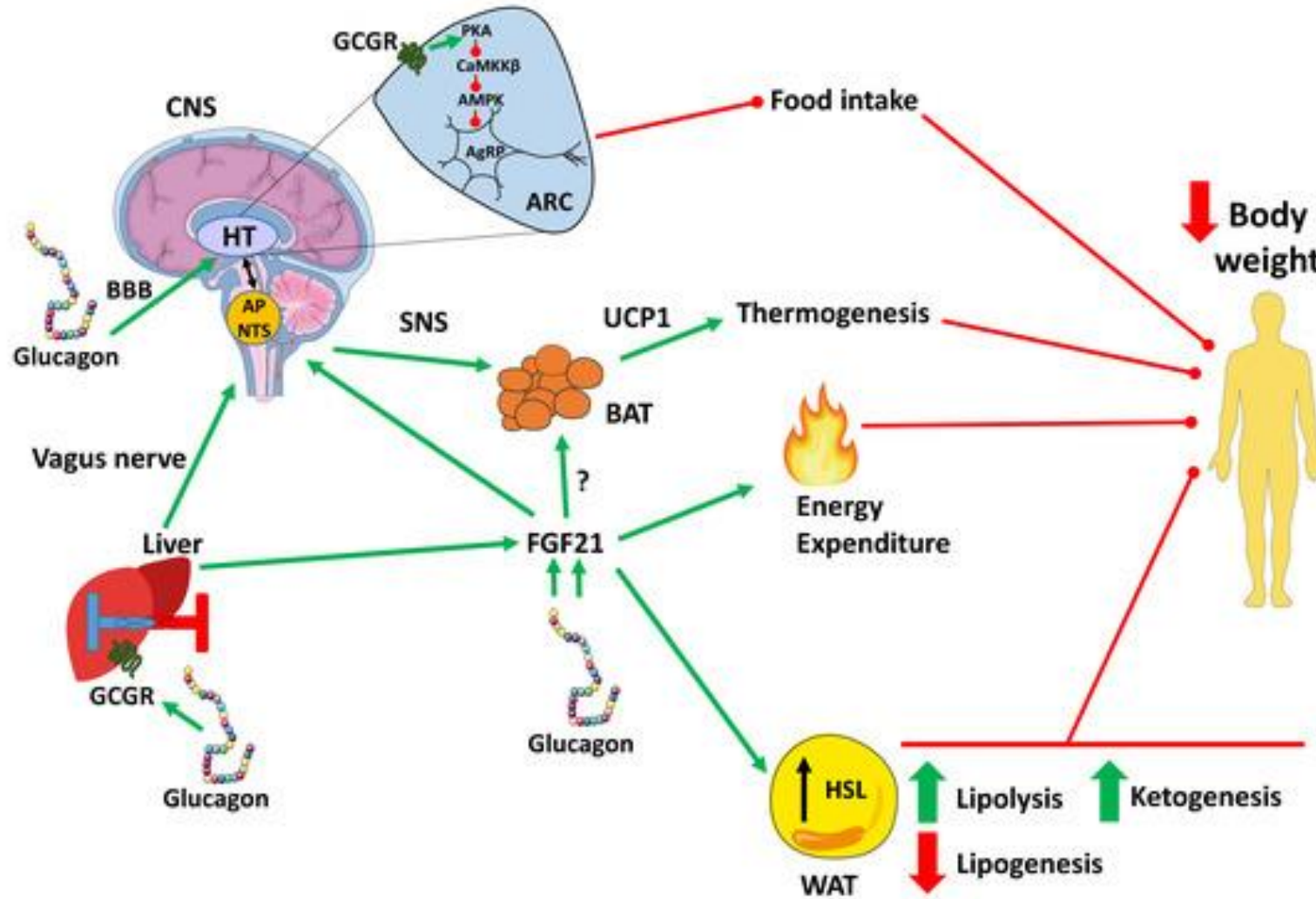
Systemic

- ↓ Hyperglycemia
- ↓ Dietary Triglyceride

Skeletal Muscle

- ↑ Insulin Sensitivity
- ↑ Metabolic Flexibility
- ↓ Ectopic Lipid Accumulation

Effects of Glucagon on Energy intake and energy expenditure



Efficacy and Safety of Tirzepatide for the Treatment of Obesity in Adults with Type 1 Diabetes—The Mayo Clinic Experience

Retrospective study

N=52 patients: BMI 36 kg/m² [32-42].

TBWL at 6, and 12 months was 8% (n=29), and 14% (n=13), respectively (p<0.001 for all).

HbA1c reduce by 1%, TDD by 32% [6-45], and TAR by 28% [8-48], p<0.001 for all.

TIR increased by 29% [3-55], p<0.001.

No episodes of severe hypoglycemia or DKA were recorded. The incidence of side effects was 26%.

Tama et al/ Diabetes 2024;73(Supplement_1):1660-P

Efficacy and Safety of Tirzepatide in Adults With Type 1 Diabetes: A Proof of Concept Observational Study

N=26; mean BMI of 36.7 ± 5.3 kg/m².

Significant reduction in HbA1c by 0.45% at 3 months and 0.59% at 8 months

Significant reduction in body weight by 10.5%, and 10.1% at 6, and 8 months

TIR and TITR increased (+12.6%, P = .002; +10.7%, P = .0016, respectively)

TAR >180 mg/dL decreased (-12.6%, P = .002) at 3 months, and sustained over 8 months.

The drug was relatively safe and well tolerated with only 2 patients discontinuing the medication

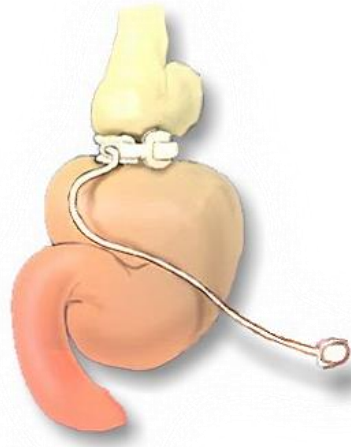
Akturk et al J Diabetes Sci & TEchn 2024

SUMMARY – INCRETIN BASED THERAPY IN Type 1 and Type 2 Diabetes

DRUG	DOSE	POPULATION	% WEIGHT LOSS
Liraglutide (VICTOZA)	1.8mg OD	T2D	~6%
Liraglutide (VICTOZA)	1.8mg OD	T1D	~4.6-6.1%
Liraglutide (SAXENDA)	3.0mg OD	with or without T2D	~8%
Semaglutide (OZEMPIC)	1.0mg OW	T2D	~7%
Semaglutide (Ozempic)	0.5-1.0mg OW	T1D	~7.6% - 11%
Semaglutide (WEGOVY)	2.4mg OW	T2D	~10%
Semaglutide (WEGOVY)	2.4mg OW	with or without T2D	~17%
Tirzepatide (MOUNJARO)	15mg OW	T2D	~13%
Tirzepatide (MOUNJARO)	15mg OW	with or without T2D	~22%
Tirzepatide (Mounjaro)	up to 15mg OW	T1D	~10 – 14%

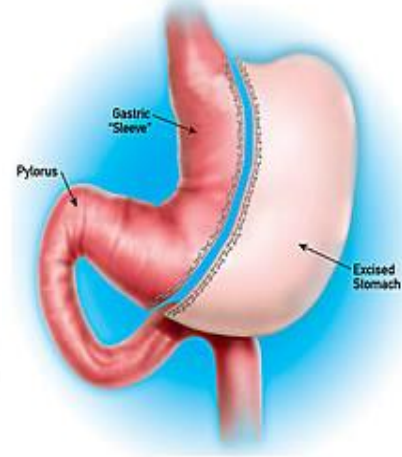
Bariatric Surgery in Type 1 diabetes?

Restriction



Gastric Band

Restriction



**Sleeve
Gastrectomy**

**Restriction &
Malabsorption**



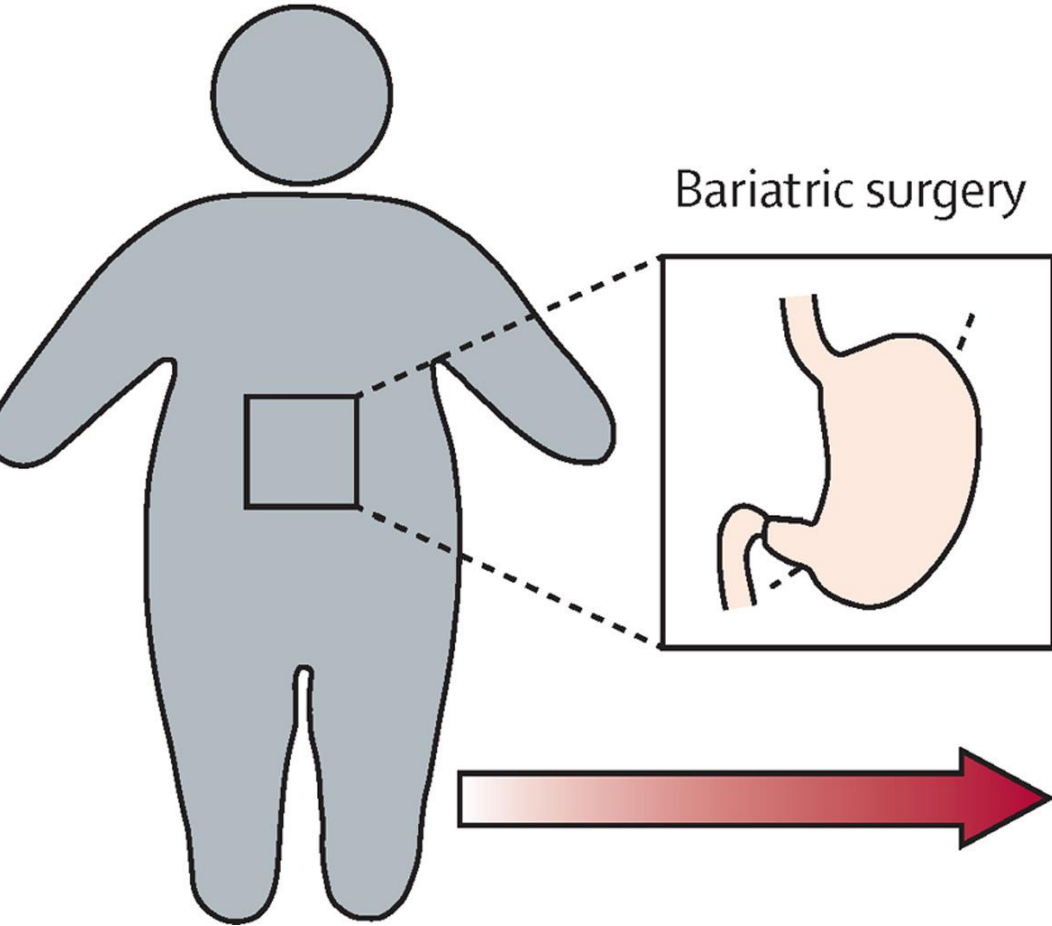
Gastric Bypass

>99% successfully completed laparoscopically

Bariatric surgery in type 1 Diabetes

- Systematic review (30 studies, N-706): weight loss ~25% to 34%
- Insulin dose reduce from 92.3U to 35.8U
- Glycaemic control may not achieve target Hba1c
- RYGB most common, Sleeve gastrectomy is less common option (but gaining popularity due to lower risk of dumping syndrome)
- Several common short-term problems, such as marginal ulcers, incisional hernias, oesophageal dysmotility, prolonged nausea, and nutritional deficits, were experienced by a range of 4.0%–25.0% of patients with T1D who underwent bariatric surgery
- The risks for hypoglycaemia and DKA episodes increasing by up to 28.6% and 25.0% respectively.
- The predisposing factors for DKA include surgical stress, suboptimal care, sudden halt or non-compliance with insulin therapy, infection, and electrolyte imbalance.

Person living with obesity



- Weight loss
- Improved HbA_{1c} (?)
- Reduction of insulin dose requirements
- Decreased risk of cardiovascular disease



- Increased risk of hypoglycaemia
- Increased risk of diabetic ketoacidosis (?)
- Nutrient deficiency
- Complications of surgery

CONCLUSION

