SID Società Italiana di Diabetologia
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AMD ASSOCIAZIONE MEDICI DIABETOLOGI
1974 ANNO DI FONDAZIONE

Diabete tipo 1: Solo insulina?

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Barts and The London
Queen Mary's School of Medicine and Dentistry

Disclosure

Il Prof. Paolo Pozzilli dichiara di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

- Dompè

Dichiara altresì il proprio impegno ad astenersi, nell'ambito dell'evento, dal nominare, in qualsivoglia modo o forma, aziende farmaceutiche e/o denominazione commerciale e di non fare pubblicità di qualsiasi tipo relativamente a specifici prodotti di interesse sanitario (farmaci, strumenti, dispositivi medico-chirurgici, ecc.).

THE LANCET
Diabetes & Endocrinology

Review

Obesity in people living with type 1 diabetes

Bart Van der Schueren, Darcy Ellis, Raquel N Faradji, Eeba Al-Ozairi, Jonathan Rosen, Chantal Mathieu

Lancet Diabetes Endocrinol, 2021

International Journal of Obesity

REVIEW ARTICLE

Clinical Research

The emergence of obesity in type 1 diabetes

Martin T. W. Kueh[1,2], Nicholas W. S. Chew[3], Ebaa Al-Ozairi[4,5] and Carel W. le Roux[6]

International Journal of Obesity (2024)

Taylor & Francis

Expert Review of Endocrinology & Metabolism

Obesity in type 1 diabetes: an overlooked immune-metabolic issue

Ernesto Maddaloni & Dario Tuccinardi

Expert Review of Endocrinology & Metabolism, 2024

Contents lists available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.journals.elsevier.com/diabetes-research-and-clinical-practice

Review

Beyond the insulin pump: unraveling diabetes tech dependency

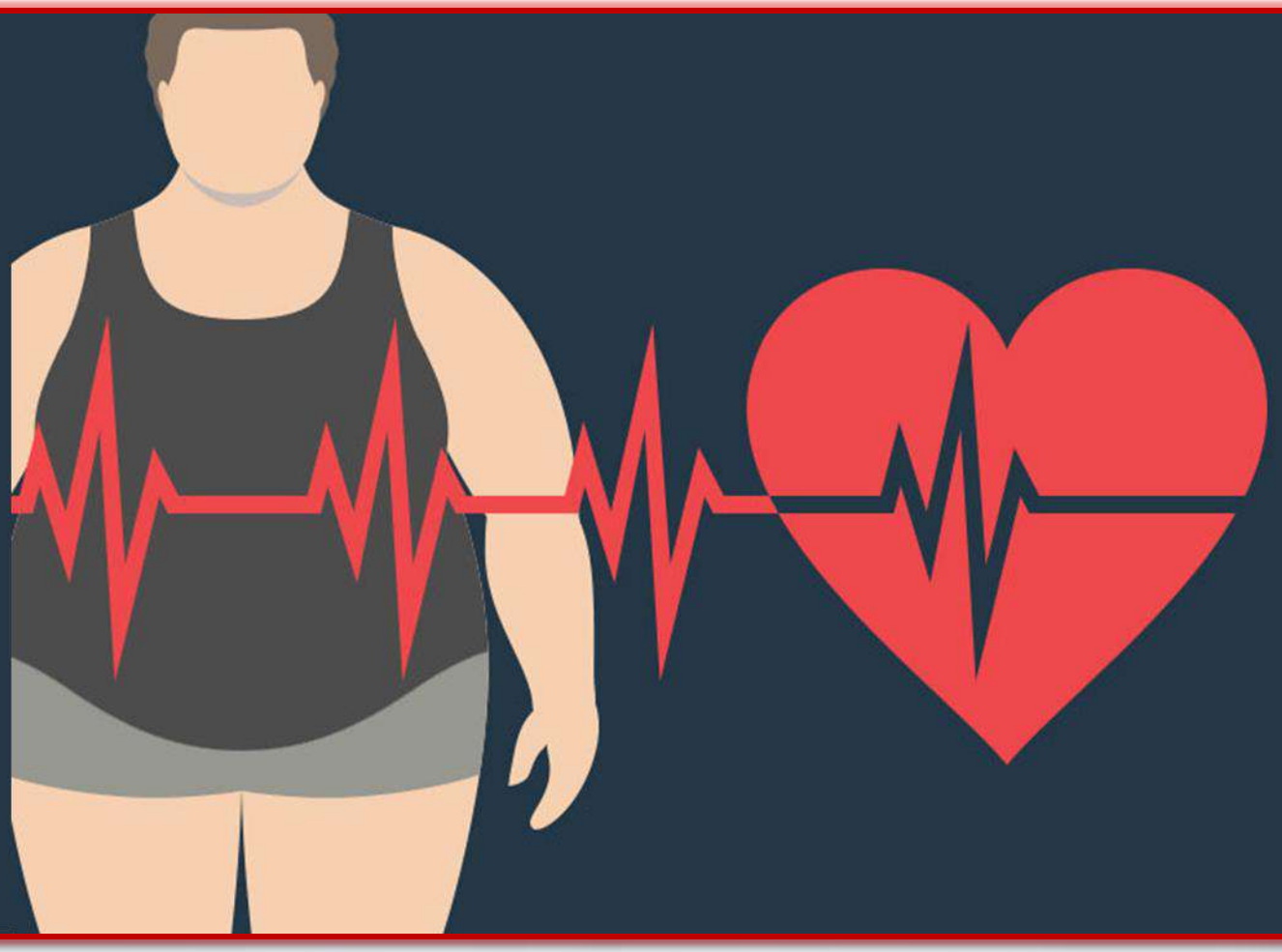
Emanuele Feliziani, Maria Caterina Chios, Paolo Pozzilli

Diabetes Res Clin Pract, 2024

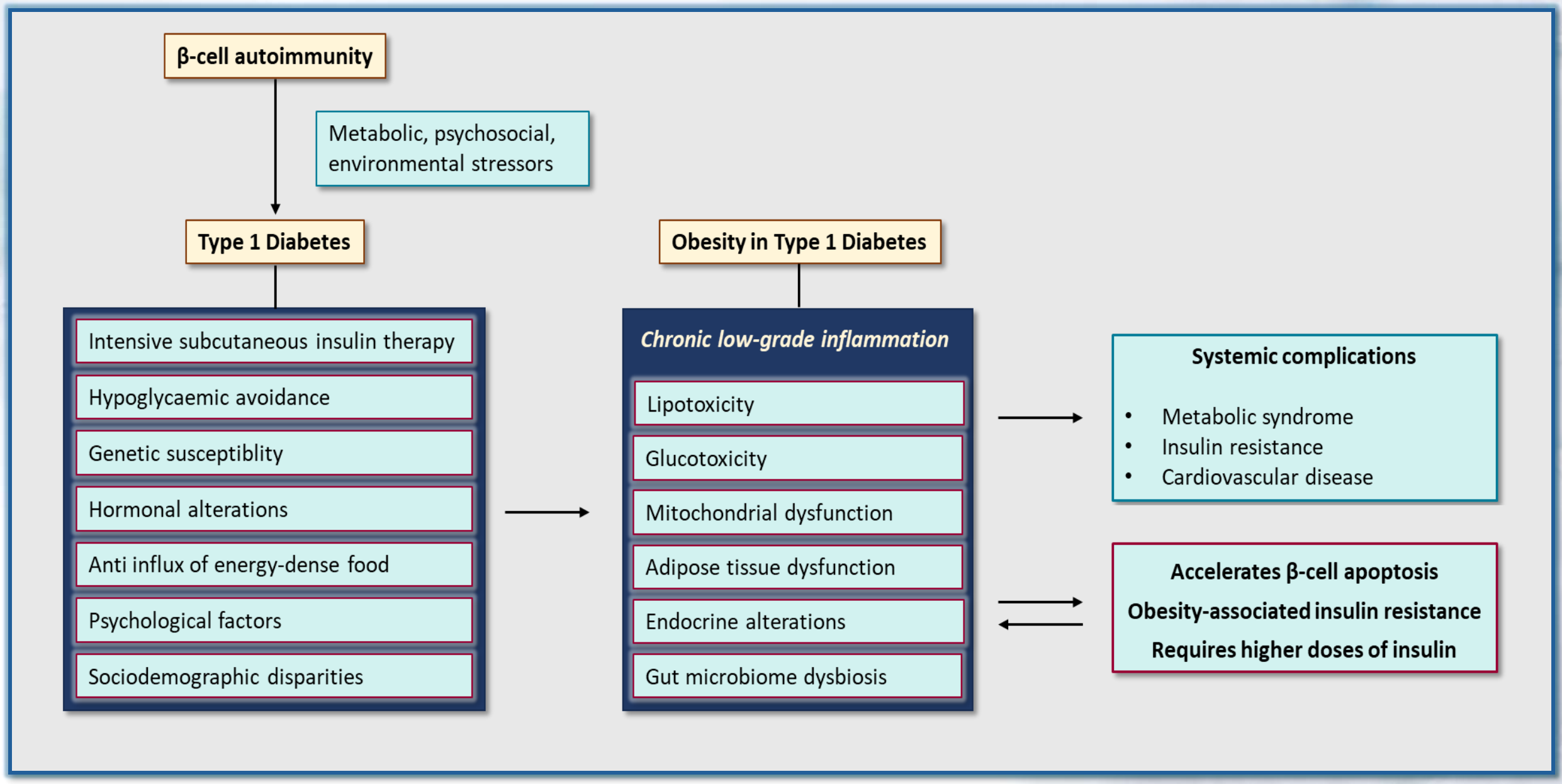
Obesity and type 1 diabetes

- Overweight/obesity affects a large number of patients with type 1 diabetes (T1D) across their lifetime, with rates ranging between 3% and 37%

- Patients with T1D and obesity are characterized by presence of insulin resistance, high insulin requirements for treatment, a greater cardio-metabolic risk and an **ENHANCED RISK OF DEVELOPING CHRONIC COMPLICATIONS** when compared to normal-weight subjects with T1D.

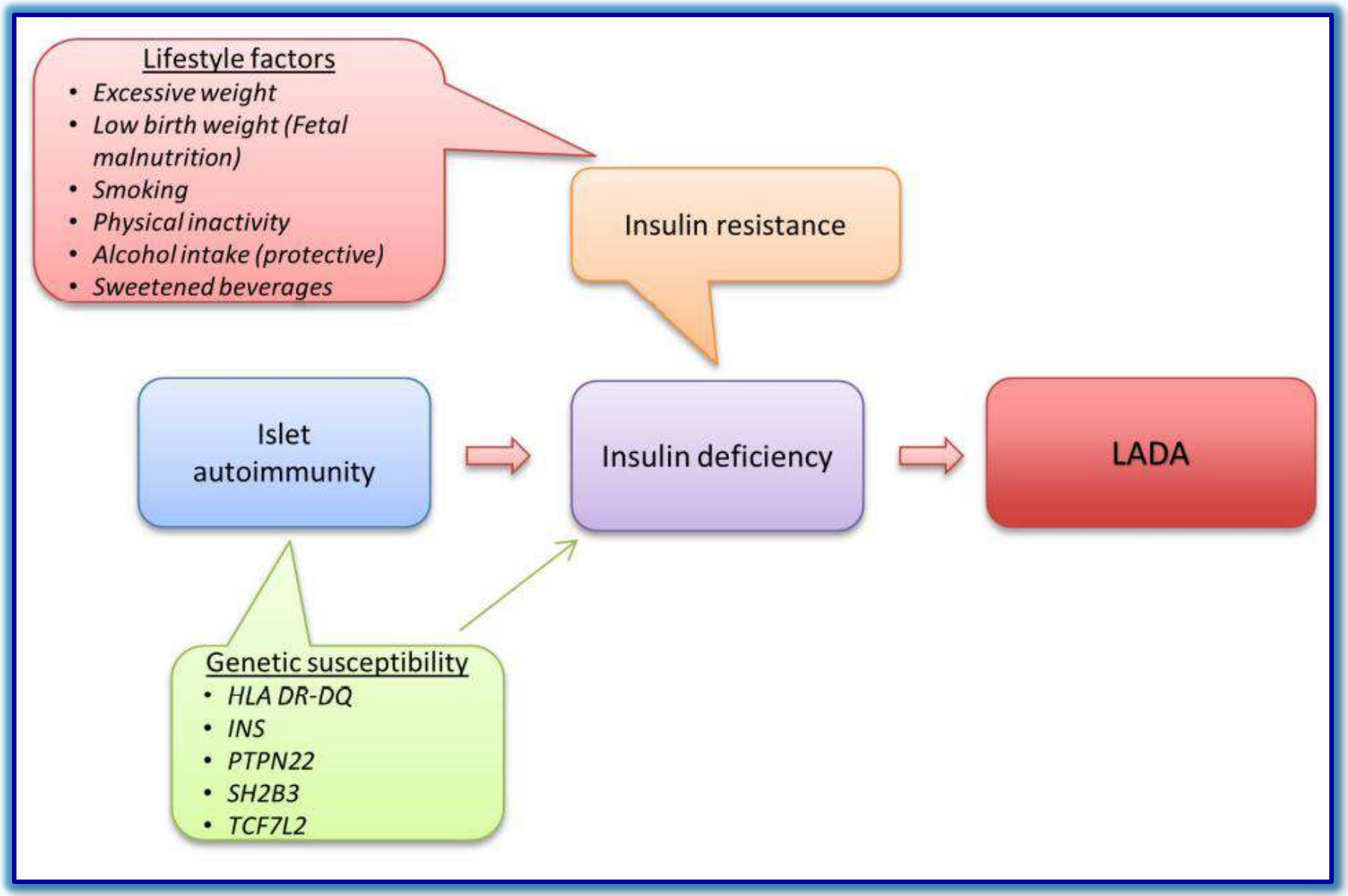


A summary of variables contributing to obesity in T1D



Modified from M.T.W. Kueh et al. International Journal of Obesity 2024

Autoimmune diabetes in adults (LADA) associated with overweight/obesity: a model based on current knowledge



LADA may share several environmental risk factors with T2D including:

- Overweight;
- Physical inactivity;
- Alcohol consumption;
- Smoking.

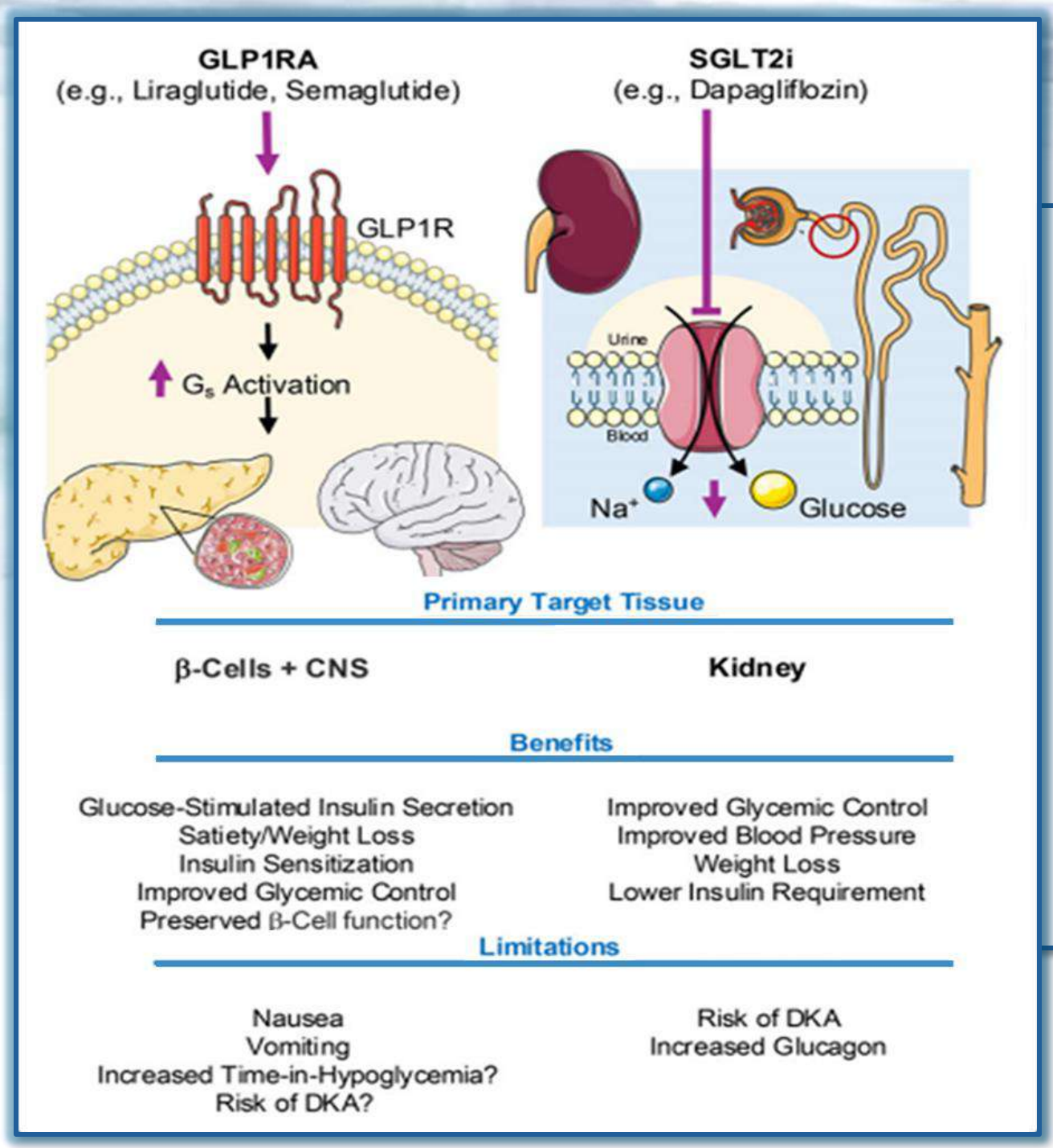
Carlsson S., Frontiers in Physiology 2019

The importance of targeting metabolic control for T1D management and treatment

- Metabolic interventions, through their direct and indirect impacts on β-cells, have shown promise in preserving β-cell function.

- These interventions can reduce glucose toxicity, alleviate oxidative stress and inflammation, enhance insulin sensitivity, and indirectly mitigate the autoimmune responses.

- By preserving β-cell function, individuals with T1D attain better glycaemic control, reduced complication risks and exhibit improved overall metabolic health.

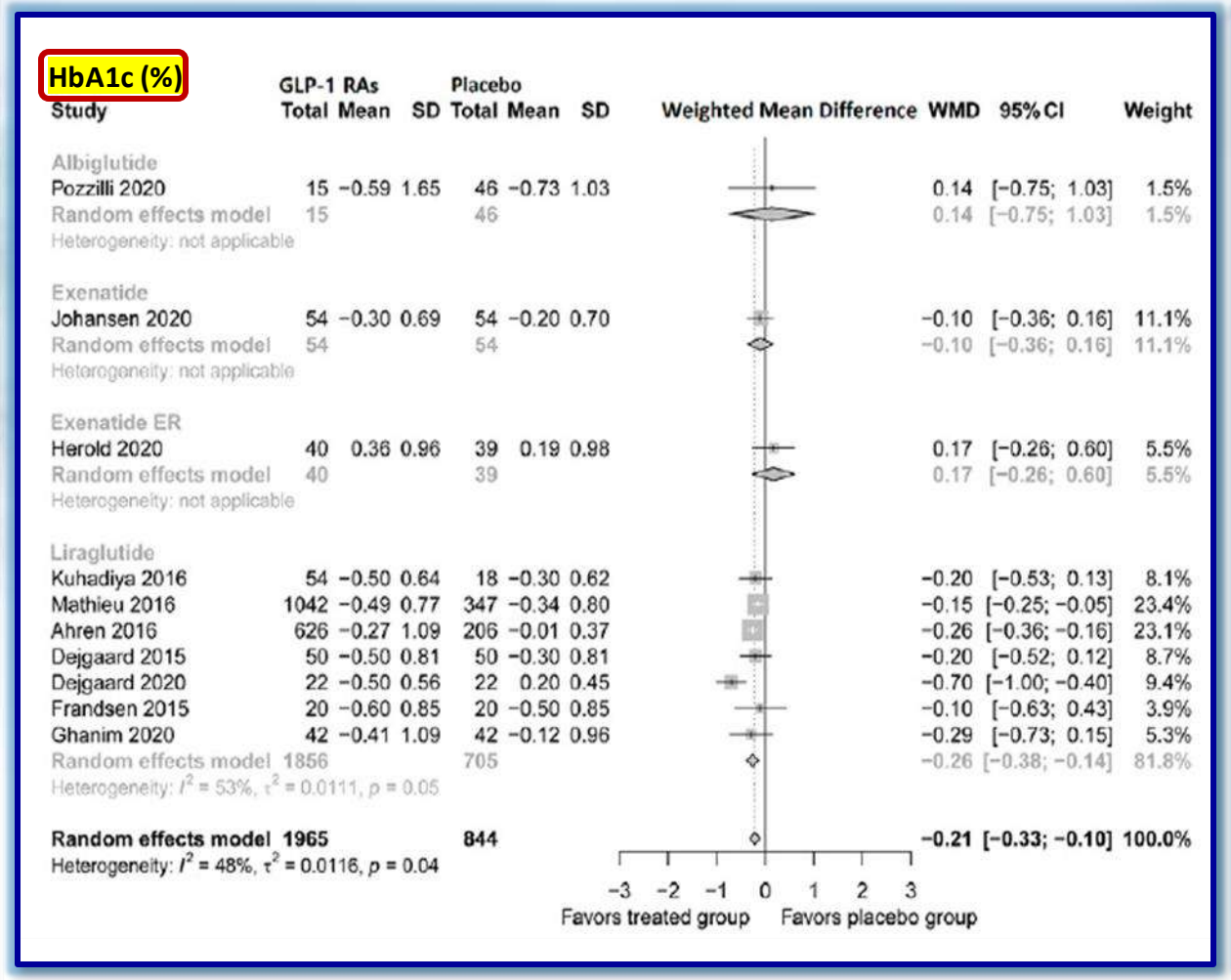


Overview of metabolic interventions as adjuncts to insulin therapy for the treatment of T1D

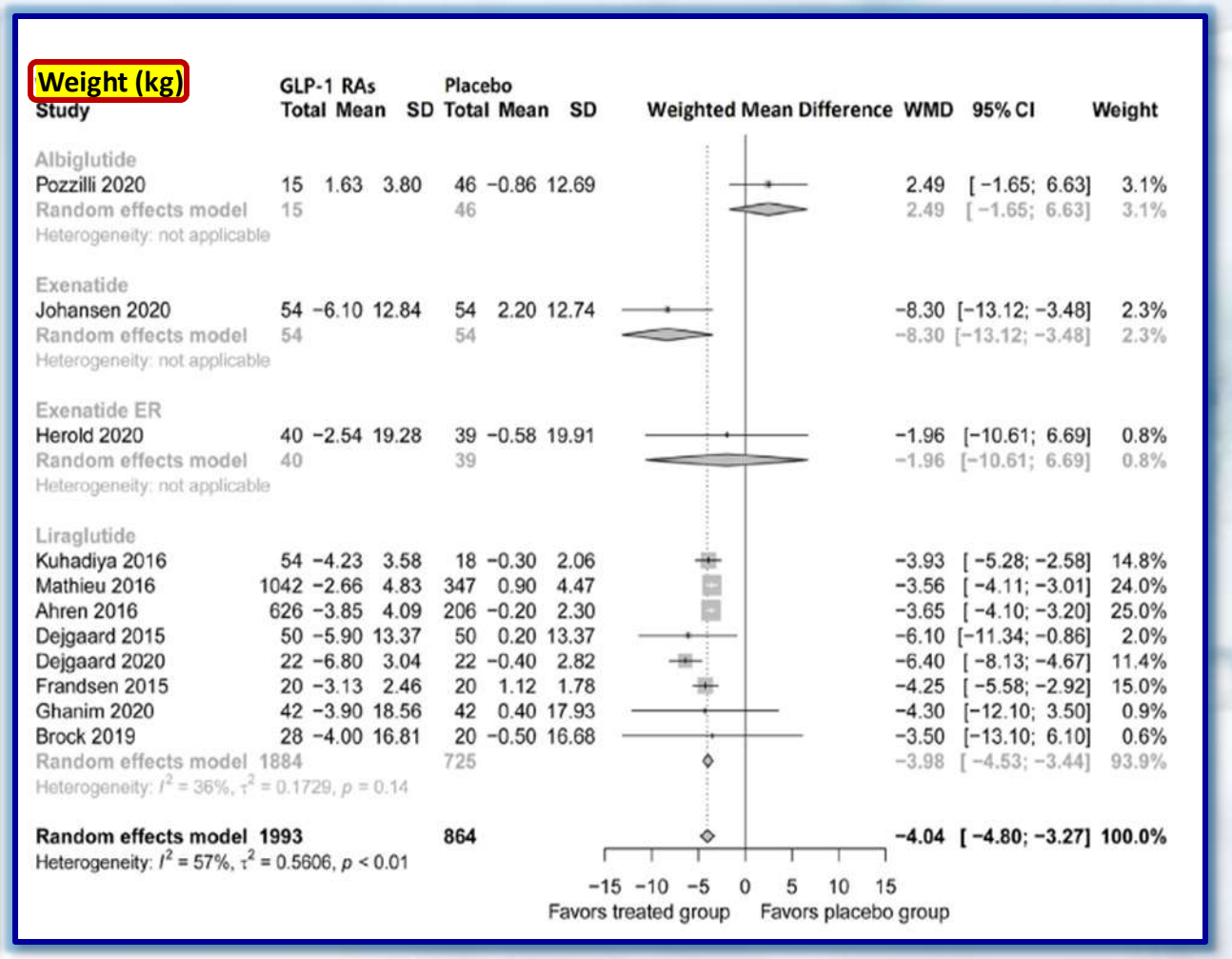
Podobnik J, Prentice KJ, Diabetes Obes Metab. 2025

Glucagon-like peptide-1 receptor agonists as add-on therapy to insulin for T1D

HbA1c (%)



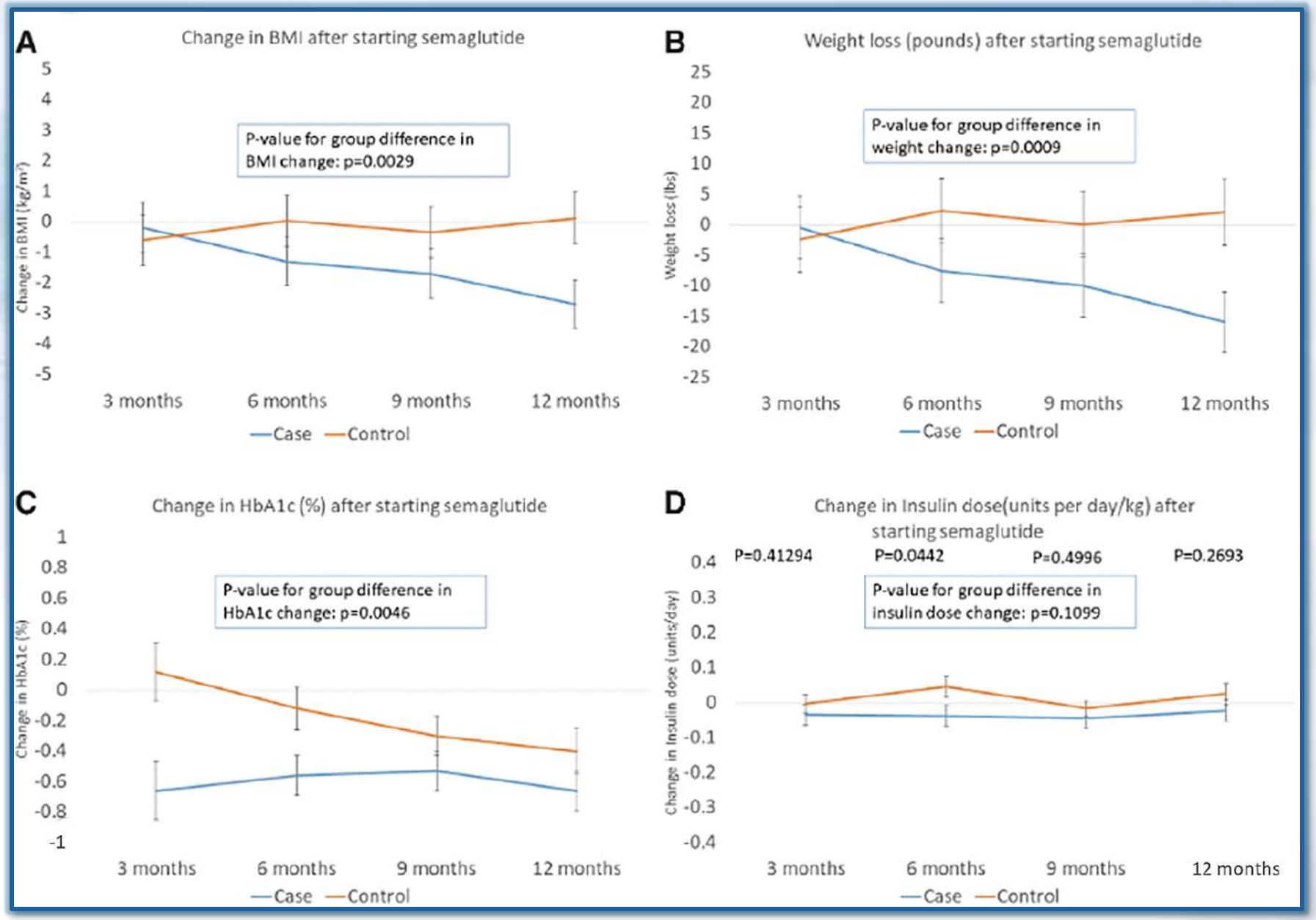
Weight (kg)



This meta-analysis of randomized clinical trials suggests moderate beneficial effects of GLP-1 RAs on the metabolic profile in patients with T1D, without an increased risk of serious adverse events.

Tan X. Et al., Front. Pharmacol. 2023

Efficacy of Semaglutide in Overweight and Obese Patients with T1D

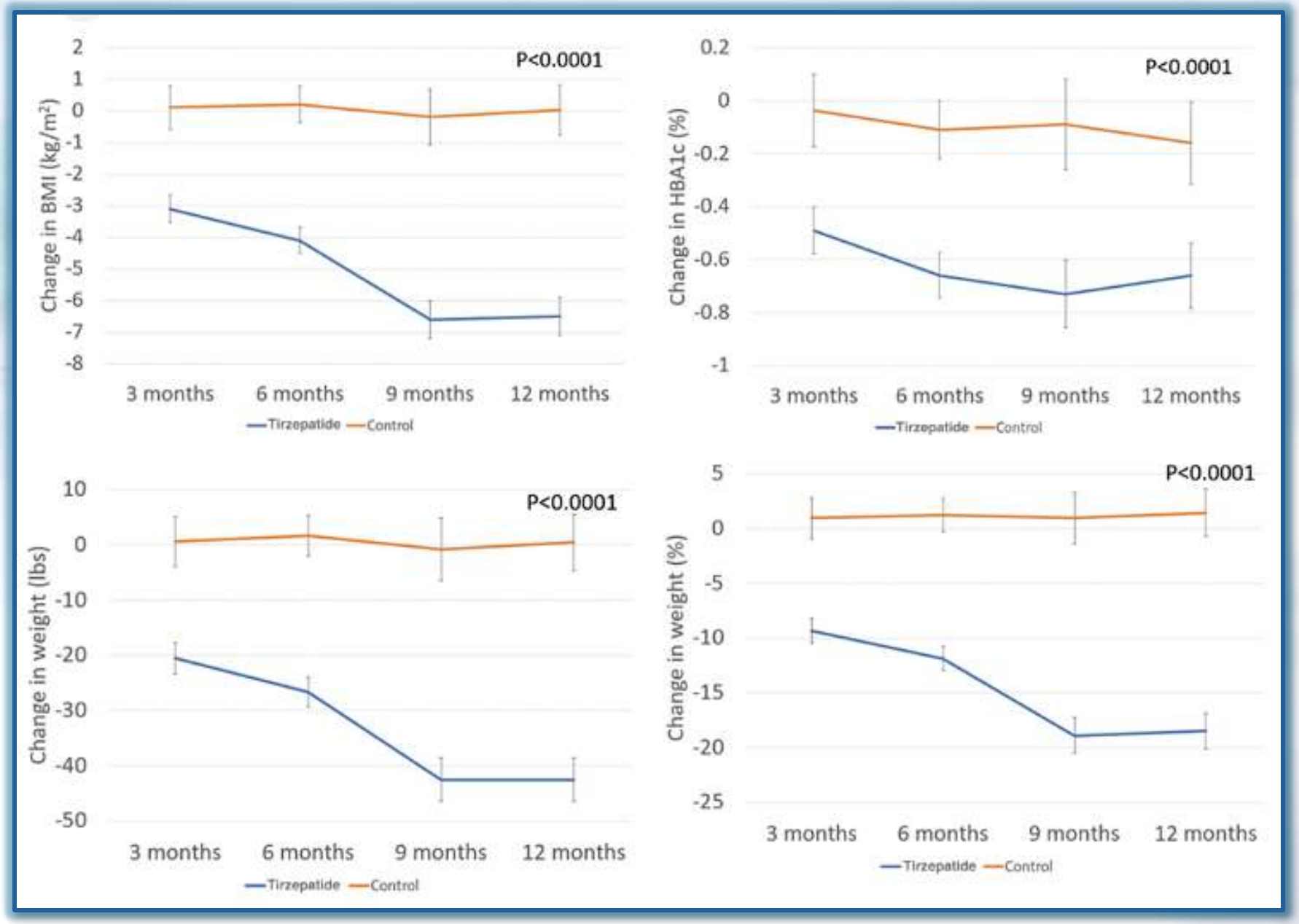


The use of semaglutide in patients who are OW and/or OB with T1D is effective in lowering body weight and BMI and improving glycemic metrics in this pilot real-world study.

Prospective, large-randomized clinical trials with newer GLP-1 analogs like semaglutide and tirzepatide for subjects with T1D associated with OW and/or OB are strongly recommended.

Garg SK et al., Diabetes Technology & Therapeutics 2024

Efficacy and Safety of Tirzepatide in Overweight and Obese Adult Patients with T1D



In this pilot (off label) study, tirzepatide facilitated an average 18.5% weight loss and improved glucose control in OW/OB patients with T1D at 1 year.

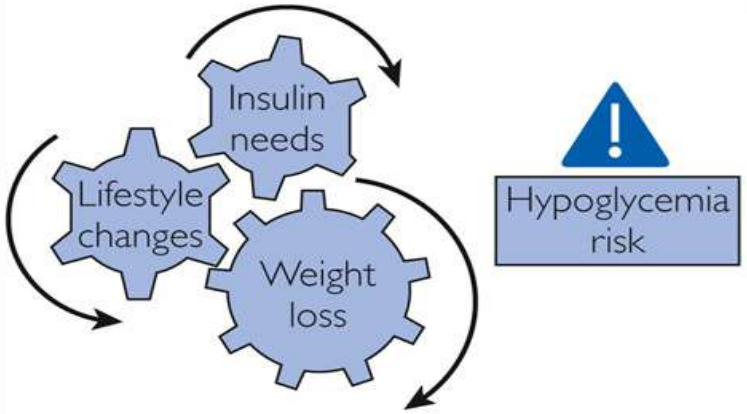
For safe use of tirzepatide in patients with T1D, a large prospective randomized control trial in OW/OB patients with T1D is strongly recommended.

Garg SK et al., Diabetes Technology & Therapeutics 2024

Effect of Tirzepatide on Body Weight and Diabetes Control in Adults With T1D and Overweight or Obesity

Background

The treatment of overweight and obesity in individuals with type 1 diabetes poses a clinical challenge.



Objective

To determine the effect of tirzepatide on weight, diabetes control, and insulin requirements, and its safety profile in adults with type 1 diabetes and overweight or obesity.

Methods

Retrospective chart review of 51 adults with type 1 diabetes using tirzepatide for overweight or obesity for at least 3 months.

Results

Over a median follow-up time of 8 months, we observed:

- ☑ Weight loss 8.5%
- ☑ HbA1c ↓ 0.9%
- ☑ Daily insulin requirements ↓ 36%
  - Basal ↓ 36%
  - Meal ↓ 31%

*With most changes ocurring within 6 months of therapy initiation

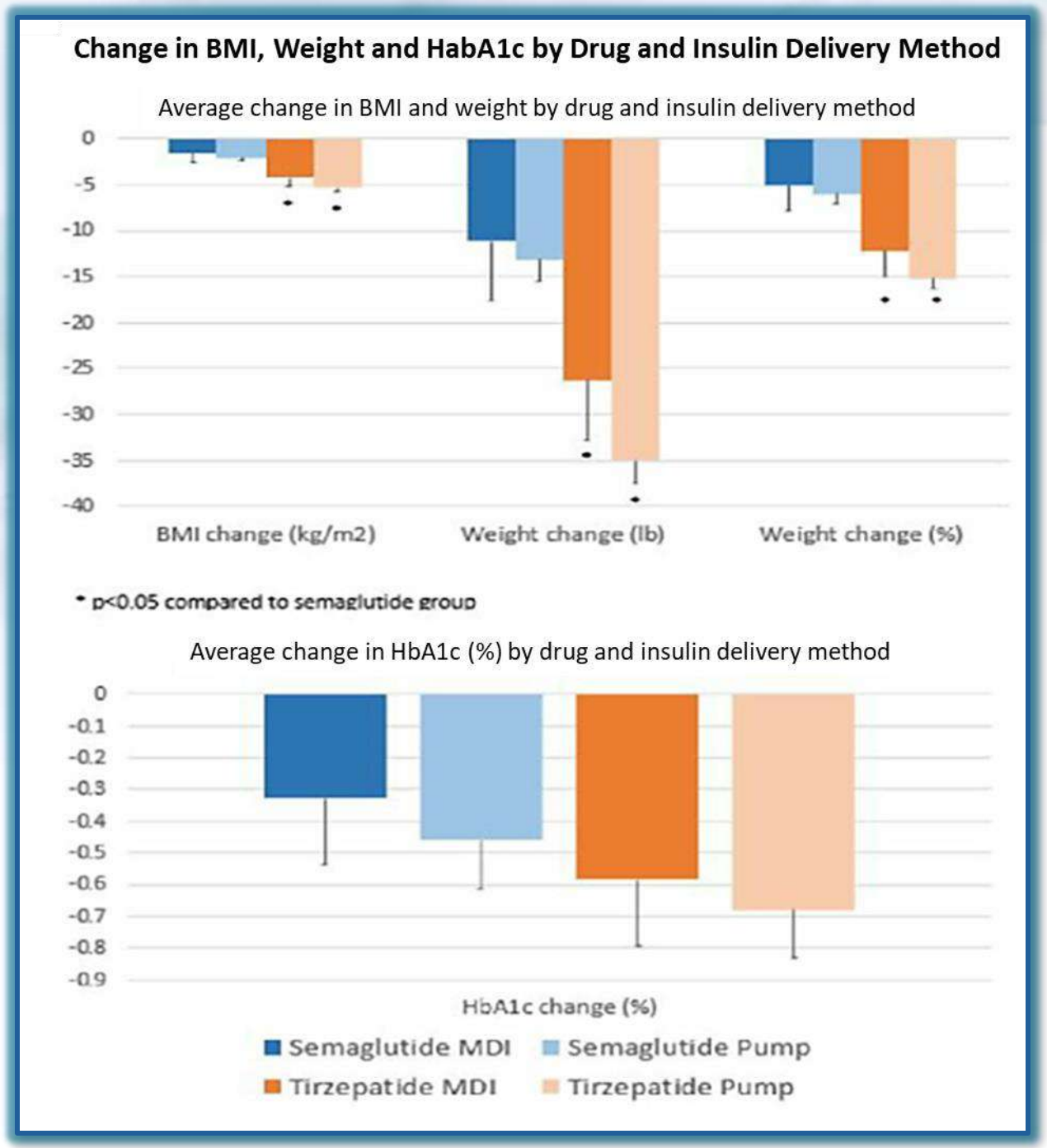
- ☑ Improvement in cardiometabolic parameters
- ☑ No increased hypoglycemia
- ☑ No diabetes ketoacidosis

Conclusions

In adults with type 1 diabetes, tirzepatide leads to substantial weight loss, better diabetes control, and decreased insulin requirements, without worsening hypoglycemia.

Gutierrez RR et al., Mayo Clin Proc. 2025

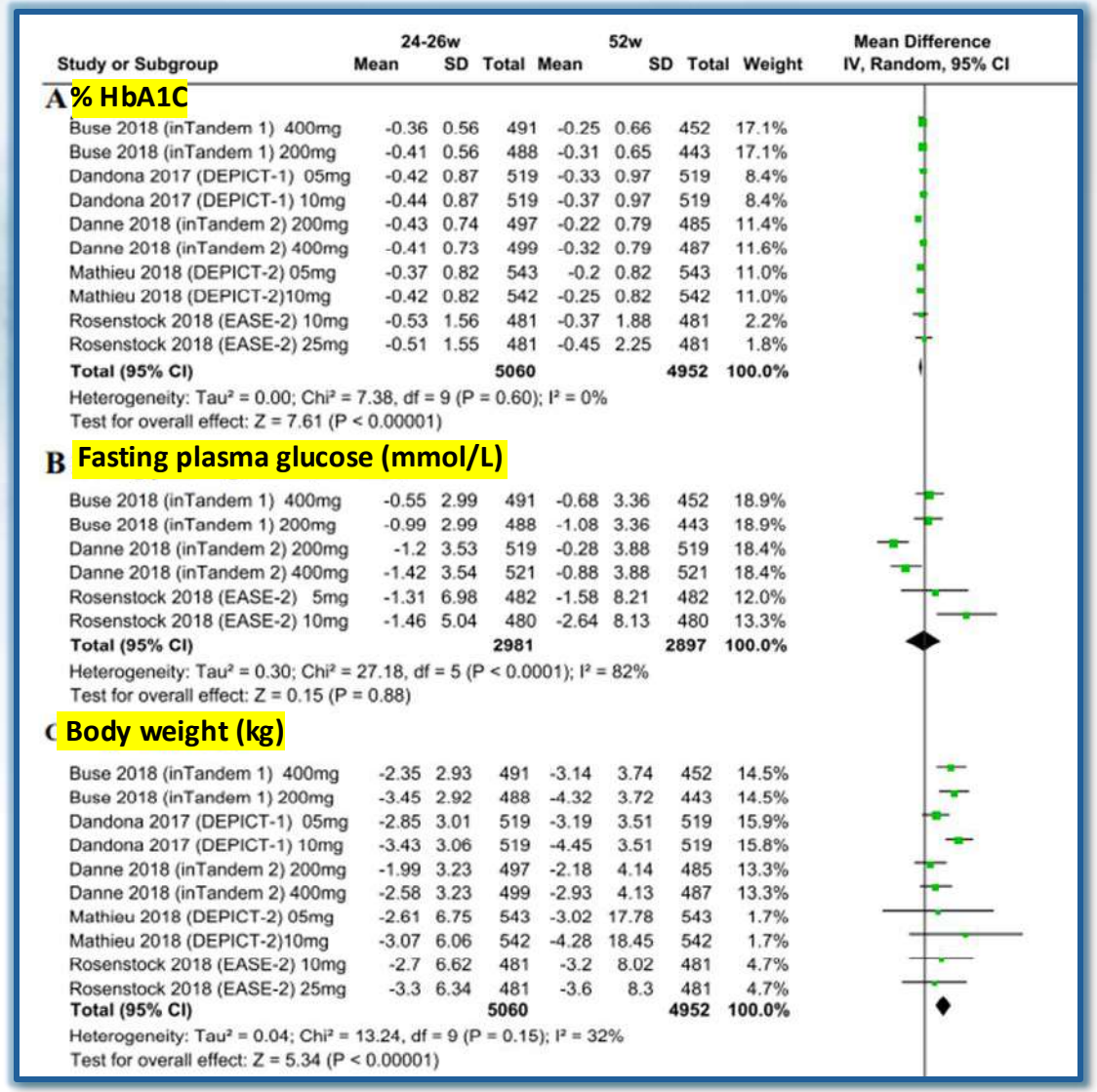
Effectiveness of Semaglutide and Tirzepatide in Overweight and Obese Adults with T1D

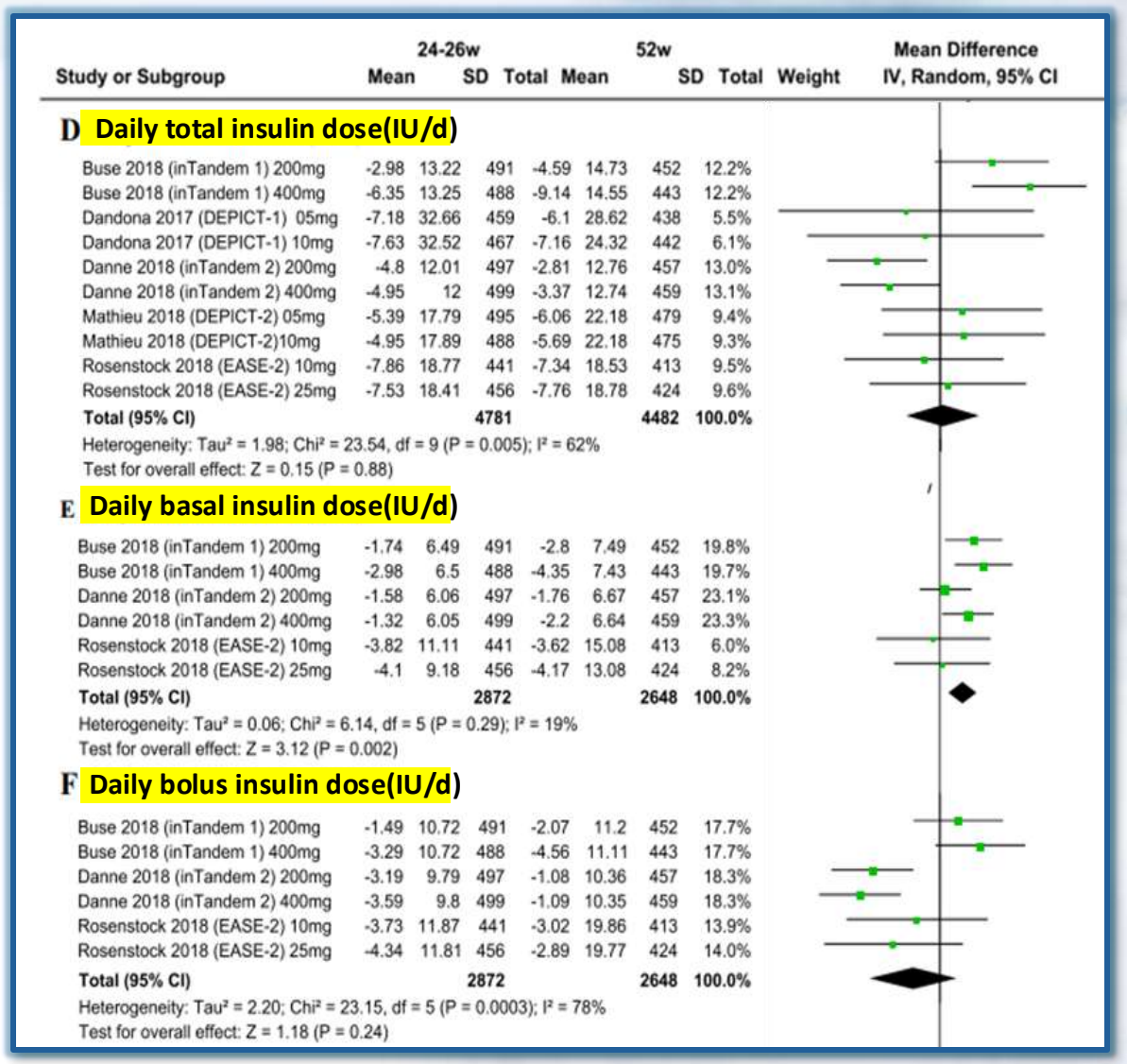


Weight loss of 9.1% and 21.4% and improved glucose control in semaglutide and tirzepatide users, respectively, after 1 year of off-label use were observed. As off-label use of these drugs is increasing in patients with T1D, larger, prospective safety and efficacy trials are needed.

Snell-Bergeon JK et al., Diabetes Technology & Therapeutics 2025

SGLT- 2 inhibitors as an add-on therapy to insulin for T1D: Meta-analysis of randomized controlled trials





SGLT2i as an add-on therapy to insulin improved glycaemic control and body weight and decreased the required dose of insulin without increasing the risk of hypoglycemia. After 6 months the benefits of SGLT2is on glycaemic control may weaken and the risks of DKA increased.

Rao L. et al., Acta Diabetologica 2021

SGLT2 Inhibitors in the Management of T1D: Ongoing Clinical Trials

- Dapagliflozin in Physical Exercise in Type 1 Diabetes (NCT04049110)
- Dapagliflozin Plus Pioglitazone in T1DM (NCT03878459)
- Ketone Monitoring in T1D: Effect of SGLT2i During Usual Care and With Insulin Deficiency (NCT05541484)
- Triple Therapy in T1DM (NCT03899402)
- Study to Explore the Effect of Dapagliflozin and Stress in Adolescent and Adults subjects With Type 1 Diabetes (T1D) (Dapa-Stress) (NCT04234867)
- Adolescent Type 1 Diabetes Treatment With SGLT2i for hyperglycEMia and hyPerfilTration Trial (ATTEMPT) (NCT04333823)
- Combination Adjunctive Therapy to Address Multiple Metabolic Imbalances in Type 1 Diabetes (SOTA) (NCT05696366)

Maffei P. et al., Diabetes, Metabolic Syndrome and Obesity 2023

Combination of SGLT-2 Inhibitor and GLP-1RA Therapy in T1D: A Randomized Clinical Trial

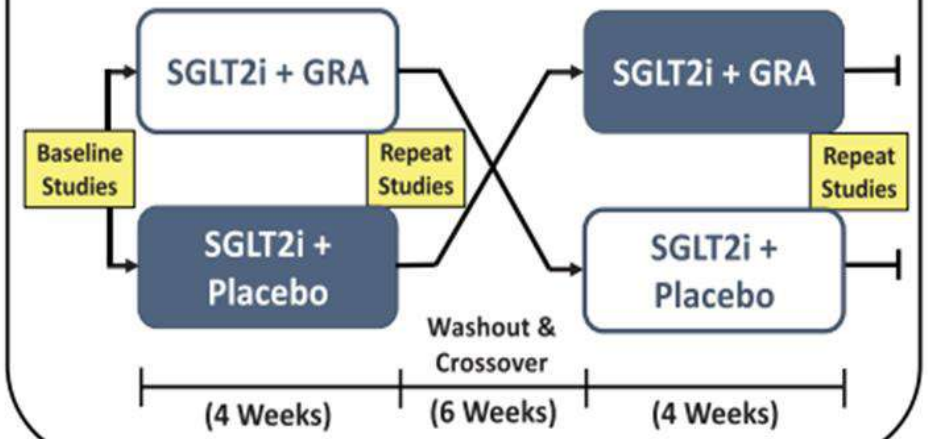
Hypothesis

Combining an SGLT2 inhibitor with a GRA will:

1. Improve glycemia
2. Reduce insulin use
3. Reduce ketogenesis during insulinopenia

Study Design (*n*=12)

SGLT2i = dapagliflozin 10 mg daily
GRA = volagidemab 70 mg weekly



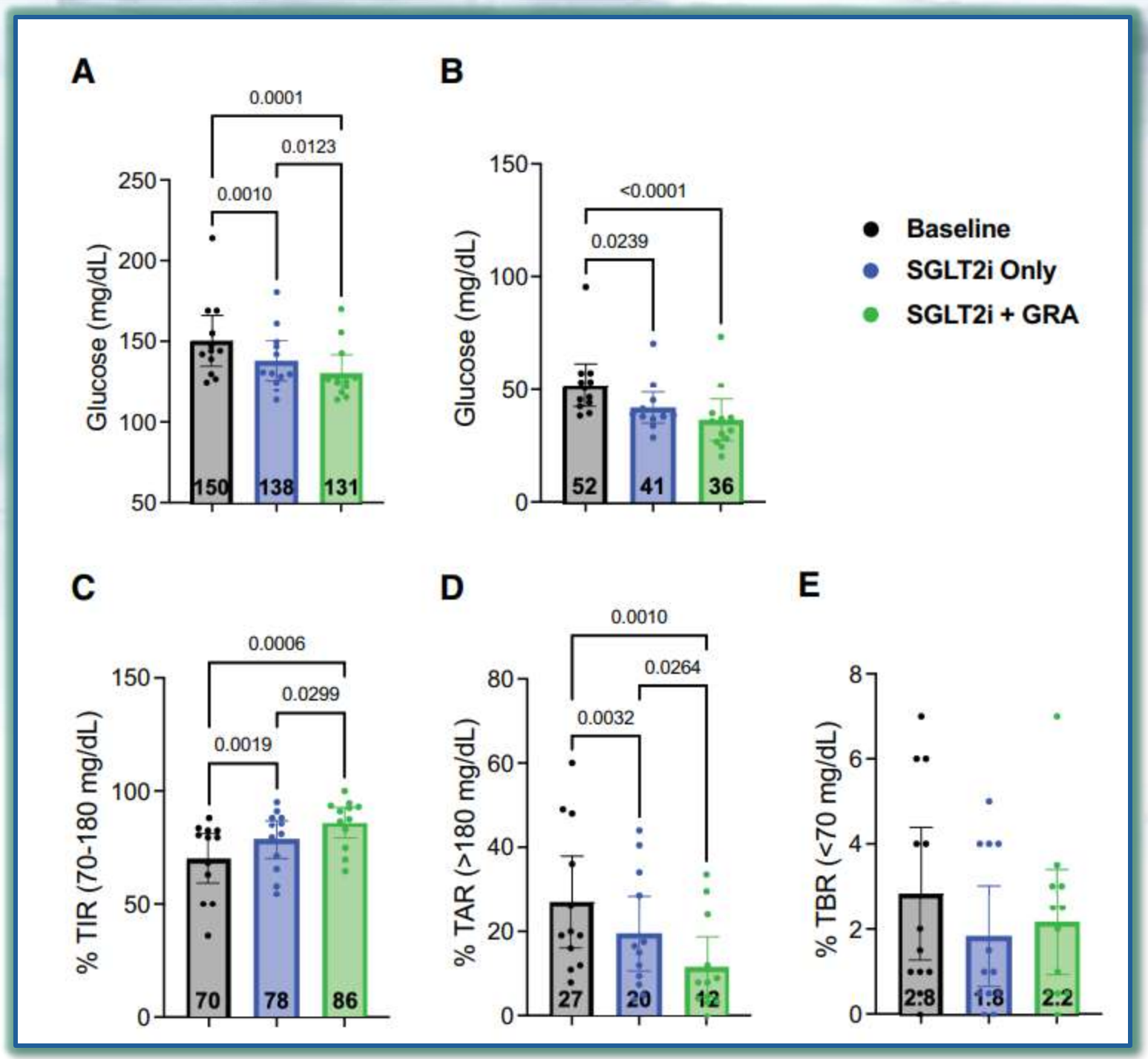
Results

With combination therapy:

- Average glucose ⬇ 19 mg/dL
- Time in range ⬆ 16%
- No increased hypoglycemia
- Total insulin use ⬇ 27%
- Ketones in insulinopenia ⬇ 17%

Conclusion: Combination SGLT2 inhibitor + GRA is a promising adjunctive therapy strategy for type 1 diabetes

Boeder SC, et al. Diabetes Care. 2025



Glucagon antagonism enhances the therapeutic effects of SGLT2 inhibition in T1D. Combination therapy improves glycemic control, reduces insulin dosing, and suggests a strategy to unlock the benefits of SGLT2 inhibitors while mitigating the risk of diabetic ketoacidosis.

Boeder SC, et al. Diabetes Care. 2025

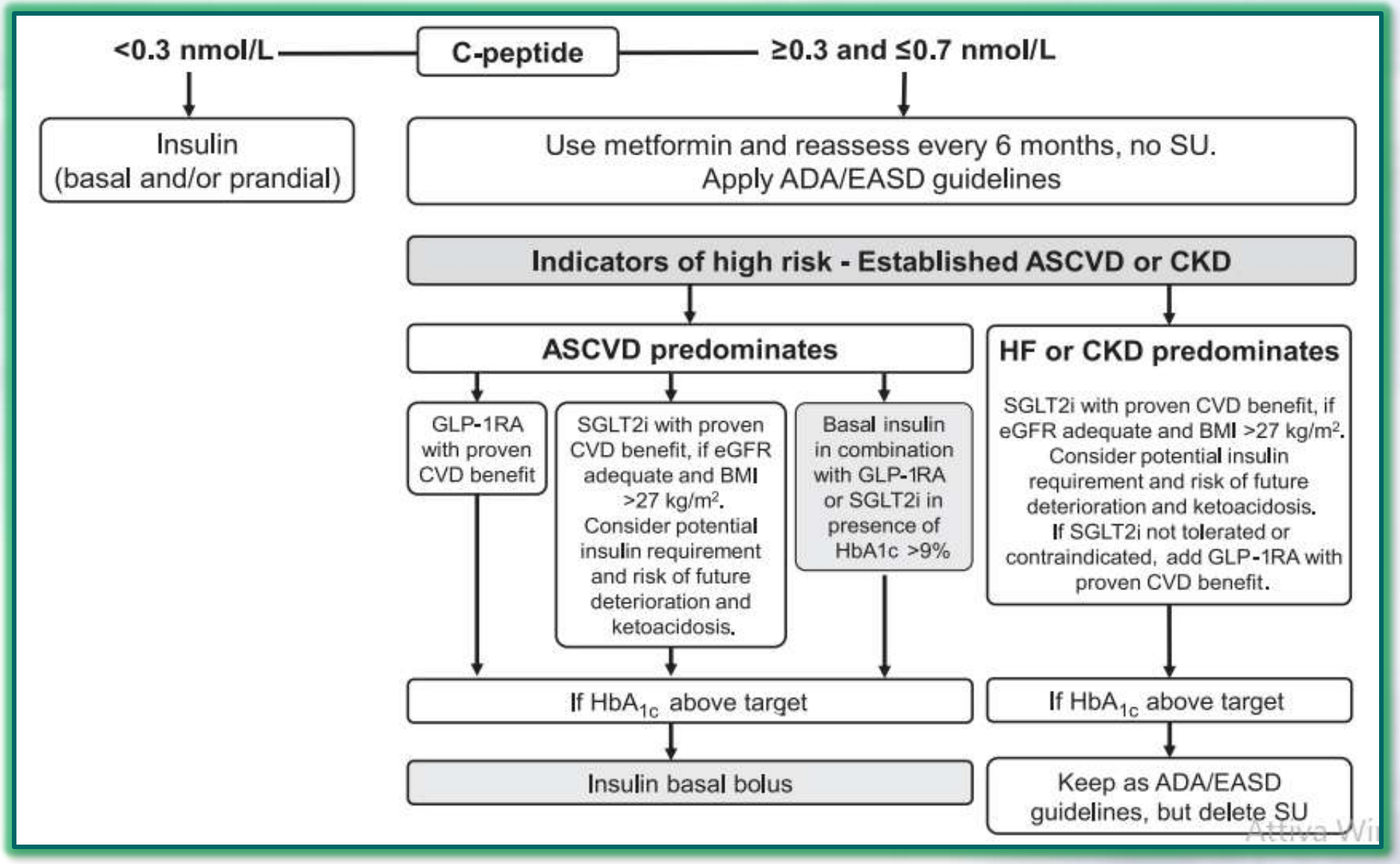
Diabetes Volume 69, October 2020

Management of Latent Autoimmune Diabetes in Adults: A Consensus Statement From an International Expert Panel

Raffaella Buzzetti,[1] Tiinamaija Tuomi,[2,3] Didac Mauricio,[4] Massimo Pietropaolo,[5] Zhiguang Zhou,[6] Paolo Pozzilli,[7,8] and Richard David Leslie[8]

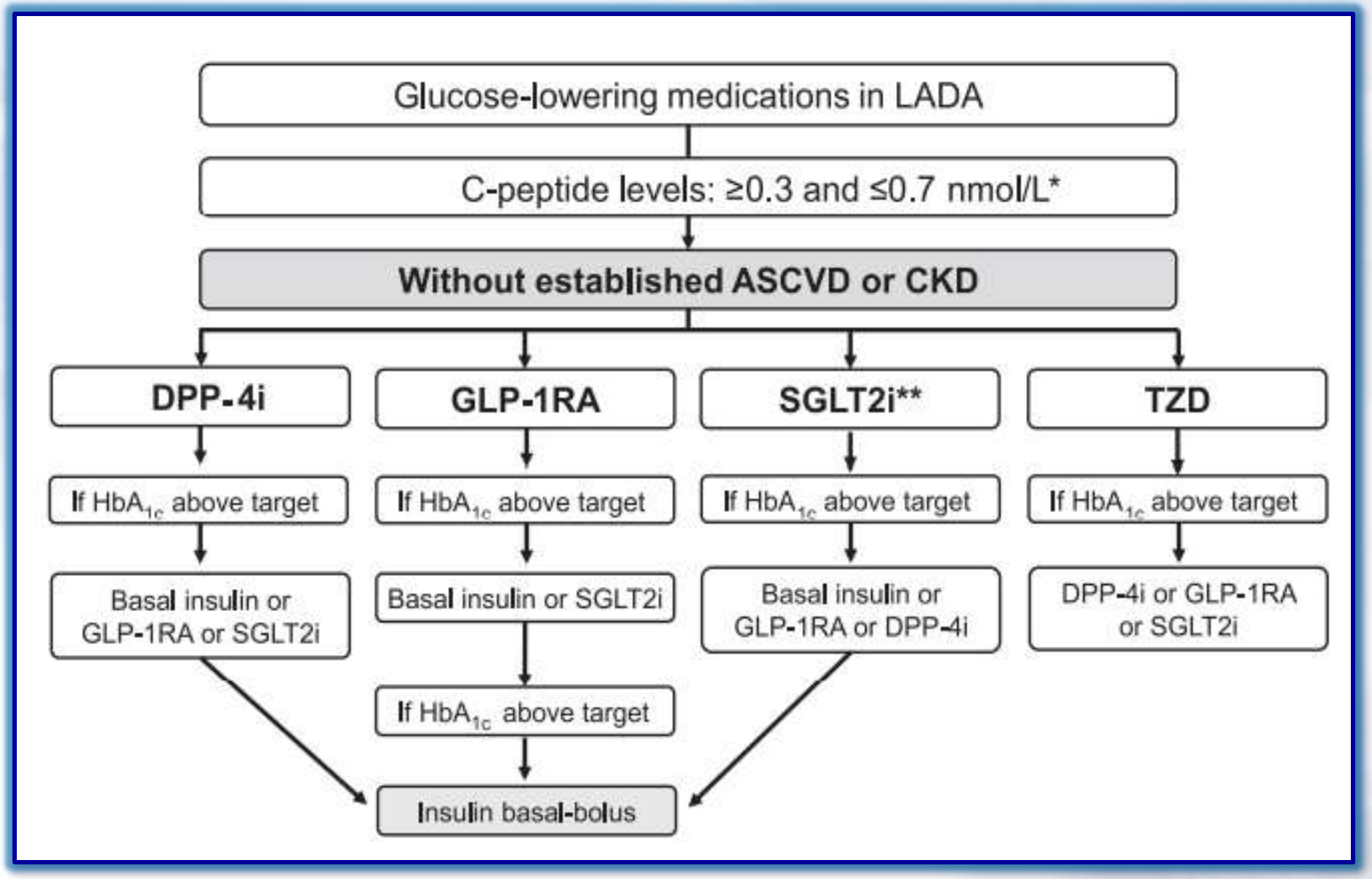
Diabetes 2020;69:1–11 | https://doi.org/10.2337/dbi20-0017

Algorithm for glucose-lowering medications in LADA patients with C-peptide ,< 0.3 mmol/L or with C-peptide ≥ 0.3 and ≤ 0.7 nmol/L

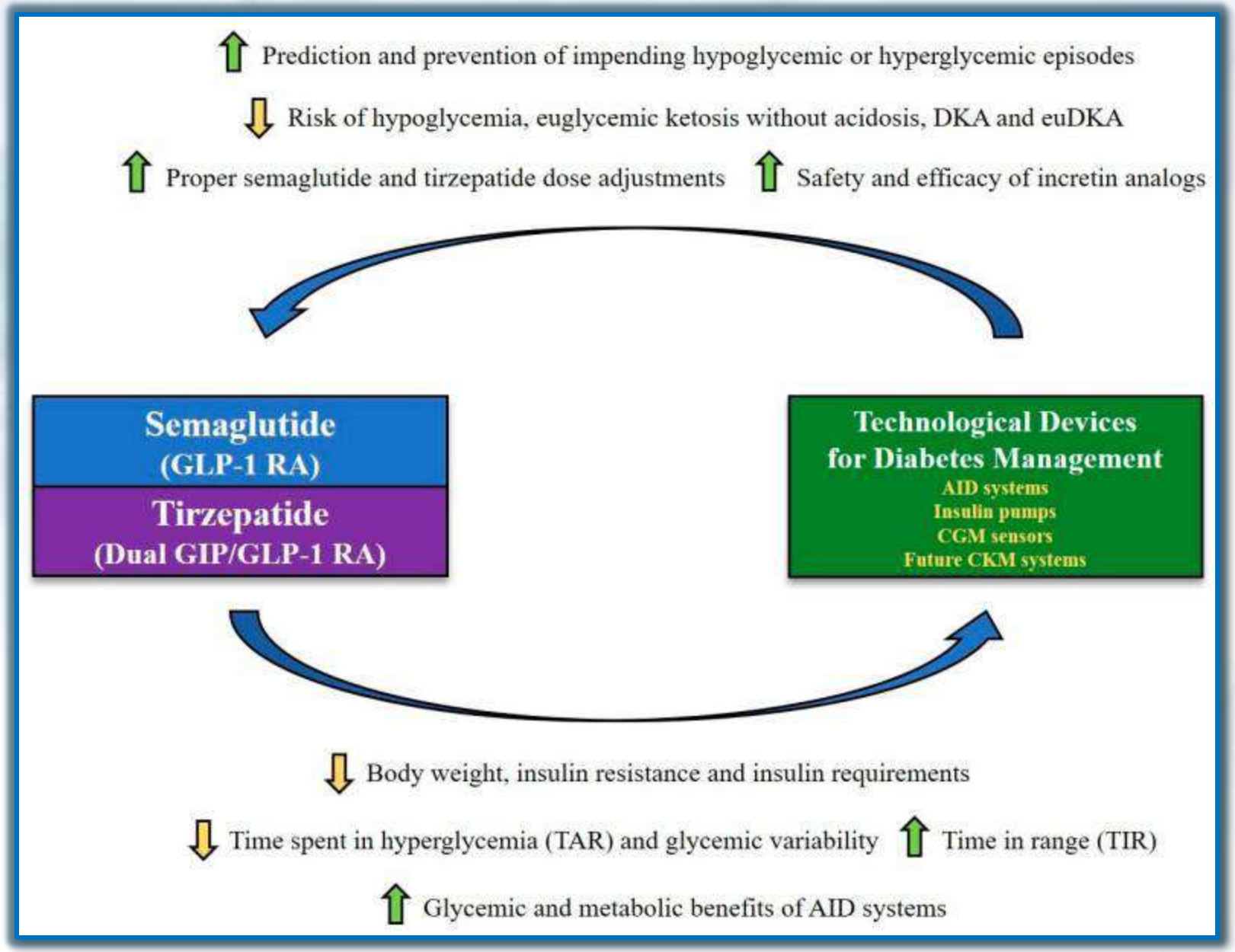


Buzzetti R.,…, Pozzilli P. et al., Diabetes 2020

Algorithm for glucose-lowering medications in LADA patients with C-peptide levels ≥ 0.3 and ≤0.7 nmol/L without established ASCVD



Buzzetti R.,…, Pozzilli P. et al., Diabetes 2020



Unveiling the Therapeutic Potential of the Second-Generation Incretin Analogs Semaglutide and Tirzepatide in T1D and Latent Autoimmune Diabetes in Adults

Potential synergistic benefits of second-generation incretin analogs (semaglutide and tirzepatide) and advanced technological devices used for diabetes management in patients with T1D, double diabetes and LADA.

Infante M et al., J Clin Med. 2025

Conclusions

- In conclusion, the adoption of metabolic-based interventions alongside insulin therapy holds strong promise for advancing T1D treatment by addressing the significant limitations of traditional insulin monotherapy.

- These adjunctive therapies for the increased obesity in T1D offer novel pathways to improve glucose control and reduce insulin dose, while also holding potential to delay or even preserving residual β-cell function.

- The use of GLP-1RAs and SGLT-2i will become an additional treatment to insulin in overweight/obese T1D improving metabolic control and modify disease trajectories.