TRATTAMENTO DEL PAZIENTE GIOVANE CON OBESITA' E DM1

Carla Micaela Cuttica

SSD ENDOCRINOLOGIA
E.O. OSPEDALI GALLIERA GENOVA

Dichiaro di non aver ricevuto negli ultimi due anni compensi o finanziamenti da Aziende Farmaceutiche e/o Diagnostiche

L’obesità è una malattia cronica, recidivante, in grado di provocare altre malattie croniche.

E’ in progressivo aumento nel mondo in tutte le età, anche in adolescenti e bambini.

NEOLOGISMI (2018)

GLOBESITA

globesita globesità s. f. inv. La diffusione dell’obesità come fenomeno globale.

Can type 1 diabetes be an unexpected complication of obesity?

Frontiers in Endocrinology
TYPE Mini Review
PUBLISHED 31 March 2023
DOI 10.3389/fendo.2023.1121303

Paulina Oboza[1], Natalia Ogarek[2], Magdalena Olszanecka-Glinianowicz[3] and Piotr Kocelak[2*]

Diabetologia (2022) 65:1473–1482
https://doi.org/10.1007/s00125-022-05722-5

ARTICLE

Obesity in late adolescence and incident type 1 diabetes in young adulthood

Inbar Zucker[1,2] · Yair Zloof[1,3] · Aya Bardugo[3,4] · Avishai M. Tsur[1,3,5] · Miri Lutski[1,2] · Yaron Cohen[3,4] · Tali Cukierman-Yaffe[1,6] · Noga Minsky[1,6] · Estela Derazne[7] · Dorit Tzur[3,4] · Cheli Melzer Cohen[1,8] · Orit Pinhas-Hamiel[7,8,9] · Gabriel Chodick[1,8] · Itamar Raz[10] · Arnon Afek[7,11] · Hertzel C. Gerstein[12] · Amir Tirosh[6,7] · Gilad Twig[1,3,4,6]

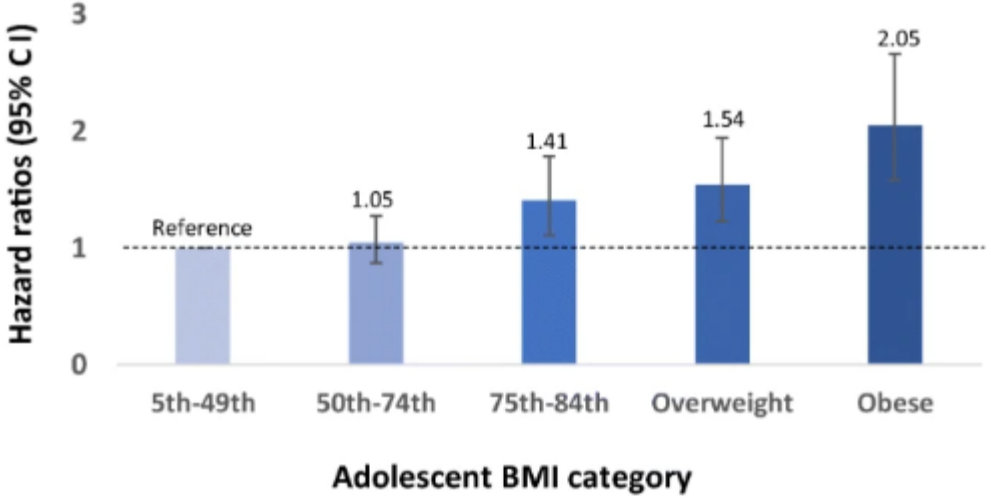
Higher BMI percentiles are **positively associated with incident T1D** among adolescents (16 to 19 years), with an **increase in risk of approximately 25% observed for each incremental standard deviation in BMI**

Israel Defense Force
Medical Corps

1.4 million adolescents who were evaluated before mandatory military service during 1996 - 2016

State of Israel
Ministry of Health

Israel National Diabetes Registry
Type 1 diabetes



REVIEW ARTICLE OPEN

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]

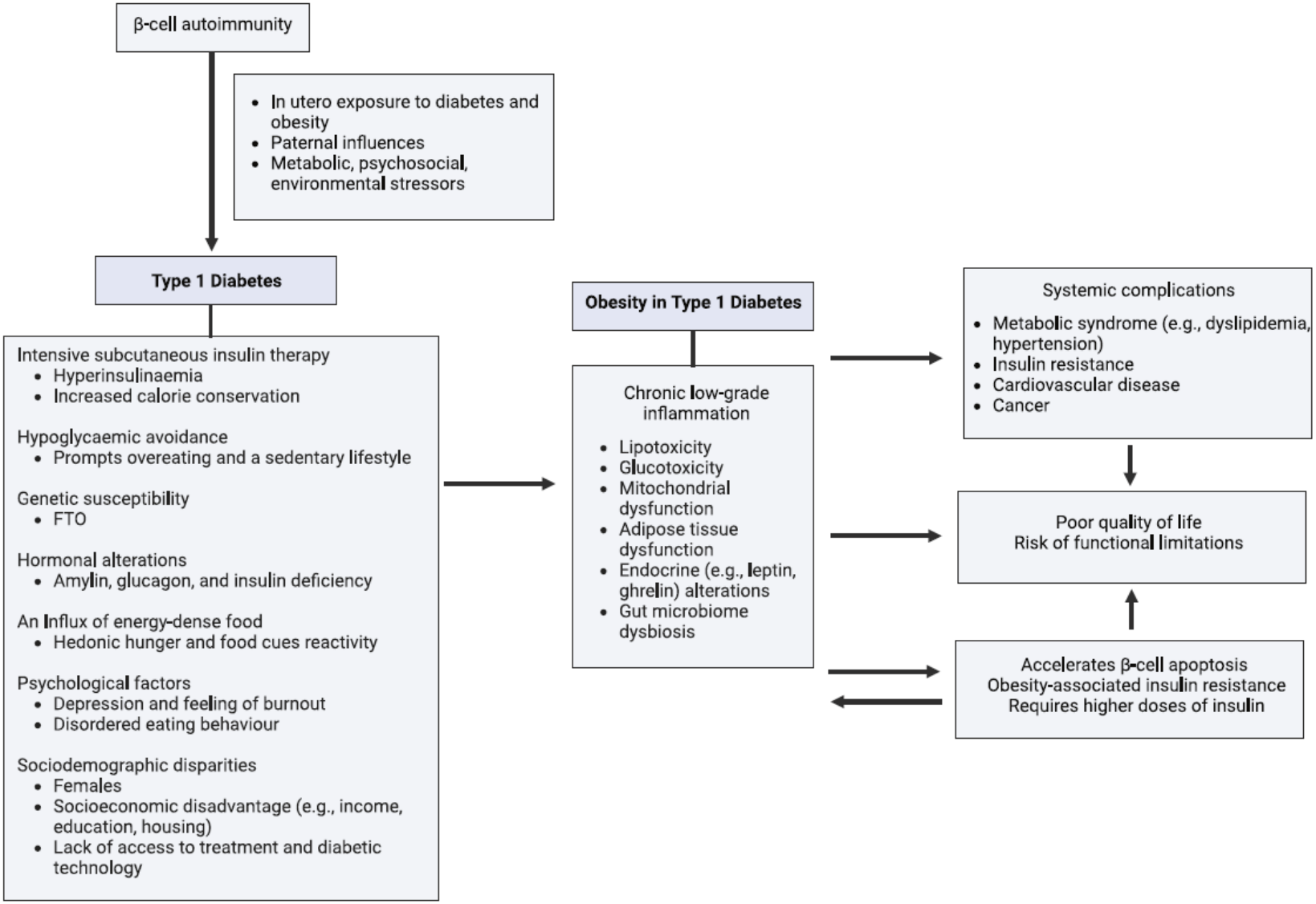


Fig. 1 A summary of variables contributing to obesity in T1D.

Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy Dovepress
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Obesity in Patients with Type I Diabetes: Links, Risks and Management Challenges

Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2021:14

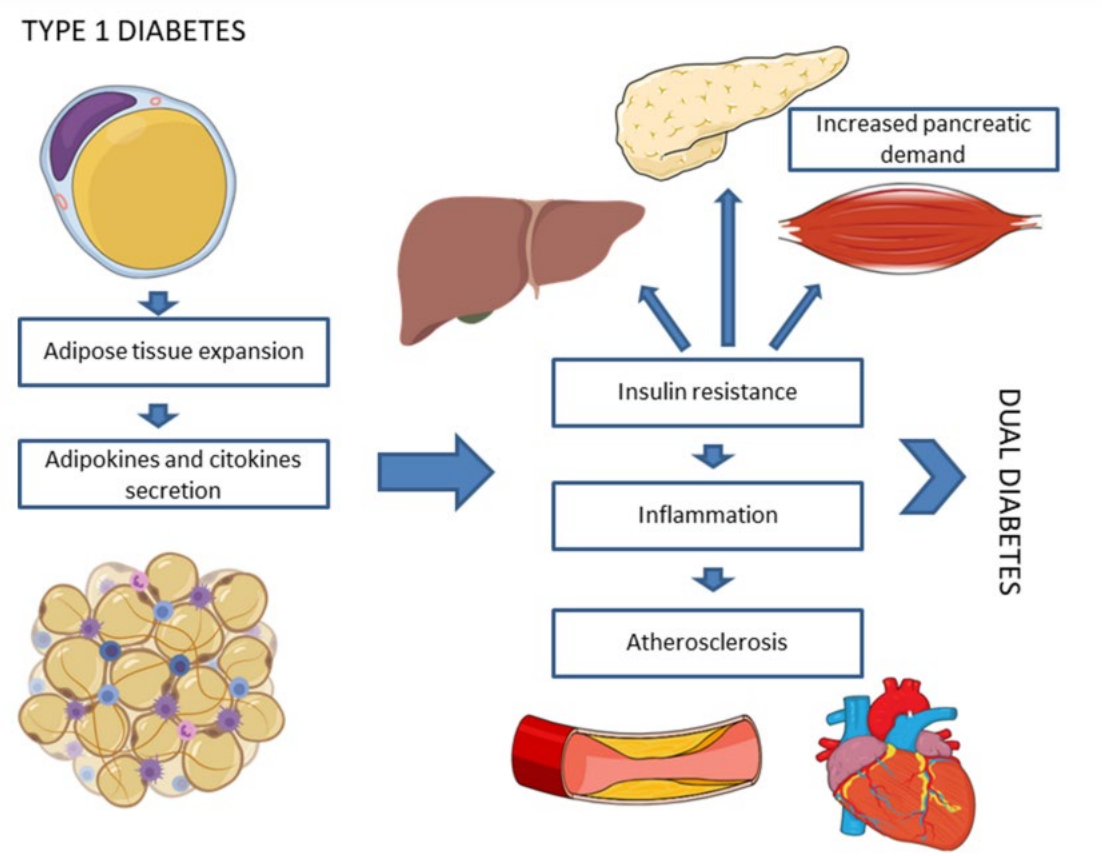

Figure 1 In patients with type I diabetes adipose tissue deposits produce adipokines and inflammatory cytokines that induce insulin-resistance contributing to the development of cardiometabolic complications. The coexistence of these clinical characteristics of type 2 diabetes in patients with type I diabetes has been referred to as double diabetes.

DUAL DIABETES : T1DM + insulino- resistenza

Nel T1DM è presente infiammazione della beta cellula pancreatica. L'obesità, attraverso una serie di eventi biochimici includenti lipotossicità, glucotossicità, disfunzione mitocondriale, disfunzione del tessuto adiposo, alterazioni nella produzione di incretine e nel microbioma intestinale, producono uno stato di infiammazione cronica. Questo «doppio danno» si associa ad un aumento delle complicanze micro e macrovascolari e ad un aumento della mortalità.

Gestione dell’obesità nel T1DM

sono essenziali cambiamenti migliorativi nello stile di vita

TERAPIA NUTRIZIONALE

Ad oggi non abbiamo studi sufficienti che possano indicare quale dieta sia superiore ad un'altra nel trattamento del paziente con diabete mellito tipo 1 ed obesità

Table 5.1—Medical nutrition therapy recommendations

	Recommendations
Effectiveness of nutrition therapy	**5.10** An individualized medical nutrition therapy program as needed to achieve treatment goals, provided by a registered dietitian nutritionist, preferably one who has comprehensive knowledge and experience in diabetes care, is recommended for all people with type 1 or type 2 diabetes, prediabetes, and gestational diabetes mellitus. A **5.11** Because diabetes medical nutrition therapy can result in cost savings B and improved cardiometabolic outcomes A, medical nutrition therapy should be adequately reimbursed by insurance and other payers. E
Energy balance	**5.12** For all people with overweight or obesity, behavioral modification to achieve and maintain a minimum weight loss of 5% is recommended. A
Eating patterns and macronutrient distribution	**5.13** There is no ideal macronutrient pattern for people with diabetes; meal plans should be individualized while keeping nutrient quality, total calorie, and metabolic goals in mind. E **5.14** A variety of eating patterns can be considered for the management of type 2 diabetes and to prevent diabetes in individuals with prediabetes. B **5.15** Reducing overall carbohydrate intake for individuals with diabetes has demonstrated the most evidence for improving glycemia and may be applied to a variety of eating patterns that meet individual needs and preferences. B
Carbohydrates	**5.16** Carbohydrate intake should emphasize nutrient-dense carbohydrate sources that are high in fiber (at least 14 g fiber per 1,000 kcal) and minimally processed. Eating plans should emphasize nonstarchy vegetables, fruits, legumes, and whole grains, as well as dairy products, with minimal added sugars. B **5.17** People with diabetes and those at risk are advised to replace sugar-sweetened beverages (including fruit juices) with water or low calorie, no calorie beverages as much as possible to manage glycemia and reduce risk for cardiometabolic disease B and minimize consumption of foods with added sugar that have the capacity to displace healthier, more nutrient-dense food choices. A **5.18** When using a flexible insulin therapy program, education on the glycemic impact of carbohydrate A, fat, and protein B should be tailored to an individual's needs and preferences and used to optimize mealtime insulin dosing. **5.19** When using fixed insulin doses, individuals should be provided with education about consistent patterns of carbohydrate intake with respect to time and amount while considering the insulin action time, as it can result in improved glycemia and reduce the risk for hypoglycemia. B
Protein	**5.20** In individuals with type 2 diabetes, ingested protein appears to increase insulin response without increasing plasma glucose concentrations. Therefore, carbohydrate sources high in protein should be avoided when trying to treat or prevent hypoglycemia. B
Dietary fat	**5.21** An eating plan emphasizing elements of a Mediterranean eating pattern rich in monounsaturated and polyunsaturated fats may be considered to improve glucose metabolism and lower cardiovascular disease risk. B **5.22** Eating foods rich in long-chain n-3 fatty acids, such as fatty fish (EPA and DHA) and nuts and seeds (ALA), is recommended to prevent or treat cardiovascular disease. B
Micronutrients and herbal supplements	**5.23** There is no clear evidence that dietary supplementation with vitamins, minerals (such as chromium and vitamin D), herbs, or spices (such as cinnamon or aloe vera) can improve outcomes in people with diabetes who do not have underlying deficiencies, and they are not generally recommended for glycemic control. C There may be evidence of harm for certain individuals with β carotene supplementation. B
Alcohol	**5.24** Adults with diabetes who drink alcohol should do so in moderation (no more than one drink per day for adult women and no more than two drinks per day for adult men). C **5.25** Educating people with diabetes about the signs, symptoms, and self-management of delayed hypoglycemia after drinking alcohol, especially when using insulin or insulin secretagogues, is recommended. The importance of glucose monitoring after drinking alcoholic beverages to reduce hypoglycemia risk should be emphasized. B
Sodium	**5.26** Sodium consumption should be limited to <2,300 mg/day. B
Nonnutritive sweeteners	**5.27** The use of nonnutritive sweeteners as a replacement for sugar-sweetened products may reduce overall calorie and carbohydrate intake as long as there is not a compensatory increase in energy intake from other sources. There is evidence that low- and no-calorie sweetened beverages are a viable alternative to water. B

Le attuali linee guida ADA suggeriscono un adeguato apporto dietetico abbinato a terapia insulinica intensiva.

Le diete chetogeniche (<55 g di carboidrati/die) nel T1DM meritano un'attenzione particolare. Benché molto popolari per perdere peso nelle persone obese, nel T1DM sono state sollevate preoccupazioni soprattutto riguardo ai rischi di ipoglicemia e di chetoacidosi.

Anche il digiuno intermittente, forma popolare di dieta per perdere peso, richiede attenzione nel T1DM per la necessità di aggiustamento della terapia per evitare l'ipoglicemia.

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Obesity in Patients with Type I Diabetes: Links, Risks and Management Challenges

Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2021:14

La componente principale di qualsiasi intervento dietetico sull'obesità, indipendentemente dalla presenza del diabete, è la riduzione dell'apporto calorico totale.

Una riduzione di energia nella dieta di 500–1000 kcal al giorno o del 25–30% dell'apporto calorico giornaliero può portare a una perdita di peso di 0,5 e 1 kg/settimana, equivalente a una perdita di peso superiore al 5% in un periodo medio di 6 mesi.

Nel T1DM è necessario concentrarsi sull'incoraggiare il consumo di carboidrati a basso indice glicemico e ad alto contenuto di fibre provenienti da verdure, legumi, frutta e cereali integrali ed evitare carboidrati raffinati, zuccheri aggiunti e alimenti altamente trasformati.

La dieta mediterranea è quella che meglio rappresenta un approccio equilibrato.

DIABETES, OBESITY AND METABOLISM
A JOURNAL OF PHARMACOLOGY AND THERAPEUTICS

ORIGINAL ARTICLE

Intensive multidisciplinary weight management in patients with type 1 diabetes and obesity: A one-year retrospective matched cohort study

Adham Mottalib MD, Shaheen Tomah MD, Samar Hafida MD, Taha Elseaidy BS, Megan Kasetty BS, Sahar Ashrafzadeh AB, Osama Hamdy MD

Programmi di intervento dietetico strutturati, ad alta intensità (con più di 14 sessioni in 6 mesi) nel contesto di un intervento completo sullo stile di vita sono la strategia più efficace, ottenendo perdite di peso del 5-10%.

ATTIVITA' FISICA

I benefici dell'attività fisica, cardiovascolari e sulla salute psicologica, sono molteplici e la sua promozione è fondamentale nella gestione dell'obesità e del T1DM.

Tuttavia, i pazienti con T1DM praticano meno attività fisica rispetto a quelli senza diabete e hanno la tendenza a vivere uno stile di vita sedentario che promuove lo sviluppo dell'obesità.

La sola attività fisica isolata come trattamento per l'obesità ha un effetto modesto sulla perdita di peso. Tuttavia, se associato ad una dieta, è in grado di diminuire la massa grassa e l'adiposità viscerale, mantenendo la massa magra e aumentando la sensibilità all'insulina.

Inoltre, l'esercizio fisico è utile nel ridurre il rischio di riprendere peso.

ATTIVITA' FISICA

L'obiettivo per bambini e adolescenti affetti da T1DM secondo le raccomandazioni ADA è di 60 minuti di attività aerobica quotidiana di intensità da moderata a intensa (camminare, fare jogging, ballare, pedalare, ecc.), con attività intense e di rafforzamento muscolare per almeno 3 giorni a settimana.

Per gli adulti, è si consigliano 150 minuti o più di attività aerobica di intensità da moderata a intensa a settimana, distribuiti su almeno 3 giorni/settimana e 2-3 sessioni/settimana di resistenza

Le stesse indicazioni possono essere date anche ai pazienti che sono affetti da obesità

ATTIVITA' FISICA

Il principale ostacolo all'esercizio fisico nel T1DM è la paura di una grave ipoglicemia.

La prescrizione dell'esercizio fisico deve essere individuale e dovrebbero essere presa in considerazione la partecipazione collaborativa di esperti della nutrizione e di professionisti dell'attività fisica per un migliore adattamento a situazione, caratteristiche e capacità funzionale del paziente, con l'obiettivo anche di migliorarne l'aderenza.

L'uso di nuove tecnologie come smartwatch e applicazioni per telefoni cellulari può contribuire a valutare e migliorare l'aderenza dei pazienti ai programmi di esercizi fisici.

5. Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes: *Standards of Care in Diabetes—2023*

Nuha A. ElSayed, Grazia Aleppo, Vanita R. Aroda, Raveendhara R. Bannuru, Florence M. Brown, Dennis Bruemmer, Billy S. Collins, Marisa E. Hilliard, Diana Isaacs, Eric L. Johnson, Scott Kahan, Kamlesh Khunti, Jose Leon, Sarah K. Lyons, Mary Lou Perry, Priya Prahalad, Richard E. Pratley, Jane Jeffrie Seley, Robert C. Stanton, Deborah Young-Hyman, and Robert A. Gabbay, on behalf of the American Diabetes Association

Diabetes Care 2023;46(Suppl. 1):S68–S96 | https://doi.org/10.2337/dc23-S005

SITTING/BREAKING UP PROLONGED SITTING

Limit sitting. Breaking up prolonged sitting (every 30 min) with short regular bouts of slow walking/simple resistance exercises can improve glucose metabolism.

STEPPING

- An increase of only 500 steps/day is associated with 2–9% decreased risk of cardiovascular morbidity and all-cause mortality.
- A 5- to 6-min brisk-intensity walk per day equates to ~4 years' greater life expectancy.

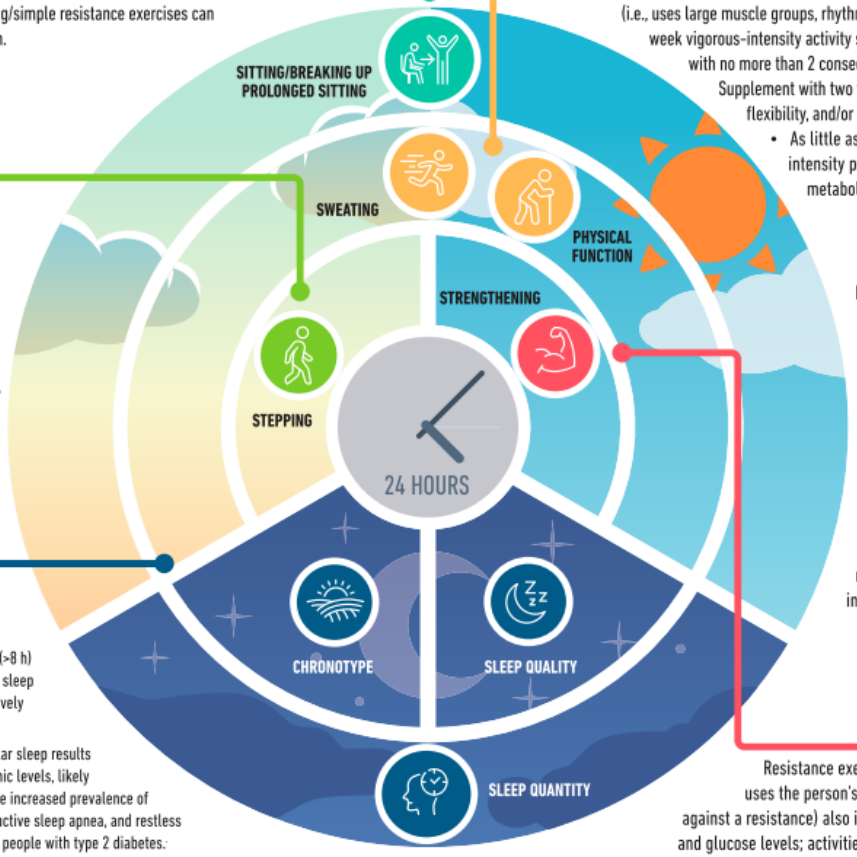
SLEEP

Aim for consistent, uninterrupted sleep, even on weekends.

Quantity – Long (>8 h) and short (<6 h) sleep durations negatively impact A1C.

Quality – Irregular sleep results in poorer glycemic levels, likely influenced by the increased prevalence of insomnia, obstructive sleep apnea, and restless leg syndrome in people with type 2 diabetes.

Chronotype – Evening chronotypes (i.e., night owl: go to bed late and get up late) may be more susceptible to inactivity and poorer glycemic levels vs. morning chronotypes (i.e., early bird: go to bed early and get up early).



SWEATING (MODERATE-TO-VIGOROUS ACTIVITY)

- Encourage ≥150 min/week of moderate-intensity physical activity (i.e., uses large muscle groups, rhythmic in nature) OR ≥75 min/week vigorous-intensity activity spread over ≥3 days/week, with no more than 2 consecutive days of inactivity. Supplement with two to three resistance, flexibility, and/or balance sessions.
  - As little as 30 min/week of moderate-intensity physical activity improves metabolic profiles.

Physical function/frailty/sarcopenia

- The frailty phenotype in type 2 diabetes is unique, often encompassing obesity alongside physical frailty, at an earlier age. The ability of people with type 2 diabetes to undertake simple functional exercises in middle age is similar to that in those over a decade older.

STRENGTHENING

Resistance exercise (i.e., any activity that uses the person's own body weight or works against a resistance) also improves insulin sensitivity and glucose levels; activities like tai chi and yoga also encompass elements of flexibility and balance.

Check for updates

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	Glucose/insulin	Blood pressure	A1C	Lipids	Physical function	Depression	Quality of life
SITTING/BREAKING UP PROLONGED SITTING	↓	↓	↓	↓	↑	↓	↑
STEPPING	↓	↓	↓	↓	↑	↓	↑
SWEATING (MODERATE-TO-VIGOROUS ACTIVITY)	↓	↓	↓	↓	↑	↓	↑
STRENGTHENING	↓	↓	↓	↓	↑	↓	↑
ADEQUATE SLEEP DURATION	↓	↓	↓	↓	?	↓	↑
GOOD SLEEP QUALITY	↓	↓	↓	↓	?	↓	↑
CHRONOTYPE/CONSISTENT TIMING	↓	?	↓	?	?	↓	?

IMPACT OF PHYSICAL BEHAVIORS ON CARDIOMETABOLIC HEALTH IN PEOPLE WITH TYPE 2 DIABETES

↑ **Higher levels/improvement** (physical function, quality of life); ↓ **Lower levels/improvement** (glucose/insulin, blood pressure, A1C, lipids, depression); ? no data available;
↑ **Green arrows = strong evidence;** ↑ **Yellow arrows = medium-strength evidence;** ↑ **Red arrows = limited evidence.**

Terapia psicologica

I pazienti in sovrappeso o obesi sono vulnerabili allo stigma e alla discriminazione sul posto di lavoro, a scuola, in ambito sanitario e nella società in generale, con conseguenti conseguenze psicologiche negative.

Table 5.2—Situations that warrant referral of a person with diabetes to a qualified behavioral or mental health professional for evaluation and treatment

- A positive screen on a validated screening tool for depressive symptoms, diabetes distress, anxiety, fear of hypoglycemia, or cognitive impairment
- The presence of symptoms or suspicions of disordered eating behavior, an eating disorder, or disrupted patterns of eating
- Intentional omission of insulin or oral medication to cause weight loss is identified
- A serious mental illness is suspected
- In youth and families with behavioral self-care difficulties, repeated hospitalizations for diabetic ketoacidosis, failure to achieve expected developmental milestones, or significant distress
- Declining or impaired ability to perform diabetes self-care behaviors
- Before undergoing bariatric or metabolic surgery and after surgery, if assessment reveals an ongoing need for adjustment support

Endocrine Practice 29 (2023) 849–854

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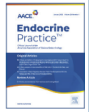

Original Article

Diabulimia: A Risky Trend Among Adults with Type 1 Diabetes Mellitus

Eric J. Ip, PharmD [1, 2], Shadi Doroudgar, PharmD [3], Aava Salehi, BS [3], Fojan Salehi, PharmD [2], Mitra Najmi, PharmD [3, *]

***Diabulimia** is an eating disorder in which patients with type I diabetes restrict insulin to lose weight*

Highlights

- Diabulimia is prevalent among adults with type 1 diabetes mellitus (1 in 11 of screened individuals)
- Diabulimia is linked with major depressive disorder, more hospital visits, and high A1C
- This study may help clinicians to identify patients who may be at risk of diabulimia

Clinical Relevance

Screening adults with type 1 diabetes mellitus for diabulimia is crucial, especially those with high A1C, history of depression, or recent diabetes-related emergency department visit or hospitalization. Health care professionals require increased awareness and training to detect diabulimia signs. Education regarding insulin misuse, alongside psychological support, is essential.

Pramlintide

Clinical Trial > Diabet Med. 2004 Nov;21(11):1204-12. doi: 10.1111/j.1464-5491.2004.01319.x.

Amylin replacement with pramlintide as an adjunct to insulin therapy improves long-term glycaemic and weight control in Type 1 diabetes mellitus: a 1-year, randomized controlled trial

R E Ratner [1], R Dickey, M Fineman, D G Maggs, L Shen, S A Strobel, C Weyer, O G Kolterman

A synthetic analogue of amylin, a hormone that is secreted together with insulin, pramlintide supplements the action of insulin by decreasing postprandial glucagon output, delaying gastric emptying and promoting satiety. Pramlintide contributes toglucose control during the postprandial period.

The Food and Drug Administration has officially approved pramlintide as the only drug that can be used as a additional therapy to insulin to treat patients with T1DM in United States, not in Europe.

Studies show that pramlintide as an add-on therapy to insulin for patients with type 1 diabetes brings beneficial effects such as improving glycaemic control, reducing insulin dose and body weight, while causing transient hypoglycemia and gastrointestinalside effects such as nausea, vomiting and anorexia at the beginning of treatment. There are limited data regarding the use of this drug in children with type 1 diabetes, but few studies show the beneficial effect of using such therapy in the pediatric population.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use SYMLIN safely and effectively. See full prescribing information for SYMLIN.

SYMLIN® (pramlintide acetate) injection for subcutaneous use
Initial U.S. Approval: 2005

WARNING: SEVERE HYPOGLYCEMIA
See full prescribing information for complete boxed warning.

- **SYMLIN use with insulin has been associated with an increased risk of severe hypoglycemia, particularly in patients with type 1 diabetes**
- **Hypoglycemia risk may be reduced by appropriate patient selection, careful patient instruction, and insulin dose reduction (5.1, 5.2)**

----------INDICATIONS AND USAGE----------

SYMLIN is an amylin analog indicated for patients with type 1 or type 2 diabetes who use mealtime insulin and have failed to achieve desired glycemic control despite optimal insulin therapy.

----------DOSAGE AND ADMINISTRATION----------

- Upon initiation of SYMLIN, reduce mealtime insulin dose by 50%. Monitor glucoses frequently and individualize subsequent insulin dose adjustments.
- Type 1 Diabetes: Start at 15 mcg subcutaneously before major meals. Increase in 15 mcg increments to a maximum premeal dose of 30 or 60 mcg; if not tolerated, reduce to 30 mcg, as tolerated (2.2).
- Type 2 Diabetes: Start at 60 mcg subcutaneously before major meals then increase to 120 mcg before meals, as tolerated (2.2).
- Wait at least 3 days between dose titrations to minimize nausea.

DIABETES, OBESITY AND METABOLISM
A JOURNAL OF PHARMACOLOGY AND THERAPEUTICS

ORIGINAL ARTICLE

A co-formulation of pramlintide and insulin A21G (ADO09) improves postprandial glucose and short-term control of mean glucose, time in range, and body weight versus insulin aspart in adults with type 1 diabetes

Grit Andersen MD, Rosy Eloy MD, Susanne Famulla PhD, Tim Heise MD, Grégory Meiffren PhD, Cyril Seroussi MSc, Martin Gaudier PhD, Claire Mégret PhD, You-Ping Chan PhD ... See all authors

First published: 12 January 2023 | https://doi.org/10.1111/dom.14972

Review
Type 1 Diabetes
Diabetes Metab J 2021;45:312-325
https://doi.org/10.4093/dmj.2020.0171
pISSN 2233-6079 · eISSN 2233-6087

dmj
DIABETES & METABOLISM JOURNAL
Check for updates

Non-Insulin Antidiabetes Treatment in Type 1 Diabetes Mellitus: A Systematic Review and Meta-Analysis

Xiaoling Cai[1], Chu Lin[1], Wenjia Yang[1], Lin Nie[2], Linong Ji[1]

Compared with placebo, in adjunct to insulin treatment, **Pramlintide** resulted in significant reduction in HbA1c (-0.26%; 95% CI, –0.41% to –0.11%; P<0.01), and in NS reduction in body weight (–1.18 kg; 95% CI, –2.31 to –0.04 kg; P=0.04), required a more decreased dosage of insulin change from baseline (- 8.25 unit/day), did not increase the risk of hypoglycemia and of ketoacidosis, did increase the risk of GI side effects.

Review
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DIABETES & METABOLISM JOURNAL
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Non-Insulin Antidiabetes Treatment in Type 1 Diabetes Mellitus: A Systematic Review and Meta-Analysis

Xiaoling Cai[1], Chu Lin[1], Wenjia Yang[1], Lin Nie[2], Linong Ji[1]

Compared with placebo, in adjunct to insulin treatment, **metformin** exhibited significant reduction in HbA1c (–0.29%; 95% CI, –0.50% to –0.08%; *P*<0.01) and body weight (–2.08 kg; 95% CI, –2.84 to –1.33 kg; *P*<0.01), required a more decreased dosage of insulin change from baseline (-4.83 unit/day), did not increase the risk of hypoglycemia and of ketoacidosis, did increase the risk of GI side effects.

Review
Type 1 Diabetes
Diabetes Metab J 2021;45:312-325
https://doi.org/10.4093/dmj.2020.0171
pISSN 2233-6079 · eISSN 2233-6087

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Compared with placebo, in adjunct to insulin treatment, **GLP-1RA** exhibited significant reduction in HbA1c (–0.19%; 95% CI, –0.29% to –0.1%; *P*<0.01) and body weight (–4.76 kg; 95% CI, –4.95 to –4.57 kg; *P*<0.01), required a more decreased dosage of insulin change from baseline (- 5.53 unit/day), did not increase the risk of hypoglycemia and of ketoacidosis, did increase the risk of GI side effects.

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Compared with placebo, in adjunct to insulin treatment, **alpha glucosidase inhibitors** exhibited significant reduction in HbA1c (–0.58%; 95% CI, -0.829% to –0.33%; *P*<0.01), but not in body weight (0.9 kg; 95% CI, –0.67 to 2.47 kg; *P=0.26*), did not show significant decrease in dosage of insulin change from baseline, did not increase the risk of hypoglycemia and of ketoacidosis , did increase the risk of GI side effects.

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Compared with placebo, in adjunct to insulin treatment, **thiazolidinedione** resulted in non-significant increases in HbA1c (WMD, 0.05%; 95% CI, –0.33% to 0.42%; P=0.81) and body weight (WMD, 0.99 kg; 95% CI, –1.10 to 3.09 kg; P=0.35), did not show significative decrease in dosage of insulin change from baseline.

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Compared with placebo, in adjunct to insulin treatment, **DPP-4i** led to non significant reduction in HbA1c –0.15%; 95% CI, –0.34% to 0.04%; P=0.13), and body weight (WMD, 0.1 kg; 95% CI, –0.94 to 1.14 kg; P=0.85), did not show significative decrease in dosage of insulin change from baseline, did not increase the risk of hypoglycemia, did increase the risk of GI side effects.

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Compared with placebo, in adjunct to insulin treatment, **SGLT-2i** conferred significant reduction in HbA1c (–0.42%; 95% CI, –0.47% to –0.37%; *P*<0.01) and body weight (–2.70 kg; 95% CI, –3.15 to –2.25 kg; *P*<0.01), required a more decreased dosage of insulin change from baseline (-5.95 unit/day), did not increase the risk of hypoglycemia, did increase the risk of ketoacidosis.

Table 2 Studies Analysing the Effects of Oral Glucose-Lowering Drugs as Adjuncts to Insulin Treatment in T1D

		n	Duration (Weeks)	Change in HbA_{1c} (%)	Change in Weight (kg)	Change in Insulin Dose
Biguanides						
REMOVAL[113]	Metformin 1000 mg	428	156	−0.13**	−1.17**	−0.05 IU/kg/d
GLP1a						
Lira-1[120]	Liraglutide 1.8 mg	100	24	−0.2	−6.80*	−0.1 IU/kg/d
ADJUNCT ONE[121]	Liraglutide 1.8 mg Liraglutide 1.2 mg Liraglutide 0.6 mg	1398	52	−0.2 ** −0.15* −0.09*	−4.90 ** −3.55** −2.19**	−5%* (ΔBL) −2% (ΔBL) +4% (ΔBL)
ADJUNCT TWO[122]	Liraglutide 1.8 mg Liraglutide 1.2 mg Liraglutide 0.6 mg	853	26	−0.35 ** −0.23** −0.24**	−5.10** −4.00** −2.50**	Ratio 0.90** Ratio 0.93** Ratio 0.95**
iSGLT2						
DEPICT-1[124]	Dapagliflozin 10 mg Dapagliflozin 5 mg	833	52	−0.36** (ΔBL) −0.33** (ΔBL)	−3.90** −2.56**	NR NR
DEPICT-2[125]	Dapagliflozin 10 mg Dapagliflozin 5 mg	815	24	−0.42** −0.37**	−3.74%† −3.21%†	−16.71% −11.19%
EASE-1[126]	Empagliflozin 25 mg Empagliflozin 10 mg Empagliflozin 2.5 mg	75	4	−0.53* −0.38** −0.49**	−1.90** −1.80** −1.50**	−0.07 IU/kg/d* −0.09 IU/kg/d * −0.08 IU/kg/d *
EASE-2[127]	Empagliflozin 25 mg Empagliflozin 10 mg	730	52	−0.45*** −0.39***	−3.60*** −3.20***	−12.9%*** −12.0%***
EASE-3[127]	Empagliflozin 25 mg Empagliflozin 10 mg Empagliflozin 2.5 mg	977	26	−0.52*** −0.45*** −0.28***	−3.40*** −3.00*** −1.80***	−12.6%*** −9.5%*** −6.4%***
InTandem1[128]	Sotagliflozin 400 mg Sotagliflozin 200 mg	793	52	−0.31** −0.25**	−4.34** −3.14**	−12.64%** −8.02**
InTandem1[129]	Sotagliflozin 400 mg Sotagliflozin 200 mg	782	52	−0.32%* −0.21%*	−2.18** −1.98**	−8.17%** −6.26%*
InTandem1[130]	Sotagliflozin 400 mg	1402	24	−0.46**	−2.98**	−5.3 UI/d **
Amylin mimetics						
Whitehouse et al[133] Edelman et al[134] Ratner et al[135]	Pramlintide 30μg or 60μg Pramlintide 30μg or 60μg Pramlintide 60μg or 90μg	480 296 651	52 29 52	−0.39** −0.19 −0.29**	NR −1.3***(ΔBL) NR	+2.3%* (ΔBL) −12% (ΔBL) NR

Notes: †Mean percent change. *p<0.05. **p<0.001. ***p<0.0001.
Abbreviations: ΔBL, change from baseline; NR, not reported.

Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy Dovepress
REVIEW

Obesity in Patients with Type 1 Diabetes: Links, Risks and Management Challenges

Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2021:14

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DOI: 10.1111/dom.15364

ORIGINAL ARTICLE

WILEY

Effect of the dual sodium-glucose co-transporter-1 and -2 inhibitor sotagliflozin on renal outcomes in type 1 diabetes and type 2 diabetes: A systematic review and meta-analysis of randomized controlled trials

Maria Anna Bantounou MPharm[1] | Panagiotis Sardellis BSc (Hons)[1] | Rosa Thuemmler BSc (Hons)[1] | Daniel Black Boada[1] | Justyna Kaczmarek BSc (Hons)[1] | Ribeya Mahmood BSc (Hons)[1] | Josip Plascevic BSc (Hons)[1] | Sam Philip MD[1,2]

Sotagliflozin, a sodium-glucose co-transporter-1 and -2 (SGLT1/2) inhibitor, increases renal glucose excretion through SGLT2 inhibition and inhibits intestinal glucose absorption by acting on the SGLT1 transporter, leading to additional glucose-lowering effects. It significantly reduced HbA1c, body weight, systolic blood pressure and the incidence of myocardial infarction and heart failure (HF) compared with placebo. Sotagliflozin had a favourable renal safety profile in both T1D and T2D participants, with or without pre-existing renal impairment.

Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy Dovepress
REVIEW

Obesity in Patients with Type 1 Diabetes: Links, Risks and Management Challenges

sity: Targets and Therapy 2021:14

Table 1 Anti-Obesity Pharmacological Therapy in Randomised Clinical Trials (>1 Year of Duration), Including Subjects with Type 2 Diabetes

	Duration (Years)	Participants (n)	Weight Loss		≥5% Weight Loss		Dropouts	Side Effects	Contraindications
			Drug	Placebo	Drug	Placebo			
Orlistat[92] Meta-analysis	1–4	6196	−6.4%	−3.5%	54%	33%	≈ 30%	Oily spotting, flatus with discharge, diarrhea, fecal urgency	Chronic malabsorption syndrome, cholestasis and oxalate nephrolithiasis
Naltrexone-Bupropion								Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, and diarrhea	Uncontrolled hypertension, seizures, eating disorders, chronic opioid use, concurrent use with monoamine oxidase inhibitors within 14 days
COR-1[93]	1	1742	−6.1%	−1.3%	48.0%	16.0%	50%		
COR-2[94]	1	1496	−6.4%	−1.2%	50.5%	17.1%	46%		
COR-BMOD[95]	1	793	−9.3%	−5.1%	66.4%	42.5%	48%		
COR-DIABETES[96]	1	505	−5.0%	−1.8%	44.1%	26.3%	48%		
Liraglutide 3.0 mg (SCALE studies)[101]								Nausea, vomiting, constipation or diarrhea	Personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia type 2
Obesity/ prediabetes[102]	1	3731	−8.0%	−2.0%	63.2%	27.1%	18%		
	3	2254	-6.1%	-1.9%	49.6%	23.7%	47.4%		
Maintenance diabetes[104]	1	422	-6.2%	-0.2%	50.5%	21.2%	25%		
	1	846	-6.0%	-2.0%	69.2%	27.2%	26.7%		

Sebbene i farmaci antiobesità non siano controindicati nel T1DM, i dati sul loro utilizzo in questi pazienti non esistono poiché sono stati esclusi dai principali studi.

International Journal of Obesity

REVIEW ARTICLE OPEN

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✉]

Table 1. An overview of ongoing, recruiting, and upcoming trials of anti-obesity medications as adjunct therapies in T1D.

Adjunct medication	ClinicalTrials.gov identifier	Phase(s)	Age inclusion (years)	Estimated sample size	BMI inclusion (kg/m^2)	Other intervention(s)	Placebo-controlled	Primary outcome	
								Measure(s)	Timeframe
GLP1-RA									
GLP1	NCT04355832[b]	1	18–50	40	<40	/	✓	Catecholamines levels	3 years
Liraglutide	NCT02516657[c]	3	15–21	5	NR	/		Mean weekly blood glucose	2 weeks
Liraglutide	NCT03011021[b]	1 and 2	≥18	40	NR	Umbilical cord blood-T regulatory cells infusion [biological]		Adverse events and signs of toxicity	2 years
Liraglutide	NCT05794581[b]	1	18–65	24	25–35	CT-868 [dual GLP1 and GIP receptor modulator]	✓	Area under the curve in glucose metabolism	Up to 4 days
Liraglutide	NCT03182426[c]	1 and 2	18–45	60	<35	Plerixafor, Alemtuzumab Anakinra Etanercept		C-peptide area under curve and serious adverse event rate	3, 6, 9, 12, 18 and 24 months
Semaglutide	NCT05537233[b]	2	18–60	80	≥30		✓	Continuous glucose monitoring-measured time in range >70% with time below range of <4% and reduction in body weight by 5%	26 weeks
Semaglutide	NCT05819138[b]	3	18–40	60	20–35		✓	Central and peripheral arterial stiffness	4 weeks
Semaglutide	NCT05822609[a]	2	≥18	60	NR		✓	Kidney cortical relaxation rate	26 weeks
Semaglutide	NCT05205928[b]	2 and 3	≥18	28	≥22	Closed-loop insulin system	✓	Percentage of time of plasma glucose levels spent in target range (3.9 to 10.0 mmol/L)	4 weeks
Dulaglutide	NCT05478707[a]	2	18–40	64	19–27	Exercise training	✓	Microvascular blood volume	14 weeks
SGLT2 inhibitor									
Sotagliflozin	NCT05696366[a]	1 and 2	18–70	22	18.5–35	Volagidemab	✓	HbA1c changes	12 weeks
Dapagliflozin	NCT05541484[b]	4	18–75	20	NR	Biosense breath ketone analyser		Blood and breath ketone levels	4 weeks
Dapagliflozin	NCT04333823[b]	3	12–18	100	Within 99.9th percentile	/	✓	Glomerular filtration rate	16 weeks
Dapagliflozin	NCT04049110[b]	3	18–65	24	20–29	/		Mean amplitude of Glucose Excursions upon exercise	From completion of physical exercise at day 7 of each intervention period to 72 h after
Dapagliflozin	NCT03878459[b]	4	≥18	120	NR	Pioglitazone,	✓	HbA1c change	28 weeks
GLP1-RA + SGLT2 inhibitor									
Liraglutide, semaglutide, dapagliflozin	NCT05390307[a]	N/A	21–65	60	≥25	Intensive nutrition, bariatric surgery, and usual care		Weight change	26 weeks
Semaglutide, dapagliflozin	NCT03899402[b]	2 and 3	18–75	114	≥25	Insulin	✓	HbA1c change	6 months

CHIRURGIA BARIATRICA

› Obes Surg. 2022 Dec;32(12):3992-4006. doi: 10.1007/s11695-022-06321-4. Epub 2022 Oct 22.

Choice of Bariatric Surgery in Patients with Obesity and Type 1 Diabetes Mellitus? an Up-to-Date Systematic Review

30 studi, età media 40 anni, BMI 40.9 kg/m2, calo ponderale medio del 74.6% a 6 mesi. Riduzione della media giornaliera di insulina da una media di 92.3 IU/day pre- intervento a 35.8 IU/day post-intervento.

Le procedure chirurgiche più usate sono la Sleeve gastrectomy e la Roux-en-Y Gastric Bypass (RYGB). Vi è un miglioramento in pertensione arteriosa (42,8%), dislipidemia (25%), OSAS (66%), microalbuminuria (25%).

Particolare attenzione va posta al rischio di ipoglicemia (28,6%) e di chetoacidosi (25%), gestiti in team multidisciplinare.

Although surgery has been shown to improve the metabolic profiles of people with type 1 diabetes, larger and longer term studies are needed to determine the role of metabolic surgery in such individuals

8. Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes: *Standards of Care in Diabetes—2023*

Diabetes Care 2023;46(Suppl. 1):S128–S139 | https://doi.org/10.2337/dc23-S008

International Journal of Obesity

REVIEW ARTICLE OPEN

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✉]

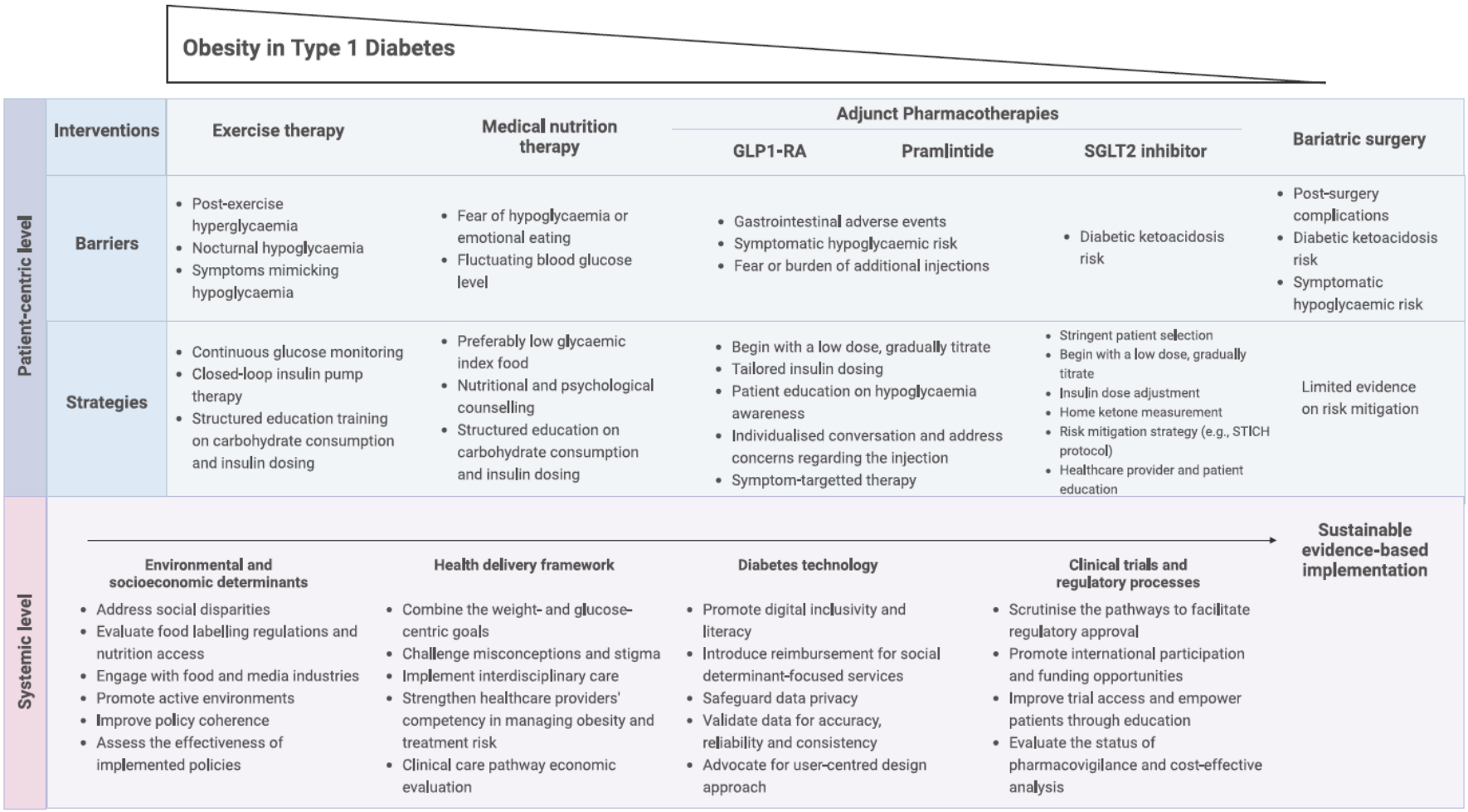
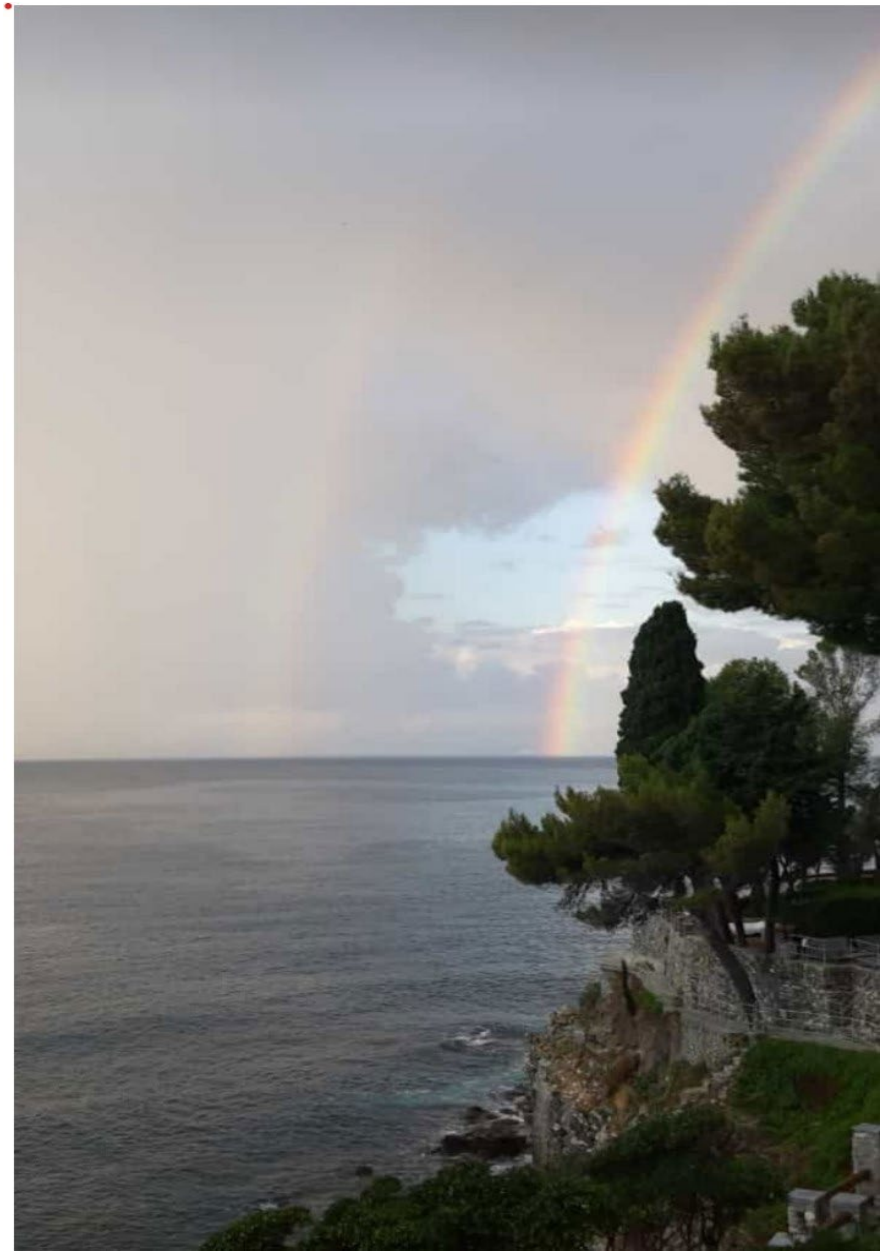


Fig. 2 An overview of the barriers and strategies for different weight management interventions, and proposed systemic-level strategies.



Grazie per l'attenzione