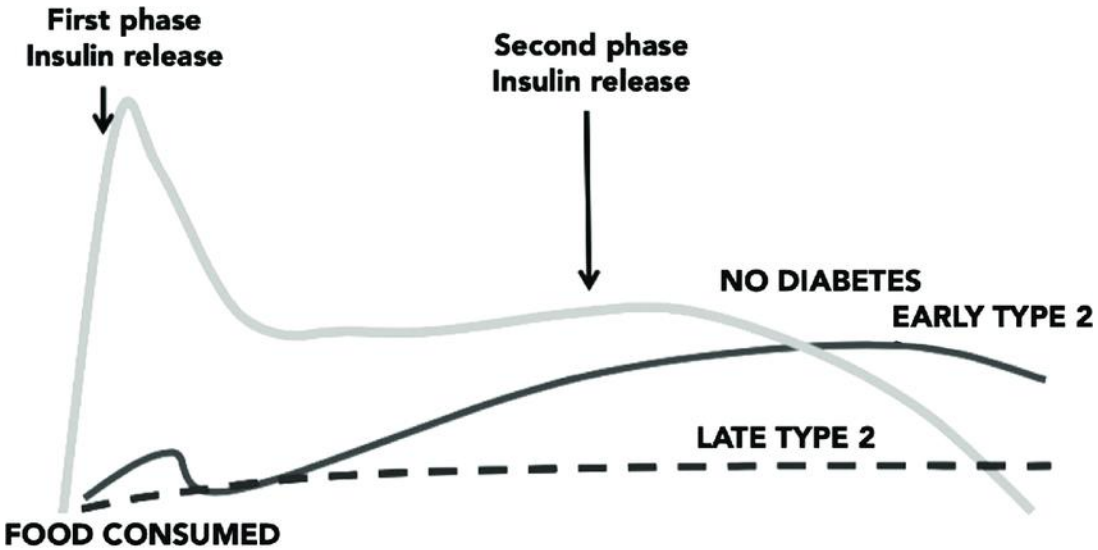
Diagnosis and Treatment of Type 2 Diabetes in Adults
A Review

The number of people with diabetes worldwide was estimated to be between 589 million and 828 million during 2022 to 2024,[1,2] with type 2 diabetes comprising 90% to 95% of cases.[1,3,4] Insulin resistance may be present for 10 years or longer prior to diagnosis.[5] Although the global prevalence is rising (estimates range from 11%-14% of adult population), the incidence of type 2 diabetes has stabilized or decreased in most places worldwide.[6,7] The prevalence of diabetes in US adults is 15.8%.[4] In individuals with prediabetes, type 2 diabetes can be prevented or delayed with changes in health behaviors that lead to weight loss or pharmacotherapy.[8]

Risk factors for type 2 diabetes include overweight and obesity, physical inactivity, age, family history, race and ethnicity, history of gestational diabetes, and presence of other conditions (eg, hypertension, dyslipidemia, cardiovascular disease).[9-14] More than 600 genetic variants are associated with an increased risk of type 2 diabetes.[15] Although body mass index has a stronger association with type 2 diabetes than genetic risk scores,[16] approximately 10% of individuals with type 2 diabetes do not have overweight or obesity.[3]

Globally, 32.2% of people with type 2 diabetes have cardiovascular disease.[17] In the US, 1 in 10 individuals with diabetes have severe vision loss or blindness.[3] Diabetes is a leading cause of kidney failure, nontraumatic lower extremity amputation, and death (30.4 deaths per 100 000 population).[3,18] Diabetes-related comorbidities also include metabolic dysfunction–associated steatotic liver disease,[19] cancers such as colorectal and breast,[20] and dementia.[21]

secretion from pancreatic β-cells, following a two-phase pattern. The first phase, occurring in the first 10 min after carbohydrate ingestion, represents the release of pre-stored insulin from islet vesicles whereas the second phase, occurring during the subsequent 2–3 h, is characterized by the release of newly synthesized insulin and replenishment of islet cell insulin stores[19]. High levels of insulin mainly stimulate skeletal muscle glucose uptake and storage as glycogen but also favour NEFA uptake and esterification to triglycerides in adipose tissue. Hyperinsulinaemia, along with suppression of glucagon, by insulin and incretins, such as glucagon-like peptide 1 (GLP1) and glucose-dependent insulinotropic polypeptide (GIP)[20–22], favour hepatic glycogen storage and decrease gluconeogenesis, collectively reducing endogenous glucose production and maintaining normoglycaemia. At a cellular level, insulin action allows for the uptake of glucose, amino acids, and NEFA and the synthesis of storage forms of these metabolites such as glycogen, proteins and triglycerides, respectively. During meal ingestion or an OGTT, skeletal muscle accounts for the vast majority of glucose uptake and non-oxidative storage as glycogen[18]. The interaction of insulin with its receptor initiates a cascade of phosphorylation events, ultimately activating AKT (protein kinase B), which collectively favours the recruitment of intracellular vesicles containing glucose transporters (GLUT4) to the cell membrane, thereby stimulating glucose uptake (Fig. 2). In parallel, activated AKT2 inhibits glycogen synthase kinase (GSK3α/β), leading to disinhibition of glycogen synthase and stimulation of glycogen synthesis from glucose-6-phosphate[18,23–26].



Sinais e sintomas TÍPICOS de hiperglicemia
• Poliúria • Polidipsia • Polifagia • Perda de peso inexplicada • Desidratação
Sinais e sintomas SUGESTIVOS de hiperglicemia
• Noctúria • Visão turva • Cansaço • Infecções recorrentes (Candidíase e Periodontite) • Má cicatrização de feridas • Albuminúria transitória em pacientes com DM1 com menos de 5 anos de doença

Tabela 1. Critérios laboratoriais para diagnóstico de DM e pré-diabetes.

Critérios	Normal	Pré-diabetes	DM
Glicemia de jejum (mg/dl)	< 100	100-125	≥ 126
Glicemia ao acaso (mg/dl) + sintomas	-	-	≥ 200
Glicemia de 1 hora no TTGO (mg/dl)	< 155	155-208	≥ 209
Glicemia de 2 horas no TTGO (mg/dl)	< 140	140-199	≥ 200
HbA1c (%)	< 5,7	5,7-6,4	≥ 6,5

AVALIAÇÃO DE RISCO DE DIABETES TIPO 2

Circule a alternativa correta e some os seus pontos.

1. Idade

0 p. Abaixo de 45 anos
2 p. Entre 45-54 anos
3 p. Entre 55-64 anos
4 p. Acima de 64 anos

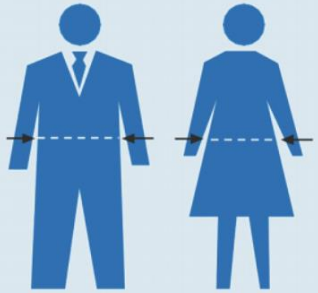
2. Índice de massa corporal (IMC)

(Ver verso do formulário)

0 p. Abaixo de 25kg/m²
1 p. 25-30kg/m²
3 p. Acima de 30kg/m²

3. Circunferência da cintura medida abaixo das costelas (geralmente na altura do umbigo)

	HOMENS	MULHERES
0 p.	Menor que 94 cm	Menor que 80 cm
3 p.	94-102 cm	80-88 cm
4 p.	Maior que 102 cm	Maior que 88 cm



4. Você pratica pelo menos 30 minutos de atividade física diária no trabalho e/ou durante o horário de lazer (incluindo as atividades diárias normais)?

0 p. Sim
2 p. Não

5. Com que frequência você come legumes, verduras, frutas ou grãos?

0 p. Todos os dias
1 p. Não todos os dias

6. Você já tomou regularmente algum medicamento para pressão alta?

0 p. Não
2 p. Sim

7. Alguma vez você já apresentou glicose alta no sangue (por exemplo, em um exame médico de rotina, durante uma doença, durante gravidez)?

0 p. Não
5 p. Sim

8. Algum membro de sua família ou parente próximo já foi diagnosticado com diabetes (tipo 1 ou tipo 2)?

0 p. Não
3 p. Sim: avós, tia, tio ou primo de 1° grau (exceto pai, mãe, irmão, irmã ou filhos)
5 p. Sim: pai, mãe, irmão, irmã ou filho

Pontuação Total de Risco

☐ **O risco de desenvolver diabetes tipo 2 em 10 anos é:**

Menor que 7	**Baixo**: cerca de 1 em cada 100 pessoas irá desenvolver a doença
7-11	**Levemente elevado**: cerca de 1 em cada 25 pessoas irá desenvolver a doença
12-14	**Moderado**: cerca de 1 em cada 6 pessoas irá desenvolver a doença
15-20	**Alto**: cerca de 1 em cada 3 pessoas irá desenvolver a doença
Maior que 20	**Muito alto**: cerca de 1 em cada 2 pessoas irá desenvolver a doença

Indicações para rastreamento de DM2 em adultos assintomáticos[2]

• Idade acima de 35 anos (universal)
• Idade abaixo de 35 anos com sobrepeso ou obesidade, e mais um fator de risco
  • História familiar de DM2 em parente de primeiro grau
  • História de doença cardiovascular
  • Hipertensão arterial
  • HDL abaixo de 35 mg/dl
  • Triglicerídeos acima de 250 mg/dl
  • Síndrome de ovários policísticos
  • Acantose nigricans
  • Sedentarismo
• Pré-diabetes em exame prévio
• Diabetes gestacional prévio ou recém-nato grande para idade gestacional
• FINDRISC alto ou muito alto

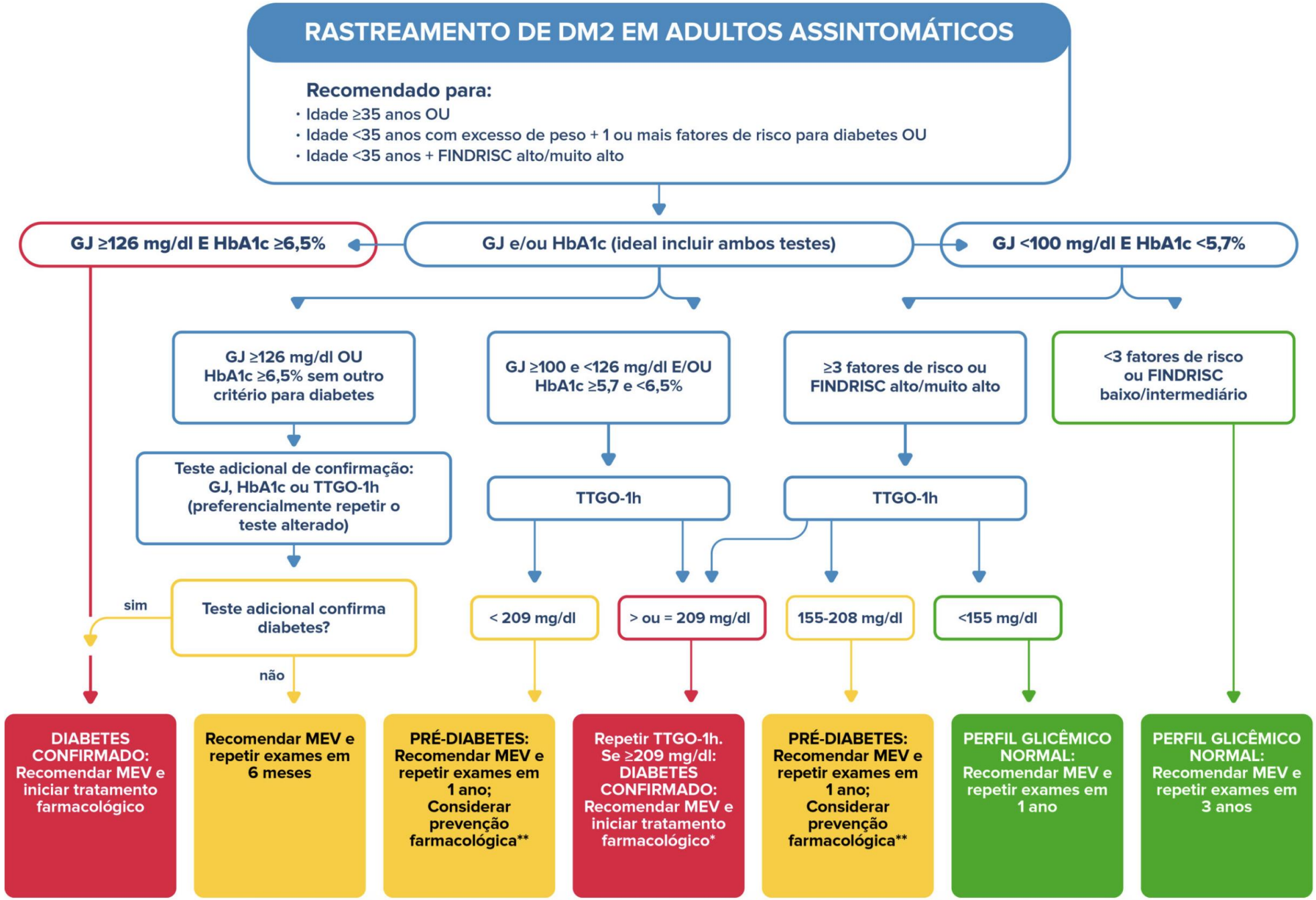
Tabela 2. Rastreamento inicial do DM em indivíduos assintomáticos no Brasil

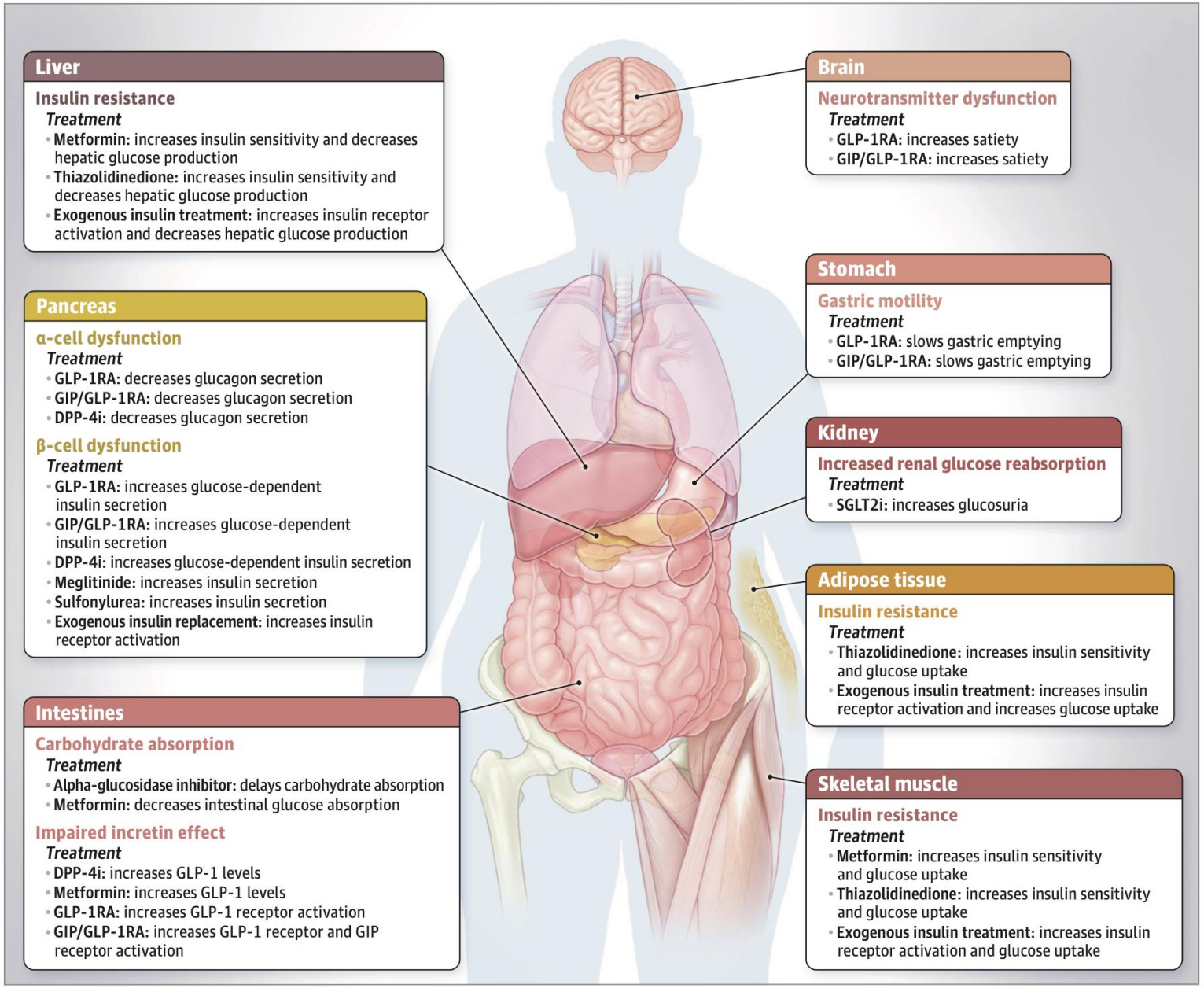
Locais com viabilidade financeira e disponibilidade técnica total	**Locais com viabilidade financeira e disponibilidade técnica parciais**
Medida simultânea da glicemia plasmática e HbA1c em amostra de sangue obtida em jejum de 8 a 12 horas	Medida da glicemia plasmática em amostra de sangue obtida em jejum de 8 a 12 horas

R9. No rastreamento do DM2, se houver glicemia de jejum menor a 100 mg/dl e HbA1c menor que 5,7% em pessoas com 3 ou mais fatores de risco ou FINDRISC alto/muito alto, **É RECOMENDADO** realizar o TTGO-1h para complementar a investigação de DM e pré-diabetes.

Tabela 3. Frequência de repetição do rastreamento de DM2 conforme a situação clínica apresentada na investigação inicial

Situação clínica	**Frequência de rastreamento de DM2**
Pessoas sem sintomas e com apenas um exame preenchendo critérios para DM.	Semestral
Pessoas com pré-diabetes confirmada.	Anual
Pessoas com exames normais e ≥ 3 fatores de risco.	Anual
Pessoas com exames normais e FINDRISC alto/muito alto.	Anual
Pessoas com exames normais e < 3 fatores de risco.	Trianual
Pessoas com exames normais e FINDRISC baixo/moderado.	Trianual


RASTREAMENTO DE DM2 EM ADULTOS ASSINTOMÁTICOS
Recomendado para:
• Idade ≥35 anos OU
• Idade <35 anos com excesso de peso + 1 ou mais fatores de risco para diabetes OU
• Idade <35 anos + FINDRISC alto/muito alto
GJ ≥126 mg/dl E HbA1c ≥6,5%
GJ e/ou HbA1c (ideal incluir ambos testes)
GJ <100 mg/dl E HbA1c <5,7%
GJ ≥126 mg/dl OU HbA1c ≥6,5% sem outro critério para diabetes
GJ ≥100 e <126 mg/dl E/OU HbA1c ≥5,7 e <6,5%
≥3 fatores de risco ou FINDRISC alto/muito alto
<3 fatores de risco ou FINDRISC baixo/intermediário
Teste adicional de confirmação: GJ, HbA1c ou TTGO-1h (preferencialmente repetir o teste alterado)
TTGO-1h
TTGO-1h
sim
Teste adicional confirma diabetes?
não
< 209 mg/dl
> ou = 209 mg/dl
155-208 mg/dl
<155 mg/dl
DIABETES CONFIRMADO: Recomendar MEV e iniciar tratamento farmacológico
Recomendar MEV e repetir exames em 6 meses
PRÉ-DIABETES: Recomendar MEV e repetir exames em 1 ano; Considerar prevenção farmacológica**
Repetir TTGO-1h. Se ≥209 mg/dl: DIABETES CONFIRMADO: Recomendar MEV e iniciar tratamento farmacológico*
PRÉ-DIABETES: Recomendar MEV e repetir exames em 1 ano; Considerar prevenção farmacológica**
PERFIL GLICÊMICO NORMAL: Recomendar MEV e repetir exames em 1 ano
PERFIL GLICÊMICO NORMAL: Recomendar MEV e repetir exames em 3 anos



There are multiple pathophysiological defects in various organs that contribute to the development of hyperglycemia in type 2 diabetes.[54] Different classes of glucose-lowering medications are currently available, each with specific mechanisms of action to lower blood glucose that target these defects. Commonly used medication for type 2 diabetes are included. DPP-4i indicates dipeptidyl peptidase-4 inhibitor; GIP/GLP-1RA, glucose-dependent insulinotropic polypeptide/ glucagon-like peptide-1 receptor agonist; GLP-1RA, glucagon-like peptide-1 receptor agonist; SGLT2i, sodium-glucose cotransporter 2 inhibitor.

In a 4-year retrospective observational study including 669 individuals with obesity and prediabetes (defined as HbA1c ≥5.7% and <6.5%) who underwent metabolic surgery[181], the respective remission rates of prediabetes, that is, return to normoglycaemia, were 82%, 73%, 66% and 58% in the first, second, third and fourth years, respectively. Older patients (49–67 years of age) had lower odds of prediabetes remission from the third year of follow-up than younger patients (19–38 years of age).

In a study in the USA that compared the effects of metabolic surgery versus usual care on the incidence of T2DM in individuals with obesity aged 21–65 years[184], 3,060 met criteria for prediabetes at baseline. The usual-care group had a relative risk of progressing to T2DM of 33.7 at 1 year (95% CI 13.8–82.2) and 138.8 at 3 years (95% CI 19.3–992.7) compared with the surgical group.

Long-term studies also support the cost-effectiveness of metabolic surgery compared with lifestyle intervention and medications. This is mainly due to sustained effects on weight loss with avoidance of escalating treatment and drug costs. Progression rates to T2DM were lower 5 years postoperatively in patients who lost >25% of their baseline weight than in those who lost <15% of their weight during the first postoperative year (4.7% versus 14.0%; P <0.001)[185]. This progression was independent of baseline weight, age and sex.

Category	Type 2 diabetes	Type 1 diabetes	Monogenic diabetes syndromes (ie, MODY)	Types of diabetes secondary to other medical conditions
Epidemiology[a]	90%-95%	5%-10%	<5%	<5%
Pathophysiology	Nonautoimmune progressive loss of insulin secretion from β cells, usually in the setting of insulin resistance	Autoimmune β-cell destruction, usually leading to absolute or near-absolute insulin deficiency	Rare form of diabetes caused by a variant in a single gene disrupting β-cell glucose sensing or insulin production, inherited in an autosomal dominant manner; the most common forms are GCK-MODY (MODY2; glucose-sensing defect), HNF1A-MODY (MODY3), and HNF4A-MODY (MODY1)	Many different secondary forms of diabetes exist; examples include diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), diabetes due to endocrinopathies such as Cushing syndrome or acromegaly, or diabetes secondary to SARS-CoV-2 infection
Age at diagnosis	Usually ≥35 y but increasingly seen in youth and younger adults, especially in the setting of obesity and/or family history	Can occur in adults at any age, often with more indolent onset compared with children (termed *latent autoimmune diabetes in adults*)	Usually <25 y	Any age
Degree of hyperglycemia on presentation	Usually mild (blood glucose <250 mg/dL) if detected early; however, can be moderate or severe in long-standing undiagnosed diabetes.	Usually moderate (blood glucose of 250-600 mg/dL); can be severe (blood glucose >600 mg/dL) in some cases	Mild; usually HbA_{1C} <7.5% at diagnosis	Mild, moderate, or severe
Symptoms	Can be asymptomatic or with symptoms	Usually with catabolic symptoms (polyuria, polydipsia, weight loss); can be asymptomatic in adults	Usually asymptomatic	Can be asymptomatic or with symptoms
BMI	Usually BMI ≥25	Usually BMI <25, but can be diagnosed in those with overweight or obesity	Variable, but obesity usually not present	Any
Family history	Often a first-degree relative with type 2 diabetes, but not always	Sometimes a first-degree relative with type 1 diabetes or other autoimmune disease; 85% have no family history	Autosomal dominant family history, confirmed to be MODY diabetes	Not usually
Diabetic ketoacidosis	Can be seen on presentation in those with severe insulin deficiency or glucotoxicity (termed *ketosis-prone type 2 diabetes*); euglycemic diabetic ketoacidosis has been described in individuals taking SGLT2is	Ketoacidosis common on presentation in children; variable on presentation in adults	Unlikely	Rare; has been reported with SARS-CoV-2 infection and can occur with severe pancreatitis
Autoantibodies present	Not usually seen, but can be present in up to 10% of individuals, depending on the population	Common, but 5%-10% will not have antibodies present on diagnosis, and levels can wane over time; the following antibodies are often tested: glutamic acid decarboxylase (GAD), islet tyrosine phosphatase-related islet antigen 2 (IA-2), zinc transporter 8 (ZnT8) and/or insulin autoantibodies (IAA)	Unlikely	Unlikely
Race and ethnicity	Any; more common in Asian American and Pacific Islander, Black, Latino, and Native American individuals than White individuals	Any; more common with European ancestry	Any; most described in populations of European ancestry	Any
Genetic testing	Not commercially available	Not commercially available; currently only in research studies	Yes; required for definitive diagnosis	Not commercially available
Duration prior to diagnosis	Long (years)	Short (months)	Long (years; potentially lifelong undiagnosed in mild cases)	Variable
Stimulated C-peptide[b]	Detectable	Low or undetectable (<200 pmol/L); may be detectable soon after diagnosis or for prolonged duration in adult-onset	Detectable	Variable
Drugs that may exacerbate or contribute to development of diabetes	Long-term glucocorticoids, use of immunosuppressant drugs after organ transplant such as tacrolimus and cyclosporine (ie, new-onset diabetes after transplant),[c] and second-generation antipsychotics such as olanzapine and clozapine[d]	Immune checkpoint inhibitors such as nivolumab and pembrolizumab (for cancer)	None	Antiretroviral therapies (ie, certain protease inhibitors and nucleoside reverse transcriptase inhibitors) in people with HIV[d]; glucocorticoid treatment with active COVID-19

Study; country; year	Prediabetes phenotype	Baseline BMI mean (kg/m^2) (s.d.); study size	Mean follow-up	Study groups	Relative risk reduction for T2DM (95% CI)	Absolute risk reduction for T2DM
TRIPOD; USA; 2002	IGT (women with history of gestational diabetes)	30 (5.7); 266	2.5 years	Troglitazone vs placebo	55% (17–75)	12.1% vs 5.4%
STOP-NIDDM; multinational; 2002	IGT and IFG	31 (4.2); 1,429	3.3 years	Acarbose vs placebo	25% (10–37)	42% vs 32%
DPP; USA; 2002	IGT and IFG	34 (6.7); 3,234	2.8 years	Metformin vs placebo	31% (17–43)	11.0% vs 7.8%
DPP; USA; 2005	IGT	NR; 585	0.9 years	Troglitazone vs placebo	75% (NR)	3.0% vs 12.0%
XENDOS; multinational; 2006	Normal glucose regulation and IGT	37 (4.4); 3,305	4 years	Orlistat vs placebo	37% (14–54)	9% vs 6.2%
Indian DPP-1; India; 2006	IGT	25.8 (3.5); 531	2.5 years	Metformin vs placebo	26.4% (19.1–35.1)	55.0% vs 40.5%
Indian DPP-2; India; 2006	IGT	25.9 (3.3); 407	3 years	Pioglitazone vs placebo	2% (–44 to 33)	31.6% vs 29.8%
DREAM; multinational; 2006	IGT and IFG	30.9 (5.6); 5,269	3 years	Rosiglitazone vs placebo	62% (56–67)	25.0% vs 10.6%
DREAM; multinational; 2006	IGT and IFG	30.9 (5.6); 5,269	3 years	Ramipril vs placebo	9% (–3 to 20)	19.5% vs 18.1%
Voglibose Trial; Japan; 2006	IGT	25.8 (3.8); 1,780	0.9 years	Voglibose vs placebo	40% (18–57)	17% vs 8%
NAVIGATOR; multinational; 2010	IGT and IFG	30.5 (5.4); 9,306	5 years	Nateglinide vs placebo	–7% (–15 to 0)	34% vs 34%
NAVIGATOR; multinational; 2010	IGT and IFG	30.5 (5.4); 9,306	5 years	Valsartan vs placebo	14% (8–20)	36.8% vs 33.1%
ACT NOW; USA; 2010	IGT	33.7 (s.e. 0.4); 602	2.4 years	Pioglitazone vs placebo	72% (51–84)	7.6% vs 2.1%
CANOE; Canada; 2010	IGT	31.7 (27.1–36.8); 207	3.9 years	Metformin and rosiglitazone vs placebo	66% (41–80)	39% vs 14%
ACE; China and Hong Kong; 2010	IGT	24.5 (3.1); 6,522	5 years	Acarbose vs placebo	18% (6–29)	3.8% vs 3.2%
SCALE; multinational; 2010	IGT and IFG	38.9 (6.4); 2,254	3 years	Liraglutide vs placebo	79% (66–87)	6% vs 2%
STEP-I; multinational; 2021	HbA1c <6.4	>30; 1,961	1.3 years	Semaglutide	NA	Regression to normoglycaemia: 84.1% vs 47.8%
SURMOUNT; multinational; 2025	(2 of 3 criteria HbA1c, fasting plasma glucose, OGTT)	38.8 (7.1); 2,539 (1,032 with prediabetes)	3 years	Tirzepatide vs placebo	NR	13.3% vs 1.3%

guidelines recommend metformin as the first medication in those without cardiovascular comorbidities (ie, atherosclerotic cardiovascular disease or heart failure) or chronic kidney disease. This recommendation is based on the high glycemic efficacy, low hypoglycemia risk, general tolerability, and low cost of metformin.[84] The major barrier to use of metformin is gastrointestinal adverse effects such as diarrhea (**Table 2**), which may be ameliorated by slow dose titration (eg, starting with 500 mg once daily followed by gradual dose escalation by 500 mg every week until target dose is reached)[89] or switching to an extended-release formulation. A meta-analysis of 15 randomized clinical trials (N = 3765) reported that extended-release metformin was associated with a nonsignificant reduction in gastrointestinal adverse effects compared with immediate-release metformin (24.6% vs 28.1%; odds ratio, 0.76 [95% CI, 0.58-1.00]).[90]

Drug (glucose-lowering dose)	Glucose-lowering efficacy[55,56,b]	Impact on weight[56,57,c]	Hypoglycemia risk as monotherapy	Impact on comorbidities[d]	Cost[58,f]	Common adverse effects[59,g,e]	Practical considerations[59]
Alpha-glucosidase inhibitors: Acarbose (25-100 mg orally at each meal) Miglitol (25-100 mg orally at each meal)	Intermediate (0.5%)	Neutral	No	Atherosclerotic cardiovascular disease: neutral[8] HF[5]: neutral[85]	$-$$$	Most common adverse effects: abdominal pain (12%-19%), diarrhea (29%-31%), elevated transaminases (14% [acarbose]), flatulence (42%-74%) Contraindications :cirrhosis, inflammatory bowel disease, colonic ulceration, intestinal obstruction, hypersensitivity Warnings/precautions: hypoglycemia (add-on to sulfonylurea and/or insulin); use oral glucose (not sucrose) to treat hypoglycemia	When to use Add-on treatment in individuals who require intermediate levels of HbA_{1C} lowering (0.5%-1% above target); not as commonly used due to gastrointestinal adverse effects Can reduce postprandial hyperglycemia Dosing considerations: Take only when eating Start low dose, titrate slowly to minimize gastrointestinal adverse effects
Biguanides: Metformin (500-2000 mg orally daily)	High (1.0%-2.0%)	Neutral (potential for modest weight loss)	No	Atherosclerotic cardiovascular disease: likely long-term benefit[38,60] Chronic kidney disease: neutral HF: neutral	$	Most common adverse effects[h]: diarrhea (10%-53%), nausea/vomiting (7%-26%), abdominal discomfort (1%-6%) Contraindications: estimated glomerular filtration rate <30 mL/min/1.73 m^2, acute or chronic metabolic acidosis, hypersensitivity Warnings/precautions: vitamin B12 deficiency, lactic acidosis	When to use First-line treatment when initial HbA_{1C} <9%-10% and in absence of life-threatening hyperglycemic crisis (ie, diabetic ketoacidosis or hyperosmolar hyperglycemic state) Can be used at reduced doses (ie, 1000 mg) with estimated glomerular filtration rate 30-45 mL/min/1.73m^2 If gastrointestinal symptoms develop Hold or reduce dose to assess the relationship of symptoms to metformin Consider switching to extended-release formulation Take with food to improve tolerability and/or continue at reduced dose When to hold Prior to procedure with nothing per mouth or illness Day of procedure Resume when eating normally
Dipeptidyl peptidase-4 inhibitors: Alogliptin (6.25-25 mg orally daily) Linagliptin (5 mg orally daily) Saxagliptin (2.5-5 mg orally daily) Sitagliptin (25-100 mg orally daily)	Intermediate (<0.5%)	Neutral	No	Atherosclerotic cardiovascular disease: neutral Chronic kidney disease: neutral HF: potential risk with saxagliptin[77]	$$-$$$	Most common adverse effects: upper respiratory infection (4%-8%), nasopharyngitis (5%-7%), headache (4%-7%) Contraindications: hypersensitivity Warnings/precautions: pancreatitis, hypersensitivity reactions, arthralgia, bullous pemphigoid	When to use Add-on treatment in individuals who require intermediate levels of HbA_{1C} lowering (0.5%-1% above target) without risk of hypoglycemia For patients who desire to maintain weight Combination therapy: Dipeptidyl peptidase-4 inhibitors should not be combined with GLP-1RAs or dual GLP-1/GIP RAs because they act on the same pathway

Drug (glucose-lowering dose)	Glucose-lowering efficacy[55,56,b]	Impact on weight[56,57,c]	Hypoglycemia risk as monotherapy	Impact on comorbidities[d]	Cost[58,f]	Common adverse effects[59,g,e]	Practical considerations[59]
GIP/GLP-1RA: Tirzepatide (2.5-15 mg subcutaneously once weekly)	High (1.0%-2.0%) to very high (2.0%-2.5%)	Loss (high)	No	Atherosclerotic cardiovascular disease: safe[i] Chronic kidney disease: safe[i] HF: benefit in obesity-related HFpEF[109]	$$$$	Most common adverse effects: nausea (18%), diarrhea (17%), vomiting (9%), constipation (7%), dyspepsia (5%), abdominal pain (5%) Contraindications: personal or family history of medullary thyroid cancer or in patients with multiple endocrine neoplasia 2 Warnings/precautions: pancreatitis, hypoglycemia (add-on to sulfonylurea and/or insulin), diabetic retinopathy complications, acute kidney injury, hypersensitivity reactions, acute gallbladder disease	When to use Add-on treatment in individuals taking ≥1 oral glucose-lowering drugs at maximally tolerated doses who require high to very high levels of HbA_{1C} lowering (ie, HbA_{1C} >1.0%-2.5% above goal) Can be used for patients who desire substantial weight loss When to hold Prior to procedures, consider dietary adjustments (eg, liquid diet) or holding therapy (eg, day of procedure for daily formulations or 1 week prior for weekly formulations) in those at high risk for delayed gastric emptying When adding to insulin Reduce then stop prandial insulin Reduce the basal insulin dose as GLP-1 dose increases, guided by glucose monitoring
GLP-1RAs: Dulaglutide (0.75-4.5 subcutaneously once weekly) Exenatide extended release (2 mg subcutaneously once weekly) Liraglutide (0.6-1.8 mg subcutaneously daily) Semaglutide (0.25-2 mg subcutaneously once weekly or 3-14 mg orally daily or 1.5 - 9 mg orally daily)	High (1.0%-2.0%) to very high (2.0%-2.5%)	Loss (intermediate to high)	No	Atherosclerotic cardiovascular disease: benefit on major cardiovascular events with dulaglutide,[70] liraglutide,[71] and semaglutide[72,86] Chronic kidney disease: benefit on progression with semaglutide (subcutaneous)[73] HF: evidence of benefit in obesity-related HFpEF with semaglutide (subcutaneous)[74,75]	$$$$	Most common adverse effects[j]: nausea (8%-21%), vomiting (3%-13%), diarrhea (9%-13%), abdominal pain (6%-11%), constipation (2%-5%) Contraindications: personal or family history of medullary thyroid cancer or in patients with multiple endocrine neoplasia 2 Warnings/precautions; pancreatitis, hypoglycemia (add-on to sulfonylurea and/or insulin), diabetic retinopathy complications, acute kidney injury, hypersensitivity reactions, acute gallbladder disease	When to use First-line treatment in atherosclerotic cardiovascular disease, chronic kidney disease, obesity-related HFpEF Add-on treatment in individuals without cardiovascular or kidney comorbidities taking 1 or more oral glucose-lowering drugs at maximally tolerated doses who require high to very high levels of HbA_{1C} lowering (ie, HbA_{1C} level >1.0%-2.5% above goal) Can be used for patients who desire moderate weight loss When to hold: Prior to procedures, consider dietary adjustments (eg, liquid diet) or holding therapy (eg, day of procedure for daily formulations or 1 week prior for weekly formulations) in those at high risk for delayed gastric emptying Switching GLP-1 formulations: Although there is no standard dose equivalence, the following may be used as a guide: semaglutide oral 14 mg ~ semaglutide subcutaneous 0.5 mg ~ dulaglutide 1.5 mg ~ liraglutide 1.8 mg ~ tirzepatide 2.5 mg[76,80] When adding to insulin: Reduce, then stop prandial insulin Reduce the basal insulin dose as GLP-1 dose increases, guided by glucose monitoring

Drug (glucose-lowering dose)	Glucose-lowering efficacy[55,56,b]	Impact on weight[56,57,c]	Hypoglycemia risk as monotherapy	Impact on comorbidities[d]	Cost[58,f]	Common adverse effects[59,g,e]	Practical considerations[59]
Thiazolidine-dione: Pioglitazone (15-45 mg orally daily)	High (1%-2%)	Gain	No	Atherosclerotic cardiovascular disease: likely benefit[78,79] Chronic kidney disease: neutral HF: increased risk	$	Most common adverse effects: upper respiratory infection (13%), headache (9%), sinusitis (6%), myalgia (5%), pharyngitis (5%) Contraindications: New York Heart Association class III or IV HF, hypersensitivity Warnings/precautions: HF, liver toxicity, bladder cancer, fluid retention/edema, fractures, macular edema	When to use Add-on treatment in individuals who require high levels of HbA_{1C} lowering (1%-2% above target) Inexpensive, can be used when cost is a concern Dosing considerations[82] Benefits maximized and adverse effects minimized at doses of 15 or 30 mg Weight gain, edema, and heart failure risk higher at 45-mg dose Fracture risk similar across all doses
SGLT2 inhibitors[k]: Bexagliflozin (20 mg orally daily) Canagliflozin (100-300 mg orally daily) Dapagliflozin (5-10 mg orally daily) Empagliflozin (10-25 mg orally daily) Ertugliflozin (5-15 mg orally daily)	Intermediate (0.5%)	Loss (intermediate)	No	Atherosclerotic cardiovascular disease: benefit on major cardiovascular events with canagliflozin[61] and empagliflozin[62] Chronic kidney disease: benefit on progression with canagliflozin,[63] dapagliflozin,[64] and empagliflozin[65] HF: benefit in HFpEF and HFrEF with dapagliflozin [66,69,88] and empagliflozin [67,68]	$-$$$	Most common adverse effects: genital mycotic infections (6%-12%), urinary tract infection (4%-8%), increased urination (2%-7%) Contraindications: hypersensitivity Warnings/precaution: euglycemic diabetic ketoacidosis, volume depletion, severe urinary tract infections, hypoglycemia (add-on to sulfonylurea and/or insulin), Fournier gangrene; lower limb amputation, fractures with canagliflozin	When to use First-line treatment in atherosclerotic cardiovascular disease, chronic kidney disease, HF Add-on treatment in individuals without cardiovascular or kidney comorbidities who require intermediate levels of HbA_{1C} lowering (0.5%-1% above target) Can be used for patients who desire moderate weight loss When to hold Hold 3-4 d prior to procedures Consider holding if risk of dehydration (eg, religious fasting, strenuous exercise on hot day)
Sulfonylureas: Glimepiride (1-8 mg orally daily) Glipizide (IR: 2.5-40 mg orally daily; extended release: 2.5-20 mg orally daily) Glyburide (1.25-20 mg orally daily)	High (1%-2%)	Gain	Yes	Atherosclerotic cardiovascular disease: neutral Chronic kidney disease: neutral HF: neutral	$	Most common adverse effects (glimepiride)[e]: hypoglycemia (20%), headache (8%), nausea (5%), dizziness (5%) Contraindication: hypersensitivity Warnings/precautions: severe hypoglycemia risk, hemolytic anemia (glucose-6-phosphate dehydrogenase deficiency), special warning for increased risk of cardiovascular mortality based on studies with an older-generation sulfonylurea (tolbutamide); glimepiride demonstrated safety[81]	When to use Add-on treatment in individuals who require high levels of HbA_{1C} lowering (1%-2% above target) Inexpensive and can be used when cost is a concern When to hold Day of procedure; resume when eating normally To minimize hypoglycemia In those at higher risk (eg, older adults, chronic kidney disease), do not use glyburide, which is longer-acting and associated with higher risk of hypoglycemia vs other sulfonylureas Glimepiride or glipizide are shorter-acting and preferred Dose cautiously; do not overtreat

Drug class and agents[b]	Usual dosing range for glucose-lowering[59]	Glucose-lowering efficacy	Cost[58,c]	Safety/tolerability[59,d]	Considerations for dosing and titration [14,92]	Practical considerations
Basal insulin: Human NPH Degludec Glargine Glargine biosimilar (glargine-yfgn, glargine-aglr) and follow-on products[b] Bolus insulin: Human regular Aspart Aspart biosimilar (aspart-szjj)[b] Fast-acting aspart Lispro Lispro biosimilar (lispro-aabc) and follow-on products[b] Glulisine Inhaled insulin Premixed insulin: Aspart 70/30 Lispro 75/25 Lispro 50/50 NPH/regular 70/30 Fixed dose combinations: Degludec/liraglutide Glargine/lixisenatide	Typically up to 200-300 units; above this, consider concentrated insulins[a]	In theory, no limit to HbA_{1C} lowering potential	$ - $$$ Human insulin (NPH, regular) is lower cost than analog insulins; follow-on and biosimilar insulins often lower cost than the reference insulin product	Most common adverse effects Hypoglycemia Injection site reactions Lipohypertrophy or lipoatrophy Weight gain Contraindications: Hypersensitivity Warnings/precautions Never share insulin delivery devices between patients, even if the needle is changed Increased risk of fluid retention/edema; risk increased further when used in combination with thiazolidinediones	Adding basal insulin: Start 10 units or 0.1-0.2 units/kg/d Increase 2 units every 3 d until at FPG target without overnight or midday hypoglycemia If not already on GLP-1RA or dual GLP-1/GIP RA, consider adding Adding prandial insulin: Start with 4 units (or 10% of basal dose) to the largest meal of the day, titrate based on response, then add additional injections in step-wise manner to second and third meals Titrate by 1-2 units (10%-15%) twice weekly Consider premixed insulin in people with meal patterns that match premixed insulin kinetics (eg, large breakfast and supper, small mid-day meal) Switching insulin formulations: If close to glycemic target: Sum the total daily dose of insulin and reduce by 10%, then titrate based on glucose monitoring If well above glycemic target, switch to the equivalent dose, then titrate Anticipate total daily insulin dose reduction with treatment of glucose toxicity and resolution of insulin resistance as counter-regulatory hormone levels and volume depletion resolve	When to use First-line treatment with severe hyperglycemic symptoms (ie, polyuria or polydipsia) and life-threatening hyperglycemic crisis (ie, diabetic ketoacidosis or hyperosmolar hyperglycemic state) and/or HbA_{1C} >10% Add-on treatment for individuals taking 1 or more oral glucose-lowering drugs at maximally tolerated doses who require injectable therapies to meet glycemic targets (ie, HbA_{1C} level more than 1.5%-2% above goal) Basal insulin can be used to target elevated fasting glucose levels (ie, >80-130 mg/dl) Prandial insulin can be used to target elevated postprandial glucose levels within 1-2 h after meal (ie, >180 mg/dl) Impact on key comorbidities: Neutral cardiovascular[93] and kidney effects Hypoglycemia: Analog insulins generally have less hypoglycemia than human insulins When to hold: If nothing per mouth, hold or reduce insulin by 50%-80% to weight- based basal requirement (eg, 0.2-0.3 units/kg ideal body weight)

In a meta-analysis and systematic review of 15 randomized clinical trials and observational studies (783 255 patients) comparing intensive control (HbA_{1C} <7.5%) vs standard care in adults 60 years or older or frail adults of any age with type 2 diabetes, there was no difference in mortality, but intensive control was associated with both a reduction in microvascular and macrovascular complications and increased risk for severe hypoglycemia.[45] Older adults with cognitive or functional limitations and those with reduced life expectancy experience less benefit from intensive glycemic targets and more harm from overtreatment, including increased risk of severe hypoglycemia, which may lead to falls and fractures.[46]

	Pacientes DM1 ou DM2	Idoso Saudável*	Idoso Comprometido (Frágil)*	Idoso Muito Comprometido*	Criança e adolescente
HbA1c %	<7,0	<7,5	<8,0	Evitar sintomas de hiper ou hipoglicemia	<7,0
Glicemia de Jejum e Pré Prandial	80-130	80-130	90-150	100-180	70-130
Glicemia 2h Pós-Prandial	<180	<180	<180	-	<180
Glicemia ao deitar	90-150	90-150	100-180	110-200	90-150
TIR 70-180 mg/dL	>70%	>70%	>50%	-	>70%
T Hipog <70 mg/dL	<4%	<4%	<1%	0	<4%
T Hipog <54 mg/dL	<1%	<1%	0	0	<1%

Valores normais de glicemia de jejum para adultos não gestantes: 70-99mg/dL; Valores normais de HbA1c para adultos não gestantes < 5,7%; *Ver tabela 2; TIR: Tempo no alvo ("*Time in Range*"); T Hipog: Tempo em hipoglicemia.

IDOSO		
Saudável	**Comprometido**	**Muito Comprometido**
Poucas comorbidade crônicas Estado funcional preservado Estado cognitivo preservado	Múltiplas comorbidades crônicas* Comprometimento funcional leve a moderado Comprometimento cognitivo moderado	Doença terminal** Comprometimento funcional grave Comprometimento cognitivo grave

risk.[14,94,97-100] Many evidence-based guidelines continue to recommend metformin as first-line treatment,[94-97,99-102] particularly in patients without cardiovascular or kidney comorbidities, although some guidelines no longer state that metformin be used prior to using GLP-1RAs or SGLT2is in patients with atherosclerotic cardiovascular disease, HF, or CKD.[14,94,98] Some guidelines recommend combination SGLT2i and GLP-1RA in patients with type 2 diabetes and cardiovascular disease or those at high risk of CVD if glycemic targets are not met (Table 4). Studies have been limited by small sample sizes in combination therapy subgroups and trials have not consistently shown benefit for the combination of SGLT2is and GLP-1RAs on cardiovascular and kidney outcomes.[73,112]

The major disadvantage of SGLT2is, GLP-1RAs, and dual GIP/GLP-1RAs, aside from their specific adverse effects (Table 2), is limited access in the US due to high cost for individuals without insurance or with high-deductible health plans.[113] Strategies such as co-payment cards, manufacturer patient assistance programs, and the Medicare low-income subsidy may help patients navigate high prescription drug costs.[114] Generic formulations of liraglutide and dapagliflozin have been approved in the US, but are not widely available.

Patients with type 2 diabetes are commonly treated by primary care clinicians. HbA_{1C} should be assessed at least every 6 months or every 3 months for patients not meeting their glycemic targets or for those with recent glucose-lowering medication dose adjustments. Referrals to a diabetes care and education specialist for diabetes self-management education and to a registered dietitian for medical nutrition therapy are recommended for all individuals with type 2 diabetes.[14] Most adults with type 2 diabetes should be counseled to engage in moderate- to vigorous-intensity aerobic physical activity such as brisk walking, swimming, or running (≥150 minutes/week) and resistance exercise (2-3 sessions/week). Patients should be counseled to lose weight or maintain weight if weight loss is not advisable. Multidrug regimens, complicated insulin regimens (ie, multiple daily injections), high-dose insulin (ie, >200 units/d), and consideration of use of diabetes technology (such as CGMs or insulin pumps) may warrant consultation with endocrinology. Lack of expected response to treatment or persistent hyperglycemia in patients with new-onset diabetes who are adherent to metformin or other oral glucose-lowering therapy should prompt screening for type 1 diabetes with islet autoantibodies (eg, glutamic acid

R1 - Em pessoas com pré-DM e sobrepeso ou obesidade, É RECOMENDADO a restrição calórica, associada à prática de atividade física para a perda de peso e redução do risco de desenvolver DM2.
R2 - Em pessoas com pré-DM, o consumo de fibras (25-30g ao dia) É RECOMENDADO por estar associado a menor risco de desenvolver DM2.
R3 - A redução do consumo de bebidas contendo açúcares (naturais ou adicionados) É RECOMENDADA por estas estarem associadas a um maior risco de desenvolver DM2.
R4 - Em pessoas com DM2 que apresentem sobrepeso ou obesidade É RECOMENDADO a perda de, no mínimo, 5% do peso corporal inicial para melhora do controle glicêmico.
R5 - Diversas abordagens nutricionais são capazes de melhorar o controle glicêmico no DM2. De uma forma geral, É RECOMENDADO que pessoas com DM2 sigam uma dieta balanceada, com restrição de carboidratos simples ou refinados de rápida absorção.
R6 - Em adultos, não-gestantes, com pré-diabetes ou DM2, a redução de carboidratos totais PODE SER CONSIDERADA para melhora do controle glicêmico.
R7 - A utilização do índice glicêmico e da carga glicêmica para melhorar o controle glicêmico em pessoas com DM2 PODE SER CONSIDERADA, quando os alimentos forem consumidos de forma isolada.
R8 - Em pessoas com DM2, com função renal preservada, É RECOMENDADO o consumo de proteínas entre 15 a 20% do valor energético total diário, podendo variar entre 1 a 1,5g/kg/dia.
R9 - Em relação à ingestão de gorduras, em pessoas com DM2, DEVE SER CONSIDERADO priorizar o uso de ácidos graxos mono e poliinsaturados por estarem associados à menor incidência de doenças cardiovasculares.
R10 - Em adultos com DM2, É RECOMENDADO o uso de fibras dietéticas na quantidade 14g/1000 kcal, com um mínimo de 25g por dia, para melhorar o controle glicêmico e atenuar hiperglicemia pós-prandial.

CASO CLÍNICO: PACIENTE COM DISLIPIDEMIA

CASO CLÍNICO: PACIENTE COM DISLIPIDEMIA

🔍 Critérios clínicos e laboratoriais para dislipidemia

Parâmetro	Valor Desejável (adultos)	Níveis considerados anormais
Colesterol total (CT)	< 190 mg/dL	≥ 190 mg/dL
LDL-C (colesterol ruim)	< 100 mg/dL (baixo risco) < 70 mg/dL (alto risco) < 55 mg/dL (muito alto risco)	≥ 130–160 mg/dL
HDL-C (colesterol bom)	> 40 mg/dL (homens) > 50 mg/dL (mulheres)	< 40 mg/dL
Triglicerídeos (TG)	< 150 mg/dL	≥ 150 mg/dL
Não-HDL-C (CT - HDL-C)	< 130 mg/dL (baixo risco) < 100 mg/dL (alto risco)	> 160–190 mg/dL

1.9% Low — **Current 10-Year ASCVD Risk****

Lifetime ASCVD Risk: **36%** Optimal ASCVD Risk: **0.7%**

Unit of Measure: **US** SI

Reset All

App should be used for primary prevention patients (those without ASCVD) only.

Current Age * : 41
Age must be between 20-79

Sex *: ✔ Male | Female

Race *: ✔ White | African American | Other

Systolic Blood Pressure (mm Hg) *: 130
Value must be between 90-200

Diastolic Blood Pressure (mm Hg) *: 80
Value must be between 60-130

Total Cholesterol (mg/dL) *: 190
Value must be between 130 - 320

HDL Cholesterol (mg/dL) *: 35
Value must be between 20 - 100

LDL Cholesterol (mg/dL) ○: 120
Value must be between 30-300

History of Diabetes? *: Yes | ✔ No

Smoker? *: Current | Former | ✔ Never

On Hypertension Treatment? *: Yes | ✔ No

On a Statin? ○: Yes | ✔ No

On Aspirin Therapy? ○: Yes | ✔ No

🎯 Metas de LDL-C segundo risco (SBC/DA 2022 e ESC 2021)

Risco Cardiovascular	Meta de LDL-C
Muito alto risco	**< 55 mg/dL**
Alto risco	**< 70 mg/dL**
Risco intermediário	**< 100 mg/dL**
Baixo risco	**< 130 mg/dL**

🔍 Critérios clínicos e laboratoriais para dislipidemia

Parâmetro	Valor Desejável (adultos)	Níveis considerados anormais
Colesterol total (CT)	< 190 mg/dL	≥ 190 mg/dL

Table 1 Risk categories and target levels for total cholesterol/HDL-C, LDL-C/HDL-C and apoB/apoA-I ratios, in primary and secondary prevention, stratified by gender[6,7,14]

Ratio	Primary prevention				Secondary prevention*			
	Risk level		Target		Risk level		Target	
	Men	Women	Men	Women	Men	Women	Men	Women
TC/HDL-C	>5.0	>4.5	<4.5	<4.0	>4.0	>3.5	<3.5	<3.0
LDL-C/HDL-C	>3.5	>3.0	<3.0	<2.5	>3.0	>2.5	<2.5	<2.0
ApoB/ApoA-I	>1.0	>0.9	<0.9	<0.8	>0.8	>0.7	<0.7	<0.6

Note: *Or equivalent risk situation.
Abbreviations: Apo, apolipoprotein; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol.

Não-HDL-C (CT - HDL-C)	< 130 mg/dL (baixo risco) < 100 mg/dL (alto risco)	> 160–190 mg/dL

TABLE 5 FH Diagnostic Categories

ICD-10 Category	Clinical Criteria	With Genetic Testing Performed
Heterozygous FH	LDL-C ≥160 mg/dL (4 mmol/L) for children and ≥190 mg/dL (5 mmol/L) for adults and with 1 first-degree relative similarly affected or with premature CAD or with positive genetic testing for an LDL-C–raising gene defect (LDL receptor, apoB, or PCSK9)	Presence of 1 abnormal LDL-C–raising gene defect (LDL receptor, apoB, or PCSK9) Diagnosed as heterozygous FH if LDL-C–raising defect positive and LDL-C <160 mg/dL (4 mmol/L) Occasionally, heterozygotes will have LDL-C >400 mg/dL (10 mmol/L); they should be treated similarly to homozygotes Presence of both abnormal LDL-C–raising gene defects (LDL receptor, apoB, or PCSK9) and LDL-C–lowering gene variant(s) with LDL-C <160 mg/dL (4 mmol/L)
Homozygous FH	LDL-C ≥400 mg/dL (10 mmol/L) and 1 or both parents having clinically diagnosed FH, positive genetic testing for an LDL-C–raising gene defect (LDL receptor, apoB, or PCSK9) or autosomal-recessive FH If LDL-C >560 mg/dL (14 mmol/L) or LDL-C >400 mg/dL (10 mmol/L) with aortic valve disease or xanthomata at <20 years of age, homozygous FH highly likely	Presence of 2 identical (true homozygous FH) or nonidentical (compound heterozygous FH) abnormal LDL-raising gene defects (LDL receptor, apoB, or PCSK9); includes the rare autosomal-recessive type Occasionally, homozygotes will have LDL-C <400 mg/dL (10 mmol/L)
Family history of FH	LDL-C level not a criterion; presence of a first-degree relative with confirmed FH	Genetic testing not performed

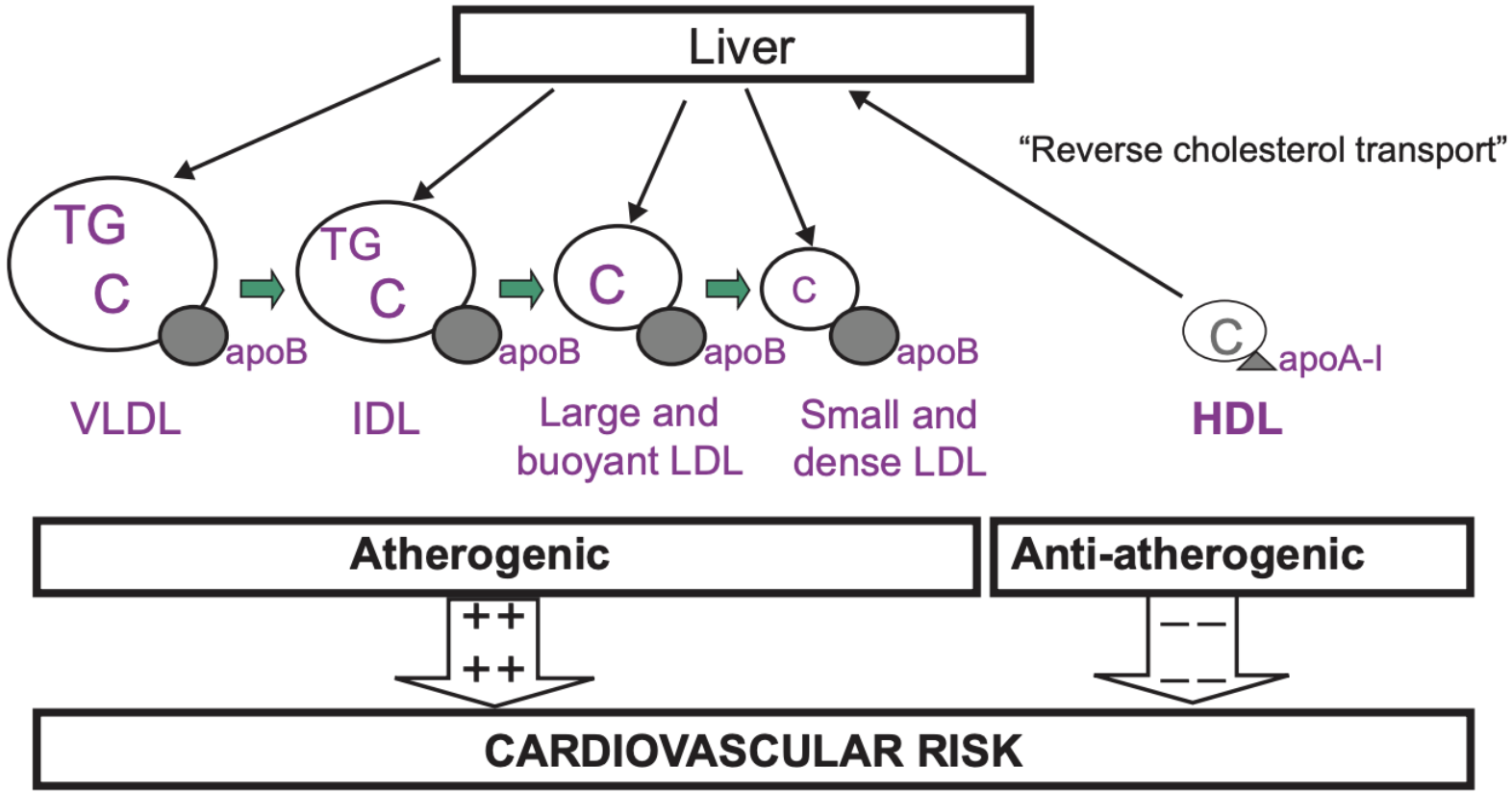
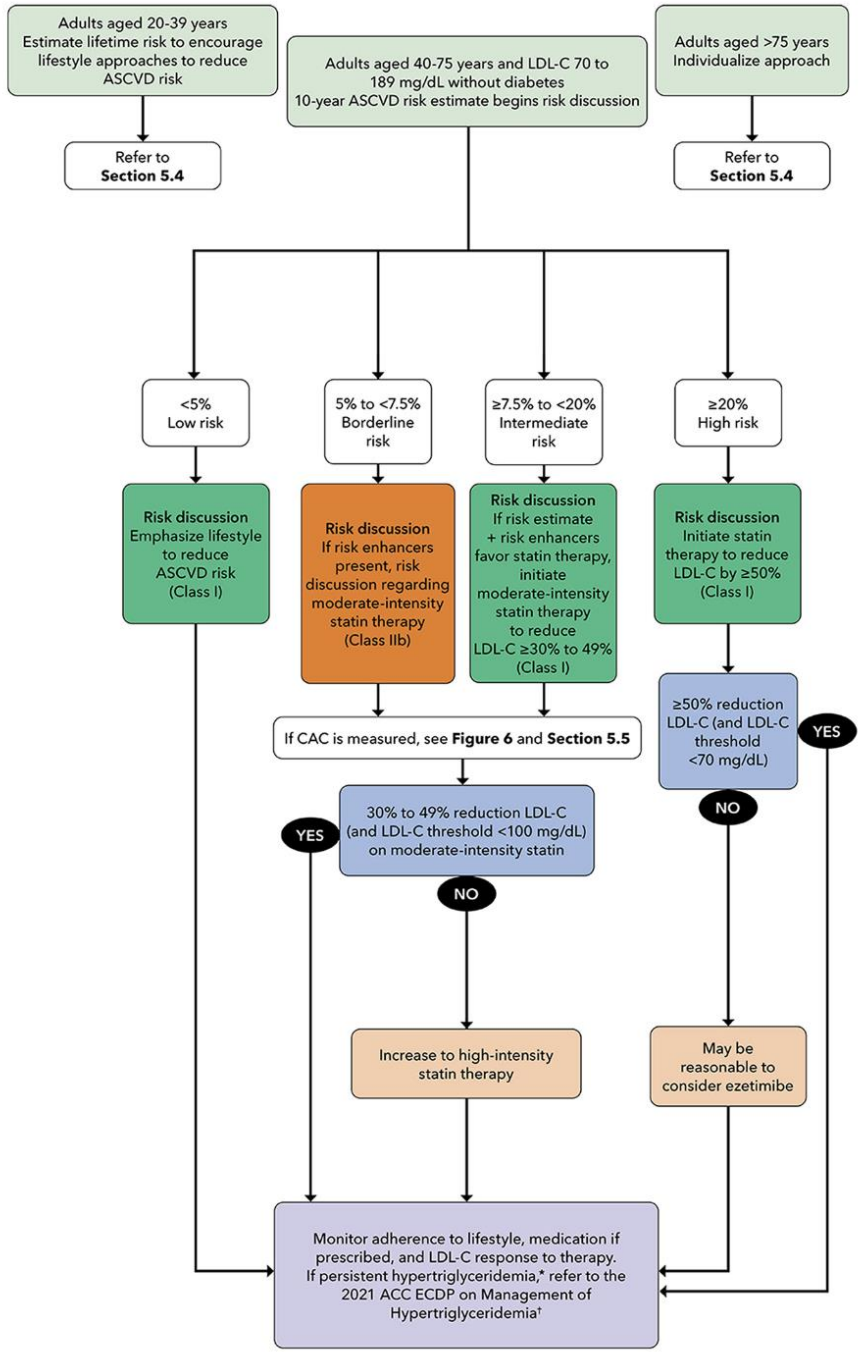

Liver
"Reverse cholesterol transport"
TG
C
apoB
VLDL
TG
C
apoB
IDL
C
apoB
Large and buoyant LDL
C
apoB
Small and dense LDL
C
apoA-I
HDL
Atherogenic
Anti-atherogenic
++
++
– –
– –
CARDIOVASCULAR RISK

FIGURE 5 Adults Without Clinical ASCVD or Diabetes (LDL 70-189 mg/dL)



Calculadora	Usada por	Parâmetros incluídos	Comentários
SCORE2 / SCORE2-OP	Diretriz Europeia (ESC 2021)	Idade, sexo, PAS, colesterol total, HDL-C, tabagismo	Usada na Europa. SCORE2 para < 70 anos, SCORE2-OP para ≥ 70 anos. Estima risco de **eventos fatais e não fatais**.
ASCVD Risk Estimator Plus	Diretriz americana (AHA/ACC 2018)	Idade, sexo, raça, PAS, uso de anti-hipertensivos, colesterol total, HDL-C, tabagismo, diabetes	Estima risco de **eventos em 10 anos**. Usado nos EUA. Define início de estatinas e metas de LDL.
Framingham Risk Score	Diretriz Brasileira e outras	Idade, colesterol total, HDL-C, PA, tabagismo, diabetes	Clássico, ainda muito usado. Subestima risco em alguns grupos.
Reynolds Risk Score	Alternativa para mulheres	Idade, PCR-us, PA, colesterol total e HDL-C, tabagismo, histórico familiar	Usa proteína C reativa. Foco maior em mulheres.
Calculadora da Diretriz Brasileira (SBC/DA 2022)	Brasil	Adaptação de Framingham com fatores como síndrome metabólica, história familiar precoce	Define metas conforme risco: baixo, intermediário, alto ou muito alto.

ias

Gorduras insaturadas: em substituição às saturadas

Intensity of lipid lowering treatment

Treatment	Average LDL-C reduction
Moderate intensity statin	≈ 30%
High intensity statin	≈ 50%
High intensity statin plus ezetimibe	≈ 65%
PCSK9 inhibitor	≈ 60%
PCSK9 inhibitor plus high intensity statin	≈ 75%
PCSK9 inhibitor plus high intensity statin plus ezetimibe	≈ 85%

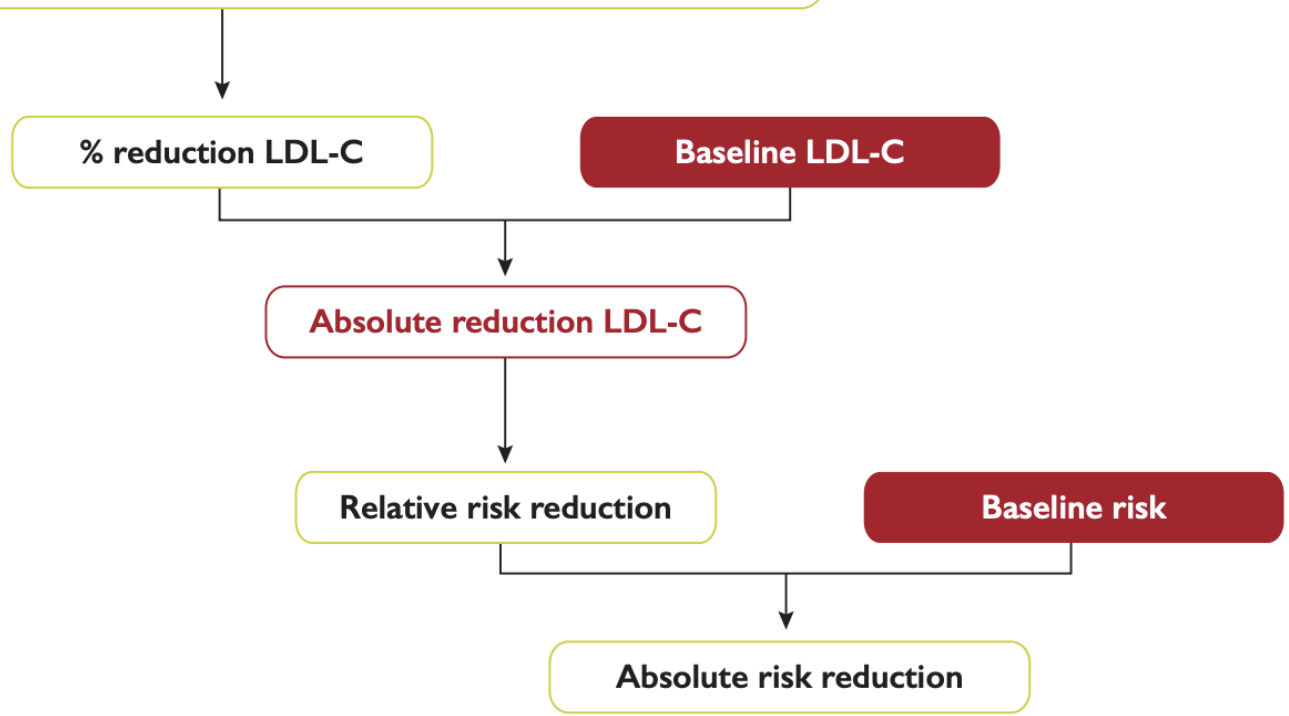
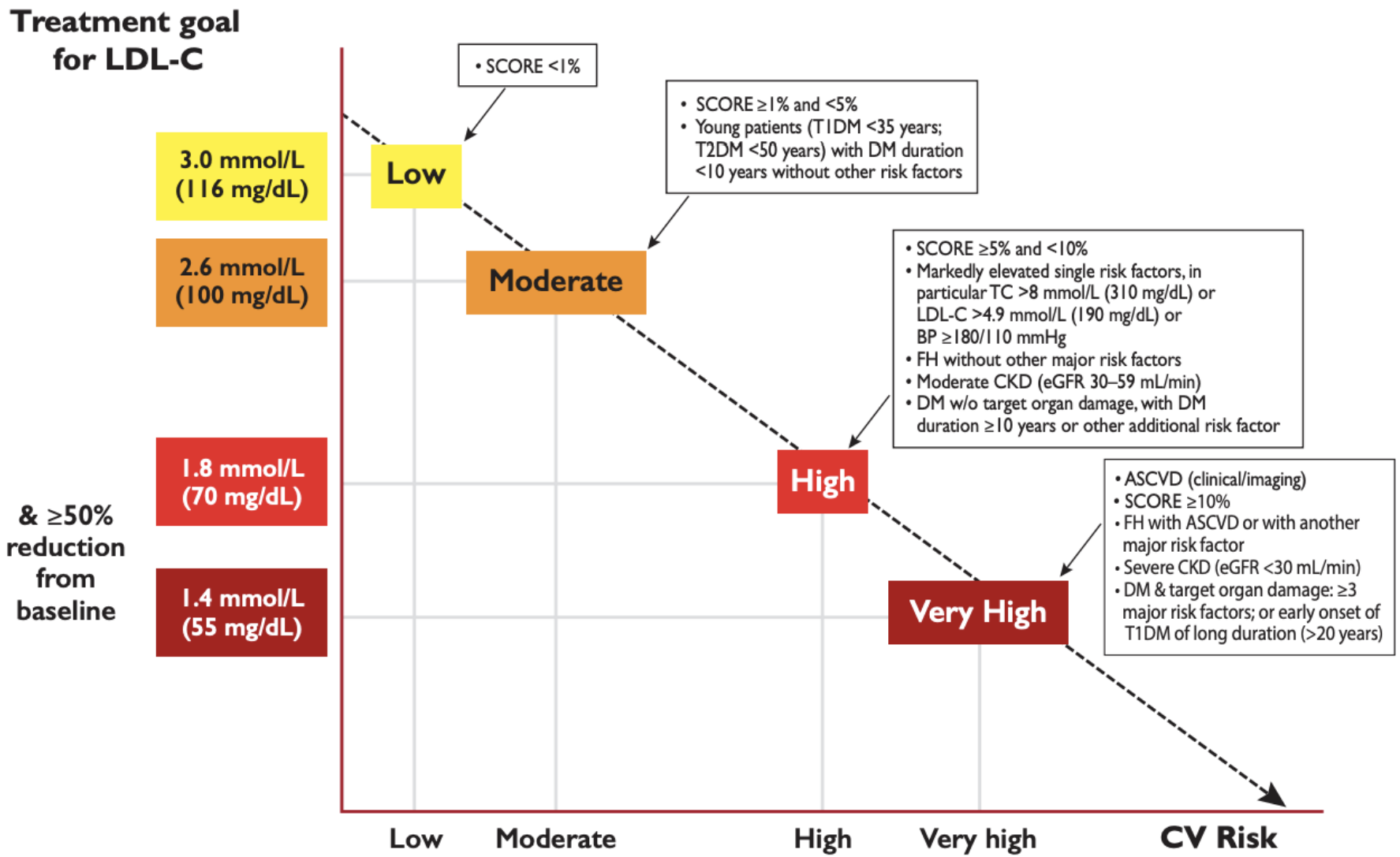


Table 4 **Cardiovascular risk categories**

Very-high-risk	People with any of the following: Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes previous ACS (MI or unstable angina), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke and TIA, and peripheral arterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis), or on carotid ultrasound. DM with target organ damage,[a] or at least three major risk factors, or early onset of T1DM of long duration (>20 years). Severe CKD (eGFR <30 mL/min/1.73 m^2). A calculated SCORE ≥10% for 10-year risk of fatal CVD. FH with ASCVD or with another major risk factor.
High-risk	People with: Markedly elevated single risk factors, in particular TC >8 mmol/L (>310 mg/dL), LDL-C >4.9 mmol/L (>190 mg/dL), or BP ≥180/110 mmHg. Patients with FH without other major risk factors. Patients with DM without target organ damage,[a] with DM duration ≥10 years or another additional risk factor. Moderate CKD (eGFR 30–59 mL/min/1.73 m^2). A calculated SCORE ≥5% and <10% for 10-year risk of fatal CVD.
Moderate-risk	Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years, without other risk factors. Calculated SCORE ≥1 % and <5% for 10-year risk of fatal CVD.
Low-risk	Calculated SCORE <1% for 10-year risk of fatal CVD.


Treatment goal for LDL-C
3.0 mmol/L (116 mg/dL)
2.6 mmol/L (100 mg/dL)
1.8 mmol/L (70 mg/dL)
1.4 mmol/L (55 mg/dL)
& ≥50% reduction from baseline
• SCORE <1%
Low
• SCORE ≥1% and <5%
• Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years without other risk factors
Moderate
• SCORE ≥5% and <10%
• Markedly elevated single risk factors, in particular TC >8 mmol/L (310 mg/dL) or LDL-C >4.9 mmol/L (190 mg/dL) or BP ≥180/110 mmHg
• FH without other major risk factors
• Moderate CKD (eGFR 30–59 mL/min)
• DM w/o target organ damage, with DM duration ≥10 years or other additional risk factor
High
• ASCVD (clinical/imaging)
• SCORE ≥10%
• FH with ASCVD or with another major risk factor
• Severe CKD (eGFR <30 mL/min)
• DM & target organ damage: ≥3 major risk factors; or early onset of T1DM of long duration (>20 years)
Very High
Low
Moderate
High
Very high
CV Risk

- Banana (Grama: 140)
- Morango (Grama: 200)
- Mamão (Grama: 150)
- Arroz integral (cozido) (Grama: 200)
- Feijão carioca (Grama: 300)
- Filé de frango (Grama: 150)
- Aveia, flocos, crua (Grama: 80)
- Ovo de galinha Cozido(a) (Unidade: 1)
- Queijo minas frescal (Grama: 30)
- Castanha do Pará sem sal (Grama: 30)
- Azeite de oliva (Grama: 10)
- Iogurte desnatado (Grama: 320)
- Beterraba (Grama: 200)
- Tomate (Grama: 200)
- Cenoura (crua) (Grama: 200)

PTN	1,74 g/kg	121,64 g (22,5 %)	111 g (1,58 g/kg) ↓
CHO	3,95 g/kg	276,37 g (51,2 %)	256 g (3,65 g/kg) ↓
LIP	0,90 g/kg	62,88 g (26,2 %)	60 g (0,86 g/kg) ↓
Kcal		2.102 kcal	2.000 kcal ↓

Micronutrientes

Açucar Total	38,79 g
Cálcio	953,35 mg
Colesterol	324,7 mg
Ferro	12,46 mg
Fibra alimentar	46,87 g
Fósforo (P)	1.621,76 mg
G. Monoinsaturada	22,25 g
G. Poli-insaturada	15,02 g
G. Saturada	12,21 g
G. Trans	0,14 g

CASO CLÍNICO: PACIENTE USANDO SEMAGLUTIDA

The NEW ENGLAND JOURNAL of MEDICINE

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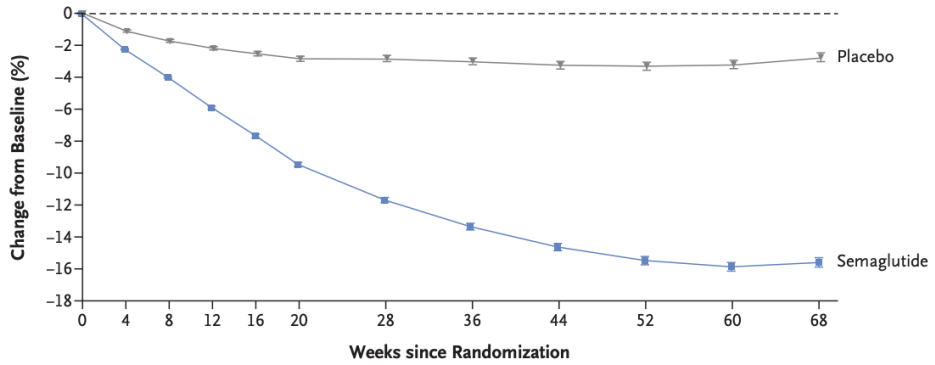
Once-Weekly Semaglutide in Adults with Overweight or Obesity

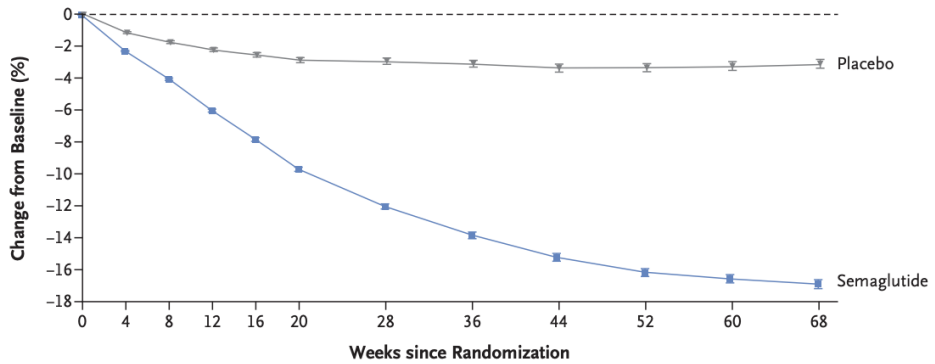
A Body Weight Change from Baseline by Week, Observed In-Trial Data



No. at Risk

Placebo	655	649	641	619	615	603	592	571	554	549	540	577
Semaglutide	1306	1290	1281	1262	1252	1248	1232	1228	1207	1203	1190	1212

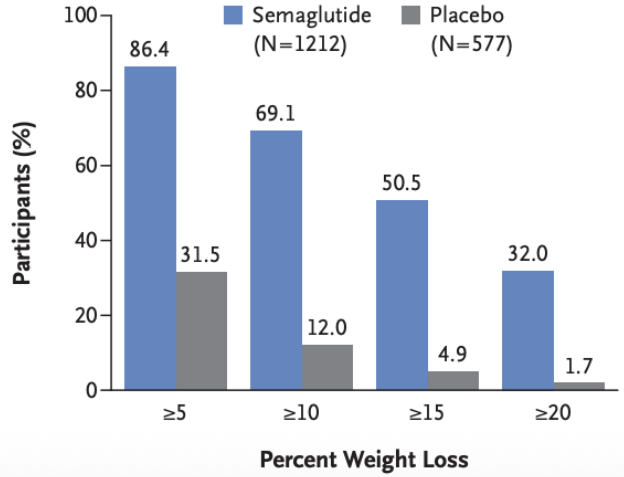
B Body Weight Change from Baseline by Week, Observed On-Treatment Data



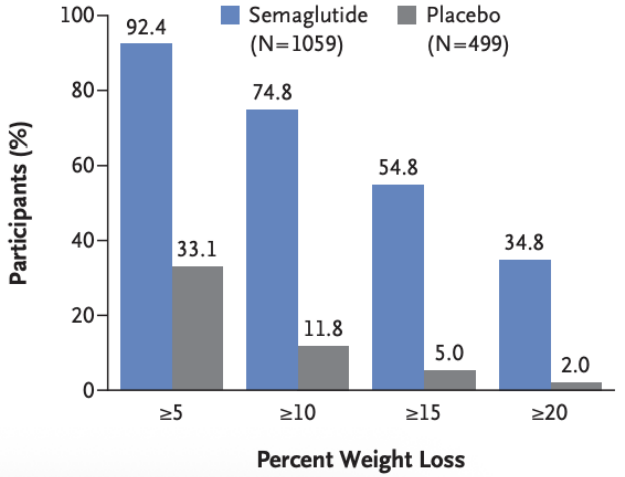
No. at Risk

Placebo	655	647	637	613	607	593	576	555	529	520	514	499
Semaglutide	1306	1283	1259	1225	1206	1193	1176	1166	1135	1115	1100	1059

C In-Trial Data at Wk 68

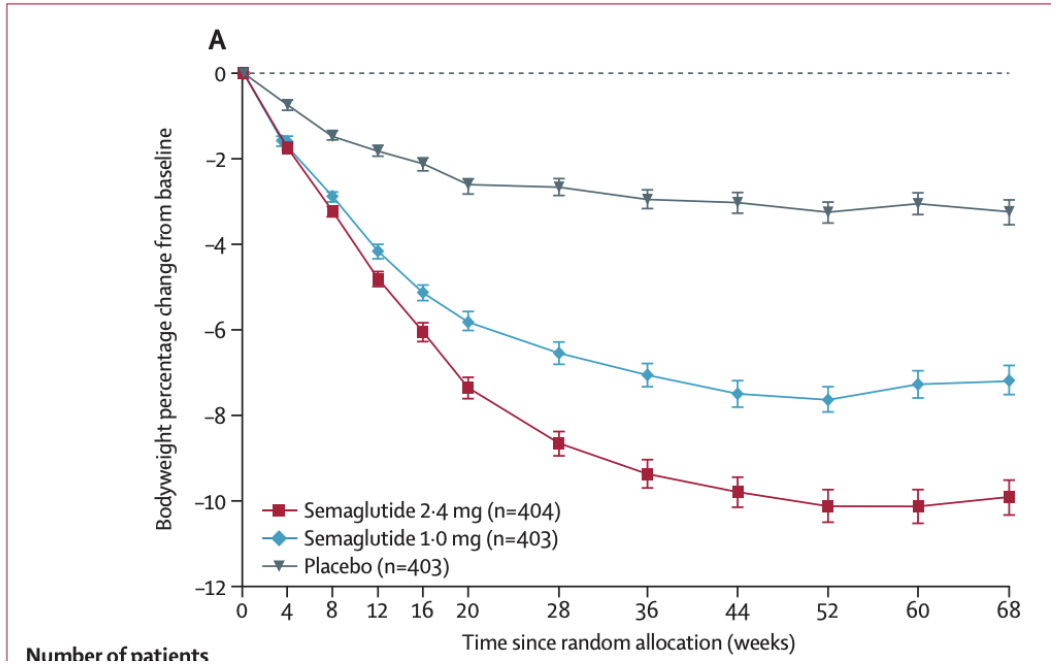


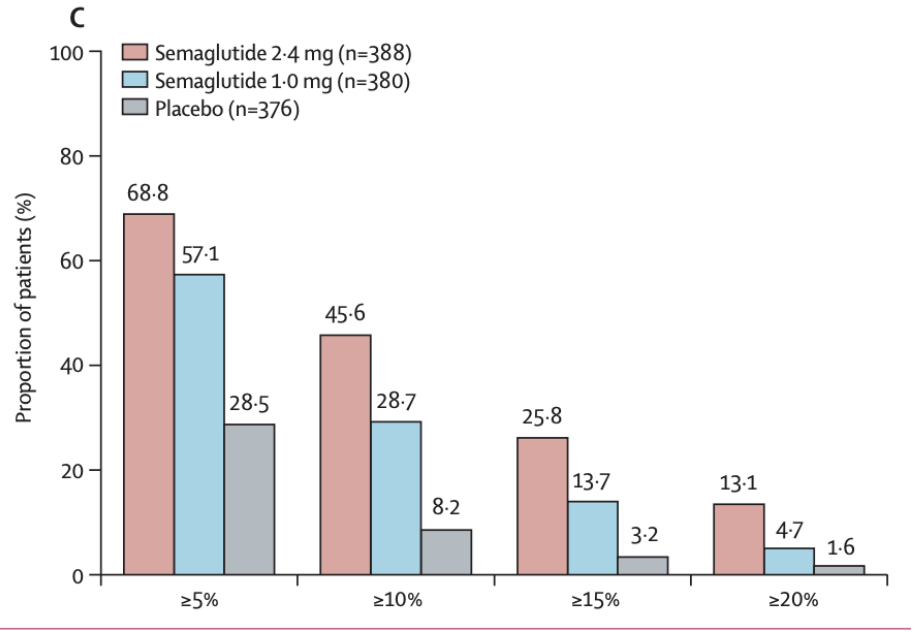
D On-Treatment Data at Wk 68



Semaglutide 2·4 mg once a week in adults with overweight or obesity, and type 2 diabetes (STEP 2): a randomised, double-blind, double-dummy, placebo-controlled, phase 3 trial

*Melanie Davies, Louise Færch, Ole K Jeppesen, Arash Pakseresht, Sue D Pedersen, Leigh Perreault, Julio Rosenstock, Iichiro Shimomura, Adie Viljoen, Thomas A Wadden, Ildiko Lingvay, for the STEP 2 Study Group**





🧪 Estudo STEP 2 (Semaglutide Treatment Effect in People with Obesity and Type 2 Diabetes)

Referência:

Davies, M. J., et al. (2021). *Semaglutide 2.4 mg once a week in adults with overweight or obesity, and type 2 diabetes (STEP 2)*. **The Lancet**, 397(10278), 971–984.

📎 DOI: 10.1016/S0140-6736(21)00213-0

🧍 Método

- **Tipo de estudo:** Ensaio clínico randomizado, duplo-cego, controlado por placebo.
- **Duração:** 68 semanas.
- **Participantes:** 1.210 adultos com DM2 e sobrepeso/obesidade.
- **Grupos:**
  - **Semaglutida 2,4 mg/semana**
  - **Semaglutida 1,0 mg/semana** (comparador ativo)
  - **Placebo**
- Todos os grupos receberam orientação comportamental e plano alimentar hipocalórico.

📊 Resultados

Desfecho principal	Semaglutida 2,4 mg	Semaglutida 1,0 mg	Placebo
Perda de peso (%)	-9,6%	-7,0%	-3,4%
≥5% de perda de peso	68,8%	57,1%	28,5%
Redução do peso (kg)	-9,7 kg	-6,4 kg	-3,4 kg
Redução de HbA1c (%)	-1,6	-1,5	-0,4

🧪 Estudo STEP 1 (Semaglutide Treatment Effect in People with Obesity)

Referência:

Wilding, J. P. H., et al. (2021). *Once-weekly semaglutide in adults with overweight or obesity.* New England Journal of Medicine, 384(11), 989-1002.

📎 DOI: 10.1056/NEJMoa2032183

🧍 Método

- **Tipo de estudo:** Ensaio clínico randomizado, duplo-cego, controlado por placebo.
- **Duração:** 68 semanas.
- **Participantes:** 1961 adultos (sem diabetes).
- **Intervenções:**
  - **Grupo Semaglutida:** 2,4 mg/semana + intervenção de estilo de vida.
  - **Grupo Placebo:** Placebo semanal + mesma intervenção de estilo de vida.
- **Co-intervenção:** Todos receberam orientações comportamentais e redução calórica (~500 kcal/dia) + aumento de atividade física.

📊 Resultados

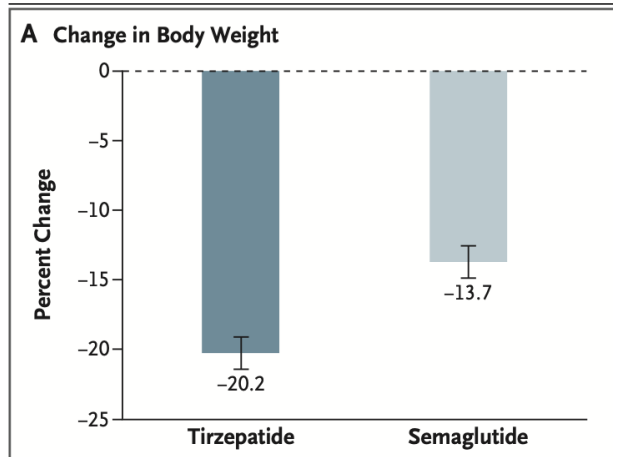
Desfecho	Semaglutida	Placebo	Diferença absoluta
Perda de peso média (%)	-14,9%	-2,4%	**-12,4%**
≥5% de perda de peso	86,4%	31,5%	
≥10% de perda de peso	69,1%	12,0%	
≥15% de perda de peso	50,5%	4,9%	
Redução média de peso (kg)	-15,3 kg	-2,6 kg	

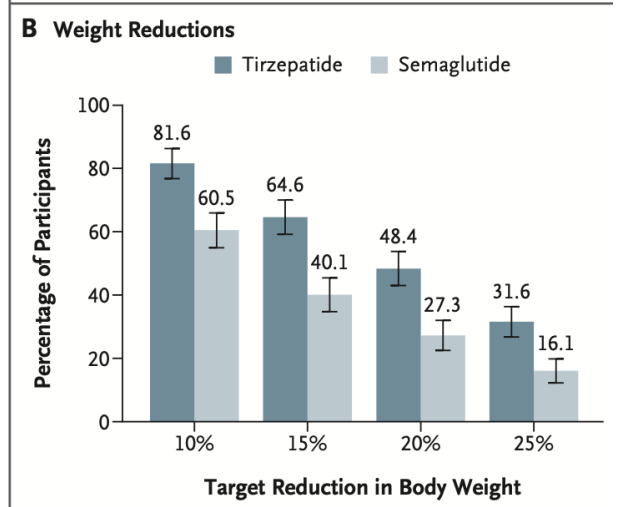
ORIGINAL ARTICLE

Tirzepatide as Compared with Semaglutide for the Treatment of Obesity

METHODS

In this phase 3b, open-label, controlled trial, adult participants with obesity but without type 2 diabetes were randomly assigned in a 1:1 ratio to receive the maximum tolerated dose of tirzepatide (10 mg or 15 mg) or the maximum tolerated dose of semaglutide (1.7 mg or 2.4 mg) subcutaneously once weekly for 72 weeks. The primary end point was the percent change in weight from baseline to week 72. Key secondary end points included weight reductions of at least 10%, 15%, 20%, and 25% and a change in waist circumference from baseline to week 72.





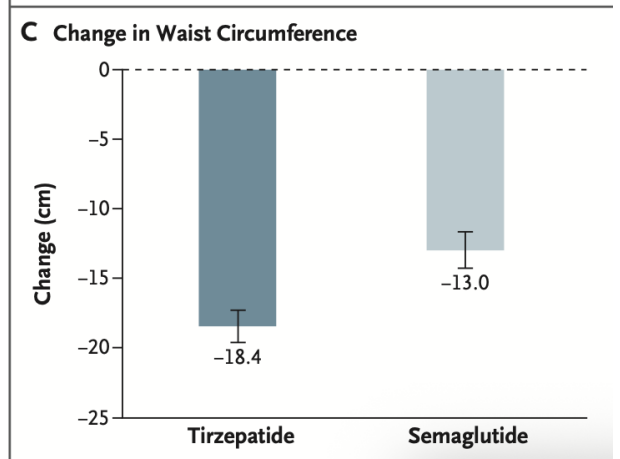


Table 3. Adverse Events and Safety.*

Variable	Tirzepatide (N=374)	Semaglutide (N=376)	Total (N=750)
	number of participants (percent)		
Adverse events that occurred or worsened during the treatment period	287 (76.7)	297 (79.0)	584 (77.9)
Serious adverse events	18 (4.8)	13 (3.5)	31 (4.1)
Adverse events leading to death	0	0	0
Discontinuation from the trial because of adverse events	6 (1.6)	6 (1.6)	12 (1.6)
Discontinuation of the trial treatment because of adverse events	23 (6.1)	30 (8.0)	53 (7.1)
Discontinuation of the trial treatment because of gastrointestinal adverse events	10 (2.7)	21 (5.6)	31 (4.1)
Adverse events occurring in ≥5% of participants in either group†			
Nausea	163 (43.6)	167 (44.4)	330 (44.0)
Constipation	101 (27.0)	107 (28.5)	208 (27.7)
Diarrhea	88 (23.5)	88 (23.4)	176 (23.5)
Vomiting	56 (15.0)	80 (21.3)	136 (18.1)
Coronavirus disease 2019	51 (13.6)	47 (12.5)	98 (13.1)
Fatigue	39 (10.4)	46 (12.2)	85 (11.3)
Eructation	37 (9.9)	29 (7.7)	66 (8.8)
Injection-site reaction	32 (8.6)	1 (0.3)	33 (4.4)
Upper respiratory tract infection	32 (8.6)	43 (11.4)	75 (10.0)
Alopecia	31 (8.3)	23 (6.1)	54 (7.2)
Abdominal distention	27 (7.2)	24 (6.4)	51 (6.8)
Headache	27 (7.2)	27 (7.2)	54 (7.2)
Abdominal pain	24 (6.4)	26 (6.9)	50 (6.7)
Dizziness	24 (6.4)	18 (4.8)	42 (5.6)
Gastroesophageal reflux disease	23 (6.1)	40 (10.6)	63 (8.4)

- Morango (Grama: 200)
- Mamão (Grama: 150)
- Arroz integral (cozido) (Grama: 60)
- Filé de frango (Grama: 100)
- Feijão carioca (Grama: 60)
- Aveia, flocos, crua (Grama: 20)
- Castanha do Pará sem sal (Grama: 30)
- Iogurte desnatado (Grama: 320)
- Whey Protein Concentrado - DUX (Grama: 30)

PTN	0,83 g/kg	82,97 g (33,4 %)	83 g (0,83 g/kg) ↑
CHO	0,96 g/kg	95,66 g (38,5 %)	106 g (1,06 g/kg) ↑
LIP	0,31 g/kg	31,10 g (28,1 %)	27 g (0,27 g/kg) ↓
Kcal		975 kcal	1.000 kcal ↑