

Supplementary Material

Search strategies:

Literature search conducted in PubMed, Web of Science, and Cochrane CENTRAL covering studies between 2015 and 2025.

The searches included search concepts with words, phrases, synonyms and index terms: (("Obesity"[MeSH Terms] OR ("obeses"[All Fields] OR "Obesity"[MeSH Terms] OR "Obesity"[All Fields] OR "obese"[All Fields] OR "obesities"[All Fields] OR "obesity s"[All Fields]) OR ("overweight"[MeSH Terms] OR "overweight"[All Fields] OR "overweighted"[All Fields] OR "overweightness"[All Fields] OR "overweights"[All Fields]) OR ("adipose"[All Fields] OR "adiposities"[All Fields] OR "adiposity"[MeSH Terms] OR "adiposity"[All Fields]) OR "visceral adiposity"[All Fields] OR "ectopic fat"[All Fields] OR "central obesity"[All Fields] OR "waist-to-height ratio"[All Fields] OR "BMI"[All Fields]) AND ("Cardiovascular Diseases"[MeSH Terms] OR ("cardiovascular system"[MeSH Terms] OR ("cardiovascular"[All Fields] AND "system"[All Fields]) OR "cardiovascular system"[All Fields] OR "cardiovascular"[All Fields] OR "cardiovasculars"[All Fields]) OR ("ascvd"[All Fields] OR "ascvds"[All Fields]) OR "coronary artery disease"[All Fields] OR "heart failure"[All Fields] OR "HFpEF"[All Fields] OR "HFrEF"[All Fields] OR "atrial fibrillation"[All Fields] OR "AF"[All Fields] OR "peripheral artery disease"[All Fields] OR ("pathog dis"[Journal] OR "pad"[All Fields])) AND ("Weight Loss"[MeSH Terms] OR "lifestyle"[All Fields] OR ("exercise"[MeSH Terms] OR "exercise"[All Fields] OR "exercises"[All Fields] OR "exercise therapy"[MeSH Terms] OR

("exercise"[All Fields] AND "therapy"[All Fields]) OR "exercise therapy"[All Fields] OR "exercising"[All Fields] OR "exercise s"[All Fields] OR "exercised"[All Fields] OR "exerciser"[All Fields] OR "exercisers"[All Fields]) OR ("diet"[MeSH Terms] OR "diet"[All Fields]) OR "bariatric surgery"[All Fields] OR "metabolic surgery"[All Fields] OR "Roux-en-Y gastric bypass"[All Fields] OR "RYGB"[All Fields] OR "sleeve gastrectomy"[All Fields] OR "anti-obesity"[All Fields] OR ("semaglutide"[Supplementary Concept] OR "semaglutide"[All Fields]) OR "oral semaglutide"[All Fields] OR ("semaglutide"[Supplementary Concept] OR "semaglutide"[All Fields] OR "rybelsus"[All Fields]) OR ("tirzepatide"[Supplementary Concept] OR "tirzepatide"[All Fields] OR "tirzepatide"[MeSH Terms]) OR ("liraglutid"[All Fields] OR "liraglutide"[Supplementary Concept] OR "liraglutide"[All Fields] OR "liraglutide"[MeSH Terms] OR "liraglutide s"[All Fields])) AND ("randomized controlled trial"[All Fields] OR "RCT"[All Fields] OR "clinical trial"[All Fields] OR ("cohort"[All Fields] OR "cohort s"[All Fields] OR "cohorte"[All Fields] OR "cohorts"[All Fields]) OR "systematic review"[All Fields] OR "meta-analysis"[All Fields] OR ("guideline"[Publication Type] OR "guidelines as topic"[MeSH Terms] OR "guideline"[All Fields]) OR "practice guideline"[All Fields]) AND ("myristica"[MeSH Terms] OR "myristica"[All Fields] OR "mace"[All Fields] OR "major adverse cardiovascular events"[All Fields] OR "cardiovascular mortality"[All Fields] OR "heart failure hospitalization"[All Fields] OR "renal outcomes"[All Fields] OR "kidney outcomes"[All Fields] OR "KCCQ"[All Fields] OR ("curr res psychol"[Journal] OR "crp"[All Fields]))) AND (2015:2025[pdat])

Inclusion and exclusion criteria:

Participants: Include adults (≥ 18 years) with overweight or obesity. There are no limits on gender, ethnicity, or country of origin. Exclude studies involving under 18 years, pregnant participants.

Interventions: lifestyle intervention, pharmacological intervention, surgical therapy.

Outcome: cardiovascular outcomes and weight outcomes.

Study Design: high-quality randomized trials, prospective and/or retrospective cohorts, systematic reviews and meta-analyses, international clinical guideline/consensus statements were included. Case reports, studies without obesity definition or without outcomes relevant to CVD were excluded.

Table 1. Benefits of Lifestyle, Pharmacological, and Surgical Interventions on Weight and Cardiovascular Risk Management in Normoglycemic Individuals

Studies	Characteristic of Study and Population	CVD Phenotype and/or Risk (BMI/diabetes)	Intervention and Control	Weight Change	CV risk/Outcomes
Lifestyle Intervention					
Ge et al. 2020 ¹	Systematic review and network meta-analysis (median 26 weeks), 21,942 adults	Median BMI 33.0kg/m ²	14 diets (Atkins, DASH, Zone etc.) and 3 control diets	At 6 months: Low-carb -4.63 kg; Low-fat -4.37 kg; Moderate-macro -3.06 kg; Best named diets: Atkins -5.5 kg, DASH -3.6 kg, Zone -4.1 kg. Weight loss diminished by 12 months.	At 6 months (low-carb vs low-fat vs moderate-macro): SBP: -5.14 vs -5.05 vs -3.59 mm Hg; DBP: -3.21 vs -2.85 vs -1.57 mm Hg; LDL-C: -1.01 vs -7.08 vs -5.22 mg/dL; HDL-C: +2.31 mg/dL only with low-carb diet; Benefits on BP/LDL-C largely lost by 12 months except Mediterranean diet retained LDL-C reduction.
Kitzman et al. 2016 ²	RCT (20 weeks), 100 older adults	HFpEF, BMI 39.3±5.6kg/m ²	Caloric restriction diet ± exercise vs control	Exercise: -3kg (95%CI, -5 to -1); Diet: -7kg (95%CI, -9 to -5); Diet + Exercise: -11±1kg (10%).	Reduction in cardiac mass with diet (-4g, 95%CI -7 to 0), relative wall thickness with diet (-0.03, 95%CI -0.05 to -0.01). Increase in E/A ratio with exercise (+0.09, 95%CI 0.02 to 0.17). Improvement in peak VO ₂ with exercise (+1.2 mL/kg/min, 95%CI 0.7 to 1.7), diet (+1.3 mL/kg/min, 95%CI 0.8 to 1.8), additive effects combined (+2.5 mL/kg/min).
Ma et al. 2017 ³	Systematic review and meta-analysis (follow-up ≥1 year), 30,206 adults	BMI≥30kg/m ² , subset with T2D	Diet ± exercise vs control	-3.42kg at 1 year (95%CI -4.09 to -2.75); -2.51kg at 2 years (95%CI -3.42 to -1.60); -2.56kg at ≥3 years (95%CI -3.50 to -1.62).	Reduction in all-cause mortality (RR 0.82, 95%CI 0.71 to 0.95), CV mortality (RR 0.93, 95%CI 0.67 to 1.31), and CV events (RR 0.93, 95%CI 0.83 to 1.04).
Pathak et al. 2015 ⁴	Prospective cohort (5 years follow-up), 825 adults	Symptomatic paroxysmal/persistent AF, BMI≥27kg/m ²	A structured motivational and goal-directed program a diet + physical activity diary	Group ≥10% weight loss: -16.0±3.0 kg; 3–9% weight loss: -6.0±0.4 kg; <3% weight gain: +2.0±1.0kg. 66% of those with ≥10% weight in year 1 maintained at 34.5±15.5 months. This corresponded with higher	Weight loss program improved AF outcomes, arrhythmia-free without rhythm control: 45.5% (≥10% weight loss) vs 22.2% (3–9% weight loss) vs 13.4% (<3% weigh gain); total arrhythmia-free survival: 86.2% vs 65.5% vs 39.6%. Weight loss ≥10% resulted in a 6-fold (95%CI 3.4 to 10.3) greater probability of arrhythmia-free survival compared with the

				participation in the dedicated weight management clinic (84% vs 57% vs 30%, p<0.001).	other 2 groups. Weight fluctuation >5% partially offset this benefit, with a 2-fold (95%CI 1.0 to 4.3) increased risk of arrhythmia recurrence. SBP reduction 18/10/7 mmHg across three groups; larger LDL/TG/TC and hsCRP reductions in higher weight loss group; LA volume index and IVS decreased with weight loss, increased/unchanged in weight gain group.
Pharmacological Intervention					
Kosiborod et al. 2023⁵	RCT (52 weeks), 529 adults	HFpEF, BMI≥30kg/m ²	GLP-1RA (Semaglutide 2.4mg weekly) vs placebo	Mean percentage weight change -13.3 % with Semaglutide vs -2.6 % with placebo (estimated difference -10.7 percentage points, 95%CI -11.9 to -9.4).	Semaglutide improved KCCQ-CSS (difference 7.8 points, 95%CI 4.8 to 10.9), increased 6-min walk distance (difference 20.3 m, 95%CI 8.6 to 32.1), and lowered CRP (ratio 0.61, 95%CI 0.51 to 0.72) vs placebo. Serious adverse events were less frequent with Semaglutide (13.3% vs 26.7%).
Lincoff et al. 2023⁶	RCT (mean 39.8 months), 17,604 adults (age ≥45 years)	No prior CVD (MI, stroke, PAD), BMI ≥27kg/m ²	GLP-1RA (Semaglutide 2.4mg weekly) vs placebo	Semaglutide: -9.4% (at 3 years), sustained >10% loss at 4 years; Placebo: -1.5%; over 10% absolute weight loss sustained 4 years with Semaglutide.	Reduction in CV events (HR 0.80, 95%CI 0.72 to 0.90).
McMurray et al. 2019⁷	RCT (median 18 months), 4,744 adults	HFrEF, EF≤40%, NYHA class II-IV, BMI 28.2kg/m ²	SGLT2i (Dapagliflozin 10mg daily) vs placebo	-0.88±3.86kg (Dapagliflozin) vs 0.10±4.09 (placebo).	Reduction in HF event (HR 0.70, 95%CI 0.59 to 0.83), CV mortality (HR 0.82, 95%CI 0.69 to 0.98), all-cause mortality (HR 0.83, 95%CI 0.71 to 0.97). Improved KCCQ scores (HR 1.18, 95%CI 1.11 to 1.26).
Packer et al. 2025⁸	RCT (median 2 years), 731 adults (age≥40 years)	HF, EF≥50%, BMI ≥30kg/m ²	GLP-1RA (Tirzepatide up to 25mg weekly) vs placebo	No weight data documented.	Lower risk of the primary composite (CV death or HF worsening) with Tirzepatide vs placebo (9.9% vs 15.3%; HR 0.62, 95%CI 0.41 to 0.95), mainly fewer HF-worsening events (8.0% vs 14.2%; HR 0.54, 95%CI 0.34 to 0.85). CV death alone was uncommon and not different (HR 1.58, 95%CI 0.52 to 4.83).

					Greater change in KCCQ-CSS at 52 weeks (between-group difference 6.9, 95%CI 3.3 to 10.6).
Surgical Intervention					
Schiavon et al. 2018⁹	RCT (12 months), 100 adults (age 18–65 years)	Hypertension, no prior CVD, BMI 30.0–39.9kg/m ²	Roux-en-Y gastric bypass (RYGB) + medical therapy vs medical therapy alone	Reduction in BMI (difference –9.6kg/m ² , 95%CI –10.9 to –8.3), body weight (difference –26.9kg, 95%CI –32.4 to –21.4), waist circumference (difference –23.3cm, 95%CI –26.9 to –19.7).	Reduction in fasting plasma glucose (–14.7mg/dL, 95%CI –20.2 to –9.1), HbA1c (–0.4%, 95%CI –0.6 to –0.2), HOMA-IR (–3.75, 95%CI –4.8 to –2.7), LDL-C (–28.2mg/dL, 95%CI –41.8 to –14.8), triglycerides (–44.8mg/dL, 95%CI –65.9 to –23.8), CRP (–4.2mg/L, 95%CI –5.6 to –2.7), interventricular septum thickness (–0.56 mm, 95%CI –1.06 to –0.06), 10-year Framingham risk score (–2.46%, 95%CI –4.18 to –0.74), serum creatinine (–0.13mg/dL, 95%CI –0.19 to –0.07), number of antihypertensive medications (–3, 95%CI –3 to –2). Increased glomerular filtration rate (+14.37 mL/min, 95%CI 6.05 to 22.68).
van Veldhuisen et al. 2022¹⁰	Systematic review and meta-analysis (10–15 years), ~1 million adults	Severe obesity, subset with T2D	Bariatric surgery vs non-surgical	No weight data documented.	Reduction in all-cause mortality (HR 0.55, 95%CI 0.49 to 0.62), CV mortality (HR 0.59, 95%CI 0.47 to 0.73), HF (HR 0.50, 95%CI 0.38 to 0.66), myocardial infarction (HR 0.58, 95%CI 0.43 to 0.76), and stroke (HR 0.64, 95%CI 0.53 to 0.77).

Cardiovascular disease (CVD) phenotype was reported only when explicitly specified by the original study. Statistically significant outcomes reported only unless stated otherwise. Negative values indicate reduction (i.e., weight loss) relative to the control group unless stated otherwise. Values are mean differences, hazard ratios (HR), rate ratios (RR) or odds ratios (OR) with 95 % confidence intervals (CI). Abbreviations: AF, atrial fibrillation; BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; CV, cardiovascular; DBP, diastolic blood pressure; EF, ejection fraction; GLP-1RA, glucagon-like peptide-1 receptor agonist; HDL-C, high-density lipoprotein cholesterol; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HIIT, high-intensity interval training; HR, hazard ratio; KCCQ-CSS, Kansas City Cardiomyopathy Questionnaire clinical summary score; LDL-C, low-density lipoprotein cholesterol; RCT, randomized controlled trial; RR, risk ratio; SBP, systolic blood pressure, VO₂, oxygen consumption.

Table 2. Benefits of Lifestyle, Pharmacological, and Surgical Interventions on Weight and Cardiovascular Risk Management in Individuals with Type 2 diabetes

Studies (Years)	Characteristic of Study and Population	CVD Phenotype and/or Risk (BMI/diabetes)	Intervention and Control	Weight Change	CV risk/Outcomes
Lifestyle Intervention					
Lean et al. 2018¹¹	RCT (12 months intervention + ongoing maintenance), 306 adults	BMI 27–45kg/m ² , T2D	Intensive weight-loss programme vs usual care	–8.8kg (95%CI –10.3 to –7.3); 24% weight lost ≥15 kg with intervention (none in control)。	Reduction in HbA1c (–0.85%, 95%CI –1.10 to –0.59), oral antidiabetic medications (–0.97, 95%CI –1.11 to –0.84), antihypertensive medications (–0.58, 95%CI –0.75 to –0.42).
Taheri et al. 2020¹²	RCT (12 months), 158 adults (age 18–50 years)	BMI≥27kg/m ² , T2D	Intensive lifestyle vs usual care	–6.08kg (95%CI –8.37 to –3.79). 21% (Intensive lifestyle) vs 1% (usual care) achieved >15% weight loss.	Reduction in HbA1c (–0.62%, 95%CI –0.92 to –0.33), antidiabetic medications (–1.54, 95%CI –1.84 to –1.24); higher odds of diabetes remission (OR 12.03, 95%CI 5.17 to 28.03) and normoglycaemia (OR 12.07, 95%CI 3.43 to 42.45). Reduction in antihypertensive medications (–0.36, 95%CI –0.58 to –0.14), and resting heart rate (–3.2 bpm, 95%CI –6.1 to –0.4). Increase in HDL-C (+0.08 mmol/L, 95%CI 0.01 to 0.15, total cholesterol (+0.86 mmol/L, 95%CI 0.52 to 1.18), LDL-C (+0.82 mmol/L, 95%CI 0.51 to 1.13). Increase in walking MET-min/week (+410.3, 95%CI 160.3 to 660.3).
Pharmacological Intervention					
Badve et al. 2025¹³	Meta-analysis (≥12 months), 85,373 adults	HFpEF, BMI≥30kg/m ² , T2D	GLP-1RA vs placebo	No weight data documented.	Reduction in kidney composite (HR 0.82, 95%CI 0.73 to 0.93), HF (HR 0.84, 0.72 to 0.99), MACE (HR 0.87, 0.81 to 0.93), all-cause mortality (HR 0.88, 0.83 to 0.93).
Davies et al. 2015¹⁴	RCT (56 weeks), 846 adults	BMI≥27kg/m ² , T2D	GLP-1RA (Liraglutide 3.0mg or 1.8mg) vs placebo; alongside a 500 kcal/day deficit and ≥150 min/week activity	–4.00 % (95%CI –5.10 to –2.90) with Liraglutide 3.0 mg; –2.71 % (95%CI –4.00 to –1.42) with Liraglutide 1.8mg.	Reduction in HbA1c (–0.93%, 95%CI –1.08 to –0.78) with 3.0mg, –0.74% (95%CI –0.80 to –0.21) with 1.8mg; fasting plasma glucose (–31.89mg/dL, 95%CI –38.02 to –25.59) with 3.0mg, (–23.06 mmol/dL, 95%CI –30.27 to –15.86) with 1.8mg, net use of concomitant oral hypoglycaemic agents (5.63, 95%CI 3.62 to 8.76) with 3mg and (3.36, 95%CI 2.07 to 5.47) with 1.8mg. Reduction in total cholesterol (0.96, 95%CI 0.94 to 0.99), VLDL (0.87, 95%CI 0.81 to 0.93), triglycerides (0.86, 95%CI 0.80 to 0.92); increase in HDL-C (1.03, 95%CI

					0.72 to 6.57) with 3.0mg.SBP reduction (-2.59 mmHg, 95%CI -4.56 to -0.62) with 3.0mg, (-2.68 mmHg, 95%CI -4.98 to -0.38) with 1.8mg. hsCRP reduction (0.73, 95%CI 0.64 to 0.83) with 3.0mg, and (0.75, 95%CI 0.65 to 0.88) with 1.8mg.
Frías et al. 2021¹⁵	RCT/Phase 3 trial (40 weeks active treatment + 4 weeks follow-up), 1,879 adults	BMI≥25kg/m ² , T2D	GLP-1RA: Tirzepatide 5mg, 10mg, 15mg vs Semaglutide 1mg	-1.9kg (95%CI -2.8 to -1.0) with Tirzepatide 5mg, -3.6kg (95%CI -4.5 to -2.7) with 10mg, -5.5kg (-6.4 to -4.6) with 15mg vs Semaglutide 1mg.	Reduction in HbA1c -0.15% (95%CI -0.28 to -0.03) with Tirzepatide 5mg, -0.39 (-0.51 to -0.26) with Tirzepatide 10mg, -0.45 (-0.57 to 0.32) Tirzepatide 15mg vs Semaglutide 1mg.
Gerstein et al. 2019¹⁶	RCT (median 5.4 years), 9,901 adults (aged≥50 years)	BMI≥32kg/m ² , T2D	GLP-1RA (Dulaglutide 1.5mg weekly) or placebo	-1.46kg (95%CI -1.67 to -1.25).	Reduction in MACE (HR 0.88, 95 % CI 0.79–0.99), with the greatest single-component benefit seen in non-fatal stroke (HR 0.76, 95 % CI 0.61–0.95). Lowered the composite micro-vascular outcomes (HR 0.87, 95 % CI 0.79–0.95), driven by renal events (HR 0.85, 95 % CI 0.77 to 0.93).Reduction in total cholesterol (-0.07mM, 95%CI -0.10 to -0.03), LDL-C (-0.05mM, 95%CI -0.08, -0.02), SBP (mm Hg, 95%CI -2.07, -1.33), mean BP (-0.49mm Hg, 95%CI -0.73 to -0.25).
Kosiborod et al. 2024¹⁷	RCT (52 weeks), 616 adults	HFpEF, BMI≥30kg/m ² , T2D,	GLP-1RA (Semaglutide 2.4mg weekly) vs placebo	-6.4% (95%CI, -7.6 to -5.2).	Reduction in HF events HR 0.40 (95 % CI 0.15 to 0.92), HbA1c (-0.8%, 95 % CI -1.0 to -0.6), CRP ratio 0.67 (95%CI, 0.55 to 0.80); NT-proBNP ratio 0.80 (95 % CI 0.70 to 0.90).Increase in KCCQ-CSS (+7.3 points; 95%CI 4.1 to 10.4), walk distance (+14.3m, 95%CI 3.7 to 24.9).
McGuire et al. 2025¹⁸	RCT (median 49.5 months), 9,650 adults	Established CVD and/or CKD, T2D	GLP-1RA (oral semaglutide, once/daily, dose started at 3 mg, escalated to 7 mg and then 14 mg + standard care) vs	-4.22 kg (semaglutide) vs -1.27 kg (placebo); estimated difference -2.95 kg (95%CI -3.18 to -2.73).	Primary MACE: 12.0% vs 13.8% (HR 0.86, 95%CI 0.77 to 0.96). CV death: 6.2% vs 6.6% (HR 0.93, 95%CI 0.80 to 1.09). Nonfatal myocardial infarction 4.0% vs 5.2% (HR 0.74, 95%CI 0.61 to 0.89). Major adverse limb events number 71 vs 99 (HR 0.71, 95%CI 0.52–0.96).

			matching placebo + standard care		
Surgical Intervention					
Aminian et al. 2019¹⁹	Matched cohort study (median 3.9 years, up to 8 years), 13,722 adults	BMI \geq 30kg/m ² , T2D	Bariatric surgery (various) vs usual medical care (matched by baseline risk factors)	-20.3 kg (95%CI, 20.1-20.6) at 8 years.	Reduction in MACE (HR 0.61, 95%CI 0.55 to 0.69), all-cause mortality (HR 0.59, 95%CI 0.48 to 0.72), HF (HR 0.38, 95%CI 0.30 to 0.49, CAD (HR 0.69, 95%CI 0.54 to 0.87), cerebrovascular disease (HR 0.67, 95%CI 0.48 to 0.94), nephropathy (HR 0.40, 95%CI 0.31 to 0.52), atrial fibrillation (HR 0.78, 95%CI 0.62 to 0.97); HbA1c -1.1% (95%CI 1.0% to 1.2%).
Mingrone et al. 2021²⁰	10-year follow-up of RCT; 60 adults	BMI \geq 35kg/m ² , T2D	Biliopancreatic diversion (BPD) or RYGB vs medical therapy	-35.7kg (95%CI, -49.7 to -21.6) with BPD, -30.8kg (95%CI, -44.8 to -16.7) with RYGB.	Reduction in diabetes complications with surgery (RR 0.07, 95 % CI 0.01 to 0.48); reduced anti-diabetes drugs/day to 0.7 \pm 0.9 (BPD) and 1.4 \pm 0.9 (RYGB) vs 2.9 \pm 0.8; reduced insulin to 0 % (BPD) and 2.5 % (RYGB) vs 53.3 %; reduced anti-hypertensive tablets/day to 0.6 \pm 0.8 (BPD) and 1.6 \pm 1.5 (RYGB) vs 3.2 \pm 2.0.
Schauer et al. 2017²¹	RCT (5 years), 150 adults	BMI 27-43kg/m ² , T2D	Bariatric surgery (RYGB or sleeve gastrectomy) + medical therapy vs intensive medical therapy	-23% (bypass) and -19% (sleeve) vs -5% (medical therapy) in body weight change.	Reduction in HbA1c with bariatric (-2.1%) vs medical therapy (-0.3%); 29% RYGB and 23% sleeve achieved HbA1c \leq 6% vs 5% in medical therapy; triglyceride level -40%, -29%, and -8% in RYGB, sleeve, and medical therapy, respectively; HDL-C: 32%, 30%, and 7%, insulin use: -35%, -34%, and -13%. Sleeve-gastrectomy uniquely lowered urinary albumin-to-creatinine ratio.

Cardiovascular disease (CVD) phenotype was reported only when explicitly specified by the original study. Statistically significant outcomes reported only unless stated otherwise. Negative values indicate weight loss relative to the control group unless stated otherwise. Values are mean \pm SD/mean differences, hazard ratios (HR), rate ratios (RR) or odds ratios (OR) with 95 % confidence intervals (CI). Abbreviations: BMI, body mass index; BPD, biliopancreatic diversion; CAD, coronary artery disease; CI, confidence interval; CRP, C-reactive protein; CV, cardiovascular; DBP, diastolic blood pressure; GLP-1RA, glucagon-like peptide-1 receptor agonist; HDL-C, high-density lipoprotein cholesterol; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HIIT, high-intensity interval training; KCCQ-CSS, Kansas City Cardiomyopathy Questionnaire Clinical Summary Score; LDL-C, low-density lipoprotein cholesterol; MACE, major adverse cardiovascular events; NS, not significant; RCT, randomized controlled trial; RR, risk ratio; RYGB, Roux-en-Y gastric bypass; SBP, systolic blood pressure; SGLT2i, sodium glucose transporter-2 inhibitors; VLDL, very-low-density lipoprotein.

Table 3. Summary of Lifestyle and Pharmacological Interventions on Weight and Cardiovascular Risk Management in Individuals with Type 1 Diabetes

Studies (Years)	Characteristic of Study and Population	CVD Phenotype and/or Risk (BMI/diabetes)	Intervention and Control	Primary Outcome(s)	Secondary Outcome(s)	Weight Change	Side-effects
Lifestyle Intervention							
Tomah et al. 2023²²	Longitudinal cohort study (12 weeks intervention, and 10 years follow-up), 128 adults (Group A: <7% weight loss in a 12-week ILI, Group B: ≥7% weight loss in a 12-week ILI)	BMI 30–45kg/m ² , T1D/T2D	Intensive lifestyle intervention (ILI)	Group B (≥7% weight loss at 1 year) maintained 9.3% weight loss at 10 years vs 4.3% in Group A; significantly lower HbA1c in Group B at 10 years (7.3% vs 8.0%).	Improved lipid profile maintained in both groups; Group B had lower TG increase; 68% reduced risk of nephropathy in Group B (HR 0.32, p=0.007); no difference in retinopathy or neuropathy.	–10.8±4.6kg at 12 week, –9.1±0.8 at 1 year, and 7.7±10kg at 10y compared with baseline; Group A maintained 4.3±9.5kg (–4.3%) vs 10.8±9.3kg (–9.3%) in group B at 10 years.	None reported.
Yardley et al. 2014²³	Systematic review and meta-analysis (minimum 8 weeks, up to 9 months), 323 adults	T1D	Exercise interventions	HbA1c decreased by 0.78% (95%CI – 1.14 to –0.41, p<0.0001); greater reduction seen in those with baseline HbA1c >8.5%.	VO ₂ max increased by 3.45 mL/kg/min (p=0.02); weight reduced by 1.1 kg (p=0.03); insulin dose reduced in those with poor baseline control; no consistent effect on lipids.	No significant BMI change (MD –0.02, 95%CI –0.40 to 0.37) in 3 trials.	Only one study reported adverse events; no post-exercise hypoglycaemia observed.
Pharmacological Intervention							
Ahren et al. 2016²⁴	RCT (26 weeks), 835 adults	35kg/m ² , T1D	GLP-1RA (Liraglutide 1.8, 1.2, and 0.6mg daily) vs placebo	Significant HbA1c reduction vs placebo at all doses: –0.35% (1.8 mg), –0.23% (1.2 mg), –0.24% (0.6	Reduced total daily insulin dose (dose-dependent, mostly prandial): –10–15% vs baseline increased TRIM-D QoL scores in all liraglutide groups.	–5.1kg (1.8mg), –4.0kg (1.2mg), –2.5kg (0.6mg) vs –0.2kg (placebo).	Increased nausea (dose-dependent), symptomatic hypoglycaemia with 1.2 mg (21.3 vs 16.6 events/patient/year), ketosis with 1.8 mg

				mg) vs 0.01% (placebo).	More patients achieved composite targets (HbA1c <7% and no severe hypo) with liraglutide 1.8 mg increased 1,5-anhydroglucitol with 1.8 mg (suggesting improved postprandial control); no effect on fasting glucose, C-peptide, or fasting glucagon.		(0.5 vs 0.1 events/patient/year); low discontinuation due to AE.
Anson et al. 2023²⁵	Retrospective cohort study (5 years), adult participants from TriNetX database; SGLT2i (n=992), GLP-1RA (n=1822); PSM (n=933)	T1D	SGLT2i or GLP-1RA	GLP-1 RA: HbA1c decreased by -5.4 mmol/mol (-0.5%); SGLT2i: HbA1c decreased by -2.6 mmol/mol (-0.2%)	GLP-1 RA: decreased cholesterol; SGLT2i: increased eGFR (+3.5 vs -7.2 ml/min); decreased CKD, HF, and hospitalisation.	-2.4kg with SGLT2i; +1.5kg with GLP-1RA.	SGLT2i: increased DKA (RR 2.08), UTI/pyelonephritis (RR 2.27); GLP-1 RA: fewer adverse events overall.
Dandona et al. 2018²⁶	Phase 3 RCT (52 weeks), 833 adults	T1D	SGLT2i (Dapagliflozin 5mg or 10mg) vs placebo	HbA1c significantly reduced: -0.33% (5 mg), -0.36% (10 mg) vs placebo	Body weight decreased (-2.95% and -4.54%), insulin dose decreased, 43-46% achieved ≥0.5% HbA1c reduction without severe hypoglycaemia, decreased fasting glucose, decreased SBP in hypertensive group.	-2.31 kg (5mg), -3.65kg (10mg) vs placebo.	Increased DKA: 4.0% (5 mg), 3.4% (10 mg), vs 1.9% (placebo); mostly mild-moderate. Genital infections (especially in women), UTIs, rashes, and hypersensitivity also reported.

Mathieu et al. 2016²⁷	RCT 52 weeks, treat-to-target, 1,398 adults	T1D	GLP-1RA (Liraglutide 1.8, 1.2, or 0.6mg) vs placebo	Reduction in HbA1c (up to -0.54%), reduction in insulin dose (up to 8%), and body weight (~-4.9kg).	Quality of life TRIM-D total score was significantly higher for all liraglutide groups, particularly for diabetes management. No significant treatment differences in the SF-36 overall physical and mental scores.	~ -4.9kg Dose-dependent weight loss.	Increased symptomatic hypoglycaemia (RR ~1.31), increased ketosis (notably at 1.8mg, RR 2.22), GI side-effects (dose-dependent nausea), DKA (n=8, all in liraglutide groups).
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Cardiovascular disease (CVD) phenotype was reported only when explicitly specified by the original study. Negative values indicate reduction unless stated otherwise. Abbreviations: BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; chronic kidney disease; CV, cardiovascular; DBP, diastolic blood pressure; GLP-1RA, glucagon-like peptide-1 receptor agonist; HDL-C, high-density lipoprotein cholesterol; HF, heart failure; HR, hazard ratio; LDL-C, low-density lipoprotein cholesterol; RCT, randomized controlled trial; RR, risk ratio; SBP, systolic blood pressure.

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