Weight Centric Management of Type 2 Diabetes: Current Evidence and Future Directions

Arshid Rafiq[1], Amit Gupta[2], Nagendra Kumar Sing[3], Shahnawaz Bandh[4], Rutba Maqbool[5]
[1,2,3,4,5] *AMRL Ventures Pvt Ltd*

Abstract—**Background: Overweight and obesity affect most people with type 2 diabetes (T2D) and drive insulin resistance, beta-cell failure and cardiorenal risk. Treatment paradigms have shifted from glucose-centric to weight-centric care, in which substantial, sustained weight loss is a primary therapeutic target alongside glycaemic control.**

Scope: This narrative review summarises the pathophysiological basis for weight-centric management and the evidence from 2013 to 2026 for lifestyle, pharmacological and surgical interventions. It draws on the ADA Standards of Care 2026, the 2025 Lancet Commission on clinical obesity, and recent trials including SURPASS-CVOT, SOUL, ACHIEVE-1, TRANSCEND-T2D-1 and REIMAGINE 2.

Index Terms—**Weight loss of 5–7% improves glycaemia and cardiovascular risk factors, while losses of 10–15% or more can induce remission. Intensive dietary programmes achieve remission in 46–61% of people with early T2D at one year, though durability is limited. Incretin-based agents now deliver 10–17% weight loss in T2D, with proven cardiovascular and kidney benefits for semaglutide and favourable cardiorenal outcomes for tirzepatide versus dulaglutide. Metabolic surgery provides the most durable glycaemic control and remission over 7–12 years.**

Conclusions: Weight should be assessed and targeted at every stage of T2D care. Priorities include durable weight maintenance, preservation of lean mass, population-specific adiposity thresholds for South Asians, and equitable access to effective therapies.

I. INTRODUCTION

Type 2 diabetes and obesity are converging global epidemics. The International Diabetes Federation estimated 537 million adults with diabetes in 2021, projected to reach 783 million by 2045 [1]. Over the same period, more than one billion people worldwide were living with obesity by 2022 [2]. In India, the ICMR-INDIAB study reported diabetes in 11.4% and generalised obesity in 28.6% of adults, with abdominal obesity in 39.5% [3].

Around 80–90% of people with T2D have overweight or obesity. Yet for decades, management focused almost exclusively on lowering glucose, often with agents such as insulin, sulfonylureas and thiazolidinediones that promote weight gain. This approach treated the consequence, hyperglycaemia, rather than a major cause, excess and dysfunctional adiposity.

A weight-centric paradigm proposes that weight management be a primary goal of T2D treatment, not an adjunct [4]. This view is now embedded in the ADA Standards of Care [5] and the ADA/EASD consensus on hyperglycaemia management [6]. It has been made practical by incretin-based therapies that achieve weight losses once possible only with surgery.

This review examines the biological rationale for weight-centric care, the evolution of guidelines, and current evidence for lifestyle, pharmacological and surgical strategies. It also addresses remission, considerations for South Asian populations, and future directions.

II. PATHOPHYSIOLOGICAL LINK BETWEEN ADIPOSITY AND TYPE 2 DIABETES

Excess adiposity causes T2D through insulin resistance and progressive beta-cell dysfunction, and both are at least partly reversible with weight loss.

Adipose tissue dysfunction and insulin resistance. When subcutaneous fat stores exceed their capacity, enlarged adipocytes release more non-esterified fatty acids, pro-inflammatory cytokines (TNF-α, IL-6) and less adiponectin [7]. These signals impair insulin action in muscle and liver. Visceral fat drains directly to the liver via the portal circulation, amplifying hepatic insulin resistance.

Ectopic fat and the twin-cycle hypothesis. Taylor proposed that T2D results from two interacting vicious cycles [8]. In the liver, fat accumulation causes hepatic insulin resistance and raised fasting glucose production. Excess hepatic triglyceride is exported as VLDL and deposited in the pancreas, where lipotoxicity impairs beta-cell function. Each individual appears to have a personal fat threshold beyond which diabetes develops, irrespective of BMI.

Reversibility. Mechanistic studies within the DiRECT trial showed that remission followed falls in liver and pancreatic fat, with recovery of first-phase insulin secretion [9]. This establishes the biological basis for remission and explains why early; substantial weight loss is most effective.

Incretin and gut–brain pathways. GLP-1 and GIP act on the pancreas, brain and adipose tissue to reduce appetite, slow gastric emptying and improve insulin secretion. Targeting these pathways now allows pharmacological weight loss of a magnitude sufficient to reverse ectopic fat accumulation.

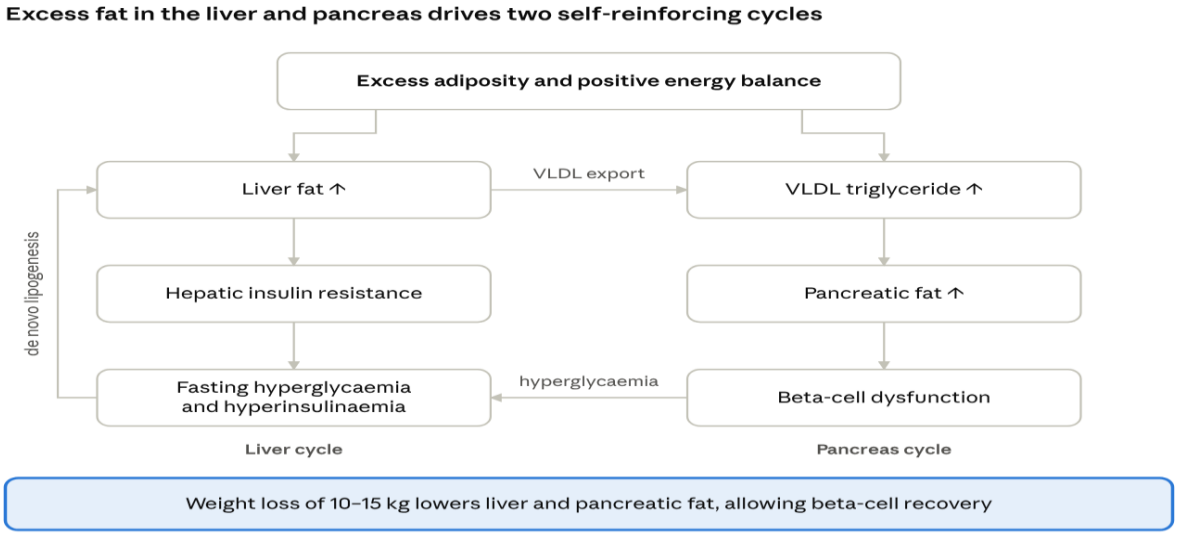


Figure 1 twin-cycle hypothesis, adapted from Taylor [8,9]

Figure 1. The twin-cycle hypothesis of type 2 diabetes. Liver fat drives hepatic insulin resistance and hyperinsulinemia, which further promotes hepatic lipogenesis. Exported VLDL triglyceride accumulates in the pancreas and impairs beta-cell function, worsening hyperglycaemia. Sustained weight loss reverses both cycles [8,9].

Beta-cell reserve and disease duration. Beta-cell function declines progressively after diagnosis. In DiRECT, people who did not achieve remission despite similar fat loss had longer diabetes duration and lower insulin secretory capacity at baseline [9]. This supports intervening early, before beta-cell dedifferentiation becomes irreversible.

Ethnic differences in fat distribution. South Asians store more fat in visceral and ectopic depots, and less in subcutaneous tissue, than Europeans of the same BMI [35]. Their personal fat threshold is therefore reached at a lower body weight, which explains the earlier onset of T2D and supports lower diagnostic thresholds for obesity (section 8).

Systemic consequences. The same ectopic fat that drives T2D also underlies MASLD, atherogenic dyslipidaemia, hypertension and heart failure with preserved ejection fraction [7]. Weight reduction therefore addresses multiple cardiometabolic complications at once, a key argument for weight-centric rather than glucose-centric care.

III. EVOLUTION OF GUIDELINES

Current guidelines place weight management alongside glycaemic control as a co-primary goal in people with T2D and overweight or obesity.

The 2022 ADA/EASD consensus report first framed weight management as a core component of T2D care and favoured agents with high weight-loss efficacy, such as semaglutide and tirzepatide, when weight is a

priority [6]. The ADA Standards of Care have progressively strengthened this position. The 2026 Standards recommend annual screening for overweight and obesity using BMI plus a second measure to confirm excess adiposity, such as waist circumference [5,10]. They state that 5–7% weight loss improves glycaemia and intermediate cardiovascular risk factors, while greater losses yield larger benefits, including possible remission.

New elements in the 2026 Standards include guidance on individualising obesity pharmacotherapy doses, monitoring nutritional intake during treatment, and maintaining physical activity to preserve lean mass [10]. The pharmacological algorithm now lists dual GIP/GLP-1 receptor agonists for people with T2D and obesity, symptomatic heart failure with preserved ejection fraction, or metabolic dysfunction-associated steatotic liver disease (MASLD/MASH) [5].

In parallel, the 2025 Lancet Diabetes & Endocrinology Commission redefined obesity [11]. It distinguishes preclinical obesity (excess adiposity with preserved organ function) from clinical obesity (excess adiposity causing organ dysfunction or limitation of daily activities). Under this framework, obesity with T2D is a form of clinical obesity warranting active treatment. The Commission also recommends confirming excess adiposity with body-composition or anthropometric measures rather than BMI alone.

3.1 Clinical assessment of adiposity

BMI alone misclassifies risk, particularly in Asian populations and older adults, so assessment should combine BMI with a measure of fat distribution and a review of obesity-related complications [5,11].

Anthropometry. Waist circumference is the simplest marker of visceral adiposity. Thresholds of 90 cm for men and 80 cm for women are widely used for South Asians, compared with 94 cm and 80 cm for Europeans. A waist-to-height ratio above 0.5 is a useful, population-independent alternative [36]. Where available, bioimpedance or DXA can quantify fat and lean mass, which also provides a baseline for monitoring lean-mass loss during treatment.

Complications and staging. Assessment should include MASLD (for example using the FIB-4 score), obstructive sleep apnoea, osteoarthritis, heart failure, CKD and psychological wellbeing. Under the Lancet Commission framework, people with T2D already meet the definition of clinical obesity once excess adiposity is confirmed [11]. The Indian classification similarly places T2D with abdominal adiposity in Stage 2, warranting intensive treatment [36].

Weight history and medications. A history of weight trajectory, previous attempts and eating behaviour guides the choice of intervention. Weight-promoting drugs, including insulin, sulfonylureas, pioglitazone, some antidepressants, antipsychotics and glucocorticoids, should be reviewed and substituted where possible.

Setting a target. Benefits rise with the magnitude of weight loss (Figure 2). A target of at least 5–7% is appropriate for most people, while 10–15% or more is the goal when remission or major improvement in comorbidities is sought [5].



Figure 2 weight-loss magnitude and expected benefits [5,13,14]

Figure 2. Weight-loss magnitude and expected benefits in T2D. Modest loss improves glycaemia and risk factors; larger, sustained losses are associated with fewer cardiovascular events and remission [5,13,14].

IV. LIFESTYLE AND DIETARY INTERVENTIONS

Structured dietary programmes with total diet replacement can induce remission in about half of people with early T2D, but maintaining weight loss remains the central challenge.

Look AHEAD. This trial randomised 5,145 adults with T2D and overweight to intensive lifestyle intervention or diabetes support and education [12]. Despite 8.6% weight loss at one year and better glycaemic and risk-factor control, it was stopped for futility after 9.6 years with no reduction in cardiovascular events (HR 0.95). A post-hoc analysis, however, found that participants losing at least 10% of body weight in year one had a 21% lower risk of the primary outcome [13]. This suggested the magnitude of weight loss, not the intervention itself, determined benefit.

DiRECT. In this UK primary-care trial, an 825–853 kcal/day total diet replacement for 12–20 weeks, followed by food reintroduction and maintenance support, achieved remission in 46% of intervention participants at 12 months versus 4% of controls [14]. Remission was achieved by 86% of those who lost 15 kg or more. At two years, 36% remained in remission [15]. In the five-year extension, 13% of the extension cohort were in remission, and 26% of those in remission at year two remained so [16]. Notably, the original intervention group had fewer serious adverse events needing hospital admission than controls (4.8 vs 10.2 per 100 patient-years).

DIADEM-I. In young adults (18–50 years) of predominantly South Asian and Middle Eastern origin with early T2D in Qatar, an intensive lifestyle programme produced 12 kg mean weight loss and 61% remission at 12 months, versus 12% with usual care [17]. This is directly relevant to Asian populations, in whom remission may occur at lower absolute weight loss.

Practical implications. Low-calorie and very-low-calorie diets, meal replacements and structured behavioural support are effective when offered early, ideally within six years of diagnosis. Long-term maintenance support, regular physical activity including resistance training, and adjunctive pharmacotherapy for weight regain are increasingly recommended.

Dietary patterns, physical activity and behavioural support

No single eating pattern is superior for weight loss in T2D; the best diet is one that creates a sustained energy deficit and that the individual can maintain [5].

Energy restriction. A daily deficit of about 500–750 kcal typically produces 0.5–1 kg weight loss per week. Low-calorie diets (800–1,200 kcal/day) and total diet replacement (about 800–900 kcal/day using formula products) achieve larger and faster losses. These approaches require medication review before starting, because insulin and sulfonylurea doses usually need to be reduced or stopped to avoid hypoglycaemia, and antihypertensives may need adjustment [14].

Macronutrient composition. Mediterranean-style, low-carbohydrate, plant-based and DASH-style patterns all improve glycaemia and weight when energy intake falls [5]. Low-carbohydrate diets often lower HbA1c faster in the short term, but differences between patterns tend to narrow by 12–24 months. In South Asian settings, where diets are often high in refined carbohydrate, reducing white rice, refined wheat and sugar-sweetened beverages while increasing protein, legumes and vegetables is a practical, culturally adaptable target.

Time-restricted eating and intermittent fasting. These strategies can reduce energy intake for some people, but they offer no clear advantage over continuous energy restriction of the same size. People on insulin or sulfonylureas need careful dose adjustment, particularly during religious fasting such as Ramadan.

Physical activity. At least 150 minutes per week of moderate-intensity aerobic activity, plus resistance training on two or three days per week, is recommended [5]. Exercise alone produces modest weight loss, but it improves insulin sensitivity independent of weight change and is associated with better weight maintenance. Resistance training has become more important in the incretin era, because it helps preserve lean mass during rapid weight loss [10].

Behavioural support. High-intensity programmes, with at least 16 sessions over six months, achieve greater weight loss than brief advice [5]. Effective components include self-monitoring of food intake and weight, goal setting, problem solving and relapse prevention. Digital and telehealth delivery can widen access where dietitians are scarce. Screening for depression, diabetes distress and disordered eating should precede intensive dietary interventions.

V. PHARMACOTHERAPY

Incretin-based agents have transformed weight-centric management, delivering 10–17% weight loss in people with T2D together with cardiovascular and kidney benefits in outcome trials.

5.1 GLP-1 receptor agonists

Semaglutide 2.4 mg weekly reduced body weight by 9.6% versus 3.4% with placebo over 68 weeks in adults with T2D and overweight (STEP 2) [18]. Weight loss in T2D is consistently smaller than in people without diabetes, reflecting older age, concomitant weight-promoting drugs and reduced glycosuria with better control.

Orforglipron, an oral small-molecule non-peptide GLP-1 receptor agonist taken without food or water restrictions, lowered HbA1c by up to 1.48% and weight by 7.6% at 40 weeks in early T2D (ACHIEVE-1) [21]. Oral agents of this type could widen access by avoiding injection and cold-chain storage.

5.2 Dual and triple agonists, and amylin combinations

Tirzepatide, a GIP/GLP-1 receptor agonist, was superior to semaglutide 1 mg for both HbA1c and weight in SURPASS-2 [19]. In SURMOUNT-2, tirzepatide 15 mg produced 14.7% weight loss in adults with T2D and obesity [20].

Retatrutide, a GIP/GLP-1/glucagon triple agonist, lowered HbA1c by up to 2.0% and weight by up to 16.8% at 40 weeks in early T2D, without a weight plateau (TRANSCEND-T2D-1) [22]. CagriSema, combining the amylin analogue cagrilintide with semaglutide, was superior to semaglutide 2.4 mg for HbA1c and weight at 68 weeks (REIMAGINE 2) [23].

Table 1. Glycaemic and weight outcomes of key incretin-based trials in T2D

Agent (highest dose)	Trial	Population	Duration	HbA1c change	Weight change
Semaglutide 2.4 mg weekly	STEP 2 [18]	T2D, BMI ≥27	68 weeks	−1.6%	−9.6% (placebo −3.4%)
Tirzepatide 15 mg weekly	SURPASS-2 [19]	T2D on metformin	40 weeks	−2.30% (semaglutide 1 mg −1.86%)	−11.2 kg (semaglutide −5.7 kg)
Tirzepatide 15 mg weekly	SURMOUNT-2 [20]	T2D, BMI ≥27	72 weeks	−2.1%	−14.7% (placebo −3.2%)
Orforglipron 36 mg daily (oral)	ACHIEVE-1 [21]	Early T2D, diet and exercise	40 weeks	−1.48% (placebo −0.41%)	−7.6% (placebo −1.7%)
Retatrutide 9–12 mg weekly	TRANSCEND-T2D-1 [22]	Early T2D, diet and exercise	40 weeks	Up to −2.0% (placebo −0.8%)	Up to −16.8% (12 mg)
CagriSema 2.4/2.4 mg weekly	REIMAGINE 2 [23]	T2D on metformin ± SGLT2i	68 weeks	−1.91% (semaglutide 2.4 mg −1.76%)	−14.2% (semaglutide −10.2%)

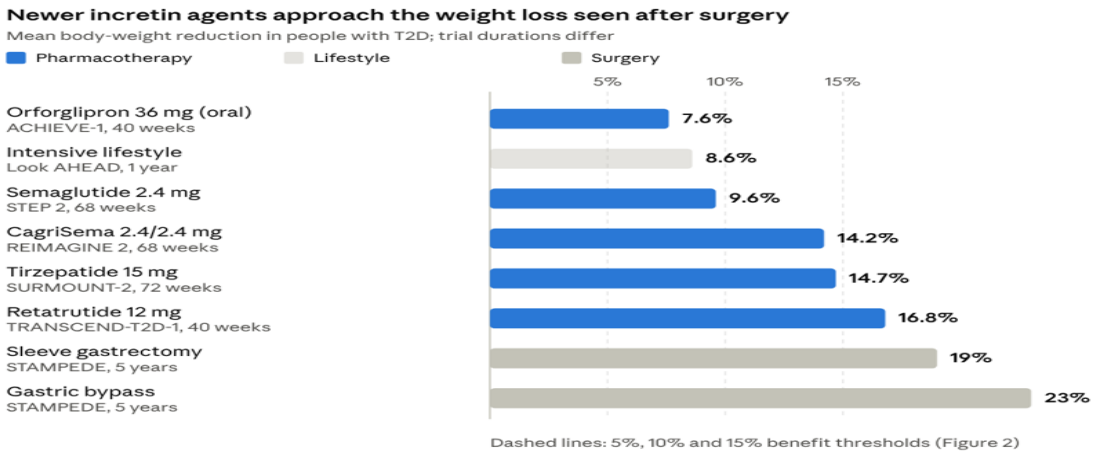


Figure 3 mean % weight loss from Look AHEAD [12], STEP 2 [18], SURMOUNT-2 [20], ACHIEVE-1 [21], TRANSCEND-T2D-1 [22], REIMAGINE 2 [23], STAMPEDE [30]

Figure 3. Mean weight loss across interventions in people with T2D. The newest incretin agents achieve 14–17% weight loss, narrowing the gap with metabolic surgery (19–23% at five years). Cross-trial comparisons are indicative only, because populations, durations and estimands differ.

5.3 Cardiovascular and kidney outcomes

Weight-lowering incretin agents also reduce hard outcomes. Injectable semaglutide (SUSTAIN-6) and dulaglutide (REWIND) reduced major adverse cardiovascular events (MACE) in T2D [24,25]. Oral semaglutide reduced MACE by 14% in T2D with atherosclerotic disease or CKD, independent of SGLT2 inhibitor use (SOUL) [26].

SURPASS-CVOT, the first active-comparator cardiovascular outcomes trial, randomised 13,299 adults with T2D and atherosclerotic disease [27]. Tirzepatide was non-inferior, but not superior, to dulaglutide for MACE. All-cause mortality was 16% lower, and weight loss (about 12% vs 5% at 36 months) and kidney outcomes were better, although these secondary findings were not adjusted for multiplicity. In people with obesity but without diabetes, semaglutide reduced MACE by 20% (SELECT), indicating benefit beyond glucose lowering [28]. Semaglutide also reduced major kidney events by 24% in T2D with CKD (FLOW) [29].

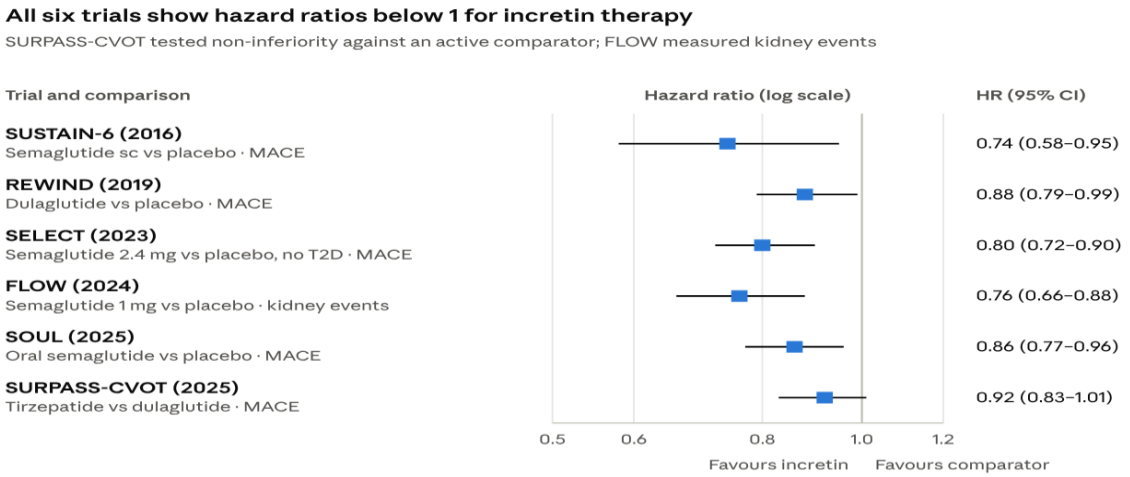


Figure 4 primary outcomes of SUSTAIN-6 [24], REWIND [25], SELECT [28], FLOW [29], SOUL [26], SURPASS-CVOT [27]

Figure 4. Primary outcomes of cardiorenal trials of incretin-based therapy. Squares show hazard ratios and lines show 95% confidence intervals. MACE, three-point major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction or non-fatal stroke). SELECT enrolled people with obesity and cardiovascular disease but without diabetes.

Taken together, these trials show that weight-lowering incretin therapy reduces cardiovascular and kidney events beyond its effects on glucose. The benefit in SELECT, in people without diabetes, and mediation analyses from these trials suggest that weight loss, reduced inflammation and direct vascular actions all contribute.

5.4 Other agents and safety

SGLT2 inhibitors produce modest weight loss of 2–3 kg but offer robust heart failure and kidney protection, and combine well with incretin agents [6]. Metformin is weight-neutral. Insulin and sulfonylureas should be minimised or de-escalated when potent weight-lowering agents are started, to reduce hypoglycaemia and weight gain.

Incretin therapies commonly cause nausea, vomiting and diarrhoea, mostly during dose escalation. Other considerations include gallbladder disease, pancreatitis, early worsening of diabetic retinopathy with rapid HbA1c reduction, and loss of lean mass. Gradual titration, adequate protein intake and resistance exercise help mitigate these effects.

5.5 Mechanisms of action and practical prescribing

How the newer agents differ. GLP-1 receptor agonists act on hypothalamic and hindbrain centres to reduce appetite and food reward, slow gastric emptying, and enhance glucose-dependent insulin secretion while suppressing glucagon. Adding GIP agonism, as in tirzepatide, appears to enhance weight loss and improve tolerability, possibly through central effects on nausea and direct actions on adipose tissue. Glucagon receptor agonism, the third component of retatrutide, increases energy expenditure and hepatic fat oxidation, which may explain its large effects on weight and liver fat [22]. Amylin analogues such as cagrilintide add satiety signalling through the area postrema and complement GLP-1 action [23].

Choosing an agent. Selection should consider the weight-loss target, cardiovascular and kidney comorbidities, route of administration, cost and availability [5,6]. For people with established atherosclerotic disease, agents with proven MACE reduction (semaglutide or dulaglutide) are preferred, and tirzepatide is a reasonable alternative given its non-inferiority to dulaglutide [27]. For CKD, semaglutide has dedicated kidney outcome data, and SGLT2 inhibitors should be added where eGFR allows [29]. Where weight loss of 15% or more is the goal, tirzepatide currently offers the greatest efficacy among approved agents [20].

Initiation and titration. Doses are escalated every four weeks to limit gastrointestinal effects. The 2026 ADA Standards advise individualising titration, including slower escalation or holding at a tolerated dose rather than forcing the maximum [10]. Advice to eat smaller meals, stop eating at satiety, limit fatty foods and maintain hydration reduces nausea and the risk of dehydration-related acute kidney injury.

De-escalating other glucose-lowering drugs. When a potent incretin agent is started in people with HbA1c near target, sulfonylureas should usually be stopped and insulin doses reduced by about 10–20%, with closer glucose monitoring. Continuous glucose monitoring, now recommended more widely in the 2026 Standards, helps guide this process safely [10].

Monitoring. Weight, HbA1c, blood pressure and lipids should be reviewed about three months after reaching the maintenance dose. People with pre-existing diabetic retinopathy need ophthalmic review when rapid HbA1c reduction is expected. Antihypertensive doses often need reduction as weight falls.

VI. METABOLIC AND BARIATRIC SURGERY

Metabolic surgery remains the most effective and durable weight-centric intervention, with superior glycaemic control and remission sustained over 7–12 years.

In STAMPEDE, 150 adults with uncontrolled T2D were randomised to intensive medical therapy, Roux-en-Y gastric bypass or sleeve gastrectomy [30]. At five years, HbA1c ≤6.0% was achieved by 29% after bypass and 23% after sleeve gastrectomy, versus 5% with medical therapy. In an Italian trial with 10-year follow-up, 37.5% of surgical patients remained in remission versus 5.5% with conventional therapy [31]. The ARMMS-T2D consortium pooled four US randomised trials with a median follow-up of 11 years [32]. At seven years, surgery lowered HbA1c by 1.6% versus 0.2% with medical and lifestyle management. Remission rates were 18.2% versus 6.2% at seven years and 12.7% versus 0% at 12 years. Insulin use at seven years was 16% after surgery versus 56% with medical care.

The 2022 ASMBS/IFSO guidelines recommend surgery for BMI ≥35 kg/m² regardless of comorbidity, and consideration for BMI 30–34.9 kg/m² with metabolic disease [33]. They advise lower thresholds in Asian populations, with surgery considered from BMI ≥27.5 kg/m². Risks include micronutrient deficiency, dumping, post-bariatric hypoglycaemia and, uncommonly, reoperation. As incretin therapies approach surgical efficacy, comparative trials of surgery versus modern pharmacotherapy are a research priority.

VII. TYPE 2 DIABETES REMISSION

Remission is achievable in a substantial minority of people with T2D, and is most likely with early, large and sustained weight loss.

An international consensus defines remission as HbA1c <6.5% (48 mmol/mol) measured at least three months after stopping glucose-lowering medication [34]. The term "remission" rather than "cure" reflects the risk of relapse with weight regain. People in remission still require monitoring of HbA1c, retinopathy, kidney function and cardiovascular risk.

Predictors of remission include shorter diabetes duration, greater weight loss, lower baseline HbA1c, and not requiring insulin. In DiRECT, remission was

achieved by most participants who lost more than 10 kg, and 86% of those who lost 15 kg or more [14]. Remission rates fall over time with weight regain, as seen in the five-year DiRECT and 12-year ARMMS-T2D data [16,32].

Remission with incretin therapy is harder to define, because the drug that drives weight loss also lowers glucose directly. Normoglycaemia on treatment, such as the 26% of ACHIEVE-1 participants reaching HbA1c <5.7%, should be described as glycaemic normalisation rather than remission [21]. Trials testing whether planned drug withdrawal after major weight loss can preserve remission are needed.

VIII. SPECIAL CONSIDERATIONS

South Asian phenotype. Asian Indians develop T2D at lower BMI and younger age than Europeans, owing to greater visceral and ectopic fat and lower muscle mass at any given BMI. WHO recommended lower BMI action points for Asian populations in 2004 [35]. A 2025 revised Indian definition uses BMI >23 kg/m² as the threshold and adds abdominal adiposity and comorbidity [36]. Stage 1 denotes increased adiposity without organ dysfunction, and Stage 2 denotes adiposity with consequences such as T2D. Pharmacotherapy is advised for Stage 2 or BMI ≥27.5 kg/m². This aligns with the Lancet Commission's clinical obesity concept [11]. Under these criteria, most South Asians with T2D qualify for active weight management even at "normal" Western BMI.

Lean mass and sarcopenia. Lean tissue may account for roughly 25–40% of weight lost with incretin therapy [37]. This matters most in older adults and those with pre-existing sarcopenia or frailty. Adequate protein intake (about 1.0–1.5 g/kg/day), resistance training and monitoring of function are recommended, consistent with the 2026 ADA emphasis on nutrition and physical activity [10].

Weight regain after discontinuation. Obesity is a chronic relapsing disease. When semaglutide was switched to placebo after 20 weeks, participants regained 6.9% of body weight over 48 weeks (STEP 4) [38]. One year after stopping semaglutide in STEP 1, participants regained two-thirds of the weight lost, and cardiometabolic improvements reverted [39]. Similar regain occurred after tirzepatide withdrawal (SURMOUNT-4) [40]. Long-term treatment, or structured maintenance strategies, should be planned from the outset.

Cost and access. High drug costs, supply shortages and limited insurance coverage restrict access, particularly in low- and middle-income countries where the T2D burden is growing fastest. Generic semaglutide following patent expiry in several countries, and oral small molecules such as orforglipron, may improve affordability. Health systems must also fund structured dietary programmes, which are cost-effective and scalable.

IX. A STEPWISE WEIGHT-CENTRIC TREATMENT ALGORITHM

Integrating the evidence above, we propose a stepwise approach in which every person with T2D and excess adiposity receives a weight goal, a lifestyle foundation and a treatment route matched to their priorities (Figure 5).

Step 1: Assess. Measure BMI using ethnicity-appropriate thresholds, waist circumference, and screen for obesity-related complications, cardiovascular disease, CKD and heart failure [5,11,36].

Step 2: Set a goal. Agree a target of at least 5–7% weight loss for most people, and 10–15% or more when remission or major comorbidity improvement is the aim. Shared decision-making should consider the person's preferences, motivation, cost and access.

Step 3: Build the lifestyle foundation. All people should receive nutrition counselling, a physical activity plan including resistance training, and behavioural support [5].

Step 4: Choose a route. People with recent-onset T2D who are motivated to pursue remission can be offered a structured total diet replacement programme, ideally within six years of diagnosis [14]. People whose priority is weight loss with cardiorenal protection, or who cannot undertake intensive dietary therapy, should start a high-efficacy incretin agent, with an SGLT2 inhibitor added for heart failure or CKD [6]. The two routes can be combined, for example using pharmacotherapy to treat weight regain after dietary remission.

Step 5: Review and adjust. Response should be reviewed about three months after reaching a maintenance dose or completing the weight-loss phase. If goals are met, treatment continues with

attention to lean mass and weight regain. If they are not, the dose can be escalated, the agent switched, or metabolic surgery considered for eligible people [33].

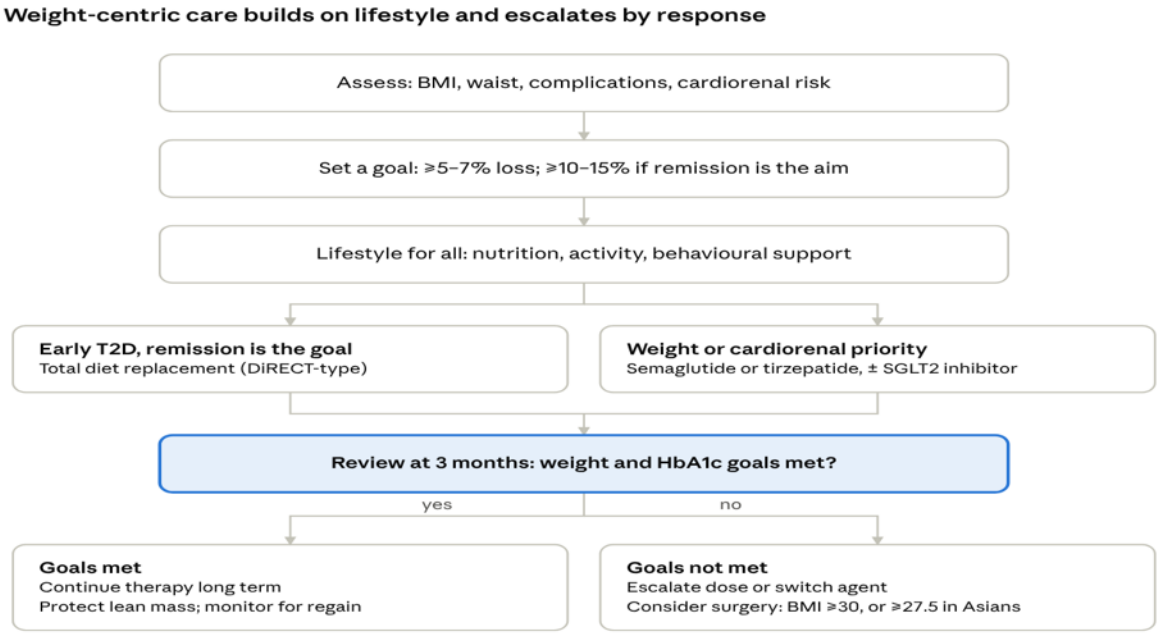


Figure 5 proposed stepwise algorithm, synthesised from [5,6,11,14,33,36]

Figure 5. Proposed stepwise weight-centric treatment algorithm for type 2 diabetes. Surgical thresholds follow the 2022 ASMBS/IFSO guidance, with lower thresholds for Asian populations [33].

X. FUTURE DIRECTIONS AND CONCLUSIONS

Future directions. Several developments will shape weight-centric care over the next five years:

- Next-generation agents. Triple agonists (retatrutide), amylin-based combinations (CagriSema, amycretin) and oral GLP-1 receptor agonists (orforglipron) are completing phase 3 programmes, with head-to-head and outcome trials under way [22,23].
- Lean-mass preservation. Agents targeting myostatin and activin pathways are being tested in combination with incretins to protect muscle during weight loss.
- Durable maintenance. Strategies such as dose tapering, intermittent therapy and sequential pharmacotherapy after dietary remission need evaluation.
- Precision approaches. Body-composition measures, ectopic fat imaging and beta-cell function markers may identify who can achieve remission and who needs long-term therapy.
- Population-specific evidence. More trials in South Asian, African and Latin American populations are needed to validate adiposity thresholds and treatment targets.
- Comparative effectiveness. Trials comparing metabolic surgery with modern incretin therapy, and cost-effectiveness analyses in low-resource settings, are a priority.

Conclusions. Weight-centric management treats a principal driver of T2D rather than only its glycaemic consequence. Weight loss of 5–7% improves metabolic control, while 10–15% or more can induce remission, especially early in the disease. Structured dietary programmes, incretin-based pharmacotherapy and metabolic surgery each have a defined role, and are complementary rather than competing. With semaglutide showing cardiovascular and kidney benefits, and tirzepatide showing non-inferior

cardiovascular outcomes with lower all-cause mortality than dulaglutide, weight should be assessed and actively treated at every stage of T2D care. The challenges ahead are sustaining weight loss, preserving lean mass, adapting thresholds for high-risk ethnic groups, and ensuring equitable access.

REFERENCES

[1] Sun H., Saeedi P., Karuranga S., et al., "IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045," *Diabetes Research and Clinical Practice*, vol. 183, Art. no. 109119, 2022.

[2] NCD Risk Factor Collaboration (NCD-RisC), "Worldwide trends in underweight and obesity from 1990 to 2022: A pooled analysis of 3663 population-representative studies with 222 million children, adolescents, and adults," *The Lancet*, vol. 403, pp. 1027–1050, 2024.

[3] R. M. Anjana, R. Unnikrishnan, M. Deepa, et al., "Metabolic non-communicable disease health report of India: The ICMR-INDIAB national cross-sectional study (ICMR-INDIAB-17)," *The Lancet Diabetes & Endocrinology*, vol. 11, pp. 474–489, 2023.

[4] Lingvay, P. Sumithran, R. V. Cohen, and C. W. le Roux, "Obesity management as a primary treatment goal for type 2 diabetes: Time to reframe the conversation," *The Lancet*, vol. 399, pp. 394–405, 2022.

[5] American Diabetes Association Professional Practice Committee for Diabetes, "8. Obesity and weight management for the prevention and treatment of diabetes: Standards of Care in Diabetes—2026," *Diabetes Care*, vol. 49, suppl. 1, 2026.

[6] M. J. Davies, V. R. Aroda, B. S. Collins, et al., "Management of hyperglycemia in type 2 diabetes, 2022: A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)," *Diabetes Care*, vol. 45, pp. 2753–2786, 2022.

[7] S. E. Kahn, R. L. Hull, and K. M. Utzschneider, "Mechanisms linking obesity to insulin resistance and type 2 diabetes," *Nature*, vol. 444, pp. 840–846, 2006.

[8] R. Taylor, "Type 2 diabetes: Etiology and reversibility," *Diabetes Care*, vol. 36, pp. 1047–1055, 2013.

[9] R. Taylor, A. Al-Mrabeh, S. Zhyzhneuskaya, et al., "Remission of human type 2 diabetes requires decrease in liver and pancreas fat content but is dependent upon capacity for β cell recovery," *Cell Metabolism*, vol. 28, pp. 547–556, 2018.

[10] American Diabetes Association Professional Practice Committee for Diabetes, "Summary of revisions: Standards of Care in Diabetes—2026," *Diabetes Care*, vol. 49, suppl. 1, pp. S6–S12, 2026, doi: 10.2337/dc26-SREV. [Online]. Available: https://pmc.ncbi.nlm.nih.gov/articles/PMC12690167

[11] F. Rubino, D. E. Cummings, R. H. Eckel, et al., "Definition and diagnostic criteria of clinical obesity," *The Lancet Diabetes & Endocrinology*, vol. 13, pp. 221–262, 2025.

[12] Look AHEAD Research Group, R. R. Wing, P. Bolin, F. L. Brancati, et al., "Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes," *The New England Journal of Medicine*, vol. 369, pp. 145–154, 2013.

[13] Look AHEAD Research Group, E. W. Gregg, J. M. Jakicic, G. Blackburn, et al., "Association of the magnitude of weight loss and changes in physical fitness with long-term cardiovascular disease outcomes in overweight or obese people with type 2 diabetes: A post-hoc analysis of the Look AHEAD randomised clinical trial," *The Lancet Diabetes & Endocrinology*, vol. 4, pp. 913–921, 2016.

[14] M. E. J. Lean, W. S. Leslie, A. C. Barnes, et al., "Primary care-led weight management for remission of type 2 diabetes (DiRECT): An open-label, cluster-randomised trial," *The Lancet*, vol. 391, pp. 541–551, 2018.

[15] M. E. J. Lean, W. S. Leslie, A. C. Barnes, et al., "Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DiRECT open-label, cluster-randomised trial," *The Lancet Diabetes & Endocrinology*, vol. 7, pp. 344–355, 2019.

[16] M. E. J. Lean, W. S. Leslie, A. C. Barnes, et al., "5-year follow-up of the randomised Diabetes

Remission Clinical Trial (DiRECT) of continued support for weight loss maintenance in the UK: An extension study," *The Lancet Diabetes & Endocrinology*, vol. 12, pp. 233–246, 2024, doi: 10.1016/S2213-8587(23)00385-6. [Online]. Available: https://eprints.gla.ac.uk/315287

[17] S. Taheri, H. Zaghloul, O. Chagoury, et al., "Effect of intensive lifestyle intervention on bodyweight and glycaemia in early type 2 diabetes (DIADEM-I): An open-label, parallel-group, randomised controlled trial," *The Lancet Diabetes & Endocrinology*, vol. 8, pp. 477–489, 2020.

[18] M. Davies, L. Færch, O. K. Jeppesen, et al., "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," *The Lancet*, vol. 397, pp. 971–984, 2021.

[19] J. P. Frías, M. J. Davies, J. Rosenstock, et al., "Tirzepatide versus semaglutide once weekly in patients with type 2 diabetes," *The New England Journal of Medicine*, vol. 385, pp. 503–515, 2021.

[20] W. T. Garvey, J. P. Frias, A. M. Jastreboff, et al., "Tirzepatide once weekly for the treatment of obesity in people with type 2 diabetes (SURMOUNT-2): A double-blind, randomised, multicentre, placebo-controlled, phase 3 trial," *The Lancet*, vol. 402, pp. 613–626, 2023.

[21] J. Rosenstock, S. Hsia, L. Nevarez Ruiz, et al., "Orforglipron, an oral small-molecule GLP-1 receptor agonist, in early type 2 diabetes," *The New England Journal of Medicine*, vol. 393, pp. 1065–1076, 2025, doi: 10.1056/NEJMoa2505669. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/40544435/

[22] TRANSCEND-T2D-1 Investigators, "Efficacy and safety of retatrutide, a GIP, GLP-1, and glucagon receptor agonist, in people with type 2 diabetes and inadequate glycaemic control with diet and exercise (TRANSCEND-T2D-1): A double-blind, randomised, phase 3 trial," *The Lancet*, 2026, doi: 10.1016/S0140-6736(26)00967-0. [Online]. Available: https://www.ccjm.org/page/ada-2026/retatrutide-diabetes

[23] Novo Nordisk A/S, "CagriSema demonstrated superior HbA1c reduction of 1.91%-points and weight loss of 14.2% in adults with type 2 diabetes in the REIMAGINE 2 trial," company announcement no. 2/2026, Feb. 2, 2026. [Online]. Available: https://www.novonordisk.com/news-and-media/news-and-ir-materials/news-details.html?id=916481

[24] S. P. Marso, S. C. Bain, A. Consoli, et al., "Semaglutide and cardiovascular outcomes in patients with type 2 diabetes," *The New England Journal of Medicine*, vol. 375, pp. 1834–1844, 2016.

[25] H. C. Gerstein, H. M. Colhoun, G. R. Dagenais, et al., "Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): A double-blind, randomised placebo-controlled trial," *The Lancet*, vol. 394, pp. 121–130, 2019.

[26] D. K. McGuire, N. Marx, S. L. Mulvagh, et al., "Oral semaglutide and cardiovascular outcomes in high-risk type 2 diabetes," *The New England Journal of Medicine*, vol. 392, pp. 2001–2012, 2025, doi: 10.1056/NEJMoa2501006. [Online]. Available: https://www.acc.org/latest-in-cardiology/clinical-trials/2025/03/27/15/04/soul

[27] S. J. Nicholls, I. Pavo, D. L. Bhatt, et al., "Cardiovascular outcomes with tirzepatide versus dulaglutide in type 2 diabetes," *The New England Journal of Medicine*, vol. 393, pp. 2409–2420, 2025. [Online]. Available: https://www.acc.org/latest-in-cardiology/journal-scans/2026/01/07/14/20/surpass-cvot

[28] M. Lincoff, K. Brown-Frandsen, H. M. Colhoun, et al., "Semaglutide and cardiovascular outcomes in obesity without diabetes," *The New England Journal of Medicine*, vol. 389, pp. 2221–2232, 2023.

[29] V. Perkovic, K. R. Tuttle, P. Rossing, et al., "Effects of semaglutide on chronic kidney disease outcomes in patients with type 2 diabetes," *The New England Journal of Medicine*, vol. 391, pp. 109–121, 2024.

[30] P. R. Schauer, D. L. Bhatt, J. P. Kirwan, et al., "Bariatric surgery versus intensive medical therapy for diabetes—5-year outcomes," *The New England Journal of Medicine*, vol. 376, pp. 641–651, 2017.

[31] G. Mingrone, S. Panunzi, A. De Gaetano, et al., "Metabolic surgery versus conventional medical therapy in patients with type 2 diabetes: 10-year follow-up of an open-label, single-centre, randomised controlled trial," *The Lancet*, vol. 397, pp. 293–304, 2021.

[32] P. Courcoulas, M. E. Patti, B. Hu, et al., "Long-term outcomes of medical management vs bariatric surgery in type 2 diabetes," *JAMA*, vol. 331, pp. 654–664, 2024, doi: 10.1001/jama.2024.0318. [Online]. Available: https://www.nih.gov/news-events/news-releases/bariatric-surgery-provides-long-term-blood-glucose-control-type-2-diabetes-remission

[33] D. Eisenberg, S. A. Shikora, E. Aarts, et al., "2022 American Society for Metabolic and Bariatric Surgery (ASMBS) and International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO): Indications for metabolic and bariatric surgery," *Surgery for Obesity and Related Diseases*, vol. 18, pp. 1345–1356, 2022.

[34] M. C. Riddle, W. T. Cefalu, P. H. Evans, et al., "Consensus report: Definition and interpretation of remission in type 2 diabetes," *Diabetes Care*, vol. 44, pp. 2438–2444, 2021.

[35] WHO Expert Consultation, "Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies," *The Lancet*, vol. 363, pp. 157–163, 2004.

[36] Misra, N. K. Vikram, A. Ghosh, et al., "Revised definition of obesity in Asian Indians living in India," *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, vol. 19, Art. no. 102989, 2025, doi: 10.1016/j.dsx.2024.102989.

[37] J. Neeland, J. Linge, and A. L. Birkenfeld, "Changes in lean body mass with glucagon-like peptide-1-based therapies and mitigation strategies," *Diabetes, Obesity and Metabolism*, vol. 26, suppl. 4, pp. 16–27, 2024.

[38] D. Rubino, N. Abrahamsson, M. Davies, et al., "Effect of continued weekly subcutaneous semaglutide vs placebo on weight loss maintenance in adults with overweight or obesity: The STEP 4 randomized clinical trial," *JAMA*, vol. 325, pp. 1414–1425, 2021.

[39] J. P. H. Wilding, R. L. Batterham, M. Davies, et al., "Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension," *Diabetes, Obesity and Metabolism*, vol. 24, pp. 1553–1564, 2022.

[40] L. J. Aronne, N. Sattar, D. B. Horn, et al., "Continued treatment with tirzepatide for maintenance of weight reduction in adults with obesity: The SURMOUNT-4 randomized clinical trial," *JAMA*, vol. 331, pp. 38–48, 2024.