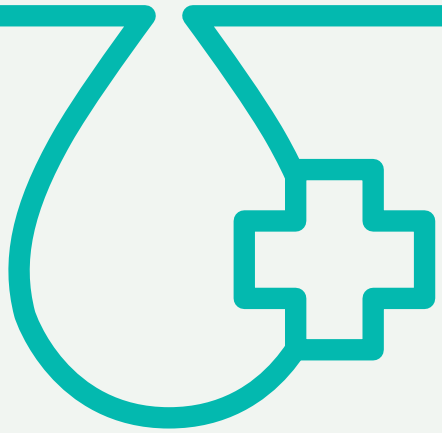
OPTIFAST®
PROGRAM

Diabetes Management Guidelines



OPTIFAST VLCD is for the dietary management of overweight and obesity and must be used under the supervision of a healthcare professional. Information for healthcare professional use only.

Nestlé HealthScience

We would appreciate any feedback or comments you may have on how to further improve the management guidelines and make them more relevant to you and your practice.

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The OPTIFAST Program

Diabetes Management Guidelines

The OPTIFAST Program is designed to assist with the dietary management of overweight and obesity, and this can often be accompanied by co-morbid conditions such as diabetes. These guidelines have been developed to assist the healthcare professional manage patients with diabetes and excess weight who may be at greater health risk.

These guidelines are designed to be used alongside the existing Clinical Treatment Protocol, Management of Complex Cases Protocol and Preoperative Protocol for OPTIFAST VLCD. These documents are designed to support professional standards and best practice methodologies for the healthcare professionals using them. The information provided here is general in nature and not intended to be a substitute for assessment of a individual patient's requirements. All clinical decisions should be made by a qualified healthcare professional, taking into account the individual patient's circumstances and needs.

Continuity of care is important, particularly where co-morbid conditions exist. Contacting other healthcare professionals who are treating a specific individual can help all involved to work together as a co-ordinated team. At all times the patient should be under the supervision of a qualified medical practitioner, and a multi-disciplinary approach to diabetes management is advised for optimal management.

We would like to thank the following experts for their contribution, feedback and review:

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Type 1 Diabetes

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Main points

- **Care needs to be taken if using a very low energy diet (VLED, <3350kJ/800kcal per day) in patients with Type 1 Diabetes (T1D).**
- **An increasing number of patients with T1D also have obesity in keeping with the increasing prevalence of obesity in the population.**
- **Patients with T1D using a VLED are at risk of hypoglycaemia and ketoacidosis so should monitor their blood glucose and ketones regularly.**
- **Glycaemic control is critical to reducing the risk of diabetic complications. Reduction of insulin dose needs to be matched to the change in carbohydrate and energy intake. The established targets of glycaemia, with avoidance of hypoglycaemia, and management of other established cardiovascular risk factors should be priority issues in the management of T1D.**

Review of clinical evidence

- Along with the rising epidemic of obesity, the prevalence of obesity in T1D is also increasing and evidence is emerging that obesity can accelerate the onset of T1D in susceptible individuals.[1] Obesity also exacerbates both micro-and macrovascular complications in people with T1D.[2]
- The landmark Diabetes Control and Complications Trial (DCCT) in T1D showed an average 5.1 kg vs 3.7 kg increase in weight with intensive insulin therapy compared to conventional treatment.[3]
  - An 18-year follow-up of this trial found an increase in obesity from 3.4% at baseline to 22.7% likely due to the community rise in obesity as well as an increase in the intensification of insulin therapy.[4]
  - Thus increasingly patients who have obesity and T1D will be seeking assistance with weight loss.
- Reduction in body weight is associated with an increase in hypoglycaemia that may be due to several factors including reduced carbohydrate intake, increased insulin sensitivity and change in physical activity.
- VLEDs are associated with ketosis, a metabolic response in which ketones (acetoacetate and β-hydroxybutyrate) are produced by the liver from the breakdown of fatty acids as an alternative fuel source when glucose is in short supply. This process is primarily driven by a reduced carbohydrate intake and is likely to occur with carbohydrate intakes of 50–100g/day. The OPTIFAST Intensive Level provides approximately 60–70g carbohydrate/day.
  - The blood ketone levels seen in people consuming VLEDs using moderate carbohydrate restriction (60-70 g/day), usually range between 0.3-1.0 mmol/L.[5,6]
  - These levels are much lower than the levels in diabetic ketoacidosis which are usually above 3 mmol/L and often much higher.[7]
- The appetite suppressive capability of VLEDs may be improved with the genesis of mild ketosis.[7] The insulin dose can be adjusted to maintain mild ketosis with avoidance of ketoacidosis. Thus the ketosis seen with a VLED should not pose any problems for people with T1D. However, there are no studies on the continuous use of a VLED in people with T1D.
- In a study in which people with T1D (n=14) were fasted for a week and then placed on a low energy diet (LED, 5000kJ and 150g carbohydrate) for 3 weeks, there was a reduction in fat mass, preservation of lean mass and a reduction in insulin dose but HbA1c was unchanged.[8]
  - There were no adverse events with fasting (in which patients just received a basal dose of insulin and essential electrolytes and vitamins) or the LED.[8]
- A pilot trial in adults with type 1 diabetes and overweight or obesity demonstrated the safety and feasibility of the intermittent use of a VLED. Participants (n=10) were randomised to either severe energy restriction on two 24-hour periods per week (2510 kJ/day using three OPTIFAST VLCD Shakes) with 5 days per week of eating to appetite or continuous moderate energy restriction (30% energy-restricted diet) for 12 weeks.
  - There were no adverse events during the study and rates of hypoglycaemia were unchanged.
  - Finger capillary blood β-hydroxybutyrate levels exceeded 1.0mmol/L twice following the overnight fast in one participant in the intermittent fasting arm.
  - Blood β-hydroxybutyrate levels reached 1.6 mmol/L but fell to below 0.4 mmol/L after breakfast and a mealtime dose of rapid acting insulin.
  - Body weight was reduced by both intermittent fasting (–7.0%, range –5.2% to –8.0%) and continuous energy restriction (–3.9%, range –1.0% to –11.1%).
  - Trunk fat was also reduced by both interventions (intermittent fasting: –12.2%, range –1.0% to –15.3%; 30% energy reduction: –10.1%, range 2.3% to –10.7%).
  - Blood pressure, HbA1c and lipids were unchanged.[9]
- While there is little literature on the use of VLEDs in patients with type 1 diabetes, with appropriate medical supervision, patient education and patient selection, VLEDs can be used in patients with T1D.

Recommendations for management

a) Patient suitability

The OPTIFAST Program can be considered for weight loss in selected patients with T1D if used with close supervision by their diabetes team. Extra care should be taken soon after the diagnosis of T1D. Patients should be very familiar with all aspects of self-management before starting a VLED.

b) Adaptations to OPTIFAST Program

The major clinical issue for patients with T1D is hypoglycaemia because of the severe reduction in carbohydrate intake that a VLED supplies. Therefore, it is imperative that the insulin dose be adjusted at the start of a VLED program.

In Australia, people with Type 1 diabetes can access government subsidised continuous glucose monitoring (CGM). Available systems can be set to alert people to impending hypoglycamia so commencement of CGM is strongly recommended before use of VLED. Alerts can be individualised but it is recommended the low alert is set at 3.6 to 4.4 mmol/L. Patients must monitor glucose more frequently for the first few days (at least 4 times – once before each meal and before going to bed if not using CGM). For optimum management, it is recommended that patients start the regimen on the weekend, when they can be at home and thus more attentive to the symptoms of hypoglycaemia. If someone is experiencing severe hypoglycaemia they should be referred to their diabetes team for review of their management and further education. Patients should be counselled to avoid activities where hypoglycaemia poses a high risk (e.g. driving, swimming) until they are familiar with the effect of the OPTIFAST Program on their glycaemic profile.

Most patients with T1D are on a basal bolus regimen of intermediate or long acting insulin once or twice a day, and short acting insulin three times per day before each meal; however, an increasing number of patients are using insulin pump therapy.

The short acting or bolus insulin covers the carbohydrate load with each meal. OPTIFAST VLCD products provide approximately 18-23g of carbohydrate per serve, so it is important to reduce the short acting insulin dose. In patients who are aware of their insulin to carbohydrate ratio, a suitable dose adjustment should be made. Patients using insulin pump therapy can administer a bolus dose of insulin according to the carbohydrate content of the OPTIFAST VLCD product.

If a patient is unaware of their insulin to carbohydrate ratio, one method to estimate the insulin to carbohydrate ratio is the '500 rule' where 500 is divided by the total insulin daily dose.

- For example, if the total insulin daily dose is 100 units, then divide 500/100=5.
  - The Insulin:Carbohydrate ratio is 5. This equates to 1 unit of insulin for 5g carbohydrate.
- If taking an OPTIFAST VLCD product with 20g of carbohydrate, divide the carbohydrate content of the meal by the Insulin:Carbohydrate ratio.
  - In this case: 20/5=4.
  - Therefore, the dose should be 4 units of rapid acting insulin with the OPTIFAST VLCD meal.

It is recommended to start with replacing 1 or 2 meals with OPTIFAST VLCD products on initiation to work out the bolus (rapid insulin) dose before embarking on the full Intensive Level.

A reduction in the basal insulin dose is also necessary due to the expected reduction in hepatic glucose production with a VLED. At the commencement of the full Intensive Level of the OPTIFAST Program, a 20% reduction in the dose of the basal insulin is suggested as a starting point, but the study by Overland *et al* suggests hypoglycaemia can be avoided with a more modest insulin adjustment of around 10% reduction of the basal dose.[9]

If using a standalone insulin pump, the basal setting should be weakened by 20% when starting the Intensive Level of the OPTIFAST Program. Insulin delivery settings need to be reviewed and likely weakened every 2 to 4 weeks. Little or no change to basal insulin patterns is likely to be needed for people with T1D using hybrid closed loop insulin pumps. These pumps adjust basal insulin in response to sensor glucose readings, reducing or suspending basal insulin delivery when the glucose level is falling, and giving additional insulin if the glucose level is trending high. If someone is deemed at high risk of hypoglycaemia, selection of one of the settings that either reduces the amount of insulin released or raises the level of the glucose target is recommended. These settings differ with each hybrid closed loop insulin pump and include Ease-Off, Exercise or Temp Target settings.

Patients should be instructed to monitor their blood glucose levels more frequently and the results should be reviewed regularly. Further adjustment of both basal and bolus insulins should be made to prevent hypo- and hyperglycaemia.

Mild ketosis may be present while on the Intensive Level of the OPTIFAST Program. The expected blood ketone level is 0.3–1.0 mmol/L and this is likely to persist while remaining on the VLED.[5,6] It is unlikely that there would be an increased risk of ketoacidosis, especially if the blood glucose remains acceptable and insulin is taken regularly. It is recommended that blood ketones be monitored at least in the first week that patients are on a VLED. A finger prick ketone level >1.5 mmol/L should be discussed with a diabetes professional.

It is extremely important that patients with type 1 diabetes do not have their insulin stopped, no matter how low the insulin dose is, otherwise they risk developing ketoacidosis. Healthcare professionals should also be aware of the possibility that patients may significantly reduce or withhold insulin as a weight management strategy. The risks of this practice may need to be discussed with your patient.

c) Contraindications and precautions

Care must be taken in people with type 1 diabetes who also have chronic kidney disease.

Another potential side effect is an aggravation of postural hypotension in patients with autonomic neuropathy. Caution is needed in people with severe retinopathy as sudden lowering of glucose levels can exacerbate this condition. A less intensive energy restriction may be more appropriate in such patients.

Care should be taken if the patient has a history of an eating disorder, as these patients are more likely to omit insulin.

Case study

Tara is a recently married 26 year old woman with T1D for 10 years, complicated by mild non-proliferative retinopathy and microalbuminuria. She weighs 100kg, has a BMI of 40kg/m² and has slowly gained weight at about 2 kg per year since adolescence.

Tara's blood pressure is 130/84. She also has dyslipidaemia with total cholesterol 6.0, HDL 1.1, LDL 4.0 and triglycerides 1.9 mmol/L and mildly elevated liver transaminases.

Her HbA1c is generally between 8 and 9% and she is on a basal bolus regimen using 88 units of insulin daily (40 units long acting and 16 units short acting with each meal). She has tried Metformin but is unable to tolerate the gastrointestinal side effects.

She finds it frustrating that the pattern of meal-time insulin and BGL monitoring (at least 4 times daily) appear to not follow a particular pattern in that sometimes her glucose levels are very high but at other times she has unexplained hypoglycaemic episodes. She has seen dietitians over the past 10 years and implemented recommended dietary behaviour but her weight has not reduced. Screening for other associated conditions that may exacerbate food absorption and weight, including coeliac disease, gastroparesis and hypothyroidism, is negative.

INTERVENTION & OUTCOME

Her diabetes specialist suggests a trial of the OPTIFAST Program while being closely monitored. The goal is to reduce her weight to see if it helps control her blood glucose levels, blood pressure, lipids and liver function tests.

She starts with replacing one meal a day with an OPTIFAST VLCD product to see how to adjust her short acting insulin dose. She has not previously determined an insulin to carbohydrate ratio, but using the 500 rule she starts with a ratio of 1 unit: 6 grams of carbohydrate. She tries the OPTIFAST VLCD Berry Crunch Flavour Bar, which contains 19.5g carbohydrate and takes 3 units of short acting insulin, which is about a quarter of her usual meal time dose. She does a blood glucose check 2 hours after she has eaten the bar to see the effect of the dose, which is higher than her recommended post prandial target.

When she next has an OPTIFAST VLCD Bar she takes 4 units of her short acting insulin and has a better post prandial glucose level.

She then replaces 2 meals a day while trialling a range of the OPTIFAST VLCD products to see which products she likes best. She finds that her dose is 3–4 units of rapid acting insulin with each OPTIFAST VLCD product depending on the carbohydrate content. She starts to have some overnight and early morning borderline low glucose levels (3.5-5 mmol/L) and reduces her long acting insulin from 40 to 30 units. After finding that she is stable on this dose, she decides to embark on the Intensive Level of the OPTIFAST Program, replacing 3 meals daily with OPTIFAST VLCD products. She does additional monitoring before and 2 hours after each replacement meal.

She continues this for 10 days and finds that she feels quite well on the program. Her blood glucose levels range between 4.5–10mmol/L with no hypoglycaemia. She checks her blood ketone level and it is 0.6mmol/L. After 3 weeks she has reduced her weight by 6kg and, due to borderline hypoglycaemia, reduces long acting insulin dose to 24 units.

She is able to continue the Intensive Level for 12 weeks by which time she has reduced her weight by 16 kg and her blood pressure is 120/70. She finds physical activity easier and feels happier. Her HbA1c has dropped to 6.2%, she no longer has albuminuria and her lipids have improved (total cholesterol 4.3, HDL 1.5, LDL 2.3 and triglycerides 1.1 mmol/L). She has an ophthalmic review and her retinopathy is stable. Her insulin doses are 20 units long acting, and 3–4 units short acting with meals. She reduces her meal replacements to 2 per day, and consumes 1 low carbohydrate meal for a further 6 weeks, reducing her weight to 80 kg. She then starts a healthy, regular diet with the occasional OPTIFAST VLCD product, usually at lunch time. She is very keen to maintain her current weight and tries to exercise regularly. She usually manages to swim or walk 1 hour daily and does this after her evening meal to minimise hypoglycaemia.

Together with her diabetes specialist team, Tara decides that if her weight increased to 84 kg she would recommence the Intensive Level of the OPTIFAST Program for at least 4 weeks.

This case study is an example of the possible management of an individual with type 1 diabetes who is living with obesity. Name and image used are for illustrative purposes only.

Type 2 Diabetes

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Main points

- **Type 2 Diabetes (T2D) is one of the main metabolic consequences of obesity as the two conditions share pathophysiological drivers. Perpetuating factors common to both conditions should be the focus of management in patients with T2D. Tackling obesity will help to achieve health targets, reduce complications and improve quality of life.**
- **The two key abnormalities of T2D are multi-organ insulin resistance and a progressive decline in pancreatic beta-cell function. Weight loss can address both these abnormalities.**
- **Use of a very low energy diet (VLED, <3350kJ/800kcal per day), such as the Intensive Level of the OPTIFAST Program, is a well-established method of weight loss in T2D.**
- **Improvement in beta cell function and glycaemia can occur in some patients early in the course of a VLED, which may be independent of weight loss, but rather related to the reduction in energy intake.**
- **Methods to improve glycaemia and reduce obesity should be implemented as soon as possible in the course of T2D as it is more likely to result in preservation of beta cell function.**
- **A VLED can result in weight loss (10-15% body weight) over a period of ~12 weeks, which is sufficient to produce remission of T2D in those with disease duration of 6 years or less, and possibly longer.**
- **Transition to less obesogenic agents is recommended by avoiding insulin or sulphonylurea therapy and adding Metformin, SGLT2 inhibitors, acarbose, DPP-4 inhibitor or GLP-1 agonist therapy. SGLT2 inhibitors and acarbose should not be used during a VLED.**
- **Agents that promote satiety, such GLP-1 agonists and dual GLP-1/GIP agonists, may have an additional benefit of improving compliance with a VLED, or limiting intake when on a healthy regular diet.**

Review of clinical evidence

- In Australia, the prevalence of obesity and overweight based on both waist circumference and BMI continues to increase. In 2022, 67.9% of adults had an elevated waist circumference compared to 62.9% in 2011-12. Similarly, the rate of overweight and obesity has increased from 62.8% in 2011-12 to 65.8% in 2022. This increase is primarily driven by a higher prevalence of obesity, from 27.5% in 2011-12 to 31.7% in 2022.[10]
  - The estimated prevalence of T2D in Australian adults is 7.5% with a further 17% of adults aged over 25 years estimated to have pre-diabetes presently.[11] Obesity is a major risk factor for T2D and compounds cardiovascular risk when diabetes is present.[12,13] In Australia from 1990 to 2019, in association with the increased prevalence of obesity, that of diabetes has tripled.[11]
- People who can store fat in their lower body such as the buttocks and thighs are less likely to develop T2D and related metabolic diseases. Conversely, those who have more upper body fat (abdominal subcutaneous and intra-abdominal fat) are more likely to store fat in tissues such as the liver, pancreas and skeletal muscle where the presence of fat impairs function.
  - Fat stored in tissues that usually contain only a small amount of fat is referred to as ectopic fat. Ectopic fat appears to drive the key abnormalities of T2D, insulin resistance (hepatic and inter- and intramyocellular fat in skeletal muscle) and reduced insulin production by pancreatic beta-cells (pancreatic fat).
  - Weight loss is associated with reductions in these ectopic fat depots and results in improvements in insulin action (insulin sensitivity) and insulin secretion as well as other metabolic abnormalities related to T2D including hypertension, dyslipidaemia, liver steatosis, menstrual disturbances in women (polycystic ovarian syndrome) and hypogonadism in men.[14]
- In the Look AHEAD trial, a study that assessed the effect of lifestyle intervention on several health outcomes in over 5000 middle-aged participants with T2D (median duration 5 years) and BMI >25kg/m², the energy intake was restricted to approximately 1200–1500 kcal per day and included the option for meal replacements such as OPTIFAST VLCD products to achieve this. Patients were randomised to the intensive lifestyle intervention or standard therapy for 4 years and monitored for up to 12 years.
  - After 4 years, an 8% weight loss was associated with better measures of glycaemia and other metabolic risk factors including blood pressure and dyslipidaemia.[15]
  - During 12 years of follow up, 12.7% of participants experienced T2D remission in at least one follow-up visit. The chance of remission was related to the degree of weight loss achieved and was greater in the interventional lifestyle group.
  - In post hoc analyses, participants who experienced any remission had a 33% lower rate of chronic kidney disease and 40% lower rate of cardiovascular disease.[16]

Type 2 diabetes remission

- With advances in the treatment of T2D, remission is now possible. Remission of T2D, defined as a HbA1c below 6.5% while not being on glucose-lowering treatment for at least 3 months, means not having active disease.[17] T2D remission can be achieved with the substantial weight loss associated with bariatric surgery and VLEDs. When in remission one can still be at risk of the complications of diabetes, but this risk reduces over time.[18] However, with weight regain, T2D quickly recurs.
- In the UK DiRECT trial, a total diet replacement program in people with T2D of up to 6 years' duration, remission of T2D was achieved in 46% of patients in the intervention group. The chance of remission increased with greater weight loss such that remission occurred in 86% of patients with a weight loss of 15% or more, and 57% of patients with a weight loss of 10% to 15% at 12 months.[19] Remission of diabetes was maintained at 2 years after the intervention for 64% of those who maintained a weight loss of at least 10kg.[20] Associated with the weight loss there was a significant increase in quality of life.[19] At 5 years, data were available on 118/149 in the intervention group and 93/149 in the control group. There was 5% body weight loss in both groups and, while there was a numerically higher rate of remission in the intervention group (10% vs 5% in the control group), this outcome was not statistically significant.[21]
- There have been similar findings in two other trials. In the Qatari DIADEM-I, 61% of people with T2D of up to 3 years' duration treated with a total diet replacement were in remission at 12 months.[22] In the DiRECT-AUS trial people with T2D of up to 6 years' duration followed a total diet replacement which incorporated OPTIFAST VLCD products, via primary care. Overall, 56% achieved diabetes remission at 12 months and the chance of remission was greater in those with more weight loss, occurring in 87% with > 15% weight loss, 75% of those with 10-15% weight loss and 42% of those with 5-10% weight loss.[23]
- Diabetes remission is strongly linked to maintenance of weight loss. In the DiRECT trials patients were offered to resume meal replacements if they gained weight (> 2-4 kg) or HbA1c increased above 6.5%.
- Independent of weight loss, soon after the initiation of a VLED, significant improvements in glycaemic control can be seen. In a study including people with T2D, after just 3 days of a VLED, there was a reduction in fasting glucose which was related to the reduced carbohydrate intake. There was also a reduction in basal hepatic glucose output and increased insulin suppressibility of hepatic insulin action. By 4 weeks, after significant weight loss, there was an improvement in peripheral insulin sensitivity which was strongly related to loss of abdominal fat.[24] Normalisation of beta cell function and hepatic insulin sensitivity has been shown after 1 week of energy restriction in association with decreased pancreatic and liver triacylglycerol fat stores measured by magnetic resonance imaging.[25]
- The mechanisms involved in the improvements in insulin action and secretion induced by weight loss include reductions in muscle and liver glycogen as well as liver, pancreatic and skeletal muscle fat. Restriction of carbohydrate leads to lipolysis and the formation of ketone bodies by the liver. Energy restriction also reduces liver fat which results in improved hepatic insulin signalling. Together these responses lead to reductions in hepatic glucose output via inhibition of gluconeogenesis and reduced glycogenolysis. Circulating ketone bodies have also been shown to increase satiety.[26] With weight loss, there is a reduction in circulating glucose and lipid levels as well as pancreatic fat all of which have been associated with better pancreatic beta cell function resulting in improvements in insulin production and dynamic insulin secretion.[25]
- The main determinant of remission is the potential for pancreatic insulin secretion, which is linked to duration of diabetes with longer disease duration associated with greater risk of long-term pancreatic dysfunction. However, there is evidence that even people with longstanding diabetes may be able to achieve remission with sufficient weight loss.[27] Conversely, there are subgroups of patients in whom remission does not occur despite weight loss. Such patients include those with late onset autoimmune diabetes, pancreatic disease related diabetes, cystic fibrosis related diabetes and genetic forms of diabetes (maturity onset diabetes of the young, MODY).
- Most international guidelines on diabetes management recommend weight loss with energy restriction. With the positive outcomes of the DiRECT trials, the prescription of greater energy restriction with a VLED resulting in 10-15% body weight loss is a treatment option, particularly early in the diagnosis of T2D. With this weight loss and improved metabolic parameters, there is also evidence that diabetes complications can be both delayed and reduced.[18]

Recommendations for management

a) Patient suitability

The OPTIFAST Program should be considered:

- For all patients with a BMI > 27kg/m² (or BMI > 23 kg/m² in Australian indigenous and Asian people) at diagnosis of T2D to induce diabetes remission. Weight maintenance is critical to maintaining diabetes remission.
- For patients within 6 years of diagnosis of T2D with a BMI > 27kg/m² (or BMI > 23 kg/m² in Australian indigenous and Asian people) and not taking insulin to induce diabetes remission.
- For most patients with a BMI >27kg/m² (or BMI > 23 kg/m² in Australian indigenous and Asian people) who have T2D, including those with associated complications such as microalbuminuria, non-proliferative retinopathy, obstructive sleep apnoea, metabolic dysfunction associated steatotic liver disease and diastolic cardiac dysfunction as part of an overall program that emphasises the importance of ongoing weight maintenance.
- For patients with more severe complications such as proteinuria >1g/d, eGFR <60 or risk of fluid balance complications, however these patients need to be carefully monitored (creatinine, eGFR, electrolytes, fluid status) while on a VLED.
- Before bariatric surgery. The OPTIFAST Program Intensive Level is often initiated before bariatric surgery including in patients with T2D to reduce liver size thereby improving accessibility and visibility for laparoscopic procedures. Other metabolic markers are likely to improve preoperatively, and perioperative complications may reduce with the weight loss associated with the OPTIFAST Program.
- For patients with poor glycaemic control despite multiple agents or those in whom insulin treatment is being considered. If the OPTIFAST Program Intensive Level is used in this setting a considerable improvement in glycaemic control usually occurs within 1–2 weeks. If not, other hypoglycaemic measures should be instituted. Patients with poor glycaemic control starting the Intensive Level should monitor their blood glucose levels regularly and be reviewed within 1–2 weeks of commencing.

b) Adaptations to the OPTIFAST Program

In the DiRECT trial all hypoglycaemic and antihypertensive treatments were ceased at initiation of the total diet replacement. However, patients were closely reviewed by the treating team and treatment was introduced according to guidelines. It is recommended to reduce or cease any medications that may result in hypoglycaemia and to maintain other hypoglycaemic treatments apart from SGLT2-inhibitors and acarbose. SGLT2-inhibitors should be ceased as carbohydrate restriction increases the risk of euglycaemic ketoacidosis.[28] It is recommended acarbose be ceased as it is unlikely to be effective when following a VLED. Acarbose lowers glucose levels by reducing carbohydrate absorption through the inhibition of intestinal alpha glucosidase, an enzyme in the small intestine that hydrolyses ingested carbohydrate.

If glycaemic control is good (HbA1c < 7.5%), consideration can be given to reducing or ceasing glucose lowering medications as glucose levels are likely to further reduce with weight reduction. Alternatively, agents can be progressively reduced with monitoring of HbA1c on completion of the OPTIFAST Program Intensive Level (*refer Table 1*).

Patients on insulin or sulphonylureas should be careful to avoid hypoglycaemia and simplifying the insulin regimen or changing to an oral agent that does not increase basal insulin secretion is recommended.

Unless glycaemic control has been poor, the insulin or sulphonylurea dose should be ceased or reduced on commencement of a VLED and glucose levels should be closely monitored. It is recommended that if the HbA1c is below 7.5%, insulin and sulphonylurea treatment should be ceased. If the HbA1c is above 7.5%, the doses should be halved. Treatment should be further modified according to the glucose levels bearing in mind there is a high chance neither insulin nor sulphonylureas will be required with weight loss.

On the OPTIFAST Program Intensive Level, patients on basal bolus insulin usually do not need pre-meal insulin bolus doses and require a reduction in the basal dose. A practical recommendation is to initially cease all prandial insulin and halve the basal dose and review frequently with self-blood glucose monitoring. When only 1 or 2 meals are replaced with OPTIFAST VLCD products, the bolus dose may only need to be reduced or withheld before these meals.

Patients on twice daily pre-mixed insulin (breakfast and dinner) who are starting the Intensive Level of the OPTIFAST Program, are often best managed by changing their insulin regimen to a single basal insulin injection at half the dose of their usual total insulin dose.

The OPTIFAST Program to assist with achieving T2D remission

- A VLED can be implemented as a first line treatment at diagnosis of T2D and for patients within 6 years of diagnosis with HbA1c < 10% and not using insulin.
- Cease all hypoglycaemic medications, and consider ceasing or reducing antihypertensive treatment if blood pressure is well-controlled.
- Implement the OPTIFAST Program Intensive Level for 12 weeks or until the patient achieves 10-15% body weight loss.
  - Fortnightly review is recommended.
  - Monitor blood pressure and adjust anti-hypertensive treatment if necessary.
- On completion of the Intensive Level, OPTIFAST VLCD products are weaned and food is reintroduced over 4-8 weeks. Patients step down to Active 2 Level in which 2 meals are replaced daily for 2-4 weeks and then Active 1 Level in which 1 meal is replaced with OPTIFAST VLCD daily for 2-4 weeks. See the OPTIFAST Clinical Treatment Protocol for more information on each of the program levels.
- It is recommended patients weigh themselves weekly. Weight should be monitored in the clinic monthly and HbA1c should be checked 3-monthly.
- If there is a weight gain of 2-4 kg, recommence Active 1 Level for 4 weeks.
- If there is a weight gain > 4 kg or HbA1c > 6.5%, recommence the Intensive Level for 4 weeks, followed by Active 2 Level for 2-4 weeks, and then Active 1 Level for 2-4 weeks.
- If HbA1c remains > 6.5% despite weight loss, recommence hypoglycaemic treatment.

c) Contraindications and precautions

Blood pressure may reduce while on a VLED. Antihypertensive treatment should be reduced or ceased in those with very well-controlled blood pressure (< 110/60 mmHg) while on the OPTIFAST Program Intensive Level. Blood pressure needs to be closely monitored in all patients taking antihypertensive medication while on the OPTIFAST Program Intensive Level as with weight loss there is a high chance blood pressure will reduce necessitating a reduction in antihypertensive treatment. The only serious adverse events in the DiRECT-AUS study were related to hypotension in people taking antihypertensive medication.[14]

The OPTIFAST Program is not recommended for people with diabetes with normal or low weight, women with diabetes associated with pregnancy, or people with cystic fibrosis-related diabetes.

Case study

Erica has had T2D for 7 years with associated obesity, complicated by hypertension, dyslipidaemia, macroalbuminuria (0.6g/d) with stage III chronic kidney disease (eGFR 55ml/min/1.73m²) and sleep apnoea (on CPAP).

Erica is on Metformin, dapagliflozin, maximum dose ACE-Inhibitor, a calcium channel blocker and a statin. Six months ago, her HbA1c was 9% and she was commenced on twice daily mixed insulin. She is now on 60 units BD. Her HbA1c has improved to 7.6% but she has gained 10kg and her BMI is now 40kg/m². She has now developed gastro-oesophageal reflux and is finding physical activity very difficult because of knee pain.

INTERVENTION & OUTCOME

After consultation with her doctor, Erica decides to go on the OPTIFAST Program. Dapagliflozin is ceased because of the small risk of euglycaemic ketoacidosis with the low carbohydrate and energy content of the diet. In anticipation of a fall in her glucose levels, she is changed to a basal insulin at 60 units before bed and achieves target blood glucose readings. With increasing weight reduction, her glucose levels start to fall to 4–5mmol/L and her insulin dose is progressively reduced so that by the time she has been on the Intensive Level of the program for 6 weeks she is no longer requiring any insulin. Her blood pressure also falls and she stops the calcium channel blocker.

After having been on the VLED for 3 months Erica starts having 1 regular healthy evening meal and replaces breakfast and lunch with an OPTIFAST VLCD product. She gradually weans off the OPTIFAST VLCD products over the next month and is extremely happy with her progress. She has managed to reduce her weight by 14kg so that her BMI is now 35kg/m².

Erica recommences dapagliflozin because of the presence of significant renal disease but no longer requires insulin or a calcium channel blocker and her dose of ACE-inhibitor has been halved. Her knee pain has resolved and her ability to exercise is much improved. She is intent on maintaining her weight by walking regularly and eating a healthier diet. Erica realises that she will need to monitor her weight regularly and if it starts to increase, she would consider recommencing the OPTIFAST Program either to replace all meals or 1–2 meals daily, in consultation with her doctor.

This case study is an example of the possible management of an individual with type 2 diabetes who is living with obesity. Name and image used are for illustrative purposes only.

Table 1: Considerations for Medications used in Type 2 Diabetes with the OPTIFAST Program

Medication	Mode of action	Weight effect	Considerations with OPTIFAST VLCD	Recommendations when used with OPTIFAST VLCD
Metformin	Reduces glucose production by liver; reduces intestinal glucose absorption	Small reduction	Minimal hypoglycaemia risk	Maintain or cease if good glycaemic control (HbA1c < 7.5%)
Sulphonylureas - Gliclazide - Glipizide	Stimulate pancreatic beta cell insulin secretion	Increases	Risk of hypoglycaemia	Cease (HbA1c < 7.5%) or reduce dose (HbA1c > 7.5%) with monitoring of glucose levels
Glitazones - Pioglitazone	Increase insulin sensitivity, reduce visceral fat and increase gluteal fat	Increases	Minimal hypoglycaemia risk	Maintain or cease if good glycaemic control (HbA1c < 7.5%)
Acarbose	Reduces glucose absorption from gut	Small reduction	Unlikely to be useful while on OPTIFAST as low carbohydrate intake	Cease, may be recommenced in food reintroduction phases
SGLT2 inhibitors - Empagliflozin - Dapagliflozin	Reduce renal glucose reabsorption	Small reduction	Can increase risk of euglycaemic ketoacidosis	Cease, may be recommenced in food reintroduction phases
DPP-4 inhibitors - Linagliptin - Sitagliptin - Vildagliptin	Blocks action of enzyme DPP4, resulting in reduced breakdown of GLP1	Neutral	Minimal hypoglycaemia risk	Maintain or cease if good glycaemic control (HbA1c < 7.5%)
GLP1-analogues - Dulaglutide - Liraglutide - Semaglutide	Reduces appetite and increases insulin release in glucose dependent manner	Modest-large weight loss depending on agent	Minimal hypoglycaemia risk	Maintain as may help with adherence to VLED
Dual GIP/GLP1 analogues - Tirzepatide	Reduces appetite and increases insulin release in glucose dependent manner	Large weight loss	Minimal hypoglycaemia risk	Maintain as may help with adherence to VLED
Insulin		Increases	Risk of hypoglycaemia	Cease if HbA1c < 7.5%; if HbA1c > 7.5% cease any prandial insulin, reduce total insulin dose by at least 50% and closely monitor glucose levels as with weight loss further dose reduction likely to be necessary

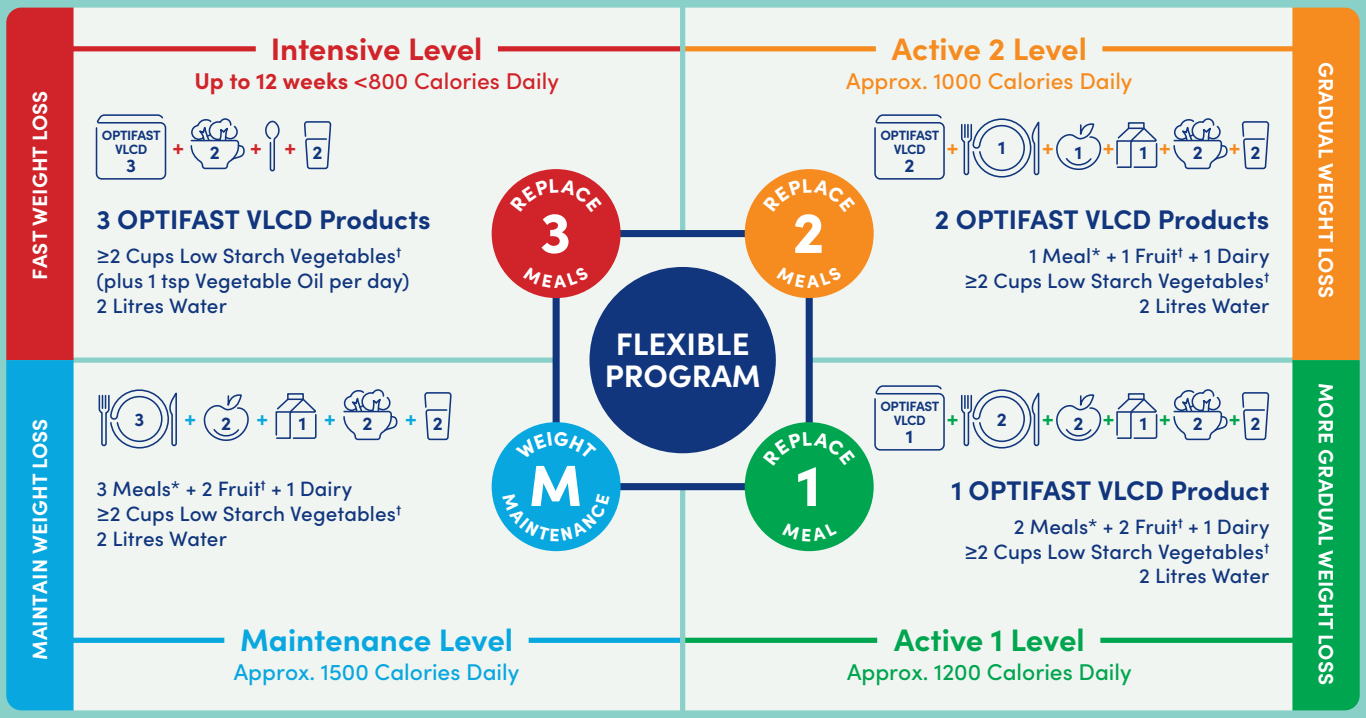
Information is general in nature and not intended to be a substitute for assessment of an individual patient's requirements. All clinical decisions should be made by a qualified healthcare professional, taking into account the individual patient's circumstances and needs.

OPTIFAST® PROGRAM

The OPTIFAST Program is a nutritionally complete, very low energy diet for the dietary management of obesity. It includes a range of OPTIFAST VLCD products (Shakes, Soups, Desserts and Bars) and is structured into four simple levels.

Each of the OPTIFAST VLCD products can be used interchangeably throughout the program, depending on individual preference.

The OPTIFAST Program can be modified to suit individual requirements.



*Meals should equal approximately 350 calories each.
†See 'Additional Foods' table on optifast.com.au for allowed low starch vegetables and fruit.

Recommended for:

- BMI ≥30kg/m²
- BMI >27kg/m² with associated health conditions (including type 1 or type 2 diabetes, sleep apnoea and heart disease).

Not recommended for:

- Pregnancy or breastfeeding
- Children under 18 years of age
- Presence of porphyria
- Recent myocardial infarction or unstable angina
- Renal or Liver disease.

Individuals aged over 65 years and those with existing medical conditions may require a modified program and should speak to their healthcare professional.

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OPTIFAST® PROGRAM

Clinically proven for safe and effective weight loss

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OPTIFAST VLCD is for the dietary management of overweight and obesity and must be used under the supervision of a healthcare professional.

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