Therapeutic options in the management of obesity

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Abstract
In New Zealand 28.4% of adults now classify as obese, whilst a total of 63.8% are overweight or obese (BMI >25 kg/m²). This presents an ever increasing social and economic burden to individuals, families and the healthcare system. Obesity is a major risk factor for cancer, cardiovascular, metabolic, and respiratory disorders. Preventing obesity is the optimal long-term population strategy and must be a government priority. There are many approaches which could be taken to facilitate this, however it is important not to forget those who are currently overweight or obese.

This review addresses the current therapeutic options in the treatment of obesity, focusing on lifestyle changes, medications, and surgery in New Zealand. It also presents a suggested algorithm for the clinician assessing and managing obese patients in New Zealand.

The prevalence of obesity is increasing at an alarming rate worldwide. Approximately 35% of the adult population of the United States are classified as obese (BMI ≥30 kg/m²). Of more concern is that the average BMI of the US population is now 28 kg/m², well above the “healthy” range of 19–25 kg/m².1

The picture in New Zealand is equally disturbing. The ‘Health of New Zealand adults’ survey of 2012 demonstrated that 28.4% of New Zealand adults now classify as obese, whilst a total of 63.8% would be considered overweight or obese (BMI >25 kg/m²).2

Of particular concern are the marked disparities in prevalence rates between ethnic groups in New Zealand, and the increased rates in high deprivation communities. The rates in Caucasians approximate to the national averages; however, the rates of obesity and overweight in Māori (44.4% and 75.3% respectively) and Pacific adults (62.1% and 84.8% respectively) place them amongst the most overweight groups in the world.

Whilst a multitude of factors contribute to the increasing rates of obesity, the major contemporary promoter is a marked increase in the intake of energy across almost all populations.3 At a fundamental level obesity results when energy intake exceeds energy expenditure over a prolonged period of time.

An increase in the consumption of high energy foodstuffs, both portion size and energy density, coupled with a reduction in exercise levels, has resulted in a population where obesity has surpassed tobacco smoking as the major cause of morbidity. Obesity-related comorbidity, well reviewed elsewhere, places an enormous burden on our health service and will only worsen unless measures are taken to reduce the obesity rate.4
Of prime importance is effective public health measures aimed at obesity prevention. Such interventions may include targeting improved dietary patterns, reduced availability of nutritionally poor, high energy foods with increased availability of healthy choices, and improved physical activity levels.

Recent studies support the notion that instigating these interventions in childhood is effective, with the hope that behavioural changes made in childhood will be durable and lead to healthier lifestyle choices in adulthood.\textsuperscript{3,5} Overweight and obesity are a societal problem and therefore need a society wide solution. This must include changes in lifestyle at a personal level, but will also require community, council and governmental action for real success.

Whilst most would agree that prevention is the optimal long-term population strategy, it is important not to forget those who are currently overweight or obese. During an initial assessment it is important that overweight or obese patients are screened for the metabolic consequences of obesity and the presence of weight-related comorbidity (see Table 1).

In this review, we focus on the therapeutic options available to the New Zealand adult to achieve weight loss through lifestyle, pharmaceutical and surgical means, and suggest an approach to the management of weight loss in these individuals.

### Table 1. Metabolic and weight-related comorbidities that should be assessed at the initial clinical review of the overweight/obese patient

<table>
<thead>
<tr>
<th>Metabolic assessment</th>
<th>Comorbidities to be assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical examination</strong></td>
<td>Cardiac disease (ischaemia, LVH, arrhythmias)</td>
</tr>
<tr>
<td>Body mass index (BMI: weight (kg)/height(cm)$^2$)</td>
<td>Sleep apnoea or hypoventilation</td>
</tr>
<tr>
<td>Age</td>
<td>Diabetes microvascular complications</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>Liver dysfunction including non-alcoholic steatohepatitis</td>
</tr>
<tr>
<td>Blood pressure (mmHg)</td>
<td>Gout</td>
</tr>
<tr>
<td><strong>Blood tests</strong></td>
<td>Arthritis</td>
</tr>
<tr>
<td>HbA1c</td>
<td>Incontinence</td>
</tr>
<tr>
<td>Cholesterol profile</td>
<td>Depression</td>
</tr>
<tr>
<td>Liver function tests</td>
<td>Menstrual irregularities including PCOS</td>
</tr>
<tr>
<td>Uric acid</td>
<td></td>
</tr>
<tr>
<td>Thyroid stimulating hormone (TSH)</td>
<td></td>
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</tbody>
</table>

### Lifestyle strategies for the management of obesity

Lifestyle modification, a change in diet and physical activity to favour energy expenditure rather than energy intake, underpins the management of obesity. It is an essential component of all therapeutic options to reduce obesity and the most readily available option to New Zealanders. However, because alterations in dietary habits and physical activity require behavioural change in an individual, lifestyle modification may be the most difficult option to plan and implement. Despite this, extensive research has shown that persevering with lifestyle modification results in weight loss, and a reduction in risk factors for obesity-related disease.
Lifestyle assessment—The most important factor in developing a lifestyle modification strategy is to perform a thorough assessment of diet and physical activity habits. A diet history may be obtained by a recount of usual diet, or a recall of all food consumed in the previous 24 hours. Whilst these methods provide some insight into diet patterns there is likely to be substantial underreporting of food consumed.6

Although more time-consuming, completing a food and exercise diary, usually for 3 to 7 days, is an extremely valuable tool for the initial assessment of obesity and to develop a lifestyle modification plan. Most importantly, while completing the diary obese individuals may recognise factors in their diet which make a substantial contribution to their excess weight.

Influence of dietary macronutrients and fibre on weight loss—Whilst total energy intake is ultimately the critical factor, the macronutrient composition of the diet may influence weight loss by altering satiety and subsequent energy intake. Manipulating macronutrient composition as a percentage of total energy intake has attracted considerable research over the last 30 years.

Low fat diets, high protein diets and low carbohydrate diets have all been postulated to have advantages. A number of short-term studies have supported each as a means for achieving weight loss. Early studies demonstrated that substitution of carbohydrate for fat promoted reductions in energy intake and associated weight loss. This evidence has underpinned most national nutrition guidelines for several decades.7

It is often forgotten that these early studies also had a focus on dietary fibre intake. It is now common for low fat:high carbohydrate diets to contain a high proportion of refined carbohydrate and relatively low fibre intake, which may explain the relative lack of efficacy when used as comparator diets.

More recently there has been a focus on protein. In short-term experimental studies, high-protein meals have been shown to increase satiety and reduce subsequent energy intake to a greater degree than isoenergetic high-fat or high-carbohydrate meals.8 Conversely, increasing dietary fat in a meal results in 'high-fat hyperphagia’ with increases in hunger and total energy intake.9

Low carbohydrate diets such as the “Atkins diet” have received much popular attention and in short-term studies can be shown to be effective.10 However, many short term studies are conducted in highly controlled environments and do not represent what is achievable in more “real world” settings.

Longer-term studies may provide some insight into potential lifestyle modification strategies. Reductions in weight gain and increases in weight loss have been shown when low-fat, high-carbohydrate11,12 or low-fat, high protein diets13–15 are followed for 6 to 24 months, even when energy intake is not intentionally restricted.

There is a suggestion that high-protein diets may favour weight loss14,16 or prevent weight regain after weight loss17 and improve body composition and lipid profiles, thereby reducing the metabolic complications of obesity13,18 possibly due to increased acceptability of the study diet.17 However these findings are not supported by all studies.15
From all of the dietary macronutrient research, there is no one approach which is clearly superior, but importantly all are able to promote modest weight loss over the short to medium term. Furthermore whatever the macronutrient composition a focus on a diet high in fibre enhances weight loss or prevents weight gain.\textsuperscript{10}

**Adherence to lifestyle interventions**—What is most apparent in these studies is that compliance with the study diet is the key factor in successful weight loss. The importance of compliance was illustrated by Sacks et al (2009) with the inability to distinguish between two-year weight loss effects of four diets varying in protein, carbohydrate and fat composition.\textsuperscript{20} In this study the attendance at diet counselling sessions was the strongest factor associated with weight loss. Likewise, increased adherence to one of four popular diets was associated with greater reductions in weight and cardiovascular disease risk factors irrespective of the diet followed.\textsuperscript{21}

Similar findings are reported in a series of recent meta-analyses of macronutrient modification trials reinforcing that identifying strategies to improve adherence is the main current priority. Because adherence to a diet is the most important and yet the most difficult component to successful weight loss a variety of strategies to increase the acceptability of altering energy balance have been proposed.

A recent approach has been to follow an intermittent fast, with energy intake reduced to 25\% of an individuals recommended daily energy intake on 2 days per week and \textit{ad libitum} eating on the other 5 days. This approach appears to be at least as effective as continuous energy restriction for achieving weight loss with further research underway.\textsuperscript{22}

Another strategy is to participate in a commercial weight loss programme. Over twelve months, subjects attending the commercial programme Weight Watchers lost twice as much weight as those following standard care suggesting that this approach may be an effective alternative strategy for weight management that can be delivered on a large scale.\textsuperscript{23}

A systematic review of reviews demonstrated the effectiveness of community based lifestyle interventions (based on the Diabetes Prevention Program\textsuperscript{24}) with an average weight loss of 3-5kg at 12 months and 2-3kg at 36 months.\textsuperscript{25} Physical activity increased and factors that were important to the effectiveness of the intervention were identified—social supports, self-regulation and self-monitoring, behaviour change techniques, motivational interviewing and the use of pedometers, highlighting the importance of actively engaging individuals to adhere to lifestyle modification.

**Lifestyle interventions and risk of cardiovascular disease**—Although it is clear that following a lifestyle intervention results in modest weight loss, it is important to identify whether the weight lost leads to a reduction in risk factors for obesity-related disease. Perhaps the strongest evidence for this comes from the Diabetes Prevention Programme and the Diabetes Prevention Study.\textsuperscript{24,26} Both studies compared an intensive lifestyle intervention with standard advice in those with pre-diabetes and demonstrated a 58\% reduction in the incidence of diabetes with lifestyle intervention compared to placebo over 4 years.

However the benefits of lifestyle intervention and weight loss on cardiovascular disease risk is less clear, particularly in light of the recent publication of the 10 year Look AHEAD data.\textsuperscript{27} The lifestyle intervention produced a significant and sustained
weight loss and a reduction in HbA1C but no difference was seen in the primary endpoint of a CV disease score. This study was complicated by fewer than expected CV incidents in the control group and a change in the definition of the CVD score during the study. What is clear is that this intensive lifestyle intervention was not detrimental to the risk for CV disease and produced effective weight loss and improvements in glucose metabolism.

**Influence of dietary patterns on weight, adherence and cardiovascular disease risk**—Dietary patterns have been explored to investigate whether a broader group of food or nutrients, rather than manipulation of specific dietary components, may be more closely associated with obesity.

Diets high in fat or sugar and low in fibre have been associated with obesity, while a change to a diet lower in fat and sugar and high in fibre over 10 years resulted in a reduction in BMI in obese women and less increase in BMI in lean women. In children, high fat, low fibre, energy dense dietary patterns are associated with an increase in fat mass and linked to excess gain in body mass.

Another example of a dietary pattern is the “Mediterranean Diet”, characterised by replacing most red meat with fish and poultry, including wine in moderation and ample vegetables, legumes, grains, fruit, nuts and olive oil.

Adopting a Mediterranean dietary pattern has been shown to reduce cardiovascular events in those at high risk when compared with a low fat dietary prescription. Favourable effects of the Mediterranean diet on glycaemic control (compared with the favourable effects on lipids with a low-carbohydrate diet for example) suggest that personal preferences and metabolic considerations might inform individualised tailoring of dietary interventions.

**Exercise as a component of lifestyle interventions**—A reduction in physical activity is associated with increasing rates of obesity, and overweight individuals often report low exercise levels. An increase in physical activity alone, without dietary adjustment is unlikely to have a significant weight loss effect, and may even promote weight gain through an increase in appetite. Thus, activity should be viewed as an adjunct to dietary interventions to achieve weight loss, but thereafter as a key factor in weight maintenance.

As with dietary change, the critical factor in the effectiveness of activity for weight control is adherence. Individuals should be encouraged to select their preferred form of exercise, recognising that exercise undertaken as part of normal daily activity (e.g. walking to work) is as effective for weight control as scheduled activity (e.g. gym classes). Furthermore, regular short bouts of exercise are comparable to the same intensity of exercise undertaken over longer periods. A pedometer is a useful self-monitoring tool, with a target of at least 10,000 steps per day during periods of active weight loss, and higher targets during weight maintenance when caloric restrictions may be relaxed. A full review of the role of physical activity in weight management is beyond the scope of this paper.

**Summary of lifestyle strategies**—Long-term lifestyle intervention studies show clinically significant, albeit quantitatively modest, reductions in weight which result in a reduction in risk for metabolic disease. Dietary modification and increased physical activity to achieve a reduction in total energy intake is critical, however
adherence to the intervention, and hence behavioural change, appears to be the predominant factor in producing successful long-term weight loss, rather than the nature of the dietary intervention. Therefore allowing an individual to choose from the range of available evidence-based interventions may be the most effective strategy.

**Pharmaceutical options in the management of obesity (see Table 2)**

Medical options for the management of obesity are currently limited, following the withdrawal of a number of previously used drugs as a result of significant side effects. The development of new agents has been protracted and is not without difficulty. Regulators are wary of the likely very high population exposure to anti-obesity agents that become available.

Previous guidelines have suggested the consideration of pharmaceutical agents for the treatment of obesity, alongside dietary and physical activity interventions, in those with a BMI >30 kg/m$^2$ or >27 kg/m$^2$ if obesity-related comorbidities are present.

These criteria apply to an increasingly large proportion of the New Zealand population, and thus any unforeseen complications resulting from these medications would likely have a hugely significant adverse population health effect. Furthermore, it is likely that pharmaceutical therapy, once commenced, would need to be continued in the long-term unless significant alterations can be made to the lifestyle and other circumstances that lead to obesity in the first place. Thus the individual exposure to these agents would be significant.

Criteria for obesity drug licensing have tended to favour, but not enforce, placebo subtracted weight loss of >10%, on the basis that this degree of weight loss is required to gain health benefits.

Currently only 2 anti-obesity agents (orlistat and phentermine) are available in New Zealand, and three new anti-obesity agents are either in use or are close to market internationally (Table 2). Additionally, existing medications such as the incretin mimetics have shown great promise as anti-obesity agents.

Whilst pharmaceutical agents could potentially target either energy intake or expenditure, no agent has yet been produced which can successfully increase energy expenditure without unacceptable side effects. Agents acting on energy intake can be divided between those resulting in reduced digestion or absorption of foods, or those acting on appetite or satiety.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Usual dose</th>
<th>Mechanism</th>
<th>PSWL (kg)</th>
<th>Side effects</th>
<th>Licensed in New Zealand?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orlistat</td>
<td>120mg up to TDS</td>
<td>Lipase inhibitor</td>
<td>2.8</td>
<td>Oily stool, flatulence, change in bowel habit</td>
<td>Yes (NS) 1</td>
</tr>
<tr>
<td>Phentermine</td>
<td>37.5mg OD</td>
<td>Increased central noradrenaline activity</td>
<td>3.6</td>
<td>Tachycardia, palpitation, Hypertension, GI upset</td>
<td>Yes (NS) 2</td>
</tr>
<tr>
<td>Phentermine/topiramate 3</td>
<td>46/7.5mg OD</td>
<td>Increased central noradrenaline activity/</td>
<td>6.7</td>
<td>Dry mouth, paraesthesia, constipation, respiratory infections</td>
<td>No</td>
</tr>
<tr>
<td>Lorcaserin 4</td>
<td>10mg OD/BD</td>
<td>Hypothalamic Serotonin receptor agonism</td>
<td>2.9</td>
<td>Neuropsychiatric, cognitive-related adverse events</td>
<td>No</td>
</tr>
<tr>
<td>Naltrexone/bupropion 5</td>
<td>32/360mg OD</td>
<td>Opioid receptor antagonist/ dopaminenoradrenaline reuptake inhibitor</td>
<td>2.9% (change in kg not reported)</td>
<td>Nausea, constipation, headache</td>
<td>No</td>
</tr>
<tr>
<td>GLP-1 receptor agonist 6</td>
<td>Exenatide 10mg BD/ Liraglutide up to 1.8mg OD</td>
<td>Increased central satiety/ Delayed gastric emptying</td>
<td>1.9</td>
<td>Nausea, vomiting</td>
<td>No</td>
</tr>
</tbody>
</table>

PSWL = Placebo subtracted weight loss; TDS = Thrice daily; OD = Once daily; BD = Twice daily; NS = Not subsidised.

1. Weight control in adults with initial BMI ≥30 kg/m², in conjunction with low fat, calorie controlled diet;
2. Short term adjunct to medical monitored comprehensive weight reduction regimen in obese patient (BMI ≥30 kg/m²);
3. Approved by the FDA as an anti-obesity agent in 2012 on the basis of a phase 3 randomised 56 week trial of 2 dose regimens versus placebo. Phentermine/topiramate 92/15 mg daily was associated with PSWL of -8.8 kg; however, depression and/or anxiety-related adverse events occurred at almost double the frequency seen with the lower dose (phentermine/topiramate 46/7.4 mg daily, PSWL –6.7 kg) where the frequency was similar to placebo. Thus, the FDA have approved phentermine/topiramate 46/7.5 mg daily for chronic weight management in obese patients (BMI >30 mg/kg² or 27 mg/kg² if obesity-related comorbidities are present) and suggest a review after 12 weeks of therapy;
4. Serotonin 2C (5-HT₂C) agonist approved by the FDA in 2012 as an anti-obesity agent on the basis of a 12 month randomised trial of 2 dose regimens versus placebo, in conjunction with a nutritional and physical activity program. Subjects randomised to lorcaserin 10 mg BD achieved a modest mean PSWL of -2.9 kg, whilst lorcaserin 10 mg OD resulted in PSWL of -1.8 kg;
5. A phase 3 randomised study of naltrexone/bupropion (Contrave) slow release 32/360 mg versus placebo, in conjunction with lifestyle changes, demonstrated a PSWL of -2.9% in an intention to treat analysis. The FDA declined an application to approve this preparation in 2011 due to concerns about the longer-term cardiovascular safety concerns; a repeat application on the basis of further studies is likely in 2014;
6. GLP-1 acts centrally to increase satiety, and also delays gastric emptying further reducing appetite. A meta-analysis of nearly 3400 subjects enrolled in 21 studies, demonstrated a PSWL of -2.9 kg (CI -3.6 to -2.2), although the majority of these studies focused on obese patients with type 2 diabetes. When placebo controlled trials alone were considered (10 trials), the PSWL was a more modest -1.9 kg (-2.9 to -0.9).
Weight loss is modest when combined with other dietary and physical activity interventions, with most randomised studies showing placebo subtracted weight loss (PSWL) of -2.9kg, equating to approximately 2–5% of total body weight.\textsuperscript{35,40}

Reduction in total cholesterol and LDL cholesterol have been reported in large randomised studies, as well as a modest reduction in progression to type 2 diabetes in those patients who already had evidence of glycaemic dysfunction.\textsuperscript{41}

Gastrointestinal side effects occur as a consequence of increased stool fat content. Increased flatulence, oily stool, faecal urgency are seen in up to 40% of patients, although drop-out rates in clinical trials do not exceed placebo.\textsuperscript{40,42}

The frequency of gastrointestinal side effects reduces with time, although patients should be prescribed fat soluble vitamins (A, D, E, and K) together with orlistat therapy to prevent deficiencies.\textsuperscript{41} The longest trials with orlistat are out to 4 years, with no clinical trial data of the effects of longer term use on weight or comorbidities beyond this.

**Medications that act on appetite or satiety**—The majority of anti-obesity drugs that affect food intake do so primarily by affecting central neurotransmitter physiology. The sympathomimetic phentermine was the first medication approved by the FDA specifically for the treatment of obesity in 1959, and remains licensed in New Zealand (but not subsidised) for the treatment of obesity.

Numerous others have come to market since but have been withdrawn following the documentation of severe side effects (fenfluramine and dexfenfluramine (valvulopathy), aminorex (pulmonary hypertension), phenylpropanolamine (stroke), rimonabant (suicidal ideation) and sibutramine (myocardial infarction and stroke) and will not be considered in this review.\textsuperscript{33}

Other drugs (e.g. topiramate), despite showing promise as weight loss agents, have been limited by poor tolerability at the required doses. Nonetheless, weight loss outcomes with these medications are often more significant than with other current pharmaceutical strategies; thus, recent approaches to obesity drug development have focused on either combined therapy (enabling exposure to lower doses of constitutive agents) or modifications of existing therapies (e.g. lorcaserin, see Table 2) so that negative effects are avoided.

Phentermine suppresses appetite primarily by increasing the hypothalamic release of noradrenaline. A meta-analysis of 6 randomised studies showed PSWL of -3.6 kg (95% CI, -0.6 to -6.0) when phentermine was administered to obese persons for a mean of 13 weeks alongside lifestyle and dietary changes.\textsuperscript{42} However it is important to note that there are no studies of long-term use of phentermine although one small study of 108 obese women followed for 36 weeks showed PSWL of > -7.8 kg.\textsuperscript{43} Thus, it is approved only for up to 12 weeks treatment as an adjunct to other measures.

Despite concerns about the potential for addiction (as seen with other amphetamines), phentermine does not appear to cause psychological dependence or drug craving when used at the doses suggested for weight loss therapy.\textsuperscript{44}

Three new anti-obesity medications have either recently been licensed in the United States (phentermine/topiramate, lorcaserin) as anti-obesity agents, or are likely to be submitted for approval in the near future (naltrexone/buproprion).
The mechanisms and effects of these agents are summarised in Table 2, and interested readers are directed to recently published randomised studies for further details. Each will be subject to extensive post marketing (phase 4) studies given the unfortunate unforeseen consequences of historical anti-obesity treatments, and it is likely to be some time before these agents are available for use by New Zealand clinicians.

**Surgical options in the management of obesity**

Surgical procedures aimed at producing weight loss are broadly divided into those that simply restrict the stomach volume, thus reducing the capacity for food intake, and those that induce malabsorption of ingested nutrients (see Figure 1). A multitude of additional mechanisms are likely to play a role in both initial weight loss and weight loss maintenance following bariatric surgery, and the reader is directed to a recent excellent review article.  

![Figure 1. Graphic illustrating the anatomical changes associated with the common forms of bariatric surgery](image)

**Surgical notes:**

**Gastric banding** – A silicon based band is placed around the stomach within the perigastric pathway approximately 1cm inferior to the gastro-oesophageal junction, resulting in a gastric pouch above the band of approximately 15ml. A subcutaneous access port is sited and allows the injection of saline into the band resulting in band constriction. Most surgeons elect to leave the band inflated for at least 1 month after surgery to minimise band movement, with incremental inflations (via the injection of saline into the subcutaneous port) thereafter to achieve adequate restriction.

**Roux-en-Y gastric bypass** – The stomach is bisected and a small volume (15-50ml) pouch is fashioned. The jejunum is divided approximately 50cm below the pyloric sphincter, and the distal segment is anastomosed to the gastric pouch (the Roux limb). The distal end of the proximal segment (consisting of the remainder of the stomach, the pancreatojejunal tree and the duodenum/proximal jejunum) is anastomosed back to the small bowel forming the ‘Y’ limb. 50 to 150cm from the gastric/jejunum anastomosis. Thus, patients who undergo this surgery feel rapidly full, and ingested food is not exposed to the digestive secretion of the pancreaticobiliary tree, the proximal small bowel and the majority of the stomach until much later in small bowel transit. Additionally, these tissues are prevented from direct contact with ingested food which appears to have significant neuroendocrine consequences.

**Vertical sleeve gastrectomy** – A bougie (dilator) is placed transorally through to the pylorus. A starting point for resection is then chosen 5-10cm (proximal to the pylorus). A stapler is inserted and fired along the length of the bougie such that the bougie is enclosed by a formed gastric tunnel, and 75–80% of the entire stomach volume is resected.
The three most commonly performed bariatric procedures in New Zealand are laparoscopic adjustable gastric banding (LAGB, purely restrictive), sleeve gastrectomy, and Roux-en-y gastric bypass (RYGB, both restrictive and malabsorptive).

The majority of bariatric surgery in New Zealand is performed in the private sector, with access to publically funded bariatric surgery District Health Board dependent and on the basis of clear selection criteria. The majority of studies exploring outcomes following bariatric surgery have included patients with a BMI in excess of 35 kg/m². Most experts therefore recommend that a BMI greater than this is required for consideration of bariatric surgery, and the role of bariatric surgery in those patients with obesity-related comorbidities but a BMI lower than this threshold remains to be clarified.

Bariatric surgery results in more significant and durable weight loss than any other current therapeutic option, although it should be acknowledged that high quality randomised data reflecting longer term outcomes (>2 years) following bariatric surgery is lacking, especially in specific sub groups such as those with preoperative diabetes. Nonetheless, resolution of diabetes is seen in the majority of those undergoing bariatric surgery, although the effects on microvascular outcomes (retinopathy, nephropathy, etc) are unknown; thus, current practice is to continue regular review of micro/macrovascular risk factors in these patients.

Gastric banding was developed over 30 years ago as a weight loss therapy, and the procedure provided by most surgeons today has changed little in the last 20 years. Adjustable gastric banding is the least invasive of all bariatric surgery options and can nearly always be performed via a laparoscopic technique.

Average excess body weight loss (EBWL%) following LAGB has been shown to be in the order of 30–60% in most studies with maximal weight loss seen at 24–36 months post-surgery.

A number of modified surgical approaches to achieve bariatric gastrectomy exist, with vertical sleeve gastrectomy (VSG) being the most commonly performed option. The average excess weight loss following this procedure is approximately 50-80%. RYGB is the most commonly performed bariatric operation in the United States and is widely performed internationally. The majority of studies comparing types of bariatric surgery have shown greater earlier and long-term weight loss following RYGB (approximately 70% EBWL%) than that seen with gastric banding, although few randomised trials have been performed.

In a recent randomised controlled study of bariatric surgery versus intensive medical therapy in obese patients with type 2 diabetes, weight loss following vertical sleeve gastrectomy was comparable to that seen following Roux-en-Y gastric bypass at 12 months. Subjects who underwent sleeve gastrectomy lost -24.7% of their bodyweight by 12 months (81% excess body weight loss), whilst those who underwent Roux-en-Y gastric bypass lost -27.5% of their body weight (88% excess body weight loss).
A similar study comparing outcomes following RYGB and biliopancreatic diversion (a more invasive malabsorptive procedure and performed only rarely in New Zealand) in obese patients with type 2 diabetes showed weight loss of -33% at 2 years in those undergoing RYGB (68% excess body weight loss). In both studies weight loss in the intensive medical therapy control groups was approximately 5%.

Early complication rates following laparoscopic banding are low with band slippage or port problems most commonly reported. Gastric erosions have been reported at alarmingly high rates in longer term follow up studies (1 in 3 patients), although other authors argue that more modern surgical techniques alleviate this problem.

Perioperative and short-term mortality rates are also favourable towards LAGB when compared with other bariatric procedures, although it should be noted that rates in well-selected patients are very low for all procedures (<0.2% for all procedures). Short-term complications occur in less than 10% post VSG or RYGB and include venous thromboembolism, infection, and perforation.

Dumping syndrome is very common following RYGB, and results from the movement of fluid into the intestinal lumen due to the increased osmotic potential of undigested carbohydrates. Patients are advised to avoid foodstuffs or situations that predictably provoke episodes and maintain a healthy fluid intake. As foodstuffs provoking dumping are often unhealthy choices, ‘dumping’ may act as a positive deterrent in some patients.

Many authors reporting on outcomes beyond 3-4 years have also suggested an increased risk of longer term complications with LAGB than with other bariatric procedures, and the high re-operation (approximately 60% and mostly related to weight regain) and band removal rate (approximately 50%) have resulted in cautions against recommending the wide spread use of LAGB as the bariatric procedure of choice.

**Follow up of bariatric surgery patients**—Increasingly, New Zealand clinicians will encounter patients who have previously undergone bariatric surgery, and an awareness of the side effects, intentional or otherwise, of surgery is required. Weight regain is particularly common following LAGB, but is reported in up to 50% during long-term follow up of all bariatric procedures.

Frequently, weight regain is associated with poor compliance with recommend dietary and physical activity practice post surgery, although a multitude of other physiological, surgical and genetic factors are likely to be important. Reinforcement of post surgery lifestyle recommendations via a multidisciplinary team skilled in the management of post bariatric surgery patients is advised but rarely available in New Zealand. There is little evidence to guide the use of pharmacological anti-obesity therapies in this context.

Consideration of a surgical cause of weight regain should be entertained when weight regain is refractory to further intervention. Re-operation rates specifically for this indication are higher with LAGB than they are with more invasive initial procedures.

Vitamin and mineral deficiencies, if untreated, should be expected to result following all malabsorptive bariatric procedures. Thus, the use of daily multivitamin tablets
incorporating recommended daily intake levels of vitamin D and folate amongst others is strongly recommended.\textsuperscript{56}

Menstruating women are at particular risk of iron deficiency, which should be prophylactically treated. Vitamin B12 deficiency, due to both reduced intrinsic factor production and B12 complex absorption, is common following RYGB, and replacement using oral, intranasal or injectable B12 preparations is recommended.

Protein deficiency, usually seen at 3–6 months post surgery, is the most serious potential malabsorptive issue. Dietary support, occasionally requiring hospitalisation for parenteral nutrition is required. Numerous groups have reported an increased incidence of secondary hyperparathyroidism following RYGB.\textsuperscript{54} The exact mechanism remains unclear, but an annual assessment of parathyroid hormone levels (± vitamin D) is advisable; bone mineral density scanning (DEXA) is recommended at 2–3 yearly intervals postoperatively.

**Summary**

Obesity is a long-term condition with many associated comorbidities. In this review we have summarised the evidence for weight loss from effective lifestyle, pharmacotherapy and surgical interventions. Whilst weight loss is achievable through these interventions there are strong physiological drivers which make weight loss maintenance a lifelong battle for individuals.

**Figure 2. An approach to therapeutic weight loss in overweight/obese individuals**

![Figure 2](image-url)
An approach to weight loss in overweight or obese individuals in New Zealand as developed by the Ministry of Health in 2010 (see Figure 2) must be centred on lifestyle changes primarily. The diet should be assessed ideally by a dietitian, with the immediate removal of high energy, nutritionally poor foodstuffs and an aim to reduce daily caloric intake to approximately 500 calories below the individuals recommended daily intake. The exact dietary prescription should be tailored to the individual, based on the most likely pattern that they can adhere to and sustain in the long-term.

Physical activity should be increased through whichever activity is most likely to be durable for that individual. For best results the increased physical activity should be built into normal daily activities. The patient should be counselled that both dietary changes and increased physical activity should be seen as long-term interventions. A comprehensive national strategy for implementation of these guidelines is urgently needed. Achieving comparable results to the diabetes prevention programme requires adequate resourcing for community based multidisciplinary teams to assist individuals with all of the elements of behavioural change described.

The additional use of pharmaceutical agents for weight loss may be considered in those with a BMI of >30 kg/m\(^2\), although ideally the effect of lifestyle changes should be observed first. Bariatric surgery is generally reserved for those with a BMI >35 kg/m\(^2\) who have been unable to lose weight through other methods.

Despite the above therapeutic strategies, the greatest effect New Zealand healthcare workers can have on the increasing obesity prevalence in New Zealand is to promote the lifestyle choices that help to prevent obesity developing in the first place.

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