



# Adjunctive therapies for obesity

## VLEDs, pharmacotherapy and bariatric surgery

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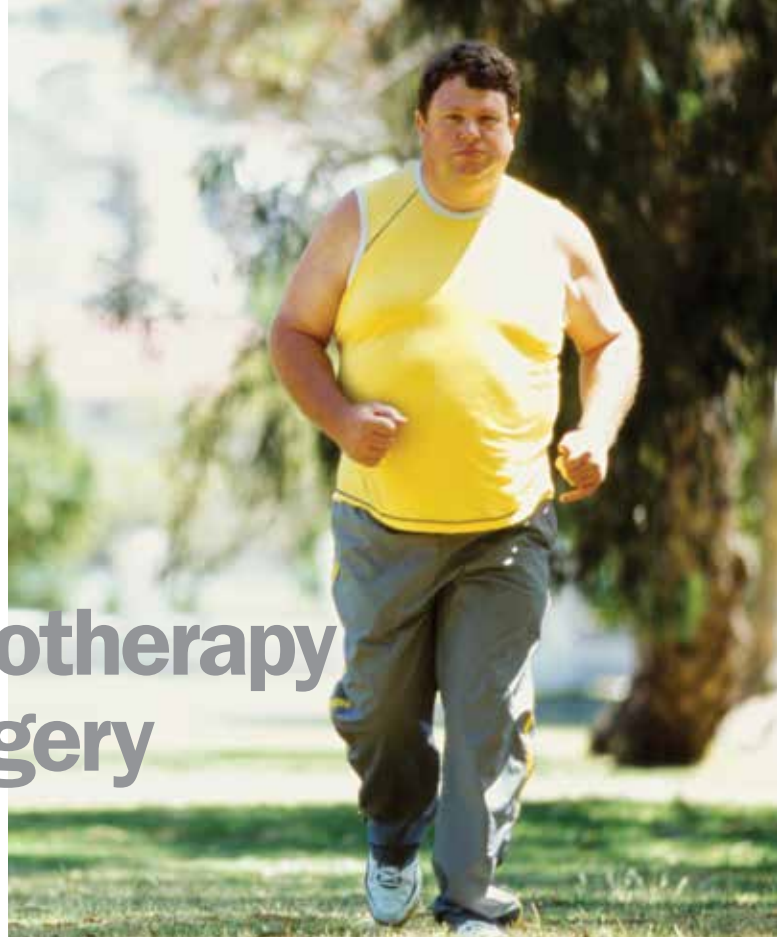
*Although lifestyle interventions remain the cornerstone of obesity treatment, this article highlights additional approaches to management that may help reduce and maintain weight. These adjunctive therapies include the role of the multidisciplinary team in obesity management, and the use of very low energy diets, pharmacotherapy and bariatric surgery.*

### Key points

- **Obesity is a multifactorial disease requiring a comprehensive and often diverse management approach to both the disease itself and its related comorbidities.**
- **Adjunctive therapy, including pharmacotherapy and very low energy diets, can be used to aid weight loss and maintenance.**
- **Multidisciplinary obesity clinics are best placed to address the complex causes of obesity and its related comorbidities.**
- **Bariatric surgery should be considered for patients who have BMI above 40 kg/m<sup>2</sup> or BMI above 35 kg/m<sup>2</sup> with comorbidities.**
- **Lifestyle intervention remains the cornerstone of treatment irrespective of the type of adjunctive therapy used.**

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Seeking effective solutions to obesity is arguably one of the greatest public health challenges currently facing Australia. Primary and community-based healthcare professionals are at the forefront of this challenge, often with limited time and resources to sufficiently address the multifactorial aspects of obesity management.

In a previous article, published in the October 2012 issue of *Endocrinology Today*,<sup>1</sup> we focused on practical approaches to lifestyle interventions for the management of obesity. The cause of obesity, particularly for patients with very high body mass indices (BMIs), is multifactorial (e.g. physical and sexual abuse,<sup>2,3</sup> periods of inactivity, disordered eating, medical problems, medications, genetics, lifestyle). It follows then that the management approach to obesity must address these many causes in addition to addressing obesity-related comorbidities. Although lifestyle interventions remain the cornerstone of obesity treatment, there are additional approaches to management, highlighted in this article, that may help reduce and maintain weight. These include the role of the multidisciplinary team in obesity management, in addition to the use of very low energy diets (VLEDs), pharmacotherapy and bariatric surgery. These adjunctive therapies should be considered when lifestyle interventions have failed to achieve sufficient weight loss or improvement in obesity-related comorbidities after a minimum of three months (Figure 1),<sup>4</sup> or initially if the patient has obesity of grade II or above and psychological, financial and social barriers have been addressed.<sup>4</sup> Ensuring the patient is ready to start adjunctive therapy is vital for success.

GPs play a crucial role in the management of obesity. They should aim to reinforce diet and exercise recommendations and highlight possible lifestyle changes at each consultation in a nonjudgemental

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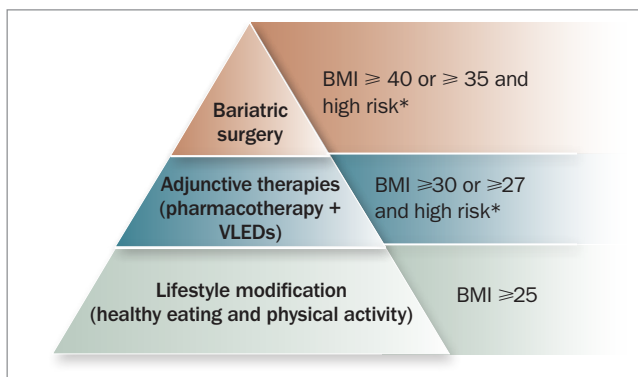


Figure 1. Hierarchical approach to obesity management.<sup>4</sup>

\* High risk: a waist circumference  $\geq 102$  cm in men and  $\geq 88$  cm in women; or the presence of risk factors, including type 2 diabetes/impaired glucose tolerance, hypertension, coronary heart disease, dyslipidaemia and obstructive sleep apnoea.

and empathetic way.<sup>5</sup> They should also ensure there is adequate psychological support for the patient, and identify and manage obesity-related complications. The 2013 NHMRC clinical practice guidelines for the management of overweight and obesity<sup>6</sup> can be used to inform and guide this process. These guidelines are structured according to the 5A's (Ask, Assess, Advise, Assist, Arrange follow up), which has recently been shown to facilitate weight management by promoting physician-patient communication and emphasises follow-up care.<sup>5</sup> Referral of the patient to a specialised obesity multidisciplinary team should be considered when the patient has multiple obesity-related issues or disease complications that require specialist expertise. Figure 2 outlines a recommended obesity referral pathway.

### Multidisciplinary specialist obesity clinics

Obesity is caused by a complex interplay of different aspects of a patient's life, and thus the multidisciplinary team is well placed to deal with the multifactorial nature of obesity. The team uses diverse skills from multiple health disciplines, which usually include a medical practitioner, dietitian, physiotherapist or exercise physiologist, and psychologist. The aim is for the team to communicate regularly about the ongoing care of the patient and to identify and treat most, if not all, factors contributing to a patient's excess weight (see Appendix 1 in the online version of this article). The team is also involved in screening, treating and/or facilitating specialist referrals for any obesity-related comorbidities. It is important that all members of the team enquire or are informed about all aspects of the patient's obesity as issues will often cross disciplines.

### Interventions considered beyond lifestyle VLEDs

VLED, sometimes called a very low calorie diet, is the most intensive dietary intervention for the management of obesity. It involves completely or partially replacing all usual food intake with nutritionally complete commercial products, which provide between 1845 and 3280 kJ (450 to 800 kcal) per day and which are fortified with the recommended daily allowances of vitamins, minerals and electrolytes. The severe energy restriction results in rapid weight loss (which is very motivating for the patient), typically 1.5 to 2.0 kg for women and 2.0 to 2.5 kg for men per week.<sup>7</sup> However, the rate of

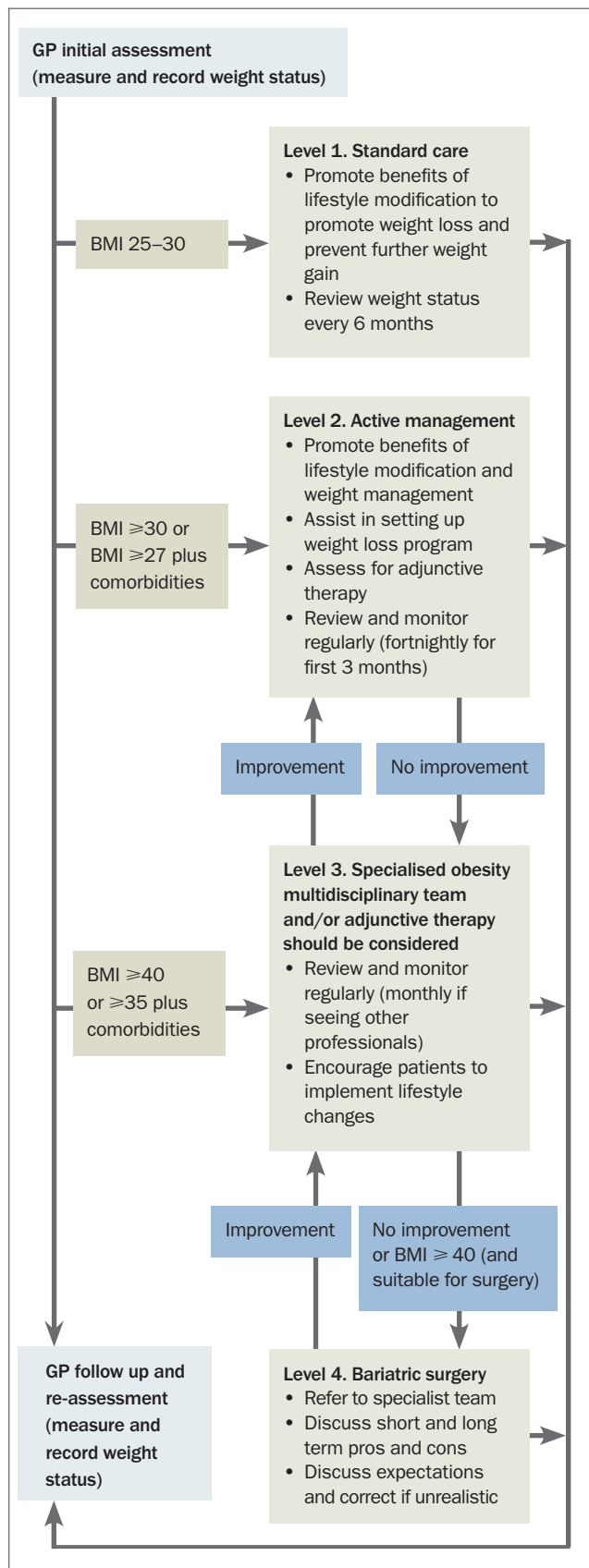
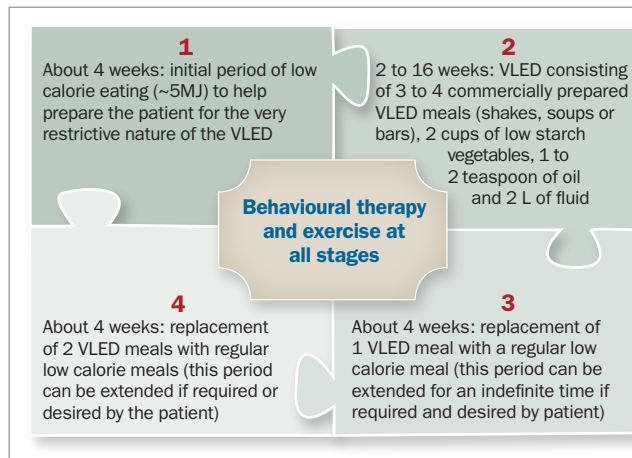


Figure 2. Decision tree for weight management and referral.

GPs play an integral role regardless of the level of intervention by providing regular follow-up and support.



**Figure 3. Typical structure of a very low energy diet (VLED) program.<sup>9</sup>**

1. It can be helpful to start patients on a 4-week run in period that aims to cut back on intake. Establishing good habits beforehand may also help when food is reintroduced as healthy habits are familiar.
2. The intensive phase can last between 2 and 16 weeks and in some cases longer if required and supervision is possible.
3. Start weaning the patient back onto food by introducing one meal at a time. Breakfast is usually best as it typically has the lowest total energy content but patients with families may find reintroducing a meal at dinner easier.
4. When the patient feels ready and the clinician agrees, reintroduce another meal. This can be any meal, but keeping the meal replacement at the time of the usual biggest meal will aid weight control. Stopping meal replacements completely can be confronting for some patients. Extra support during this time is often required. The process can be repeated but is often more difficult the second time around. Using partial meal replacement can be a long-term solution for when weight starts to increase. Reintroduction of meal replacements should be implemented when weight has increased by 1 to 2 kg rather than waiting until it has reached 5 kg or more.

weight loss subsequently slows due to a decrease in energy requirements, spontaneous physical activity and hormonal alterations; and thus a weight plateau may not necessarily indicate a lack of treatment adherence.<sup>8</sup> Although modern VLEDs are accepted as being safe, there are several potential complications associated with VLEDs (see Appendix 2 in the online version of this article). VLEDs should ideally be commenced in consultation with a medical practitioner, particularly if the patient has comorbidities such as liver, renal and cardiovascular disease, or diabetes. If initiated without medical supervision, support and encouragement from a health professional should not be underestimated, particularly during the weaning and weight maintenance phases. A typical VLED program is shown in Figure 3.<sup>9</sup>

Most commercial VLED preparations recommend three meals per day and provide approximately 70 g of protein. However, to attenuate the loss of lean body mass, aim for a minimum protein intake of 0.8 g/kg of body weight per day.<sup>10,11</sup> Therefore, patients weighing over 85 kg may require four or more meal replacement sachets per day. Alternatively, to keep total calories and carbohydrate intake low, a whey protein isolate supplement could be added to the VLED preparations or a small serving of lean protein could be included in addition to the meal replacements.<sup>10,11</sup>

Patients often find the first three to five days of the VLED the most difficult as first glycogen, then fat stores, are used for energy. This results in the production of ketone bodies leading to appetite suppression.<sup>12,13</sup> However, even with this ketosis it is difficult to completely replace all usual food intake and initiation of a VLED should involve discussion about filling in the time a patient would usually spend preparing and eating food, and what to do when socialising and eating with the family. One of the reasons VLEDs are effective is that their restrictive nature can take away the anxiety of deciding what to eat. Consequently, it is often when patients transition back to 'real' food that they will require the most support. VLEDs can be used intermittently (or partially) to help with weight maintenance.<sup>14</sup>

Weight reduction of 5 to 10% from baseline is associated with improvement in obesity-related comorbidities.<sup>15-17</sup> Accordingly, as

a VLED proceeds, ongoing review by a medical practitioner is recommended as antihypertensive therapy may need to be decreased and adequate fluid intake encouraged. In people with diabetes, their diabetic therapy almost always requires significant dose reduction and should be adjusted before commencing a VLED with subsequent regular blood glucose level monitoring and ongoing dose titration in consultation with a medical practitioner. On average, a single serve of a VLED will contain between 15 and 24 g of carbohydrate, depending on the brand used. See the following references for more information on VLEDs.<sup>6,14,18</sup>

### Pharmacotherapy

Lifestyle interventions for the treatment of obesity are frequently limited by significant weight regain in the long term. For patients who already demonstrate good compliance to lifestyle modification or those who have lost a significant amount of weight but are struggling to maintain weight loss, pharmacotherapy can be an effective adjunct to their treatment. When pharmacotherapy is combined with lifestyle modification the proportion of body weight lost is usually 2 to 5% higher than with lifestyle alone (i.e. a loss of 10% initial body weight with pharmacotherapy, compared with 6% with lifestyle alone).<sup>19</sup>

Pharmacotherapy options remain limited in Australia. Phentermine monotherapy is approved for a short duration (<3 months) as an adjunct to lifestyle modification, usually commencing at a dose of 15 mg daily and increasing to 30 mg or 40 mg if required. Phentermine is associated with a 3.6 kg (confidence interval [CI], 0.6 to 6.0 kg) greater weight loss compared with placebo in major studies<sup>20,21</sup> and, before the recently FDA-approved combination therapy phentermine/topiramate ER (not available in Australia), phentermine monotherapy was the most effective obesity pharmacotherapy for both weight reduction and improvement in comorbidities. Phentermine causes appetite suppression; however, its use is often associated with poorly tolerated adverse effects relating to its stimulant properties, including dry mouth, agitation, insomnia and decreased concentration. Of greatest concern is its effect on cardiovascular risk factors – in particular, blood pressure and heart rate. For this reason

it is not recommended in patients with hypertension and is relatively contraindicated in individuals with hypertension, existing heart valve abnormalities or heart murmurs, cerebrovascular disease, severe cardiac disease (including arrhythmias and advanced arteriosclerosis), eating disorders and states of agitation or psychosis. Long-term clinical trials also indicate increased tolerance and habituation associated with prolonged use,<sup>22</sup> and thus phentermine is not recommended in people with psychiatric disorders, including anorexia or depression, or in those at risk of drug dependency.<sup>23</sup>

Orlistat is a gastrointestinal lipase inhibitor that reduces the amount of fat absorbed from the diet by approximately 30%, leading to weight loss through reduction in total energy intake. Orlistat is associated with 2.89 kg (CI, 2.27 to 3.51 kg) or 2.9% (95% CI, 2.3 to 3.4%) greater reduction in body weight, in combination with lifestyle modification, compared with placebo.<sup>24,25</sup> Initially available only with a prescription, it was reclassified as a 'pharmacist-only medicine' in 2003. It is currently available over the counter in 120 mg capsules (84 capsules per pack) and patients are advised to take one with every meal. It remains the only obesity therapy with long-term safety and efficacy data. However, its clinical use is predominantly limited by its gastrointestinal side effects, including increased defecation, liquid/oily stools, anal leakage, increased urgency and flatulence. Although these symptoms are significantly reduced on a low-fat diet, patients often will avoid taking the tablet with high-fat foods rather than

changing their diet. If patients have not lost weight within the first three months of commencing orlistat it is unlikely that it will have a significant benefit.

The FDA recently approved two new pharmacotherapies, lorcaserin and phentermine/topiramate ER as an adjunct to lifestyle intervention for the treatment of overweight adults with comorbidities and obese patients. These are yet to be approved in Australia or Europe. Although there are no head-to-head studies, recent evidence suggests that these new therapies may be more effective at achieving and maintaining weight loss than currently available pharmacotherapy.<sup>26</sup>

### **Surgery**

The most common surgeries offered in Australia for obesity are laparoscopic adjustable gastric banding (LAGB), laparoscopic sleeve gastrectomy (LSG) and laparoscopic Roux-en-Y gastric bypass (LRYGB) (Figure 4).<sup>27,28</sup> The bilio-pancreatic diversion with or without duodenal switch (BPD DS) was a common bariatric procedure worldwide; however, is now less commonly performed due to the increased risk of complications and nutritional deficiency long term. These surgeries were previously thought to be purely restrictive or malabsorptive procedures; however, it is now recognised that they have significant neuroendocrine implications that affect intake and metabolism.<sup>29</sup>

**1. Patient criteria for weight loss surgery<sup>29</sup>**

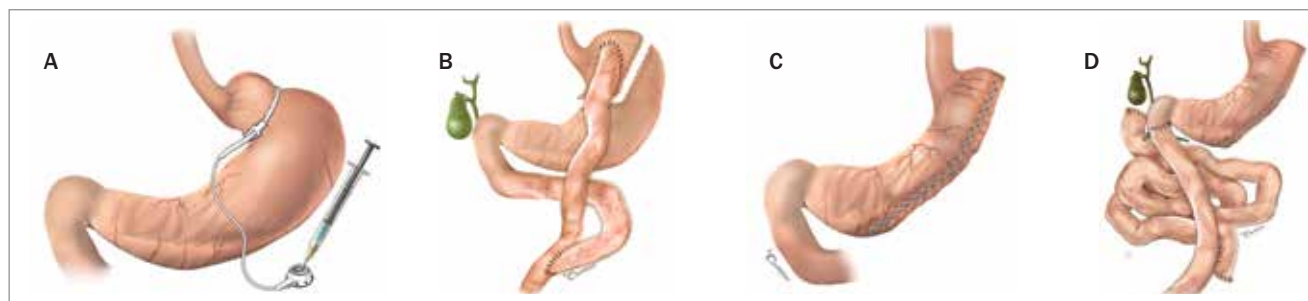
- Past history of weight loss attempts using recognised methods
- Have received counselling and assessment by a multidisciplinary obesity management team
- Have a comprehensive medical evaluation
- Must commit to lifelong surveillance
- BMI >40 kg/m<sup>2</sup>
- BMI >35 to 39.9 kg/m<sup>2</sup> with an associated comorbidity, such as:
  - type 2 diabetes
  - hypertension
  - hyperlipidaemia
  - obstructive sleep apnoea
  - obesity-hypoventilation syndrome
  - nonalcoholic fatty liver disease
  - nonalcoholic steatohepatitis
  - benign intracranial hypertension
  - gastro-oesophageal reflux disease
  - asthma
  - venous stasis disease
  - severe urinary incontinence
  - debilitating arthritis
- Be of sound operative risk
- No underlying endocrine abnormality contributing to the obesity e.g. Cushing's syndrome
- No current substance abuse disorders
- No uncontrolled psychiatric disorders

Bariatric surgery helps people to feel satisfied on a smaller amount of food. The criteria to determine suitability for surgery is outlined in Box 1.<sup>29</sup> Surgery has been shown to lead to greater weight loss and improvements in comorbidities than lifestyle change alone. Most of the weight loss occurs in the first 12 months; subsequently

weight will generally plateau or start to increase regardless of the type of surgery used.<sup>30</sup> Some patients do eventually regain all lost weight. However, the average weight loss achieved is 15 to 40% of baseline weight or 12 to 17 BMI units depending on surgery type.<sup>30-33</sup> Malabsorptive procedures (BPD DS and LRYGB) are generally regarded as producing greater weight loss and improvement of obesity-related comorbidities.<sup>6,32-35</sup> However, the amount of weight loss produced by all surgeries varies significantly between studies and may depend on the team involved.<sup>6,34,36,37</sup> Despite patient expectations, most individuals remain in the obese if not severely obese category after surgery.

Poorer prognosis with regards to maintenance of postsurgical weight loss has been associated with older age, binge eating, emotional eating, sweet cravings and a lack of exercise.<sup>38-40</sup> Lifestyle modification therefore remains crucial, even after surgery. In addition, diet quality and lifelong micronutrient supplementation becomes important due to the reduced intake. Micronutrients should be checked before surgery and corrected to decrease risk of nutrient deficiency after surgery. In particular, levels of vitamin D and calcium should be checked because they are often low in obese individuals and may increase the risk of postsurgical osteoporosis.<sup>41,42</sup>

Many patients have unrealistic expectations relating to outcomes from surgery. For example, although it is generally emphasised in education before surgery, patients often think they can return to old habits and ignore the long-term commitment to lifestyle change. Poor food choices can lead to weight gain over time even if portions are small. Patients may also not fully appreciate the ongoing medical management that is required. The pros and cons of surgery should be repeatedly discussed with patients, as should the wider social, dietary and psychological implications (see Table).<sup>4,6,34,41,42</sup> This is often best done with a multidisciplinary team but should also be covered by all health professionals involved with the patient's care, especially the primary physician.



**Figure 4. Bariatric surgeries for obesity.<sup>27,28</sup>**

- A) Laparoscopic adjustable gastric banding (LAGB) is a restrictive procedure with some reduction in appetite. It involves the placement of a prosthetic band around the upper part of the stomach partitioning the stomach into two, a small upper pouch of approximately 10 to 20 mL and a larger distal remnant connected through a narrow restriction that can be adjusted via an inflatable balloon.
- B) Laparoscopic Roux-en-Y gastric bypass (LRYGB) is a restrictive and malabsorptive procedure but with less of the deficiencies seen with the biliopancreatic diversion. It also leads to significant neuroendocrine changes. The LRYGB divides the stomach into a small proximal pouch and a separate large, distal remnant. The upper pouch (~5% of stomach) is joined to the proximal jejunum through a narrow gastrojejunal anastomosis.
- C) Laparoscopic sleeve gastrectomy (LSG) is a restrictive procedure and leads to significant reduction in appetite. LSG removes and discards 80 to 90% of the greater curvature of the stomach leaving a tubular sleeve. In particular, it removes part of the stomach that releases ghrelin into the body.
- D) Biliopancreatic diversion (BPD) is a restrictive and malabsorptive procedure where the sleeve is created as in B) and the duodenum is transected 2 cm distal to the pylorus. It is then reconnected to the distal jejunum thus bypassing more of the small intestine than the LRYGB procedure.<sup>27,28</sup>

**Table. Pros and cons of the different types of bariatric surgeries<sup>4,6,34</sup>**

Type of surgery	Pros	Cons
LAGB	<p>Hospital stay 1 to 2 days</p> <p>Reversible</p> <p>The band can continue to be filled or emptied for the life of the band and patient, allowing long-term weight manipulation</p> <p>Low acute morbidity or mortality</p> <p>Low risk of nutrient deficiencies</p> <p>Can reduce restriction during times of increased nutrient/energy need (e.g. pregnancy)</p>	<p>The small pouch above the band can dilate increasing the ability to eat larger portions and thus reducing the effectiveness of the band</p> <p>Enlargement of oesophagus</p> <p>Increased risk of gastro-oesophageal reflux disease</p> <p>The band can erode the stomach</p> <p>The band can slip up or down reducing its effectiveness</p> <p>The tubing to the band can leak or disconnect</p> <p>Potential for infection around port site</p> <p>Often whole solid foods become problematic to eat (e.g. meat and vegetables)</p> <p>Close follow up required</p> <p>Must wait 12 months before falling pregnant</p> <p>About 50% require reoperation in 10 years due to any number of the conditions mentioned above</p>
LSG	<p>Hospital stay 2 to 4 days</p> <p>Greater improvements in comorbidities</p> <p>Weight loss starts sooner, greater reduction in sweet cravings and appetite, less invasive than LRYGB</p> <p>Requires less ongoing follow up</p> <p>Greater improvements in comorbidities compared with LAGB</p> <p>No foreign body inside patient</p>	<p>Leakage can occur at suture line</p> <p>Decreased absorption of calcium, iron and B<sub>12</sub> may occur</p> <p>Strictures may occur</p> <p>Greater morbidity and reoperation rates at 30 days after surgery compared with LAGB</p> <p>Increased risk of sepsis compared with LAGB</p> <p>Potential for GORD</p> <p>Oesophageal enlargement may occur</p> <p>Should wait 12 months before falling pregnant</p> <p>Possible osteoporosis in the long term</p>
LRYGB	<p>Hospital stay 2 to 4 days</p> <p>Greater weight loss</p> <p>Greater neuroendocrine changes thus greater reduction in desire to eat/hunger signals</p> <p>Greatest resolution in obesity-related comorbidities including diabetes</p> <p>No foreign body inside patient</p>	<p>Associated with the highest short (30 days) and long-term (1 year) mortality risk of the three procedures (mostly due to embolism and sepsis)</p> <p>Greater 30-day reoperation rates compared with LSG</p> <p>Highest risk of nutrient deficiencies (particularly iron, calcium, B<sub>1</sub> and B<sub>12</sub>)</p> <p>Increased risk of dumping syndrome (from increased rate of sugars and fats reaching small intestines and causing fluid changes, nausea/vomiting, stomach cramps/pain, diarrhoea, sweating/flushing/light headiness and rapid heartbeat)</p> <p>Increased risk of deep vein thrombosis, anastomotic leaks, internal hernias, gastrointestinal bleeding, ulcers in the bypassed segments, torsions of roux limb, closed loop obstruction, stomal stenosis, wound complications, staple line disruption and gallstone formation</p> <p>Possible osteoporosis in the long term<sup>41,42</sup></p> <p>Should wait 12 months before falling pregnant</p>

Abbreviations: LAGB = laparoscopic adjustable gastric banding; LRYGB = laparoscopic Roux-en-Y gastric bypass; LSG = laparoscopic sleeve gastrectomy.

## Conclusion

Obesity is a multifactorial disease requiring a comprehensive multidisciplinary management approach to both the disease itself and its associated comorbidities. VLEDs, pharmacotherapy and bariatric surgery represent effective adjuncts to ongoing lifestyle modification and may be used as either single therapies or in combination throughout the patient's life, reflecting the nature of obesity as a chronic illness. Nevertheless, lifestyle modification remains the cornerstone of obesity therapy, particularly in maintenance of weight loss. A multidisciplinary team within a tertiary obesity service is frequently best placed to address the complex causes of obesity and its related comorbidities for an individual patient. However, this approach will

be most effective in the long term when supported by the GP in the primary care setting. **ET**

## References

A list of references is included in the website version ([www.medicinetoday.com.au](http://www.medicinetoday.com.au)) of this article.

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## References

- Gibson A, Franklin J, Sim KA, Partridge SR, Caterson ID. Lifestyle approaches to obesity: making it a less weighty issue. *Endocrinology Today* 2013; 2(4): 8-15.
- Wadden TA, Butryn ML, Sarwer DB, et al. Comparison of psychosocial status in treatment-seeking women with class III vs. class I-II obesity. *Surg Obes Relat Dis* 2006; 2: 138-145.
- Noll JG, Trickett PK, Harris WW, Putnam FW. The cumulative burden borne by offspring whose mothers were sexually abused as children: descriptive results from a multigenerational study. *J Interpers Violence* 2009; 24: 424-449.
- Gibson A, Sim K, Caterson ID. Obesity, in nutrition for the primary care provider. 2013 Karger: In Press.
- Rueda-Clausen CF, Benterud E, Bond T, et al. Effect of implementing the 5As of obesity management framework on provider-patient interactions in primary care. *Clinical Obesity* 2013; 4: 39-44.
- National Health and Medical Research Council. Clinical practice guidelines for the management of overweight and obesity in adults, adolescents and children in Australia - Systematic Review, 2013, National Health and Medical Research Council: Melbourne.
- Atkinson R. Very low-calorie diets. *JAMA* 1993; 270: 967-974.
- Leibel RL, Rosenbaum M, Hirsch J. Changes in energy expenditure resulting from altered body weight. *New Engl J Med* 1995; 332: 621-628.
- Wadden TA. The treatment of obesity: an overview. In *Obesity: theory and therapy*. Stunkard AJ, Wadden WA, Eds. Raven Press: New York 1993. p. 197-217.
- Soenen S, Martens EA, Hochstenbach-Waelen A, Lemmens SG, Westerterp-Plantenga MS. Normal protein intake is required for body weight loss and weight maintenance, and elevated protein intake for additional preservation of resting energy expenditure and fat free mass. *Nutr* 2013; 143: 591-596.
- Westerterp-Plantenga MS, Lemmens SG, Westerterp KR. Dietary protein – its role in satiety, energetics, weight loss and health. *Br J Nutr* 2012; 108 Suppl 2: S105-S112.
- Sumithran P, Prendergast LA, Delbridge E, et al. Ketosis and appetite-mediating nutrients and hormones after weight loss. *Eur J Clin Nutr* 2013; 67: 759-764.
- Chearskul S, Delbridge E, Shulkes A, Proietto J, Kriketos A. Effect of weight loss and ketosis on postprandial cholecystokinin and free fatty acid concentrations. *Am J Clin Nutr* 2008; 87: 1238-1246.
- Delbridge E, Proietto J. State of the science: VLED (very low energy diet) for obesity. *Asia Pac J Clin Nutr* 2006; 15 Suppl: 49-54.
- Goldstein DJ. Beneficial health effects of modest weight loss. *Int J Obes Relat Metab Disord* 1992; 16: 397-415.
- Poirier P, Giles TD, Bray GA, et al. Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss: an update of the 1997 American Heart Association Scientific Statement on Obesity and Heart Disease from the Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. *Circulation* 2006; 113: 898-918.
- Goldstein D. Beneficial effects of modest weight loss. *Int J Obes Relat Metab Disord* 1992; 16: 397-415.
- Lau NS, Caterson ID. Meal replacement products and very low calorie diets in adult obesity. *Royal College of Pathologists Bulletin* 2011; 155: 172-174.
- Wittert G, Caterson ID, Finer N. The clinical effectiveness of weight loss drugs. *Obes Res Clin Pract* 2007; 1: 1-5.
- Li Z, Maglione M, Tu W, Mojica W, et al. Meta-analysis: pharmacologic treatment of obesity. *Ann Intern Med* 2005; 142: 532-546.
- O'Connor HT, Richman RM, Steinbeck KS, Caterson ID. Dexfenfluramine treatment of obesity: a double blind trial with post trial follow up. *Int J Obes Relat Metab Disord* 1995; 19: 181-189.
- Douglas A, Douglas JG, Robertson CE, Munro JF. Plasma phentermine levels, weight loss and side-effects. *Int J Obes* 1983; 7: 591-595.
- Administration, FDA Advisory Committee Meeting for Phentermine/Topiramate. 2012 May 2013; Available online at: <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/EndocrinologicandMetabolicDrugsAdvisoryCommittee/UCM218824.pdf> (accessed February 2014).
- Padwal R, Li SK, Lau DC. Long-term pharmacotherapy for overweight and obesity: a systematic review and meta-analysis of randomized controlled trials. *Int J Obes Relat Metab Disord* 2003; 27: 1437-1446.
- Zhou YH, Ma XQ, Wu C, et al. Effect of anti-obesity drug on cardiovascular risk factors: a systematic review and meta-analysis of randomized controlled trials. *PLoS One* 2012; 7: e39062.
- Holes-Lewis KA, Malcolm R, O'Neil PM. Pharmacotherapy of obesity: clinical treatments and considerations. *Am J Med Sci* 2013; 345: 284-288.
- Yurcisin BM, Gaddor MM, DeMaria EJ. Obesity and bariatric surgery. *Clin Chest Med* 2009 30: 539-553.
- Laddu D, Dow C, Hingle M, Thomson C, Going S. A review of evidence -based strategies to treat obesity in adults. *Nutr Clin Pract* 2011; 26: 512-525.
- Kissane NA, Pratt JS. Medical and surgical treatment of obesity. *Best Pract Res Clin Anaesthesiol* 2011; 25: 11-25.
- Sjöström L, Narbro K, Sjöström CD, et al., Effects of bariatric surgery on mortality in Swedish obese subjects. *New Engl J Med* 2007; 357: 741-752.
- Dorman RB, Serrot FJ, Miller CJ, et al. Case-matched outcomes in bariatric surgery for treatment of type 2 diabetes in the morbidly obese patient. *Ann Surg* 2012; 255: 287-293.
- Ikramuddin S, Livingston EH. New insights on bariatric surgery outcomes. *JAMA* 2013; 310: 2401-2402.
- Chang SH, Stoll CR, Song J, Varela JE, Eagon CJ, Colditz GA. The effectiveness and risks of bariatric surgery: an updated systematic review and meta-analysis, 2003-2012. *JAMA Surg* 2013. doi: 10.1001/jamasurg.2013.3654 [Epub ahead of print].
- Hutter MM, Schirmer BD, Jones DB, et al. First report from the American College of Surgeons Bariatric Surgery Center Network: laparoscopic sleeve gastrectomy has morbidity and effectiveness positioned between the band and the bypass. *Ann Surg* 2011; 254: 410-420.
- Courcoulas AP, Christian NJ, Belle SH, et al. Weight change and health outcomes at 3 years after bariatric surgery among individuals with severe obesity. *JAMA* 2013; 310: 2416-2425.
- O'Brien PE, McPhail T, Chaston TB, Dixon JB. Systematic review of medium-term weight loss after bariatric operations. *Obes Surg* 2006; 16: 1032-1040.
- Lanthaler M, Aigner F, Kinzl J, Sieb M, Cakar-Beck F, Nehoda H. Long-term results and complications following adjustable gastric banding. *Obes Surg* 2010; 20: 1078-1085.
- Wölnershanzen BK, Peters T, Kern B, et al. Predictors of outcome in treatment of morbid obesity by laparoscopic adjustable gastric banding: results of a prospective study of 380 patients. *Surg Obes Relat Dis* 2008; 4: 500-506.
- Colles SL, Dixon JB, O'Brien PE. Grazing and loss of control related to eating: two high-risk factors following bariatric surgery. *Obesity* 2008; 16: 615-622.
- Colles SL, Dixon JB. Night eating syndrome: impact on bariatric surgery. *Obes Surg* 2006; 16: 811-820.
- Scibora LM, Ikramuddin S, Buchwald H, Petit MA. Examining the link between bariatric surgery, bone loss, and osteoporosis: a review of bone density studies. *Obes Surg* 2012; 22: 654-667.
- Brzozowska MM, Sainsbury A, Eisman JA, Baldock PA, Center JR. Bariatric surgery, bone loss, obesity and possible mechanisms. *Obes Rev* 2013; 14: 52-67.

## APPENDICES

<b>Appendix 1. Aspects potentially covered by each discipline in the management of obesity</b>	
<b>Discipline</b>	<b>Factors covered</b>
Medical officer	<p>All aspects of medical status:</p> <ul style="list-style-type: none"> <li>• clinical examination including anthropometric measurements and blood pressure</li> <li>• dietary and physical activity assessment including reasons for weight regain and barriers to change</li> <li>• screen for underlying medical causes of obesity e.g. Cushing's syndrome, thyroid diseases, polycystic ovary syndrome (PCOS), medications (antipsychotic, anticonvulsants, glucocorticoids, hypoglycaemic drugs, beta blockers)</li> <li>• screen for obesity-related complications, including metabolic syndrome, diabetes, hypertension as well as benign intracranial hypertension, cardiovascular disease, stroke, nonalcoholic fatty liver disease, liver and gallbladder disease, respiratory disease (asthma is increased), obstructive sleep apnoea, osteoarthritis, pain, depression, gynaecological problems (infertility, PCOS, abnormal menses) incontinence, low testosterone (men), lymphoedema</li> <li>• treat relevant issues</li> </ul> <p>Information obtained by examination, interview and pathology/medical tests</p>
Dietitian	<p>All aspects related to food and lifestyle including:</p> <ul style="list-style-type: none"> <li>• focusing on type, quantity, place and frequency of intake</li> <li>• hunger and satiety sensations</li> <li>• sabotages</li> <li>• reasons for eating and choosing food</li> <li>• cooking techniques and available facilities</li> <li>• eating disorders, dieting attempts</li> <li>• social support and interaction</li> <li>• nutrient deficiency and sufficiency</li> <li>• supplementation use</li> </ul>
Physiotherapist physiotherapist or exercise physiologist	<p>All aspects related to physical movement:</p> <ul style="list-style-type: none"> <li>• physical activity assessment including strength and aerobic fitness</li> <li>• dealing with pain</li> <li>• past history of exercise and injuries</li> <li>• joint and mobility issues</li> <li>• overcoming barriers and sabotages to movement</li> <li>• appropriate exercise prescription</li> <li>• equipment prescription</li> </ul> <p>Information obtained by examination, interview and questionnaires if appropriate</p>
Psychologist	<p>All aspects of a psychological status:</p> <ul style="list-style-type: none"> <li>• motivation</li> <li>• psychological barriers to change</li> <li>• sabotaging behaviour</li> <li>• past history of abuse</li> <li>• body image, self-esteem</li> <li>• schemers, personality traits</li> <li>• depression</li> <li>• eating disorders and disordered eating/thinking</li> <li>• psychiatric illness</li> </ul> <p>This would be obtained by both clinical interview and psychological testing</p>
Any, if not all, team Members	<p>Weight, diet and physical activity history, including any previous use of bariatric surgery, adjunctive therapy and meal replacements. Plus noting associated life events or family history of similar weights and shapes (genetic component)</p> <p>Anthropometric measurements (height, weight, waist and blood pressure)</p>

## Appendix 2. Potential complications of VLED and some possible solutions

- Ketosis\*
- Lethargy, weakness, fatigue\*
- Light headedness, dizziness\* (ensure adequate fluid intake)
- Constipation\* (add fibre supplement to replacements)
- Menstrual irregularity\*(ensure proper contraception is being used as menstrual cycle may return)
- Gastrointestinal upset\*
- Increased uric acid
- Cold intolerance\*
- Dry skin\* (include omega-3 supplementation)
- Electrolyte imbalances
- Dehydration (ensure adequate noncalorie fluid intake)
- Decrease in exercise tolerance (if struggling aim for only light exercise during intensive phase)
- Decrease voluntary physical activity
- Cardiac changes (rare and mostly with older version of the product)
- Nutrient deficiencies
- Postural hypotension (often related to a lack of fluid intake)
- Anaemia (may require addition iron supplementation)
- Hair loss (may indicate inadequate protein intake)
- Muscle cramping
- Nausea
- Diarrhoea (add fibre supplement to replacement)
- Gout (may require prophylactic gout medication)
- Gall bladder disease (particularly if losing >1.5 kg per week)
- Brittle nails (normally only occurs after prolonged use of full program)
- Oedema

\* Common symptoms