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Weight management

By Dr Luke Bereznicki and Professor Gregory Peterson

Learning objectives:

After reading this article, the reader should be able to:

- Discuss the definition, prevalence and health implications of obesity.
- Discuss ways in which pharmacists can assist in the prevention and management of obesity.
- Discuss the advantages and disadvantages of various weight management strategies.

'The devil has put a penalty on all things we enjoy in life. Either we suffer in health or we suffer in soul or we get fat.' Albert Einstein, 1870-1955

Introduction

In Australia, more than one in two adults[1,2] and more than one in four children or adolescents are overweight (Body Mass Index [BMI] ≥ 25 kg/m^2) or obese (BMI ≥ 30 kg/m^2).[3] A recent Australian report, which received considerable media attention, found that seven out of 10 men and six out of every 10 women aged between 45 and 64 years are overweight or obese.[2] This age group has the highest combined rates of overweight and obesity compared to other age groups, the highest risk of type 2 diabetes and cardiovascular disease and, therefore, are most likely to experience preventable obesity-related hospital admissions and premature death within the next 20 years.[2]

Obesity is causally linked to a range of metabolic diseases, and the medical complications of obesity include a decreased life expectancy,[4] a five-fold increased risk of hypertension,[5] a four-fold increase in the risk of coronary heart disease[6] and an increased risk of cancer. It is estimated that approximately 10% of all cancer deaths in non-smokers are related to obesity.[6] Overweight and inactivity account for a quarter to a third of cancers of the breast, colon, endometrium, kidney and oesophagus.[7,8] There is such a close relationship between obesity and the development of type 2 diabetes that the term 'diabesity' was coined in the 1970s.[9] These days, much of the focus is on 'metabolic syndrome' (type 2 diabetes or impaired glucose tolerance, plus hypertension, central obesity and hyperlipidaemia) and its relationship with cardiovascular mortality. A BMI greater than 30 kg/m^2 is associated with increased all-cause mortality and death from cardiovascular disease.[10] Waist circumference is an independent predictor of these outcomes, particularly the risk of metabolic and vascular complications,[11] and should also be measured routinely.[10]

Overweight and inactivity account for a quarter to a third of cancers of the breast, colon, endometrium, kidney and oesophagus.

Obesity may also lead to, increase the risk of, or complicate depression, stroke, intracranial hypertension, cataracts, pulmonary disease, pancreatitis, hepatic and gall bladder disease, back pain, gynaecological abnormalities, osteoarthritis, thrombophlebitis, many skin disorders and gout.[12]

'Corpulence is not only a disease itself, but the harbinger of others.' Hippocrates, 460BC-370BC

Weight loss knowledge is vital for community pharmacists. Coupled with our accessibility and professional credibility, the ability to combat obesity through evidence-based health promotion, education and pharmaceutical services (including the prescribing of effective over-the-counter products) should be seen as a key deliverable from the pharmacy profession to the Australian public.

From the public's point of view, there is a vast array of products available in community pharmacies, many of which are unproven.[13] From an ethical and societal viewpoint, pharmacists should focus on providing the public with advice and products that have proven effectiveness, and promote strategies to prevent obesity. This article will review the evidence for a range of non-surgical strategies to combat overweight and obesity, the majority of which can be provided independently by pharmacists.

'While we have made dramatic progress over the last few decades in achieving so many of our health goals, the statistics on overweight and obesity have steadily headed in

the wrong direction. If this situation is not reversed, it could wipe out the gains we have made in areas such as heart disease, diabetes, several forms of cancer, and other chronic health problems.' US Surgeon General, 2001[14]

Benefits of weight management

Bear in mind that a relatively small, sustained weight loss can result in large reductions in metabolic risk.[15] A reduction of 5% to 10% in body weight may be sufficient to favourably modify waist circumference, blood pressure, fasting blood glucose levels, triglycerides and high-density lipoprotein (HDL) cholesterol.[16] The metabolic and vascular benefits of this degree of weight loss are summarised in Table 1. Weight loss assists in the management of many chronic conditions (e.g. cardiovascular disease, respiratory disease and diabetes), improves fertility in women and reduces the risk of many cancers. While dramatic interventions, such as surgery, have been shown to be beneficial for obese individuals, the most important benefits in proportional terms are achieved with moderate weight loss (i.e. 5% to 10% of body weight).[17]

Weight loss is only one element of weight management. Weight management encompasses weight loss (short term, three to 12 months), weight maintenance (long term, > 12 months) and priority reduction of risk factors.[18] Therefore, successful weight management does not necessarily require weight loss; it could reflect, for example, weight maintenance in a person who has gained weight in the past. Generally, the lifestyle modification strategies to achieve weight loss, maintenance and improved risk factors are identical.[18]

Table 1: Estimated metabolic and vascular benefits of 10% weight loss. Modified from Haslam *et al.*, 2006.[17]

Blood pressure:
• Fall of approximately 10 mmHg in systolic and diastolic blood pressure in hypertensive patients
Diabetes:
• Fall of up to 50% in fasting glucose for newly diagnosed patients
People at risk for diabetes (e.g. impaired glucose tolerance):
• > 30% increase in insulin sensitivity
• 40 to 60% reduction in the incidence of type 2 diabetes
Lipids:
• Fall of 10% in total cholesterol
• Fall of 30% in triglycerides
• Fall of 15% in LDL cholesterol
• Rise of 8% in HDL cholesterol
Mortality:
• > 20% fall in all-cause mortality
• > 30% fall in deaths related to diabetes
LDL = low-density lipoprotein; HDL = high-density lipoprotein

Individuals may respond differently to various components of lifestyle interventions (e.g. low fat or low carbohydrate diets, or physical activity).

Non-surgical strategies to manage obesity

Lifestyle modification

The most important component of any weight loss strategy is energy balance; for weight loss to occur, energy intake must be less than energy expenditure. Either decreasing energy intake or increasing physical activity can achieve a change in energy balance. However, a combination of these strategies is preferable.

Exercise

Increased physical activity alone, in the absence of caloric restriction, is not associated with dramatic weight reduction,[19] although it can reduce visceral fat tissue and improve insulin resistance.[20] When an increase in physical activity is combined with caloric restriction, greater weight loss occurs, together with improved body composition, than with diet or physical activity alone.[20] Resistance training may be particularly beneficial in improving body composition (fat mass versus lean mass). Aerobic exercise combined with dietary change results in greater improvements in HDL cholesterol levels, triglyceride levels and blood pressure than dietary changes alone.[21]

The minimum amount of exercise recommended to complement dietary intervention for weight loss is approximately 150 minutes or 2,500 kcal/week.[22] This equates to 70,000 steps per week for an 80 kg person. While exercise is a necessary component of weight management strategies, it is usually not sufficient alone unless carried out at high levels.[23] Exercise alone is unlikely to be effective for weight loss unless a person engages in approximately 200-300 minutes (3,500 kcal/week) exercise per week. For patients who have been previously inactive, reducing inactivity should be the initial goal, rather than simply 'doing more exercise', which can have negative connotations. This might include less sitting and more standing, walking to work and less television.

Dietary interventions

Reduced calorie diets include very low (less than 800 kcal/day), low (800-1,500 kcal/day) and moderate (approximately 500 kcal/day less than normal daily intake).[10] Without accompanying changes in the level of physical activity, consumption of a reduced calorie diet (approximately 500 kcal/day reduction) is associated with a weight loss of approximately 0.5 kg per week. It is unclear whether a greater degree of initial dietary restriction (e.g. such as that associated with meal replacement strategies) predicts a greater weight loss at two years.[24]

There is currently no consensus regarding the optimal macronutrient composition of diet to produce weight loss.[10]

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Low fat diets (LFDs) produce significant weight loss at 36 months (mean weight loss 3.6 kg) in randomised controlled trials (RCTs).[25] In these trials, blood pressure, lipids and blood glucose all improved; LFDs may also prevent the onset of diabetes and reduce antihypertensive medication for up to three years.[25] Randomised trials show that low carbohydrate diets (e.g. the Atkins diet) result in significantly more weight loss in the first six months than LFDs.[26,27] However, this difference was not significant in the long term (12 months). Compared with LFDs, diets low in carbohydrate result in lower glucose levels in patients with hyperglycaemia, lower fasting triglycerides and higher HDL cholesterol; however, they also increase low-density lipoprotein (LDL) levels.[10] Substituting proteins for carbohydrates during weight loss is currently being emphasised because protein may enhance satiety, protect lean body mass and decrease energy efficiency.[28] However, diets high in protein are also often high in fat. In RCTs, the substitution of protein for carbohydrates in low-fat, calorie-restricted diets resulted in increased weight loss.[29,30]

Commercial diets

Few results of commercial weight management programs are reported. In one trial, the Weight Watchers program (caloric restriction) was compared to self-help (e.g. self-motivated lifestyle change) in overweight and obese participants.[31] Participants in the commercial program had greater reductions in weight and waist circumference than those in the self-help program. Other trials have compared a variety of different strategies, including commercial programs.[32-34] In general, no differences in the degree of weight loss were reported between the diets studied (including diets aimed at caloric restriction, carbohydrate restriction, fat restriction, or a combination of fat, carbohydrate and protein restriction).

Meal replacements

Recent research suggests that meal replacements are safe, economical, effective and can assist in the reduction of co-morbidities.[35] They can be either low (< 1,200 kcals/day) or very low (< 800 kcals/day) in energy. The effect of meal replacements is to reduce portion size and energy intake.[36] For patients with morbid obesity requiring rapid weight loss (BMI > 40kg/m^2), very low calorie diet (VLCD) forms of meal replacement can be used in place of all meals, under medical supervision. A recent case study was published involving a morbidly obese patient, who was treated successfully with a VLCD program for 12 months under close medical supervision.[37] For other overweight and obese patients, partial meal replacements (low calorie) are usually used to replace some, rather than all, meals or are used in combination with pre-prepared meals.

In the past, there have been several concerns regarding the use of meal replacements. These have included concerns regarding the nutritional balances of some commercially available products; potential rebound weight gain on discontinuing use, when this use is unsupervised; and the fact that they may not teach users good long-term eating habits.[35] However, these issues have been largely overcome by improvements in food technology, better training of health professionals about weight management, and the provision of meal replacements as a component of weight loss programs (many of which are delivered by community pharmacies). The use of partial meal replacements commonly results in weight loss of approximately 9% to 10% of total body weight in the short term (six to 12 months) and 6% to 8% in the long term (one to five years), with few reported adverse effects when used as part of an overall weight management plan.[36,38,39] Studies have also shown improvements in metabolic risk factors, particularly for patients with diabetes,[40] exceeding those achieved by dietary change alone.[38]

One of the key advantages of meal replacements is that rapid effects in the short term may result in increased motivation to implement long-term lifestyle change.[41] It is suggested that two meals per day should be replaced initially, followed by one meal per day (preferably a high energy meal) for weight maintenance.[38] Partial meal replacements can be used with minimal supervision,[42] and result in increased patient satisfaction and lower drop-out rates than with other diets (possibly because they result in less hunger).[43] VLCDs (e.g. *Optifast VLCD* and *OptiSlim 2000*) result in a mild ketosis (which may suppress hunger), and contain only enough protein, carbohydrate and fat to preserve lean body mass, maintain normoglycaemia, and stimulate gall bladder contraction, respectively.[44,45] They also contain the recommended daily allowances of minerals, vitamins, trace elements and essential fatty acids. Because of this minimalistic composition, it is recommended that liver function, lipid profile, full blood count, iron, electrolytes, creatinine and uric acid measurements should be assessed when beginning a VLCD and six weeks following commencement.[37] Normally, VLCDs are used for 12 weeks, followed by a transition to partial use (1-2 normal meals replaced per day with VLCD meals) which is sufficient for weight maintenance.[46]

VLCDs may result in transient adverse effects, including cold intolerance, dry skin, hair loss, constipation, headaches, fatigue and dizziness.[37] Other more serious effects include gallstones, increased serum uric acid levels and precipitation of gout, and reduced bone mineral density.[37]

Behavioural modification

Behavioural modification includes a range of counselling activities, including goal setting, self-monitoring, stimulus control (local environmental modification to support weight management), cognitive restructuring (increased awareness of body weight) and prevention of relapse (weight regain).[47] Most studies of behavioural treatment have been conducted in weekly individual or small-group sessions in academic medical centres, and have reported positive results (weight loss of 8-10% at 6 months).[48]

Pharmacological approaches

Complementary medicine

Complementary and alternative medicines are being used increasingly in Australia. From 1996 to 2006, more than 1,000 weight loss products were listed on the Australian Register of Therapeutic Goods. Most contained multiple unevaluated ingredients (herbs, vitamins, minerals), many of which were (or currently are) promoted and sold in community pharmacies and health food shops.[13] Despite their increased use, reviews consistently find that there is no convincing evidence of efficacy for the majority of these products.[49-51]

Ephedrine-containing supplements may promote a short-term weight loss compared to placebo, but their use is associated with psychiatric, gastrointestinal, autonomic and cardiac adverse effects.[52] The beneficial effects of chromium picolinate also appear limited (1.1-1.2 kg weight loss compared to placebo at 6-14 weeks).[53]

Prescribed medicine

The currently available medications that may be prescribed by pharmacists (orlistat) or medical practitioners (orlistat, sibutramine and phentermine) to manage obesity should be considered in patients who have been unsuccessful losing weight through lifestyle changes and who have a BMI > 30 kg/m^2 or BMI > 27 kg/m^2 with co-morbidities. Table 2 shows a comparison of these agents and another weight loss medication, rimonabant, which may become available in Australia in the future.

When combined with lifestyle interventions in RCTs, these medications lead to a reduction in initial weight that is 3% to 5% greater than with placebo.[10] Reductions in risk factors for cardiovascular disease are generally related to the degree of weight reduction.[10] A systematic review of RCTs (eight small RCTs; 885 patients in total) comparing orlistat to sibutramine found that sibutramine was more effective than orlistat at achieving weight loss in head-to-head trials of three to 12 months duration (mean difference 2.2 kg; $P < 0.001$).[54] The

Table 2: Pharmacological agents prescribed for weight loss. Modified from Eckel, 2008.[10]

Drug	TGA-approved for weight loss	Mechanism of action	Dose	Approximate weight loss (beyond that achieved with placebo)	Adverse effects	Clinical issues
Orlistat (*Xenical*)	Yes	Lipase inhibition in gastrointestinal tract	120mg three times a day	3%	Oily spotting, flatus with discharge, faecal urgency	Adverse effects decrease with time; may be more effective when fat remains in diet, but this increases the incidence of adverse effects; decreases LDL cholesterol; may reduce absorption of fat-soluble vitamins, rarely causing deficiency
Phentermine (*Duromine*)	Yes	Sympathomimetic	15, 30 or 40mg daily	4%	Dry mouth, insomnia, dizziness, mild increase in BP (rarely more severe) and heart rate	Insufficient data from RCTs; requires monitoring of BP; limited role in the long-term management of obesity; may be subject to misuse; not indicated for long-term use – use should be limited to 12 weeks
Sibutramine (*Reductil*)	Yes	Inhibition of noradrenaline and serotonin reuptake	10 or 15mg daily	5%	Mild increase in BP and heart rate (rarely more severe), palpitations	Requires monitoring of BP; may result in clinically modest improvement in blood glucose and lipid control
Rimonabant (*Acomplia; not available in Aust*)	No	Inhibition of cannabinoid receptor CB1	5 or 20mg daily	5%	Nausea, diarrhoea, anxiety, depression	Prototype in a new class of medication; monitor for mood disorders

LDL = low-density lipoprotein; RCT = randomised controlled trial; BP = blood pressure

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Table 3: Level of supporting evidence for weight loss strategies. Modified from Egger, 2008.[23]

Strategies with limited or no supporting evidence: • Most complementary and alternative medicines • Alternative non-ingestible treatments (e.g. creams, soaps, body wrapping, aromatherapy, acupuncture)
Strategies with some supporting evidence: • Commercial diet-oriented weight loss programs • Self help
Strategies with good supporting evidence: • Exercise based programs • Counselling and behavioural approaches • Pre-prepared low energy meals • Meal replacements • Prescribed medication (including pharmacist-prescribed orlistat) • Surgery

combination of orlistat and sibutramine has not been well researched, but three small studies have investigated the combination of sibutramine and orlistat.[55,57] In two of these studies, the combination was found to be superior to orlistat alone, but not sibutramine alone.[55,56] The third study focussed on weight maintenance and found that the combination was unlikely to be superior to monotherapy.[57] In summary, sibutramine appears to be more efficacious than orlistat for weight loss, although this finding is based on pooling of studies of small sample size; the combination of orlistat and sibutramine does not appear to be superior to sibutramine alone.

Both orlistat and sibutramine are indicated for long-term use (> 1 year). In studies of one to four years' duration, orlistat reduced weight by 2.9 kg (2.9%) more than placebo (dietary and/or exercise intervention), and increased the absolute proportion of participants achieving 5% and 10% weight loss thresholds by 21% (54% versus 33%) and 12% (26% versus 14%), respectively.[58] Orlistat reduced the incidence of diabetes, and improved total cholesterol and LDL cholesterol, blood pressure and glycaemic control in patients with diabetes, but increased rates of gastrointestinal adverse effects and lowered HDL cholesterol. Sibutramine reduced weight by 4.2 kg (4.3%) more than placebo (dietary and/or exercise intervention), and increased the absolute proportion of participants achieving 5% and 10% weight loss thresholds by 32% (59% versus 27%) and 18% (28% versus 10%), respectively. Sibutramine raised HDL cholesterol and lowered triglycerides, but raised blood pressure and pulse rate.

Rimonabant is a selective antagonist of the cannabinoid receptor CB1. The cannabinoid system contributes to the regulation of food intake, energy balance and body weight.[59] In RCTs, participants taking rimonabant lost approximately 5% more weight than those given placebo; and the possibility has been raised that the drug possesses lipid-lowering effects independent of weight loss.[60] Rimonabant is approved for long-term use in obese patients in most of Europe, but not currently in the US or Australia. There are some concerns surrounding its adverse effect profile, which includes depression and anxiety, as well as nausea and diarrhoea.[10]

Summary and conclusion

A range of evidence-based strategies is available to help patients lose weight. Table 3 shows a summary of some of these approaches to weight management and the quality of the evidence supporting them. Table 4 shows the recommended approaches to the management of obesity using

Table 4: Weight loss treatment guidelines from the US National Heart, Lung and Blood Institute. Modified from Eckel, 2008.[10]

Treatment	BMI				
	25.0-26.9	27.0-29.9	30.0-34.9	35.0-39.9	>40.0
Diet, physical activity, behavioural therapy, or all three	Yes	Yes	Yes	Yes	Yes
Pharmacotherapy†	Not recommended	In patients with obesity-related disease	Yes	Yes	Yes
Surgery‡	Not recommended	Not recommended	Not recommended	In patients with obesity-related disease	Yes

† Pharmacotherapy should be considered only in patients who are not able to achieve adequate weight loss with available conventional lifestyle modifications and who have no absolute contraindications for drug therapy.

‡ Bariatric surgery should be considered only in patients who are unable to lose weight with available conventional therapy and who have no absolute contraindications for surgery.

lifestyle management options, prescribed medication and surgery, according to BMI. It is likely that the best outcomes in weight management will arise as a result of tailoring single or multiple strategies to the needs of the overweight or obese patient.

It is important to remember that weight management involves two phases: weight loss and weight maintenance, which may require a different emphasis.[23] In the initial weight loss phase, meal replacements or a prescribed medication may result in an acceptable weight loss that will help to motivate the patient to continue to implement lifestyle changes to maintain their weight. A combination of strategies, which may include pre-prepared meals, caloric restriction, a graduated exercise program, or prescribed medication could then be used to build on or maintain this initial weight loss. The ability to combat overweight and obesity through health promotion, education and pharmaceutical services (including the prescribing of effective over-the-counter products) should be seen as a key deliverable from the pharmacy profession to the Australian public. With the current focus on managing obesity and obesity-related diseases, it would be of great benefit to the profession if we could demonstrate the effectiveness of pharmacist-delivered weight management services.

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