

## Obesity: A Review of Pathogenesis and Management Strategies in Adult

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### Abstract

*Obesity is a chronic metabolic disease characterized by an increase of body fat stores. It is a gateway to ill health, and has become one of the leading causes of disability and death, affecting not only adults but also children and adolescents worldwide. Obesity is a major risk factor for cancer, cardiovascular, metabolic, and respiratory disorders. This presents an ever increasing social and economic burden to individuals, families and the healthcare system. Preventing obesity is the optimal long-term population strategy. A comprehensive history, physical examination and laboratory assessment relevant to the patient's obesity should be obtained. Appropriate goals of weight management emphasize realistic weight loss to achieve a reduction in health risks and should include promotion of weight loss, maintenance and prevention of weight regain. Management of co-morbidities and improving quality of life of obese patients are also included in treatment aims. Treatment should be based on good clinical care, and evidence-based interventions; should focus on realistic goals and lifelong multidisciplinary management. A comprehensive obesity management can only be accomplished by a multidisciplinary obesity management team. We conclude that physicians have a responsibility to recognize obesity as a disease and help obese patients with appropriate prevention and treatment. This review addresses the current therapeutic options in the treatment of obesity, focusing on pathogenesis, lifestyle changes, medications, and surgery. It also presents a suggested algorithm for the clinician assessing and managing obese patients.*

### Search strategy:

*We searched journal of obesity, clinical guideline for obesity, Pub Med for reviews and original articles related to obesity management. Keywords used included obesity, pathogenesis, multidisciplinary management, and pharmacotherapy.*

**Keywords:** Obesity; pathogenesis; multidisciplinary management.

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### Introduction

Obesity is a metabolic disease that has reached epidemic proportions. The World Health Organization (WHO) has declared obesity as the largest global chronic health problem in adults which is increasingly turning into a more serious problem than malnutrition.<sup>1</sup> In 2014, more than

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1.9 billion adults (18 years and older) were overweight. Of these over 600 million were obese. 42 million children under the age of 5 were overweight or obese in 2013.<sup>2</sup> It has been further projected that 60% of the world's population, i.e. 3.3 billion people, could be overweight (2.2 billion) or obese (1.1 billion) by 2030 if recent trends continue.<sup>3</sup> In 2010, overweight and obesity were estimated to cause 3.4 million deaths, 4% of years of life lost, and 4% of disability-adjusted life years (DALYs).<sup>4</sup> Obesity is a risk factor for several of the leading causes of preventable death, including cardiovascular disease, diabetes mellitus, and many types of cancer. Thus, successful treatment and control of obesity should be major imperatives. However, multiple studies have shown that detection and counseling rates among physicians remain low.<sup>5-8</sup> Thus, a gap exists between the need to provide obesity care and the actual provision of care. In this article, current recommendations for the medical evaluation of the obese adult patient are reviewed, followed by management approaches to using lifestyle therapy, pharmacotherapy, and surgery.

### Definition and classification

In clinical practice, the body fatness is usually estimated by BMI. BMI is calculated as measured body weight (kg) divided by measured height squared (m<sup>2</sup>). Patients with a BMI of 25 kg/m<sup>2</sup> or greater are classified as being overweight. Pre obesity and obesity class I, II and III (extreme obesity) are defined as a BMI of 25 kg/m<sup>2</sup> to 29.9 kg/m<sup>2</sup>, 30 kg/m<sup>2</sup> to 34.9 kg/m<sup>2</sup>, 35 kg/m<sup>2</sup> to 39.9 kg/m<sup>2</sup>, and 40 kg/m<sup>2</sup> or greater, respectively. (Table I)

**Table I: BMI categories<sup>9</sup>**

Category	BMI (kg/m <sup>2</sup> )
Underweight	<18.5
Healthy weight	18.5–24.9
Pre-obese state	25.0–29.9
Obesity grade I	30.0–34.9
Obesity grade II	35.0–39.9
Obesity grade III	≥40

However, obesity-related disease risk is also increased in individuals with normal weight and BMI who have an increased waist circumference (WC): a waist circumference of more than 102 cm (40 inches) in men and more than 88 cm (35 inches) in women.<sup>10</sup> Waist circumference is an indirect measurement of visceral adiposity, which is metabolically active and responsible for the secretion of pro-inflammatory cytokines that are, in part, responsible for the pathogenesis of insulin resistance and the metabolic syndrome. Accumulation of intra-abdominal fat is associated with higher metabolic and cardiovascular disease risk.<sup>11,12</sup> The amount of abdominal fat can be assessed by waist circumference which highly correlates with intra-abdominal fat content. The WC is measured in the horizontal plane midway in the distance of the superior iliac crest and the lower margin of the last rib.<sup>13</sup>

### Pathogenesis and etiology

The etiology of obesity is multifactorial, involving a complex interaction among genetics, hormones and the environment. Though multiple candidate genes have been implicated in the pathogenesis of obesity, these findings are inconsistent.<sup>14,15</sup> These genes include the beta-3-adrenergic receptor gene, peroxisome-proliferator-activated receptor gamma 2 genes, chromosome 10p, melanocortin-4 receptor gene and other genetic polymorphisms.<sup>14</sup>

Multiple hormones are involved in the regulation and pathophysiology of obesity, including gut-related hormones, adipokines and others. Ghrelin is a circulating peptide hormone derived from the stomach. It is the only known peripherally acting orexigenic hormone and is responsible for stimulating appetite.<sup>16</sup> All other gut-derived hormones serve as anorectic agents that are responsible for limiting food intake to achieve optimal digestion and absorption while avoiding the consequences of overfeeding, such as hyperinsulinemia and insulin resistance. These

anorectic gut hormones are Peptide YY (PYY)<sup>17</sup>, Cholecystokinin (CCK)<sup>18</sup>, Glucagon-like peptide -1,<sup>19</sup>, etc.

Several hormones, collectively referred to as adipokines, are produced by the adipocytes. The key secretory products are tumour necrosis factor-alpha (TNF- $\alpha$ ), interleukin-6 (IL-6), leptin and adiponectin. The role of TNF- $\alpha$  in obesity has been linked to insulin resistance through the liberation of free fatty acids, reduction in adiponectin synthesis and impairment of insulin signaling. Leptin acts as a dominant long-term signal responsible for informing the brain of adipose energy reserves. Leptin is transported across the blood-brain barrier and binds to specific receptors on appetite-modulating neurons and the arcuate nucleus in the hypothalamus, inhibiting appetite.<sup>20</sup> Adiponectin is an adipokine derived from plasma protein. It is insulin sensitizing, anti-inflammatory and antiatherogenic and adiponectin levels are restored to normal levels after weight loss.<sup>21,22</sup>

Secondary causes of obesity include drugs, and neuroendocrine diseases (hypothalamic, pituitary, thyroid and adrenal).<sup>22</sup> High energy density diet, increased portion size, low physical activity and adoption of a sedentary lifestyle as well as eating disorders are considered as important risk factors for the development of obesity.<sup>23,24</sup> These behavioral and environmental factors lead to alterations in adipose tissue structure (hypertrophy and hyperplasia of adipocytes, inflammation) and secretion (e.g. adipokines).<sup>25, 26</sup>

### **Clinical evaluation of the obese patient**

A comprehensive history, physical examination and laboratory assessment relevant to the patient's obesity should be obtained.<sup>27-29</sup>

### **Taking an obesity-focused history**

The first step in initiating obesity care is to take a comprehensive history that addresses issues and concerns specific to obesity treatment. This obesity-focused history allows the physician to develop tailored treatment recommendations that

are more consistent with the needs and goals of the individual patient.<sup>30</sup> For many patients, weight gain initially occurs with or is accelerated coincident to smoking cessation, initiation of a medication, or change in life events such as a change in marital status, change in occupation, or illness.<sup>30</sup> At-risk times for women include pregnancy and menopause. Stressful life events often result in a change in eating and physical activity habits. Insight into predisposing genetic factors is obtained by taking a family history.<sup>31</sup>

Similarly, it is important to ascertain whether the patient was overweight as a child or adolescent because early onset of obesity is a predictor of severe obesity in adulthood.<sup>32</sup> A dietary and physical activity history should be assessed in all patients before counseling is initiated. Assessment of psychological health and psychiatric history should be done routinely during the history.<sup>33</sup> Probing for conditions of disordered eating such as binge eating disorder, bulimia, or night-eating syndrome or other psychological conditions that may impair treatment such as attention deficit disorder or post traumatic stress disorder should be part of a comprehensive obesity history.<sup>34</sup>

### **Physical examination of the obese patient**

According to the World Health Organization, assessment of risk status resulting from overweight or obesity is based on the patient's BMI, waist circumference, and existence of comorbid conditions.<sup>9,35</sup>

Presence and impact of obesity-related diseases (diabetes, hypertension, dyslipidaemia, cardiovascular, respiratory and joint diseases; non-alcoholic fatty liver disease (NAFLD), sleep disorders, etc should be assessed.

Presence of acanthosis nigricans as a sign of insulin resistance should be looked for.

### **Laboratory examinations**

The minimum data set required will include fasting blood glucose, serum lipid profile (total, HDL and LDL cholesterol, triglycerides), uric

acid, thyroid function (thyroid-stimulating hormone [TSH] level), liver function (hepatic enzymes), liver investigation (ultrasound, biopsy) if abnormal liver function tests suggest NAFLD or other liver pathology, cardiovascular assessment, if indicated, endocrine evaluation if Cushing’s syndrome or hypothalamic disease suspected and sleep laboratory investigation for sleep apnoea.<sup>27-29</sup>

**Comprehensive obesity management**

Appropriate goals of weight management emphasize realistic weight loss to achieve a reduction in health risks and should include promotion of weight loss, maintenance and prevention of weight regain. Weight loss occurs by generating a negative energy balance, which is achieved by consuming fewer calories than energy expended. A physician should discuss with the patient before deciding the initial level of intervention. (Table II)

**Table II: A guide to deciding the initial level of intervention to discuss with the patient<sup>36</sup>**

BMI, kg/m <sup>2</sup> *	WC, cm*	men ≥ 94, women ≥ 80	Co-morbidities
25.0–29.9	L	L	L ± D
30.0–34.9	L	L ± D	L ± D ± S**
35.0–39.9	L ± D	L ± D	L ± D ± S
≥40.0	L ± D ± S	L ± D ± S	L ± D ± S

L = Lifestyle intervention (diet and physical activity); D = consider drugs; S = consider surgery. \*BMI and waist circumference cut-off points are different for some ethnic groups. \*\*Patients with type 2 diabetes on individual basis.

The evidence and recommendations for nonpharmacological management of obesity, including diet therapy, physical activity and behavioural therapy, as well as pharmacotherapy, and bariatric surgery are discussed in the present review.

**Lifestyle treatment**

The foundation of obesity care is assisting the

patient in making healthier dietary and physical activity choices that will lead to a net negative energy balance. The initial goal is to achieve a 5% to 10% weight loss over the initial 6 months of treatment.<sup>37</sup> A comprehensive review of lifestyle modification for obesity was previously provided by Wadden et al.<sup>38</sup> It is important to remember that personal choices are heavily influenced by exposure to environmental factors, i.e., home and work life, access, affordability, media, and advertising, so all recommendations must have a contextual perspective.<sup>39</sup> Caloric reductions is the most important component in achieving weight loss, whereas increased and sustained physical activity is particularly important in maintaining the lost weight.<sup>40-44</sup>

**Diet therapy**

Weight loss is dependent primarily on reducing total caloric intake, not the proportions of carbohydrate, fat, and protein in the diet.<sup>43</sup> The macronutrient composition (i.e., proportion of calories from carbohydrate, fat, and protein) will ultimately be determined by the patient’s taste preferences, cooking style, and culture. However, the patient’s underlying medical problems are also important in guiding the recommended dietary composition. A consultation with a registered dietitian for medical nutrition therapy is particularly useful,<sup>45</sup> along with the importance of emphasizing collaborative care and self-management of chronic disease.<sup>46</sup> Incorporating meal replacements into the diet is another useful strategy. Meal replacements are foods designed to take the place of a meal or snack while providing nutrients and good taste within a fixed caloric limit.<sup>47,48</sup> Dietary advice should encourage healthy eating and emphasize the need to increase consumption of vegetables, beans, legumes, lentils, grain, unsweetened cereals and fiber, and to substitute low-fat dairy products and meats for high-fat alternatives. It should also emphasize increased intake of seafood. It is recommended to avoid foods containing added sugars and solid fats, as well as consumption of

sugary drinks and alcohol-containing beverages.<sup>49-52</sup>

### General advice

- Decrease energy density of foods and drinks
- Decrease the size of food portions
- Avoid snacking between meals
- Do not skip breakfast and avoid eating in the night time
- Manage and reduce episodes of loss of control or binge eating.

### Physical Activity

Obesity is related to a sedentary lifestyle. Exercise causes lipolysis, resulting in free fatty acid release from triglycerides stored in fat for use as an energy source by muscle, increasing energy expenditure.<sup>53</sup> Although some reports indicate that exercise alone can produce a 2% to 3% reduction in BMI, it is a more effective weight loss tool when used in conjunction with dietary modification. The majority of the literature suggests that physical activity alone is ineffective in achieving initial weight loss or results in only modest weight loss of a few kilograms.<sup>54</sup> However, physical activity can help in long-term weight loss maintenance.<sup>55</sup>

A starting program of 30 min to 45 min of moderate exercise (e.g., brisk walking) at least three days per week is recommended. This amount of physical activity expends approximately 150 kcal/day (500 to 1000 calories per week). For some, this may not be adequate energy expenditure and these individuals may require a loss of 2000 calories or more per week to ensure weight loss maintenance. Any form of physical activity is appropriate as long as it increases heart rate and energy expenditure. Walking is the most common, safe and accessible mode of exercise that is prescribed. The National Weight Control Registry recommends that individuals initially walk 4000 steps per day, with a gradual increase to 12,000 steps per day over a period of six months.<sup>53</sup>

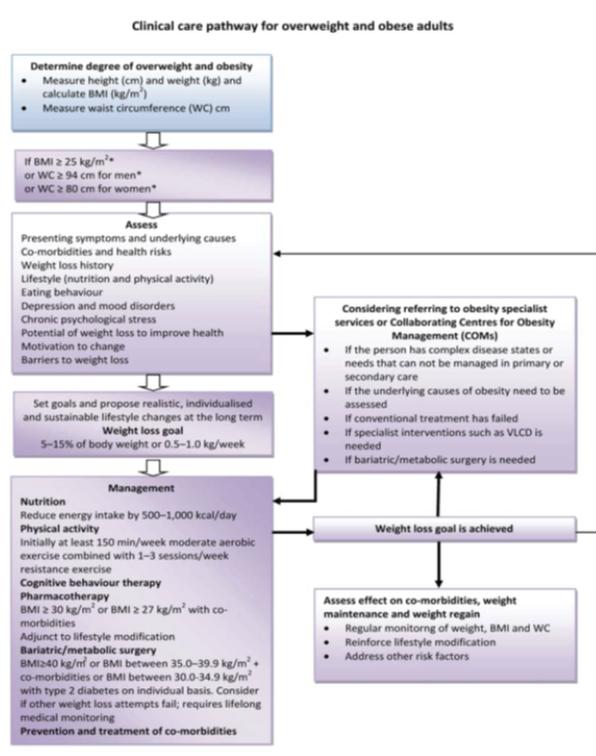
### Behavioral modification

Behavioral strategies are designed to change patients' dietary and exercise habits. They target obstacles that limit adherence to diets. These strategies include self-monitoring of eating habits and physical activity, stress management of situations that lead to overeating, avoiding situations that lead to incidental eating, cognitive restructuring to correct unrealistic goals and misconceptions about weight loss and body image, social support from family and friends, and relapse prevention after episodes of overeating or weight gain. Individuals who receive regular behavioral therapy such as regular contact with treatment providers are more likely to achieve and maintain long-term weight loss.<sup>53</sup>

### Treatment

#### Aims of treatment

The management and treatment of obesity (Fig. 1) have wider objectives than weight loss alone and include risk reduction and health improvement. Significant clinical benefits may be achieved even by modest weight loss (i.e., 5-10% of initial body weight), and lifestyle modification.<sup>56-59</sup> More attention is to be paid to WC and the improvement in body composition which is focusing on ameliorating or maintaining free fat mass (FFM) and decreasing fat mass.<sup>60</sup> Management of co-morbidities, improving quality of life and well-being of obese patients are also included in treatment aims. Obesity management may reduce the need to treat co-morbidities by drugs.<sup>49,61,62</sup> Referral to an obesity specialist (or an obesity management team) should be considered if the patient fails to lose weight in response to the prescribed intervention ( Fig. 1). Weight cycling, defined by repeated loss and regain of body weight, is more frequent in women and may be linked to increased risk for hypertension, dyslipidaemia and gallbladder disease.<sup>63</sup> Obesity is a chronic disease. A follow-up and continued supervision is necessary to prevent weight regain, and to monitor disease risks.<sup>64</sup>



**Fig. 2: Algorithm for the assessment and stepwise management of overweight and obese adults**

\*BMI and WC cut-off points are different for some ethnic groups.<sup>36</sup>

### Pharmacotherapy

Antiobesity drug therapy is indicated for those individuals who cannot achieve weight loss despite an adequate trial of lifestyle modification. Pharmacotherapy should only be prescribed in conjunction with lifestyle modifications, and not as monotherapy for obesity. According to current Food and Drug Administration (FDA) guidance, pharmacotherapy is approved for patients with a BMI  $\geq 30$  kg/m<sup>2</sup> or  $\geq 27$  kg/m<sup>2</sup> when complicated by obesity comorbidity<sup>49</sup> (Table II). Although sound in principle, few agents are currently approved for treatment of obesity. They fall into 2 major categories: appetite suppressants or anorexiant and gastrointestinal fat blockers.<sup>65-67</sup> Regardless of whether new antiobesity agents are available, it is important to avoid or minimize weight-gaining medications when possible.<sup>68</sup> Although there are a wide variety of weight loss agents that have been tested in the treatment of

obesity, currently only sibutramine and orlistat are approved worldwide.<sup>69</sup> Drugs should be used according to their licensed indications and restrictions. The efficacy of pharmacotherapy should be evaluated after the first 3 months. If weight loss achieved is satisfactory (>5% weight loss in non-diabetic and >3% in diabetic patients), treatment should be continued.<sup>49,70-73</sup> Treatment should be discontinued in non-responders.

### Orlistat

Orlistat is a potent, irreversible inhibitor of gastric and pancreatic lipases that reduce systemic absorption of dietary fat by 30%. Randomized clinical trials reveal a 3 kg weight loss or 3% greater reduction in weight than with the ingestion of a placebo. It also reduced low density lipoprotein and cholesterol levels independently of body weight reduction, delayed diabetes, improved glycemic control in diabetic patients and significantly reduced systolic and diastolic blood pressure. Orlistat has been evaluated in weight loss maintenance. At one year, patients treated with 120 mg of orlistat, three times per day had significantly less weight regain than those in the placebo group.<sup>74</sup> Side effects include liquid stools, steatorrhea, fecal urgency, incontinence, flatulence, abdominal cramping and fat-soluble vitamin deficiencies.

### Sibutramine

Sibutramine was initially developed as an anti-depressant and was incidentally found to reduce body weight, decrease appetite and increase satiety. It inhibits norepinephrine and serotonin reuptake without stimulating their release.<sup>69</sup> Three trials lasting at least one year demonstrated a weight loss of 4 kg or 5% more than placebo; 35% more patients achieved at least 5% weight loss and 15% more patients achieved at least 10% weight loss compared to patients ingesting the placebo. Patients who received 10 mg/day or 15 mg/day of sibutramine experienced a greater weight loss than those who received the

placebo with dietary advice over a one-year period, with a weight reduction of 4.4 kg, 6.4 kg and 1.6 kg ( $p \leq 0.01$ ), respectively.<sup>75</sup> Sibutramine has also been shown to be effective at weight loss maintenance.<sup>76</sup> The main side effects of sibutramine are tachycardia and increase in blood pressure, nervousness and insomnia. Some patients may also complain of dry mouth and constipation. The drug is contraindicated in patients using monoamine oxidase inhibitors and selective serotonin reuptake inhibitors.

### **Lorcaserin**

Lorcaserin is a serotonin type 2C receptor agonist with hypophagic effects.<sup>77</sup> Lorcaserin has been available in the USA since June 2013. The recommended dose is 10 mg twice daily. The product license requires 5% weight loss after 12 weeks of treatment. If a patient does not reach this target, the drug should be discontinued.<sup>70-73,78,79</sup> The efficacy and safety of the drug were assessed in the following RCTs: BLOOM<sup>65</sup>, BLOOM-DM<sup>80</sup> and BLOSSOM<sup>81</sup>. In the BLOOM-DM trial, both fasting blood glucose and haemoglobin A1C (HbA1c) levels were improved.<sup>80,82</sup> The most common adverse events associated with lorcaserin included blurred vision, dizziness, somnolence, headache, gastrointestinal disturbance and nausea.

### **Phentermine/Topiramate**

Phentermine and extended-release topiramate is based on the principle of a synergistic combination of two drugs at a lower dose to obtain efficacy with less toxicity. Phentermine is an atypical amphetamine analogue that suppresses appetite by norepinephrine agonism in the CNS. Topiramate is an atypical anticonvulsant drug previously evaluated as a potential anti-obesity drug after reports of weight loss occurring in epileptic patients taking this drug. The mechanisms by which topiramate induces a weight loss are unknown and may include carbonic anhydrase inhibition of taste or influences on GABA

transmission, thus reducing appetite.<sup>83</sup> After approval by the FDA, the drug was launched in the USA in September 2012. The recommended dosage is 7.5 mg phentermine / 46 mg topiramate once a day. The product license requires 5% weight loss after 12 weeks of treatment. If a patient does not reach this target, the drug should be discontinued.<sup>70-73</sup> The efficacy and safety of the drug were assessed in the following RCTs: EQUIP<sup>84</sup>, CONQUER<sup>67</sup>, SEQUEL<sup>85</sup> and EQUATE<sup>86</sup>. Adverse events associated with treatment were dry mouth, constipation, insomnia, palpitations, dizziness, paraesthesia, disturbances in attention, metabolic acidosis and renal calculi, headache, dysgeusia (distortion of sense of taste), alopecia and hypokalaemia.<sup>70-73,87</sup> The combination is contraindicated during pregnancy due to its teratogenic potential. Owing to this risk, the drug has been approved with a risk evaluation and mitigation strategy recommendation by the FDA.<sup>88</sup>

### **Bupropion/Naltrexone**

Bupropion/naltrexone combines two centrally acting medications that had already been approved. Bupropion is used for treating depression and to aid smoking cessation. It is a nonselective inhibitor of the dopamine and norepinephrine transporters. Naltrexone is an opioid receptor antagonist widely used to treat alcohol and opiate dependence syndromes. The anorectic effect of the bupropion/naltrexone combination is believed to result from activation of POMC neurons in the arcuate nucleus. POMC neurons release a melanocyte stimulating hormone ( $\alpha$ -MSH), which is a potent anorectic feeding neuropeptide, and these neurons project to other hypothalamic areas involved in feeding and body weight control. After approval by the FDA and the European Medicinal Agency (EMA), the drug is available in the USA since September 2012 and will be launched in Europe in approximately mid 2016. The recommended dosage is 16 mg naltrexone / 180 mg bupropion twice a day. The product license requires 5% weight loss after 12

weeks of treatment. If a patient does not reach this target, the drug should be discontinued.<sup>70-73,89</sup> The efficacy and safety of the drug were assessed in the following RCTs: COR-I<sup>66</sup>, COR-II<sup>90</sup>, COR-BMOD<sup>91</sup> and COR-DM<sup>92</sup>. Nausea, headache, dizziness, insomnia and vomiting were the most common adverse events that led to discontinuation.<sup>89</sup>

### Liraglutide

Liraglutide is an injectable long-acting GLP-1R agonist designed to resist rapid metabolism by dipeptidyl peptidase-IV. While glucose-induced insulin release is stimulated, the glucagon response is reduced and appetite suppressed with additional effects on gastric emptying.<sup>92</sup> It has already successfully been introduced in type 2 diabetic patients (1.2-1.8 mg) once daily. After approval by the FDA and EMA, the drug (in a dosage of 3 mg once daily) was launched for obesity treatment in the USA in November 2014 and in Europe in March 2015. The product license requires 5% weight loss after 12 weeks of treatment. If a patient does not reach this target, the drug should be discontinued.<sup>70-73,93-97</sup> The efficacy and safety of the drug were assessed in the following RCTs: SCALE-Maintenance<sup>98</sup>, SCALE-Obesity<sup>99</sup> and LEADER<sup>100-102</sup>. Liraglutide is generally well tolerated. Nausea and vomiting are the transient side-effects, but they may actively contribute to weight loss.<sup>103</sup>

### Bariatric and metabolic surgery

According to the 1991 NIH Consensus Development Conference Panel on bariatric surgery,<sup>104</sup> patients with a BMI  $\geq 40$  kg/m<sup>2</sup> or those with a BMI  $\geq 35$  kg/m<sup>2</sup> who have associated high-risk co-morbid conditions such as cardiopulmonary disease or type 2 diabetes mellitus could be considered surgical candidates. Surgical weight loss can be achieved by restrictive, malabsorptive or combination procedures.

Roux-en-Y gastric bypass surgery results in weight loss by gastric restriction, causing early

satiety and malabsorption, as well as reduction in hunger due to a decrease in ghrelin levels and increased PYY. The approximate weight loss at one year is 50%.<sup>105</sup> Complications associated with this surgery include deficiencies in iron, calcium, vitamin B12, fat-soluble vitamins, folic acid and electrolytes.

Vertical banded gastroplasty is a purely restrictive procedure by which the patient is left with a pouch that dilates to only 250 mm in diameter. Vomiting is a common side effect. Weight loss with compliance is 60%.<sup>106</sup> Drawbacks of the procedure are that high calorie beverage ingestion can eventually lead to weight gain. Furthermore, the pouch can expand with overeating.

Laparoscopic adjustable gastric banding, another purely restrictive procedure, involves placing a small silicone band around the fundus of the stomach. It is a short day-surgery and can be adjusted after placement. Weight loss seen after this procedure is also approximately 60%.<sup>106</sup> Contraindications include an extremely high operative risk, active substance abuse, or a major unstable or uncontrolled psychopathological condition such as major depressive disorder, schizophrenia, or bulimia. All patients who are considering weight loss surgery should undergo a comprehensive assessment by a multidisciplinary team of healthcare providers that includes a physician, registered dietitian, and mental health professional.<sup>107</sup>

### Treatment of co-morbidities

Active treatment of obesity-related co-morbidities should be integral part of the comprehensive management of the obese patients. Appropriate management of obesity complications in addition to weight management should include:<sup>49,108</sup>

- Management of dyslipidaemia
- Optimising glycaemic control in type 2 diabetics
- Normalising blood pressure in hypertension
- Management of pulmonary disorders
- Attention to pain control and mobility needs in osteoarthritis

– Management of psychosocial disturbances, including affective disorders, eating disorders, low self-esteem and body image disturbance.

The presence of obesity and the effects that treatments have on body weight, body composition or metabolic status should be taken into account in the selection of the drugs used to treat obesity-related co-morbidities or even non-obesity-related diseases occurring in a patient with obesity.<sup>72</sup>

### Conclusions

Obesity is a serious and highly prevalent disease associated with increased morbidity and mortality. A thorough medical assessment is required to identify patients who are obese or at risk for obesity or obesity-related complications. Treatment should be based on good clinical care and evidence-based interventions and it should be individualized and multidisciplinary, focus on realistic goals, weight maintenance and prevention of weight regain. All patients should be provided lifestyle therapy with consideration for pharmacotherapy and bariatric surgery when indicated. Physicians have a responsibility to recognize obesity as a gateway to disease and help patients with appropriate prevention and treatment schemes for obesity and its co-morbidities.

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