

Obesity: When weight becomes unbearable

Diana Raffelsbauer

Freelance Medical Writer and Journalist, PharmaWrite Medical Communications Network, Germany

Correspondence to:

Diana Raffelsbauer,
Freelance Medical Writer
and Journalist,
PharmaWrite Medical
Communications
Network, Giebelstadt,
Germany
diana.raffelsbauer@
pharmawrite.de

Abstract

Obesity is associated with many chronic diseases. The dramatic rise in its prevalence worldwide has become a major health concern. This article discusses some of the controversies on its causes, consequences, and standard treatments, with a focus on anti-obesity drugs and bariatric surgery.

Keywords: Obesity, Overweight, Diet, Anti-obesity drug, Bariatric surgery, Gastric bypass

What is obesity?

Obesity is defined by the World Health Organization as a body mass index (BMI) of $\geq 30 \text{ kg/m}^2$, whereas overweight lies in the transition zone between this and the normal weight limit (BMI < 25).¹ The prevalence of obesity has risen dramatically over the last two decades, and this has serious consequences for our healthcare and financial systems. Overweight and obesity are associated with a variety of chronic diseases, including musculoskeletal problems, type 2 diabetes mellitus, cardiovascular diseases, and cancer. Weight reduction lowers not only their incidence but also the severity of symptoms or associated health risks once they become chronic. Therefore, keeping body weight within the normal range ($18.5 < \text{BMI} < 25$) is a good strategy to prevent life-threatening diseases.

Causes

Apart from specific endocrine and neurological disorders, the cause of overweight is simple: more calorie intake than calorie expenditure. This leaves us three options: (1) to eat fewer calories; (2) to expend more calories through physical activity; or (3) both. If we are becoming obese, then the logics is that: (1) we are eating more or foods and drinks with more calories; (2) we are physically less active; or (3) both. If the problem is clear, then the solution should also be, at least in theory. All we need to do is: (1) to eat less or less caloric foods;

(2) to become physically more active; or (3) both. But if the principle is so simple, why is obesity becoming a global epidemic with huge impacts on our healthcare systems and economies? Don't we know what to do to avoid becoming obese? If we know, why doesn't it work? These questions aren't simple at all, and there are many possible answers: (1) we don't know exactly what we are eating (think about industrialised, energy-dense foods, and drinks); (2) we know what we are eating and eat it anyway; (3) we can't change our sedentary lifestyle, either because we don't have time to, don't want to, or both; (4) we don't care about our body weight, either because we are not aware of the health risks associated with obesity or because we don't care about our health. But obesity is a burden in most aspects of life: a health-related, quality of life-related, social, professional, and economical burden. It also affects psychological dimensions such as self-acceptance, self-esteem, mood, social interactions, and sexuality.

It seems though that overweight is not simply the result of a mathematical equation. There are various genetic, epigenetic, endocrine, neurological, and environmental factors that contribute to its genesis (see article by M. Price in this issue). And there are also many psychological, social, cultural, and economical aspects in gaining, maintaining, or losing weight.

A few social and economic aspects

Centuries ago, obesity was a synonym of wealth, and this perception is still valid in some cultures where undernourishment is present. But worldwide, today's reality shows the opposite: overweight and obesity are highly prevalent across all social classes. They have recently been linked to lower educational status and professional achievement, and consequently lower incomes, a situation that reminds us of Aristotle's 'the chicken or the egg causality dilemma.' A small, but interesting

experimental study published recently showed that obese people are discriminated by human resource professionals in Germany when they apply for a job.² Obese people (and especially women) were more often disqualified from being hired and less often nominated for a supervisory position, while non-ethnic normal-weight individuals were favoured. This study suggests that weight-related stigmatisation is not only a public health problem, but also a social and economical one.

Obesity is the leader of a wealthy market that incessantly demands new products (weight-management programmes, diets, drugs, and surgical approaches), not least fostered by the ideal of beauty. Everyone who takes a brief look at the newspaper stand is astonished at the number of different diet recipes in most women's magazines, which often also provide details on which diets were effective in whom among prominent people. The food industry has long identified the huge market potential of diet products, as anyone can see in every supermarket. Of course, it is important to look at the calorie content of the food we buy. But aren't 'diet' potato chips a kind of legitimisation to consume an unhealthy product or even the consent to eat double the amount with 50% less calories each?

Prevention and conventional treatment

The most successful programmes for long-term weight control involve combinations of diet, physical activity, and behaviour modification. Physical activity is recommended as a component of weight management for prevention of weight gain, for weight loss, and for prevention of weight regain after weight loss. The American College of Sports Medicine published a Position Stand that recommended moderate-intensity physical activity between 150 and 250 minutes/week to prevent weight gain, whereas greater amounts of physical activity of at least 250 minutes/week are necessary for clinically significant weight loss as well as weight maintenance after weight loss.³ In observational studies, individuals who successfully maintained large weight loss during at least a year typically engaged in about 7 hours/week of moderate- to vigorous-intensity exercise. Physical activity seems to be more important than a normal weight to reduce the risk of type 2 diabetes and cardiovascular diseases.

It is beyond the scope of this article to give an overview on the different types of diets, as not only their scientific evidence and efficacy vary, but also their use and popularity according to personal

preferences and vogue. For instance, according to the *Medical News Today*,⁴ the eight most popular diets in 2009 were: the Atkins diet (low-carbohydrate (carb), high-protein, high-fat), the Zone diet (balance of 40% carbohydrates, 30% fats, and 30% proteins in every meal), the Vegetarian diet, the Vegan diet, the Weight Watchers diet (diet based on a points system, exercise, and a support network), the South Beach diet (low-glycaemic index (GI) products, whole grains, specific fruits and vegetables, olive oil, and lean protein sources), the Raw Food diet (foods and drinks which are not processed, are completely plant-based and ideally organic), and the Mediterranean diet (plant foods, fruits, beans, nuts, cereals, seeds, olive oil, cheese and yogurts, moderate amounts of fish and poultry, up to four eggs per week, small amounts of red meat, and low/moderate amounts of wine). Two years later, the British Dietetic Association's⁵ list of the 10 most popular commercial diets was: the Dukan diet (low-carb, high-protein, restricted vegetables and fat), the Atkins diet, the Cambridge diet (meal replacement products), the South Beach diet, the Slimming World diet (low-fat foods and support network), the Slim-Fast diet (meal replacement products), the LighterLife diet (meal replacement products and weekly counselling), the Weight Watchers diet, the Rosemary Conley diet (low-fat, low-GI diet, and regular exercise), and the Jenny Craig diet (one-to-one support, a meal delivery service, and tailored exercise plans).

Most of us with overweight would be happy to get rid of a couple of excess kilograms. Willingness and self-discipline come spontaneously to my mind. It is however difficult to lose weight because it requires a whole change in behavioural patterns to which we are usually resistant. Otherwise, we wouldn't be overweight. It is also extremely frustrating to regain weight as soon as we return to normal eating habits after following a fad diet. To lose weight and maintain weight loss over the long term, it is necessary to modify one's diet and engage in regular physical activity. So maintaining the new weight needs sustainability. Not only this, depending on the extent of overweight, some people may need additional medical treatment, particularly when their physical and/or psychological health is seriously compromised (for instance, when they are unable to engage in physical activity). These are patients who are at increased medical risk because of their weight. They may be considered for a pharmacological therapy or a bariatric surgery. But before this, they should ideally have tried conventional measures to lose weight through dieting and physical activity without success.

Anti-obesity drugs

Anti-obesity drugs act through one of three distinct mechanisms: suppression of appetite, increase of the body's metabolism (i.e. caloric expenditure), or impairment of digestion and absorption of nutrients (e.g. fat). Since amphetamines were banned from diet pills in 1979, a number of anti-obesity drugs have been launched and withdrawn from the market due to safety concerns. These include aminorex (withdrawn in 1972 due to pulmonary hypertension), fenfluramine, and dexfenfluramine (withdrawn in 1997 due to case reports of heart valve disease and pulmonary hypertension), rimonabant (withdrawn in 2008 due to increased risks of depression and suicidal ideation), and sibutramine (withdrawn in 2010 due to increased risk of heart attacks and strokes).

Weight-loss medications currently approved by the Food and Drug Administration (FDA) for short-term use (≤ 12 weeks) include the appetite suppressants phentermine, diethylpropion, phendimetrazine, and the newcomer lorcaserin. People taking these drugs usually lose 5 kg more than they would normally lose without medication, with the maximum effect seen within the first 6 months. Currently, the only anti-obesity medicine approved by the FDA for long-term use (< 1 year) is the lipase inhibitor orlistat (Xenical®).⁶ It was approved by the FDA in 1999 and is available over the counter in the USA since 2007. Drugs used off-label to combat overweight include some anti-depressants (e.g. bupropion), the anti-convulsants topiramate and zonisamide, and anti-diabetic medicines metformin, exenatide, and pramlintide. These substances are currently being studied in more detail regarding their benefit against obesity.

As seen by the number of drugs withdrawn from the market, anti-obesity medicines may cause serious and life-threatening side effects, and these side effects are often inherent to their mechanism of action. Therefore, caution is recommended for prescription and use of any anti-obesity drug. For instance, it is obvious that stimulants increase heart rate and blood pressure, and cause restlessness and insomnia. One of the main issues with anti-obesity drugs is the fact that we do not fully understand the neurological basis of appetite and how to modulate it, as there are so many hormones and neurotransmitters involved in eating, generating, and processing satiety signals. Likewise, there are many parameters controlling storage, bioavailability, and expenditure of energy to keep an adequate balance between anabolism and catabolism. Anti-obesity drugs are not a practical long-term solution

for people who are chronically overweight or obese. In general, they are approved only for people with a BMI ≥ 30 , or a BMI ≥ 27 with an obesity-related condition, such as hypertension, type 2 diabetes, or dyslipidaemia.⁶

What is bariatric surgery?

A different option for extremely obese people is bariatric (weight loss) surgery. Weight loss is achieved by reducing the size of the stomach with an implanted, adjustable medical device (gastric banding), or through removal of a portion of the stomach (sleeve gastrectomy or biliopancreatic diversion with duodenal switch), or by resecting and re-routing the small intestine to a small stomach pouch (gastric bypass surgery).⁷ The gastric bypass is considered the 'gold standard' in the USA (140 000 procedures performed in 2005), and its most common form is the Roux-en-Y gastric bypass.

Bariatric surgery is scientifically proven to be more successful in reducing weight in moderate and severe obesity than conventional treatments.⁸ It allows loss of huge amounts of weight (up to 50 kg) by reducing the size of the stomach as well as the levels of ghrelin (the hormone that causes hunger) it produces.⁹ The smaller stomach constrains the daily amount of food taken and requires a thorough change of dietary patterns after surgery, as overeating causes nausea and vomiting. Also, the resulting reduction in the absorption surface of the small intestine may lead to the need of nutritional supplementation with minerals and vitamins, often for life.¹⁰

Bariatric surgery results in resolution of major obesity-related co-morbidities, including type 2 diabetes, hypertension, dyslipidaemia, metabolic syndrome, non-alcoholic fatty liver disease, nephropathy, left ventricular hypertrophy, and obstructive sleep apnoea in the majority of morbidly obese patients.¹¹ Through these effects, bariatric surgery appears to reduce cardiovascular morbidity and mortality.

The US National Institutes of Health recommend bariatric surgery for obese people with a BMI ≥ 40 , or for people with BMI ≥ 35 , and serious co-morbidities.¹² In line with this, the American Diabetes Association recommends bariatric surgeries only for adults with BMI > 35 and type 2 diabetes, especially if the diabetes or its associated co-morbidities are difficult to control with lifestyle and pharmacological therapy.¹³ In its 2012 Standards of Medical Care in Diabetes, the Association states that 'gastric reduction surgery (either gastric

banding or procedures that involve bypassing, transposing, or resecting sections of the small intestine) can be an effective weight loss treatment for severe obesity, and US national guidelines support its consideration for people with type 2 diabetes who have BMI > 35.' Furthermore, they note that 'bariatric surgery has been shown to lead to near or complete normalization of glycaemia in 55–95% of diabetes patients, depending on the surgical procedure.'

A meta-analysis of studies of bariatric surgery involving 3188 patients with diabetes reported that 78% had remission of diabetes (normalisation of blood glucose levels in the absence of medications), and that the remission rates were sustained in studies with follow-up exceeding 2 years.¹⁴ Weight loss and diabetes remission rates were higher with procedures that bypass portions of the small intestine than with those that only constrict the stomach. This and other studies suggest that intestinal bypass procedures may have glycaemic effects that are independent of their effects on body weight, perhaps involving the incretin axis (hormones that increase insulin release). In a study published in 2010 involving 110 patients with type 2 diabetes and a mean BMI of 47, Roux-en-Y gastric bypass resulted in a mean loss of excess weight of 63% at 1 year and 84% at 2 years.¹⁵ Diabetic medication was discontinued in 68% of the patients and reduced in a further 14%. Two recently published single-centre studies comparing bariatric surgeries with conventional medical therapy in obese diabetic patients reported greater weight loss, better glycaemic control, and reduced use of medicines to treat co-morbid conditions in significantly more patients in the surgical groups,^{16,17} and these effects were independent of pre-operative BMI and post-operative weight loss.¹⁷

Rates of morbidity and mortality directly related to bariatric surgeries have been reduced considerably in recent years.¹³ In a systematic review and meta-analysis published in 2007, total mortality at ≤30 days was 0.28% and total mortality at >30 days to 2 years was 0.35%.¹⁸ Mortality rates were dependent on the type of procedure (open × laparoscopic, restrictive × malabsorptive type), the surgeon's experience, as well as on the pre-operative health status of patients. The most common post-operative complications of bariatric surgery include gastric dumping syndrome (bloating and diarrhoea after eating), anastomotic and staple line leaks, hernia, infections, pulmonary events, and haemorrhage.¹⁹ Morbidity rates are lower after laparoscopic procedures, which is the largest proportion of bariatric operations. Longer-term concerns include

vitamin and mineral deficiencies, hypocalcaemia, osteopaenia, osteoporosis, hyperparathyroidism, development of gallstones, renal diseases, and rarely, Wernicke's encephalopathy and hypoglycaemia resulting from insulin hypersecretion.^{7,19}

In line with the higher incidence of obesity and reflecting improvements in the surgical technique, the number of bariatric surgeries performed worldwide is rising exponentially. Recent scientific evidence suggests that bariatric surgery could be appropriate for those with a BMI = 35–40 with no co-morbidities, or a BMI = 30–35 with significant co-morbidities,^{19–21} further expanding the number of patients who could be considered for the procedure. Bariatric surgery appears to be a clinically effective and cost-effective intervention for moderately to severely obese people compared with non-surgical interventions.^{22,23} However, studies so far available on whether bariatric surgery reduces long-term morbidity and mortality by curing or preventing the onset of chronic diseases are limited and in general difficult to conduct due to several confounders. More efforts are required to monitor the long-term safety and efficacy (particularly in regard to quality of life and overall life expectancy) of bariatric surgery, for instance, by setting up large patients registries and following patients for a longer time.

Conclusions

Diet, physical activity, and behavioural changes remain the first-line treatment for overweight and obesity, but these measures may not be sufficient to promote a clinically significant and sustained weight loss in morbidly obese people. Current anti-obesity drugs also have limited efficacy. If all else fails, bariatric surgery may be considered for people with BMI ≥ 35 at increased health risk. Bariatric surgery results in greater weight loss than conventional treatment, remission of obesity-related diseases such as diabetes and hypertension, and significant improvements in quality of life.^{8,11} However, the pros and cons of each procedure must be carefully weighed up individually in view of short- and long-term benefits and risks.

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The body mass index (BMI) was proposed by Adolphe Quetelet as long ago as 1835. He based it on average measurements from a population of Scottish soldiers.

Author information

Diana Raffelsbauer is a freelance medical writer, journalist, and translator. She has an MSc in Biology and a PhD in Medical Microbiology. She has been a member of EMWA since 2007. In 2011, she founded PharmaWrite Medical Communications Network, a network of freelancers providing services in different areas of medical writing, journalism, and translations in various European languages.