

## Special Article

# Obesity Epidemiology and Management - Up to Date Short Review

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### Abstract

Obesity is currently considered to be the most common metabolic disease, whose contagion has pandemic character. During the last decades, its incidence has dramatically risen both in developed and developing countries, while the prevalence of overweight and obese people has become an upward trend in many European countries including Greece over the last 20 years. During the period between 2010 and 2014 the percentage of obesity has remained constant worldwide and the same applies for Europe and Greece. Identifying effective long term treatment strategies for overweight and obesity is of paramount importance.

**Key words:** Obesity , Epidemiology , Treatment

### Background

Obesity is currently considered to be the most common metabolic disease, whose contagion has pandemic character. During the last decades, its incidence has dramatically risen both in developed and developing countries, while the prevalence of overweight and obese people has become an upward trend in many European countries including Greece over the last 20 years. During the period between 2010 and 2014 the percentage of obesity has remained constant worldwide and the same applies for Europe and Greece. importance. The US Preventive Services Task Force recommends referral of all obese adults to intensive, multi component interventions including behavioral interventions, pharmacological therapies, and surgical weight loss procedures (US Preventive Services Task Force, 2003).

The Endocrine Society also suggests the use of approved weight loss medications for long term weight maintenance, to ameliorate comorbidities, and to enhance adherence to

behavior changes Identifying effective long term treatment strategies for overweight and obesity is of paramount (Apovian et al., 2015)

- According to Organisation for Economic Co-operation and Development (OECD), in 2015 the percentage of self-reported obesity in Greek adults ( > 15 years old ) ranged at 17%, while the percentage of self-reported overweight ranged at 39.2 % (OECD, 2017).
- ‘‘Hydria study’’ shows that 7 out of 10 Greeks are either overweight or obese and that it is more common for men to be overweight and for women to be obese (HYDRIA Project, 2016).
- The highest overweight rate was observed in the age group of 50-64 years, while the corresponding rate of obesity was reported in the age of 65-79 years. (HYDRIA Project, 2016).
- Almost half of the population is at risk of metabolic complications due to their somatometric characteristics. (HYDRIA Project, 2016).

- As far as childhood obesity is concerned, data which have been collected over the last 20 years demonstrate that the rate of children and adolescents with excessive body weight has been increased. Greece occupies one of the highest positions of childhood obesity not only among Europe countries, but also worldwide. (Ng et al., 2014).
- Since 1998, an upward trend in the percentage of children and adolescents with excessive body weight had been reported, which seems to reach a plateau in 2010. Specifically, in 2010 Greece was at the first place of obesity in Europe as far as the age of 13 is concerned. (Blundell et al., 2017).
- Almost 5 thousand children participated in the "GRECO study" which demonstrated the serious problem of childhood obesity in Greece. The results of the study were that 30% of the pupils of the last 2 years of the elementary school are overweight, while the 13% are obese. These evidence illustrate that the 40-45% of children have serious weight problem from a very young age. (Farajian et al., 2011).
- As far as the global classification is concerned, the same study mentions that the rates of overweight and obesity in both children and adolescents have been raised significantly compared to those of 1975 when the percentage was less than 1%, which is equal to 5 million girls and 6 million boys. In 2016, there were 6% more girls with excessive body weight (50 million) and 8% more boys (76 million). Overall, the number of obese young people between 5-19 years in 2016 was 10 times higher than in 1975, starting from 11 million and resulting in 124 million all over the world. (Farajian et al., 2011).
- Childhood and adolescent obesity seems to be notably frequent in low income families. The long-term financial crisis in Greece in combination with the sedentary lifestyle, the excessive use of electronic devices such as mobile phones, P.C., T.V., tablets etc. and the absence of nutritional education in school may lead to continual weight gain due to the consumption of cheap, high-calorie foods. (Farajian et al., 2011).
- Obesity has been correlated to a great range of diseases and metabolic disorders, including diabetes type 2, hypertension, dyslipidemia, musculoskeletal disorders and

malignancies that drastically affect overweight people's quality of life and life expectancy. Annually in Greece, almost 7.000 people die as a result of obesity related disorders. It has been mentioned that a middle-aged person with BMI > 40 kg/m<sup>2</sup> has decreased life expectancy compared to a normal weight person at 10 years. (Ng et al., 2014).

- Given the expense of the medical treatment of both the disease and its complications, the obesity has obviously financial consequences. (Ng et al., 2014).

### **Obesity assessment by healthy and nutritional practice**

The targets of weight assessment include a realistic weight loss, the subsequent maintenance and the prevention of weight gain. All the obese patients should realize that obesity is a chronic disease, thus the weight management is a lifelong procedure.

### **Aim of the therapy**

Obesity assessment should not only focus on weight loss and on a lower BMI. Great emphasis has to be given on both the waist circumference and body composition so that the muscle mass be improved or at least remain constant and the fat mass level be reduced. Some equally important aims of the therapy are the assessment of the related to the obesity diseases, the improvement of obese people's quality of life and their well-being. (US Preventive Services Task Force, 2003) An effective obesity management may decrease the chances of taking medication as a therapy of the accompanying diseases.

### **Attainable targets of weight loss**

Weight loss between 5-15% of body weight within 6 months is realistic and has been proven to be beneficial for the human health. A higher weight loss ( $\geq 20\%$ ) could be considered in the case of severe obesity (BMI  $\geq 35$  kg/m<sup>2</sup>). The keys to a successful weight management are the maintenance of the lost weight and the correction of the unhealthy habits. (US Preventive Services Task Force, 2003)

Even a moderate weight loss, between 5-10% of the body weight, and modification of the lifestyle, which includes healthy diet, calorie restriction and physical exercise, may lead to important clinical benefits. (Level of evidence A) (Yumuk et al., 2015) When there are obesity

related diseases the above mentioned target may be altered (Garvey et al., 2016). Thus, while for an obese patient suffering from dyslipidemia the target of 5-10% is suitable (Garvey et al., 2016), for an obese with metabolic syndrome or prediabetes or with high risk of diabetes type 2, the aim is 10% weight loss. (Yumuk et al., 2015) The target of 5-15% weight loss is appropriate for overweight or obese patients with hypertension or diabetes type 2 (regardless of the duration and the severity of diabetes) and that concerns both new cases and patients with long-term diabetes and medication. (Knowler et al., 2002) For those with excessive body weight or obesity and NAFLD it is recommended a weight loss between 4-10% or 10-40% so that the hepatic inflammation, the hepatocellular damage and cirrhosis get improved. (Garvey et al., 2016, Sampsel & May, 2007)

Patients with BMI between 25-29.9 kg/m<sup>2</sup> without any obesity related disease need to prevent weight gain by following nutritional advice and increase their physical activity. These alterations may be more appropriate for them than weight loss strategies. Undoubtedly, all the targets of weight loss should be realistic and personalised.

### **Diet**

The most important part of the weight loss progress is the restriction of energy intake. (Level of evidence A) This restriction should be based on each individual's dietary patterns taking also into consideration their usual physical exercise, obesity related diseases and previous attempts to assess their weight. (Garvey et al., 2016)

A restriction of 15-30% of the dietary intake is sufficient and appropriate for those who maintain a constant body weight. (Level of evidence A)

However, it is very common for the obese people to underreport their usual energy intake. Energy requirements vary according to many factors such as the age, gender, physical activity and BMI. One practical way to calculate the energy requirements is that a person needs 25 kcal/ kg of body weight daily. This method causes an important deficit of energy as far as men are concerned. Usually, taking into consideration that a diet plan should be personalised, a restriction of 600-750 kcal/day is suggested so that there will be a weight loss of 0.5-1kg within a week. (Level of evidence A) (Yumuk et al., 2015)

Low calorie balanced diets can be considered those which provide  $\geq 1200$  kcal/day. Low calorie diets of less than 1200 kcal/day may lead to micronutrients deficiency. However in clinical practice, an extent restriction of the energy intake may be essential. Low calorie diets provide 800-1200 kcal/day. Very low calorie diets provide less than 800kcal/day and can be applied as one of the parameters of a total intervention program which is under the control of either an obesity expert or a doctor specialized in nutrition and diet. The use of such diets should be addressed only to specific patients for a short period of time. (Yumuk et al., 2015, Tsai & Wadden, 2006)

Balanced diets result in clinically significant weight loss regardless of its composition in macronutrients and in addition, they enhance diet adherence and the feeling of satiety. (Level of evidence A) Every balanced diet should be personalized and based on each individual's personal and cultural characteristics and thus, a long-term success is more possible. While the macronutrient content of a diet has less influence in weight loss compared to the adherence on the diet plan, its modification may improve the metabolic and clinical profile of specific patient groups. An illustration is that low carbohydrates diets improve the lipidemic profile and the glycemic index resulting in restriction of some risk factors for cardiovascular disease. (Knowler et al., 2002) High protein diets have long term results as far as waist circumference and fat mass are concerned, while they cause restriction of the diameter of the fat cells and prevent muscle mass loss. (Level of evidence A) . Mediterranean diet reduces the risk of cardiovascular disease and metabolic syndrome, prevents the onset of some cancers and has anti-inflammatory effect. Moreover, it has a positive influence in renal function, hepatic steatosis and insulin sensitivity. (Level of evidence A) (Jensen et al., 2014).

### **Exercise**

Every scientific guideline recommends a combination of 150min/week moderate aerobic exercise (e.g. fast walking) and 3 sessions of resistance exercise to increase the muscle strength. (Level of evidence A) Exercise results in abdominal fat restriction, increase on the muscle and bone mass, while it prevents the weight loss induced reduction of the BMR. Moreover, it decreases blood pressure and has a positive effect on the lipidemic profile and the insulin resistance. What is also important,

exercise helps the person to both adhere to the diet plan and, thus, it is more likely to maintain a weight loss, and increase the sense of self-esteem and wellbeing by reducing the levels of stress and depression. Further goals should be the restriction of sedentary life (e.g. tv and pc overuse) and the increase of everyday activities (e.g. walking or cycling instead of car, climbing stairs instead of using the elevator). All exercise advice should be personalised according to the patient's abilities and health and not to overcome the safety levels. (Garvey et al., 2016, Geliebter et al., 2015, Poirier & Despres, 2001)

### Pharmaceutical treatment of obesity

Medication should be considered as a parameter of an holistic approach that aims to obesity management, as it enhances the dietetic factor and the physical activity which results in weight loss. (Level of evidence A)

Pharmaceutical treatment may also help the patients to adhere to their health and diet plans and manage their obesity related diseases or even more to reduce the risk of their development particularly as far as diabetes type 2 is concerned.

For many years, the indication of the pharmaceutical use is clear and stable:

- Patients who, despite a health and diet intervention, continue to be obese ( $BMI \geq 30 \text{ kg/m}^2$ ), regardless of any obese related disease or
- Overweight patients ( $BMI \geq 27 \text{ kg/m}^2$ ) with any comorbidity (e.g. diabetes type 2, hypertension, dyslipidemia, obstructive sleep apnea)
- Although these drugs are not compensated by the social Security funds, they should be prescribed according to their indications and limitations that go along with their marketing authorization. (Mechanick et al, 2013).
- The correspondence to the treatment should be monitored by the doctor and if within 3 months from the beginning of the treatment the patient has not achieved clinically important weight loss ( $>5\%$  of the body weight or  $>3\%$  for those with diabetes type 2), the treatment should be interrupted. Continuation of the medication to those who do not show signs of improvement is not recommended for its financial cost and side effects. (Level of evidence A) (Toplak et al., 2015, Pucci & Finer, 2015)

- There are three (3) approved and available medical treatments in Greece:
- Orlistat: it is a powerful inhibitor of pancreatic and intestinal lipase enzymes, which decreases part of absorption ( $\approx 30\%$ ) of dietary fat. There are 2 available types: 120mg which is prescribed and 60mg which is not. Both types are simultaneously consumed with the meal. The effectiveness of the orlistat, as far as weight loss is concerned, is moderate ( $\approx 3\%$  additional weight loss against a placebo). There are some side effects which mainly the gastrointestinal system (e.g. steatorrhea, urge for evacuation), while, less frequently, orlistat may result in mild deficiencies of fat-soluble vitamins. (Ballinger & Peikin, 2002)
- Naltrexone and bupropion combination: naltrexone is an opioid antagonist which is used for alcohol and opioid detoxification, while bupropion constitutes a dopaminergic factor which act as an antidepressant and helps stop smoking. They are administered by tablets that contain 8mg of the first and 90mg of the second drug (full dose: 32/360mg or 4 tablets per day) seems to have a synergistic effect on weight loss by enhancing the feeling of satiety and influence reward mechanisms. COR clinical trials (Greenway et al., 2010) showed that this drug is satisfactorily effective as far as weight loss is concerned: 8.1% in COR-I, 8.2% in COR-II and 5.9% in COR-DM with diabetic (type 2) patients. When this treatment was combined with health and diet intervention in COR-BMOD trial (Wadden et al., 2011), the weight loss was impressive (11.5%). The main side effect of the treatment, which otherwise has sufficient safety level, is the transient and dose-dependent nausea ( $\approx 20\text{-}30\%$  of the patients).
- Liraglutide 3mg: it is administered subcutaneously once and constitutes a GLP-1 receptor agonist that has been successfully used with its maximum dose of 1.8mg in the treatment of type 2 diabetes for several years. It affects hypothalamus and brain stem by influencing the satiety feeling which results in weight loss of diabetic patients. Thus, it was tested in increasing doses to obese patients without diabetes and the outcome was that a dose of 3mg leads to significant weight loss. In 2015, liraglutide was

approved in Europe and since the September of 2017 it has been available in Greece (Pucci et al., 2015). SCALE trials are going to confirm its effectiveness. SCALE OBESITY and PREDIABETES TRIAL (le Roux et al., 2017) showed 9.2% weight loss during the 1<sup>st</sup> year, 7.1% weight loss within the following 3 years and 79% decrease in the risk of diabetes onset. SCALE DIABETES TRIAL (Pi-Sunyer et al., 2015) resulted in 5.9% loss of the body weight. Impressive results were the ones of the SCALE maintenance which referred to people that had already lost 6.0% of their body weight after a 3-month intensive health and diet intervention. The trial showed that after that intervention, liraglutide administration resulted in further 6.2% weight loss (in total more than 12%). It has been found that those patients who end the 3-month treatment period having lost >5% of their body weight have greater results at the end of the first year. The main side effect of the treatment is the dose-dependent nausea ( $\approx$ 30-40% of the patients). Recent scientific data on the effect of treatment with orlistat or lorcaserin or naltrexone-bupropion or phentermine-topiramate, or liraglutide, compared with placebo among overweight or obese adults, showed that each one was associated with achieving at least 5% weight loss at 52 weeks. Phentermine-topiramate and liraglutide were associated with the highest odds of achieving at least 5% weight loss. (Rohan et al., 2016)

### Bariatric surgery

- Bariatric or metabolic surgery includes special surgeries that aim either to food consumption restriction (gastric band, sleeve gastrectomy) or to food malabsorption (gastric bypass, biliopancreatic diversion) or to both of them (mixed type) (Mechanick et al., 2013).
- The malabsorption type of surgeries (gastric bypass, biliopancreatic diversion) is recommended for obese people with diabetes (Mechanick et al., 2013).
- These surgeries that refer to diabetic patients (type 2) with  $BMI > 35 \text{ kg/m}^2$  result in great weight loss and improvement or regression of the diabetes. (Raffaelli et al., 2015)
- Randomized clinical trials that include 1-5 years post-surgery monitoring have shown that diabetes regression fluctuates between 30-63% of the patients. However, there are 35-50% or even more chances for a diabetes reappearance. (Ribaric et al., 2014)
- Regardless of diabetes regression, the majority of the patients who are subjected to a surgery maintain glycemic control from 5 to 15 years. (Yumuk et al., 2015)
- Moreover, bariatric surgeries lead to restriction of obesity related diseases and mortality and have positive effects on microvascular and macrovascular side effects of diabetes type 2. (Raffaelli et al., 2015)
- Conventional methods of body weight loss result in 1-1.5% HbA1c reduction, while bariatric surgeries lead to 2-3.5% reduction. (Yumuk et al., 2015)
- In order for an obese diabetic patient to be subjected to bariatric surgery, he or she must fulfill all the following requirements (Fried et al., 2013):
  - $BMI \geq 40 \text{ kg/m}^2$  regardless of glycemic control or  $BMI > 35 \text{ kg/m}^2$  with insufficient glycemic control (level of evidence A)
  - Obese diabetic patients with  $BMI = 30-35 \text{ kg/m}^2$  and with insufficient glycemic control (injectable or per os treatment) may be subjected to bariatric surgery (Level of evidence B)
  - Willingness to lose body weight after multiple unsuccessful attempts with conventional methods of body weight loss
  - Approval of the surgery risk according to the type and case of the surgery
  - Age 18-60 years old
- Contraindications:
  - Cardiovascular disease (unless it is surgically recovered before the bariatric surgery)
  - Alcoholism
  - Psychiatric disorders
  - Eating disorders (e.g. bulimia nervosa)
  - Established renal disease
  - Lack of motivation and social support
- Bariatric surgeries should take place in specialized centers which deal with a great amount of such cases and include a team of expert therapists who are able to assess diabetes and put through gastrointestinal surgeries. (level of evidence C) (Tsigos et al., 2011)
- Patients who have been subjected to bariatric surgeries should be monitored lifelong from a

doctor and have nutritional support. (Fried et al., 2013)

- The advantage of bariatric surgeries is that they lead to normal or almost normal level of blood sugar within 2 years from the intervention (younger age, shorter duration of diabetes, lower levels of HbA1c, higher levels of insulin, non-administration of insulin result in higher possibility of diabetes regression after the surgery). Bradley et al., (2012)
- As far as drawbacks are concerned, apart from the surgery's high cost, the long-term side effects are the dumping syndrome, vitamin deficiencies and high risk of drug and substances abuse. The percentage of the major side effects rates between 2-6%, while the one of the minor side effects is 15%. Post-bariatric surgery mortality rates at 0.1-0.5% which is almost the same as the one either of the cholecystectomy or hysterectomy. (Ribaric et al., 2014)

### Conclusions

Obesity is a chronic disease and a significant global health challenge. Its associated comorbidities include cardiovascular morbidity and mortality, type 2 diabetes, certain cancers, dyslipidemia, and obstructive sleep apnea. Moreover, obesity reduces health-related quality of life.

Weight loss is recommended for all patients. As with all chronic medical conditions, effective management of obesity must be based on a partnership between a highly motivated patient and a committed team of health professionals. Achieving and maintaining weight loss through lifestyle interventions alone is often difficult, partly because of the multiple obesity-related hormonal, metabolic, and neuronal adaptations that favor weight regain. Few pharmacological options are currently available for the treatment of obesity. Their effectiveness is limited to palliation (ie, production and maintenance of weight loss) rather than cure, with benefits fading when the drugs are stopped.

Because all medications inherently have more risks than diet and exercise do, pharmacologic therapy should be used only in patients in whom the benefit justifies the risk. In patients with morbid obesity associated with comorbidities, bariatric surgery is the only available

therapeutic modality associated with clinically significant and relatively sustained weight loss. Well-performed bariatric surgery, in carefully selected patients and with a good multidisciplinary support team, substantially ameliorates the morbidities associated with severe obesity.

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