Review Article

Health Consequences of Obesity: A Review

Abstract:

Obesity is a worldwide epidemic that is threatening to overwhelm health-care resources by increasing the incidence of diabetes, heart disease, hypertension, and cancer. Obesity is the largest cause of preventable death globally, affecting both adults and children, and is regarded as one of the most important public health issues of the twenty-first century. Obesity has two effects: a rise in the bulk of adipose tissue and an increase in the release of pathogenetic products by larger fat cells. This view of obesity as a disease allows for a simple separation of the negative effects of obesity into those caused by fat bulk and those caused by fat cell metabolic effects. Social difficulties coming from the stigma associated with obesity, sleep apnea caused in part by increased parapharyngeal fat deposits, and osteoarthritis caused by the wear and tear on joints caused by carrying an enlarged quantity of fat fall under the first category. A wide range of policy issues could have an impact on food ecosystems. Fiscal food policies, obligatory nutrition panels on the formulation and reformulation of manufactured foods, food and nutrition labelling implementation, and limiting marketing and advertising prohibitions on unhealthy foods are among these topics. In this review, we overview current evidences on health consequences of obesity.

Introduction:

Overweight and obesity are defined by the World Health Organization (WHO) as abnormal or excessive fat accumulation that poses a health risk. Overweight is

defined as a body mass index (BMI) of 25 kg/m2, whereas obesity is defined as a BMI of 30 kg/m2. Obesity and overweight are well-known worldwide problems, with high incidence in both developed and developing countries. [1] According to the 2017 global nutrition report, 2 billion adults and 41 million children worldwide are overweight or obese. [2] Obesity has increased globally in the last three decades; unexpectedly, it is also increasing in low- and middle-income nations as a result of uncontrolled urbanization and nutrition transition (moving from a traditional to a westernized diet). [3, 4] Overweight prevalence in children under the age of five years has grown somewhat globally. In low- and middle-income countries, the overweight trend was varied. Obesity prevalence in children aged 2–4 years has increased moderately in the meantime. Obesity in children aged 5 to 19 years was uncommon in 1975, but it is now very common in 2016.[5] It is In the last ten years, the prevalence has climbed from 10% to 40% in the majority of European countries, and it has increased more than twofold in England [6].

Obesity is a worldwide epidemic that is threatening to overwhelm health-care resources by increasing the incidence of diabetes, heart disease, hypertension, and cancer. Obesity has two effects: a rise in the bulk of adipose tissue and an increase in the release of pathogenetic products by larger fat cells. This view of obesity as a disease allows for a simple separation of the negative effects of obesity into those caused by fat bulk and those caused by fat cell metabolic effects. Social difficulties coming from the stigma associated with obesity, sleep apnea caused in part by increased parapharyngeal fat deposits, and osteoarthritis caused by the wear and tear on joints caused by carrying an enlarged quantity of fat fall under the first category [1, 3].

The metabolic variables linked to the far-reaching impacts of molecules generated from larger fat cells fall into the second category. Increased release of fatty acids from fat cells, which are then deposited in the liver or muscle, is likely to cause the insulin-resistant condition that is so common in obesity. Diabetes develops when the pancreas' secretory capacity is overwhelmed by the fight against insulin resistance. Because of the close link between increasing fat, particularly visceral fat, and diabetes, this result is particularly alarming for health-care expenses. The production of cytokines from fat cells, notably IL-6, may contribute to the proinflammatory state that characterises obesity. Increased release of prothrombin activator inhibitor-1 from fat cells may contribute to obesity's procoagulant state,

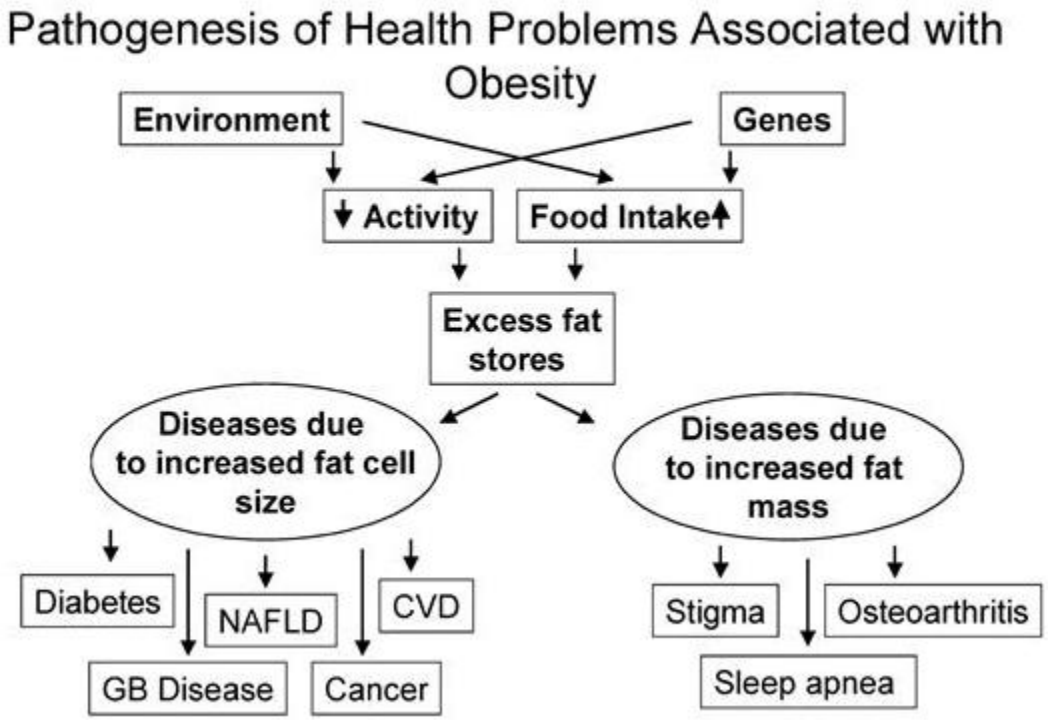
as well as changes in endothelial function, which may contribute to the increased risk of cardiovascular disease and hypertension. The synthesis of estrogens by the larger stromal mass has been linked to an increased risk of breast cancer. Other types of proliferative proliferation may be aided by increased cytokine release. The combined effect of these pathogenetic implications of increasing fat reserves is a higher likelihood of life expectancy being decreased. [7]

Early malnutrition contributes to obesity and metabolic diseases later in life. The link between childhood malnutrition and the development of obesity later in life is unexplained; nevertheless, scientists have proposed an alternative hypothesis. The first is when the socioeconomic level improves, and living standards rise, as well as exposure to obesogenic conditions outside the uterus, resulting in obesity. This could be due to a discrepancy between intrauterine and postnatal nutritional requirements. Second, obesity may result from the positive response of undernutrition in the womb to protect essential organs, as well as exposure to an obesogenic environment. Furthermore, obesity may result from the positive response of undernutrition in the foetus to protect essential organs, as well as exposure to an obesogenic environment. [8] That's why nutritionists often utilise the saying "what you eat today determines your life tomorrow" to illustrate the impact of diet on our health. Dietary habits, not just obesity, are a fundamental driver of our health. That is why the Consumption of energy-dense foods, such as confectionaries, sugars, soft drinks, fats, and alcohol, has been linked to obesity and chronic diseases in studies [10, 14, 15]. Obesity is increased by a variety of factors, including feeding habit culture [16], consuming pastry foods [16], consuming ultraprocessed food (refined carbohydrate) [13], excessive alcohol use [9, 11], and a monotonous diet or poor diet quality [10, 14, 17, 18]. Obesity is reduced when breakfast and fruit are consumed [17], whereas obesity is induced when an evening snack is consumed [19]. Additionally, the grocery shop and school food environments [12] for school-aged children expose them to obesity. Obesity is also associated with a family history of obesity and a variety of genetically arranged genes [12, 16]. More than 250 genes/loci have been linked to obesity, according to genome-wide association studies (GWAS). The fat mass- and obesity-associated gene (FTO) was found to play a key role in the development of obesity and type 2 diabetes among these genes.

Pathogenesis of Obesity:

Obesity is a progressive, chronic, and recurrent medical disorder characterised by a pathological accumulation of adipose tissue in absolute values and percentages in relation to lean mass, to the point that it adversely affects health. It's a true metabolic disorder that wreaks havoc on hunger control and energy metabolism [20]. Therefore, each disease with an increased risk due to obesity can be divided into one of two pathophysiological groups. The first group of disabilities is caused by an increase in fat mass. Obesity stigma and the behavioural responses it causes, osteoarthritis, and sleep apnea are just a few of them. The dangers connected with metabolic alterations caused by excess fat fall under the second category. Diabetes mellitus, gallbladder disease, hypertension, cardiovascular disease, and several cancers linked to obesity are among them (Fig. 1). [21].

FIG. 1.



Obesity's excess adiposity can lead to difficulties due to its anatomical and metabolic impacts.

Subcutaneous adipose tissue acts as a'metabolic sink,' storing extra calories as triglycerides and protecting lean visceral organs including the heart, kidney, liver, and pancreas through adipocyte hyperplasia and hypertrophy. When the capacity of subcutaneous adipose tissue is exceeded, hypertrophied adipocytes rupture, causing inflammation and triglycerides to be deposited in visceral adipose tissue[22]. Obesity is linked to diastolic heart failure, chronic kidney disease (CKD), non-alcoholic fatty liver disease (NAFLD), and type 2 diabetes mellitus (T2DM). [23].

Obesity and atherosclerosis:

Atherosclerosis is a condition in which the arteries' walls harden over time, losing their suppleness, and eventually blocking or narrowing them, obstructing blood flow. Fatty and fiber-like deposits cause the obstruction. The most common cause of cardiovascular disease is atherosclerosis. It can cause coronary artery disease and heart attacks when it affects the heart. Strokes occur when this affects the brain, and peripheral artery disease occurs when it affects the blood vessels. And a high BMI is inextricably linked to the development of atherosclerosis. Atherosclerosis is strongly linked to increased waist circumference, waist hip ratio, and abdominal subcutaneous fat deposition. The link is made with the intimal–medial thickness (IMT) of the carotid artery, which is a marker for atherosclerosis. Furthermore, men may have a stronger link between high body weight and atherosclerosis than women who have not yet reached menopause. [24].

Liver disease:

Obese people are more likely to develop fatty liver disease, also known as nonalcoholic steatohepatitis (NASH). This occurs when the liver becomes clogged with fat. Cirrhosis is a condition in which excess fat damages the liver or causes scar tissue to form, and Fatty liver disease normally has no symptoms, but it can develop to liver failure if left untreated. Losing weight, exercising, and avoiding alcohol consumption are the only ways to reverse or manage the illness. [25].

Pregnancy in Young Women with Obesity:

With the rise in young adults who are overweight or obese at the time of conception, it is critical that they receive sound nutritional advice at a time when they are most likely to accept it in order to improve pregnancy outcomes. In developed countries, there has been a trend toward less stringent monitoring of pregnancy weight gain, while in emerging economies, there has been a trend toward more intensive interventions aimed at improving maternal nutrition and avoiding the negative effects of small for gestational age (SGA) births. For overweight and obese women, current US recommendations indicate total pregnancy weight gains of 7–11.5 kg and 5–9 kg, respectively, for overweight and obese women. [26].

Obese young women experience increased maternal and foetal risks during pregnancy [27, 28]. Hypertension and pre-eclampsia, as well as gestational diabetes (GDM), are among these risks [29]. Miscarriage and stillbirth rates are also higher in pregnant women with gestational obesity [30]. Because young women may present to obstetric care later than older women for a variety of reasons, earlier antenatal care could potentially enhance outcomes.

Obesity and Lung Function/Respiratory Disease:

Through mechanical and metabolic processes, excess weight inhibits respiratory function. The accumulation of abdominal fat, for example, might impede diaphragm descent and, as a result, lung expansion, whereas the accumulation of visceral fat can diminish chest wall flexibility, sap respiratory muscle strength, and narrow airways in the lungs. (31) Lung function may be hampered by cytokines produced by the low-grade inflammatory state that comes with obesity. Obesity has also been linked to asthma and obstructive sleep apnea, two common respiratory diseases. Obesity raised the probability of acquiring asthma in both men and women by 50% in a meta-analysis of seven prospective trials including 333,000 individuals. (32) Obesity is also a major contributor to obstructive sleep apnea (OSA), which affects one out of every five adults; one out of every 15 adults has moderate or severe OSA. Daytime sleepiness, accidents, hypertension, cardiovascular disease, and premature death are all linked to this disorder. Obesity affects between 50 and 75 percent of people with OSA. (31) Small weight loss

appears to be beneficial in the treatment of sleep apnea in clinical trials. (33) and (34).

Obesity and Cancer:

The link between fat and cancer is less evident than the link between diabetes and cardiovascular disease. This is due in part to the fact that cancer is a collection of separate diseases rather than a single disease, however, an expert panel set up by the World Cancer Research Fund and the American Institute for Cancer Research concluded in 2007 that there was convincing evidence of a link between obesity and cancers of the oesophagus, pancreas, colon and rectum, breast, endometrium, and kidney, as well as a possible link between obesity and gallbladder cancer. [36] Obesity in the abdomen and weight gain in adulthood have also been associated to a variety of malignancies. Obesity is linked to malignancies of the breast, colon, and rectum, endometrial, oesophagus, kidney, ovary, and pancreas, according to a later comprehensive review and meta-analysis. [35] Because obesity has been linked to a reduction in immunocompetence in humans, hence immune system changes may play a role in the increased cancer incidence rates in obese people. According to Moulin et al., very obese people have significantly decreased natural killer (NK) cell cytotoxic activity when compared to normal individuals of the same age and gender, as well as inferior defence against invaders such precancerous and cancerous cells [46]. After 6 months of gastric bypass surgery, weight loss (26 percent less than initial weight) is associated with an increase in NK cytotoxic activity [46]. Lynch et al. recently discovered that the frequency of omental invariant NKT (iNKT) cells was reduced in individuals with extreme obesity compared to lean healthy people, implying that the omentum plays a new function in immune modulation and tumour immunity [47]. Therefore, obesity is the cause of 20% of cancer deaths in women and about 14% of cancer deaths in men, according to data published over the last 25 years. These rates are second only to smoking in terms of the number of malignancies that could have been avoided [48]. According to Jaggers et al., there is a positive multivariable-adjusted correlation between cancer mortality and abdominal obesity, which raises cancer mortality risk by up to 24% [49]. Obesity has also been linked to an increase in the incidence and mortality of malignancies of the colon, endometrium, kidneys, and breast (in postmenopausal women) in epidemiological studies [50, 51].

Diseases of the bones, joints, muscles, connective tissue, and skin:

Overweight people are more likely to get osteoarthritis. The trauma associated with the degree of extra body weight may be directly related to the osteoarthritis that develops in the knees and ankles [37]. Increased osteoarthritis in non-weight-bearing joints, on the other hand, implies that some aspects of the overweight syndrome affect cartilage and bone metabolism independently of weight bearing. A major portion of the cost of being overweight is due to increased osteoarthritis, and excess weight is linked to a number of skin abnormalities. Stretch marks, also known as striae, are frequent and are caused by the forces exerted on the skin by increasing lobular fat deposits. Many overweight people develop acanthosis nigricans, which causes deeper pigmentation in the folds of the neck, knuckles, and extensor surfaces, although it is not linked to an increased risk of cancer. Hirsutism in women could be a result of their altered reproductive state [21].

Obesity and hypertension:

Hypertension is a component of the metabolic syndrome that commonly coincides with obesity and is also a risk factor for cardiovascular disease. [38]. Although the exact processes behind the link between obesity and hypertension are unknown, adipose tissue has been shown to produce angiotensinogen, angiotensin converting enzyme (ACE), and angiotensin receptor 1 (AT 1) [39,40]. Obesity also increases renin activity and aldosterone levels [41]. These changes increase plasma volume and cause vascular smooth muscle contractions, both of which can lead to an increase in blood pressure. According to ganglionic nerve studies, heart rate variability studies, and renal norepinephrine spillover studies [42], obesity is related with a sympathovagal system imbalance. Due to the activation of 1-adrenoreceptors in the myocardium, this enhanced sympathetic nervous system activation may also contribute to higher blood pressure in the setting of obesity, resulting in an increased left ventricular (LV) dP/dt (rate of rise of LV pressure). Due to alpha1-adrenoreceptor activation, increased sympathetic tone associated with obesity may cause arterial vasoconstriction, which can raise blood pressure. Finally, obesity is linked to a low-grade inflammatory condition in the body. Interleukin-6 (IL-6) and tumour necrosis factor- (TNF-) are proinflammatory cytokines produced by adipose tissue, and these can control other inflammatory

markers including C-reactive protein (CRP) [43]. This increased inflammation is now being linked to an increase in blood pressure [44]. The 7th report of the Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure recommends weight loss as a first step based on these mechanisms. Weight loss is related with a dose-dependent improvement in hypertension [45]. Thiazide-type diuretics, ACE inhibitors, AT1 receptor blockers, and -adrenergic blockers, all of which are listed as initial therapies for Stage 1 hypertension in the 7th JNC report, are also rational therapies to consider in the obese patient with hypertension based on the mechanisms described above.

Obesity and Type 2 Diabetes Mellitus:

Type 1 diabetes, type 2 diabetes, prenatal diabetes, mature onset diabetes of the young, drug-induced diabetes, diabetes secondary to pancreatic damage, and diabetes secondary to pancreatic damage are all examples of diabetes mellitus (52). Type 2 diabetes mellitus (T2DM) accounts for up to 90% of all diagnosed diabetic cases in adults and is frequently related with obesity of varied degrees. BMI over 25 kg/m2 is present in 50-90 percent of T2DM patients, depending on ethnicity, age, and gender, and patients with BMI over 35 kg/m2 are about 20 times more likely to develop T2DM than those with BMI in the normal range (18.5-24.9 kg/m2 for Caucasians) (52, 53). Indeed, T2DM rates have been rising in both industrialised and developing nations in response to confirmed obesity prevalence trends (54, 55); as a result, the term "diabesity" has been coined to represent this twin epidemic (55-56).

Cardiovascular risk:

Obesity is a well-known independent risk factor for cardiovascular disease (CVD) and one of the leading causes of disorders such dyslipidemia, insulin resistance, high blood pressure (HBP) or hypertension, and atherosclerosis in both adults and children [57] The development of atherosclerosis is influenced by obesity and increasing adipose tissue. White adipose tissue (WAT) and brown adipose tissue (BAT) are two types of adipose tissue that are involved with metabolic and

inflammatory systems and have protective effects on energy homeostasis. WAT secretes peptides and proteins that affect obesity, insulin resistance, inflammatory and immunological activities, atherosclerosis, and cardiovascular disease via modulating biological and physiological circumstances [58] And a diponectin is a peptide generated in adipose tissue that is expressed at high levels by lean, healthy persons but becomes dysregulated in those who are obese [59]. Obesity is characterised by an increase in adipose tissue and a decrease in adiponectin levels, limiting its ability to control inflammatory processes and thereby maintaining the inflammatory state. Adipocyte dysregulations contribute to body homeostasis imbalances and pro- and anti-inflammatory pathways, which contribute to obesity-induced metabolic problems and vascular breakdown, resulting in cardiometabolic changes [59]. Inflammatory cell infiltrate occurs in the adipose tissue, the pancreas, and other tissues in tandem with the development of obesity [60]. In adolescents with metabolic syndrome, this inflammatory state can be diagnosed early [61], and a link between inflammatory biomarkers and cardiovascular events has been demonstrated [62].

Obesity Prevention:

Obesity is a complicated etiology, necessitating a diverse prevention and treatment strategy at both the community and individual level. [63] The social ecology model can be used to identify the human and environmental factors that influence obesity, making intervention development easier. [64] Obesity prevention, both primary and secondary, necessitates participation and collaboration from a variety of sources, including the government, policymakers, legislative powers, and the healthcare system. Figure 2 depicts a selection of interventions that have been applied in several nations, placed on a modified social ecology model. No country has yet successfully devised a population-level approach to reverse obesity's growing trends. [65].

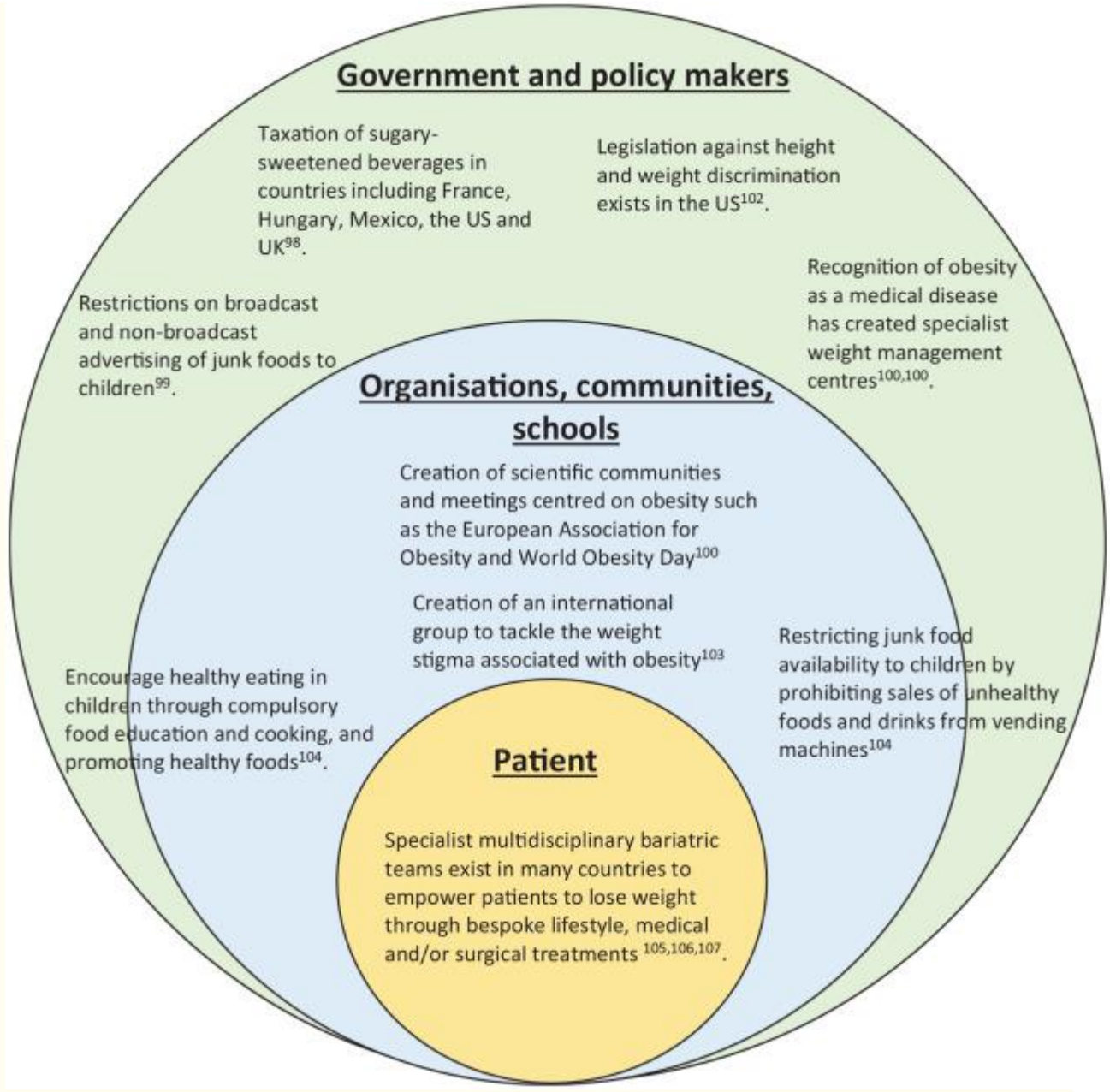


Figure 2 **Government and policy makers**

Obesity prevention policies aim to change the food environment so that healthy choices are easier to make, as well as the physical activity environment to encourage higher levels of physical activity and discourage sedentary behaviour. A wide range of policy issues could have an impact on food ecosystems. Fiscal food policies, obligatory nutrition panels on the formulation and reformulation of manufactured foods, food and nutrition labelling implementation, and limiting

marketing and advertising prohibitions on unhealthy foods are among these topics [66]. Urban planning policies, transportation policies, and organisational policies on the supply of physical activity facilities are all policy areas that influence physical activity surroundings [67] Education about excellent nutrition and a healthy weight should also be included in school curricula to enable all children to understand how to choose the right foods. These educational themes should be reflected in the foods served during the school's breakfast and lunch programs. [68].

Conclusions

The global prevalence of obesity continues to grow at an exponent. That is why obesity should be considered a real disease. Worldwide, the risk of developing diseases such as: arterial hypertension, dyslipidemia, type 2 diabetes, coronary heart disease, cerebral angiopathy, cholelithiasis, arthropathy, spherocytosis, sleep apnea increases, some tumors, increasing morbidity and mortality. Therefore, work on preventing obesity was very important because of its dire consequences.

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