Academy of Romanian Scientists
Annals Series on Biological Sciences

Volume 14, No. 1, 2025, pp. 169-184
Online ISSN 2285 – 4177
ORIGINAL PAPERS

OBESITY – THE NEW PANDEMIC. A CARCINOGENIC RISK FACTOR AFFECTING LONGEVITY AND IMPACTING THE GLOBAL ECONOMY

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Abstract. *A representative public health issue of the 21st century is the obesity pandemic, a medical condition that affects people of all age groups worldwide, with severe impacts on health. This paper is a narrative review about obesity and its consequences, aiming to highlight the magnitude of the effects of excess weight by analyzing numerous representative references from the specialized literature. The main objectives focused on identifying the mechanisms involved in the carcinogenic process and their interference with chemotherapy pharmacokinetics, assessing prognosis and the impact on reduced life expectancy, analyzing economic effects, and the necessity of initiating public health policies. The initiative stemmed from the recognition of the phenomenon embodied by the severity of obesity from the association with multiple chronic diseases to its transformation into a redoubtable factor in the increased incidence of neoplasms (13 types of cancers). This approach supports clinicians in improving disease management while also raising awareness among the population about the dimensions of the obesity pandemic. The collection of data on the economic impact of obesity and its associated costs highlights the urgent need for fiscal measures and policies aimed at mitigating the severity of obesity's effects and improving quality of life.*

Keywords: obesity, cancer, longevity, prevalence, economic impact.

DOI 10.56082/annalsarscibio.2025.1.169

Introduction

According to studies, obesity has reached pandemic proportions, with its prevalence increasing among both adults and children, including adolescents. Obese patients are significantly more susceptible to developing chronic diseases, including neoplastic forms, with impaired quality of life and premature death, reducing life expectancy by up to four years. This paper aims to highlight the

major risks faced by overweight patients, the importance of implementing public health policies designed to introduce measures for health education and regulations within the food industry. The acquisition of data regarding the global economic impact influenced by the scale of obesity, predicts a budget of approximately 4.32 trillion USD allocated to obesity in 2035, with the associated healthcare costs being much more considerable compared to investments in prevention.

Obesity. General considerations and epidemiological data

Obesity, the most common eating disorder, is currently a major public health issue worldwide, and while it was recently considered only a risk factor, it is now recognized as a chronic disease of excess adipose tissue, anthropometrically quantified by a body mass index (BMI) value greater than or equal to 30 kg/m² [1].

Obesity is the result of an energy homeostasis imbalance, specifically the imbalance between energy intake and expenditure, through a positive caloric balance, with excessive energy storage [2].

The etiology of obesity is multifactorial, including genetic, neurohormonal, environmental, and behavioral causes. The epigenetic perspective suggests that obesity cannot be determined exclusively due to genetic causes or environmental factors, but by an association of these, to which lifestyle contributes, reversible changes under the influence of proper conduct.

Increased food intake along with reduced energy consumption, constitutes the main cause of overweight, the comorbidities associated with obesity thus impairing quality of life [3].

Overweight has significant consequences on all organs and systems, impacting incidence, prevalence, and mortality, through endocrine, cardiovascular, respiratory, neurological comorbidities, etc., up to at least 13 different types of cancer [4].

The World Health Organization cites a study published in The Lancet, highlighting that, in 2022, over 1 billion people worldwide live with obesity. Globally, obesity among adults has doubled since 1990 and has increased fourfold among children and adolescents. Data also shows that 43% of adults were overweight in 2022 [5].

According to data provided by the WHO in 2022, 2.5 billion adults (18 years and older) were overweight [5].

Additionally, according to WHO reports, 37 million children under the age of 5 were overweight. Over 390 million children and adolescents aged 5 to 19 were overweight in 2022, including 160 million who were obese [5].

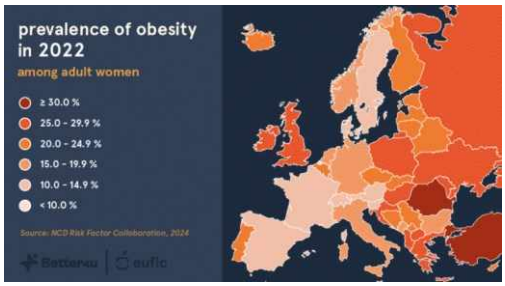

Fig. 1. Prevalence of obesity among women globally
(source: The European Food Information Council) [6].

Thus, the global prevalence of obesity has been labeled as a pandemic, representing an extremely concerning phenomenon worldwide [7, 8, 9]

In Romania, in 2022, 2 out of 100 people were officially registered with a diagnosis of obesity. The analysis of newly reported cases during the same period indicates a higher incidence of obesity among women and the urban population [10].

Childhood obesity in our country represents one of the most redoubtable health issues, with an incidence of excess weight among children marking a value of 165.94%000 inhabitants in 2020, a significant increase to 196.14%000 inhabitants in 2021, and 173.02%000 inhabitants in 2022 [10].

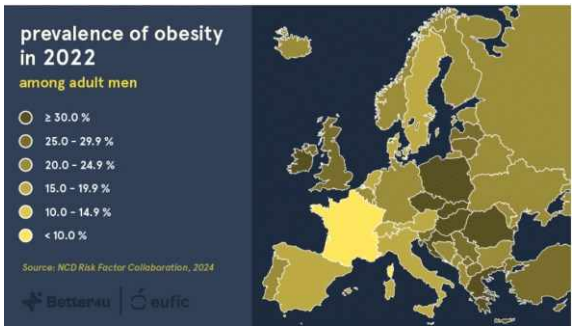

Fig. 2. Prevalence of obesity among men globally
(source: The European Food Information Council) [6]

Obesity is a medical condition that can be prevented and treated, according to the principles of lifestyle medicine, pharmacological options and surgical interventions. Obese patients are more prone to the risks of premature death due to

associated conditions, such as diabetes, coronary heart disease, or cerebrovascular diseases.

In these conditions, the patient requires medical, nutritional, and psychological counseling, aiming at lifestyle changes through the adoption of intervention measures regarding diet optimization (by reducing caloric intake), behavior modification (by encouraging lifestyle improvement), the addition of pharmacological treatment as an adjunct to the diet, and ultimately, if the previously adopted strategies do not yield the expected results, bariatric surgery may be a solution.

Surgical treatment is performed only under certain conditions, such as morbid obesity (BMI > 40 kg/m2) or patients with a BMI > 35 kg/m2 who have multiple comorbidities induced by excess weight, and when conventional strategies have been ineffective. The evaluation of patients who opt for this type of treatment must be thorough (clinical-biological), in order to assess the risks and benefits for the patient, in order to improve both health status and quality of life.

Obesity - risk factor in over 13 types of cancer. Negative impact on pharmacokinetics and unfavorable prognosis

Studies have shown that obesity is a redoubtable factor in the increased incidence of cancers, such as breast, uterine, ovarian, thyroid, colorectal, renal, pancreatic, hepatic, gallbladder, meningioma, multiple myeloma, gastric (cardia), and esophageal (adenocarcinoma).

The pathophysiological mechanisms underlying the connection between obesity and cancer have not yet been fully elucidated. There are several theories supporting the involvement of adipokines, such as leptin, whose elevated levels in obesity contribute to tumorigenic processes [11].

Obesity is associated with elevated lipid profile levels, and the increase in triglyceride values in adipose tissue leads to the expansion of the beta-oxidation process, inducing the overproduction of reactive oxygen species [12].

Thus, the prolonged inflammatory status maintained by adipokines leads to the excessive production of reactive oxygen species, a condition that triggers a proinflammatory response aimed at favoring the predisposition to neoplastic transformation [11].

The influence of oxidative stress, along with metabolic imbalance, leads to neoplastic transformation. Excessive dysfunctional adipose tissue releases cytokines in high amounts, causing changes at the cellular microenvironment level, leading to the progression and survival of cancer cells.

In the context of obesity, the gut microbiome also undergoes changes, favoring dysbiosis under the influence of high-fat and high-sugar diets, with the development of flora rich in pathogenic bacteria. Pathogenic bacteria sustain the inflammatory process, thereby contributing to the support of the carcinogenic microenvironment formation [11].

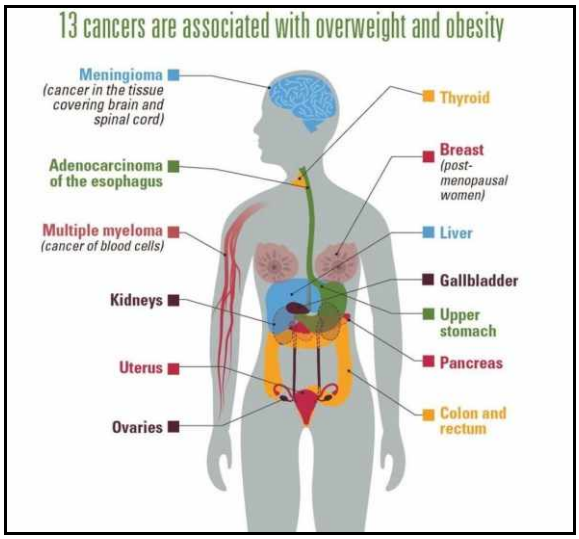

Fig 3. Types of cancers associated with obesity
(source: Centers for Disease Control and Prevention – Cancer) [13].

It should be emphasized that obesity is an unfavorable prognostic factor in cancer patients, as excess weight also affects the effectiveness of therapies, increasing the risk of recurrence and mortality.

Hormones play another decisive role in the development of carcinogenesis alongside obesity, such as in breast, endometrial, and ovarian cancer in postmenopause, through the increased activity of aromatase, involved in the mechanism of converting androgens into estrogen, inducing cellular division and mutations that promote neoplastic progression.

In men, obesity influences testosterone levels, reducing them, which increases the risk of prostate cancer.

Colorectal and hepatic cancers are other neoplasms influenced by obesity, but the influence on long-term prognosis has not yet been sufficiently studied. The mechanism by which obesity contributes to neoplastic development consists in the systemic increase of proinflammatory cytokines, such as tumor necrosis factor α (TNFα) and interleukin-6 (IL-6), influenced by excess adipose tissue, which not only affects insulin action in metabolic tissues but also promotes carcinogenesis development [14].

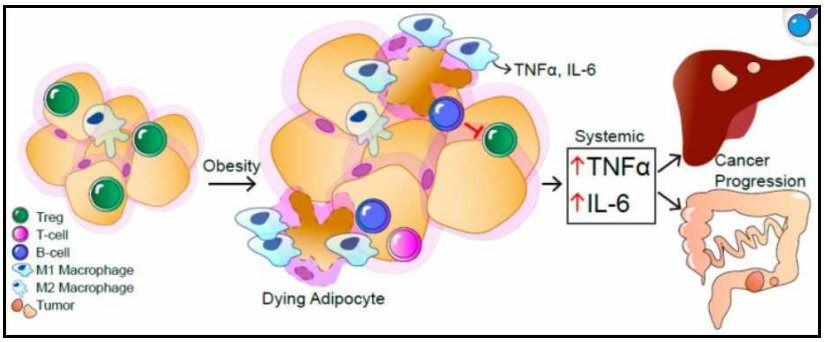

Fig. 4. Effects of excess adipose tissue, such as: induction of mechanical stress with the release of free fatty acids and inflammatory cytokines
(source: National Cancer Institute) [14]

In conclusion, the mechanisms known to date through which excess weight contributes to carcinogenesis, such as chronic inflammation influenced by adipokines, insulin resistance and hormonal imbalances, can be improved through the adoption of a balanced hygienic-dietary regimen, along with a healthy lifestyle and regular physical activity.

The adoption of health policies focusing on the consequences of obesity, the promotion of the principles behind lifestyle medicine that prioritize improving the individual's quality of life, as well as public awareness programs on the necessary strategies for a healthy lifestyle, can reduce the incidence of obesity and associated neoplasms [15].

The impact of obesity on the pharmacokinetics of chemotherapeutic drugs

Currently, it has been found that obesity has reached pandemic proportions worldwide [7,8,9], but obesity is not only a risk factor in carcinogenesis, but also an element that can influence the response to chemotherapy treatment. Studies have suggested that individuals with obesity have a poor prognosis, an increased risk of metastasis and mortality, and also resistance to anti-neoplastic therapies [16].

According to the American Society of Clinical Oncology, the pharmacokinetics of chemotherapy drugs are affected in overweight patients, with 40% of them receiving insufficient doses and exposure to chemotherapy. This aspect leads to a decrease in the effectiveness of chemotherapy, highlighting the need for guidelines regarding adequate and personalized dosing for this category of patients [17].

The way obesity influences oncological treatment involves affecting the absorption, distribution, metabolism, and elimination of drugs. Thus, adipose tissue can sequester certain cytostatic substances, reducing their effective

concentration in the body. Hepatic enzymes responsible for metabolizing chemotherapeutic drugs can be affected, leading either to rapid elimination or to toxic accumulation of the drugs.

Additionally, adipose tissue produces pro-inflammatory cytokines such as IL-6 and TNF-α, which promote the survival of cancer cells and resistance to treatment.

Excessive adipose tissue promotes the stimulation of angiogenesis and the selection of neoplastic cells resistant to chemotherapy, with angiogenesis being essential for tumor development and metastasis formation [18].

An effective solution for addressing the impact of pharmacokinetics involves adjusting chemotherapy doses based on actual body weight rather than ideal body weight, controlling blood sugar levels and insulin resistance, which can help improve treatment response, and, not least, identifying specific metabolic markers alongside adopting a healthy lifestyle.

Thus, excess weight not only affects the risk of developing a neoplasm but also the response to treatment, including chemotherapy. The multidisciplinary approach, which includes oncologists, nutritionists and endocrinologists, is essential for optimizing therapy in patients with obesity and cancer.

The impact of obesity on longevity

Obesity is a risk factor that contributes to a decreased life expectancy by increasing the risk of severe chronic diseases. Excess weight affects almost all systems of the body, accelerating senescence and promoting the appearance of complications that can lead to premature death.

According to studies, obesity is an unfavorable factor regarding longevity, as an increase in body mass index by 5 units is associated with up to a 30% higher risk of overall mortality. In the case of individuals with a BMI between 30 and 35 kg/m2, average survival decreases by up to 2-4 years [19].

The findings of prospective studies conducted on a group of 1.46 million adults (Berrington de Gonzalez et al., 2010) revealed that obese or severely obese women had a much higher risk of death, with similar results being highlighted in the studies of Alune, 2016, and in the studies of Di Angelantonio, 2016 [20].

Flegal, in 2013, highlighted alarming data in a meta-analysis regarding mortality reported for standardized BMI categories. The result highlighted a mortality ratio of 1.18 for overweight individuals compared to those with normal values [20].

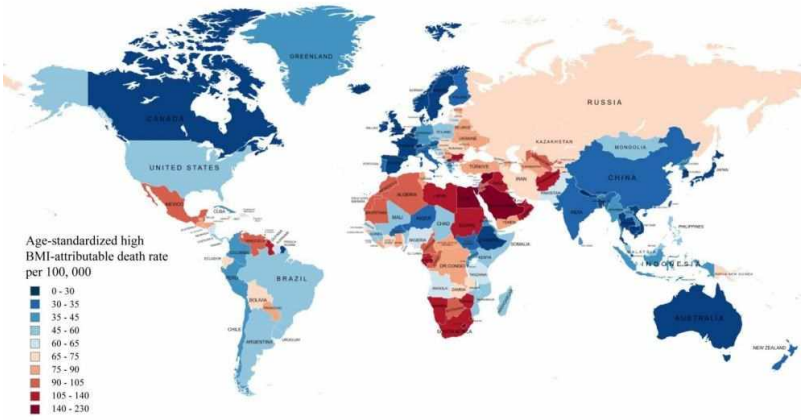

Fig. 5. Distribution of age-standardized death rates, reported per 100,000 inhabitants (source: Global Burden of Disease Study) [20]

According to the reports from the "Global Burden of Disease 2021" based on the most recent and available databases, the trends associated with high body mass index suggest a significant increase in global rates of high BMI values over the past 30 years among individuals over 20 years old [20].

At the same time, there are significant differences between countries regarding mortality rates, the ratios between mortality and increased BMI values, with specific regional variables [20].

In conclusion, obesity is not only a public health issue but also a major economic challenge. The costs associated with treating obesity-related conditions exceed the investments required for preventive strategies. An effective approach that includes well-structured public health policies, economic regulations and nutritional education can contribute to a significant reduction in the financial impact of obesity on healthcare systems.

Psychological considerations regarding the emotional impact of obesity on self-esteem

Excess weight has a significant psychological impact on patients, affecting self-esteem, as these individuals are often exposed to social stigma, discrimination, and prejudice. These situations generate feelings of shame and guilt, with effects on social interactions and professional opportunities, leading to social isolation.

Pertinent to this context, the assessment of self-worth is influenced by the stereotype threat theory, the social identity theory based on body weight, and the Cyclic Obesity/Weight-Based Stigma (COBWEBS) model-concepts that highlight the negative impact of body weight perception on health status [21].

Self-identifying as an overweight person can influence health through the adverse effects of chronic stress and anxiety related to social rejection, which can lead to unhealthy behaviors. In addition to these mechanisms related to social identity and stress, the internalization of weight stigma can play an independent role in explaining the relationship between body self-perception and health risks [21].

Weight stigma has profound consequences on self-perception, impacting both the physical and emotional health of individuals. Studies show that obesity is perceived as highly undesirable, with a significant proportion of the population preferring to experience major difficulties, such as divorce (30%) or infertility (25%), rather than being obese. According to social identity theory, the sense of personal value is influenced by belonging to certain social groups. Inspired by social identity threat theory, this perspective suggests that weight stigma has negative implications for individuals who identify as overweight. Awareness of belonging to a stigmatized group can contribute to adverse effects on physical and mental health, amplifying psychosocial stress and decreasing motivation for healthy behaviors [21].

At the same time, in addition to obesity management and clinical effects, numerous pieces of evidence suggest the impact on mental health, through the negative effects on self-esteem. A series of cross-sectional studies have highlighted that individuals who self-identify as overweight are predisposed to developing anxiety and depression.

It has been proven that the emotional experiences of patients influence both the therapeutic process and its effect, as well as the perspective of improving health [22]. In this sense, psychological counseling, discussions with the family doctor or other health specialists, can contribute to the easier management of obesity and its health effects, improving physical appearance, self-esteem, and quality of life.

The economic impact of obesity at the global level

According to estimates:

- 4.32 trillion USD - will be the global economic impact regarding medical costs generated by obesity in 2035.
- 1.9 billion - will be the number of people worldwide who will live with obesity in 2035.
- 100% increase in childhood obesity between 2020 and 2035.
- 1 in 4 people will have obesity by 2035, compared to the current ratio of 1 in 8 [5].

The global economic impact of overweight and obesity was estimated at 2.4% of GDP in 2020 and is projected to rise to 4.32 trillion USD by 2035 [23].

Given the increase in demographic size and changes in age group configurations, as well as estimates of current trends in obesity prevalence, the global economic costs associated with overweight and obesity are expected to rise significantly. From approximately 2 trillion USD in 2020, these costs are estimated to exceed 3 trillion USD by 2030 and reach over 18 trillion USD by 2060 (all indices are expressed in 2019 prices). This increase in costs will particularly affect middle-income countries as well as high-income countries, with effects in all regions of the world [24].

Fig. 6. Estimated economic costs in the World Health Organization regions, 2019 and 2060, in USD at 2019 prices
(source: World Obesity Federation) [24]

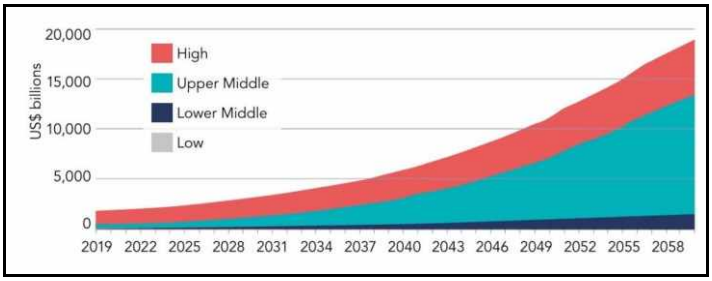

Fig. 7. Estimated economic costs from 2020 to 2060 by the World Bank
(source: World Obesity Federation) [24]

On the other hand, reports on the, invisible" indirect economic costs-resulting from poor health status and deaths due to comorbidities associated with obesity, as well as the subsequent loss of economic productivity-are actually much more significant compared to the, visible" costs, which include both medical and social care costs [24].

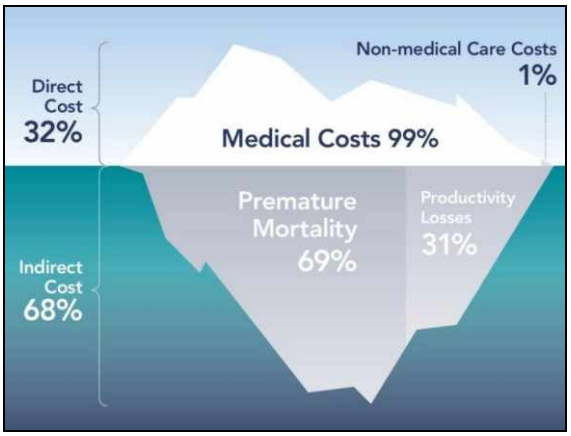

Fig. 8. The ratio of direct and indirect economic costs generated by obesity and comorbidities (values recorded in 2019)
(source: World Obesity Federation) [24]

It should be emphasized that funding for obesity does not reflect the real level of the impact of obesity on global health and economies, which is why it is urgently necessary to adopt sustainable funding programs and public health policies aimed at effectively managing the effects generated by obesity. Thus, multidisciplinary approaches and collective efforts from both public and private medical sectors can ensure the sustainability of medium-and long-term objectives, with positive effects both clinically and economically.

Public health policies and regulations with an impact on the effects of obesity

The changes in the global dimensions of obesity and associated comorbidities require the approach and implementation of a set of policies and regulations aimed at improving the obesity pandemic, with the goal of enhancing the quality of life for populations worldwide.

A concerning phenomenon is the influence of ultraprocessed foods and beverages on excess weight, foods that are high in calories, added sugars, sodium, and unhealthy fats, while being low in fiber, proteins, and micronutrients, with negative effects on human health and the environment. There is a growing global trend for food manufacturers to add micronutrients to ultra-processed products to promote their health benefits, ingredients that regulatory authorities classify as fake foods [25].

Public health sectors are vital for adopting initiatives in the interest of communities, being the most competent institutions in implementing programs based on tools aimed at strengthening measures to improve the quality of life of the population. This process becomes feasible through the adoption of health policies regarding lifestyle, diet, and physical activity, evidence-based concepts

focused on improving the environment, changing consumer behaviors, and modifying the availability of foods and drinks, including through fiscal policies (e.g., taxes on sugary products).

It must be recognized that health policies are an investment, not a cost, incorporating this aspect into the interpretation of economic analyses of policies and cost-effectiveness studies [26].

Thus, it is necessary to develop policies and strategies with secure and long-term effects, such as:

Prevention policies, strategies and health education:

- Nutritional education programs.
- Promotion of a healthy lifestyle.
- Lifestyle medicine courses and skills.
- Awareness campaigns on the health effects of obesity
- The adoption and implementation of evidence-based lifestyle interventions
- Medical and nutritional therapy [27].

Food industry regulation:

- Proper labeling and regulation of food products.
- The obligation for producers to display clear information about sugar, salt, fats, and calorie content on food packaging.
- Development a simplified visual labeling system (Nutri-Score) to help the population make healthier choices.
- Regulating advertisements for foods high in sugar, salt, and saturated fats [28].

A French health care survey, based on 97,848 individual data points, developed a Markov model to analyze the progression from overweight to obesity and the onset of diabetes mellitus, providing forecasts on obesity between 2022 and 2027.

The model indicated that, in the status quo scenario, the global prevalence of obesity and diabetes mellitus will reach significant levels between 2022 and 2027, with estimates ranging from 17.3% to 18.2% for obesity, and values from 7.3% to 8.1% for diabetes. Additionally, the lifetime risk of developing diabetes for 25-year-old men and women is estimated at 33.1% and 30.1%, respectively. This model serves as a valuable tool for assessing the impact of public health policies on the burden of obesity and diabetes mellitus [29].

The results highlighted that a more effective strategy would be to prevent the increase in the percentage of patients with a high BMI, rather than focusing on interventions aimed at reducing BMI in individuals who are already overweight or obese.

On the other hand, the model suggests that the prevalence of severe obesity could serve as a useful surrogate indicator for assessing the success or failure of public health strategies at an early stage [29].

Mathematical models serve as optimal methods for predicting disease progression and determining the extent of necessary parameter adjustments. The Markov model, widely used in medical decision-making, can also be applied to estimate the incidence and lifetime risk of a disease, its trends over time, and its correlation with age and gender - essential indicators for better understanding the magnitude of obesity's effects and developing the most effective public health policies.

For public health policies to be considered effective in stabilizing the prevalence of general obesity, it is necessary for the progression rate from one BMI category to a higher BMI class to be reduced by at least 22% [29].

Global public health objectives focus on preventing excessive weight gain at the population level. The implementation of these strategies helps reduce the number of new cases of overweight, obesity and diabetes. The mathematical model used indicated that measures aimed at reducing progression between BMI categories are more effective than those promoting regression to a lower category [29].

Thus, public policies play a key role in shaping behaviors that contribute to the prevention of obesity. Obesity can be influenced through regulatory strategies and an increasing number of governments recognize that preventing this issue is a collective responsibility requiring coordinated actions and effective population-level strategies [30].

Conclusions

Obesity remains a topic of interest and concern for health specialists due to its scale and associated consequences. Data analysis has revealed alarming obesity rates among children and adults worldwide, with the prevalence of associated cancers on the rise. Studies have shown that excess adipose tissue contributes to sustaining chronic inflammatory status through elevated adipokine levels, a factor implicated in carcinogenesis and chemotherapy resistance.

Data on longevity have shown that women with obesity have a higher risk of mortality, with life expectancy in the general population decreasing by up to four years. Psychological studies have also highlighted how excess weight affects

quality of life, with individuals affected by obesity being subjected to stigmatization, which impacts self-perception and leads to episodes of anxiety and depression; conditions that negatively influence disease progression and treatment response.

Through a multidisciplinary extrapolation, it is important to emphasize that excess weight affects not only individual health but also the sustainability of healthcare systems and the global economy. Obesity contributes to economic losses by reducing workforce productivity, increasing absenteeism and disability, and shortening active life expectancy. Therefore, implementing effective prevention and early intervention policies is a essential investment in public health and long-term economic stability.

Compliance with Ethics Requirements:

"The author declares no conflict of interest regarding this article "

"The author declare that all the procedures and experiments of this review respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study "

"No funding for this study "

Acknowledgements: *None*

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