THE EUROPEAN SOCIETY OF MEDICINE
Medical Research Archives, Volume 13 Issue 12

REVIEW ARTICLE

Towards Better Understanding of the Complex Obesity Cancer Link

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OPEN ACCESS

PUBLISHED
31 December 2025

CITATION
Vucenik, I., 2025. Towards Better Understanding of the Complex Obesity Cancer Link. Medical Research Archives, [online] 13(12). https://doi.org/10.18103/mra.v13i12.7149

DOI
https://doi.org/10.18103/mra.v13i12.7149

ISSN
2375-1924

ABSTRACT

Obesity is presently one of the major health concerns worldwide, associated with multiple metabolic abnormalities and cardiometabolic diseases. Obesity is also playing a significant role in cancer development and pathogenesis, affecting not only health and quality of life of cancer patients, but also mortality. Additionally, it is a social and economic burden in developed and in developing countries. The potential biological mechanisms linking obesity to cancer development, progression and mortality are not well understood and are still a big challenge. Therefore, the aim of this paper is to clarify some underlying pathological mechanisms linking obesity and cancer, including energy imbalance, insulin resistance, and chronic inflammation. The role of inositol, inositol phosphates and inositol compounds against both obesity and cancer are highlighted in this report. Better understanding of the mechanisms involved in the complex obesity-cancer link is needed, not only to prevent both diseases and to propose dietary strategies and interventions for effective weight management, but also for developing potential therapeutics and pharmacological agents targeting weight loss.

Keywords:
Obesity, cancer, mechanisms, inositol compounds, prevention, interventions

Introduction

Because obesity rates have increased worldwide, WHO has declared it a global epidemic. It is predicted that by 2030 the number of people with obesity globally will have doubled since 2010.[1] The World Obesity Federation's expects that 51% of the world, or more than 4 billion people, will be obese or overweight within the next 12 years.[2] Of a big concern is the finding that rates of obesity are rising particularly quickly among children and in lower-income countries.[2] For the USA, it is projected that by 2030, about fifty percent of adults will be obese.[3]

There are multiple consequences of obesity on human health and wellbeing. Metabolic complications include type 2 diabetes, fatty liver disease, hypercholesterolemia, chronic kidney disease and atherosclerotic cardiovascular disease.[4] Associated with obesity are also some musculoskeletal disorders, especially osteoarthritis, some cancers, many psychological effects, psychosocial problems and increased mortality.[4] Additionally, almost in all societies, people with obesity are often subject to stigmatization, and this stigma is manifested in many ways, and is associated with employment discrimination, depression, and health disparities.[4] However, obesity costs, and health-care expenses for obesity-related problems are increasing with a serious global economic impact that will reach $4.32 trillion annually, if the prevention and treatment of obesity do not improve.[2]

Obesity is defined by WHO as an abnormal or excessive accumulation of fat that might impair health. By far the most widely used weight-for-height measure is the body mass index (BMI), which is defined as weight (in kilograms) divided by height (in meters squared); BMI of 18.8-24.0 kg/m^2 indicates healthy weight, 25.0-29.9 overweight, and BMI of 30 kg/m^2 or higher obesity.[5] Herein, an overview of the global obesify and cancer burden is presented, some recent advances and molecular mechanisms are discussed, as well as challenges in our prevention and treatment strategies.

Obesity and Cancer

The worldwide burden of cancer continues to grow. Obesity (body fatness or adiposity) is associated with the risk of developing several types of cancer. Over 500 observational epidemiologic studies have examined some aspects of the association between obesity, physical activity, and cancer incidence.[6] In addition to many preclinical (experimental) and clinical data that have provided a possible cause-effect relationship, it seems that further studies are needed to prove a causality process linking obesity and cancer.[7,8] Many of the global concerns that relates environmental factors and diet, nutrition, obesity, and cancer are addressed by the World Cancer Research Fund (WCRF) and American Institute for Cancer Research (AICR)[9] and their various publications.[10] World Cancer Research Fund and American Institute for Cancer Research conducted a comprehensive and systemic evaluation of the available literature on diet, physical activity, weight, and cancer prevention, considering epidemiologic, clinical, and experimental data. Their Continuous Update Project (CUP) is an ongoing program that analyzes global research on how diet, nutrition and physical activity affect cancer risk and survival and provides a continuous update of 17 different types of cancer: endometrial, ovarian cancer, esophageal, stomach, postmenopausal breast cancer, liver, colorectal, kidney, gallbladder, pancreatic, prostate, bladder, skin, lung, mouth, pharynx and larynx cancer. The main obesity-related cancers are endometrial, ovarian, esophageal, stomach, postmenopausal breast cancer, liver, colorectal, kidney, gallbladder, pancreatic and prostate. The latest CUP, released in April 2025, has a specific focus on breast and colorectal cancer, the two most common cancers influenced by dietary and lifestyle factors. Further, WCRF/AICR has estimated that about 21% of these cancers in the United States can be attributed to obesity, 17% in Great Britain, 13% in Brazil, and 11% in China.[9,10] In addition to WCRF/AICR, this evidence has been evaluated and summarized for the Physical Activity Guidelines for Americans (PAGA) 2018 Report as part of their recommendations on physical activity for cancer risk reduction.[11] Regarding the association of physical activity and cancer, multiple reviews and analyzes have shown strong evidence that physical activity reduces the risk of bladder, breast, colon, endometrial, esophageal adenocarcinoma, and gastric cancers.[6] However, there seems to be moderate evidence linking higher levels of physical activity with lower occurrence of renal, ovarian, pancreatic, and lung cancers.[6]

Potential Mechanisms Linking Obesity and Cancer

The link between obesity and cancer is complex and currently a very active area of research. It seems that adipose tissue and cancer "crosstalk" and communicate through several mechanisms that they share, and that this determines cancer development and progression. Obesity is a perfect "setting", a perfect "storm" for carcinogenesis, enabling all hallmarks of cancer, a set of biological capabilities that cancer cells acquire to survive and spread **(Figure 1)**.[12] Altered adipose tissue and inflammation seem to be the main drivers of these diseases and conditions.[7,13]

The complex physiological changes that occur with obesity include alterations in the adipose tissue production of bioactive factors, growth factors, hormones and reactive oxygen species (ROS) that can impact the development of cancer.[14,15] Underlying the co-morbid disease states that are associated with obesity, including many cancers, is a state of chronic, low-level inflammation.[14,15]

Inflammation has been implicated in every stage of cancer development including transformation, survival, proliferation, invasion, angiogenesis and metastasis.[16] This complex biological response can result in both local and systemic changes. Acute inflammation is a rapid, high-grade response to tissue damage or pathogen invasion, where a cascade of chemokines, cytokines and immune cells infiltrate damaged, necrotic, or infected tissue. These chemokines recruit circulating neutrophils from the microvasculature into the damaged tissue, and these activated neutrophils then release anti-microbial peptides and ROS to kill invading pathogens. At this point, either the wound healing response will continue or assistance from the adaptive immune system (B and T cell-mediated) will be initiated. The wound healing process involves tissue remodeling including cellular hyperplasia and angiogenesis triggered by cytokines and growth factors released into the local environment.[17]

Obesity is the result of a hypertrophic and hyperplastic response of adipocytes within adipose tissue to caloric intake "in excess" of the requirement for metabolic homeostasis. This is usually the result of chronic positive energy balance and/or decreased energy expenditure. However, adipose tissue is very heterogeneous, and the heterogeneity of adipose tissue is influenced by genetics, environment, age, and gender. Adipose tissue is heterogenous even at the cellular level, consisting of two types of fat with morphological and functional diversity. While white adipose tissue (WAT) stores energy reserves as fat, the function of brown adipose tissue (BAT) is lipid oxidation to produce heat.[18] Recently, BAT has been considered as a promising target for obesity treatment strategies.

Obesity is characterized by a state of a chronic, low-grade inflammation and the release of pro-inflammatory cytokines, such as tumor necrosis factor-α (TNF-α) and chemokines, like monocyte chemoattractant protein-1 (MCP-1). Pro-inflammatory M1 macrophages release additional cytokines, interleukin-1 (IL-1) and interleukin-6 (IL-6), and chemokines, such as interleukin-8 (IL-8) and macrophage inflammatory protein-1α (MIP-1α). These secreted pro-inflammatory cytokines contribute to systemic inflammation. Type 2 diabetes, dyslipidemia, hypertension, endothelial dysfunction and hepatic steatosis, leading to cardiovascular disease, renal failure, and several types of cancer are co-morbidities, attributed directly or indirectly to a prolonged, chronic inflammatory state.[13] The prominent link between inflammation and obesity has been further emphasized by finding that the inflammasomes may contribute to the pathology.[19]

Insulin and insulin-like growth factors (IGFs) have been implicated in a wide range of cancers due to their anti-apoptotic and growth-promoting properties.[14,15,19] Obesity is associated with inflammation-dependent increases in insulin resistance resulting in hyperglycemia and compensatory hyperinsulinemia, and eventually type 2 diabetes.[14,15] High levels of insulin promote insulin-like growth factor-1 (IGF-1) production. Caloric restriction, which increases insulin sensitivity and reduces circulating insulin and IGF-1, is a potent suppressor of carcinogenesis.[20] In several preclinical models, the effect of caloric restriction on carcinogenesis is evident by reduction of the PI3K/Akt/mTOR pathway activation *via* AMPK activation and can be abrogated by restoration of IGF-1 levels.[20]

The common effector pathways for many growth factors including insulin, IGF and leptin, are the PI3K/Akt/mTOR and Ras/Raf/MAPK, that regulate tumor survival, growth and proliferation[13]. PI3K/Akt/mTOR inhibition has been an active target to reduce both carcinogenesis and tumor incidence.

Adipose tissue is an endocrine organ that produces many bioactive proteins, called adipokines, which include leptin, adiponectin and numerous others including cytokines and chemokines as well as bioactive lipids and steroid hormones.[13] Leptin acts centrally as an anorexic neuroendocrine hormone, and in the periphery, as a regulator of energy metabolism, reproduction and immune function.[21] Adiponectin is also secreted from adipose tissue and has insulin-sensitizing, anti-inflammatory actions and promotes fatty acid oxidation. In contrast to leptin, adiponectin decreases with increasing adiposity[22], inhibits proliferation of colon, prostate, endometrial and breast cancer cells and is associated with decreased risk of cancers of the uterus, colon and breast in epidemiological studies.[13,22] The association between the adiponectin-to-leptin ratio and metabolic syndrome as well as some types of cancer has been suggested as an additional important parameter.

The role of novel adipokines, such as omentin-1, visfatin and vaspin in obesity and cancer is under investigation.[13] Furthermore, interactions with the tumor microenvironment, activity of NK (Natural Killer) cells, role of the microbiome, role of epigenetics, kynurenine are some emerging mechanisms and new concepts in a complex obesity and cancer link, that need to be also addressed.

The framework of "hallmarks of cancer", a seminal work by Hanahan and Weinberg, was used to delineate how obesity might influence the carcinogenic process in somatic cells, and the effects of obesity on sustaining proliferative signaling, evading growth suppressors, resisting cell death, enabling replicative immortality, inducing angiogenesis, activating invasion and metastasis, reprogramming energy metabolism, on avoiding immune destruction, its effects on genome instability and tumor-promoting inflammation was discussed.[12] This concept is presented in Figure 1A. Clarifying this remarkable and unique "obesity-cancer relationship" is extremely important not only for better management of obesity and cancer, but also for development of novel prevention and treatment strategies.

Prevention and Interventions

Obesity is preventable and it is usually an indicator of an unhealthy lifestyle. Therefore, strategies, such as healthy diet, change in lifestyle, or even pharmacology, that disrupt the obesity-cancer link may be useful for reducing cancer development.

World Cancer Research Fund and American Institute for Cancer Research (WCRF/AICR) developed guidelines and personal recommendations for individuals, as well as goals for the population, made by world experts including those from the International Obesity Task Force, to prevent both obesity and cancer.[9,10] Similar recommendations and guidelines on nutrition and physical activity for cancer prevention were given by the American Cancer Society (ACS)[23], by the Physical Activity Advisory Committee[11] and by the European Society for the Study of Obesity (EASO).[7]

By interacting with inflammatory and growth factor signals underlying the obesity-cancer link, some phytochemicals, such as resveratrol, curcumin and quercetin have potential in breaking this link.[24] Also naturally appearing and widely distributed in animal and plant tissues are inositol phosphates[25,26] that have also shown implications in obesity, diabetes, and cancer. This will be discussed later.

The Mediterranean Diet, a healthy combination of dietary factors and lifestyle, with an extremely important social aspect, has proved to be beneficial for cardiovascular diseases, and to have a preventive role in cancer.[27] The combination of polyphenols contained in fruits, vegetables, grains, legumes, and olive oil have been recognized for their antioxidant and anti-inflammatory properties contributing to anti-tumor and anti-atherogenic abilities. It was shown that polyphenols control and reduce inflammation through a series of pathways preventing cancer and other age-related diseases with inflammatory pathogenesis.

The number of cancer survivors is steadily increasing, and the results from diet and weight loss studies show that cancer survivors are very motivated and able to make dietary and lifestyle modifications. One of the first such studies were the Women's Intervention Nutrition Study (WINS)[28] and the Woman's Healthy Eating and Lifestyle (WHEL)[29] trials conducted among early-stage breast cancer survivors, testing the effects of dietary interventions on cancer recurrence and survival. There were significantly lower rates of recurrence observed in the intervention arm at 5 years.[30,31] The Exercise and Nutrition to Enhance Recovery and Good Health for You (ENERGY) trial is designed as a vanguard component of a fully powered trial of at least 2,500 women with breast cancer recurrence endpoints.[32] With a goal to reduce breast cancer recurrence, and with a high potential to have a major impact on clinical management and outcomes after a breast cancer diagnosis, this study also initiated the efforts to establish the weight loss support for overweight or obese breast cancer survivors, as a new standard of clinical care. This multicenter trial, the ENERGY study, is the largest weight loss intervention trial among survivors of breast cancer to date, showing that a behavioral weight loss intervention, can lead to clinically meaningful weight loss in overweight/obese survivors of breast cancer.[33] Further studies to test methods that support sustained weight loss and to examine the potential benefit of intentional weight loss on breast cancer recurrence and survival are indicated and needed.

The Mediterranean Diet (MedDiet), a healthy pattern diet, has originally been proposed to reduce the risk of cardiovascular diseases and overall mortality. However, there is a strong correlation between a higher adherence to the MedDiet and a lower incidence of several forms of cancer.[7,13,27] On the contrary, a ketogenic diet, characterized by high fat intake, moderate to low protein consumption, and very low carbohydrate intake, has become very popular recently not only for obesity management, but also as an adjuvant therapy for cancer treatment.[7,34] It was hypothesized that ketogenic diets selectively starve tumors by providing the fat and protein that otherwise could not be used by glucose-dependent tumor cells. However, some new studies link the keto diet to cancer metastasis. Another strategy to control obesity is intermittent fasting (IF), that involves periodic episodes of minimal to no calorie consumption. IF may be considered in adults seeking prevention of cancer through weight management but still it is uncertain whether IF itself affects cancer and related metabolic and molecular pathways.[35]

While lifestyle interventions for weight loss are efficacious, sometimes their long-term durability is limited. In addition to these nutritional interventions, bariatric surgery and pharmacotherapy are available for long-term obesity management targeting obesity cancer risk. Bariatric surgery is an invasive approach that is also not consistently durable to all patients, although there has been some recent evidences are indicating safety and long-term effect.[4] However, the new obesity medications, like semaglutide and tirzepatide, are transforming the way the disease of obesity can be treated. Semaglutide and tirzepatide are medications used to treat type 2 diabetes and obesity, that belong to a class of drugs called glucagon-like peptide-1 (GLP-1) receptor agonist. Among several pharmacological interventions, SELECT was the first randomized cardiovascular outcome study powered for superiority evaluating an obesity pharmacotherapy, due to sample size large enough to have high probability of detecting a statistically significant difference between the treatments.[4,36] The follow-up of this landmark study shows that pharmacological treatment of obesity can reduce cardiovascular events, and that a large population of patients with atherosclerotic cardiovascular disease who have overweight or obesity and heart failure, could benefit from semaglutide, without the need for previous detailed cardiovascular risk stratification.[4,37,38]

In a recent study, Dr. Wang was investigating the clinical evidence supporting the potential benefits of glucagon-like peptide receptor agonists (GLP-1Ras) for the prevention of 13 human malignant neoplasm that have been identified as obesity-associated cancers, where the presence of excess body fat is associated with increased risk of developing cancer and worse prognosis in patients with these specific tumors.[39] In their study, they demonstrated that GLP-1Ras were associated with lower risks of specific types of obesity-associated cancers compared with insulin or metformin in

patients with T2D, type 2 diabetes mellitus.[39] Metformin is a medication commonly used to treat type 2 diabetes, that has shown a potential anti-cancer effect, by targeting obesity-associated physiology and signaling pathways.[13]

However, there are multiple risks associated with weight loss. Prevalence of sarcopenia, bone mineral loss and fractures are challenging, and rapid weight loss can be associated with formation of gallstones due to changes in cholesterol metabolism. Additionally, mental health issues and nutritional deficiencies are added outstanding issues, that a complementary oncological approach should include.[4,7,13]

The ongoing NIH clinical trial is investigating fiber-rich foods to treat obesity and prevent colon cancer, and testing whether a high-legume, high-fiber diet will simultaneously increase weight loss and suppress intestinal biomarkers of cancer risk compared to a control diet.[40] Interestingly, inositol and inositol phosphates, particularly phytic acid (inositol hexaphosphate) are fiber-rich components with the ability to fight both cancer and obesity through their metabolites and pathways.[25,26,41]

The Role of Inositol and Inositol Phosphates

Inositol is a naturally occurring glucose isomer, critically important for survival of mammalian cells. It is a six-carbon sugar, with nine possible stereoisomers, belonging to a family of cyclitols. Myo-inositol and its phosphorylated derivatives, inositol phosphates, are abundant in plants, but are found in high amount in mammalian cells, as well. Inositol is also a component of phospholipids found in eukaryotic cell membranes. These bioactive compounds participate in many cellular processes and are involved in various physiological functions, supporting critical cellular functions, such as cell permeability, membrane trafficking, gene expression, embryonic development, stress response, antioxidant and anti-inflammatory activities, energy homeostasis, signal transduction, and are also at the interface between cells and their microenvironment.[41,42] It seems that inositol phosphates have always been at the crossroads and between cell signaling and cell metabolism, affecting multiple signal transduction pathways and cascades. These molecules are known to decrease insulin resistance, increase insulin sensitivity, and have many other diverse properties and importance, acting from cell signaling to cell metabolism.

Due to diverse range of cellular functions, inositol phosphates are known to possess multiple beneficial properties for human health and have been widely studied.[43] Their anticancer properties, particularly of inositol hexaphosphate (IP6), known also as phytic acid, have been well established.[43,44] A striking anticancer action of IP6 was demonstrated in different experimental models.[44] Studies in humans show that IP6 and inositol, its precursor molecule, given in combination, appear to enhance the anticancer effect of conventional chemotherapy, control cancer metastases, and improve quality of life.[44]

It has been indicated that insulin resistance is involved in pathogenesis of number of diseases, including type 2 diabetes and cancer, and that insulin sensitizers, synthetic or natural, exert both anti-diabetic and anti-cancer properties. So, biochemical network shared by insulin resistance and cancer metabolism are the same, and interestingly, both are affected by inositol.[45] Inositol may directly interfere with both glucose metabolism and carcinogenesis by affecting several critical pathways downstream of insulin stimulation: antioxidant and endocrine modulation, but also PI3K/Akt, PDH and AMPK-related pathways.[45] Effect of inositol on adipokines have been studied, and inositol was shown to have effect on both leptin and adiponectin, the main adipokines involved in energy homeostasis and insulin-mediated functions.[46] It was indicated that inositol derivatives increase adiponectin levels, which in turn decreases obesity.[46] The utility of inositol supplementation in obesity in humans was indicated in few recent clinical trials. In a double-blind placebo-controlled randomized clinical trial, it was shown that inositol supplementation improved the cardiometabolic factors, anthropometric measures and liver functions in obese patients with non-alcoholic fatty liver disease.[47] Pregnancy is complicated by obesity that represents increased risk of unfavorable outcomes. There are no established nutritional guidelines for managing obesity in pregnancy, but there is an urgent need to establish and implement new nutritional programs to enhance the perinatal outcomes.

Knowing for its values in both obesity and neonatology, it is not surprising that inositol has been included in the intervention to optimize the perinatal wellbeing in pregnancy with obesity.[48]

Inositol hexakisphosphate kinase 1 (IP6K), an inositol pyrophosphate biosynthetic enzyme, has been a target in diet-induced obesity and obesity-related metabolic diseases. The inhibition of IP6K has emerged as a potential therapeutic strategy for obesity and related diseases. Several strong and potent IP6K inhibitors for the treatment of obesity and associated disorders, such as Li-2242[49] and inhibitor 20[50], have been developed by Dr. Anutosh Chakraborty. Additionally, valuable guidance on the design of novel IP6K1 inhibitors, that employ multiple in silico ligand-based modeling techniques, have emerged as a potential therapeutic strategy for obesity.[51] This work is based on the findings, that inositol pyrophosphates inhibit Akt signaling, thus regulating insulin sensitivity and weight gain.[52]

While white fat has been the primary focus of obesity research, in contrast to white adipose tissue that stores energy, brown fat dissipates energy and produces heat. However, brown fat has been inversely correlated with obesity and BMI, and the therapeutic potential of activating brown fat in humans is under investigation. And, evidence has indicated that inositol phosphates might enhance the browning of white adipocytes, and thus directly improve insulin sensitivity through adipocytes.[26,41]

Therefore, the impact of inositol and inositol phosphates on obesity, diabetes and related diseases, and cancer has been significant, particularly since these natural alternatives to pharmaceuticals are safe and much cheaper. It is important to note that both Ins and IP6 meet specifications of the FDA, and both have been given GRAS (Generally Recognized As Safe) status.

Discussion

Although obesity is a global epidemic, childhood obesity has become one of the major health challenges of this 21st century. In the United States obesity affects a staggering 40% of adults and 20% of children. It has been shown that youths with extreme obesity are at high risk-group for pain and mental health impairments.

In this "Ozempic era", the power of trendy weight-loss injectable prescription medication, primarily meant to treat type 2 diabetes, but popularized for their ability to aid in weight loss, like Ozempic and Wegovy, Zepbound and Mounjaro. These drugs mimic a natural hormone called glucagon-like peptide 1 (GLP-1), which helps regulate blood sugar and appetite. They also boost insulin production, slow digestion and make people feel full longer, helping them to slim down in record time. In the US, about 1 in 8 adults report using these medications. Recent guidelines from the American Academy of Pediatrics went so far to tell clinicians to offer kids with obesity weight loss medications but did not recommend specific agents.

Five scientists who helped develop these groundbreaking, blockbuster diabetes and weight-loss drug semaglutide (Ozempic Wegovy) were among recipients of the 2025 $3 million Breakthrough Prize in Life Sciences in April 2025.

However, are these weight-loss medications for everybody? These drugs have sent several people to the emergency room developing severe side effects. Although these are primarily gastrointestinal complications, there are multiple other medical and biological changes affecting some taking semaglutide medications, like hair loss, their impact on oral health causing dry mouth, gum inflammation, and tooth decay. Also, mixed dermatological effect, "Ozempic breast", "Ozempic vagina", "Ozempic penis", confusing scans, and unusual patterns on the PET-CT scans have been reported by medical community. However, it also has been shown that these drugs are good for sleep apnea, knee osteoarthritis, psoriasis and psoriatic arthritis, and can help in rheumatic arthritis. But, what happens to your body when you stop taking Mounjaro and other weight-loss medications, we still do not know. The risk and effectiveness of GLP-1 receptor agonists have been recently evaluated, providing useful guidelines for clinical care, but also directing the development of mechanistic and clinical research.[53]

While these popular therapies help to tackle and challenge the epidemic of obesity, there is still so much that researchers do not understand about brain-body connection that regulates appetite. A new population of neurons in the hypothalamus that regulate food intake and could be a promising

new target for obesity drugs, have been discovered and could be a promising new target for obesity. BNC2 neurons in the hypothalamus, which are activated by leptin, provide the potential for a completely new class of obesity drugs.[54]

Medical experts have called for new ways to more accurately measure obesity, and new definition has been proposed, although yet needs to be adopted. Almost 70% of US adults would be deemed obese, based on new definition, study finds. Experts are also proposing to split obesity into two categories: clinical obesity, where there are signs of illness, and pre-obesity, without any clinical signs.

Guidelines from the European Association of Obesity (EASO) are to pick GLP-1s as first drug option in obesity. A new treatment algorithm from EASO recommends opting for semaglutide (Wegovy) or tirzepatide (Zepbound) first when substantial weight loss is needed in a patient. Tailoring treatment to the individual is possible, although that is a complex task. The EASO recommendations go further than current guidance in the US. EASO puts an emphasis on selecting the right medication to manage obesity and its complications, prompting the revision of criteria for the diagnosis and staging of obesity.[55] Oral alternatives of these drugs are under development and approval.

Conclusion

Strategies, either diet, lifestyle, or pharmacological, that disrupt the obesity-cancer link are useful in reducing both obesity and cancer. However, we cannot apply all knowledge we know about prevention of obesity and cancer, because of multiple obstacles known as social determinants of health (SOD), non-medical factors that affect our health, like socioeconomic status and politics, as depicted in Figure 1B. The conditions in which people are born, live, work and age affect health outcomes, and can be more influential on health than genetics or healthcare access alone.

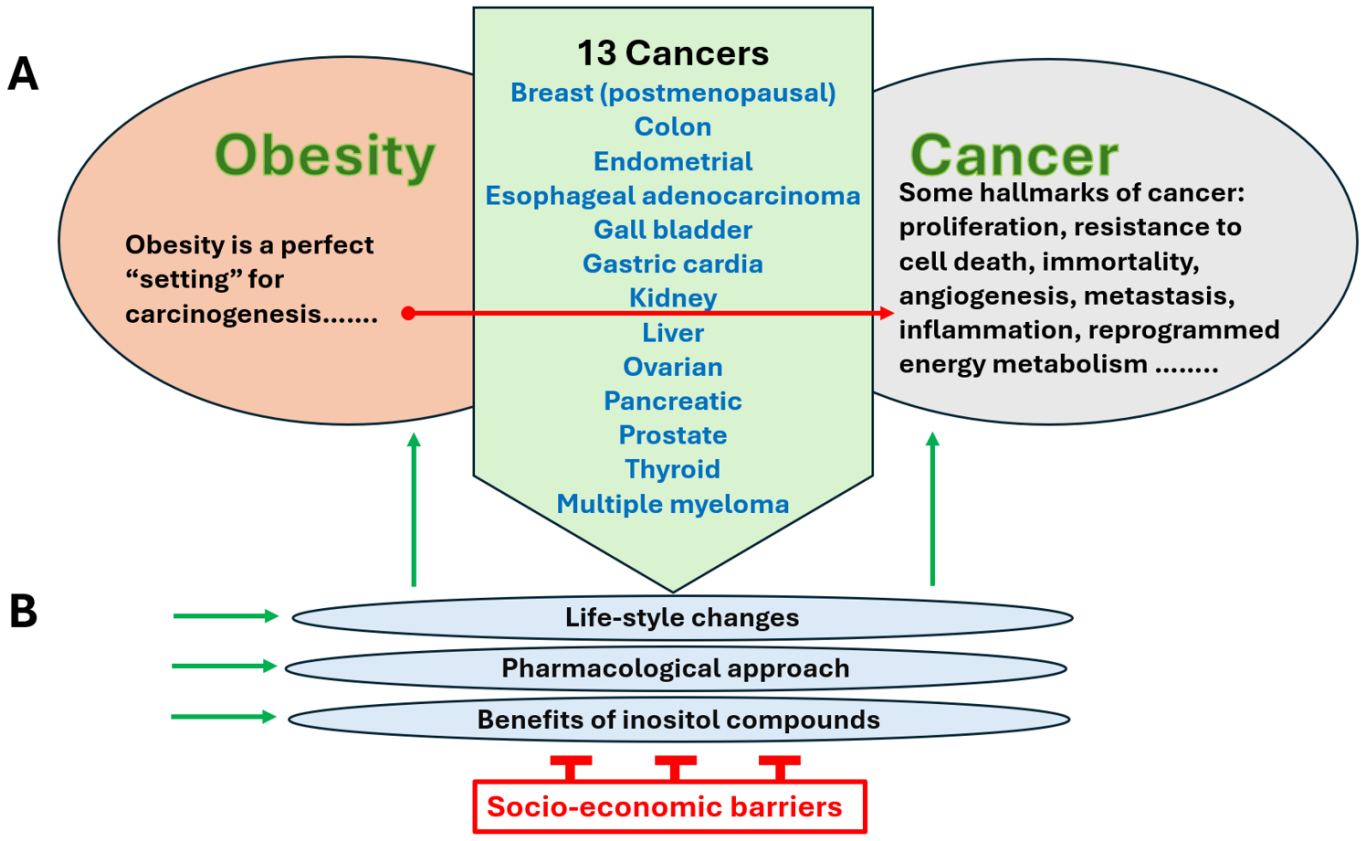

Figure 1. **A)** Obesity is a perfect setting for carcinogenesis, eliciting "hallmarks" of cancer. **B)** But, because of the socioeconomic barriers, we cannot apply all we know to prevent the obesity and cancer. Therefore, all sectors of society need to work together: science and academia, industry and government, to fight against obesity, that is not only health, but also a cultural crisis.

The question is, can we boost GLP-1 with diet and lifestyle? Also, are diet and exercise, in addition to medication, the keys to health longevity? It seems that we need an environment that makes the "healthy choice the easy choice" - because obesity is both health and cultural crisis.

Conflict of Interest Statement:

None.

Funding Statement:

None.

Acknowledgements:

None.

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