Effects of dietary modifications and physical activity on cancer prevention and treatment

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INTRODUCTION

Despite the great advancement of technology, cancer remains a leading cause of death in major parts of the world [1,2]. The second leading cause of death worldwide is cancer [3]. In this paper, diet, physical activity and its relationship with the prevention of cancer will be discussed together with how it affects the efficiency of treatment. We will review the few clinical studies that have been made publicly available online and discuss possible ways that nutrition may enhance the
effectiveness of cancer treatments through a variety of pathways. Notwithstanding the lack of current data, dietary interventions and adjustments may benefit cancer patients long-term by reducing long-term consequences, improving chemotherapy efficacy, and reducing toxicity. Therefore, to enhance the result of cancer treatment, it is critical that we comprehend the current state of the knowledge surrounding dietary intervention in conjunction with physical activity and that we broaden the scope of our studies examining this crucial but challenging treatment approach [4-5].

Cancer is a disease in which some of the body’s cells grow uncontrollably and spread to other parts of the body [6-7]. It happens when the regular process of cell division is disrupted, causing damaged or aberrant cells to increase and develop when they shouldn’t. Tumors are lumps of tissue that can be formed by these cells. Cancerous or benign tumors can both occur. Malignant tumors can metastasize, or spread into, neighboring tissues. They can also migrate to far-off locations within the body to establish new tumors. Malignant tumors are another term for these types of tumors. Many malignancies, except blood cancers like leukemia, do not form solid tumors. Benign tumors do not penetrate or spread to neighboring tissues [6-7].

Cancer is a hereditary illness, meaning that alterations to the genes that regulate cells’ growth and division are the root cause of the disease [8-9]. Cancer-causing genetic alterations can result from a variety of environmental factors, including chemical exposure from tobacco smoke and UV radiation from the sun, faults in cell division, and inheritance from one’s parents. Normally, damaged DNA is eliminated by the body from cells before they become malignant. However, as we age, the body’s capacity to do so decreases. Because of this, the chance of developing cancer increases with age [6,10-11]. As seen in Figure 1, there are over 100 different forms of cancer [12]. Cancer types are typically called after the tissues or organs in which they first appear. Prostate cancer, thyroid cancer, pancreatic cancer, leukemia, liver cancer, lung cancer, melanoma, non-Hodgkin lymphoma, bladder cancer, breast cancer, colon and rectal cancer, endometrial cancer, kidney cancer, and so forth are a few examples [6,13-15].

Figure 1: Different types of cancer affecting males and females [6,13-15].
DISCUSSION

The last century has seen significant advancements in the treatment of cancer. Acute lymphoblastic leukemia in children used to be almost always fatal, but today it has a cure rate of about 90%. From 49% in 1975 to 70% in 2011, the five-year survival rate from all malignancies has improved [16]. Treatment options for cancer are diverse. The kind of cancer a person has, and its stage of progression determine the kind of treatment that is prescribed. A cancer patient may receive chemotherapy and radiation therapy in addition to surgery, or they may receive only one of these therapies. Chemotherapy, hormone therapy, photodynamic therapy, radiation therapy, immunotherapy, stem-cell transplantation, surgery, and targeted therapy are a few examples of these cancer treatments [6,17-18]. The idea that nutrition may affect cancer treatment is very appealing to the public, and around 50% of cancer patients altered their diets to increase their chances of survival [19]. A diet is a specific eating plan that a person follows to either gain or lose weight or for other health-related purposes. A nutritious diet can help ward off non-communicable diseases like diabetes, heart disease, stroke, and cancer, as well as all types of malnutrition. The two biggest global health concerns are an unhealthy diet and inactivity [1,20-21]. Dietary alterations are adjustments made to food during processing, preparation, and consumption to reduce micronutrient deficits and increase food’s bioavailability of micronutrients. It’s also known as a "therapeutic diet." Therapeutic diets are used for a variety of purposes, such as maintaining, restoring, correcting, and increasing nutritional status; supplying extra calories for weight gain; balancing the amounts of fat, carbs, and protein to control diabetes; increasing the amount of a nutrient, like protein; reducing the amount of a nutrient, like sodium; and excluding foods due to allergies or intolerances [22-23]. Because our diets and beverages have a multitude of effects on our health, this study will concentrate on the connections between certain foods, beverages, nutraceuticals, and the benefits of exercise for cancer prevention and management.

Obesity and cancer: Adverse or excessive fat buildup that may pose a health risk is a characteristic shared by obesity and overweight people [24]. An easy way to classify adults as overweight and obese is to utilize the body mass index (BMI), which is a simple way to assess weight to height [25]. It is calculated as follows: kg/m², which is the person’s weight in kilograms divided by the square of their height in meters. A BMI of 30 or higher is considered adult obesity. A BMI of 25 or higher is considered overweight [25-26]. Extra fat in the body poses a risk. It does not simply sit there. Rather it’s active, delivering signals to the rest of the body [27]. These messages may instruct cells to divide more often, which may result in the development of cancer [28]. Overweight and obesity are associated with a greater risk of developing 13 different types of cancer [29]. These cancers include meningioma (a type of brain cancer), multiple myeloma, esophageal adenocarcinoma, breast (postmenopausal), colon and rectum, uterus, gallbladder, upper stomach, kidneys, liver, ovaries, pancreas, and thyroid [30]. These tumors may also be caused by other risk factors. Hormonal imbalances, gene alterations (also known as mutations), persistent infections, and nicotine and alcohol use are a few of these risk factors. Obesity or being overweight
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Dietary supplements and nutraceuticals do not guarantee that a person will develop cancer, but it does increase their risk compared to someone who maintains a healthy weight [31-33]. Some possible mechanisms to explain how obesity might increase the risks of some cancers include:

i. Overproduction of estrogen by adipose tissue has been linked to a higher risk of developing breast, endometrial, ovarian, and other cancers. The link between BMI and postmenopausal breast cancer risk was nearly entirely explained by greater estrogenic levels in women with higher BMI [34-35].

ii. Hyperinsulinemia, a condition where blood levels of insulin and insulin-like growth factor-1 (IGF-1) are elevated, is common in people with obesity. Insulin resistance causes hyperinsulinemia, which in turn causes type 2 diabetes, another known risk factor for cancer. Colon, kidney, prostate, and endometrial cancer development may be aided by high insulin and IGF-1 levels [36-38]. Obese people frequently have chronic inflammatory diseases. Visceral fat cells are large and numerous. A low-oxygen environment due to the excess fat triggers inflammation. Chronic inflammation brought on by too much visceral fat can result in oxidative stress, which damages DNA and raises the risk of biliary tract and other malignancies [39-41].

iii. Adipokines, which are produced by fat cells, are hormones that can either promote or inhibit cell growth. For instance, as body fat accumulates, the blood level of an adipokine called leptin rises as well. Leptin levels above a certain point can encourage the development of abnormal cells.

Adiponectin, another adipokine, may have antiproliferative properties that inhibit the formation of tumors and is less prevalent in obese individuals than in individuals with a healthy weight [37,42].

Diet modifications and cancer: Modifications of diets can assist prevention of certain ailments as well as improvement of the efficacy of certain therapeutic practices. Carcinogenic foods increase the risk of the onset of cancer. These foods have been contaminated with carcinogens, and thus are capable of inducing cancer. Some of the foods containing carcinogens that may increase one’s cancer risk include processed meats, fried food, overcooked foods, and alcohol. Therefore, for one to reduce such risk, changes in one’s diet via modifications would be highly recommended [43-45]. Studies do suggest that simple lifestyle changes, such as following a healthy diet, could prevent about 30–50% of all cancers. It’s difficult to prove that eating a particular food can cause cancer. However, continuous consumption of certain foods may increase the likelihood of cancer development. Studies have shown high consumption of processed foods, fried foods, and overcooked foods may bring about an increased risk. It has also been shown that no single food can protect against cancer; but eating a diet full of diverse whole foods, such as fruit, vegetables, whole grains, spices, legumes, healthy fats, fresh fish and high-quality dairy, may bring about a reduced risk of cancer [46]. Obesity is related to about 13 different types of cancer [30]. Therefore, having a healthy diet aids one to keep a healthy weight, or lose weight, which can reduce the risk of cancer [47-49]. Thus, the intervention of dietary
modifications in an individual’s lifestyle is a necessity (Table 1).

<table>
<thead>
<tr>
<th>Type of diet</th>
<th>Physiological effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wholegrains</td>
<td>reduces the chance of colorectal cancer</td>
</tr>
<tr>
<td>Dietary fiber</td>
<td>reduces the risk of obesity, overweight, and colorectal cancer</td>
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<tr>
<td>Glycemic load</td>
<td>raises the chance of endometrial cancer</td>
</tr>
<tr>
<td>Red meat</td>
<td>raises the possibility of colorectal cancer</td>
</tr>
<tr>
<td>Processed meat</td>
<td>raises the chance of colorectal cancer</td>
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<tr>
<td>Coffee</td>
<td>Liver and endometrium cancer</td>
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<tr>
<td>High fat diets</td>
<td>increases the risk of developing cancer in the following areas:</td>
</tr>
<tr>
<td></td>
<td>pancreas, gallbladder, liver, colorectum, breast (post menopause),</td>
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<tr>
<td></td>
<td>ovary, endometrial, advanced prostate, mouth, throat, and larynx;</td>
</tr>
<tr>
<td></td>
<td>esophagus (adenocarcinoma); stomach (cardia)</td>
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<tr>
<td>Sugar sweetened drinks</td>
<td>raises the risk of obesity, and weight gain</td>
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<tr>
<td>Alcoholic drinks</td>
<td>raises the risk of developing cancer in the mouth, throat, larynx,</td>
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<tr>
<td></td>
<td>esophagus (adenocarcinoma), liver, colorectum, breast, and stomach.</td>
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<tr>
<td>High-dose beta-carotene</td>
<td>raises the risk of lung cancer, particularly for smokers who have</td>
</tr>
<tr>
<td>supplements</td>
<td>smoked in the past.</td>
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<tr>
<td>Arsenic-contaminated drinking</td>
<td>Increases risk of Cancers of the: lung; bladder; and skin</td>
</tr>
<tr>
<td>water</td>
<td></td>
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<tr>
<td>Aflatoxin-contaminated foods</td>
<td>Increases risk of Liver cancer</td>
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<tr>
<td>Foods preserved by salting</td>
<td>Increases risk of Stomach cancer</td>
</tr>
<tr>
<td>Dairy products</td>
<td>Decreases risk of Colorectal cancer</td>
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</table>

**Wholegrain, dietary fiber, vegetables, fruit and cancer risk:** Studies have shown that greater consumption of non-starchy vegetables or fruit protects against a number of aerodigestive cancers. This includes cancers of the airways of the head and neck, including the mouth, throat, larynx (voice box) and sinuses [50]. Also, with the consumption of more wholegrain and foods containing dietary fiber, the risk of some cancers decrease [51].
Sources of wholegrain and dietary fiber include grains, or cereals (wheat, rice, maize (corn), millet); pulses (beans, lentils, peas and peanuts); and vegetables (carrots, leafy vegetables, cabbage, onions, garlic [52-54]).

**Wholegrains and colorectal cancer:** Wholegrain diets are abundant in lignans, phytoestrogens, phenolic compounds, vitamin E, selenium, copper, zinc, and dietary fiber, among other bioactive nutrients and non-nutrient components [55]. Many of these substances, which are mostly present in the grain’s bran and germ, may have anti-carcinogenic qualities. Experimental investigations have demonstrated that various phenolic acids can enhance anti-oxidative activity. Additionally, alkylresorcinols, which are indicators of consumption of wholegrain wheat and rye, have been demonstrated to reduce the incidence of colon cancer [56]. By binding carcinogens and controlling the glycemic response, whole grains may also offer protection against colorectal cancer [52,57-58].

**Dietary fiber and colorectal cancer:** It is biologically conceivable that eating whole grains and consuming dietary fiber will reduce the incidence of colon cancer. By increasing faecal bulk, diluting faecal carcinogens, and shortening transit time, dietary fiber may lower the risk of colorectal cancer by minimizing interaction between carcinogens and the colorectal lining. Additionally, short chain fatty acids like butyrate are produced because of the bacterial fermentation of fiber, and these compounds may be protective against colorectal cancer. Higher dietary fiber consumption also protects against weight gain and type-2 diabetes. It is probable that some of the potential effect of fiber intake is transmitted through improved weight control and reduced insulin resistance, however these are indirect processes [59-60].

**Non-starchy vegetables, fruit, and cancer:** There are many substances in fruit and non-starchy vegetables that have the potential to be anti-tumorigenic. The advantages of fruits and vegetables can be linked to their abundance of a wide range of phytochemicals [61]. They contain glucosinolates, folate, flavonols, dietary fiber, vitamin C, and carotenoids, among other things. A lower risk of some cancers may be brought on by the potential combination of these nutrients. Sulforaphane, which is produced from glucosinolates, has been demonstrated in studies to have several potential anti-prostate cancer effects. The combined consumption of non-starchy vegetables and fruits may reduce the chance of developing bladder cancer and estrogen receptor-negative (ER-) breast cancer, according to scant research [62-64].

**Meat, dairy and cancer:** Meat and dairy can be termed as ‘animal foods’ as they are of animal origin. The risk of colon cancer generally decreases with increased dairy product consumption. It is recommended that meat eaters limit their intake to modest amounts. Consuming red meat has been linked to an increased risk of non-Hodgkin lymphoma (NHL), bladder, breast, colorectal, endometrial, esophageal, gastric, lung, and nasopharyngeal cancer in addition to an increased risk of overall cancer mortality. Additionally, consuming processed meat may raise the risk of prostate, NHL, esophageal, gastric, bladder, breast, colorectal, oropharyngeal, oral cavity, and oropharynx cancers, as well as overall cancer mortality. Many cooking methods and processing techniques, such as roasting, grilling, smoking, heating, drying, baking, ohmic infrared cooking, and so forth, have an impact on the formation of polycyclic aromatic hydrocarbons (PAHs) in processed meats and meat products, which predisposes the consumers to cancers. PAH levels are influenced by
various factors, such as the food’s distance from the heat source, the fuel source, the degree of processing, the length of time and method of cooking, and other cooking-related factors. Extremely high cooking temperatures, such as those used for frying, grilling, broiling, or barbecuing, can alter the nutritional content and chemical makeup of animal products. [52,65-66].

**Red meat, processed meat, and cancer:** High heat during meat cooking produces heterocyclic amines (HCAs) and polycyclic aromatic hydrocarbons (PAHs), both of which are carcinogenic. These drugs may increase risk of cancer by modifying the DNA of cells [45]. Polycyclic aromatic hydrocarbons (PAHs) and heterocyclic amines (HCAs) created during high-temperature cooking procedures, after metabolic activation, contribute to the development of DNA adducts in epithelial cells, with a significant potential for carcinogenesis to colorectal cancer. Heme, which is present in meat, causes multiple DNA mutations that lead to colorectal cancer through lipid peroxidation and endogenous N-nitroso compound synthesis. The development of colorectal cancer may then be accelerated by an inflammatory process brought on by a combination of heme-induced lipid peroxidation products and reactive oxygen species (ROS) found in red and processed meat [67].

**Dairy and cancer:** Overall, there is conflicting information regarding whether consuming dairy products influences cancer risk. According to research on Western populations, dairy products may reduce the incidence of colon cancer. However, dairy consumption is also associated with an increased risk of contracting several cancers, according to studies that concentrated on a sizable Chinese population [68]. Dairy consumption may increase the risk of prostate cancer [69]. Consuming dairy products raises insulin-like growth factor 1 levels (IGF-1).

This is linked to an increased risk of prostate cancer. IGF-1 may promote prostate cancer cell proliferation [45]. This may be brought on by milk's nutritional components and its derivatives, which may increase consumers’ chance of developing prostate cancer [70].

**Processed foods and cancer:** It’s possible that consuming foods that have been heavily processed causes cancer. However, more comprehensive population-based observational studies are required to corroborate the findings [71]. Processed foods generally have more total fat, saturated fat, added sugar, and salt, as well as less fiber and vitamin density. In addition to their nutritional makeup, heat-treated processed food products contain neo formed pollutants due to the Maillard reaction, some of which are carcinogenic (such as acrylamide, heterocyclic amines, and polycyclic aromatic hydrocarbons). Processed food packaging might contain substances that come into touch with food and have been linked to cancer and endocrine disruption, such as bisphenol A. Processed foods also contain approved, though controversial food additives, such as sodium nitrite in processed meat or titanium dioxide (TiO₂, a white food color), which has been linked to carcinogenesis in animal and cellular models [43]. Studies have found a marginally non-significant trend linking eating processed food to an increased risk of colorectal cancer. According to this research, a 10% rise in the percentage of processed foods in the diet is significantly linked to a 12% increase in the risk of all cancers as well as an 11% increase in the risk of breast cancer [43].

**Non-alcoholic drinks and cancer:** Untreated water, maté, coffee, and tea are examples of non-alcoholic beverages that may increase risk of cancer [72-73].
**Water:** Inorganic arsenic is a known carcinogen and the most prevalent chemical pollutant in drinking water worldwide [74]. Many countries' groundwater naturally contains large amounts of arsenic. The biggest harm to human health from arsenic comes from contaminated water used for drinking, food preparation, and irrigation of food crops. Cancer and skin sores can result from long-term exposure to arsenic in food and drinking water [75-77].

**Maté:** This is a hot beverage produced from the native South American plant known as Yerba Mate (Ilex Paraguariensis). It tastes and smells like vegetables. It is popular throughout the South and Central American continents [78-80]. The consumption of maté is linked to an increased risk of bladder cancer. This non-alcoholic drink has been linked to an increased risk of esophageal cancer. Drinking maté may cause heat damage to the esophagus mucosa, which could lead to human cancer (this increases the incidence of nitrosamine-induced tumors). Although maté is typically consumed at a relatively high temperature, this does not explain how it affects the bladder mucosa. It's probable that maté contains some undiscovered carcinogens [72,81].

**Coffee and tea:** These two hot beverages are widely consumed. Coffee is a popular beverage prepared from roasted Coffea fruit beans (Coffea arabica, Coffea canephora). It contains caffeine and chlorogenic acid [82-83]. Tea is a beverage derived from the Camellia sinensis plant. After water, tea is the most popular beverage worldwide. Tea has numerous health advantages, including anti-inflammatory, antioxidant, and effects on weight loss [84-85]. Drinking coffee and tea has been linked to bladder cancer, however the evidence for this is debatable [72,86]. According to studies, drinking coffee has an inverse relation with five cancer types: endometrial cancer, liver cancer, melanoma, oral cancer, and pharyngeal cancer [87-88]. Coffee's varied components may have an impact on how endometrial cancer is affected by coffee consumption. In addition to caffeine, coffee contains more than a thousand other compounds, some of which have been shown to have antioxidant and antimutagenic properties in cell culture systems and animal models. These include melanoidins, diterpenes (like cafestol and kahweol), and other phenolic compounds (including chlorogenic, caffeic, ferulic, and coumaric acids) [89-92]. These chemical components, particularly cafestol and kahweol, may lessen some carcinogens' genotoxicity and the detoxification of cancer-causing substances [90,93]. In addition, tea contains a complex blend of antioxidants called polyphenols and flavonoids. Additionally, flavonoids may have anti-inflammatory effects and may stop the growth of tumors [2,90,94]. Coffee intake may lead to a decreased risk in endometrial cancer and tea intake is associated with a decreased risk of cancer [90,95].

**Alcoholic drinks and cancer risk:** The chemical component ethanol, commonly referred to as "ethanol alcohol," is what is meant by "alcohol" and is found in alcoholic beverages such as wine, distilled spirits, cider, beer, and malt liquor [6,98].

People who drink alcohol may be more susceptible to certain cancer types, such as liver, esophageal, breast, and colorectal cancers; cancers of the head and neck, particularly those of the larynx, throat, and mouth. An individual's chance of acquiring certain cancers increases with alcohol consumption, particularly in the long run. Alcohol consumption directly encounters the tissues of the larynx, esophagus, and oral cavity, increasing the risk of these cancers [97-99]. A person is more likely to develop cancer if such person drinks alcohol than if the
person does not. However, using alcohol does not guarantee development of cancer. The exact risk will be determined by a variety of factors, including things one cannot influence, such as age and heredity. Reducing alcohol use can lower the risk of developing cancer. Alcohol can increase risk even in little amounts, so therefore, if one drinks less, the lower one’s risk will be [100-101]. Beer, wine, and spirits all contain alcohol in the form of ethanol. Acetaldehyde, a hazardous chemical and possible human carcinogen, is created when ethanol in alcoholic beverages is metabolized (broken down). Acetaldehyde can harm DNA (the genetic material that makes up genes) and other biological molecules [97,102-103].

Alcohol may contribute to cancer risk in these ways:

i. **Oxidative stress**: by producing reactive oxygen species (chemically reactive molecules containing oxygen), which act as free radicals in the body, damaging DNA, proteins, and lipids (fats) [6,104-105]

ii. **Impairment in breaking down and processing important nutrients**: Alcohol consumption may impair the body’s capacity to break down and absorb vital nutrients. These include carotenoids, vitamin A, vitamin C, vitamin D, vitamin E, and folate [97,106-107].

iii. **Increasing blood levels of estrogen**: a sex hormone linked to the risk of breast cancer [6,108-109]

iv. **By irritating healthy cells**: Alcohol acts as an irritant. Alcohol consumption has the potential to harm healthy cells in the mouth and throat. There may be DNA alterations that result in cancer as those cells repair themselves [97, 110-111]. Although there is no “safe” level of alcohol use, the risk of cancer decreases with decreased consumption. If one drinks no more than two standard drinks or less per day as a male, or no more than one standard drink or less per day as a woman, one can reduce the risk of cancer and other disorders [112-114]. One standard drink may be defined as: 12 fluid oz. of beer; 5 fluid oz. of wine; 1.5 fluid oz. of 80 proof distilled liquor [115-116].

Malnutrition is one of the adverse side effects of cancer and anticancer therapies, hence reinforcing the need for cancer patients to have proper dietary support. In routine clinical practice, nutrition ought to be one of the first things taken into consideration. Malnutrition has a detrimental effect on cancer patients' overall survival, reaction to treatment, and clinical outcomes. Early identification of nutritional problems appears to be important for ensuring the appropriate care of malnourished cancer patients and those who are at high risk of malnutrition. Furthermore, cost reductions are associated with appropriate nutritional support through diet management, and it appears critical to advance this intervention’s clinical and financial value to enhance outcomes and reduce management expenses [116].

In addition to being successful in preventing malnutrition, dietary therapies for cancer patients may also actively contribute to the management of various forms of disease. Growing popularity is a dietary intervention strategy for cancer treatment that targets specific nutrients to be removed, which is based on a mechanistic knowledge of the metabolic requirements of the tumor. This more nuanced approach, which one could call "precise nutrition," requires the tumors to be categorized both histologically and molecularly before treatment can begin. The variety and adaptability of metabolic alterations in malignancies suggest that altering dietary nutrition will have a variable impact on various cancers. Therefore, precise dietary strategies will need to be modified to account for the various metabolic
requirements of various malignancies. Making effective therapy options will require a precise mechanistic knowledge of how these factors interact, and significant progress in finding such interactions is now being achieved [117].

Owing to the links between obesity and unfavorable cancer outcomes discussed in the previous section, the discovery that cancer cells consume an excessive amount of glucose, amino acids, and fats as metabolic fuels as well as the strong desire of patients, families, and healthcare professionals to provide additional hope, dietary modifications have been implemented in the field of cancer treatment to improve therapeutic efficacy. Certain evidence suggest that dietary modifications may lessen the adverse effects of chemotherapy. Sadly, rumor and anecdotal evidence have dominated most of the discussion, and few nutrition interventions for cancer patients have received scientific validation [5]. Below is a summary of the most popular dietary therapies (based on preclinical and clinical research) recommended for cancer patients.

**Fasting/short-term fasting:** The health benefits of fasting have long been praised. People who observe intermittent fasting for personal or religious reasons live longer and experience a lower risk of cardiovascular disease and cancer, according to epidemiological studies. With varying and follow-ups are needed [118]. Short-term fasting (STF) strengthens healthy cells' stress resistance. Differential stress resistance (DSR) refers to the unique response of healthy vs malignant cells to STF. During food scarcity, healthy cells reinvest energy in maintenance and repair, which contributes to chemotherapy resistance, whereas malignant cells are unable to limit growth due to mutations in tumor suppressor genes and mitogenic pathways. Furthermore, low serum glucose levels during STF stress tumor cells because their energy needs are predominantly fulfilled by glycolysis under these conditions. Because of these differences in the reactions of healthy vs cancer cells to STF, chemotherapy produces more DNA damage and apoptosis in tumor cells while leaving healthy cells alone when paired with STF. Thus, STF protects healthy cells from the toxicity of chemotherapy while making tumor cells more vulnerable, a mechanism known as differential stress sensitization (DSS) [119].

STF offers less adverse effects than many cancer treatments, such as headaches, nausea, weakness, and short-term weight loss in people. As a result, STF is a promising method for improving the effectiveness and tolerability of chemotherapy in cancer patients, particularly because it is a practical, accessible, and reasonably priced strategy that may be successful in a variety of types. Patients with severe malnutrition, sarcopenia, cachexia, or weight loss, on the other hand, are most likely not the best candidates for an STF intervention. Recent recommendations urge people with cachexia to consume more protein and fat. STF may therefore be especially helpful for generally healthy individuals receiving (neo) adjuvant chemotherapy [119].

Figure 2 illustrates how food deprivation in healthy cells blocks growth pathways, freeing up energy for pathways involving maintenance and repair. Consequently, stronger cellular defense makes cells more resilient to a variety of stresses, including chemotherapy and radiation. Tumor cells are unable to initiate this protective response because of uncontrolled growth pathway activation, self-sufficiency in growth signals resulting from oncogenic mutations, or the production of autocrine growth factors, and uncontrolled growth pathway activation in tumor cells. These factors combine to cause the loss of anti-proliferative signals caused by mutations in tumor suppressor genes. Consequently, cancer cells gain the
capacity to proliferate more quickly but forfeit their capacity to adjust to challenging conditions such as starvation. Furthermore, a lot of nutrients are needed for cancer cells to continue growing at their accelerated rate. Tyrosine kinases (TKIs), radiation, and various chemotherapeutic treatments are thus more likely to cause cancer cells to develop resistance due to STF. Several growth factors and nutrition sensing pathways have been suggested as important regulators of DSR and DSS by STF, while the precise mechanism is unknown. Of them, insulin-like growth factor-1 (IGF-1) has received the greatest investigation. The ability of various species to withstand times of famine is facilitated by the activation or inhibition of nutrient-sensing pathways in response to a low concentration of available nutrients. These pathways direct cells to focus their energy on maintenance and repair instead of growth and reproduction when nutrients are few, presumably to increase survival during times of famine [119].

**Fasting-mimicking diet:** Patients who follow a modified version of fasting called a “fasting-mimicking diet” (FMD) can consume a low-calorie, low-protein, and low-sugar diet while yet experiencing similar metabolic effects as those of fasting [120]. By causing differential stress resistance, the use of FMD during chemotherapy may reduce side effects and boost therapeutic efficacy. A Fasting-Mimicking Diet (FMD) may reduce toxicity and is a safe and well-tolerated adjuvant to chemotherapy, according to small clinical trials. Patients with cancer who used FMD in addition to FEC/AC chemotherapy did not experience any more grade III/IV adverse events than those who did not adhere to a diet, even though they did not get dexamethasone during this treatment. This indicates that FMD might substitute dexamethasone as a necessary treatment to prevent the side effects of chemotherapy. Significantly, T-lymphocyte DNA damage was reduced in patients who received FMD in addition to chemotherapy as opposed to patients who only received chemotherapy, suggesting that FMD shielded these cells from the oxidative stress caused by chemotherapy [121]. Additionally, FMD is generally safe and beneficial in patients receiving treatments other than chemotherapy. An important aspect of the study's novelty is the broad feasibility and safety of a fasting regimen (FMD) in patients receiving different types of treatment and cancer types. This is because several non-chemotherapy anticancer treatments, such as TKIs, immune checkpoint inhibitors, radiotherapy, and endocrine therapies for breast cancer, may benefit from fasting or modified fasting regimens. Additionally, it is highly recommended that a nutritionist be involved to guarantee the best possible adherence to the FMD during cancer therapy [122].

**Carbohydrate restriction/ketogenic diet:** A ketogenic diet limits carbohydrates and increases fat intake. The purpose of the diet is to decrease the amount of glucose (sugar) the tumor cells can use to grow and reproduce [6,123]. There has been great interest in using a ketogenic diet as an alternative to fasting and caloric restriction. A ketogenic diet could be better tolerated in some patients, and it has a long safety record as a treatment for epilepsy. A recent meta-analysis identified 12 studies which tested unrestricted ketogenic diet against standard diet in murine cancer models, and it concluded an overall growth delay with the ketogenic diet [5].

**Other diet interventions:** There are numerous diets that have been demonstrated to lower cancer risk and outcome, but do not fall into the afore-mentioned categories. Mediterranean diets are centered around the region’s typical produce, dairy, seafood, legumes, nuts,
and olive oil. A diet rich in fruits and vegetables has been associated with a decreased risk of dying from cancer overall as well as from malignancies of the breast, colon, stomach, prostate, liver, pulmonary, and pancreatic regions. Antioxidants, mono-unsaturated fatty acids (MUFA), and other possibly advantageous ingredients are abundant in olive oil, a staple of the Mediterranean diet. Individuals with the highest olive oil consumption were also less likely to get gastrointestinal and breast cancers in addition to overall cancer. Protein restriction can slow the growth of prostate and breast cancer in human xenografts, but in prospective cohorts, decreased animal protein intake did not correlate with cancer mortality [5].

The concept of "differential stress" describes a crucial theory on the mechanism of action of fasting and perhaps calorie restriction. During fasting, certain anabolic hormones are decreased, such as insulin, IGF-1, and leptin. Together with a reduction in the availability of metabolic fuel, these modifications lessen anabolic signaling in non-cancerous cells, which raises mTOR and lowers AKT. The concept of "differential stress" describes a crucial theory on the mechanism of action of fasting and perhaps calorie restriction. During fasting, certain anabolic hormones are decreased, such as insulin, IGF-1, and leptin. Together with a reduction in the availability of metabolic fuel, these modifications lessen anabolic signaling in non-cancerous cells, which raises mTOR and lowers AKT. These signals can trigger autophagy and slow down the growth and proliferation of cells, which reduces the susceptibility of healthy cells to chemotherapy, especially when the chemotherapy targets dividing cells. However, one of the characteristics of cancer cells is their capacity to develop and multiply without regard to external cues. For this reason, fasting might not have an impact on the rates at which these cells multiply, maintaining their vulnerability to chemotherapy. Reduced availability of fuels like glucose, lipids, and amino acids may also harm cancer cells more since they might not be as flexible in their metabolism as host cells. Rapid growth in the face of fuel scarcity can therefore lead to oxidative stress, which raises the risk of aberrant DNA replication and disastrous mitotic events. More focused cancer treatment could be possible as a result of these effects, which should increase the therapeutic window between host and cancer cells [5].

Hormonal changes brought on by diet may have further consequences. Certain cancer cells exhibit sensitivity to growth hormones, such as insulin and IGF-1, and if these signals are diminished through dietary intervention, they may become more susceptible to chemotherapy. The benefit of survival during food restriction was reversed when IGF-1 was replaced, as evidenced by this result [126]. On the other hand, fasting and calorie restriction increase adiponectin levels, which may encourage cancer cells to undergo apoptosis. There could be more intricate hormonal impacts. Obese mice's leukemia cells were resistant to leptin. Nevertheless, fasting enhanced leptin receptor expression, which resulted in leukemia cell differentiation and enhanced mouse survival [5,127].

Diet modifications are likely to affect the host environment in a variety of ways, which can affect the course of cancer and the sensitivity of treatment. In those who are overweight or obese, a diet low in calories can reduce the number of inflammatory monocytes within 16 weeks. The microbiome is significantly impacted by dietary therapies, and this can change the metabolism of chemotherapy agents, inflammation, and the systemic metabolome. Restricting one's diet may lessen vascularization, which could lower the amount of oxygen and nutrients that tumors receive. The adjustment of one's diet can have these and other advantageous effects that could enhance the therapy of cancer [5].
Concept of physical activity: Any movement generated by skeletal muscles that necessitates a greater energy expenditure than when at rest is considered physical activity [128]. Since it consumes energy, it plays a crucial role in maintaining the equilibrium of energy. There are two categories for them: aerobic and anaerobic. Running is an example of aerobic exercise that improves cardiovascular health and boosts oxygen uptake. Anaerobic exercise, on the other hand, uses weights to build muscular mass and strength. Engaging in physical activity influences multiple physiological systems, including the immunological, respiratory, endocrine, and circulatory systems, in addition to regulating metabolic processes that may impact the likelihood of developing malignancies [129].

Studies have indicated that physical activity can be beneficial and safe for many people before, during, and following cancer treatment. Engaging in physical activity can also aid in managing the side effects of therapy and potentially lower the likelihood of developing new cancers in the future. Seated or resting for extended periods can result in decreased range of motion, muscle weakness, and loss of bodily function. Before, during, and after cancer treatment, many cancer care teams encourage patients to engage in as much physical activity as feasible [130].

Physical activity is now recognized as being crucial to both during and after cancer therapies since emerging research indicates that it reduces the likelihood of relapse and ameliorates several typical adverse effects of cancer treatments. These advantages may be attained biologically via a variety of routes that regulate cell development, hormone levels, gene expression patterns, and tumor immunity. Therefore, it is advisable for patients to engage in as much physical activity as possible prior to, during, and after cancer treatment [131].

Ways in which regular exercise may help one before, during, and after cancer treatment are numerous. It helps the body and in brain fog, reduces the feeling of fatigue, helps lessen depression and anxiety, may help promote better sleep, keeps or improves one's physical ability to get things done, maintains and improves muscle strength, bone health and range of motion, strengthens the immune system, increases one's appetite, prevents and reduce weight gain, may help with breast cancer-related lymphedema (and does not increase risk), improves the survival rate thereby decreasing recurrence of some types of cancer, improves quality of life, and reduces pain and treatment side effects [132].

Physical activity and cancer management: Physical activity enhances gut microbiota composition, immunological function, total antioxidant capacity, and sex-hormone binding globulin (SHBG) synthesis. It also raises the production of the anti-inflammatory plasma hormone adiponectin. In addition, engaging in moderate to vigorous physical exercise reduces oxidative stress, fatty tissue, and hyperinsulinemia, as well as the inflammatory hormone leptin and the levels of the sex hormones [133]. Regular moderate-intensity or more physical activity is linked to a lower chance of developing numerous malignancies, including endometrial, breast, and colon cancers. Longer exercise sessions, more intense workouts, or more years of exercise all reduce the chance of developing some cancers more than others. Physical activity improves insulin resistance, lowers hyperinsulinemia, and lowers diabetes risk, which could explain the link between increased physical activity and reduced risk for these cancers [134].

Colon cancer: Large-scale longitudinal studies reveal that people who exercise frequently seem to have a lower
chance of developing colon cancer. Studies have shown an adverse relationship between moderate/vigorous activity and the risk of colorectal cancer, which seems to be stronger in men, particularly in those who spend more time sitting down. A plausible explanation for the disparities in benefits between sexes could be hormonal differences [133]. People who frequently exercise have a 40% to 50% decreased risk of colon cancer compared to those who don’t, yet it isn’t proven for sure that exercise alone lowers the risk of cancer. Those who remain active throughout their lives had the lowest risk of developing colon cancer [135-137].

**Breast and endometrial cancer:** Physical activity may reduce body fat and lower circulating levels of estrogens and androgens, which may reduce the risk of endometrial and breast cancer in postmenopausal women. This is true for all women, regardless of family history or risk of breast cancer [134]. Uterine cancer, lung cancer, liver cancer, bladder cancer, and prostate cancer are further potential cancers for which physical exercise reduces risk [133]. Some health advantages can be derived from light exercise. Anything done to prevent sitting or lying down is considered a light activity. Activities that are sedentary should be avoided. Children and teenagers should exercise frequently. They should take part in activities like playing energetically at home or school, participating in sports and fitness activities, and so on. They should also limit their TV viewing, playing video games, computer use and other electronic devices, as these serve as sedentary activities that involve a long period of sitting [135,138].

**Goals and benefits of physical activity program in cancer prevention and management**

**Before treatment:** Before therapy, becoming more active or maintaining one’s existing level of physical activity may help one handle and recover from treatment more effectively. According to research, being as active as possible may prevent surgical complications and help one cope with treatment better. In addition, once treatment begins, physical activity may help one manage sadness and anxiety, have more energy, and sleep better. Many patients discover that their capacity to remain active becomes more difficult once they begin treatment. Starting off in better physical condition means being able to handle greater activities throughout and after treatment [130].

**During treatment:** Some factors affecting one’s ability to exercise during treatment, include: the type and stage of cancer; the cancer treatment; and the patient’s stamina, strength, and fitness level before and during treatment. Several studies examining the role of physical activity during cancer treatment have shown positive effects on decreasing fatigue [139]. Those who exercised prior to treatment may need to exercise less or at a reduced intensity while undergoing treatment. The idea is to remain as active as possible. People who were previously sedentary (inactive) may need to begin with brief, low-intensity activity, such as short moderate walks. Exercise during treatment, as well as the boundaries of what such a patient can accomplish, should be discussed with the cancer care team [130].

**Recovering from treatment:** Most people can gradually increase their exercise time and intensity as their negative effects subside. What a healthy person might consider a low- or moderate-intensity activity may appear to some cancer survivors to be a high-intensity activity. So, it’s recommended to be patient and to gradually increase activity [130].
Living with advanced cancer: Physical activity may also benefit patients whose cancer has spread or has progressed to the point where it cannot be cured. Exercise has been shown to increase physical function, reduce weariness, and improve quality of life. The kind and stage of cancer, side effects, present physical capacity, and any other health conditions will all influence whether a patient can tolerate additional physical exercise. The cancer care team should be involved to ensure safety during the exercises [130].

CONCLUSION
Diet and physical activity are critical components of human survival. Imbalanced and improper levels of these factors might disrupt normal homeostasis and impair resilience to external stresses. This can show in a variety of ways, such as susceptibility to infections, cardiometabolic disease, or cancer. Diet modifications coupled with physical activity may influence cancer risk in a variety of ways because some foods and drinks could predispose the consumers to cancer.

Abbreviations: BMI: Body Mass Index; IGF-1: insulin-like growth factor-1; PAHs: polycyclic aromatic hydrocarbons; HCAs: heterocyclic amines; ROS: reactive oxygen species; FMD: Fasting-Mimicking Diet; MUFA: mono-unsaturated fatty acids.

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