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Review Article

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Diet and nutrition strategies for cancer prevention: A comprehensive review

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ABSTRACT

Maintaining a healthy diet is crucial for preventing cancer, as it provides the essential nutrients needed for proper physiological functioning. It is predicted that simple lifestyle and dietary changes can lessen the risk of developing 30-40% of all malignancies. Obesity, the consumption of nutrient-deficient foods such as sugary and refined flour products, which can lead to impaired glucose metabolism and, eventually, diabetes, a lack of dietary fiber, an excess of red meat, and an imbalance in the consumption of omega-3 and omega-6 fats are all risk factors for cancer. To reduce your risk of cancer, include flax seeds, a variety of fruits and vegetables, and dietary fiber in your diet. Additionally, there is proof that nutritional supplements may help lower the risk of breast cancer recurrence. To prevent various types of cancer, it is important to include vegetables, fruits, whole grains, and specific fatty acids in your diet, alongside engaging in regular physical exercise. Furthermore, it is crucial to use advances in genetics and molecular biology to extend nutritional research from observational studies to demonstrating causative linkages. Cancer prevention strategies that involve dietary changes targeted at specific groups should be based on a thorough understanding of these fundamental principles. Such dietary methods can be effective as well as in cancer prevention but also cancer rehabilitation. This review investigates the relationship between cancer and diet, examines straightforward approaches to incorporating cancer-preventive foods into one's diet, investigates the impact of dietary variables and lifestyle choices on the risk of cancer, and investigates clinical studies focused on nutrition and cancer prevention.

KEYWORDS: Cancer, Diet, Nutrition, Physical Activity, Cancer risk, Lifestyle

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INTRODUCTION

Cancer is a medical condition characterized by abnormal cell development with the ability to invade and spread to other sections of the body. It has emerged as a leading cause of death worldwide, responsible for approximately 10 million fatalities in 2020. In 2018, cancer resulted in the loss of 9.6 million lives (World Health Organization, 2021). With the increasing global incidence of cancer, there is a growing demand for innovative approaches to manage this disease. Cancer is a multifaceted condition influenced by various factors, encompassing nutrition, lifestyle choices, exposure to radiation, and hormonal elements, all contributing to its onset and progression (Anand *et al.*, 2008). In the realm of primary prevention, primary goals often revolve around addressing Smoking, alcohol usage, and dietary patterns are all thought to play a substantial role in the development of cancer. It's imperative to investigate the possible link between food choices and the onset of cancer (Sun *et al.*, 2021). Diets strong in red and processed meats, for example, have been related to an increased risk of colon cancer, while diets high in fat have been connected to an increased risk of breast cancer (Santarelli *et al.*, 2008). Consumption of pickled, salted, or smoked items has been associated with an increased risk of stomach cancer, although diets heavy in fat and poor in fiber have been linked to an increased risk of developing colon, prostate, pancreatic, breast, endometrial, and ovarian cancers. In the realm of cancer clinical care, the choice of treatment depends on the severity and type of the disease. Typically, patients receive combined therapies, including chemotherapy, radiation therapy and surgery. Furthermore, there are innovative cancer treatments including photodynamic and thermal therapy, gene therapy and immunotherapy. Phytonutrients,

which are biologically active compounds found in plants, possess anti-inflammatory and antioxidant properties when consumed by human beings (Vakayil *et al.*, 2019). Among these phytonutrients, anthraquinones and flavonoids have proven to have the capacity to shield the body from a variety of cancers (Liskova *et al.*, 2021).

Diet plays an important role in cancer genesis and prevention. While there may be variations in research findings when it comes to the connection between nutrition and cancer, the fundamental concept that nutritional factors can elevate cancer risk is widely accepted. However, numerous questions still linger, such as identifying the precise dietary elements most strongly associated with cancer prevention, understanding the mechanisms through which food components influence cancer risk, unraveling the interactions among dietary factors affecting cancer risk, and determining effective preventive efforts to limit the potentially negative consequences of elements that appear to increase the risk of this disease (Greenwald *et al.*, 2001). The importance of diet in the treatment of cancer is crucial and continually evolving in the research field. With ongoing advancements in our understanding, it is becoming obvious that nutrition has a significant role in cancer care. Organizations like the American Institute for Cancer Research and the World Cancer Research Fund emphasize the potential impact of nutritious foods, physical activity, and body weight maintenance in preventing as much as 30-40% of all cancer cases. In certain types of tumors, this influence is likely to be even more pronounced (Donaldson, 2004). There are approximately 5,000 distinct phytochemicals, and scientific research indicates that their potent antioxidant and anti-cancer properties stem from their collaborative and cumulative interactions (Murali *et al.*, 2023). These phytochemicals are important in the regulation of nuclear receptors, apoptosis, cell cycle arrest, angiogenesis regulation, and enzyme inhibition (Mokhtari *et al.*, 2017).

Establishing the Correlation between Diet and Cancer

Substantial epidemiological research, along with findings from *in-vivo* and *in-vitro* studies, strongly supports the link between dietary choices and the risk of acquiring cancer. Broadly speaking, a diet rich in vegetables, dietary fiber, fruits as well as specific micronutrients tends to offer protection from cancer, while consumption of excessive fat, surplus calorie intake, and consumption of alcohol elevate the cancer risk (National Research Council, 1989). Nonetheless, several factors are likely accountable for the disparities observed in research data. Food items are intricate combinations of both nutrients and non-nutritive compounds, making their precise quantification challenging. Additionally, comprehending the impact of individual components and potential interactions among these constituents poses a complex challenge. Inconsistent associations in epidemiological studies between dietary elements and specific types of cancer may be attributed to individual variations, including inherited genetic susceptibilities (Slattery *et al.*, 1995). The predominant body of existing data suggests that there are indirect links between the risk of cancer and the consumption of vegetables, whole grains, fruits, dietary fiber, specific micronutrients, and specific categories of fats such as n-3 fatty acids, notably in relation to n-3/n-6 ratios, as well as physical activity. On the other hand, there are direct correlations between cancer risk and total fat consumption, specific forms of fat such as saturated fat, alcohol consumption, and obesity as measured by a high body mass index (BMI) (Glade, 1999). Several reputable organizations have formulated. These guidelines typically advocate for reduced overall fat consumption, particularly from animal-derived sources. They also emphasize the importance of greater fiber intake, eating a variety of fruits and vegetables, engaging in regular physical activity, maintaining a healthy body weight, limiting or abstaining from alcohol consumption, and limiting your intake of salt-pickled, salt-cured, or smoked items (American Cancer Society, 1996; Greenwald *et al.*, 2001). A new analysis of data from the Health Professionals Follow-Up Study (HPFS), which looked at modifiable risk variables such as obesity, red meat eating, poor folic acid intake, alcohol use, physical inactivity, and cigarette smoking in early adulthood in connection to risk of colon cancer, found that revealed that adopting healthier lifestyles could lead to substantial risk reduction. Specifically, it was found that if all men in this middle-aged cohort were to rank within the lowest 20%, 10%, and 5% of risk scores, it could potentially result in the avoidance of 39%, 48%, and 55% of colon cancer cases, respectively (Platz *et al.*, 2000). The Danish National Food Agency conducted a detailed study involving 104 consecutive individuals who were physically fit and had just been diagnosed with metastatic breast cancer, small-cell lung cancer, or ovarian cancer. A recent study has indicated that a significant number of ambulatory cancer patients are not consuming sufficient calories to sustain their body weight. Furthermore, this research has revealed that even a modest weight reduction is connected with physical discomfort as well as poor life quality (Pal *et al.*, 2012).

Incorporating Foods for Cancer Prevention: Effective Methods and Ideas

To lower your susceptibility to various types of cancer and other serious illnesses, it is advisable to focus on foods that are high in antioxidants such as vegetables and fruits, nuts, legumes, grain-based products, and good fats (Figure 1). Concurrently, it's important to aim for a reduction in the consumption of refined carbs, sugary treats, and processed and fried foods. Enhancing your intake of antioxidants can contribute to risk reduction. Plant-based foods, abundant in antioxidants, bolster your immunity and protect against cancer. Fruit-rich diets have shown the potential in reducing the occurrence of stomach and lung cancer (Greenwald *et al.*, 2001). Carotenoids-rich foods, such as carrots as well as sprouts from Brussels, and squash, may reduce the incidence of lung, oral, pharynx, and laryngeal cancer. Non-starchy veggies including spinach, broccoli, and legumes can help prevent stomach and oesophageal cancer (Greenwald *et al.*, 2001; Pal *et al.*, 2012). Foods high in vitamin C, such as berries, peas, oranges, bell peppers, and deep green leafy vegetables, may also help reduce the incidence of oesophageal cancer. Additionally, including lycopene-rich foods like tomatoes, guava, and watermelon in your diet could potentially lower the risk of prostate cancer.

Dietary and Lifestyle Factors

Dietary changes, decreased physical activity, and a growing incidence of obesity have all been interconnected to a heightened risk of chronic diseases, although many of these connections have not been extensively studied or documented (Wolin *et al.*, 2009).

Obesity and physical activity

A sedentary lifestyle and Obesity have been associated with a higher susceptibility to various cancers, including breast and endometrial cancer. Achieving and maintaining a healthy weight through physical activity is a crucial component of maintaining energy balance. Physical activity encompasses a range of activities such as working, exercising, performing household chores, and engaging in leisure pursuits like walking, jogging, running, yoga, hiking, cycling, and swimming. Furthermore, regular exercise may help to reduce the occurrence of various types of cancer, such as cancer of the colon, postmenopausal breast cancer, and endometrial cancer (Wolin *et al.*, 2009). According to a 2009 meta-analysis of 52 epidemiological studies, persons who engaged in the most physical activity had a 24% lower chance of acquiring colon cancer than those who were the least active (Narimatsu & Yaguchi, 2022). According to a meta-analysis conducted in 2013, which examined 31 prospective studies, physical activity is connected with a 12% reduction in the chance of acquiring breast cancer. In contemporary life worldwide, obesity is a substantial risk factor for cancer. Endometrial cancer risk rises by 50% for every 5-point increase in BMI, while oesophageal adenocarcinoma risk rises by 48%, kidney cancer risk rises by 30%, liver cancer risk rises by 30%, postmenopausal breast cancer risk rises by 12%, pancreatic cancer risk rises by 10%, and colorectal cancer risk rises by an undetermined amount (WCRF/AICR, 2018c).

Fruits, vegetables, and whole grains

Epidemiological studies show that a high intake of fruits, vegetables, and whole grains is closely linked to a lower risk of cancer. Block *et al.* (1992) discovered that fruits and vegetables had a statistically significant preventative impact in 128 out of 156 trials that reported relative risks in a thorough evaluation of over 200 studies on the association between cancer and the consumption of fruits and vegetables. Notably, individuals in the lowest quartile (25% of the population) who eat the fewest vegetables and fruits had almost twice the risk of developing cancer as those in the highest quartile who consumed the most fruits and vegetables (Block *et al.*, 1992). When smoking is considered, increasing your intake of fruits and vegetables is linked to a lower risk of lung cancer. This dietary change is expected to result in an additional 20 to 33 percent reduction in lung cancer risk (WCRF/AICR, 1997). Cohort studies have found that the link between a healthy diet rich in fruits and vegetables and a lower risk of cancer is most pronounced for cancers of the digestive and respiratory systems, including the colon, lung, esophagus, and oral cavity. Cancers related to hormonal variables, such as breast, ovarian, cervical, endometrial, and prostate cancers, tend to have a lesser association (Fahey *et al.*, 1997). Sulforaphane, a chemical recognized for its anti-cancer qualities, is found in cruciferous vegetables such as broccoli, cauliflower, cabbage, and Brussels sprouts. Furthermore, scientists at the Beckman Research Institute in Hope, USA, discovered grape juice components that can inhibit aromatase, a crucial enzyme involved in estrogen production. As a result, grape juice has been proposed as a possible chemo-preventive agent for breast cancer. Because sulforaphane is so good at protecting against cancer, incorporating broccoli sprouts into an anti-cancer diet makes sense. Furthermore, selenium, a mineral with well-established anti-cancer effects, aids in the catalysis of oxidation-reduction reactions. These interactions can induce apoptosis in malignant cells, thereby aiding in their eradication (Chen *et al.*, 1998).

Dietary fats and fiber

The dietary fiber, which is commonly characterized as a set of naturally occurring chemicals in plant-based meals that resist digestion by human enzymes, may play a potential but not fully known function in cancer prevention. Typically, unprocessed plant-based foods are rich sources of dietary fiber. In contrast, meat, eggs, and dairy products share a common characteristic: they contain minimal or no fiber. Furthermore, most refined grain products have had the majority of their dietary fiber removed (Holmes *et al.*, 2004). As a result, a diet that predominantly consists of animal products and processed grains, which is common among Americans, tends to be lacking in dietary fiber. Notably, in prospective health studies, decreased fiber consumption did not demonstrate a significant connection with an increased risk of breast cancer. Overall, epidemiological research provides strong evidence for dietary fiber and fiber-rich foods' cancer-preventive qualities. Furthermore, some research suggests that fiber may have the capacity to reduce the risk-enhancing effects of dietary fat (National Research Council, 1989). The relationship between overall fat intake, particularly high-fat diets such as those containing meat, and various types of fats or fatty acids and the risk of cancer development has been thoroughly examined and explored (Potter, 1997).

While data from ecological and animal research suggests a direct link between increased total fat consumption and an increased risk of cancer at various sites, including the breast, colon/rectum, prostate, and lung, the processes involved remain unknown (Zhou, 1999). Steer clear of consuming processed and fried foods, like hard taco shells, French fries, fried chicken, crackers, cookies, cakes, muffins, pie crusts, and pizza dough, which often contain trans-fat or partially hydrogenated oils. Always aim to limit your saturated fat intake to no more than 10% of your daily calorie intake, primarily from sources like dairy and red meat. Instead, increase your consumption of healthier fats found in foods such as olive oil, almonds, avocados, and olives, which are rich in unsaturated fats. Consider including omega-3 fatty acids in your diet, which can be found in foods such as salmon, tuna, and flaxseeds. These fats have the potential to reduce inflammation and promote heart and brain health (WCRF/AICR, 2018b).

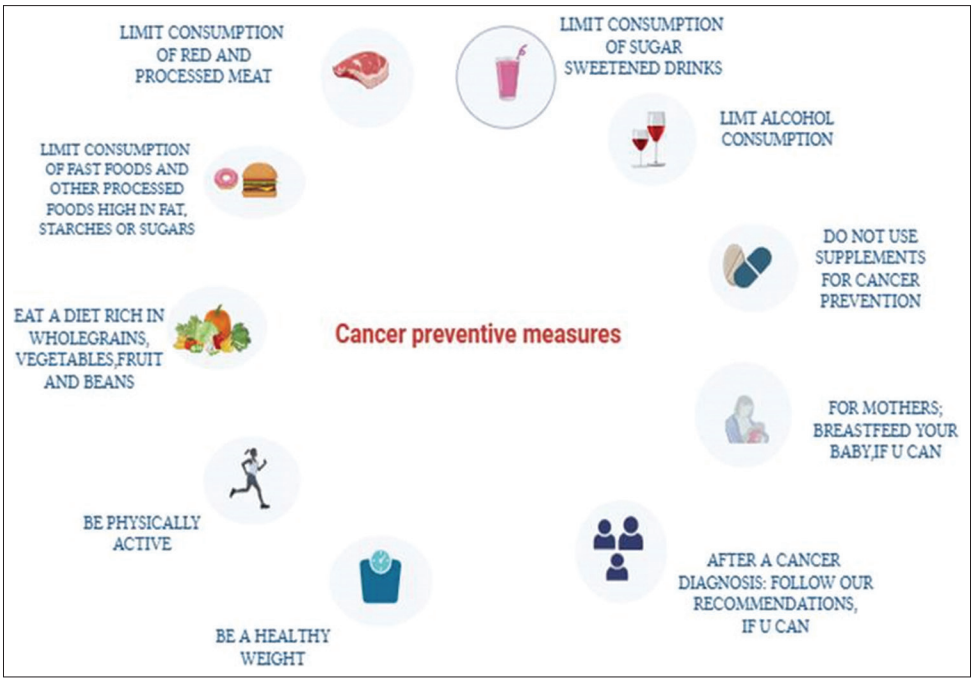

Figure 1: Schematic representation of Cancer preventive measures

Spices and food additives

India's dietary traditions have evolved over millennia, influenced by a blend of religious and secular principles. Research using human blood cancer cell lines has demonstrated that turmeric possesses the ability to inhibit and eliminate blood cancer cells (Maghimaa & Alharbi, 2020). In animal trials, turmeric has shown promise in impeding the development, progression, and metastasis of cancer (Mills *et al.*, 1989). Furthermore, a salt spice-herbal supplement known as Amrita Bindu was found to be effective in preventing cancer in rats caused by N-methyl-N-nitrosoguanidine, a powerful nitrosamine that causes cancer. Basil leaves and cumin seeds have been shown to significantly reduce the occurrence of Squamous cell carcinoma and hepatomas, while poppy seeds have shown substantial suppression of benzo[a]pyrene-induced SCC (Shanmugasundaram *et al.*, 1994).

Micronutrients

Many typical foods, particularly vegetables and fruits, are high in important micronutrients. Beta-carotene (a precursor to vitamin A), vitamin E, vitamin C, and selenium (all known for their antioxidant properties), as well as calcium, vitamin D (found in eggs, fish, and fortified dairy products), and folate, have all been the subject of extensive experimental and epidemiological research aimed at understanding their potential influence on cancer risk (IARC, 1998). Micronutrients serve an important role in safeguarding health and avoiding diseases such as cancer, through a multitude of processes such as antioxidation, anti-proliferation, and DNA repair. These essential nutrients are vital for supporting the body's defense mechanisms against cancer and other health threats (WCRF/AICR, 2018a). The potential of beta-carotene as an anticancer agent gained significant attention in the 1980s. Both case-control and cohort studies consistently show a link between a high diet of beta-carotene-rich foods and a lower risk of lung and stomach cancer. Multiple probable processes, including beta-carotene conversion to vitamin A and antioxidant characteristics, support the scientific justification for beta-carotene's position as a cancer-preventive agent (van Poppel & Goldbohm, 1995).

Research encompassing experiments, epidemiological investigations, and clinical trials has collectively revealed both direct and indirect connections between micronutrients and overall health. Notably, vitamin deficiencies, especially in vitamins C, A, and E, have been linked with a heightened prevalence of oral cancers (IARC, 1998; van Poppel & Goldbohm, 1995). This underscores the significance of adequate micronutrient intake in maintaining health and preventing diseases like oral cancer.

Alcohol

According to epidemiological studies, the connections between alcohol consumption and cancer risk are particular to both the kind of alcohol and the location of cancer. Alcohol intake has been associated with an increase in the occurrence of malignancies. in various areas, such as the larynx, pharynx, esophagus, and oral cavity, particularly when combined with smoking. Moreover, alcohol use has also been interconnected with an increased risk of breast, colorectal, liver, and pancreatic cancers (Kato & Nomura, 1994). The likelihood of developing aerodigestive malignancies is notably higher in individuals who concurrently use both tobacco and alcohol. Among this group, those who engage in regular smoking face the highest risk of developing these types of cancers (Castellsagué *et al.*, 1999; Takezaki *et al.*, 2000). In a study, it was observed that

consuming more than 150 mL of ethanol per day and smoking more cigarettes independently increased the chance of developing oesophageal cancer (with relative risks of 8.94 and 4.90, respectively). However, when these two behaviors are combined, oesophageal cancer risk will be doubled (Castellsagué *et al.*, 1999). Alcohol use and the risk of getting breast cancer have a dose-response relationship. A daily alcohol intake of two drinks, for example, relates to an estimated 25% increase in risk. This shows that higher amounts of alcohol use are associated with an increasing risk of breast cancer (Longnecker, 1994). Long-term and moderate alcohol intake may cause high insulin levels (hyperinsulinemia) in certain women, potentially stimulating the development of the IGF-I receptor in breast tissue. This activation might expedite the development of estrogen-independent precancerous lesions (Stoll, 1999). The risk of distal colon cancer associated with alcohol consumption increased after accounting for various factors such as the history of polyps/endoscopy, age, smoking, body mass index, physical activity, red meat consumption and total energy, use of multivitamins, and insufficient intake of folate and methionine. This suggests that alcohol may have a more significant impact on distal colon cancer risk when these factors are taken into consideration (Giovannucci *et al.*, 1995).

Dietary Interventions and Prevention of Cancer: Evidence from Clinical Trials

Controlled and Randomized trials in dietary modification and chemoprevention seek to answer concerns about the efficacy of various patterns of diet and ingredients in preventing cancer (primary prevention) or recurrence (secondary prevention). These trials are built upon the foundation of prior epidemiological and laboratory research on the interconnection between cancer prevention and diet (Kelloff *et al.*, 1994a). Dietary Alteration trials investigate how altering the consumption of nutritious foods like fruits, vegetables, and grains, as well as macronutrients like fats and fiber, can influence the risk of cancer. These studies seek to determine the impact of dietary changes on cancer prevention. On the other hand, chemoprevention trials examine how specific dietary components, such as vitamins, minerals, and phytochemicals found in natural foods or artificial substances like pharmaceutical drugs, can prevent or decrease the progression of cancer (Kelloff *et al.*, 1995). The initial phases of chemoprevention trials Phase I (assessing toxicological and pharmacological profiles) and Phase II (assessing biomarker endpoints), are designed to identify potential cancer-inhibitory agents and ascertain which ones offer the highest potential for both effectiveness and low toxicity. These trials play a crucial role in advancing our understanding of cancer prevention strategies and identifying promising interventions (Kelloff *et al.*, 1994b).

Chemoprevention

Chemoprevention is a potential and creative strategy for cancer prevention, like how high-risk individuals are taking cholesterol-lowering, antihypertensive, and antiplatelet drugs to reduce the risk of coronary heart disease. The idea of using chemopreventive medicines to lessen the risk of cancer is well-founded, supported by both epidemiological and experimental data accumulated over the past two decades. Research suggests that some drugs may impact carcinogenesis at numerous sites across the body, including the mouth, esophagus, stomach, colon/rectum, lung, breast, and prostate (Hakama, 1997). The National Cancer Institute (NCI) in the United States is actively engaged in a robust chemoprevention initiative, driven by the insights derived from both epidemiological and experimental research findings. Additionally, international organizations such as the International Union Against Cancer and the European Union have also expressed the belief that chemoprevention holds promise as an effective approach to reducing cancer risk. These efforts collectively underline the global recognition of chemoprevention's potential impact on cancer prevention (Greenwald *et al.*, 1995). Over 400 putative chemo-preventive drugs are now being investigated, with more than 25 compounds involved in approximately 60 ongoing clinical trials. Chemoprevention research takes a rigorous and stepwise strategy that includes several crucial stages. Identifying prospective novel medications that are either strongly indicated for preventing human cancer based on epidemiological studies or have proved efficient in preventing carcinogenesis in animal models is one of them. Following that, these promising compounds go through preclinical medication development, and if they continue to show promise, they move on to clinical intervention studies in Phases I, II, and III. This methodical approach provides for a complete assessment of prospective chemo-preventive drugs with the goal of lowering cancer risk (Sinha & Caporaso, 1999).

Gene-nutrient interaction

Human carcinogenesis likely involves a complex interplay of various genetic factors, including the function of tumor suppressor genes and oncogenes, the stability of chromosomes, cell cycle regulation, signal transduction processes, hormone pathways, vitamin metabolism routes, immune system function, receptor or neurotransmitter actions, and numerous more gene-related functions (Strickland & Groopman, 1995). The emerging field of gene-nutrient interactions has garnered significant interest in recent years and holds substantial promise in advancing the broader endeavor to minimize cancer development risk. To underscore the importance of these interactions in cancer research, consider the following examples, which also emphasize the role of genetic variations. Dietary carcinogens like polycyclic aromatic hydrocarbons (PAHs), aflatoxin B1 (AFB1), and HAAs have the capacity to modify DNA by forming adducts (Kelloff *et al.*, 1994b).

Biomarkers

Indeed, the identification of AFB1-DNA adducts secreted in urine can serve as a biomarker for aflatoxin exposure and the risk of developing liver cancer. Advancements in cancer prevention hinge on the confirmation and validation of biomarkers capable of identifying early, specific changes strongly linked to either the initiation or reversal of carcinogenesis (Greenwald & McDonald, 1997). Biomarkers play a pivotal role in pinpointing individuals at a heightened risk, making them potential candidates for

intervention studies aimed at cancer prevention. Not only do biomarkers possess the distinctive capacity to offer insights into mechanisms of action, but they also provide a strong rationale for the planning of large-scale trials, thereby enhancing the efficiency of applied preventive research (Qian *et al.*, 1994). While numerous potential biomarkers have been identified and extensively studied, none have been proven to be reliable indicators of cancer development. Genetic markers (such as micronuclei, gene amplification, and mutations), cellular markers (such as differentiation markers and measures of proliferation like the thymidine labeling index), histologic markers (such as premalignant lesions like leukoplakia and colonic polyps), and biochemical and pharmacological markers (such as ornithine decarboxylase activity) are among the many types of biomarkers (Qian *et al.*, 1994; Greenwald & McDonald, 1997). Chemopreventive agents are currently being evaluated in Phase II clinical trials for their impact on various dysplasia-based histologic biomarkers such as cervical intraepithelial neoplasia, prostatic intraepithelial neoplasia, dysplastic oral leukoplakia, colorectal adenomas, ductal carcinoma in situ, actinic keratosis and bronchial dysplastic metaplasia (Qian *et al.*, 1994).

CONCLUSION

The prevalence of cancer has risen significantly over time, making it a leading cause of death in some regions, surpassing even cardiovascular disease. This not only places a substantial burden on individuals suffering from cancer and other non-communicable illnesses but also impacts their families, caregivers, and society at large, given the significant economic implications associated with these conditions. Taking proactive steps to safeguard one's health is paramount in cancer prevention. Nearly half of all cancer cases can be averted through the adoption of a healthy lifestyle. A crucial component of cancer prevention revolves around maintaining a balanced diet. According to the NCI, it is advisable to consume alcoholic beverages in moderation. Other cancer preventive measures include frequent physical activity, the development of good eating and drinking habits, and the maintenance of a healthy body weight. Following these rules can significantly lower an individual's chance of acquiring cancer, helping to create a healthier overall environment. The integration of chemoprevention strategies with dietary adjustments can also prove effective in diminishing the cancer risk and associated death, particularly among individuals with a genetic predisposition to multiple types of tumors. These guidelines not only appear valuable in reducing personal cancer risk but also hold the potential to lay the foundation for future public education efforts and the establishment of health-promoting surroundings. Furthermore, the latest advancements in molecular and cellular biology are yielding valuable insights into the multifaceted process of carcinogenesis. These insights may open doors to novel approaches to cancer prevention and treatment, offering hope for a brighter future in the battle against cancer.

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