Chapter-5

Influence of Environment and Lifestyle on Cancer

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Abstract

Cancer remains a significant public health concern globally, with India facing its own set of challenges in combating this disease. A range of factors influencing cancer development is investigated, encompassing non-genetic factors such as lifestyle choices and environmental pollution. Lifestyle factors such as smoking, alcohol consumption and dietary habits contribute significantly to cancer incidence. The presence of carcinogens in environmental pollution, be it air, water, or soil pollution, is a factor in the increased incidence of cancers. Epidemiological evidences suggest link between exposure to pollutants and increased risk of cancer. Oxidative stress is identified as a crucial mechanism linking environmental exposures, lifestyle factors, and cancer development. Oxidative stress causes DNA damage, protein modification and changes in the transcriptional activation or repression of genes that are responsible for cellular homeostasis leading to increased risk of cancer. Present

challenges in cancer management include early detection, access to affordable treatment, and the rising burden of cancer-related morbidity and mortality. We should emphasise more on preventing the incidences of cancer. Strategies to reduce cancer incidence are crucial and encompass lifestyle modifications and efforts to mitigate environmental pollution. It has been argued that incidences of cancers can be remarkably reduced by adopting healthy lifestyles. A multidisciplinary approach focusing on lifestyle interventions and pollution reduction is essential for effective cancer prevention and treatment.

Keywords: Cancer, Oxidative stress, Lifestyle, Environment, Cancer Prevention

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1. INTRODUCTION

Cancer, an ominous word that instils fear and uncertainty in millions, stands as one of the greatest hurdles confronting modern medicine. Cancer represents a diverse array of diseases characterized by the unbridled growth and infiltration of abnormal cells. This transformation from normalcy to malignancy unfolds through a complex series of steps, involving changes in molecular composition and metabolic behaviour. The story of cancer spans millennia, with evidence of malignancies dating back to ancient civilizations. Yet, it wasn't until the dawn of modern medicine that scientists began to unravel the intricate complexities of this disease. The impact of cancer reverberates far beyond the individual patient, extending to families, communities, and societies at large. Indeed, cancer looms large as a significant public health crisis. The burden of cancer is not only measured in terms of mortality but also in terms of morbidity, diminished quality of life, and economic strain.

The transition from normal cells to invasive cancer cells is a gradual process that unfolds over years, shaped by intricate interplays among lifestyle choices, environmental factors, and individual genetics. Cancer, far from being a singular ailment, encompasses a diverse array of conditions distinguished by unique molecular signatures, clinical manifestations, and responses to treatment. Its reach spans across virtually every anatomical region of the body.

The fundamental characteristics of cancer serve as a framework for comprehending the complexities of tumorous diseases. These hallmarks include the sustained activation of signalling pathways promoting cell proliferation, evasion of mechanisms suppressing growth, resistance to programmed cell death, acquisition of limitless replicative potential, initiation of new blood

vessel formation, facilitation of invasion and metastasis, rewiring of energy metabolism, and avoidance of immune system surveillance (1). Dysregulated cellular metabolism sustains cancer cells by furnishing them with ATP energy and essential building blocks necessary for biosynthesis while maintaining the delicate balance of cellular redox status (2).

The stages of cancer can broadly be categorized into initiation, promotion, progression, and metastasis. Initiation marks the initial step in carcinogenesis, wherein normal cells undergo genetic alterations that confer them with the potential to become cancerous. The key hallmark of initiation is the acquisition of genetic mutations that disrupt normal cellular functions, allowing the affected cells to evade growth control mechanisms and proliferate autonomously. Following initiation, the promotion stage involves the clonal expansion of initiated cells, driven by mitogenic stimuli and microenvironmental cues. Proto-oncogenes may undergo further mutations, transforming them into oncogenes that drive hyperactive signalling pathways promoting cell proliferation and survival. Concurrently, tumor suppressor genes may be inactivated, removing critical checkpoints that restrain cell growth and apoptosis. This dysregulation of signalling pathways leads to the expansion of initiated cell clones, forming preneoplastic lesions or benign tumors. Progression represents the transition from benign or preneoplastic lesions to invasive and malignant tumors. During this stage, cancer cells acquire additional genetic and epigenetic alterations that confer them with increased proliferative potential, invasiveness, and resistance to cell death. These alterations may include chromosomal abnormalities, gene amplifications, and changes in DNA methylation patterns, among others.

Metastasis is the final and most devastating stage of cancer progression, wherein malignant cells spread from the primary tumor site to distant organs or tissues, establishing secondary tumors. Metastasis is a complex and orchestrated process that involves a series of sequential steps, including local invasion, intravasation, circulation through the bloodstream or lymphatic system, extravasation, and colonization of distant sites. Cancer cells may undergo phenotypic changes to adapt to the new microenvironment and evade immune surveillance, facilitating their survival and growth at metastatic sites. Metastasis is a major determinant of cancer morbidity and mortality, as it significantly reduces the effectiveness of treatment and complicates patient management.

The stages of cancer progression—from initiation to metastasis—are characterized by a sequence of genetic, molecular, and cellular alterations that drive the evolution of the disease. Each stage represents a critical juncture in the development of cancer, offering opportunities for intervention and therapeutic targeting.

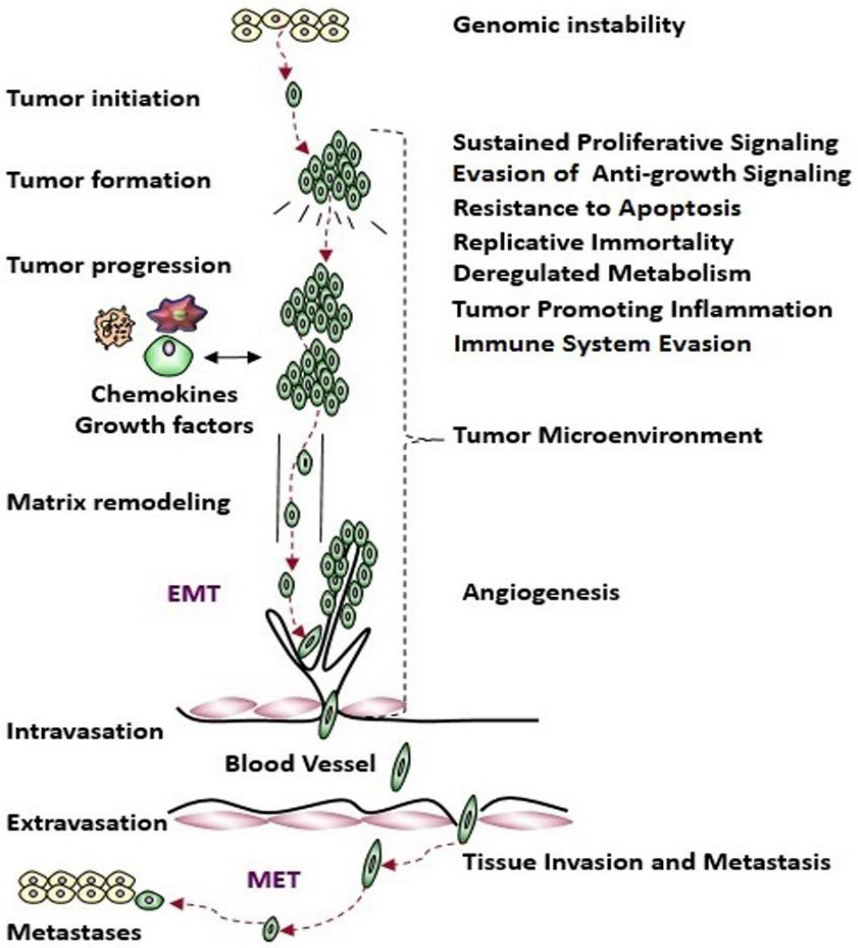

Figure 1: Stages of Cancer Development (3).

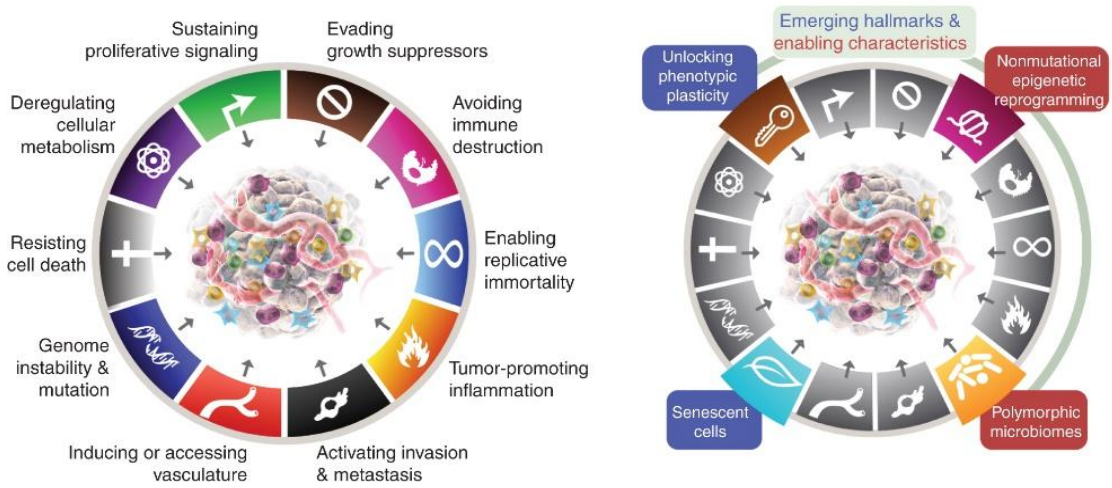

Figure 2: Hallmarks of Cancer. (A) Eight Hallmark Capabilities and Two Enabling Characteristics of Cancer (B) The Two Provisional Emerging Hallmarks of Cancer- Cellular Energetics and Avoiding Immune Destruction (1).

Attributable Cancer Burden Statistics

The International Agency for Research on Cancer (IARC), a division of the World Health Organization (WHO), annually publishes Global Cancer Statistics (GLOBOCAN). Cancer ranks as the second leading cause of death globally. Among the general population, lung, liver, and stomach cancers are the most fatal, with lung cancer being the primary cause of cancer-related mortality in men, and breast cancer holding that position in women. Statistics indicate a concerning trend: cancer morbidity and mortality rates are projected to surge. Furthermore, projections suggest that cancer will surpass all other causes of premature death by the end of this century, posing a significant obstacle to advancements in life expectancy (4).

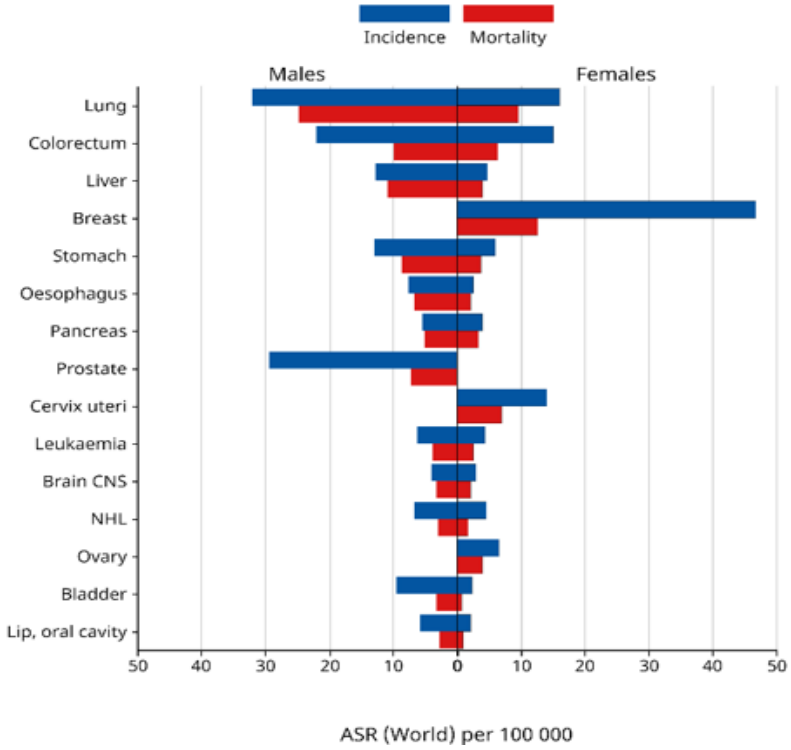

Figure 3: Age-Standardized Rate (World) per 100 000, Incidence and Mortality in 2022 (Top 15 Cancer sites).
Cancer TODAY IARC https://gco.iarc.who.int/en.

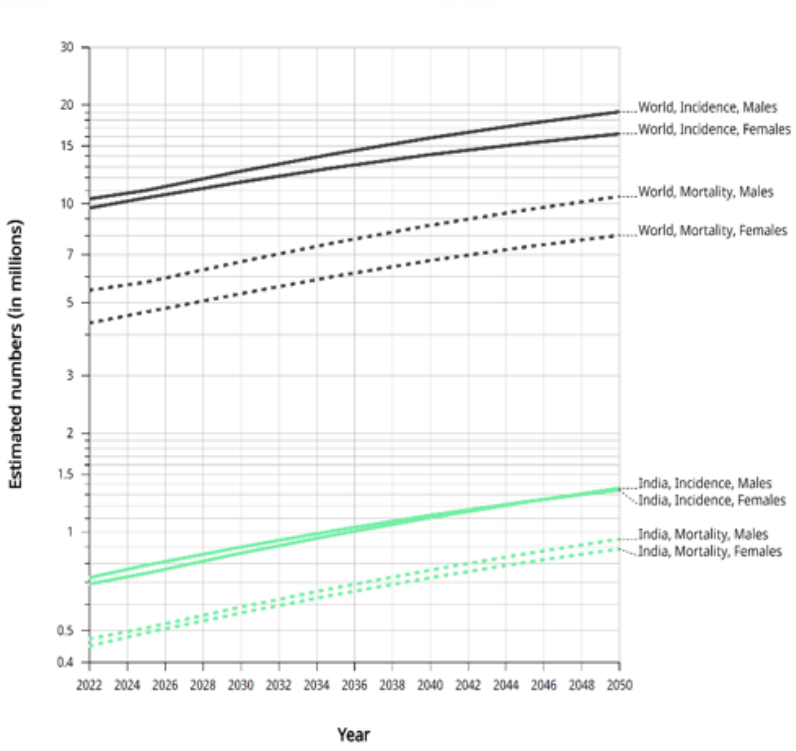

Figure 4: Estimated numbers from 2022 to 2050, (age: 0-85+). Cancer TODAY IARC https://gco.iarc.who.int/en.

Risk Factors of Cancer

Genomic researcher Craig Venter emphasizes the complexity of human biology, stating that it surpasses common perceptions. While genes inherited from parents are often discussed regarding various traits, Venter argues that their impact on life outcomes is minimal. He highlights the intricate nature of biology, which involves numerous independent factors—far beyond genetic inheritance. According to Venter, genes alone do not dictate our destiny; they may provide insights into disease risks but seldom determine actual disease causation or occurrence. Instead, he underscores the significance of the complex interplay between proteins, cells, and environmental influences in shaping biology. In essence, Venter suggests that while genes offer valuable information, the majority of biological outcomes arise from multifaceted interactions, rather than solely from genetic predisposition.

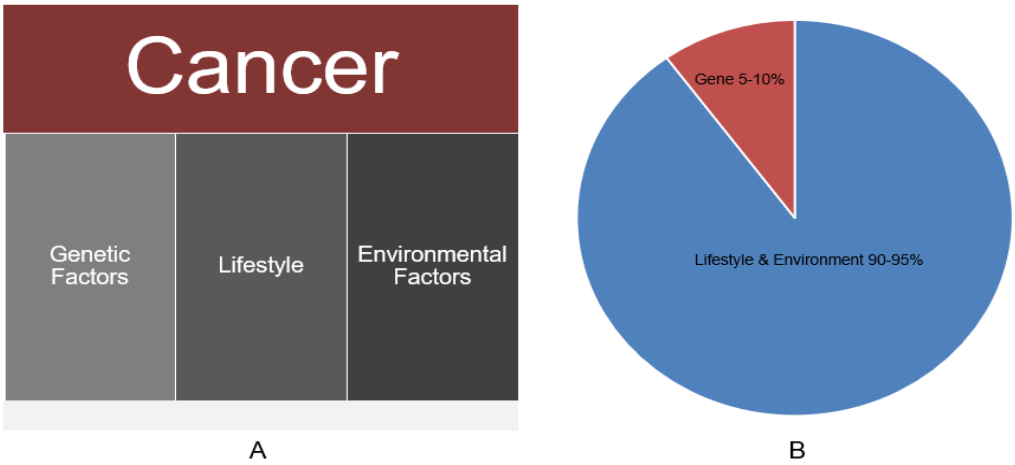

Figure 5: Risk Factors of cancer (A) Cancer arise from a complex interplay of genetic, environmental, and lifestyle factors.
(B) Lifestyle and Environment leads to more than 90% cancers.

Cancer arises from a complex interplay of genetic, environmental, and lifestyle influences. A mere 5–10% of cancers stem from inherited genetic abnormalities, while the majorities are attributed to lifestyle choices and environmental exposures. Every cancer emerges from a cascade of multiple mutations, largely influenced by interactions with the environment (5). Cancer arises from a combination of inherent and acquired factors, encompassing biological, genetic, environmental, and behavioural determinants. To grasp the complexities of cancer, a comprehensive approach is necessary, considering not only its genetic and biological underpinnings but also its social, environmental, and lifestyle components. While genetic predisposition can heighten susceptibility to certain cancers, environmental exposures and lifestyle decisions also significantly influence cancer risk. Lifestyle choices, though not direct cancer causes, serve as key risk factors linked to cancer development. Moreover, our exposure to both recognized and unidentified environmental carcinogens is continuous, underscoring the pervasive nature of cancer-inducing agents in our surroundings (6). In this in-depth analysis, we delve into the multifaceted dimensions of cancer, particularly emphasizing the influence of non-genetic factors. Influences of genetic, environmental, and lifestyle factors on cancer are:

I. **Genetic Factors:** Cancer is fundamentally a genetic disorder. While many cancer-causing mutations arise within the affected tissue during carcinogenesis, there's also a hereditary aspect. Predisposing mutations in the germline, which are inheritable, contribute to the onset of carcinogenesis. Cancer development unfolds through a series of stages marked by the accumulation of genetic mutations within a single ancestral cell. Proto-oncogenes, responsible for stimulating cell growth and survival, can undergo

mutations, transforming into oncogenes. These aberrant genes induce hyperactive signalling pathways, driving tumor expansion. Conversely, tumor suppressor genes, which typically hinder cell proliferation, may become inactive due to mutations or deletions. This loss eliminates crucial checkpoints that normally curtail the initiation of tumorigenesis.

II. Environmental Factors: Environmental factors play a pivotal role in cancer development. Carcinogens present in air, water, food, and workplace environments contribute to cancer risk. The complex relationship between cancer and the environment, shedding light on key environmental factors that shape cancer risk and the efforts to mitigate their impact.

Environmental pollutants are pervasive and often persistent, leading to daily exposure. These substances pose significant health risks and are implicated in disease development. Carcinogens, for instance, have the capacity to induce cancer by modifying cellular DNA, disrupting regular cellular functions, or fostering abnormal cell proliferation. They manifest in diverse forms within our surroundings, ranging from air and water pollutants to contaminants in soil and food, along with occupational hazards.

Table 1: Internation Agency for Research on Cancer (IARC) has classified carcinogens

Group	**Classification**
1	Carcinogen to Human
2a	Probable Carcinogenic to Humans
2b	Possibly Carcinogenic to Humans
3	Not Classified as to its Carcinogenicity to Humans

Numerous epidemiological studies indicate that exposure to certain environmental pollutants, even at minimal concentrations; can elevate the risk of cancer development (7). Intriguingly, the Asian continent, home to cities with the most elevated pollution levels (8), is so exhibits the highest incidence and mortality rates attributed to cancer (9).

The hazards of indoor pollution stemming from commonly used domestic chemicals, both historical and contemporary, are a growing concern. One such group of chemicals, known as PFAS (perfluoroalkyl and polyfluoroalkyl substances), encompasses approximately 5000 synthetic compounds employed since the 1940s to impart resistance to stains, water, and grease on surfaces. Among them, PFOA (perfluorooctanoic acid) stands out for its extensive use in non-stick cookware, despite its association with testicular and kidney cancer risks (10).

Furthermore, outdoor exposure to chemicals, particularly those utilized in agriculture, presents a significant threat to human health. Pesticides, in particular, can induce oxidative stress through complex mechanisms, disrupting the balance between pro-oxidants and antioxidants in various tissues. This imbalance often leads to alterations in antioxidant enzyme activity, contributing to health complications (11). Synthetic pesticides have been implicated in cancer development among farm workers (12).

III. **Radiation:** Radiation exposure alone can trigger genomic instability within cells, accelerating the occurrence of mutations and genetic alterations in subsequent generations of the irradiated cell after numerous replications. Ionizing radiation directly affects DNA, initiating cascades of growth factors, chemokines, and molecules that activate multiple signalling pathways. The majority of the harmful radiation we receive comes from nuclear radiation.

The Chernobyl disaster led to a rise in thyroid cancer cases in the nearby region, particularly affecting children and adolescents(13). Similarly, atomic bomb survivors in Hiroshima and Nagasaki demonstrate a notable linear dose-response relationship for thyroid nodules, encompassing both malignant tumors and benign nodules (14).

Solar radiation encompasses three primary wavelength bands: ultraviolet (UV) radiation (290- 400nm), visible light (400-760nm), and infrared (IR) radiation (760nm-1mm). Ultraviolet A radiation (UVA), can penetrate the skin gradually through cumulative exposure. UVA exposure is associated with genotoxic effects, leading to chromosome aberrations due to DNA strand breaks (15) conversely; UVB radiation induces the generation of ROS in epidermal cells and activates signalling pathways that contribute to cancer development (16). Ultraviolet radiation serves as a significant and widespread risk factor for cutaneous melanoma, emitted naturally by the sun as well as artificial sources. Cutaneous malignant melanoma primarily affects fair-skinned populations and is strongly linked to UVR exposure. Extensive epidemiological and mechanistic research has highlighted UVR exposure as the primary risk factor for both melanoma and non-melanoma skin cancers (17).

IARC has classified several metals and metalloids as known or probable carcinogens. These include iron, copper, cadmium, chromium, lead, mercury, nickel, and vanadium. These metals have the capability to generate reactive oxygen species (ROS) through processes resembling the Fenton reaction, which involves the production of superoxide anions and

hydroxyl radicals. This oxidative stress leads to molecular damage and disrupts cellular homeostasis, potentially contributing to cancer development (18).

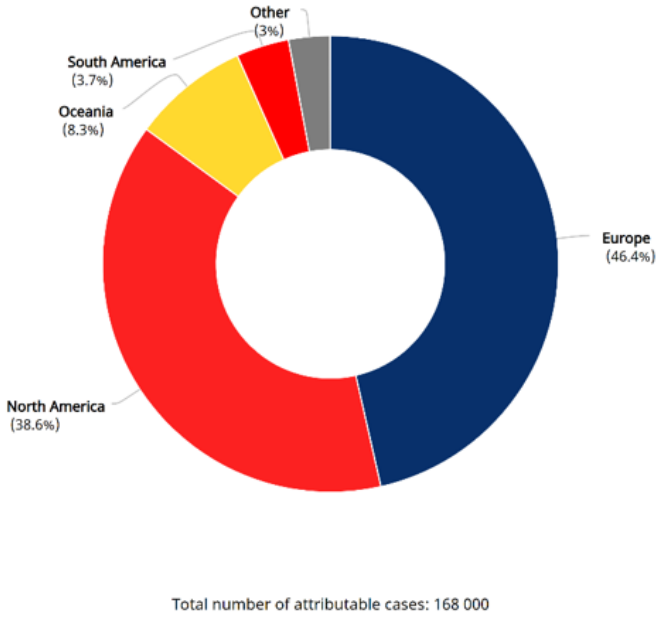

Figure 6: Cancer cases attributed to UV radiation.
Cancer TODAY IARC https://gco.iarc.who.int/en. (19).

IV. **Lifestyle:** Lifestyle decisions wield substantial influence within the complex realm of cancer, wielding significant influence, shaping individual risk profiles, and impacting disease progression. Our dietary preferences and behavioural patterns hold pivotal roles in dictating susceptibility to diverse cancer types. Moreover, the influence of lifestyle elements on cancer development was underscored in investigations involving monozygotic twins (20). The evolution of society is indispensably linked with lifestyle changes that increase cancer (21).

a. **Tobacco Smoking:** The consumption of tobacco elevates the likelihood of developing a minimum of 14 cancer types. Within tobacco are present over 50 carcinogens, including polycyclic aromatic hydrocarbons, nitrosamines, aromatic amines, aldehydes, volatile organic compounds, metals, and various others (22). A specific tobacco metabolite, benzopyrenediol epoxide, is directly linked with lung cancer (23). Smoking disrupts numerous cell signalling pathways and introduces high levels of free radicals found in cigarette smoke, which can induce DNA lesions and generate oxidized bases like 8-oxodG, a well-known biomarker of oxidative DNA damage (24). Cytochrome P450 (CYP) enzymes metabolize major carcinogens into DNA-reactive forms, with

certain CYP variants linked to increased risks of lung, esophageal, and head and neck cancers (25).

Cigarette smoking is the leading cause of lung cancer mortality globally. Understanding individual susceptibility to lung carcinogens is crucial for identifying those at highest risk. Studies on familial aggregation and linkage suggest that rare, high-penetrance genes may contribute to susceptibility differences (26).

b. Alcohol: Alcohol consumption, defined as the intake of beverages containing ethanol, is associated with an increased risk of several cancer types, including hepatocellular carcinoma, oesophageal squamous cell carcinoma, oral cancer, pharynx, colon, rectum, larynx, and breast. Scientific evidence supports the classification of alcohol as a human carcinogen based on epidemiological data (27). While alcohol itself is not mutagenic, it acts as a cocarcinogen, enhancing the effects of other carcinogens (28). Alcohol consumption promotes the production of ROS, contributing to cancer development (29).

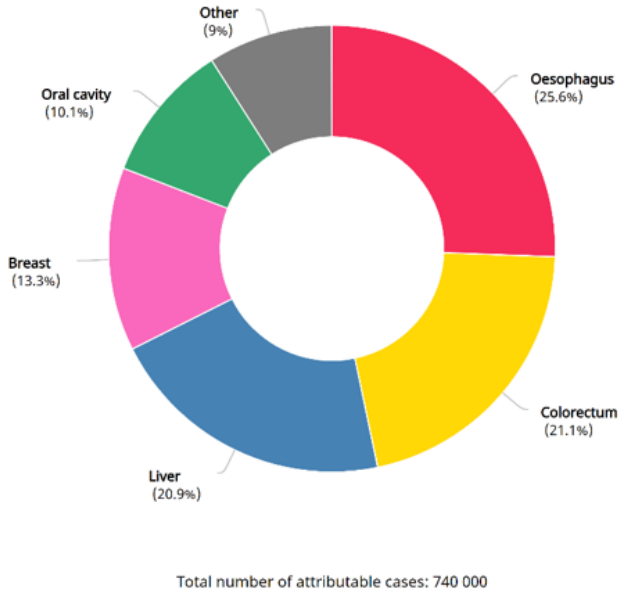

Figure 7: Estimated number of new cancer cases in 2020 attributed to alcohol drinking.
Cancer TODAY IARC https://gco.iarc.who.int/en. (30)

c. Obesity: Excess body mass index (BMI ≥ 25 kg/m²) is a well-established risk factor for various chronic diseases and mortality, including several types of cancers. These include oesophageal adenocarcinoma, colon, rectal, kidney, pancreas, gallbladder, post-menopausal breast, ovarian, and endometrial cancer (31). Moreover, higher body weight is associated with increased risks of site-specific cancers. For instance, each five-unit

increase in BMI correlates with higher risks of postmenopausal breast, colon, rectal, endometrial, oesophageal, gallbladder, kidney, liver, ovarian, pancreatic, stomach cardia, thyroid cancer, meningioma, and multiple myeloma (20). According to some studies, nearly 40% of all cancer cases can be attributed to overweight and obesity (32). The impact of overweight and obesity on cancer risks may vary based on sociodemographic factors. Epidemiological evidence indicates that the population attributable fraction of cancer is generally higher among women compared to men, and the burden of attributable cases is greater in countries with very high and high human development indices (31). Additionally, obesity leads to alterations in genes involved in insulin signalling, adipocyte metabolism, differentiation, and regulation of energy expenditure (33).

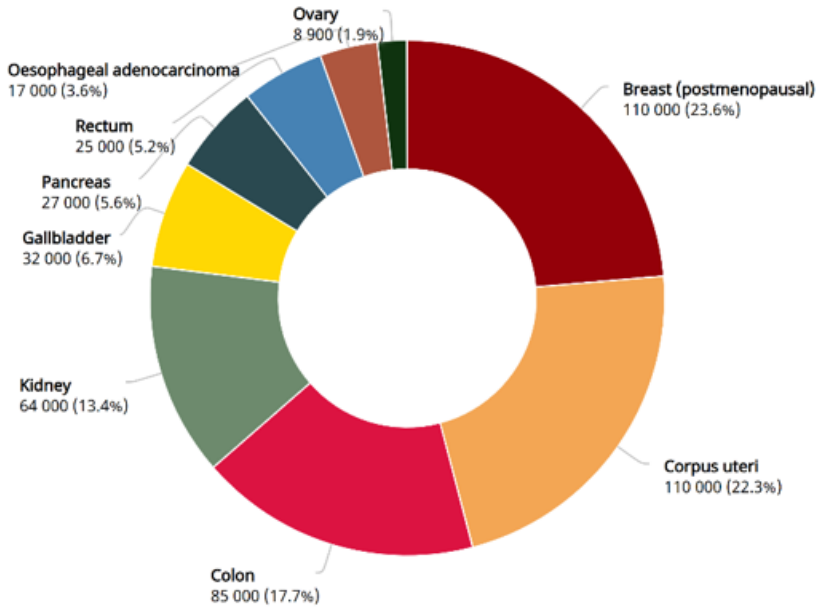

Figure 8: Cancer cases attributed to body mass index.
Cancer TODAY IARC https://gco.iarc.who.int/en. (31)

d. Diet: The familiar saying "you are what you eat" remains relevant when it comes to cancer prevention. Consuming a diet abundant in fruits, vegetables, whole grains, and lean proteins supplies vital nutrients and antioxidants, offering protection against cancer. Many ingested carcinogens, including nitrates, nitrosamines, pesticides, and dioxins, originate from food or food additives, as well as cooking methods. Diet is implicated in up to 70% of colorectal cancer fatalities. Moreover, excessive intake of red meat poses a risk factor for various cancers, particularly those affecting the gastrointestinal tract (34).

Research indicates that exposure to carcinogenic agents contributes to an overall increase in carcinogenic processes (Soffritti et al., 2008). Moreover, excessive consumption of calories derived from animal protein and fat, coupled with a deficient intake of fruits, cruciferous vegetables, carotenoid-rich vegetables, and leafy greens, has been linked to the development of certain cancers, such as non-Hodgkin lymphoma (36)

Fruits and vegetables are abundant sources of antioxidants, including vitamin C, vitamin E, carotenoids, natural flavonoids, and other compounds capable of neutralizing harmful oxidant species, thereby offering a dietary defence mechanism for our bodies (18). The World Health Organization attributes insufficient consumption of fruits and vegetables to 19% of stomach, 20% of esophagus, 12% of lung, and 2% of colorectal cancer cases worldwide (37).

e. **Occupational Exposure:** Occupational exposures were among the earliest recognized carcinogens (Purdue et al., 2015). Among these, asbestos exposure in occupational settings is recognized as the foremost contributor to the risk of lung cancer. Subsequent to asbestos, other notable occupational exposures associated with increased lung cancer risk encompass exposure to respirable crystalline silica, emissions from diesel engine exhaust, and welding fumes (39).

Preventing occupational cancers involves measures such as eliminating hazardous substances, improving worker protection, and reducing exposures. In high-income nations, there has been a decline in cancers linked to environmental and occupational carcinogens like asbestos, arsenic, and indoor and outdoor air pollution over recent decades compared to low- and middle-income countries (40). While reductions in exposure to occupational carcinogens have occurred in industrialized nations, efforts must also focus on minimizing exposure in developing countries. This necessitates comprehensive initiatives aimed at enhancing workplace safety standards, implementing effective regulations, and providing adequate training and resources for workers across all economic sectors.

f. **Infectious Agents:** Infectious pathogens represent potent and alterable factors contributing to cancer development. Among these microorganisms, oncogenic viruses stand out as the most firmly established pro-carcinogenic agents. Various groups of viruses have been associated with human cancer, indicating their capacity to initiate the process of carcinogenesis by inducing mutagenesis. Ten infectious pathogens that have been classified as carcinogenic to humans (Group 1) by IARC -

- One bacterium: *Helicobacter pylori*;
- Six viruses: hepatitis B virus (HBV), hepatitis C virus (HCV), human papillomavirus (HPV; types 16, 18, 6, 11, 31, 33, 45, 52, 58, and other HPV types), Epstein–Barr virus (EBV), human herpesvirus type 8 (HHV-8; also known as Kaposi sarcoma-associated herpesvirus), and human T-cell lymphotropic virus type 1 (HTLV-1); and
- Three parasites: *Opisthorchis viverrini*, *Clonorchis sinensis*, and *Schistosoma haematobium*.

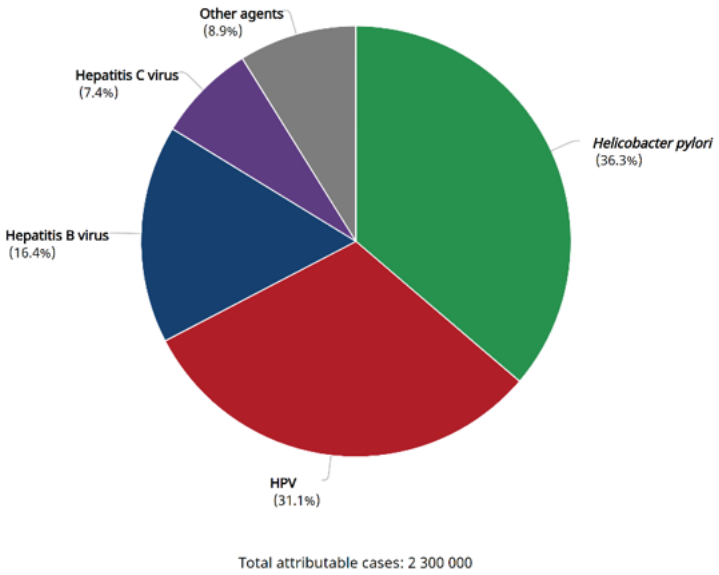

Figure 9: Cancer cases attributed to infectious agents. Cancer Today Iarc https://gco.iarc.who.int/en. (41).

2. OXIDATIVE STRESS AND CANCER

Aerobic respiration occurs within the mitochondria of eukaryotic cells to generate energy. Reactive species are categorized into four groups based on the primary atom involved: reactive oxygen species (ROS), reactive nitrogen species (RNS), reactive sulfur species (RSS), and reactive chloride species (RCS) (42). Among these, ROS are the most abundantly produced compounds derived from oxidative metabolism, including the superoxide anion radical, hydrogen peroxide, and hydroxyl radical. Major intracellular sources of ROS include the leakage of electrons to oxygen in mitochondria through reverse electron transport at complex I (43), the reduction of oxygen to superoxide by NADPH oxidases during growth factor signalling (44), and the production of hydrogen peroxide during protein folding within the endoplasmic reticulum (45). Cells naturally produce ROS during metabolism, which play roles in intracellular signalling. The antioxidant system within cells protects against oxidative damage. This system includes non-catalytic antioxidants such as

bilirubin, alpha-lipoic acid, melatonin, melanin, glutathione (GSH), and uric acid, as well as exogenously derived antioxidants like vitamin E, vitamin C, beta-carotene, and plant polyphenols (46) and catalytic antioxidants such as superoxide dismutase and catalase also contribute to cellular antioxidant defences.

Oxidative stress, characterized by an imbalance between reactive oxygen species (ROS) and antioxidants, is associated with numerous diseases (47). The detrimental effects of ROS on cells depend not only on their concentration but also on the equilibrium with endogenous antioxidant species. Disruption of the pro-oxidant/antioxidant balance leads to oxidative stress, causing damage to intracellular molecules such as DNA, RNA, lipids, and proteins (48). In cancer, cells display abnormal redox homeostasis. While ROS can be both pro-tumorigenic and cytotoxic at high levels (49), cancer cells must manage oxidative stress to maintain ROS levels within a dynamic range conducive to proliferation and avoidance of apoptosis. Imbalances induced by ROS in signalling pathways contribute to tumorigenesis (Wang, 2008). ROS play various roles in tumor development and progression, encompassing cellular proliferation activation, evasion of apoptosis, tissue invasion and metastasis, and angiogenesis. These biological processes are influenced by the effects of ROS on cellular signalling pathways and contribute to the pathogenesis of cancer.

Accumulations of genetic changes, including mutations and epigenetic modifications, play pivotal roles in the development of cancer. Mutations entail permanent alterations in the DNA sequence inherited by cells, while epigenetic changes involve modifications in the DNA structure. Both types of changes contribute to the accumulation of alterations in genes, a hallmark of cancer development. Virtually all cells are susceptible to genetic alterations, which can arise during cell division, leading to changes in the DNA sequence. Additionally, cells are constantly exposed to various agents capable of damaging DNA, including external factors such as lifestyle choices and pollution, as well as internal factors like free radicals and metabolic by-products. Cells possess mechanisms to safeguard against mutations, such as DNA repair mechanisms and apoptosis, which eliminate damaged cells. However, these protective mechanisms are not infallible and can sometimes fail, resulting in the emergence of cancerous cells. The development of cancer is closely associated with mutations that confer oncogenes with a gain of function and tumor suppressor genes with a loss of function. These genetic alterations disrupt normal cellular processes, driving the uncontrolled growth and proliferation, which is a characteristic of cancer cells.

3. PREVENTION AND REDUCTION OF CANCER – BASED ON LIFESTYLE MODIFICATIONS AND REDUCTION IN ENVIRONMENTAL POLLUTION

The treatment of cancer presents a complex challenge, with conventional methods like surgery, chemotherapy, and radiotherapy being mainstays while recent advancements offer promising alternatives. These include stem cell therapy, targeted therapy, ablation therapy, nanoparticles, natural antioxidants, radionics, chemo dynamic therapy, sonodynamic therapy, and ferroptosis-based therapy (50). Notably, cancer therapy often involves the generation of reactive oxygen species (ROS). Antioxidant treatment has shown efficacy against tumor cells by combating ROS (51). Natural polyphenols could induce apoptotic cell death in preneoplastic or neoplastic cells through various growth inhibitory mechanisms (48). ROS exhibit dual roles in cancer signalling, being both pro-tumorigenic and anti-tumorigenic, which can be manipulated for therapeutic purposes (52, 53). Chemotherapy drugs elevate ROS levels to toxic thresholds, depleting the antioxidant system and prompting programmed cell death. ROS-targeting therapy involves drugs like anthracyclines, cisplatin, bleomycin, and arsenic trioxide (54). Additionally, inhibiting ROS production in tumor cells can suppress pro-tumorigenic signalling, reducing metabolic adaptations, DNA damage, genetic instability, and ultimately inhibiting cell survival and proliferation (55).

Progress in cancer research faces persistent challenges in treatment due to cancer cells' ability to develop resistance and recur as more aggressive forms (56). However, many types of cancer are preventable, (57) and preventive measures have been shown to be cost-effective (58). Cancer prevention encompasses a range of strategies aimed at reducing cancer risk and lessening the impact of established cancer. There are three primary levels of cancer prevention (59)-

I. **Primary Prevention:** This involves eliminating or reducing cancer risk factors through adopting healthy behaviours and lifestyles. It's the simplest and most effective approach for preventing cancer in the general population.

II. **Secondary Prevention:** This entails screening to detect precancerous lesions, allowing for early intervention to prevent disease progression to malignancy.

III. **Tertiary Prevention:** This involves reducing or managing symptoms and morbidity associated with established cancer or cancer therapy.

While advancements in cancer treatment have been made, effective cancer screening and early detection remain crucial for reducing mortality.

However, only a select few cancer screening tests, such as those for cervical, breast, and colon cancers, have been widely adopted and proven to lower cancer mortality rates. Given the limited effectiveness of treatment against advanced cancer and the availability of screening for only a few cancer types, prioritizing cancer prevention is essential for reducing both cancer incidence and mortality.

The World Cancer Research Fund (WCRF) systematically evaluates and interprets the ever-growing body of scientific literature regarding the influence of diet, nutrition, and physical activity on cancer risk and survival (60). Implementing primary prevention strategies through behavioural and environmental interventions, often referred to as 'lifestyle changes,' is undoubtedly the most cost-effective approach to mitigating a significant burden of chronic and degenerative diseases globally, including cancer. These lifestyle modifications involve altering behaviours that can be adjusted to decrease disease incidence. Adopting healthy lifestyles has been shown to significantly reduce the risks of cancer morbidity and mortality, making it imperative to prioritize such measures for cancer prevention (61). However, primary prevention extends beyond individual behaviour changes; it necessitates broader transformations within social, economic, political, environmental, and cultural contexts.

The implementation of accelerated tobacco control programs, particularly in regions experiencing an increase in tobacco use, is essential for reducing tobacco-related cancer mortality rates. Tobacco consumption remains a leading preventable cause of cancer on a global scale.

There is a pressing need for concerted global efforts to address the rising prevalence of individuals with high body mass index (BMI) due to its association with various cancers (31). Evidence suggests that weight loss is linked to a reduced risk of obesity-related cancers, highlighting the importance of maintaining a healthy weight to combat non-communicable diseases (56). Regular physical activity not only enhances overall health and well-being but also serves as a critical component of cancer prevention strategies.

Helicobacter pylori (*H. pylori*) infection is recognized as a significant infectious cause of cancer worldwide, yet there is currently no vaccine available. While treatment for H. pylori infection appears to lower gastric cancer incidence, challenges remain regarding the broader implications of widespread antibiotic use on the human microbiome, optimal drug combinations in areas of rising antibiotic resistance, and cost-effective test-and-treat strategies for local settings (62).

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Access to cervical screening for detecting precancerous lesions has led to substantial reductions in incidence and mortality rates in high-income regions but remains limited in low-income and lower-middle-income countries. To achieve cervical cancer elimination targets by 2030, the World Health Organization (WHO) has set ambitious goals, including vaccinating 90% of girls against human papillomavirus (HPV) by age 15, screening 70% of women with a high-precision HPV test at ages 35 and 45, and ensuring 90% of women diagnosed with cervical disease receive treatment and care. These targets require strong commitments and concerted efforts globally (63).

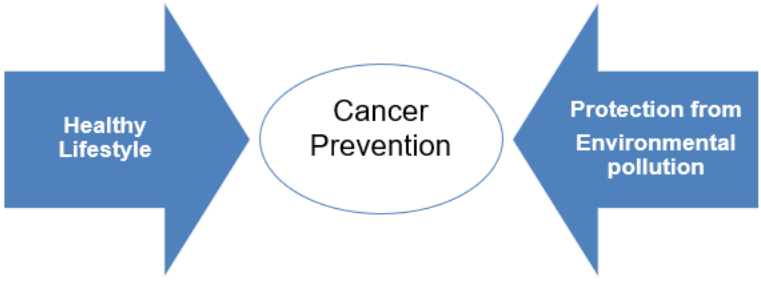

Figure 10: Cancer can be Prevented by Adopting Healthy Lifestyle and Protection from Environmental Pollution.

Based on current evidence, major health organizations such as the World Health Organization, the American Cancer Society, the World Cancer Research

Fund (WCRF), the American Institute for Cancer Research (AICR), and others advocate for the adoption of healthy lifestyles among the general population and cancer survivors to prevent cancer and enhance prognosis (61). While it's acknowledged that detectable levels of carcinogens exist in our bodies for all individuals (64), the development of cancer depends significantly on factors such as duration and intensity of exposure (65). To effectively combat cancer, it's imperative to address environmental pollution, which serves as a trigger for the disease

Given that the relationship between combined lifestyle factors and cancer morbidity and mortality remains consistent across different socioeconomic backgrounds, it's essential for each country and region to develop tailored policies that align with the preferences of local populations and the realities of public health practices. This approach can accelerate progress towards achieving Sustainable Development Goal target 3.4, which aims to reduce premature mortality from non-communicable diseases, including (20)

Table 2: WCRF/AICR Summary of Recommendations for Cancer Prevention

Risk Factor	Recommendations (66)
Obesity	Be at a healthy weight. Be physically active.
Diet	Eat a diet rich in whole grains, vegetables, fruit, and beans. Limit consumption of "fast foods" and other processed foods high in fat, starches, or sugars. Limit consumption of red and processed meat. Limit consumption of sugar-sweetened drinks.
Alcohol	Limit Alcohol consumption

4. CHALLENGES

Globally, the burden of cancer is escalating, posing significant challenges to individuals, families, communities, and healthcare systems both emotionally and financially. Particularly in low- and middle-income countries, health systems often lack the readiness to effectively address this growing burden, resulting in many cancer patients worldwide lacking access to timely and high-quality diagnosis and treatment. The root of the issue lies in our predominant focus on battling cancer rather than proactively preventing it by addressing its underlying triggers.

Environmental justice revolves around ensuring fair distribution of environmental benefits and burdens, encompassing access to clean air, water, and safe living conditions. Regrettably, marginalized communities frequently bear a disproportionate share of environmental pollution and its health

repercussions, including cancer. Efforts to mitigate environmental cancer risks involve various strategies, such as implementing stricter regulations, controlling pollution, monitoring the environment, implementing public health interventions, and empowering communities. By enacting more stringent environmental policies, advocating for clean energy sources, reducing emissions from industries and transportation, and rectifying environmental disparities, policymakers and activists can strive towards fostering healthier environments for all.

With robust evidences linking lifestyle factors to cancer risk, numerous national and international organizations have issued guidelines for cancer prevention. These guidelines emphasize the importance of measures such as smoking cessation and moderate alcohol consumption as key components of cancer prevention strategies.

5. CONCLUSIONS

In essence, the link between lifestyle, environment, and cancer is intricate and multi-layered. Cancer, being a complex ailment with numerous contributing factors, presents itself in various forms. We explore the intricate connection between lifestyle choices and the risk of cancer, highlighting areas where proactive steps can yield significant benefits.

Despite the daunting challenge that cancer poses, remarkable strides have been made in preventing, diagnosing, and treating the disease. Prevention strategies are geared towards minimizing exposure to carcinogens, encouraging healthy behaviours, and instituting screening initiatives for early detection. Continuous research, coupled with early identification and equitable access to quality healthcare, stands pivotal in the battle against cancer. Immediate policy measures are essential to encourage healthy lifestyles and foster environments that promote health, thereby reducing the risk of cancer. Preventive efforts can significantly alleviate the burden of many prevalent cancer types. A concerted global initiative, backed by sufficient resources and collaborative action, holds promise for diminishing the overall cancer burden. While primary prevention represents a long-term commitment, its implementation can substantially mitigate the suffering and fatalities caused by cancer. Moreover, by curbing the need for extensive cancer treatment, it can also alleviate healthcare costs. Therefore, primary prevention should be regarded as a fundamental component of contemporary and future cancer control strategies (67).

Although considerable headway has been achieved in comprehending and combating cancer, the journey towards comprehensive understanding and effective treatments continues. By fostering awareness, advocating for healthier

lifestyles, and bolstering cancer research endeavours, we strive towards a future where cancer's grip on human suffering and mortality is greatly diminished.

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