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RESEARCH ARTICLE

NUTRITION-LINKED DETERMINANTS OF CANCER INITIATION AND GROWTH

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Abstract: Cancer development is strongly influenced by modifiable dietary factors that shape metabolic, molecular, and inflammatory pathways involved in malignant transformation. This review synthesizes evidence from epidemiological observations, mechanistic studies, and meta-analytic findings to examine how nutrition contributes to cancer initiation and growth. Diets high in processed meats, saturated fats, refined carbohydrates, alcohol, and ultra-processed foods promote carcinogenesis through oxidative stress, chronic inflammation, genotoxic metabolite formation, and dysregulated hormonal signalling. Conversely, nutrient-dense dietary patterns rich in fiber, phytochemicals, polyphenols, and antioxidants demonstrate protective effects by modulating immune function, stabilizing the genome, improving metabolic homeostasis, and maintaining a healthy gut microbiome. The review identifies the interactions between dietary components and biological pathways such as DNA damage, epigenetic modifications, metabolic reprogramming, and cell-proliferative signalling. Challenges in isolating diet–cancer causal pathways, variation in dietary assessment methods, and population-specific risk differences are critically discussed. Overall, nutrition emerges as a central determinant of cancer risk and progression, underscoring the need for evidence-based dietary recommendations to support global cancer prevention strategies.

Keywords: Nutrition; Cancer initiation; Carcinogenesis; Dietary patterns; Processed foods; Red and processed meat; Antioxidants; Polyphenols; Fiber; Epigenetics; Oxidative stress; Gut microbiota; Metabolic pathways; Dietary carcinogens; Cancer prevention..

INTRODUCTION

Cancer remains a leading cause of morbidity and mortality worldwide, with dietary habits recognized as one of the most influential modifiable determinants of cancer risk. According to global reports, 30–50% of cancer cases could be prevented through healthier dietary and lifestyle practices. Diet influences carcinogenesis at multiple biological levels, from the formation of DNA-damaging compounds to systemic inflammation and metabolic dysregulation. High consumption of energy-dense, nutrient-poor foods—such as processed meats, fried foods, saturated fats, and sugary beverages—has been linked to elevated risks of colorectal, breast, gastric, prostate, liver, and pancreatic cancers. Conversely, plant-based dietary patterns rich in antioxidants, fibers, phytochemicals, and polyunsaturated fats provide protective benefits by reducing oxidative stress, enhancing immune defense, regulating hormones, and supporting gut microbiota diversity.

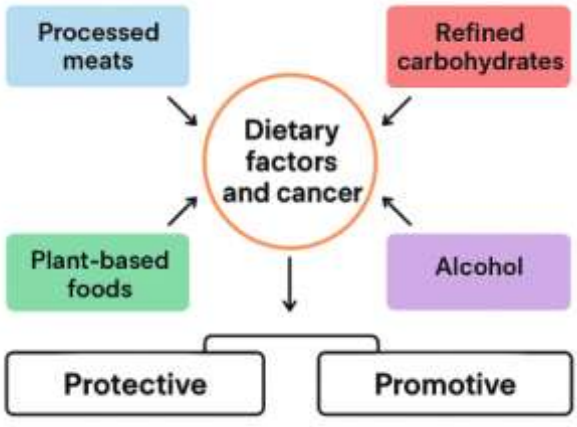

Fig 1: Various dietary factors

LITERATURE REVIEW

Dietary Patterns and Overall Cancer Risk

Large global reports consistently show that diet is one of the most influential modifiable determinants of cancer development. The World Cancer Research Fund/AICR (2018) highlighted strong evidence linking dietary patterns, obesity, and alcohol intake to the onset of several cancers. Similarly**,** Islami et al. (2018) estimated that nearly 40% of cancers in the U.S. could be prevented by addressing modifiable lifestyle factors, especially nutrition.

Mediterranean dietary patterns—rich in vegetables, fruits, whole grains, and unsaturated fats—are repeatedly associated with lower cancer incidence. Couto et al. (2011) demonstrated that high adherence to the Mediterranean diet significantly reduced overall cancer risk in the EPIC cohort, a finding supported by Morze et al. (2020) and Grosso et al. (2017) through multiple systematic reviews and meta-analyses.

Red and Processed Meat Consumption

Consumption of red and processed meat is classified as carcinogenic by the International Agency for Research on Cancer (2015) due to strong associations with colorectal cancer. This relationship is reinforced by epidemiological evidence from Aykan (2015)**,** who highlighted mechanisms involving heme iron, nitrosamines, and cooking-derived mutagens.

Formation of heterocyclic aromatic amines (HAAs**)** during high-temperature meat cooking is a key mechanistic driver of mutagenesis in colorectal tissues. Nadeem et al. (2021) reviewed the formation, occurrence, and biological consequences of HAAs, concluding that frequent exposure significantly contributes to cancer risk.

Ultra-Processed Foods and Carcinogenic Additives

Ultra-processed food intake has emerged as a modern nutritional risk factor. In a large cohort study, Fiolet et al. (2018) reported that a 10% increase in ultra-processed food consumption was associated with a significant rise in overall cancer risk, particularly breast cancer. These foods contribute to carcinogenesis through high levels of sodium, additives, refined sugars, and endocrine-disrupting contaminants.

Another concerning group of food-derived carcinogens includes acrylamide**,** a compound formed during frying or baking carbohydrate-rich foods. Systematic reviews by Virk-Baker et al. (2014) and Pelucchi et al. (2015), Vijai Krishna V et al (2025), Jeeva V et al (2025), Nirmala B et al (2025) and Ramesh M et al (2025).

revealed that long-term dietary acrylamide exposure moderately increases the risk of renal, ovarian, and endometrial cancers.

Dietary Fiber, Whole Grains, and Protective Foods

Dietary fiber plays a fundamental protective role. A large dose–response meta-analysis by Aune et al. (2011) showed that increased fiber and whole-grain intake substantially lowers the risk of colorectal cancer. Mechanisms include enhanced gut motility, dilution of carcinogens, production of protective short-chain fatty acids, and reduction of systemic inflammation.

Plant-based diets also offer protection due to lower intake of carcinogenic compounds and higher levels of phytochemicals. Findings from the EPIC-Oxford cohort **(**Key et al., 2014**)** revealed reduced cancer incidence in vegetarians, although cancer-site specificity varies.

Antioxidants, Phytochemicals, and Bioactive Compounds

Dietary antioxidants mitigate oxidative DNA damage and inhibit tumorigenesis. A comprehensive review by Zheng et al. (2020) highlighted the protective effects of vitamins C and E, carotenoids, polyphenols, and flavonoids in reducing cancer risk across multiple organ systems.

Further, Schwingshackl et al. (2015**)** reported that consumption of fruits, vegetables, legumes, and nuts significantly decreases cancer incidence, underscoring the biological relevance of anti-inflammatory and anti-proliferative compounds in plant foods.

Alcohol Consumption and Cancer Development

Alcohol is a well-established carcinogen affecting multiple organ systems. Bagnardi et al. (2015) and Rumgay et al. (2021**)** demonstrated dose–response relationships between alcohol intake and site-specific cancers, including breast, colorectal, liver, esophageal, and oropharyngeal cancers. Mechanistic pathways include acetaldehyde-induced DNA damage, hormonal disruption, and oxidative stress.

Globally, Rumgay et al. (2021**)** estimated that alcohol consumption contributed to over 741,000 new cancer cases in 2020, emphasizing its enormous public health impact.

Obesity, Weight Gain, and Diet-Related Metabolic Pathways

Obesity is strongly influenced by diet quality and caloric intake and is a major risk factor for cancer. Shi et al. (2024) found that both elevated BMI and long-term weight gain significantly increase risk for breast, colorectal, pancreatic, liver, and endometrial cancers. These effects are mediated by chronic inflammation, insulin resistance, adipokine imbalance, and increased estrogen production in adipose tissue.

Global epidemiological data, such as those from Bray et al. (2018)**,** show a dramatic rise in obesity-related cancers worldwide, driven by shifts toward Westernized dietary patterns.

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MATERIALS AND METHODS

Biological mechanisms linking diet to cancer

Diet influences carcinogenesis through multiple, often interacting biological pathways. These can be grouped into (1) direct genotoxic mechanisms, (2) metabolic/hormonal mechanisms, (3) inflammation / immune modulation, (4) microbiome-mediated mechanisms, and (5) epigenetic and signaling changes.

Direct genotoxic mechanisms

- Cooking- and processing-derived mutagens: High-temperature cooking and smoking of meat produce heterocyclic aromatic amines (HAAs) and polycyclic aromatic hydrocarbons (PAHs) which form DNA adducts that induce point mutations and chromosomal instability—key events in initiation. (Nadeem et al., 2021; IARC, 2015).
- Nitrosation/N-nitroso compounds (NOCs): Processed meats and endogenous nitrosation form NOCs that alkylate DNA bases and cause miscoding during replication (IARC, 2015; Aykan, 2015).
- Acrylamide/glycidamide: Formed in high-temperature cooking of starchy foods; metabolite glycidamide is genotoxic and has been linked in some studies to increased cancer risk (Virk-Baker et al., 2014; Pelucchi et al., 2015).

Metabolic and hormonal mechanisms

- Insulin / IGF axis: Diets high in refined carbohydrates and sugars lead to repeated hyperinsulinemia; insulin and IGF-1 stimulate proliferative signaling (PI3K/AKT/mTOR), inhibit apoptosis, and favor tumor progression (Grosso et al., 2017).
- Obesity-related hormones: Excess adiposity (often diet-driven) elevates insulin, leptin, and estrogen (via peripheral aromatization), and lowers adiponectin—conditions that promote proliferation and chronic cell survival signaling implicated in breast, endometrial and colorectal cancers (Shi et al., 2024; Bray et al., 2018).

Chronic inflammation and oxidative stress

- Pro-inflammatory diets (high in trans fats, processed foods, and red meat) raise systemic inflammatory mediators (TNF-α, IL-6, CRP) and generate reactive oxygen species (ROS), which cause oxidized bases in DNA and promote mutation accumulation and tumor-promoting microenvironments (World Cancer Research Fund/AICR, 2018; Schwingshackl et al., 2015).
- Alcohol contributes via acetaldehyde-induced DNA damage and by increasing ROS production and inflammatory signaling (Bagnardi et al., 2015; Rumgay et al., 2021).

Microbiome-mediated mechanisms

- Diet shapes gut microbiota composition; low-fiber, high-meat, and ultra-processed diets favor dysbiotic communities that generate genotoxic metabolites (secondary bile acids, hydrogen sulfide) and reduce beneficial short-chain fatty acids (SCFAs) like butyrate—SCFAs normally support epithelial health and suppress inflammation (Aune et al., 2011; Key et al., 2014).
- Certain bacteria can also convert dietary components into carcinogens (e.g., nitrate/nitrite metabolism).

Epigenetic and signaling modifications

- Nutrient availability and bioactives (folate, polyphenols, vitamin D, etc.) influence DNA methylation, histone marks and microRNA expression—changing gene expression in ways that can either suppress or promote tumorigenesis depending on timing and dose (Zheng et al., 2020; Grosso et al., 2017).
- Many phytochemicals modulate signaling pathways (NF-κB, Nrf2, Wnt/β-catenin), giving anti-inflammatory or pro-apoptotic effects.

Epidemiological associations

Epidemiology provides population-level evidence linking diet to site-specific cancer risks. Different study designs (cohort, case–control, pooled analyses, RCTs, meta-analyses) give different strengths of evidence.

Processed/red meat → colorectal cancer

- Consensus evidence: Processed meat is classified by IARC as carcinogenic (colorectal), with consistent dose–response associations in cohort and pooled analyses (IARC, 2015; Aykan, 2015).
- Magnitude: Many meta-analyses report modest but consistent relative-risk increases per 50 g/day of processed meat.

Dietary fiber/whole grains → lower colorectal cancer risk

- Strong inverse associations observed in large prospective meta-analyses (Aune et al., 2011). Mechanistic plausibility (SCFA production, reduced transit time) strengthens causal interpretation.

Mediterranean / plant-rich dietary patterns → lower overall cancer incidence

- Multiple cohorts and meta-analyses (Couto et al., 2011; Morze et al., 2020; Grosso et al., 2017) show that Mediterranean and similar plant-forward patterns associate with reduced incidence of several cancers, including gastrointestinal and breast sites.

Ultra-processed foods (UPFs) → increased cancer risk

- NutriNet-Santé reported positive associations between UPF intake and overall / site-specific cancers (Fiolet et al., 2018). Evidence is emerging and mechanistic hypotheses include additive exposures, energy density, and processing-related contaminants.

Alcohol → multiple cancers (dose-response)

- Robust dose–response evidence links alcohol to cancers of the oral cavity, pharynx, larynx, esophagus, liver, colorectum, and breast (Bagnardi et al., 2015; Rumgay et al., 2021). Population-attributable burden is substantial (Rumgay et al., 2021).

Obesity / BMI and weight gain → many cancer sites

• Higher BMI and adult weight gain are associated with increased incidence of multiple cancers, especially endometrial, postmenopausal breast, colorectal, pancreatic and liver cancers (Shi et al., 2024; Bray et al., 2018).

Dietary patterns: integrating components and interactions

Studying patterns (Mediterranean, Western, vegetarian) captures synergistic or antagonistic interactions among foods and nutrients, and generally yields more stable associations than isolated nutrients:

• Mediterranean / plant-based patterns: associated with lower all-cause and cancer-specific incidence; effects likely arise from combined high intake of fiber, antioxidants, healthy fats, and low processed food exposure (Couto et al., 2011; Morze et al., 2020).

• Western pattern: high in processed meat, refined grains, sweets and UPFs—associated with obesity and higher cancer risk (Grosso et al., 2017; Fiolet et al., 2018).

• Vegetarian patterns show mixed results by site but generally lower overall incidence for some cancers (Key et al., 2014).

Exposure measurement error

• Dietary assessment methods (FFQs, 24-hr recalls, food diaries) vary in accuracy. Misclassification attenuates true associations and can produce null or inconsistent results, especially for foods consumed episodically (e.g., grilled meat). (World Cancer Research Fund/AICR, 2018)

Residual confounding

• Lifestyle covariates (smoking, alcohol, physical activity), socioeconomic status, and other dietary factors may confound associations. If not fully controlled, apparent effects may be biased. For example, high processed-meat consumers may also smoke or exercise less.

Reverse causation and selection bias

• In some cohorts, preclinical disease may lead to dietary change (reverse causation). Case–control designs are particularly susceptible to recall bias (cases recalling diet differently).

Population heterogeneity & effect modification

• Genetic polymorphisms (e.g., in metabolizing enzymes), baseline nutrient status, gut microbiome composition, and sex/age differences can modify effects—leading to heterogeneity across studies and populations (Zheng et al., 2020).

RESULTS AND OBSERVATIONS:

Mechanistic Pathways Linking Diet to Cancer

Oxidative stress

Processed foods and alcohol increase ROS formation, causing DNA damage and promoting mutations.

Inflammatory signaling

High-fat and high-sugar diets activate NF-κB, IL-6, TNF-α, and CRP, creating a pro-tumor environment.

Epigenetic modifications

Bioactive food compounds influence methylation and histone modification, altering gene expression involved in cancer.

Microbiome alterations

Diet determines microbial diversity; dysbiosis increases carcinogen production and intestinal inflammation.

Obesity-linked hormonal disruption

Excess adiposity increases estrogen, insulin, and IGF-1 levels, accelerating tumor development.

Epidemiological Evidence

Large cohort studies confirm:

- High red/processed meat → ↑ colorectal cancer
- High alcohol consumption → ↑ liver, breast, esophageal cancers
- High UPF intake → ↑ overall cancer risk
- Mediterranean diet → ↓ cancer incidence
- High fiber intake → ↓ colorectal cancer

These findings highlight consistent dose-response trends.

The interplay between nutrition, inflammation, hormones, DNA damage, and microbiota demonstrates that cancer is multifactorial. Protective plant-based foods act through synergistic antioxidative and anti-inflammatory pathways, whereas carcinogenic dietary elements initiate early molecular changes that progress into malignancy.

Table 1: Comparison of Dietary Factors and Their Associated Cancer Risks

Dietary Factor	Primary Cancer Types Linked	Biological Mechanisms Involved	Epidemiological Evidence (Summary)
Processed Meat	Colorectal, stomach	N-nitroso compounds, heme iron, heterocyclic amines (HCAs)	Multiple cohort studies show ↑ CRC risk by 15–18%
Red Meat	Colorectal	Heme iron → oxidative stress and DNA damage	Moderate association in dose-response meta-analyses
Alcohol	Breast, liver, colorectal	Acetaldehyde toxicity, ROS, altered hormone metabolism	Strong dose-response; 100 g/week increases risk
Low Fiber Intake	Colorectal	Reduced SCFA production, impaired microbiome diversity	Consistent protective effect of whole grains and fiber
High UPF Intake	Multiple cancers	Additives, emulsifiers, neo-formed compounds, inflammation	Cohort studies show ↑ overall cancer risk 10–12%
High Sugar Intake	Obesity-related cancers	Insulin resistance, IGF-1 activation, chronic inflammation	Associated with breast and endometrial cancer risk
Mediterranean Diet	Overall cancer prevention	High antioxidants, polyphenols, anti-inflammatory components	Strong inverse association across multiple cohorts
Plant-Rich Diet	Overall reduction	Fiber, phytochemicals, gut microbiota modulation	Lower incidence in vegetarians and plant-forward diets
High Fat Western Diet	Colon, breast, prostate	Increased bile acids, lipid peroxidation, chronic inflammation	Linked to higher incidence and poor prognosis
Antioxidant-Rich Diet	Multiple cancers	Scavenges ROS, prevents DNA damage	Evidence varies but generally protective

CONCLUSION

Nutrition is a crucial determinant of cancer initiation and progression. Diets rich in processed meats, refined sugars, alcohol, and ultra-processed foods significantly promote carcinogenic processes, whereas plant-based, antioxidant-rich diets demonstrate strong protective benefits. Improving population dietary habits could substantially reduce global cancer burden. Evidence clearly supports prioritizing whole foods, increasing fiber intake, and limiting carcinogenic dietary exposures.

FUTURE SCOPE

- Integration of personalized nutrition with genomics and metabolomics
- Development of population-specific dietary guidelines
- Longitudinal studies to understand early dietary exposures
- Exploration of microbiome-targeted dietary interventions
- Improved assessment tools for dietary intake in cancer research

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