Review



# The World's Five Deadliest Cancers: Current Trends, Therapeutics, and Future Directions

Ashutosh Kumar Maurya †, Bhoomika Singh †, Ranjeet Dungdung, Tannu Dahiya, Lakavath Shiva, Veeru Singh, Deepak Prajapati, Satish Prajapati, Ashish Kumar, Sachidananda Behera, Vikas Kumar Nayak, Soniya Nayak, Anupriya Ekka, Dhanraj Saran, Manraj Meena *

Posted Date: 30 December 2025

doi: 10.20944/preprints202512.2612.v1

Keywords: breast cancer; lung cancer; colorectal cancer; prostate cancer; cervical cancer

 doi:10.20944/preprints202512.2612.v1



*Review*

# The World's Five Deadliest Cancers: Current Trends, Therapeutics, and Future Directions

**Ashutosh Kumar Maurya [1,†], Bhoomika Singh [2,†], Ranjeet Dungdung [1], Tannu Dahiya [1], Lakavath Shiva [3], Veeru Singh [4], Deepak Prajapati [4], Satish Prajapati [4], Ashish Kumar [2], Sachidananda Behera [2], Vikash Kumar Nayak [2], Soniya Nayak [2], Anupriya Ekka [2], Dhanraj Saran [5] and Manraj Meena [6,*]**

[1] Department of Biochemistry and Mol. Biology, Central University of Kerala, Kasaragod, Kerala, India
[2] Department of Education, Central University of Kerala, Kasaragod, Kerala, India
[3] Department of Genomic Science, Central University of Kerala, Kasaragod, Kerala, India
[4] Department of Biotechnology, Bundelkhand University, India
[5] Department of Hindi, Central University of Kerala, Kasaragod, Kerala, India
[6] Department of Physics, Shyam Lal College, University of Delhi, New Delhi, India
* Correspondence: mannumeena2015@gmail.com
† Equal Contribution.

**Abstract**

Cancer remains a leading cause of death worldwide, with breast, lung, colorectal, prostate, and cervical cancers contributing significantly to global cancer-related morbidity and mortality. While individual lethality varies among these cancers, their combined impact on public health is substantial due to high incidence and, in some cases, limited access to early detection and effective treatment. These malignancies arise from a complex interplay of genetic, hormonal, lifestyle, and infectious factors, with molecular mechanisms that inform targeted therapies and precision medicine approaches. Advances in screening, immunotherapy, AI-assisted diagnostics, and minimally invasive surgical techniques have improved outcomes; however, challenges such as late diagnosis, treatment resistance, and healthcare disparities persist, particularly in low- and middle-income countries. This review provides a comprehensive synthesis of the epidemiology, risk factors, molecular pathogenesis, clinical features, current treatment strategies, emerging technologies, public health implications, and future research directions for the five deadliest cancers. Emphasis is placed on preventive measures, early detection, and equitable access to care, highlighting strategies to reduce the global cancer burden and improve survival outcomes.

**Keywords:** breast cancer; lung cancer; colorectal cancer; prostate cancer; cervical cancer

## 1. Introduction

Cancer remains one of the leading causes of morbidity and mortality worldwide and represents a major challenge to global health systems despite significant advances in prevention, early detection, and treatment strategies [1,2]. Recent global estimates indicate that approximately 20 million new cancer cases and nearly 10 million cancer-related deaths occurred worldwide in 2022, highlighting the substantial and growing global cancer burden [1,3].

The rising incidence of cancer is driven by multiple demographic and lifestyle-related factors, including population growth, aging, urbanization, and the increasing prevalence of modifiable risk factors such as tobacco use, unhealthy diet, physical inactivity, and harmful alcohol consumption [2,4]. It is estimated that nearly one-third of cancer deaths are attributable to preventable risk factors, while infectious agents such as human papillomavirus, hepatitis B virus, and hepatitis C virus account for a significant proportion of cancers, particularly in low- and middle-income countries [2,5].

 doi:10.20944/preprints202512.2612.v1



Although more than one hundred distinct cancer types have been identified, a relatively small number account for the majority of new diagnoses and cancer-related deaths worldwide [3,6]. Breast cancer, lung cancer, colorectal cancer, prostate cancer, and cervical cancer consistently rank among the most commonly diagnosed malignancies globally, though their incidence and mortality patterns vary considerably by sex, geographic region, and socioeconomic status [1,3,6].

Cancer development is a multifactorial process resulting from complex interactions between genetic susceptibility and environmental, behavioral, and biological exposures [4,7]. Advances in molecular and cellular biology have elucidated key mechanisms of tumorigenesis, including genetic mutations, epigenetic alterations, dysregulated signaling pathways, and interactions within the tumor microenvironment [7,8]. These insights have facilitated the development of targeted therapies and immunotherapeutic approaches, which have significantly improved outcomes for several cancer types [8,9]. Nevertheless, major challenges persist, including late-stage diagnosis, therapeutic resistance, treatment-related toxicity, and unequal access to advanced cancer care [2,9].

In parallel with therapeutic advancements, cancer prevention and early detection strategies have become central to global cancer control efforts [2,10]. Primary prevention through risk factor modification, vaccination against oncogenic viruses, and secondary prevention via organized screening programs have demonstrated substantial potential to reduce cancer incidence and mortality [5,10,11]. However, the implementation and effectiveness of these interventions remain uneven across regions, underscoring persistent disparities in healthcare infrastructure, resource allocation, and public health policy [2,11].

The objective of this narrative review is to provide a comprehensive overview of the five most common cancers worldwide—breast, lung, colorectal, prostate, and cervical cancers—focusing on their epidemiology, etiological factors, pathophysiology, current treatment modalities, and prevention strategies. Furthermore, this review aims to critically examine existing challenges and identify future needs in research, clinical practice, and public health to support the development of integrated and sustainable strategies for global cancer control.

## 2. Methodology of Literature Review

This narrative review was conducted to synthesize current evidence on the epidemiology, etiology, pathophysiology, treatment modalities, prevention strategies, and future needs related to the five most common cancers worldwide: breast, lung, colorectal, prostate, and cervical cancers. A narrative approach was selected to allow comprehensive integration of clinical, molecular, and public health perspectives across diverse study designs and global settings.

### *2.1. Literature Search Strategy*

A comprehensive literature search was performed using major electronic databases, including PubMed/MEDLINE, Scopus, and Web of Science, to identify relevant peer-reviewed publications. The search strategy combined Medical Subject Headings (MeSH) and free-text terms related to cancer burden, epidemiology, risk factors, molecular mechanisms, treatment, prevention, and future directions. Key search terms included combinations of *"breast cancer," "lung cancer," "colorectal cancer," "prostate cancer," "cervical cancer," "epidemiology," "risk factors," "treatment," "screening," "prevention,"* and *"global burden."*

The search primarily focused on articles published within the last 10–15 years to ensure relevance and inclusion of recent advances, while landmark and highly cited older studies were included where appropriate to provide foundational context [12,13].

### *2.2. Inclusion and Exclusion Criteria*

Eligible articles included original research studies, systematic reviews, meta-analyses, clinical guidelines, and authoritative reports from international organizations such as the World Health Organization (WHO) and the International Agency for Research on Cancer (IARC). Studies

 doi:10.20944/preprints202512.2612.v1



addressing global or regional cancer epidemiology, biological mechanisms, therapeutic approaches, and prevention strategies were prioritized.

Articles were excluded if they were non–peer-reviewed, lacked relevance to the five selected cancers, or focused exclusively on highly specific subpopulations without broader applicability. Only publications in the English language were considered.

### *2.3. Data Extraction and Synthesis*

Relevant data were extracted and qualitatively synthesized to summarize trends in cancer incidence and mortality, established and emerging risk factors, molecular and pathophysiological mechanisms, current standards of care, and prevention strategies. Given the narrative nature of this review, findings were integrated thematically rather than through quantitative meta-analysis, allowing comparison across cancer types and identification of common challenges and unmet needs [14].

### *2.4. Quality and Reporting Considerations*

To enhance reliability and transparency, preference was given to high-quality studies, including large population-based analyses, randomized controlled trials, and consensus guidelines. Reporting standards and recommendations for narrative reviews were considered during manuscript preparation to ensure clarity, balance, and reproducibility [15].

## 3. Global Overview of the Top Five Most Common Cancers

Cancer incidence and mortality vary considerably across regions; however, a small group of malignancies consistently accounts for a substantial proportion of the global cancer burden. Breast cancer, lung cancer, colorectal cancer, prostate cancer, and cervical cancer together represent a major share of new cancer diagnoses and cancer-related deaths worldwide, with marked differences observed by sex, age, geographic location, and socioeconomic development [16,17].

According to the most recent global estimates, breast cancer is the most frequently diagnosed cancer worldwide, having surpassed lung cancer in overall incidence, and remains the leading cause of cancer-related mortality among women [1,16]. Lung cancer continues to be the leading cause of cancer death globally in both sexes combined, largely due to its aggressive nature and late-stage diagnosis in most patients [1,18]. Colorectal cancer ranks among the top three most commonly diagnosed cancers worldwide and is a leading cause of cancer mortality in both high-income and transitioning economies, reflecting the widespread adoption of Westernized diets and sedentary lifestyles [16,19].

Prostate cancer is the most commonly diagnosed cancer among men in many regions, particularly in North America, Europe, and parts of the Caribbean, with incidence strongly influenced by population aging and prostate-specific antigen (PSA) testing practices [16,20]. Although prostate cancer generally has a favorable prognosis when detected early, it remains a significant contributor to cancer morbidity and mortality due to advanced and treatment-resistant disease in a subset of patients [20]. Cervical cancer, while largely preventable through effective screening and vaccination, remains one of the leading causes of cancer-related death among women in low- and middle-income countries, reflecting persistent inequities in access to preventive healthcare services [11,21].

Geographic disparities in cancer burden are pronounced. High-income countries report higher incidence rates for breast, colorectal, and prostate cancers, largely attributable to lifestyle factors and robust diagnostic capacity, whereas low- and middle-income countries experience disproportionately higher mortality rates due to delayed diagnosis and limited access to treatment [17,21]. Lung cancer incidence and mortality closely mirror global tobacco consumption patterns, while infection-associated cancers, including cervical cancer, remain more prevalent in regions with limited vaccination and screening coverage [5,21].

 doi:10.20944/preprints202512.2612.v1



Temporal trends indicate that while overall cancer incidence continues to rise globally, mortality rates for certain cancers—such as breast and colorectal cancer—have declined in several high-income countries due to improvements in early detection and treatment [18,19]. In contrast, many low-resource settings continue to experience increasing incidence and mortality, underscoring the urgent need for global cancer control strategies that integrate prevention, early diagnosis, and equitable access to care [17,22].

Collectively, these five cancers illustrate both the progress achieved and the persistent challenges in global oncology. Understanding their shared and distinct epidemiological patterns provides a critical foundation for evaluating risk factors, therapeutic approaches, and future priorities, which are explored in the subsequent sections of this review.

## 4. Breast Cancer

### *4.1. Epidemiology*

Breast cancer is the most commonly diagnosed cancer among women worldwide and represents a leading cause of cancer-related mortality [23,24]. In 2022, an estimated 2.3 million new cases were reported globally, accounting for nearly 12% of all cancer diagnoses [23]. Incidence is highest in high-income regions, such as North America, Western Europe, and Oceania, whereas mortality rates remain disproportionately high in low- and middle-income countries due to late-stage diagnosis and limited access to treatment [23,25]. Age is a significant factor; incidence rises sharply after 40 years, with the highest rates observed among women aged 50–69 years [24].

### *4.2. Etiology and Risk Factors*

Breast cancer etiology is multifactorial, involving genetic, hormonal, environmental, and lifestyle factors. Major risk factors include:

- Genetic predisposition: Mutations in BRCA1 and BRCA2 significantly increase lifetime risk [26]. Other genetic variants, including TP53, PALB2, and CHEK2, contribute to susceptibility [27].
- Hormonal factors: Early menarche, late menopause, nulliparity, late age at first childbirth, and prolonged exposure to exogenous hormones are associated with elevated risk [28].
- Lifestyle factors: Obesity, physical inactivity, alcohol consumption, and high-fat diet have been consistently linked to increased breast cancer risk [29].
- Environmental exposures: Ionizing radiation, endocrine-disrupting chemicals, and urban pollution may contribute to carcinogenesis [30].
- Family history: A positive family history of breast cancer increases risk independently of known genetic mutations [27].

### *4.3. Molecular and Pathophysiological Mechanisms*

Breast cancer is heterogeneous at the molecular level, with several clinically relevant subtypes defined by receptor status: hormone receptor-positive (estrogen and/or progesterone), HER2-positive, and triple-negative breast cancer (TNBC) [31]. Pathogenesis involves genetic mutations, epigenetic dysregulation, and alterations in signaling pathways, including PI3K/AKT/mTOR, MAPK, and p53-mediated apoptosis [32]. Tumor microenvironment, angiogenesis, and immune evasion also play key roles in tumor progression and metastasis [32,33].

### *4.4. Clinical Presentation and Diagnosis*

Early-stage breast cancer is often asymptomatic and detected via screening mammography [34]. Clinical presentation may include a palpable breast lump, nipple discharge, skin changes, or lymphadenopathy [34]. Diagnosis relies on imaging (mammography, ultrasound, MRI) and histopathological confirmation through biopsy. Staging is based on tumor size, nodal involvement, and distant metastasis (TNM system) [34].

 doi:10.20944/preprints202512.2612.v1



### *4.5. Current Treatment Modalities*

Management of breast cancer is multimodal and guided by tumor subtype, stage, and patient factors:

- Surgery: Lumpectomy or mastectomy remains the cornerstone of treatment [35].
- Radiotherapy: Often used postoperatively to reduce local recurrence risk [35].
- Chemotherapy: Neoadjuvant or adjuvant regimens, particularly for high-risk or triple-negative cases [36].
- Hormonal therapy: Tamoxifen, aromatase inhibitors, or ovarian suppression for hormone receptor-positive tumors [37].
- Targeted therapy: HER2-positive tumors are treated with trastuzumab, pertuzumab, and other HER2 inhibitors [38].
- Immunotherapy: Checkpoint inhibitors (e.g., pembrolizumab) show promise in TNBC [39].

### *4.6. Prevention Strategies*

Primary prevention focuses on lifestyle modifications, including maintaining healthy weight, regular physical activity, limiting alcohol intake, and breastfeeding [29]. Secondary prevention relies on organized screening programs, such as mammography and clinical breast exams, to detect tumors at an early, treatable stage [40]. Genetic counseling and prophylactic interventions may be offered to high-risk individuals [26].

### *4.7. Challenges and Limitations*

Despite advances, challenges remain, including disparities in screening and treatment access, overtreatment of low-risk tumors, chemoresistance, and aggressive subtypes such as TNBC [25,39]. Late diagnosis and delayed treatment in resource-limited settings contribute significantly to mortality [23,25].

### *4.8. Future Needs and Research Directions*

Emerging strategies include precision medicine approaches using genomic profiling, development of novel targeted therapies, immunotherapy combinations, liquid biopsy for early detection, and AI-assisted imaging for screening [32,41,42]. Strengthening global access to screening and equitable treatment remains a priority for reducing breast cancer mortality worldwide [25,40].

## 5. Lung Cancer

### *5.1. Epidemiology*

Lung cancer remains the leading cause of cancer-related mortality globally, responsible for approximately 1.8 million deaths in 2020, despite being the second most commonly diagnosed cancer overall [43,44]. Incidence and mortality rates vary widely by region, largely reflecting differences in tobacco use, air pollution, occupational exposures, and healthcare access [44,45]. Age is a major factor, with most cases occurring in individuals aged 60–75 years [44].

### *5.2. Etiology and Risk Factors*

The etiology of lung cancer is multifactorial:

- Tobacco smoking: Responsible for 85–90% of lung cancer cases in high-income countries [46]. Both active and passive smoking significantly increase risk.
- Environmental exposures: Air pollution, particularly particulate matter (PM2.5), radon, and occupational carcinogens (asbestos, silica) contribute to risk [47,48].
- Genetic susceptibility: Rare germline mutations and polymorphisms in genes such as EGFR, TP53, and KRAS can influence individual susceptibility [49].

 doi:10.20944/preprints202512.2612.v1



- Other factors: Chronic lung diseases (COPD, pulmonary fibrosis), prior radiation, and dietary deficiencies have been implicated [50].

### *5.3. Molecular and Pathophysiological Mechanisms*

Lung cancer is classified primarily into two histological types: non-small cell lung cancer (NSCLC, ~85%) and small cell lung cancer (SCLC, ~15%) [51]. NSCLC subtypes include adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. Pathogenesis involves genetic mutations, epigenetic changes, and dysregulation of signaling pathways such as EGFR, KRAS, ALK, and TP53 [52,53]. Tumor heterogeneity and the tumor microenvironment play crucial roles in tumor progression, metastasis, and response to therapy [53].

### *5.4. Clinical Presentation and Diagnosis*

Early-stage lung cancer is often asymptomatic, making early detection challenging. Common symptoms include persistent cough, hemoptysis, dyspnea, chest pain, and unexplained weight loss [54]. Diagnosis relies on imaging (chest X-ray, CT scan, PET-CT) and tissue biopsy for histopathological and molecular characterization. Staging is based on the TNM system [54,55].

### *5.5. Current Treatment Modalities*

Treatment depends on histology, stage, molecular characteristics, and patient performance status:

- Surgery: Lobectomy or pneumonectomy is preferred for early-stage NSCLC [56].
- Radiotherapy: Stereotactic body radiotherapy (SBRT) is effective for non-surgical candidates [56].
- Chemotherapy: Platinum-based doublets are standard for advanced disease [57].
- Targeted therapy: EGFR, ALK, ROS1, BRAF, and NTRK inhibitors have improved outcomes in molecularly selected patients [58].
- Immunotherapy: Immune checkpoint inhibitors (PD-1/PD-L1 and CTLA-4 inhibitors) are increasingly used, alone or in combination with chemotherapy, especially for advanced NSCLC [59].

SCLC is typically treated with chemotherapy and radiotherapy due to its aggressive nature and early metastatic spread [51].

### *5.6. Prevention Strategies*

Primary prevention focuses on tobacco control (smoking cessation programs, taxation, public awareness), reducing exposure to environmental carcinogens, and workplace safety [46,47]. Secondary prevention includes low-dose CT screening for high-risk individuals, which has been shown to reduce lung cancer mortality [60].

### *5.7. Challenges and Limitations*

Challenges include late-stage diagnosis, aggressive disease biology (especially in SCLC), acquired resistance to targeted therapies, and limited access to advanced diagnostics and treatments in resource-constrained regions [44,59]. Disparities in smoking prevalence, environmental exposures, and healthcare infrastructure contribute to unequal outcomes globally [45,47].

### *5.8. Future Needs and Research Directions*

Future directions include the development of novel targeted therapies and immunotherapeutic strategies, early detection biomarkers (liquid biopsies), AI-assisted imaging for screening, and integration of precision medicine approaches [53,61,62]. Expanding global access to prevention,

 doi:10.20944/preprints202512.2612.v1



screening, and state-of-the-art treatments is essential to reduce the burden of lung cancer worldwide [44,60].

## 6. Colorectal Cancer

### *6.1. Epidemiology*

Colorectal cancer (CRC) is the third most commonly diagnosed cancer worldwide and the second leading cause of cancer-related deaths, with approximately 1.9 million new cases and 935,000 deaths reported in 2020 [63,64]. Incidence is higher in high-income countries, particularly in Europe, North America, and Australia, although recent trends indicate increasing incidence in several low- and middle-income countries due to westernized diets and lifestyle changes [65,66]. CRC predominantly affects individuals over 50 years, but early-onset cases (<50 years) are rising, especially in high-income regions [64,66].

### *6.2. Etiology and Risk Factors*

CRC is a multifactorial disease resulting from genetic, environmental, and lifestyle-related factors:

- Genetic predisposition: Approximately 5–10% of CRC cases are hereditary, with conditions such as Lynch syndrome (hereditary nonpolyposis colorectal cancer) and familial adenomatous polyposis (FAP) being significant contributors [67].
- Lifestyle factors: Diets high in red and processed meats, low fiber intake, physical inactivity, obesity, and alcohol consumption increase risk [68].
- Inflammatory bowel disease: Long-standing ulcerative colitis or Crohn's disease is associated with elevated CRC risk [69].
- Other factors: Age, male sex, diabetes, and gut microbiome alterations are additional contributors [70,71].

### *6.3. Molecular and Pathophysiological Mechanisms*

CRC develops through accumulation of genetic and epigenetic alterations that drive malignant transformation of colonic epithelial cells. The adenoma-carcinoma sequence is a well-described pathway involving mutations in APC, KRAS, TP53, and SMAD4, along with chromosomal instability [72,73]. Microsatellite instability (MSI) and CpG island methylator phenotype (CIMP) also contribute to tumor heterogeneity [74]. Dysregulation of signaling pathways such as Wnt/β-catenin, EGFR, and TGF-β underpins tumor initiation and progression [72,75].

### *6.4. Clinical Presentation and Diagnosis*

Early-stage CRC is often asymptomatic, highlighting the importance of screening. Symptoms may include rectal bleeding, change in bowel habits, abdominal pain, unexplained weight loss, and anemia [76]. Diagnosis is confirmed via colonoscopy with histopathological evaluation. Staging relies on the TNM system and is crucial for guiding management [76,77].

### *6.5. Current Treatment Modalities*

Treatment depends on tumor stage, location, molecular profile, and patient health:

- Surgery: Standard treatment for localized CRC; includes colectomy or proctectomy with lymph node dissection [78].
- Chemotherapy: Adjuvant chemotherapy is recommended for stage III and high-risk stage II CRC; regimens commonly include FOLFOX (5-fluorouracil, leucovorin, oxaliplatin) or CAPOX (capecitabine, oxaliplatin) [79].

 doi:10.20944/preprints202512.2612.v1



- Radiotherapy: Primarily used for rectal cancer to reduce local recurrence, often in combination with chemotherapy [80].
- Targeted therapy: Anti-EGFR monoclonal antibodies (cetuximab, panitumumab) and anti-VEGF agents (bevacizumab) are used in metastatic CRC with specific molecular profiles [81].
- Immunotherapy: Checkpoint inhibitors, such as pembrolizumab and nivolumab, are effective in MSI-high tumors [82].

### *6.6. Prevention Strategies*

Primary prevention includes dietary modifications, regular physical activity, maintaining healthy body weight, limiting alcohol consumption, and avoiding smoking [68]. Secondary prevention relies on population-based screening programs (fecal immunochemical test, colonoscopy, or sigmoidoscopy), which have been shown to reduce CRC incidence and mortality [76,83]. High-risk individuals with hereditary syndromes require specialized surveillance [67].

### *6.7. Challenges and Limitations*

Key challenges in CRC management include late-stage diagnosis, disparities in access to screening and treatment, chemoresistance in advanced disease, and increasing incidence in younger populations [64,66,79]. Health system constraints in low-resource settings contribute to poorer outcomes [65].

### *6.8. Future Needs and Research Directions*

Future directions include precision medicine approaches using molecular profiling, novel targeted therapies, microbiome-based interventions, liquid biopsy for early detection and monitoring, and AI-assisted screening for colonoscopy [73,84,85]. Strengthening global screening programs and addressing lifestyle-related risk factors remain essential for reducing CRC burden worldwide [76,83].

## 7. Prostate Cancer

### *7.1. Epidemiology*

Prostate cancer is the second most commonly diagnosed cancer among men worldwide and a leading cause of cancer-related death in many regions [86,87]. In 2020, there were an estimated 1.4 million new cases and 375,000 deaths globally [86]. Incidence is highest in high-income countries, particularly in North America, Western Europe, and parts of the Caribbean, largely due to widespread prostate-specific antigen (PSA) screening [88]. Age is a major risk factor, with most cases diagnosed in men over 65 years [87].

### *7.2. Etiology and Risk Factors*

Prostate cancer etiology is multifactorial, involving genetic, hormonal, environmental, and lifestyle components:

- Genetic predisposition: Family history of prostate cancer and inherited mutations in BRCA1, BRCA2, and HOXB13 genes increase risk [89,90].
- Hormonal factors: Androgens play a central role in prostate growth and cancer development; alterations in androgen receptor signaling contribute to tumorigenesis [91].
- Lifestyle factors: Diets high in red meat, obesity, and physical inactivity may modestly increase risk, though evidence is mixed [92].
- Ethnicity: Higher incidence and mortality rates are observed in men of African ancestry compared to Caucasian or Asian populations [87,93].

 doi:10.20944/preprints202512.2612.v1



*7.3. Molecular and Pathophysiological Mechanisms*

Prostate cancer exhibits heterogeneous molecular profiles. Key pathways implicated in pathogenesis include androgen receptor signaling, PI3K/AKT/mTOR, and TP53/RB1 alterations [94,95]. Genomic instability, epigenetic modifications, and dysregulation of cell-cycle control contribute to tumor progression. Molecular subtyping, including ETS gene fusions and DNA repair gene mutations, informs prognosis and therapeutic strategies [95,96].

*7.4. Clinical Presentation and Diagnosis*

Early-stage prostate cancer is often asymptomatic. Symptoms, when present, may include urinary frequency, nocturia, hematuria, or bone pain in metastatic disease [97]. Diagnosis involves PSA testing, digital rectal examination (DRE), and confirmatory prostate biopsy with histopathological evaluation. Multiparametric MRI is increasingly used for lesion localization and risk stratification [97,98]. Staging follows the TNM system and Gleason scoring [97].

*7.5. Current Treatment Modalities*

Management depends on disease stage, risk stratification, patient age, and comorbidities:

- Active surveillance: Recommended for low-risk localized disease to avoid overtreatment [99].
- Surgery: Radical prostatectomy is standard for localized and some locally advanced cases [100].
- Radiotherapy: External beam radiotherapy or brachytherapy is used for localized and locally advanced disease [100].
- Hormonal therapy: Androgen deprivation therapy (ADT) is the mainstay for advanced or metastatic disease, often combined with chemotherapy or novel androgen receptor inhibitors [101,102].
- Chemotherapy: Docetaxel and cabazitaxel are used in metastatic castration-resistant prostate cancer (mCRPC) [102].
- Targeted therapy and immunotherapy: PARP inhibitors (for BRCA-mutated tumors) and sipuleucel-T immunotherapy offer personalized treatment options [103,104].

*7.6. Prevention Strategies*

Primary prevention focuses on maintaining healthy body weight, regular physical activity, and dietary modification [92]. Secondary prevention includes PSA-based screening and early detection programs, with individualized risk assessment to balance benefits and harms [98,105]. Genetic counseling is recommended for high-risk individuals [89].

*7.7. Challenges and Limitations*

Challenges include overdiagnosis and overtreatment of indolent tumors, racial and socioeconomic disparities in access to screening and treatment, and development of resistance in advanced disease [87,99,102]. Accurate risk stratification and patient-centered management are critical to improving outcomes while minimizing morbidity [99].

*7.8. Future Needs and Research Directions*

Future directions involve precision medicine approaches, including genomic profiling, targeted therapies (PARP inhibitors, novel androgen receptor pathway inhibitors), liquid biopsies for monitoring disease progression, AI-assisted imaging, and biomarker-driven screening [96,104,106]. Reducing disparities in access to high-quality care globally is essential for improving prostate cancer outcomes [87,105].

 doi:10.20944/preprints202512.2612.v1



## 8. Cervical Cancer

### *8.1. Epidemiology*

Cervical cancer is the fourth most common cancer among women globally, with approximately 604,000 new cases and 342,000 deaths in 2020 [107,108]. The burden is disproportionately high in low- and middle-income countries due to limited access to screening and HPV vaccination [108,109]. Peak incidence occurs between 35 and 44 years, but precancerous lesions can develop earlier [108].

### *8.2. Etiology and Risk Factors*

Persistent infection with high-risk human papillomavirus (HPV) types, particularly HPV-16 and HPV-18, is the primary cause of cervical cancer [110]. Other risk factors include:

- Early sexual debut and multiple sexual partners [110].
- Immunosuppression, including HIV infection or prolonged immunosuppressive therapy [111].
- Smoking, which promotes carcinogenesis in cervical epithelium [112].
- Long-term oral contraceptive use and high parity may increase risk modestly [113].
- Genetic susceptibility: Rare hereditary syndromes may contribute to risk [114].

### *8.3. Molecular and Pathophysiological Mechanisms*

High-risk HPV integrates into the host genome, leading to expression of E6 and E7 oncoproteins, which inactivate tumor suppressors p53 and Rb, respectively [115]. This results in uncontrolled cell proliferation, genomic instability, and malignant transformation [115,116]. Progression typically follows a sequence from cervical intraepithelial neoplasia (CIN) to invasive carcinoma [116].

### *8.4. Clinical Presentation and Diagnosis*

Early cervical cancer is often asymptomatic. Symptoms may include abnormal vaginal bleeding, postcoital bleeding, vaginal discharge, or pelvic pain in advanced stages [117]. Diagnosis involves cytology (Pap smear), HPV testing, colposcopy, and biopsy [117]. Staging follows the FIGO system, which guides management [117,118].

### *8.5. Current Treatment Modalities*

Treatment is determined by stage, tumor size, patient age, and fertility considerations:

- Surgery: Conization or radical hysterectomy for early-stage disease [119].
- Radiotherapy: External beam radiation and brachytherapy are standard for locally advanced disease [120].
- Chemotherapy: Concurrent chemoradiation with cisplatin improves survival in locally advanced cervical cancer [120].
- Targeted therapy: Bevacizumab, an anti-VEGF monoclonal antibody, improves survival in metastatic or recurrent disease [121].
- Immunotherapy: Checkpoint inhibitors (e.g., pembrolizumab) show efficacy in PD-L1 positive recurrent/metastatic cervical cancer [122].

### *8.6. Prevention Strategies*

Primary prevention is HPV vaccination, which dramatically reduces the risk of infection with high-risk HPV types and subsequent cervical cancer [123]. Secondary prevention relies on regular screening programs (Pap smear, HPV DNA testing, or visual inspection with acetic acid) to detect precancerous lesions early [108,117]. Education, safe sexual practices, and smoking cessation complement prevention strategies [112,123].

 doi:10.20944/preprints202512.2612.v1



*8.7. Challenges and Limitations*

Challenges include limited vaccination coverage, lack of organized screening in low-resource settings, late-stage diagnosis, and disparities in access to modern therapies [108,109,123]. HPV-negative cervical cancers, though rare, present diagnostic and therapeutic challenges [115].

*8.8. Future Needs and Research Directions*

Future strategies include expanding global HPV vaccination coverage, development of therapeutic HPV vaccines, liquid biopsy for early detection and monitoring, AI-assisted cytology, and novel immunotherapeutic approaches[122,124,125]. Addressing healthcare inequities and increasing access to screening and treatment are critical to reducing the global burden [108,109].

## 9. Comparative Analysis of the Five Cancers

The top five most common cancers—breast, lung, colorectal, prostate, and cervical cancers—exhibit distinct epidemiological patterns, etiologies, and clinical behaviors, yet share several overarching characteristics.

*9.1. Epidemiology and Global Distribution*

Breast and lung cancers dominate incidence in high-income countries, largely due to lifestyle factors, screening practices, and longer life expectancy [23,43]. In contrast, cervical cancer predominantly affects women in low- and middle-income countries where HPV vaccination and organized screening programs are limited [108,123]. Colorectal and prostate cancers show a mixed distribution, influenced by diet, obesity, and genetic predispositions [63,86]. Mortality trends often mirror access to early detection and advanced treatment options, highlighting persistent global health disparities[64,108].

*9.2. Etiological Comparisons*

While each cancer has unique drivers—HPV infection in cervical cancer [110], tobacco in lung cancer [46], hormonal influences in breast and prostate cancers [24,89]—common risk factors include genetic mutations, age, lifestyle factors (diet, physical inactivity), and chronic inflammation [24,46,67,89,110]. Infection-driven and lifestyle-related cancers highlight the complementary roles of primary prevention (vaccination, smoking cessation, healthy lifestyle) and secondary prevention (screening, early detection) [123,108,64].

*9.3. Molecular and Therapeutic Insights*

Molecular heterogeneity is a unifying feature. Breast, colorectal, and prostate cancers exhibit subtype-specific genomic alterations, informing targeted therapies and precision medicine approaches [32,73,96,103]. Lung and cervical cancers also benefit from molecularly guided treatment, such as EGFR/ALK inhibitors and PD-1 checkpoint inhibitors [52,122]. Despite advances, therapy resistance and tumor heterogeneity remain common challenges across all five cancers [59,102,115].

*9.4. Screening and Prevention*

Effective screening varies by cancer type. Mammography and PSA testing detect breast and prostate cancers early [33,99], while Pap smears and HPV testing reduce cervical cancer incidence [108,117]. Colorectal cancer benefits from colonoscopy and fecal occult blood testing [71]. Lung cancer screening is largely limited to high-risk populations via low-dose CT [54]. Integrating risk-based screening with preventive strategies is crucial for reducing incidence and mortality globally [61,108,123].

 doi:10.20944/preprints202512.2612.v1



*9.5. Future Directions*

Across the five cancers, precision medicine, early detection technologies (liquid biopsy, AI-assisted imaging), immunotherapy, and equitable access to care emerge as cross-cutting priorities [41,61,84,104,125]. Collaborative efforts to expand vaccination coverage, optimize screening programs, and implement personalized treatment strategies are essential to address the rising global cancer burden.

**Table 1. Summary of Top 5 Most Common Cancers.**

| Cancer Type | Global Incidence (2020) | Major Causes / Risk Factors | Standard Treatments | Future Directions / Research Needs |
|---|---|---|---|---|
| **Breast** | 2.3 million new cases [23] | Genetic (BRCA1/2), hormonal factors, age, obesity, lifestyle [24–28] | Surgery, radiotherapy, chemotherapy, endocrine therapy, targeted therapy (HER2 inhibitors) [31–40] | Precision medicine, liquid biopsies, immunotherapy, early detection biomarkers, reducing disparities [41–42] |
| **Lung** | 2.2 million new cases [43] | Tobacco smoking, air pollution, occupational exposures, genetic mutations [46–49] | Surgery, radiotherapy, chemotherapy, targeted therapy (EGFR/ALK inhibitors), immunotherapy [56–59] | Novel targeted agents, early detection biomarkers, AI-assisted screening, global access to care [53,61–62] |
| **Colorectal** | 1.9 million new cases [63] | Diet, obesity, physical inactivity, hereditary syndromes (Lynch, FAP), IBD [67–71] | Surgery, chemotherapy (FOLFOX/CAPOX), radiotherapy (rectal), targeted therapy (anti-EGFR/VEGF), immunotherapy (MSI-high) [78–82] | Precision medicine, microbiome interventions, liquid biopsy, AI-assisted screening, global screening programs [73,84–85] |
| **Prostate** | 1.4 million new cases [86] | Age, family history, BRCA mutations, androgen signaling, lifestyle, ethnicity [89–93] | Active surveillance, surgery, radiotherapy, hormonal therapy (ADT), chemotherapy, targeted therapy (PARP inhibitors), immunotherapy [99–104] | Genomic profiling, targeted therapies, liquid biopsy, AI-assisted imaging, addressing disparities [96,104,106] |
| **Cervical** | 604,000 new cases [107] | Persistent high-risk HPV infection (16/18), immunosuppression, smoking, sexual behavior, genetics [110–114] | | |

## 10. Emerging Technologies and Innovations in Cancer Care

Advances in technology and molecular biology are transforming cancer diagnosis, treatment, and monitoring, enabling more personalized and effective care for breast, lung, colorectal, prostate, and cervical cancers.

*10.1. Precision Medicine and Genomic Profiling*

Molecular profiling of tumors allows targeted therapies tailored to genetic alterations, improving response rates and minimizing toxicity. Examples include:

- EGFR, ALK, and KRAS mutations in lung cancer guiding targeted inhibitors [137].
- HER2 amplification and PIK3CA mutations in breast cancer informing monoclonal antibodies and kinase inhibitors [138].

 doi:10.20944/preprints202512.2612.v1



- BRCA mutations in breast and prostate cancers enabling PARP inhibitor therapy [139].

Genomic-guided approaches also inform prognosis, recurrence risk, and therapy selection, making precision medicine a cornerstone of modern oncology [140].

### *10.2. Liquid Biopsies and Non-Invasive Diagnostics*

Circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), and exosome-based assays enable early detection, treatment monitoring, and minimal residual disease assessment [141,142]. These tools are particularly promising for cancers like lung, colorectal, and breast, where early detection is critical for survival [143].

### *10.3. Artificial Intelligence and Digital Health*

AI and machine learning algorithms improve imaging analysis, pathology interpretation, and risk prediction. Applications include:

- AI-assisted mammography and radiology for breast and lung cancer screening [144].
- Deep learning models for colonoscopy and polyp detection in colorectal cancer [145].
- Predictive algorithms for recurrence and therapy response across multiple cancers [146].

Digital health platforms also enable remote patient monitoring, adherence tracking, and telemedicine consultations, improving accessibility and personalized care [147].

### *10.4. Immunotherapy and Novel Therapeutics*

Checkpoint inhibitors (PD-1/PD-L1, CTLA-4) and CAR-T cell therapies have revolutionized treatment for select cancers, particularly lung, melanoma, and hematologic malignancies [148,149]. Ongoing research aims to expand their efficacy to breast, prostate, colorectal, and cervical cancers, often in combination with chemotherapy, radiotherapy, or targeted agents [150].

### *10.5. Robotics and Minimally Invasive Surgery*

Robotic-assisted surgery and laparoscopic techniques enhance precision, reduce operative morbidity, and improve recovery times. Applications include:

- Robotic radical prostatectomy [151].
- Minimally invasive hysterectomy for cervical cancer [152].
- Laparoscopic colectomy for colorectal cancer [153].

### *10.6. Future Directions*

Emerging innovations focus on integrating multi-omics data (genomics, proteomics, metabolomics), AI-driven predictive modeling, wearable biosensors, and personalized immunotherapies [154–156]. Such advances promise to enhance early detection, optimize therapeutic strategies, and improve survivorship, ultimately reducing the global cancer burden.

## 11. Public Health and Policy Implications

The global burden of breast, lung, colorectal, prostate, and cervical cancers underscores the critical role of public health initiatives and evidence-based policy in reducing incidence and mortality. Addressing these cancers requires strategies that integrate prevention, early detection, equitable access to care, and sustainable healthcare infrastructure.

### *11.1. Prevention and Risk Reduction*

Primary prevention is essential to reduce exposure to modifiable risk factors. Policies promoting tobacco control, healthy diets, physical activity, vaccination, and reduction of environmental carcinogens can substantially lower cancer incidence [157–159]. For instance:

 doi:10.20944/preprints202512.2612.v1



- HPV vaccination programs have dramatically reduced cervical cancer risk in countries with high coverage [123,157].
- Anti-smoking legislation and taxation have contributed to declining lung cancer rates in high-income countries [46,158].

*11.2. Screening and Early Detection*

Population-based screening programs detect cancers at early, more treatable stages, improving survival and cost-effectiveness. Examples include:

- Mammography for breast cancer [33].
- Colonoscopy and fecal immunochemical testing for colorectal cancer [71].
- Pap smears and HPV testing for cervical cancer [108,117].

Policy initiatives should focus on ensuring equitable access to screening, particularly in low- and middle-income countries, where disparities in mortality are highest [108,159].

*11.3. Health Systems and Access to Care*

Disparities in cancer outcomes are strongly influenced by health system capacity, availability of specialized care, and affordability of advanced treatments. Strengthening healthcare infrastructure, expanding workforce training, and implementing universal health coverage are key policy priorities [160,161].

*11.4. Research and Innovation Policy*

Investments in research, data infrastructure, and technology adoption are necessary to accelerate precision oncology, immunotherapy, AI-assisted diagnostics, and population health interventions [154,155,156]. Policies supporting multi-center collaborations, public-private partnerships, and translational research can improve global cancer care.

*11.5. Global Collaboration and Equity*

International collaboration is essential to tackle the rising global cancer burden. The WHO Global Strategy for Cervical Cancer Elimination and similar initiatives demonstrate the impact of coordinated public health policies [131]. Policies should prioritize equitable access to vaccines, screening, treatment, and palliative care, particularly in resource-limited settings [108,123,160].

*12.6. Policy Recommendations*

Key recommendations include:

1. Expanding primary prevention programs targeting lifestyle and infection-related risk factors.
2. Implementing population-based screening and early detection programs.
3. Enhancing healthcare infrastructure and workforce capacity for timely diagnosis and treatment.
4. Supporting research and innovation through funding, regulation, and collaboration.
5. Promoting global equity through international partnerships and policy alignment [157–161].

## 12. Future Perspectives

The fight against breast, lung, colorectal, prostate, and cervical cancers is entering a new era characterized by precision medicine, digital health, and integrated public health strategies. The following trends and priorities are likely to shape future cancer care and research:

*12.1. Personalized and Precision Oncology*

Advances in genomics, proteomics, and metabolomics are enabling tailored therapies based on individual tumor profiles. Multi-omic approaches, coupled with AI-driven predictive models, are expected to optimize therapy selection, reduce toxicity, and improve survival across all five cancers

 doi:10.20944/preprints202512.2612.v1



[162–164]. Expansion of biobanks and global genomic datasets will facilitate equitable access to precision medicine innovations.

### *12.2. Early Detection and Screening Innovations*

Liquid biopsies, circulating tumor DNA assays, and AI-assisted imaging are poised to revolutionize early cancer detection, particularly for lung and colorectal cancers where current screening is limited [141,144,143]. Integration of these technologies into routine clinical practice, alongside traditional screening methods, will enhance population-level outcomes and reduce late-stage diagnoses.

### *12.3. Immunotherapy and Novel Therapeutics*

Ongoing development of immune checkpoint inhibitors, CAR-T therapies, therapeutic vaccines, and combination regimens promises to expand treatment options for refractory cancers, including breast, prostate, and cervical cancers [148–150,165]. Personalized immunotherapy strategies guided by tumor microenvironment profiling are expected to improve response rates and durability of treatment.

### *12.4. Digital Health and AI Integration*

Digital health platforms, wearable biosensors, and telemedicine will facilitate remote monitoring, early symptom detection, and improved adherence to treatment protocols [147,155]. AI-driven clinical decision support can help oncologists interpret complex datasets, optimize therapy, and predict recurrence or adverse events.

### *12.5. Global Health Equity and Policy Innovation*

Future strategies must prioritize equitable access to vaccines, screening programs, diagnostics, and therapeutics, particularly in low- and middle-income countries [157,160,161]. Global collaboration, public-private partnerships, and policy frameworks that integrate prevention, early detection, and advanced treatment will be critical for reducing disparities and achieving population-level impact.

### *12.6. Research and Collaborative Priorities*

- Translational research to bridge laboratory discoveries and clinical application.
- Longitudinal studies to understand cancer etiology and therapy response across populations.
- Implementation science to optimize uptake of screening and preventive interventions.
- Multi-disciplinary collaboration among clinicians, researchers, data scientists, and policymakers to accelerate innovation and dissemination [154,156,162].

Collectively, these advances promise a future in which cancer care is more precise, personalized, accessible, and effective, reducing global morbidity and mortality while empowering patients and healthcare systems alike.

## 13. Limitations of the Review

While this review provides a comprehensive overview of the top five most common cancers—breast, lung, colorectal, prostate, and cervical cancers—certain limitations must be acknowledged:

### *13.1. Scope and Selection Bias*

The review focuses on the five most prevalent cancers and may not capture insights from less common but clinically significant malignancies. Additionally, reliance on published literature may introduce publication bias, favoring studies with significant findings over null or negative results [166].

 doi:10.20944/preprints202512.2612.v1



*13.2. Heterogeneity of Data Sources*

Global epidemiological and clinical data were sourced from multiple databases and studies, including GLOBOCAN and WHO reports. Variations in reporting standards, diagnostic criteria, and healthcare infrastructure across countries can affect comparability and may limit the generalizability of some conclusions [23,43,108,133].

*13.3. Rapidly Evolving Field*

Cancer research and treatment are evolving rapidly, with continuous developments in targeted therapies, immunotherapy, and diagnostic technologies. As a result, some emerging strategies discussed (e.g., AI-assisted screening, liquid biopsies, novel immunotherapies) may not yet be widely implemented or validated in routine clinical practice [141,144,148].

*13.4. Limited Patient-Level Data*

The review synthesizes findings at a population and literature level, without patient-level meta-analyses. Individual variability in genetics, comorbidities, treatment response, and socioeconomic factors may influence outcomes and are not fully captured in this analysis [167].

*13.5. Language and Accessibility Limitations*

Only English-language studies were included, which may exclude relevant data from non-English publications, particularly studies from low- and middle-income countries where cancer burden is high [168].

Despite these limitations, this review provides a comprehensive, up-to-date synthesis of the epidemiology, etiology, treatment, emerging innovations, and public health implications of the five most common cancers, serving as a valuable reference for researchers, clinicians, and policymakers.

## 14. Discussion

The global burden of cancer continues to rise, with breast, lung, colorectal, prostate, and cervical cancers representing the most prevalent malignancies, collectively accounting for millions of new cases and deaths annually [1,2,23,40,61,83]. This review highlights both the commonalities and distinct characteristics of these cancers, underscoring the multifactorial etiology, complex molecular mechanisms, and varying clinical presentations that influence management strategies.

*14.1. Epidemiological Trends and Risk Factors*

Epidemiological data demonstrate significant geographic, socioeconomic, and demographic disparities in incidence and mortality. High-income countries report higher incidence rates for breast and prostate cancers, largely due to lifestyle factors, increased life expectancy, and widespread screening [3,61]. Conversely, cervical cancer disproportionately affects low- and middle-income countries due to limited access to HPV vaccination and screening programs [84,157]. Lung cancer incidence remains closely tied to tobacco use and environmental exposures globally [25,46], while colorectal cancer shows increasing incidence in regions adopting Westernized diets and sedentary lifestyles [41,45].

The risk factors for these cancers are a combination of genetic predisposition, hormonal influences, lifestyle behaviors, infectious agents, and environmental exposures [4–8,25–28,85–89]. Understanding these factors is crucial for implementing effective primary prevention and public health strategies.

*14.2. Molecular Mechanisms and Pathogenesis*

The molecular landscape across these cancers reveals both shared and unique pathways. Common features include mutations in tumor suppressor genes (e.g., TP53, APC), dysregulation of

 doi:10.20944/preprints202512.2612.v1



growth factor signaling (e.g., EGFR, HER2), and aberrant DNA repair mechanisms (e.g., BRCA mutations) [9–12,29–31,68–71]. HPV-driven cervical carcinogenesis uniquely disrupts p53 and Rb pathways, demonstrating the role of infectious agents in tumor development [90–92]. Advances in genomic profiling and multi-omics analyses have enhanced understanding of tumor heterogeneity, enabling the development of targeted therapies and personalized treatment strategies [137–140,162–164].

### *14.3. Current Treatment Strategies*

Treatment paradigms for these cancers are evolving, guided by tumor biology, stage, and patient-specific factors. Surgery, radiotherapy, chemotherapy, targeted therapy, and immunotherapy form the backbone of management [9,15–20,34–37,53–57,74–79,96–100].

- Breast cancer benefits from hormone receptor-targeted therapies and HER2 inhibitors [9,15–20].
- Lung cancer management increasingly incorporates EGFR/ALK inhibitors and immune checkpoint blockade [34–37,148].
- Colorectal cancer treatment integrates surgery with chemotherapeutics and targeted monoclonal antibodies [53–57].
- Prostate cancer employs active surveillance, androgen deprivation therapy, and novel targeted agents [74–79].
- Cervical cancer is primarily treated with surgery and chemoradiation, with emerging roles for immunotherapy and targeted approaches [96–100].

Despite advances, treatment resistance, toxicity, and disparities in access continue to limit optimal outcomes, particularly in low-resource settings [108,160].

### *14.4. Emerging Technologies and Innovations*

The integration of precision medicine, liquid biopsy, AI-assisted diagnostics, immunotherapy, and minimally invasive surgery is reshaping cancer care [141–155]. Liquid biopsies and circulating tumor DNA assays enable early detection and monitoring of minimal residual disease [141–143]. Artificial intelligence improves diagnostic accuracy in imaging and pathology while optimizing clinical decision-making [144–146]. Immunotherapy, including checkpoint inhibitors and CAR-T cells, has shown durable responses in select cancers and holds promise for expansion across breast, prostate, and cervical cancers [148–150]. Robotic and minimally invasive surgical techniques reduce perioperative morbidity and accelerate recovery [151–153].

### *14.5. Public Health and Policy Implications*

Reducing the global cancer burden requires multi-level public health strategies and policy interventions [157–161]. Prevention through HPV vaccination, tobacco control, lifestyle modification, and reduction of environmental carcinogens is essential [157–159]. Population-based screening programs for breast, colorectal, and cervical cancers improve early detection and survival outcomes [33,71,108]. Health system strengthening, universal health coverage, and equitable access to diagnostics and therapeutics are critical to reducing disparities, particularly in low- and middle-income countries [160,161].

### *14.6. Integrating Research, Innovation, and Equity*

Future strategies emphasize translational research, multi-omics integration, AI-driven predictive modeling, and personalized immunotherapy [154–156,162–165]. Bridging the gap between technological innovations and real-world clinical application requires international collaboration, public-private partnerships, and policy frameworks that prioritize equity and sustainability [157,160].

 doi:10.20944/preprints202512.2612.v1



*14.7. Limitations and Challenges*

Challenges in synthesizing global cancer data include heterogeneity in reporting standards, publication bias, and rapidly evolving treatment paradigms [166–168]. Additionally, much of the current evidence is derived from high-income countries, which may limit generalizability to resource-limited settings [108,157].

## 15. Conclusion

Breast, lung, colorectal, prostate, and cervical cancers remain the most prevalent malignancies globally, posing a significant challenge to public health, healthcare systems, and patient outcomes [23,43,63,86,107]. Despite advances in screening, diagnosis, and therapeutic interventions, these cancers continue to contribute substantially to morbidity and mortality, particularly in low- and middle-income countries where access to care is limited [108,123,160].

This review highlights that while each cancer has distinct etiological factors, molecular mechanisms, and clinical features, they share common challenges, including late diagnosis, treatment resistance, and disparities in healthcare access [46,64,102]. Emerging innovations—such as precision medicine, liquid biopsies, AI-assisted diagnostics, immunotherapy, and minimally invasive surgical techniques—offer promising avenues to improve patient outcomes across all five cancers [41,141,148,155].

Public health strategies, including prevention programs, vaccination, lifestyle modification, and population-based screening, are essential to reduce the global cancer burden [157,158,123]. Integrating these strategies with research advancements and equitable policy frameworks can help bridge gaps in cancer care delivery, particularly in resource-limited settings.

Looking forward, the combination of technological innovation, translational research, and global health policy holds the potential to transform cancer management. A coordinated approach that prioritizes early detection, personalized treatment, prevention, and equity will be critical to reduce morbidity and mortality and improve survival outcomes worldwide [162,165,160].

In conclusion, addressing the top five cancers requires multifaceted, collaborative strategies that integrate scientific discovery, clinical practice, and public health initiatives, paving the way toward a future where effective, accessible, and equitable cancer care is achievable for all populations.

**Author Contribution**: Manucscript Conceptualization- AKM, MRM, RDD; Original Manuscript Drafting- AKM, BS, LS, DP, SP, VS, TD; Manuscript Editing- AE, SN, VKN, SB; Manuscript Proofreading- DS, AK

## References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.*2024;74(1):1–35.
2. World Health Organization. Cancer. WHO Fact Sheets. Geneva: WHO; 2023.
3. Bray F, Laversanne M, Weiderpass E, Soerjomataram I. The ever-increasing importance of cancer as a leading cause of premature death worldwide. *Cancer.* 2021;127(16):3029–3030.
4. Wild CP, Weiderpass E, Stewart BW, editors. *World Cancer Report: Cancer Research for Cancer Prevention.* Lyon: IARC; 2020.
5. Plummer M, de Martel C, Vignat J, Ferlay J, Bray F, Franceschi S. Global burden of cancers attributable to infections in 2018. *Lancet Glob Health.* 2021;9(4):e467–e474.
6. Ferlay J, Colombet M, Soerjomataram I, et al. Cancer statistics for the year 2020: An overview. *Int J Cancer.*2021;149(4):778–789.
7. Vogelstein B, Papadopoulos N, Velculescu VE, Zhou S, Diaz LA Jr, Kinzler KW. Cancer genome landscapes. *Science.* 2013;339(6127):1546–1558.
8. Hanahan D. Hallmarks of cancer: New dimensions. *Cancer Discov.* 2022;12(1):31–46.

 doi:10.20944/preprints202512.2612.v1




9. Ribas A, Wolchok JD. Cancer immunotherapy using checkpoint blockade. *Science.* 2018;359(6382):1350–1355.
10. Sankaranarayanan R, Swaminathan R, Brenner H, et al. Cancer survival in Africa, Asia, and Central America: A population-based study. *Lancet Oncol.* 2010;11(2):165–173.
11. Ginsburg O, Bray F, Coleman MP, et al. The global burden of women's cancers: A grand challenge in global health. *Lancet.* 2017;389(10071):847–860.
12. Green BN, Johnson CD, Adams A. Writing narrative literature reviews for peer-reviewed journals: Secrets of the trade. *J Chiropr Med.* 2006;5(3):101–117.
13. Gasparyan AY, Ayvazyan L, Blackmore H, Kitas GD. Writing a narrative biomedical review: Considerations for authors, peer reviewers, and editors. *Rheumatol Int.* 2011;31(11):1409–1417.
14. Ferrari R. Writing narrative style literature reviews. *Med Writ.* 2015;24(4):230–235.
15. Baethge C, Goldbeck-Wood S, Mertens S. SANRA—A scale for the quality assessment of narrative review articles. *Res Integr Peer Rev.* 2019;4:5.
16. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.*2024;74(1):1–35.
17. Bray F, Jemal A, Grey N, Ferlay J, Forman D. Global cancer transitions according to the Human Development Index (2008–2030): A population-based study. *Lancet Oncol.* 2012;13(8):790–801.
18. Torre LA, Siegel RL, Jemal A. Lung cancer statistics. *Adv Exp Med Biol.* 2016;893:1–19.
19. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. *Gut.* 2017;66(4):683–691.
20. Rawla P. Epidemiology of prostate cancer. *World J Oncol.* 2019;10(2):63–89.
21. Arbyn M, Weiderpass E, Bruni L, et al. Estimates of incidence and mortality of cervical cancer in 2018: A worldwide analysis. *Lancet Glob Health.* 2020;8(2):e191–e203.
22. Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): Analysis of individual records for 37,513,025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet.* 2018;391(10125):1023–1075.
23. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.*2024;74(1):1–35.
24. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68(6):394–424.
25. Ginsburg O, Bray F, Coleman MP, et al. The global burden of women's cancers: A grand challenge in global health. *Lancet.* 2017;389(10071):847–860.
26. Kuchenbaecker KB, Hopper JL, Barnes DR, et al. Risks of breast, ovarian, and contralateral breast cancer for BRCA1 and BRCA2 mutation carriers. *JAMA.* 2017;317(23):2402–2416.
27. Mavaddat N, Peock S, Frost D, et al. Cancer risks for BRCA1 and BRCA2 mutation carriers: Results from prospective analysis of EMBRACE. *J Natl Cancer Inst.* 2013;105(11):812–822.
28. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: Collaborative reanalysis. *Lancet.* 1996;347(9017):1713–1727.
29. World Cancer Research Fund/American Institute for Cancer Research. Diet, Nutrition, Physical Activity, and Breast Cancer. Continuous Update Project Report. 2018.
30. Brody JG, Rudel RA. Environmental pollutants and breast cancer. *Environ Health Perspect.* 2003;111(8):1007–1019.
31. Perou CM, Sorlie T, Eisen MB, et al. Molecular portraits of human breast tumours. *Nature.* 2000;406:747–752.
32. Polyak K. Heterogeneity in breast cancer. *J Clin Invest.* 2011;121(10):3786–3788.
33. DeNardo DG, Ruffell B. Macrophages as regulators of tumour immunity and immunotherapy. *Nat Rev Immunol.*2019;19(6):369–382.

 doi:10.20944/preprints202512.2612.v1




34. Gradishar WJ, Anderson BO, Balassanian R, et al. Breast cancer, version 3.2020, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw.* 2020;18(4):452–478.
35. Morrow M, Harris JR, Schnitt SJ. Surgical management of breast cancer. *N Engl J Med.* 2012;367:203–210.
36. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of chemotherapy and hormonal therapy for early breast cancer. *Lancet.* 2005;365(9472):1687–1717.
37. Davies C, Pan H, Godwin J, et al. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of estrogen receptor-positive breast cancer: ATLAS trial. *Lancet.* 2013;381(9869):805–816.
38. Piccart-Gebhart MJ, Procter M, Leyland-Jones B, et al. Trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer. *N Engl J Med.* 2005;353:1659–1672.
39. Schmid P, Adams S, Rugo HS, et al. Atezolizumab and nab-paclitaxel in advanced triple-negative breast cancer. *N Engl J Med.* 2018;379:2108–2121.
40. Siu AL; U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2016;164(4):279–296.
41. Gampenrieder SP, Rinnerthaler G, Greil R. Precision medicine in breast cancer: Concepts, applications, and future perspectives. *Breast Care.* 2015;10(5):335–342.
42. Esteva A, Robicquet A, Ramsundar B, et al. A guide to deep learning in healthcare. *Nat Med.* 2019;25:24–29.
43. Torre LA, Siegel RL, Jemal A. Lung cancer statistics. *Adv Exp Med Biol.* 2016;893:1–19.
44. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2022. *CA Cancer J Clin.* 2024;74(1):1–35.
45. Bray F, Jemal A, Grey N, Ferlay J, Forman D. Global cancer transitions according to the Human Development Index (2008–2030): A population-based study. *Lancet Oncol.* 2012;13(8):790–801.
46. Islami F, Torre LA, Jemal A. Global trends of lung cancer mortality and smoking prevalence. *Nat Rev Cancer.*2015;15:573–584.
47. Hamra GB, Guha N, Cohen A, et al. Outdoor particulate matter exposure and lung cancer: A systematic review and meta-analysis. *Environ Health Perspect.* 2014;122(9):906–911.
48. Vineis P, Husgafvel-Pursiainen K. Air pollution and cancer: Biomarkers of exposure and effect. *Environ Health Perspect.* 2005;113:539–550.
49. Herbst RS, Morgensztern D, Boshoff C. The biology and management of non-small cell lung cancer. *Nature.*2018;553:446–454.
50. Samet JM, Avila-Tang E, Boffetta P, et al. Lung cancer in never smokers: Clinical epidemiology and environmental risk factors. *Clin Cancer Res.* 2009;15(18):5626–5645.
51. Govindan R, Page N, Morgensztern D, et al. Changing epidemiology of small-cell lung cancer in the United States over the last 30 years. *Cancer.* 2006;107(9):2111–2117.
52. Herbst RS, Morgensztern D, Boshoff C. The biology and management of non-small cell lung cancer. *Nature.*2018;553:446–454.
53. Reck M, Rabe KF. Precision diagnosis and treatment for advanced non-small-cell lung cancer. *N Engl J Med.*2017;377:849–861.
54. Ettinger DS, Wood DE, Aisner DL, et al. Non-small cell lung cancer, version 5.2021, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw.* 2021;19(3):254–266.
55. Detterbeck FC, Boffa DJ, Tanoue LT. The new lung cancer staging system. *Chest.* 2009;136:260–271.
56. National Comprehensive Cancer Network. NCCN Guidelines: Non-Small Cell Lung Cancer. Version 2.2024.
57. Schiller JH, Harrington D, Belani CP, et al. Comparison of four chemotherapy regimens for advanced non-small-cell lung cancer. *N Engl J Med.* 2002;346:92–98.
58. Kris MG, Johnson BE, Berry LD, et al. Using multiplexed assays of oncogenic drivers in lung cancers to select targeted drugs. *JAMA.* 2014;311(19):1998–2006.
59. Brahmer J, Reckamp KL, Baas P, et al. Nivolumab versus docetaxel in advanced squamous-cell non-small-cell lung cancer. *N Engl J Med.* 2015;373:123–135.
60. National Lung Screening Trial Research Team. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med.* 2011;365:395–409.

 doi:10.20944/preprints202512.2612.v1




61. Skoulidis F, Heymach JV. Co-occurring genomic alterations in non-small-cell lung cancer biology and therapy. *Nat Rev Cancer.* 2019;19:495–509.
62. He Y, Wu Z, Chen Y, et al. Emerging biomarkers for lung cancer diagnosis and precision therapy. *Front Oncol.*2022;12:876857.
63. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide. *CA Cancer J Clin.* 2021;71(3):209–249.
64. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. *Gut.* 2017;66:683–691.
65. Dekker E, Tanis PJ, Vleugels JLA, Kasi PM, Wallace MB. Colorectal cancer. *Lancet.* 2019;394:1467–1480.
66. Bailey CE, Hu CY, You YN, et al. Increasing disparities in the age-related incidence of colon and rectal cancers in the United States. *JAMA Surg.* 2015;150:17–22.
67. Vasen HF, Tomlinson I, Castells A, et al. Hereditary colorectal cancer: ESMO Clinical Practice Guidelines. *Ann Oncol.* 2013;24 Suppl 6:vi73–vi80.
68. World Cancer Research Fund/American Institute for Cancer Research. Diet, Nutrition, Physical Activity, and Colorectal Cancer. 2018.
69. Jess T, Rungoe C, Peyrin-Biroulet L. Risk of colorectal cancer in patients with ulcerative colitis: A meta-analysis of population-based cohort studies. *Clin Gastroenterol Hepatol.* 2012;10:639–645.
70. Murphy N, Norat T, Ferrari P, et al. Lifestyle and dietary environmental factors in colorectal cancer prevention. *Curr Opin Gastroenterol.* 2019;35:43–49.
71. Tilg H, Adolph TE, Gerner RR, Moschen AR. The intestinal microbiota in colorectal cancer. *Cancer Cell.*2018;33:954–964.
72. Fearon ER, Vogelstein B. A genetic model for colorectal tumorigenesis. *Cell.* 1990;61:759–767.
73. Guinney J, Dienstmann R, Wang X, et al. The consensus molecular subtypes of colorectal cancer. *Nat Med.*2015;21:1350–1356.
74. Boland CR, Goel A. Microsatellite instability in colorectal cancer. *Gastroenterology.* 2010;138:2073–2087.
75. Kinzler KW, Vogelstein B. Lessons from hereditary colorectal cancer. *Cell.* 1996;87:159–170.
76. Rex DK, Boland CR, Dominitz JA, et al. Colorectal cancer screening: Recommendations for physicians and patients from the US Multi-Society Task Force. *Am J Gastroenterol.* 2017;112:1016–1030.
77. Edge SB, Compton CC. The American Joint Committee on Cancer: The 7th edition of the AJCC cancer staging manual and the future of TNM. *Ann Surg Oncol.* 2010;17:1471–1474.
78. Sauer R, Liersch T, Merkel S, et al. Preoperative versus postoperative chemoradiotherapy for locally advanced rectal cancer. *N Engl J Med.* 2004;351:1731–1740.
79. André T, Boni C, Mounedji-Boudiaf L, et al. Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer. *N Engl J Med.* 2004;350:2343–2351.
80. Bosset JF, Calais G, Mineur L, et al. Chemotherapy with preoperative radiotherapy in rectal cancer. *N Engl J Med.*2006;355:1114–1123.
81. Van Cutsem E, Cervantes A, Nordlinger B, Arnold D. Metastatic colorectal cancer: ESMO Clinical Practice Guidelines. *Ann Oncol.* 2014;25 Suppl 3:iii1–iii9.
82. Le DT, Durham JN, Smith KN, et al. Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade. *Science.* 2017;357:409–413.
83. Rex DK, Boland CR, Dominitz JA, et al. Colorectal cancer screening: Recommendations from the US Multi-Society Task Force. *Am J Gastroenterol.* 2017;112:1016–1030.
84. Dienstmann R, Vermeulen L, Guinney J, et al. Consensus molecular subtypes and precision medicine in colorectal cancer. *Nat Rev Gastroenterol Hepatol.* 2017;14:485–495.
85. Ahuja N, Bhanot N, Sachdeva A. Emerging biomarkers and AI-based approaches for colorectal cancer early detection. *Front Oncol.* 2022;12:927319.
86. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020. *CA Cancer J Clin.* 2021;71:209–249.
87. Rawla P. Epidemiology of prostate cancer. *World J Oncol.* 2019;10(2):63–89.
88. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin.* 2020;70:7–30.
89. Kuchenbaecker KB, Hopper JL, Barnes DR, et al. Risks of prostate and other cancers for BRCA1 and BRCA2 mutation carriers. *J Clin Oncol.* 2017;35:170–182.

 doi:10.20944/preprints202512.2612.v1




90. Ewing CM, Ray AM, Lange EM, et al. Germline mutations in HOXB13 and prostate-cancer risk. *N Engl J Med.*2012;366:141–149.
91. Feldman BJ, Feldman D. The development of androgen-independent prostate cancer. *Nat Rev Cancer.* 2001;1:34–45.
92. World Cancer Research Fund/American Institute for Cancer Research. Diet, Nutrition, Physical Activity, and Prostate Cancer. 2018.
93. Rebbeck TR, Devesa SS, Chang BL, et al. Global patterns of prostate cancer incidence, aggressiveness, and mortality in men of African descent. *Prostate Cancer.* 2013;2013:560857.
94. Robinson D, Van Allen EM, Wu YM, et al. Integrative clinical genomics of advanced prostate cancer. *Cell.*2015;161:1215–1228.
95. Cancer Genome Atlas Research Network. The molecular taxonomy of primary prostate cancer. *Cell.*2015;163:1011–1025.
96. Beltran H, Prandi D, Mosquera JM, et al. Divergent clonal evolution of castration-resistant neuroendocrine prostate cancer. *Nat Med.* 2016;22:298–305.
97. Mottet N, van den Bergh RCN, Briers E, et al. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer. *Eur Urol.* 2021;79:243–262.
98. Carter HB, Albertsen PC, Barry MJ, et al. Early detection of prostate cancer: AUA guideline. *J Urol.*2013;190:419–426.
99. Hamdy FC, Donovan JL, Lane JA, et al. 10-year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer. *N Engl J Med.* 2016;375:1415–1424.
100. Mottet N, van den Bergh RCN, Briers E, et al. EAU Guidelines on Prostate Cancer. *Eur Urol.* 2021;79:243–262.
101. Ryan CJ, Smith MR, de Bono JS, et al. Abiraterone in metastatic prostate cancer without previous chemotherapy. *N Engl J Med.* 2013;368:138–148.
102. de Bono J, Logothetis CJ, Molina A, et al. Abiraterone and increased survival in metastatic prostate cancer. *N Engl J Med.* 2011;364:1995–2005.
103. Mateo J, Carreira S, Sandhu S, et al. DNA-repair defects and olaparib in metastatic prostate cancer. *N Engl J Med.*2015;373:1697–1708.
104. Kantoff PW, Higano CS, Shore ND, et al. Sipuleucel-T immunotherapy for castration-resistant prostate cancer. *N Engl J Med.* 2010;363:411–422.
105. Fenton JJ, Weyrich MS, Durbin S, et al. Prostate-specific antigen–based screening for prostate cancer: Evidence report and systematic review. *JAMA.* 2018;319:1914–1931.
106. Wyatt AW, Gleave ME. Targeting the androgen receptor pathway in prostate cancer: Mechanisms of resistance and new therapeutic approaches. *Endocr Relat Cancer.* 2015;22:R243–R258.
107. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020. *CA Cancer J Clin.* 2021;71:209–249.
108. Arbyn M, Weiderpass E, Bruni L, et al. Estimates of incidence and mortality of cervical cancer in 2018: A worldwide analysis. *Lancet Glob Health.* 2020;8:e191–e203.
109. World Health Organization. Cervical cancer. 2021. Available from: https://www.who.int/news-room/fact-sheets/detail/cervical-cancer
110. Walboomers JM, Jacobs MV, Manos MM, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *J Pathol.* 1999;189:12–19.
111. Clifford GM, Goncalves MA, Franceschi S. Human papillomavirus types among women infected with HIV: A meta-analysis. *AIDS.* 2006;20:2337–2344.
112. Castellsagué X, Muñoz N. Chapter 3: Cofactors in human papillomavirus carcinogenesis—Role of parity, oral contraceptives, and tobacco smoking. *J Natl Cancer Inst Monogr.* 2003;31:20–28.
113. Smith JS, Green J, de Gonzalez AB, et al. Cervical cancer and hormonal contraceptives: Collaborative reanalysis of individual data for 16,573 women with cervical cancer. *Lancet.* 2003;361:1159–1167.
114. Cancer Genome Atlas Research Network. Integrated genomic and molecular characterization of cervical cancer. *Nature.* 2017;543:378–384.

 doi:10.20944/preprints202512.2612.v1




115. Moody CA, Laimins LA. Human papillomavirus oncoproteins: Pathways to transformation. *Nat Rev Cancer.*2010;10:550–560.
116. Schiffman M, Castle PE, Jeronimo J, et al. Human papillomavirus and cervical cancer. *Lancet.* 2007;370:890–907.
117. Koh WJ, Abu-Rustum NR, Bean S, et al. Cervical cancer, version 3.2020, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw.* 2020;18:660–687.
118. Bhatla N, Berek JS, Cuello Fredes M, et al. Revised FIGO staging for carcinoma of the cervix. *Int J Gynaecol Obstet.* 2019;145:129–135.
119. Covens A, Rosen B, Murphy J, et al. Radical hysterectomy for cervical cancer: Surgical techniques and outcomes. *Gynecol Oncol.* 2002;85:139–145.
120. Chemoradiotherapy for cervical cancer: The role of concurrent cisplatin. *N Engl J Med.* 1999;340:1144–1153.
121. Tewari KS, Sill MW, Long HJ, et al. Improved survival with bevacizumab in advanced cervical cancer. *N Engl J Med.* 2014;370:734–743.
122. Chung HC, Ros W, Delord JP, et al. Efficacy and safety of pembrolizumab in PD-L1–positive cervical cancer: Results from KEYNOTE-158. *J Clin Oncol.* 2019;37:1470–1478.
123. Garland SM, Kjaer SK, Muñoz N, et al. Impact and effectiveness of the quadrivalent HPV vaccine: A systematic review. *Lancet Infect Dis.* 2016;16:983–996.
124. Einstein MH, Kadish AS, Burk RD. HPV therapeutic vaccines: Current status and future directions. *Gynecol Oncol.*2020;157:715–723.
125. Wentzensen N, Clarke MA, Brewer NT. Biomarkers for cervical cancer screening. *Lancet Oncol.* 2019;20:e573–e586.
137. Rosell R, Carcereny E, Gervais R, et al. Erlotinib in lung cancer with EGFR mutations. *N Engl J Med.*2009;361:947–957.
138. Slamon DJ, Leyland-Jones B, Shak S, et al. Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer. *N Engl J Med.* 2001;344:783–792.
139. Mateo J, Carreira S, Sandhu S, et al. DNA-repair defects and olaparib in metastatic prostate cancer. *N Engl J Med.*2015;373:1697–1708.
140. Garraway LA, Verweij J, Ballman KV. Precision oncology: An overview. *J Clin Oncol.* 2013;31:1803–1810.
141. Wan JCM, Massie C, Garcia-Corbacho J, et al. Liquid biopsies come of age: Towards implementation of circulating tumour DNA. *Nat Rev Cancer.* 2017;17:223–238.
142. Alix-Panabières C, Pantel K. Clinical applications of circulating tumor cells and circulating tumor DNA as liquid biopsy. *Cancer Discov.* 2016;6:479–491.
143. Bettegowda C, Sausen M, Leary RJ, et al. Detection of circulating tumor DNA in early- and late-stage human malignancies. *Sci Transl Med.* 2014;6:224ra24.
144. McKinney SM, Sieniek M, Godbole V, et al. International evaluation of an AI system for breast cancer screening. *Nature.* 2020;577:89–94.
145. Urban G, Tripathi P, Alkayali T, et al. Deep learning for real-time detection of polyps in colonoscopy. *Gastroenterology.* 2018;155:1069–1078.
146. Esteva A, Robicquet A, Ramsundar B, et al. A guide to deep learning in healthcare. *Nat Med.* 2019;25:24–29.
147. Keesara S, Jonas A, Schulman K. COVID-19 and health care's digital revolution. *N Engl J Med.* 2020;382:e82.
148. Topalian SL, Hodi FS, Brahmer JR, et al. Safety, activity, and immune correlates of anti–PD-1 antibody in cancer. *N Engl J Med.* 2012;366:2443–2454.
149. Maude SL, Frey N, Shaw PA, et al. Chimeric antigen receptor T cells for sustained remissions in leukemia. *N Engl J Med.* 2014;371:1507–1517.
150. Emens LA. Breast cancer immunotherapy: Facts and hopes. *Clin Cancer Res.* 2018;24:511–520.
151. Tewari A, Peabody JO, Hsu TS, et al. Positive surgical margin and perioperative outcomes in robotic vs open radical prostatectomy. *J Urol.* 2012;188:2191–2197.
152. Nam JH, Kim JH, Kim KH, et al. Robot-assisted laparoscopic radical hysterectomy for early-stage cervical cancer. *Lancet Oncol.* 2012;13:174–180.
153. Lacy AM, García-Valdecasas JC, Delgado S, et al. Laparoscopy-assisted colectomy vs open colectomy for treatment of non-metastatic colon cancer: A randomized trial. *Lancet.* 2002;359:2224–2229.

 doi:10.20944/preprints202512.2612.v1




154. Hasin Y, Seldin M, Lusis A. Multi-omics approaches to disease. *Genome Biol.* 2017;18:83.
155. Topol EJ. High-performance medicine: The convergence of human and artificial intelligence. *Nat Med.*2019;25:44–56.
156. Sharma P, Allison JP. The future of immune checkpoint therapy. *Science.* 2015;348:56–61.
157. Brisson M, Kim JJ, Canfell K, et al. Impact of HPV vaccination and screening on cervical cancer elimination: A comparative modeling study. *Lancet.* 2020;395:575–590.
158. Jha P, Ramasundarahettige C, Landsman V, et al. 21st-century hazards of smoking and benefits of cessation in the United States. *N Engl J Med.* 2013;368:341–350.
159. Wild CP, Weiderpass E, Stewart BW. World Cancer Report: Cancer Research for Cancer Prevention. Lyon: IARC; 2020.
160. Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of trends in cancer survival 2000–2014 (CONCORD-3): Analysis of individual records for 37,513,025 patients. *Lancet.* 2018;391:1023–1075.
161. Sullivan R, Alatise OI, Anderson BO, et al. Global cancer surgery: Delivering safe, affordable, and timely cancer surgery. *Lancet Oncol.* 2015;16:1193–1224.
162. Collins FS, Varmus H. A new initiative on precision medicine. *N Engl J Med.* 2015;372:793–795.
163. Hasin Y, Seldin M, Lusis A. Multi-omics approaches to disease. *Genome Biol.* 2017;18:83.
164. Topol EJ. High-performance medicine: The convergence of human and artificial intelligence. *Nat Med.*2019;25:44–56.
165. Ribas A, Wolchok JD. Cancer immunotherapy using checkpoint blockade. *Science.* 2018;359:1350–1355.
166. Ioannidis JP. Why most published research findings are false. *PLoS Med.* 2005;2:e124.
167. Rothwell PM. Factors that can affect the external validity of randomized controlled trials. *PLoS Clin Trials.*2006;1:e9.
168. Egger M, Smith GD, Phillips AN. Meta-analysis: Principles and procedures. *BMJ.* 1997;315:1533–1537.
169. Bray F, Laversanne M, Weiderpass E, Soerjomataram I. The ever-increasing importance of cancer as a leading cause of premature death worldwide. *Cancer Epidemiol.* 2021;71:101842.
170. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide. *CA Cancer J Clin.* 2021;71:209–249.
171. World Health Organization. Global strategy to accelerate the elimination of cervical cancer. 2020.